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The official organ of the Egyptian Society of Surgeons

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EGYPTIAN JOURNAL OF SURGERY

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Original articles

Wolters Kluwer

Medknow

Lazy lateral technique: an innovative approach for upper outer quadrant breast cancer near the anterior axillary fold

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Context
Surgical treatment of breast cancer was challenged over years. Breast conservation is as oncologically safe as mastectomy and gives better cosmetic and psychological outcomes.

Aim
The aim of our study was to evaluate the oncological and esthetic outcomes of the lazy lateral technique as a new approach for tumor located at the upper outer quadrant near anterior axillary fold.

Patients and methods
Between October 2012 and September 2014, 18 patients with early breast cancer at the upper outer quadrant and near the anterior axillary fold were surgically treated with the lazy lateral technique.

Results
The age of our patients ranged from 36 to 58 years (median: 47 years). Most of the patients in this study were diagnosed as having infiltrating ductal carcinoma (14 patients, 77.7%). The size of the tumor ranged from 0.9 to 3.8 cm. No involved margin on frozen section. Seroma was the most common postoperative complication and developed in two (11.1%) patients. The cosmetic outcome was excellent in 12 (66.6%) patients, good in five (27.7%) patients, and satisfactory in one (5.5%) patient. No local recurrence or systemic metastasis was noticed in our patients during a median follow-up period of 38 months (range: 27–49 months).

Conclusion
The lazy lateral technique is a novel approach for surgical treatment of upper outer quadrant breast cancer near the anterior axillary fold. It is an oncologically safe procedure and promotes satisfactory esthetic outcomes.

Keywords:
breast cancer, conservative surgery, oncoplastic techniques

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Introduction

The breast is a significant symbol of femininity for women; total or partial excision of the breast alters the patient's body image and causes many psychological disorders. Surgical treatment of breast cancer was challenged over years from radical mastectomy of Halsted passing through modified radical mastectomy until the era of breast conservation and lastly oncoplastic surgery [1–6]. Oncoplastic surgery is the most recent expression of breast conserving surgery; it aims to conserve the breast parenchyma to give an excellent cosmetic outcome for the patient, respecting the oncological principles of radicality [7–9]. Breast conservation is as oncologically safe as mastectomy and gives better cosmetic and psychological outcomes [10,11]. About 60% of breast cancer occurs at the upper outer quadrant [12–14]; hence, we try to find a new approach to allow safe resection of the tumor and give better cosmetic outcomes.

Aim

The aim of our study was to evaluate the oncological and esthetic outcomes of the lazy lateral technique as a new approach for tumors located at the upper outer quadrant near the anterior axillary fold.

Patients and methods

Between October 2012 and September 2014, 18 patients with early breast cancer in the upper outer quadrant and near the anterior axillary fold were included in the study. The study was conducted at the surgical oncology unit, Zagazig University

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Hospital, and was approved by the local ethical committee of our faculty.

Preoperative

All patients were diagnosed with early breast cancer by careful clinical evaluation, investigation (breast ultrasound and mammography), and proved by true cut biopsy. Chest radiography, pelviabdominal ultrasound, and bone scan were performed for staging of the disease.

Inclusion criteria

All female patients with early breast cancer at the upper outer quadrant and near the anterior axillary fold were included in the study.

Exclusion criteria

(1) Multicentric and multifocal tumor.
(2) Inflammatory breast cancer.
(3) Breast–tumor size ratio that does not allow oncoplastic surgery.
(4) Patient preference.

The technique was discussed with all patients and informed consent was obtained. Preoperative drawing of lazy lateral incision extends from the anterior axillary fold and envelops the tumor down along the circumference of the breast to the lateral end of the inframammary fold (Fig. 1).

Intraoperative

The tumor was resected with safety margin using the designed incision; frozen section of the specimen was prepared in order to assess the safety margin (Fig. 2a and b). Axillary clearance with removal of level I and level II lymph nodes was carried out through the same incision (Fig. 2c). Closure with suction drain was performed (Fig. 3).

Postoperative

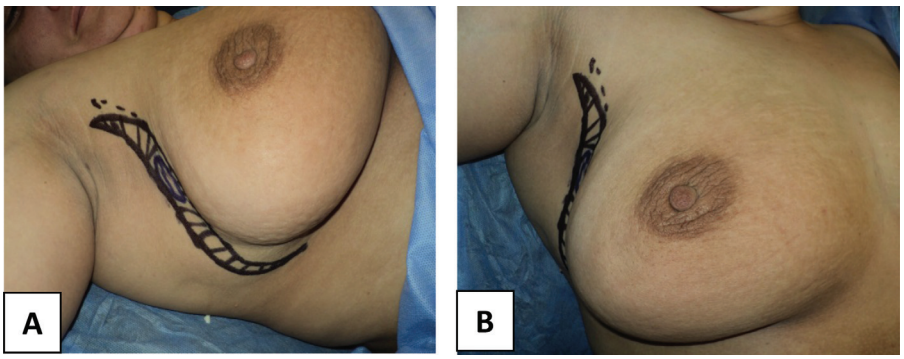
Suction drains were removed when the drain output was decreased to 20–30 ml per 24 h.

Our patients were referred to the Clinical Oncology Department to complete their adjuvant chemotherapy and radiotherapy according to protocols.

Technique-related complications

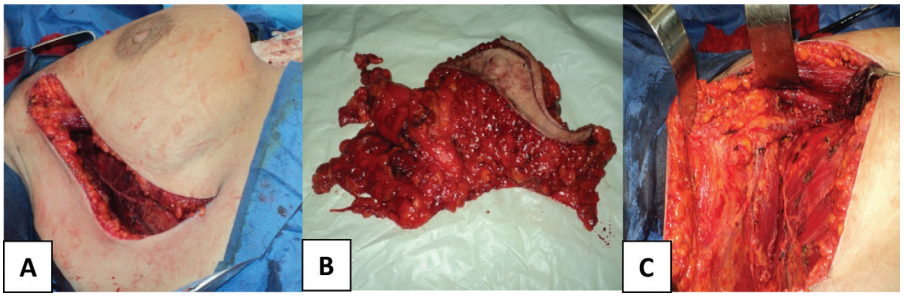
All patients were assessed for the onset of wound infection, hematoma, wound dehiscence, and seroma.

Figure 1



(a, b) Preoperative drawing of the incision

Figure 2



(a) Cavity after tumor excision. (b) Excised tumor with the axillary lymph nodes. (c) Axilla after axillary clearance

Esthetic outcomes

The cosmetic appearance was evaluated at 6 months postoperatively using objective and subjective scoring system and the mean was calculated. Using a grading system, a score of 5 to 1 (5, excellent; 4, good; 3, satisfactory; 2, poor; 1, very poor) was given after assessment of breast symmetry, nipple–areola complex symmetry, and shape of the breast (Fig. 4) [15].

Oncological outcomes

Our patients were followed up for early detection of local recurrence and patient support. Follow-up was every 2 weeks for 1 month, monthly for 3 months, every 3 months for 1 year, every 6 months for 2 years, and then annually. During follow-up, oncology nurse navigators answer questions, support patients, coordinate care, and educate patients about physical therapy, nutrition, and maintaining health after treatment.

Breast ultrasonography and CA15-3 were performed every 3 months. Mammogram was performed every year. MRI was performed when breast ultrasonography and mammography revealed suspicious data.

Results

The age of our patients ranged from 36 to 58 years (median: 47 years). All patients had tumors located at the upper outer quadrant and closely related to the anterior axillary fold. Most of the patients in this study were diagnosed as having infiltrating ductal carcinoma (14 patients, 77.7%). The size of the tumor ranged from 0.9 to 3.8 cm. Table 1 summarizes demographic, clinical, and pathological features of patients in the study.

The safety margins of our specimens ranged from 1 to 5 cm; and no involved margin on frozen section. Seroma developed in two (11.1%) patients and was treated by means of frequent aspiration. One patient developed a small firm area along the suture line at 11 months

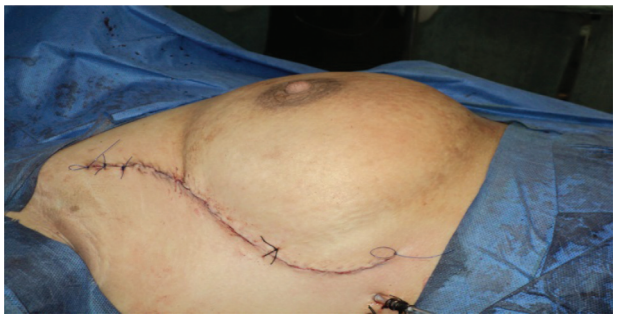
Table 1 Demographic, clinical, and pathological features of patients in the study (*N*=18)

	N
Age	
Range	36–58
Median	47
Tumor stage	
PT1	7
PT2	11
PN1	10
PN2	8
Tumor pathology	
Invasive duct carcinoma	14
Medullary carcinoma	3
Mucinous carcinoma	1
Tumor grading	
G1	5
G2	9
G3	4

Table 2 Technique-related complication (*N*=18)

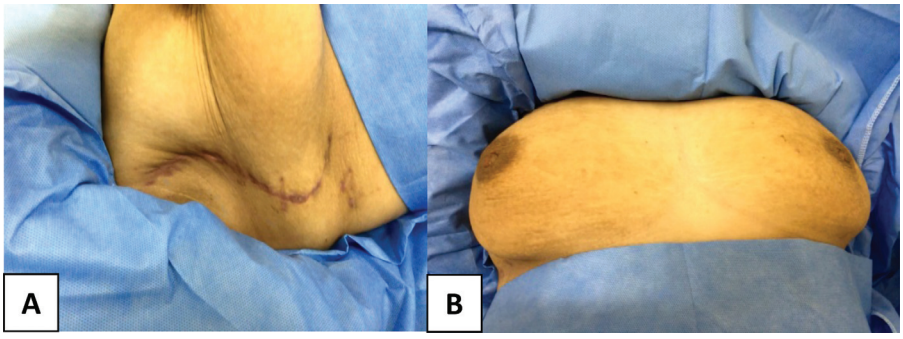
Complications	*N*
Infection	0
Hematoma	0
Wound dehiscence	0
Seroma [*n* (%)]	2 (11.1)
Traumatic fat necrosis [*n* (%)]	1 (5.5)

Figure 3



The breast after closure of the wound

Figure 4



The breast at 6 months after excision of the tumor

postoperatively and was investigated using ultrasonography and true cut biopsy revealing traumatic fat necrosis that was treated with surgical excision. Table 2 summarizes technique-related complications.

The cosmetic appearance was evaluated at 6 months postoperatively. Twelve (66.6%) patients showed excellent results, five (27.7%) women showed good results, one (5.5%) patient showed satisfactory result, and no patient showed poor result.

No local recurrence or systemic metastasis was noticed in our patients during a median follow-up period of 38 months (range: 27–49 months).

Discussion

Most of the breast tumors occur at the upper outer quadrant [12–14]. Therefore, upper quadrant techniques are commonly used in patients undergoing surgeries. Lateral mammoplasty technique is the most famous one used for the treatment of tumor located in the upper quadrant. One of the major complications of the lateral mammoplasty is obvious scar and nipple deviation [16,17]. Our incision is completely present laterally; hence, it gives better cosmetic appearance, and nipple deviation is less commonly to occur. Obtaining negative margin is an essential requirement to decrease tumor recurrence and prevent conversion to mastectomy [18–20]; our technique allows complete excision of a large tumor with safety margin and reexcision was not required. Local recurrence did not occur after a median follow-up period of 38 months (range: 27–49 months).

The oncological safety of this approach over a longer period of follow-up is going to be addressed in another publication

Finally, the advantages of this technique over different techniques used in this site are as follows: it is a very simple technique, with good cosmetic appearance and an easy learning curve, and allows easy axillary dissection.

Conclusion

The lazy lateral technique is a novel approach for surgical treatment of upper outer quadrant breast cancer near anterior axillary fold. It is oncologically safe procedure and promotes satisfactory esthetic outcomes.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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Is re-sleeve gastrectomy after sleeve gastrectomy failure feasible?

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Background
There is an increasing incidence of inadequate loss of weight or weight regain after sleeve gastrectomy (SG) accounting for 5–10%, with the potential recurrence of obesity-linked diseases.
Aim
To determine the safety and outcome of redo-SG in patients with failed SG.
Patients and methods
A total of 21 patients with failed SG who received redo-laparoscopic sleeve gastrectomy were evaluated.
Results
Entire cases were accomplished laparoscopically, with a mean operative time of 96.9±10.3 min. The mean percentage excess weight loss, percentage excess;Deg;BM;Deg;l loss, and mean;Deg;BM;Deg;l were 12.4±4.1, 13.5±3.6%, and 49.5±8.0 kg/m^2, respectively, at 1 month; 40.5±6.8, 43.3±7.8%, and 41.5±6.6 kg/m^2, respectively, at 6 months; and 56.8±8.5, 60.3±8.9% and 36.5±4.8 kg/m^2, respectively, at 12 months. At a mean follow-up of 15±2.2 months, two patients were cured of hypertension, dyslipidemia resolved in two patients, diabetes disappeared in two patients, and all patients were cured of joint problems.
Conclusion
In a short period of follow-up, redo-laparoscopic SG after failed SG is a feasible option and has good results regarding weight loss and comorbidity improvement.

Keywords:
bariatric surgery, redo sleeve gastrectomy, weight regainers

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Introduction

Sleeve gastrectomy (SG) has become now a definitive surgery for all stages of obesity, because it is a simple operation and done without implantation of foreign body with no disruption of the gastrointestinal (GI) tract [1].

Weight regain was observed during long-term follow-up, whatever the type of bariatric surgery, to a little pit significant number of patients, and it is especially common in the restrictive operations.

Development of new reflux symptoms (21%) and regain of weight were noticed between the third and the sixth years postoperatively [1]. A trend of slight weight regain is observed annually after SG as reported by studies [1,2].

Percentage of failed SG patients requiring another operation for control of morbid obesity is somewhere between 5 and 10%. Recurrence of obesity-related morbidities like hypertension and type 2 diabetes mellitus is the most important consequence of weight recidivism [3,4].

The management armamentariums for weight recidivism after SG are redo-SG; conversion to a malabsorptive bariatric procedure like gastric bypass; or achieving more restriction by implantation of adjustable gastric band to the initial sleeve. In this study, we evaluated 21 patients who had undergone redo-laparoscopic sleeve gastrectomy (re-LSG) with a follow-up period of 1 year.

Patients and methods

Eligibility

The study was done in the Department of Clinical and Experimental Surgery, Medical Research Institute, University of Alexandria, Egypt, after approval from the Ethical Committee of our Institution.

A total of 21 patients experiencing weight recidivism or unsatisfactory weight loss after LSG who received re-LSG and completed a period of 1 year after the surgery were evaluated.

The inclusion criteria were the following:

(1) Patients who underwent LSG in our institution from the period of June 2010 to December 2014

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and experienced insufficient weight loss (defined as loss of <50% of excess weigh) or progressive weight regain over a period of at least 18 months were included.
(2) Persistence of obesity-related comorbidities was evaluated by the use or discontinuation of medications in case of joint disease. Diabetic state was evaluated by fasting blood glucose and glycosylated hemoglobin preoperatively and postoperatively. Hypertension was assessed by systolic and diastolic pressure before and after surgery, and dyslipidemia was evaluated by lipid profile chemistry tests.
(3) After multidisciplinary team assessments, patients with failed LSG were subjected to an upper GI series. If the upper GI series showed the presence of large antrum and/or body and/or gastric fundus which was because of either dilatation after the initial SG or technical failure of the initial SG, then this patient is a good candidate for re-LSG.

Informed consent was signed by all patients, and they understood the possibility of alteration of the procedure to another option, for example, gastric bypass.

Surgical technique

The patients were positioned in an anti-Trendelenburg with split leg position.

(1) Adhesolyis was done using Harmonic Scalpel (Ethicon Endo-Surgery, Cincinnati, Ohio, USA).
(2) Dissection of the sleeve pouch from the liver was done along with complete dissection of the fundus with left diaphragmatic crus exposure with dissection of retrogastric adhesions till complete mobilization of the gastric pouch.
(3) Gastrectomy was done guided by a 36-Fr orogastric tube (Ethicon Endo-Surgery), which was introduced and loosely pressed against the lesser curvature by the stapler.
(4) In case of presence of large gastric antrum, it was resected closure to the pylorus as much as we can.
(5) In case of only dilated gastric fundus, it was resected completely aided by its good dissection till exposure and resection of fundic pad of fat.
(6) Green and black cartridges were used using an endoscopic linear cutter with articulation (Echelon Flex60; Ethicon Endo-Surgery).
(7) Invagination of staple line was done by 2-0 V-loc (Covidien suture, Mansfield, MA, USA).
(8) Tube drain (18-Fr) was placed along the surgical bed.

The orogastric tube was removed after completing the procedure, and the trocar wounds were closed. No nasogastric tube was left.

Study design and sample selection

A total of 21 re-LSG procedures were done in the Department of Clinical and Experimental Surgery in Medical Research Institute, University of Alexandria. The follow-up period ranged from 12 to 19 months, with a mean of 15±2.2 months.

Postoperative management

(1) Patients were started on oral liquids after upper gastrograffin study on postoperative day 1.
(2) If the condition permitted, patients were discharge on postoperative day 2, and the drain was removed before discharge.
(3) Patients' visits were planned for follow-up after 1, 3, 6, and 12 months in the postoperative period for the assessment of postoperative complications and effect of operation on weight reduction.

Statistical analysis

IBM SPSS (SPSS Inc., Chicago, IL, USA), version 20 was used for statistical analysis. The normality of distribution of variables was verified by the Kolmogorov–Smirnov test, and analysis of variance with repeated measures was assessed for comparison between different periods for normally distributed quantitative variables. All statistical tests were judged at 0.05 significance level.

Results

Data after initial laparoscopic sleeve gastrectomy

Before LSG, the mean initial BMI was 57.8±8.7 kg/m^2, mean weight was 153.7±20.8 kg, and there were four comorbid conditions among the 21 patients as shown in Table 1.

First LSG has led to a mean BMI of 53.1±8.3 kg/m^2, a mean percentage excess weight loss (%EWL) of 15.7±8.6, and a mean weight of 139.8±21.6 kg at a mean interval of 26.5±7.8 (18–42) months, as shown in Tables 2 and 3.

Table 1 Distribution of comorbidities before laparoscopic sleeve gastrectomy

	Patients [*n* (%)]
Blood hypertension	3 (14.28)
Type 2 diabetes mellitus	3 (14.28)
Joint disease	10 (47.61)
Dyslipidemia	2 (9.52)

Table 2 Descriptive analysis of the studied cases according to weight, BMI, and excess weight (*n*=21)

	Initial	After 1 year	Before re-sleeve	After re-sleeve			*P*
				1 month	6 months	1 year	
Weight	153.7±20.8	127.0±17.9	139.9±21.6	131.5±21.6	110.2±17.2	97.2±12.4	<0.001*
Excess weight loss (%)	–	29.0±11.5	15.7±8.6	12.4±4.1	40.5±6.8	56.8±8.5	<0.001*
BMI	57.8±8.7	47.8±6.7	53.1±8.3	49.5±8.0	41.5±6.6	36.5±4.8	<0.001*
Excess BMI loss (%)	–	–	–	13.5±3.6	43.3±7.8	60.3±8.9	<0.001*

Table 3 Mean weight and BMI before primary surgery and before re-sleeve

	Before initial operation	Before re-sleeve
Weight (kg)	153.7±20.8	139.9±21.6
BMI	57.8±8.7	53.1±8.3

Regarding comorbidities related to obesity, one of the three patients showed improvement with hypertension, resolution of diabetes occurred in one of the three patients, dyslipidemia was improved in one of the two patients, and joint problems resolved in two and improved in one of the 10 patients.

Data after redo-laparoscopic sleeve gastrectomy

A total of 12 patients of the included cases experienced significant weight regain whereas nine cases experienced inadequate weight loss (<50% of EW).

The study included two males and 19 female patients, with a mean age of 32.8±9.9 (20–54) years.

All cases of re-LSG were finalized by laparoscopy without intraoperative or postoperative complications, with a mean operative time of 96.9±10.3 min.

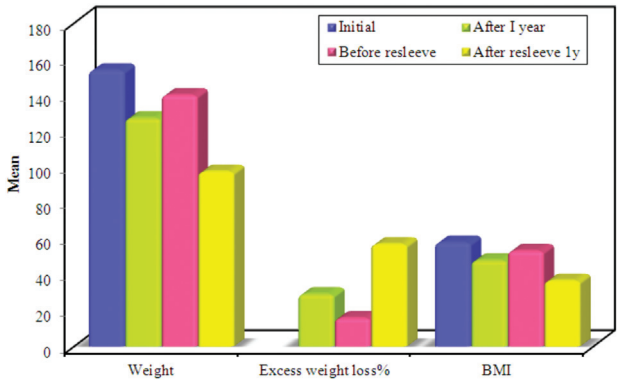
The mean %EWL, mean %EBL, and mean BMI were 12.4±4.1, 13.5±3.6%, and 49.5±8.0 kg/m^2, respectively, at 1 month; 40.5±6.8, 43.3±7.8%, and 41.5±6.6 kg/m^2, respectively, at 6 months; and 56.8 ±8.5, 60.3±8.9% and 36.5±4.8 kg/m^2, respectively, at 12 months, as shown in Fig. 1. The mean follow-up of patients was 15.0±2.2 months.

Regarding comorbidities, two patients were cured of hypertension and stopped taking antihypertensive drugs and one showed improvement, dyslipidemia resolved in two patients, diabetes disappeared in two patients and improved in one, and all patients were cured of joint problems.

Discussion

SG became the most frequently performed procedure worldwide and in the USA in 2013 and in our institute almost doubled every year. This growth can be attributed to its operational simplicity without interruption of the GI tract [5–8].

Figure 1



Descriptive analysis of the studied cases according to weight, BMI, and excess weight (n=21).

Patients who have undergone LSG but have experienced weight recidivism or have developed certain complications, such as new reflux symptoms, can be managed surgically by a second intervention, such re-LSG; conversion to biliopancreatic diversion with duodenal switch; or Roux-en-Y gastric bypass. Single anastomosis duodenoileal bypass with SG represents a new option, but data are limited in the literature and must be validated over time [9,10].

Best way of management of these patients is to take a full history at first and then to assess their weight, BMI, and their alimentary habits. All patients with maladaptive eating disorders because of their bariatric surgery should undergo further psychological assessment and should be treated before consideration for surgical revision.

The next step is to document evidence of primary or secondary dilation of the primary gastric sleeve by upper GI radiological studies. For nonconclusive results, a volumetric computed tomography scan to be done.

Mean gastric volume was studied by Braghetto and colleagues and they found that it had increased from 108 to 250 ml with computed tomography gastric

volumetry with a study conducted on 15 LSG patients on postoperative day 3, and repeated at 3 years after surgery. However, none of these patients regained weight, and they settled that even with tight sleeve, the gastric volume had increased [11].

At 1 year, upper GI radiological studies were performed by Langer *et al.* [12] for 14 LSG patients, and they found that only one patient had fit the criteria for gastric dilation. However, this patient still maintained good %EWL. Moreover, in another study by the same author, weight regain in patients was not correlated with sleeve dilation [13].

According to the literature, redo-SG can be considered when gastric volumetry study reveals a remnant gastric volume more than 250 ml in case of initially performed tight sleeve (i.e. dilatation after the initial SG) and/or when a large gastric fundus and/or antrum is present (i.e. technical failure of the initial SG) [14–16].

Conclusion

In a short period of follow-up, re-LSG for failed SG is a feasible option in presence of large fundus and has significant results regarding weight loss and comorbidity improvement.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Is single-layer better than double-layer interrupted intestinal anastomosis? A comparative study in pediatric patients

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Objective
The aim of our study was to evaluate the efficacy and safety of single-layer anastomosis compared with double-layer interrupted anastomosis in pediatric patients.
Patients and methods
The study included 60 patients, and it was carried out in Pediatric Surgery Unit, El-Minia University Hospital from February 2016 to February 2017, and the patients were classified into two groups, each group comprising 30 patients. Group A was operated with single-layer interrupted intestinal anastomosis and group B was operated with double-layer interrupted intestinal anastomosis. All patients were subjected to carful preoperative assessment and preparations. Postoperatively, intravenous fluids were continued until oral fluids begin, usually on the third day postoperatively. The patients were followed up for 1 month postoperatively with special emphasis on postoperative complications.
Results
The most frequent diagnosis was intussusception; it represented 33.3 and 36% in groups A and B, respectively. The operative time and the postoperative hospital stay were less in group A, with *P* values less than 0.001 and 0.049, respectively, which is statistically significant. Intestinal leakage was reported in two (6.7%) cases in both groups, whereas postoperative distension was reported in four (13.3%) cases in group A and 13 (43%) cases in group B, with a *P*-value of 0.01, which was statistically significant. Wound infection was reported in two cases in group A and five cases in group B. Two cases needed re-exploration in group B. Postoperative vomiting was reported in five (16.7%) cases in group A and 10 (33%) cases in group B.
Conclusion
We concluded that single-layer interrupted intestinal anastomosis is effective, safe, successful, of less operative time, less hospital stay, and valuable cost-effectiveness.

Keywords:
anastomosis, double layer, intestinal, single layer

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Introduction

Gastrointestinal anastomosis is an operation frequently performed in pediatric surgery. The choice of anastomosis technique may be influenced by the diameter of bowel ends, edema, accessibility, site of anastomosis, contamination, available time, equipment, and underlying pathology [1]. In the early 19th century through the experimental work of Travers and Lembert, double-layered intestinal anastomosis was first performed. Since then the technique has remained more or less the same, except for the use of different suture materials for the inner layer [2]. The single-layered interrupted anastomosis was first described by Hautefeuille [3]. In clinical practice, the effectiveness and safety of anastomosis have been evaluated based on the incidence of surgical complications related to the procedure, especially intestinal leakage [4]. There is no general agreement about the most appropriate surgical technique [5]. Hand-sewn techniques have traditionally been used to perform intestinal anastomosis in pediatric patients in many cases. When treating intestinal atresia and stoma closure, great discrepancy between diameters of the proximal and distal intestine caused by disuse atrophy is often observed, which may cause difficulties and complications. To overcome size discrepancy, proficiency in performing anastomosis is required when using hand-sewn techniques [6]. Numerous studies in the literature comparing techniques (e.g. one layer vs. two layers, hand-sewn vs. stapled, and end-to-end vs. end-to-side) have failed to demonstrate a clear superiority of one over another [7].

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The utility of any technique for intestinal anastomosis depends mainly on its utility to heal without a leakage. This complication has catastrophic consequences on patient's health, as well as cost of care [8]. In fact, the only technique that has been unequivocally demonstrated to be unacceptable is the everted anastomosis [9]. The indications of intestinal anastomosis in children are many and may be congenital, for example, Hirschsprung's disease, intestinal atresia, malrotation, meconium ileus, may be inflammatory, for example, necrotizing enterocolitis, or may be a part of other surgical procedures [10]. Intussusception is a common cause and the patient should be managed immediately to reduce risk [11].

Hypothesis

Single-layer interrupted anastomosis will improve the general outcome of intestinal anastomosis in pediatric surgery.

Objective

The aim of our study was to evaluate the efficacy and safety of single-layer anastomosis compared with double-layer interrupted anastomosis in pediatric patients.

Design

This is a prospective single-blinded comparative study.

Setting

This study was conducted in El-Minia University Hospital, El-Minia, Egypt.

Patients and methods

The study included 60 patients, and it was carried out in Pediatric Surgery Unit, El-Minia University Hospital from February 2016 to February 2017, and the patients were classified into two groups, each group comprising 30 patients. The study protocol was approved by the Local Ethical Committee. Group A was operated with single-layer interrupted intestinal anastomosis, and group B was operated with double-layer interrupted intestinal anastomosis. The patients were assigned to either single or double technique in a randomized manner. Informed consents from parents of all patients were taken before entering the study. The inclusion criteria included age more than 1 month and up to 14 years. Urgent cases, elective cases, small intestine, and large intestine anastomosis were included. The exclusion criteria included age less than 1 month and more than 14 years, peritonitis with local septic condition, poor nutritional status, doubtful bowel viability, malignancy, and diabetic patients. All patients were subjected to carful history taking, physical examination, and proper radiological and laboratory workup. Preoperative preparation included fluid resuscitation, antibiotic prophylaxis, chemical and mechanical bowel preparations before elective colorectal procedures, and nasogastric tube and urinary catheter inserted to decompress the stomach and urinary bladder before surgery. These tubes were removed after the operation once there was no distension or vomiting.

Intravenous fluids were continued until oral fluids were started, usually on the third day postoperatively. The patients were discharged after they passed stool and oral feeding was allowed, and there was no distension, vomiting, or high-grade fever. The patients were followed up in a surgical outpatient clinic for 1 month postoperatively with special emphasis on postoperative complications.

Operative technique

The method of anastomosis in our study was hand-sewn anastomosis, and absorbable suture materials (vicryl 3/0, 4/0) were used. The two cut ends of the bowel were brought in close apposition, and two stay sutures between the serosa of the proximal and distal ends of the bowel were taken, one at the mesenteric border and the other at the antimesenteric border. The posterior inner-layer anastomosis by interrupted full-thickness stitches were taken between the two stay sutures were tied sequentially, with care taken not to apply excessive tension; the knot lies inside the lumen. Next, a Connell stitch was made at both ends by passing the sutures from the outside in, then inside out, on one end. The same step is repeated on the other end in the form of a continuous U-shape. The suture is tied so that the knot is outside; the needle must be pulled through each edge separately. Trying to include both edges in one pass of the needle can prevent the surgeon from taking a full-thickness bite on both edges. It is necessary to include the submucosa carefully, because this is the strongest layer of the bowel wall and gives strength to the anastomosis.

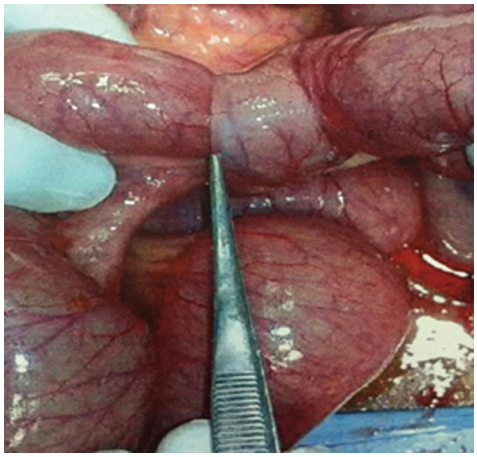
The anterior inner layer is completed in a similar manner, starting from the far end. The pouting of mucosa is prevented by taking a small amount of mucosa and a large part of the seromuscular layer, which results in inversion of the mucosa. In group B, the posterior outer layer was completed by interrupted seromuscular sutures with a 5 mm gap between each two sutures. Stitches should incorporate only the seromuscular layer, and care must be taken not to

incorporate the full thickness of the bowel wall. Sutures are tied sequentially, with care taken not to apply excessive tension so as to minimize the risk of cut-through of the seromuscular layer. The anterior outer seromuscular layer was completed in the same way. Narrowing of the lumen by including too much of the bowel into this layer should be avoided. Patency of the lumen can be confirmed by palpation acrossthe anastomosis with the tips of the thumb and the index fingers. The mesenteric defect was closed with interrupted stitches; care should be taken to avoid injuring mesenteric vessels so as to prevent ischemia of the anastomotic site. The last step was reduction of the bowel and anatomical closure. Intraperitoneal drain may or may not be inserted (Figs. 1–3).

Statistical analysis

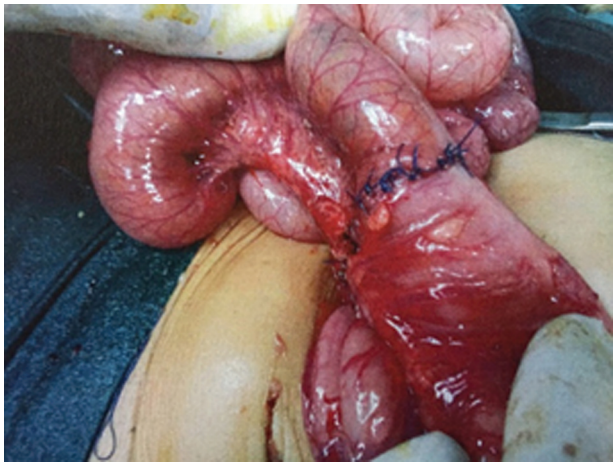
Obtained data were presented as mean±SD, ranges, numbers, and ratios. Results were analyzed using one-way analysis of variance with post-hoc Tukey's honest significant difference test and χ^2-test. Statistical analysis was conducted using the SPSS (IBM Corporation, California, USA) (version 15, 2006) for Windows statistical package. *P*-value less than 0.05 was considered statistically significant.

Figure 1



Intussusception failed simple reduction.

Figure 2



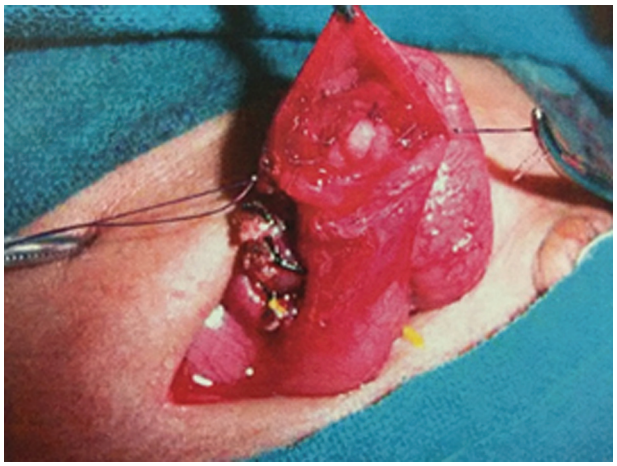
Single-layer interrupted anastomosis.

Results

Sixty cases of intestinal anastomosis were included in the study: 30 were operated by single interrupted layer (group A) and 30 were operated by double interrupted layer (group B). The age ranged between 3 months and 8 years (mean=2.08 years) in group A and 4 months and 12 years (mean=2.5 years) in group B. Fifteen cases were male and 15 cases were female in group A, whereas in group B, 21 cases were male and nine cases were female (Tables 1 and 2, Figs. 4 and 5).

Intussusception was the most common cause of anastomosis in both groups: 10 (33.3%) cases in group

Figure 3



Posterior wall anastomosis.

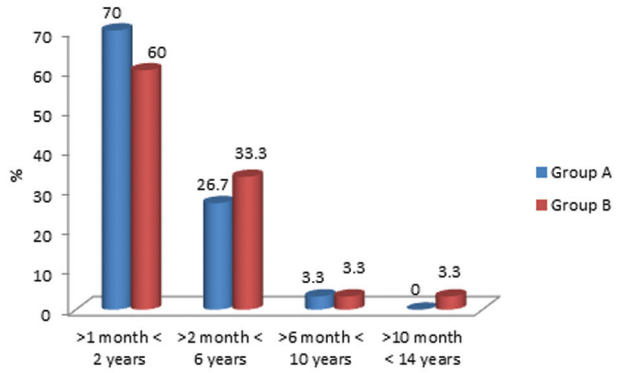
Table 1 Age distribution in both groups

	Group A (*n*=30) [*n* (%)]	Group B (*n*=30) [*n* (%)]	*P*-value
Age group			
>1 month ≤2 years	21 (70)	18 (60)	0.693
>2 months ≤6 years	8 (26.7)	10 (33.3)	
>6 months ≤10 years	1 (3.3)	1 (3.3)	
>10 months ≤14 years	0 (0)	1 (3.3)	
Age (months)			
Range	3–96	4–144	
Mean±SD	24.9±22.5	30.2±29.1	
Age (years)			
Range	0.25–8	0.29–12	
Mean±SD	2.08±1.8	2.5±1.6	

Table 2 Sex distribution in both groups

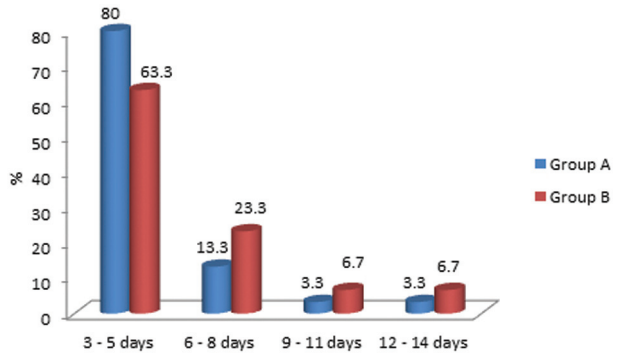
	Group A (*n*=30) [*n* (%)]	Group B (*n*=30) [*n* (%)]	*P*-value
Sex			
Male	15 (50)	21 (70)	0.114
Female	15 (50)	9 (30)	

Figure 4



Comparisons of age distribution in both groups.

Figure 5



Sex distribution in both groups.

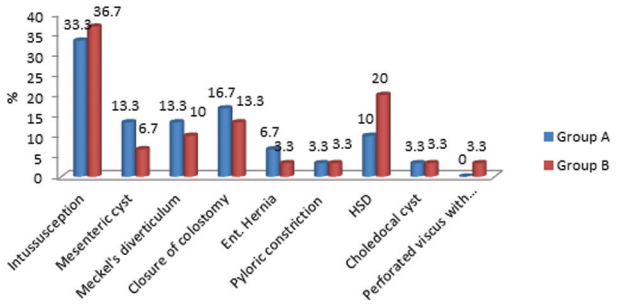
A and 11 (36.7%) cases in group B. Five (16.7%) cases and four (13.3%) cases were due to closure of colostomy in groups A and B, respectively. Four (13.3%) cases and two (6.7%) cases were mesenteric cysts in groups A and B, respectively. Cases of Hirschsprung's disease represented 10% in group A and 20% in group B, whereas cases of internal hernia represented 6.7 and 3.3% in groups A and B, respectively. Four (13.3%) cases were Meckel's diverticulum in group A, whereas it was three (10%) cases in group B. Other causes of anastomosis in our study included pyloric constriction, choledocal cyst, and perforated viscus with ischemic line (Table 3 and Fig. 6).

The operative time ranged between 50 and 155 min (mean=73.8 min) and 75 and 240 min (mean=110.8 min) in groups A and B, respectively, with *P*-value less than 0.001, which is statistically

Table 3 Diagnosis of causes of intestinal anastomosis

	Group A (*n*=30) [*n* (%)]	Group B (*n*=30) [*n* (%)]	*P*-value
Intussusception	10 (33.3)	11 (36.7)	0.914
Mesenteric cyst	4 (13.3)	2 (6.7)	
Meckel's diverticulum	4 (13.3)	3 (10)	
Closure of colostomy	5 (16.7)	4 (13.3)	
Internal hernia	2 (6.7)	1 (3.3)	
Pyloric constriction	1 (3.3)	1 (3.3)	
Hirschsprung's disease	3 (10)	6 (20)	
Choledocal cyst	1 (3.3)	1 (3.3)	
Perforated viscus with ischemic line	0 (0)	1 (3.3)	

Figure 6



Diagnosis of cause of intestinal anastomosis. HSD, Hirschsprung's disease.

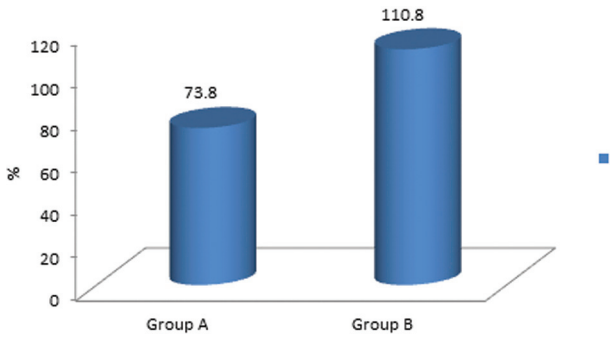
significant. As regards postoperative hospital stay, it ranged between 3 and 12 days (mean=5 days) in group A and 4 and 12 days (mean=6.1 days) in group B, with a *P*-value of 0.049, which is statistically significant (Tables 4 and 5, Fig. 7).

Fifteen (50%) patients in group A and 17 (56.7%) in group B had postoperative fever, whereas two (6.7%) cases in group A and five (16.7%) cases in group B had wound infection. In group A, we reported two (6.7%) cases of intestinal leakage and five (16.7%) cases of vomiting, whereas in group B it was two (6.7%) cases and 10 (33.3%) cases, respectively. We reported significant results as regards postoperative distention, as it was four (13.3%) cases in group A and 13 (43.3%) cases in group B, with *P*-value equal to 0.01. None of the cases required re-exploration in group A, whereas two (6.7%) cases required re-exploration in group B (Table 6 and Fig. 8).

Discussion

Intestinal anastomosis in pediatric surgery is a relevant matter because of the frequency of the procedure [12]. The two-layer interrupted anastomosis has its origins in the early 19th century, whereas the single-layer interrupted anastomosis was first described by Hautefeuille [3]. Ischemia, tension on the anastomosis,

Figure 7



Operative time in minutes.

Table 4 Operative time

	Group A (*n*=30)	Group B (*n*=30)	*P*-value
Operative time (min)			
Range	50–155	75–240	<0.001
Mean±SD	73.8±26.9	110.8±45.4	

Table 5 Postoperative hospital stay

Hospital stay (days)	Group A (*n*=30) [*n* (%)]	Group B (*n*=30) [*n* (%)]	*P*-value
3–5	24 (80)	19 (63.3)	0.914
6–8	4 (13.3)	7 (23.3)	
9–11	1 (3.3)	2 (6.7)	
12–14	1 (3.3	2 (6.7)	
Postoperative hospital stay (days)			
Range	3–12	4–12	
Mean±SD	5±2	6.1±2.2	

and poor technique are clearly the most important factors responsible for anastomotic failure [2,13].

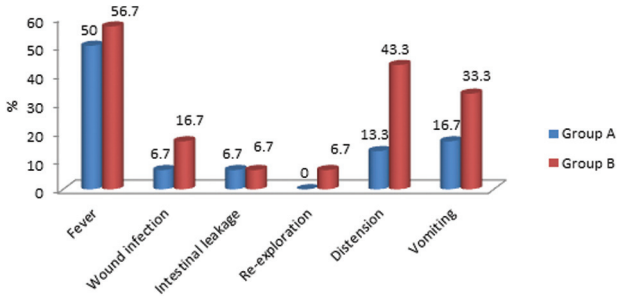
The present study assessed the efficacy and safety of the single-layer interrupted against the double-layered anastomosis in pediatric age, comparing between them mainly in operative time, postoperative complications, and postoperative hospital stay.

In our study, the mean age was 2.08 years in group A and 2.5 years in group B, whereas in the study conducted by Ordorica-Flores *et al.* [12] the mean age was 3.7 years in both groups [12] and in the study conducted by Ross *et al.* [14] the mean age was 6 months in the single-layer group [12,14].

In the present study, intussusception was the most frequent diagnosis in both groups: 10 and 11 cases in groups A and B, respectively.

In the study conducted by Ordorica-Flores *et al.* [12], the most frequent diagnosis was closure of

Figure 8



Postoperative complications.

Table 6 Presence of postoperative complications

Postoperative complications	Group A (*n*=30) [*n* (%)]	Group B (*n*=30) [*n* (%)]	*P*-value
Fever	15 (50)	17 (56.7)	0.605
Wound infection	2 (6.7)	5 (16.7)	0.228
Intestinal leakage	2 (6.7)	2 (6.7)	1
Re-exploration	0 (0)	2 (6.7)	0.150
Distension	4 (13.3)	13 (43.3)	0.01
Vomiting	5 (16.7)	10 (33.3)	0.136

colostomy postnecrotising enterocolitis, which was 53% in both groups [12], whereas in the study conducted by Garude *et al.* [15] the most frequent diagnosis was trauma, which represented 47.9% in the single-layer group and 47.2% in the double-layer group [15].

The mean operative time in our study was 73.8 min in the single-layer group and 110.8 min in the double-layer group. In the study conducted by Ordorica-Flores *et al.* [12], it was 26 min in the single-layer group and 43 min in the double-layer group, whereas in another study conducted by Saboo *et al.* [13] the mean operative times were 23.6 and 33.06 min in the single-layer and double-layer groups, respectively [13].

The operative time was longer in our study because it was estimated from the incision of the skin to the last skin stitch, but in other studies it was the time needed for constructing the anastomosis only.

In the present study, the mean hospital stay was 5 days in single-layer and 6.1 days in double-layer anastomosis, with statistically significant results. Ordorica-Flores *et al.* [12] reported a mean hospital stay of 10.4 days in both groups; also, Garude *et al.* [15] reported the same mean hospital stay in both groups (12 days), whereas Saboo *et al.* [13] reported 16.9 days in single-layer and 16 days in double-layer anastomosis [12,13,15].

The percentages of postoperative distension and vomiting were higher in group B in our study – 43 and 33%, respectively – whereas in group A they were 13.3 and 16.7%, respectively, with statistically significant *P*-value as regards postoperative distension. These results can be attributed to the decreased lumen of the intestine in double-layer intestinal anastomosis. The other studies were reviewed and they did not report postoperative distension or vomiting.

There was no difference between the two groups as regards postoperative intestinal leakage. It was two (6.7%) cases in each group in our study, whereas in the study conducted by Ordorica-Flores *et al.* [12] intestinal leakage was reported in 5% in single-layer and 7% in double-layer anastomosis [12]. In the study conducted by Askarpour *et al.* [16], intestinal leakage was found in 1.6% in single-layer and 6.3% in double-layer anastomosis. Saboo *et al.* [13] reported intestinal leakage in 10 and 6.66% and Garude *et al.* [15] reported it in 5.3 and 4% in single- and double-layer anastomosis, respectively [13,15].

Re-exploration due to intestinal leakage in our study was needed in two cases of group B, whereas in group A no cases re-explored. Saboo *et al.* [13] reported re-exploration in 10% in single-layer and 3.33% in double-layer anastomosis [13].

In our study, wound infection was found in two (6.7%) cases in single-layer and five (16.7%) cases in double-layer anastomosis, whereas in the study conducted by Ordorica-Flores *et al.* [12] wound infection was found in two (5%) cases in single-layer and three (7%) cases in double-layer anastomosis and in the study conducted by Askarpour *et al.* [16] wound infection was found in five (7.9%) cases in single-layer and seven (11%) cases in double-layer anastomosis [12,16]. Saboo *et al.* [13] reported wound infection in four (13.3%) cases in single-layer and six (20%) cases in double-layer anastomosis [13].

In this study, we can conclude that single-layer anastomosis is more successful and effective and this can be attributed to less damage to the blood supply because less mesentery is cleared off of the two cut edges and less damage to the submucosal vascular plexus, as in this technique sutures are taken sparing the mucosa. Also there is less inversion of tissue that can lead to narrowing of the lumen.

In our study, we did not exclude the duodenum and rectum from the inclusion criteria, whereas other studies did that. In addition, emergency cases were included in our study. The limitation of our study was that we did not conduct contrast studies to cases with distension to detect whether the cause was stricture in the anastomosis, especially in double-layer interrupted anastomosis.

Conclusion

The present study assessed the efficacy and safety of the single-layer interrupted against the double-layer interrupted anastomosis, comparing between them mainly in operative time, postoperative complications, and postoperative hospital stay. We concluded that single-layer anastomosis is effective, safe, and successful, of less operative time, less hospital stay, and valuable cost-effectiveness.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Platelet-rich plasma versus conventional dressing: does this really affect diabetic foot wound-healing outcomes?

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Purpose
This study aimed to compare platelet-rich plasma (PRP) versus conventional ordinary dressing in the management of diabetic foot wounds.
Background
Diabetic foot wound treatment poses a considerable burden on the medical system, with long waiting times for healing in the public hospital system. PRP enables efficient treatment of many patients with hemostatic, anti-inflammatory, and analgesic substances.
Patients and methods
This prospective study was focused on 80 diabetic feet wounds. Patients were divided into two groups: group A received conventional ordinary dressing (*N*=40, 50%) and group B received PRP dressing (*N*=40, 50%). The mean follow-up period was 12 weeks.
Results
The estimated time of wound healing was 12 weeks for 82.5% of the patients in group A and 97.5% of the patients in group B; the PRP group was found to be more effective with fewer complications, less infection, exudates, pain, and failed healing: 17.5, 12.5, 32.5, and 2.5% versus 27.5, 42.5, 62.5, and 17.5% in group B, respectively (*P*=0.001). The highest healing rate was observed for both groups at the fourth week, but it was better for the PRP group (group B): 0.89±0.13 versus 0.49±0.11 cm^2/week in group A.
Conclusion
There have been considerable advancements in the use of PRP in therapeutic processes in recent years in tissue regeneration therapy. PRP is a powerful tool for the treatment of chronic wounds and very promising for diabetic foot wounds; PRP enables healing, and reduces infection rates and exudates.

Keywords:
conventional ordinary dressing, diabetic foot wounds, healing outcomes, platelet-rich plasma

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Introduction

One of the most common causes of chronic wounds is growth factor abnormality. Platelets are considered a rich source of growth factors. Platelet-rich plasma (PRP) enhances wound healing by either the barrier effect to prevent bacterial invasion into the wound or the growth factors stimulate wound healing [1].

About 15% of diabetic patients will develop chronic wounds and about 25% of these patients will have to undergo foot amputation. The healing process is impaired in part because of deficiency of growth factors [2,3]. Becaplermin, a recombinant human platelet-derived growth factor-BB, is the only growth factor preparation approved by the US Food and Drug Administration for the treatment of diabetes mellitus (DM) wounds, but it requires daily applications for weeks to months [4].

Cell therapy and cell-containing tissue-engineered skin represent a significant advancement in the treatment of difficult to treat wounds. Currently, there are two cell-containing tissue-engineered skin products with US Food and Drug Administration approval available for use in the treatment of wounds. Apligraf (a bilayered bicellular product containing keratinocytes and fibroblasts in a bovine collagen matrix) and Dermagraft (fibroblast on a polyglactin matrix) accelerate wound healing, but also require frequent (weekly) applications, have a short shelf-life, and are expensive [5].

The use of adenovirus encoding human platelet-derived growth factor formulated in bovine collagen gel (GAM501) for the treatment of small nonhealing diabetic foot wounds has been reported. Despite these advanced researches, a more practical and effective

therapy for nonhealing diabetic wounds is clinically needed [6,7].

Plasma samples with platelet concentration above baseline values are referred to as PRP [8,9]. The clinical efficacy of the PRP was discovered in the early 1990s when new 'biological glues' were being discovered. They are at present used extensively in many clinical and surgical fields requiring tissue regeneration such as orthopedics, dentistry, wound healing, and maxillofacial surgeries [10].

The therapeutic effect of PRP is attributed to the abundance of various growth factors such as platelet-derived growth factor, transforming growth factor-β, fibroblast growth factor, insulin-like growth factor-1, insulin-like growth factor-2, vascular endothelial growth factor, epidermal growth factor, and also some cytokines primarily stored in alpha granules [11,12].

PRP can be prepared either from an autologous or an allogenic source. The majority of studies documented have used autologous platelet preparations as they are more acceptable by the patient and have a lower risk of transmission of viral infections [13].

PRP is easy to produce, with minimal effort. In a two-step process, whole blood from the patient is first centrifuged to separate plasma from packed red blood cells (RBCs) and then further centrifuged to separate PRP from platelet-poor plasma (PPP). This concentrate is then activated with the addition of thrombin or calcium, resulting in a gelatinous platelet gel. Clinically valuable PRP contains at least one million platelets per microliter [14].

Lower concentrations cannot be used to enhance healing and higher concentrations have not been shown to increase healing [15]. Blinded, multicentric, randomized-controlled studies with large sample sizes are urgently needed to establish their therapeutic efficacy. There are no universally established standards for the collection, quality control, and administration of the product [16,17].

Patients and methods

After receiving approval from the local ethical committee of Benha University and obtaining written fully informed consent from patients on the two methods of dressing and their benefits, risks, alternative interventions, and possible complications, the current study was carried out at the Vascular Unit, General Surgery Department, Benha University Hospitals, from October 2015 to July 2017, to allow a 12-week follow-up period for the last patient dressed on. This prospective randomized-controlled study was carried out on 80 diabetic patients with nonhealing feet wounds. Patients were allocated randomly using a computer-generated random number table into two groups according to the dressing method used: group A received conventional ordinary dressing (N=40, 50%) and group B received PRP dressing (N=40, 50%).

Patients included in this study had nonhealing feet wounds and fulfilled the following criteria: patients aged between 31 and 66 years, diabetic patients, both type I diabetes (insulin dependent) and type II diabetes (noninsulin dependent), with controlled blood sugar levels with nonhealing wounds on their feet, persistent wound for 3–6 months, wound size of the foot ranging from 6.5 to 8.5 cm^2, transcutaneous oxygen tension more than 30 mmHg, patients awaiting revascularization surgery, patients who had a normal peripheral platelet count ($>150\ 000/mm^3$), and patients with screening serum albumin level of more than 2.5 g/dl or hemoglobin more than 10.5 g/dl.

Pregnant women, patients with ischemic changes of the foot (transcutaneous oxygen tension$<$30), patients with radiological evidence of chronic osteomyelitis, patients not awaiting revascularization surgery, patients with severe cardiovascular disorders, patients who had received conventional skin grafting in the past, critically ill patients with immunological disturbances, and patients who were receiving or had received radiotherapy or chemotherapy within 3 months before the study were excluded.

All patients with nonhealing wounds on their feet were subjected to a formal assessment and investigations to determine the risk factors and treatment of diabetic foot disorders that required the expertise of a specialized practitioner to diagnose, manage, treat, and counsel the patient. Integration of knowledge and experience through a multidisciplinary team approach promoted more effective treatment, thereby improving outcomes and limiting the risk of lower extremity amputation.

Intervention

Sharp debridement of heavily infected wounds or nonhealing wounds was performed using a scalpel, curette, and scissors. Debridement converted a chronic or a heavily infected wound to one that was acute by removing nonviable tissue that could stimulate excessive inflammation and bacterial growth. Simple

incisions were used to open the infected area. Excision of necrotic tissue was extended as deeply and proximally as necessary until healthy, bleeding soft tissue and bone were encountered.

Any callus tissue surrounding the wound was removed. Evidence of pus on tendon sheaths indicated the need for more extensive debridement. Tendons were cut under tension to allow them to retract away from the open wound. The wounds should always be left open and inspected at 24–36 h.

Further debridement was carried out as necessary until the wound was clean and healing was underway. In the presence of an adequate arterial supply, rapid healing could occur following a thorough debridement. If healing did not occur, this was usually because of failure to drain all areas of infection or unrecognized ischemia. The decision on whether a foot could or could not be saved was made by the experienced surgeon. In case of doubt, all dead tissues were excised and the wounds were left open.

Postintervention dressing

Group A

This group of patients was treated by conventional ordinary dressing; surgical debridement was carried out for all necrotic tissues, and pus loculi were drained as discussed before and the dressing material used was prepared. Irrigation of the wound was performed with saline, and a dressing was selected by matching the properties of the dressing (such as control of exudates) with the characteristics of the wound and the patient, followed by packing of the wound. Appropriate dressing types were determined on the basis of wound location, depth, amount of slough present, amount of exudates, condition of the wound margins, and presence of infection. In general, betadine ointment with or without glycerin were used as wound-dressing materials. This dressing was performed every day and sometimes twice per day (Fig. 1).

Group B

This group of patients were treated by PRP therapy. The dressing protocol of these patients included PRP. PRP was applied to the diabetic foot after being prepared (within half an hour after preparation), followed by Vaseline gauze and then a dressing. The dressing was changed once weekly. This protocol was performed up to 12 weeks or stopped whenever healing occurred.

Each patient was sprayed with PRP around the wound edges (subdermal) and the floor (if deep). PRP was prepared from the patients' own blood (autologous PRP). Venous blood samples were drawn into 5 ml sterile tubes containing an anticoagulant (citrate dextrose – 3.2% sodium citrate) to avoid platelet activation and degranulation (10 ml). Whole blood was centrifuged at ×300*g* for 5 min at 18°C. The first centrifugation was called a 'soft spin' (×100*g*), which enabled the separation of blood into three layers: the bottommost layer comprised RBCs (55% of the total volume), the topmost layer comprised cellular plasma called PPP (40% of the total volume), and an intermediate PRP layer (5% of the total volume) called the 'buffy coat'. The upper fraction (PRP1) was separated, without disturbing the buffy coat, and was transferred into a sterile tube; this was done using a sterile syringe. The PPP, PRP, and some RBCs (i.e. the upper two layers and a very minimal 'unavoidable' amount of the bottom layer) were transferred into another tube without an anticoagulant. This tube was subjected to a second round of centrifugation (×447*g*) and was called a 'hard spin'.

This enabled the platelets (PRP) to settle at the bottom of the tube with very few RBCs. The cellular plasma, PPP (80% of the volume), was found on the top. Most of the PPP was removed with a syringe and the remaining PRP was shaken well. PRP1 was centrifuged at ×700*g* for 17 min at 18°C. The platelet pellet obtained from PRP1 was resuspended in 1 ml PPP (PRP2). Platelet activation was performed immediately by adding 0.5 ml $CaCl_2$. Application was performed immediately after the activation of wound edges and floor. Dressing was performed and lifted for 1 week until a follow-up session. Reinjection was performed after 2 weeks. However, for large wounds, more than 5.5 cm, reinjection was performed every week during a follow-up session and dressing was performed twice weekly – that is, every 3–4 days (Fig. 2).

Follow-up

The patients were advised to avoid pressure on the wound area. A special shoe with a molded insole was used. Elevation of the feet was recommended when sitting or lying down to decrease edema. The patients were seen once or twice weekly throughout the course of treatment and a clinical evaluation was performed once weekly. Clinical laboratory tests were performed every 4 weeks for all treatment groups – that is, complete blood count, random blood sugar, and serum albumin.

The patients were evaluated for the rate of wound healing in about 12 weeks and this evaluation was carried out by taking photos and measuring the wound's dimensions (length and width) using a

Figure 1

Cases of group A: conventional ordinary dressing.

metric tape at the initial visit and then every week. Characteristics of the wound such as exudates, necrotic tissue, infection, and granulation tissue were documented. The primary outcome evaluated: was reduction in the size of the wound, which was determined from photos taken every week. The secondary outcome parameters were the presence of infection, exudates, and pain.

Statistical analysis

Analysis of data was carried out using Statistical Package for Social Sciences (SPSS) (version 16; SPSS Inc., Chicago, Illinois, USA) (Bristol University, UK). Quantitative data were presented as mean and SD and were analyzed using a one-way unpaired *t*-test to compare quantitative variables as parametric data (SD<50% mean). Qualitative data were presented as numbers and percentages and were analyzed using χ^2 and Fisher's exact tests. A *P*-value of less than 0.05 was considered significant whereas a *P*-value of less than 0.01 was considered highly significant. However, a *P*-value of more than 0.05 was considered insignificant.

All these data are shown in Figs. 1, and 2.

Figure 2

Cases of group B: platelet-rich plasma (PRP) dressing.

Results

This was a prospective study that included 80 diabetic patients with nonhealed foot wounds recruited from Benha University Hospitals and were followed up for 12 weeks; patients were divided according to the dressing performed into two groups: group A included 40 patients who received conventional ordinary dressing. Group B included 40 patients who received PRP dressing. Their ages ranged from 31 to 66 years, with a mean of 49±5.06 years. All patients presented with nonhealed foot wounds and none of them presented with any other symptoms; the majority of patients were men [50 (62.5%)]. The wound was mostly present on the sole of the foot [67 (83.75%)]. The duration of diabetes in the patients ranged between 7.5 and 12.5 years, with a mean of 10.3±2.3 years, and the size of the wound ranged between 4.9 and 8.6 cm, with a mean of 7.4± 0.8 cm (Table 1 and Graph 1a and b).

Upon review of DM-related comorbidities, foot angiopathy and retinopathy, which affected wound healing and care, were observed in 15 (18.75%) and eight (10%) cases in group A versus 17 (21.25%) cases and nine (11.25%) cases in group B,

respectively. Of these diabetic patients, 64 (80%) patients were on oral hypoglycemic drugs, whereas 16 (20%) patients were on insulin injections. Other risk factors encountered were medically controlled hypertension in 31 (38.75%) patients, nephropathy in 15 (30%) patients, and smoking in 48 (60%) patients that could have impaired wound healing. There was no significant difference between both groups in terms of the presence of these risk factors (χ^2=0.104 and P=0.706) (Table 2 and Graph 2).

In terms of the previous clinical parameters, previous foot wound and minor amputations were reported in nine (11.25%) and 10 (12.5%) cases in group A versus 11 (13.75%) and 12 (15%) cases in group B, respectively. Intermittent claudication with transcutaneous O_2 tension more than 30 mmHg and foot neuropathic pain were reported in 15 (18.75%) and 25 (31.25%) cases in group A versus 17 (21.25%) and 27 (33.75%) cases in group B. Previous hyperbaric O_2 therapy was reported equally in both groups in 21 (42%) cases (P=0.736) (Table 3 and Graph 3).

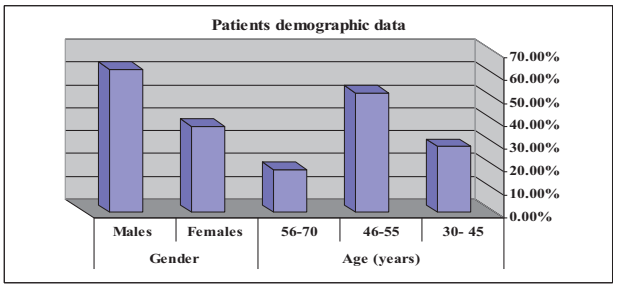
No mortality was recorded and all patients attended follow-up. PRP was shown to be more effective than conventional dressing after the second week

Table 1 Patients' demographic data

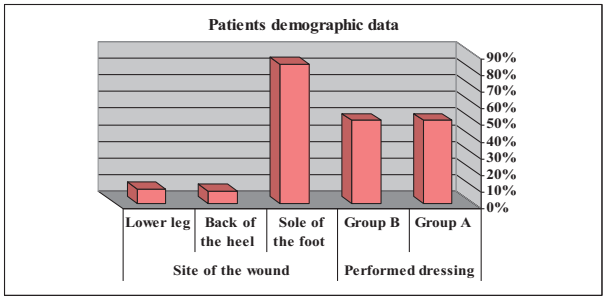
Data	Findings [*n* (%)]
Age (years)	
Strata	
31–45	23 (28.75)
46–55	42 (52.25)
56–66	15 (18.75)
Mean±SD	49±5.06
Sex	
Female	30 (37.5)
Male	50 (62.5)
Performed dressing	
Group A: conventional ordinary dressing	40 (50)
Group B: PRP dressing	40 (50)
Site of the wound	
Sole of the foot	67 (83.75)
The heel	6 (7.5)
Lower leg	7 (8.75)
Duration of diabetes [range (mean±SD)] (years)	7.5–12.5 (10.3 ±2.3)
Size of the wound [range (mean±SD)] (cm)	4.9–8.6 (6.4±0.7)

PRP, platelet-rich plasma.

Graph 1



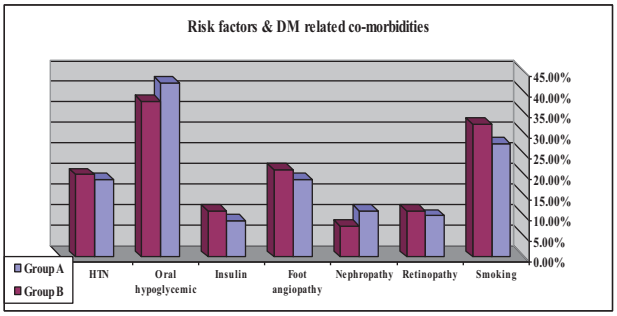
Graph. (1_A): Patients demographic data.



Graph. (1_B): Patients demographic data.

Patients' demographic data: (a) sex and age; (b) site of the wound and performed dressing.

Graph 2



Risk factors of impaired healing and diabetes mellitus-related comorbidities. HTN, hypertension.

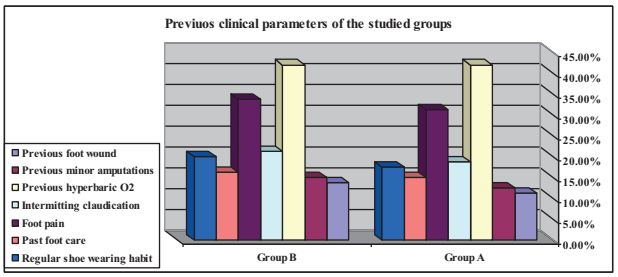
Table 2 Risk factors of impaired healing and diabetes mellitus-related comorbidities

Risk factors and DM-related comorbidities	Group A (*n*=40 patients) [*n* (%)]	Group B (*n*=40 patients) [*n* (%)]	χ^2	*P*-value
Smoking	22 (27.5)	26 (32.25)	0.104	0.706 (NS)
Retinopathy	8 (10)	9 (11.25)		
Nephropathy	9 (11.25)	6 (7.5)		
Foot angiopathy	15 (18.75)	17 (21.25)		
Insulin	7 (8.75	9 (11.25		
Oral hypoglycemic	34 (42.25)	30 (37.75)		
Hypertension	15 (18.75)	16 (20.0)		

DM, diabetes mellitus.

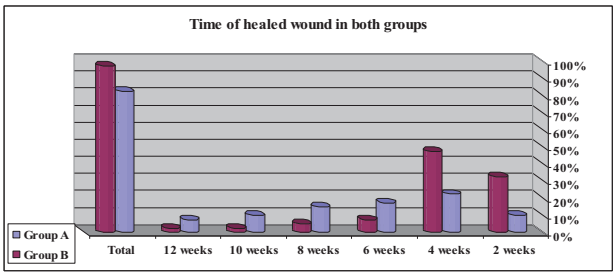
[13 (32.5%) patients vs. 4 (10%) patients, respectively]. The same result was found at the fourth week [19 (47.5%) cases versus nine (22.5%) cases, respectively]. However, subsequently, the number of healed wounds started to decline – that is, at the sixth week [three (7.5%) cases in group B versus seven (17.5%) cases in group A]. Wounds healed in 39 (97.5%) patients in group A versus 33

Graph 3



Previous clinical parameters of the studied groups.

Graph 4



Rate of healing of wound in both groups with respect to time.

Table 3 Previous clinical parameters of the studied groups

Clinical parameters	Group A (*n*=40 patients) [*n* (%)]	Group B (*n*=40 patients) [*n* (%)]	χ^2	*P*-value
Previous foot wound	9 (11.25)	11 (13.75)	0.114	0.736 (NS)
Previous minor amputations	10 (12.5)	12 (15)		
Previous hyperbaric O_2	21 (42)	21 (42)		
Intermitting claudication	15 (18.75)	17 (21.25)		
Foot pain	25 (31.25)	27 (33.75)		
Past foot care	12 (15)	13 (16.25)		
Regular shoe-wearing habit	14 (17.5)	16 (20)		

Table 4 Rate of healing of wound in both groups with respect to time

Durations	Group A (*n*=40 patients) [*n* (%)]	Group B (*n*=40 patients) [*n* (%)]	χ^2	*P*-value
2 weeks	4 (10)	5 (32.5)	21	0.001 (HS)
4 weeks	9 (22.5)	19 (47.5)		
6 weeks	7 (17.5)	3 (7.5)		
8 weeks	6 (15)	2 (5)		
10 weeks	4 (10)	1 (2.5)		
12 weeks	3 (7.5)	1 (2.5)		
Total	33 (82.5)	39 (97.5)		

HS, highly significant.

Table 5 Rate of healing (cm^2/week) in the first 8 weeks in both groups

Rates of healing	Group A (*n*=40 patients)	Group B (*n*=40 patients)	τ	*P*-value
At 2 weeks (cm^2/week)				
Mean±SD	0.41±0.20	0.80±0.21	10.9	0.001 (HS)
Range	0.21–0.61	0.59–1.01		
At 4 weeks (cm^2/week)				
Mean±SD	0.49±0.11	0.89±0.13	9.3	0.001 (HS)
Range	0.38–0.60	0.76–1.02		
At 6 weeks (cm^2/week)				
Mean±SD	0.32±0.15	0.60±0.91	10.6	0.001 (HS)
Range	0.17–0.47	0.31–1.51		
At 8 weeks (cm^2/week)				
Mean±SD	0.29±0.14	0.50±0.12	8.2	0.001 (HS)
Range	0.15–0.43	0.38–0.62		

Data are presented as ranges and mean±SD, HS, highly significant, Statistically significant difference was determined using an unpaired *t*-test (significance was towards group B).

(82.5%) patients in group B (P=0.001) (Table 4 and Graph 4).

In terms of the rate of healing (cm^2/week), after the second week, there was a higher rate of healing per week (0.80±0.21 cm^2/week in group B versus 0.41±0.20 cm^2/week in group A). At the fourth week, the highest healing rate was found for both groups, but was better for the PRP group B (0.89±0.13 vs. 0.49±0.11 cm^2/week in group A). At the sixth and eighth weeks, a higher healing rate was found for the PRP group B: 0.60±0.91, 0.50±0.12 cm^2/week vs. 0.32±0.15, 0.29±0.14 cm^2/week in group A (P=0.001) (Table 5 and Graph 5).

At 10th and 12th weeks, a higher rate of healing per week was observed (0.40±0.12, 0.39±0.11 cm^2/week in group A vs. 0.20±0.13, 0.19±0.11 cm^2/week in group B). The lowest rate of healing was reported for the PRP group at the 10th and 12th weeks. However, for the conventional group, the lowest rate of healing was reported at the eighth week (0.29±0.14 cm^2/week). There was a statistically significant difference between both groups, but towards the group B in this period of dressing, with τ of 7.1 at the 10th week and 6.9 at the 12th week (P=0.001) (Table 6 and Graph 6).

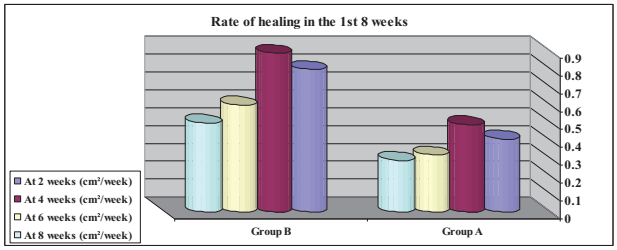
The total rate of healing (cm^2/week) was 6.8±0.54 in group A versus 7.3±0.90 in group B (Table 7 and Graph 7).

Upon review, complications occurred during the dressing period; infection, exudates, and pain were observed more in group A: 11 (27.5%) cases, 17 (42.5%) cases, and 25 (62.5%) cases, respectively, versus seven (17.5%) cases, five (12.5%) cases, and 13 (32.5%) cases, respectively, in group B. Eleven (27.5%) patients required a longer duration than the estimated time of healing (12 weeks) in group A, but this was observed in only one (2.5%) patient in group B (Table 8 and Graph 8).

Discussion

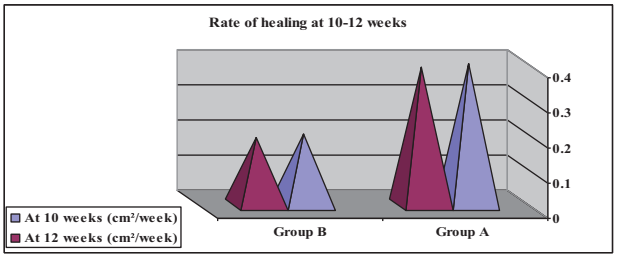
Diabetic foot wound is a common clinical problem. Because of population aging and an increase in risk factors and comorbidities such as tobacco use, obesity, hypertension, and atherosclerosis, there is a clear trend

Graph 5



Rate of healing (cm^2/week) in the first 8 weeks in both groups.

Graph 6



Rate of healing (cm^2/week) over a period of 10–12 weeks.

Table 6 Rate of healing (cm^2/week) over the period of 10–12 weeks

Rate of healing	Group A (n=40 patients)	Group B (n=40 patients)	τ	P-value
At 10 weeks (cm^2/week)				
Mean±SD	0.40±0.12	0.20±0.13	7.1	0.001 (HS)
Range	0.28–0.25	0.07–0.33		
At 12 weeks (cm^2/week)				
Mean±SD	0.39±0.11	0.19±0.11	6.9	0.001 (HS)
Range	0.29–0.50	0.08–0.30		

Data are presented as ranges and mean±SD, HS, highly significant, Statistically significant difference was determined using an unpaired t-test (significance was towards group A).

Table 7 Total rate of healing (cm^2/week) in both groups

Total rate of healing	Group A (n=40 patients)	Group B (n=40 patients)	τ	P-value
Mean±SD	6.8±0.54	7.3±0.90	4.3	0.01 (S)
Range	6.26–7.34	6.40–8.20		

HS, highly significant, Statistically significant difference was determined using an unpaired t-test (significance was towards group B).

toward increased risk of chronic wounds. The social and economic effects are inevitable [18].

PRP is defined as a proportion of the plasma fraction of autologous blood with a platelet concentration above the baseline. PRP is also known as platelet-enriched plasma, platelet-rich concentrate, and autologous platelet gel. PRP have been used to treat wounds since 1985 [19].

For more than 20 years, the PRP gel has been used to promote wound healing. Autologous PRP is composed of cytokines, growth factors, chemokine, and fibrin scaffold derived from a patient's blood. The mechanism of action of the PRP gel is believed to be the molecular and cellular induction of normal wound-healing response similar to that found with platelet activation [14].

The present study was carried out to evaluate the effectiveness of PRP in promoting healing of diabetic foot wounds, preventing infection, and reducing exudates, besides its preventive action by reducing amputation rates. There have been considerable advances in the use of PRP in therapeutic processes in recent years in tissue regeneration therapy.

On the basis of the last 10 years of research, the results of the systematic review with meta-analysis published by Carter *et al.* [20] suggest that PRP therapy can positively impact wound healing and associated factors such as pain and infection in both chronic and acute cutaneous wounds.

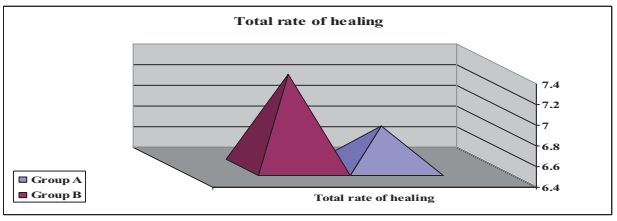
The current study was carried out on 80 patients with diabetic foot wounds; the patients' ages ranged from 31 to 66 years, with a mean of 49±5.06 years; the majority of patients were men [50 (62.5%)]. The study of Saad *et al.* [21] was carried out on 24 patients with chronic ulcers ranging in age from 40 to 60 years; they concluded that sex and age are insignificant in correlation with the rate of healing of their ulcers.

In the present study, the site of diabetic feet wounds was generally the sole of the foot [67 (83.75%)]. The duration of diabetes ranged between 7.5 and 12.5 years, with a mean of 10.3±2.3 years. It was observed that there was no correlation between the site and the rate of healing. This result was reported by Gui-Qiu *et al.* [22], who studied the effect of PRP on healing of lower extremity chronic ulcers in 21 patients; they concluded that 'there was no significant difference between type and site of ulcers in correlation with rate of healing'.

In this study, wounds varied in size and ranged between 4.9 and 8.6 cm, with a mean of 6.4±0.7 cm. It was observed that there was a significant and strong inverse correlation between the rate of healing and the size of the wounds, and there was a significant and strong proportional correlation between the size of the wounds and treatment duration (P=0.001). Also, there was a significant and strong proportional correlation between the size of the wounds and the number of injections. Many trials concluded that the larger the ulcer, the longer the duration required for treatment and the greater the number of injections [23,24].

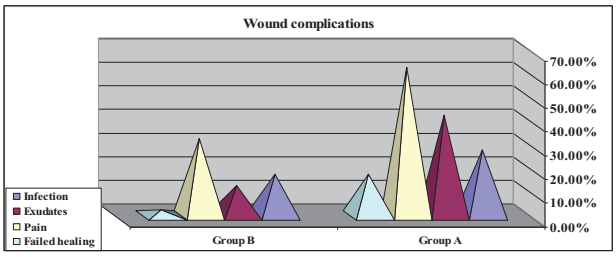
Upon review of risk factors and comorbidities, diabetes represents a worldwide public health issue, affecting ~5% of the population of the USA. Its high prevalence places this disease among one of the main pathologies

Graph 7



Total rate of healing (cm^2/week) in both groups.

Graph 8



Wound dressing complications.

Table 8 Wound dressing complications

Complications	Group A (n=40 patients) [n (%)]	Group B (n=40 patients) [n (%)]	χ^2	P-value
Infection	11 (27.5)	7 (17.5)	25	0.001 (HS)
Exudates	17 (42.5)	5 (12.5)		
Pain	25 (62.5)	13 (32.5)		
Failed healing	7 (17.5)	1 (2.5)		

HS, highly significant.

that can progress to chronic ulceration [25]. Other risk factors found in this study included DM-related comorbidities, foot angiopathy, and retinopathy, which affected wound healing and care, and smoking in 48 (60%) patients, which might have impaired wound healing directly or indirectly through vascular bad effect of smoking [26,27].

In the current study, PRP was found to be more effective than conventional dressing after the second week [13 (32.5%) vs. four (10%) patients, respectively). The same effect was reported at the fourth week [19 (47.5%) vs. nine (22.5%) cases, respectively]. This could be explained by the fact that during wound healing, platelets are activated by contact with collagen and released into the bloodstream after endothelial injury. Platelets secrete stored intercellular mediators and cytokines from the cytoplasmic pool and release their α-granule content after aggregation. More than 800 different proteins are secreted into the surrounding media, exerting a paracrine effect on different cells. This secretion is intense in the first hour and platelets continue to synthesize more cytokines and growth factors from their mRNA reserves for at least another 7 days [23].

However, after the first 4 weeks, the number of healed wounds started to decrease – that is, at the sixth week, three (7.5%) cases in group B versus seven (17.5%) cases in group A. The total number of patients in whom wounds healed was 39 (97.5%) in group A versus 33 (82.5%) in group B (P=0.001). In terms of the rate of healing, after the second week, there was a higher rate of healing per week (0.80±0.21 cm^2/week in group B vs. 0.41±0.20 cm^2/week in group A). At the fourth week, the highest healing rate was found for both groups, but was better for the PRP group B: 0.89± 0.13 vs. 0.49±0.11 cm^2/week in group A.

All systematic reviews have shown that PRP can stimulate healing of wounds. Gui-Qiu *et al.* [22] recruited 21 patients with refractory diabetic lower extremity ulcers who showed no response to conventional treatments; these patients were treated with homologous PRP. Their data indicated that homologous PRP was effective in enhancing and accelerating healing of diabetic lower extremity wounds.

Martinez-Zapata *et al.* [16] reported that the percentage of total healing in PRP-treated wounds increased compared with the controls. In a meta-analysis of chronic wound studies, Carter *et al.* [20] confirmed that the use of PRP treatment promotes complete healing compared with control care. Villela *et al.* [27] also reached the same conclusions.

All the above-mentioned studies concluded that on the basis of the meta-analysis and scientific evidence of consistent favorable outcomes, 'PRP is a treatment of choice for the topical care of wounds' [28]. This could be attributed to the fact that PRP functions as a tissue sealant and drug-delivery system, with the platelets initiating wound repair by releasing locally acting growth factors by α-granule degranulation. These growth factors aid healing by attracting undifferentiated cells to the newly formed matrix and triggering cell division and by interacting with macrophages to improve tissue healing and regeneration, promoting new capillary growth, and accelerating epithelialization in chronic wounds [29].

Seven (17.5%) patients required longer duration than the estimated time of healing (12 weeks) in group A, but this was found in only one (2.5%) patient in group B. Most of the wounds healed within the estimated time of healing (12 weeks); all these cases showed more than 50% healing after the first 4 weeks. These results were confirmed by Gelf *et al.* [30], who stated that 'It is generally accepted that a reasonable goal is healing by 12 weeks. Healing rates at 4 weeks predict overall healing rates, and a 10–15% area reduction weekly suggests an excellent prognosis'.

The use of antibiotics was more frequent in group A because of infection. Complications that developed during the dressing period were infection, exudates, and pain, which were observed more in group A: 11 (27.5%), 17 (42.5%), and 25 (62.5%), cases, respectively, versus 7 (17.5%), 5 (12.5%), and 13 (32.5%) cases, respectively, in group B. Paola *et al.* [23] reported that the fewer complications in group B could have been because of the fact that platelets exert anti-inflammatory and analgesic effects, which was confirmed by Asfaha *et al.* They reported PAR4-mediated analgesic effects *in vitro*. Also, El-Sharkawy *et al.* studied platelet secretions and their effect on macrophage cultures, concluding that 'platelet concentrates function as an anti-inflammatory agent, because of the high RANTES and LXA4 concentrations'. Also, the anti-inflammatory effect of platelets could be explained by the fact that 'PRP may suppress cytokine release and limit inflammation' [31]. On reviewing studies, the infection rate of the PRP group of the current study was higher than that stated by Anitua *et al.* [32], who reported only one patient with superinfection of his ulcer developed in PRP group.

Conclusion

There have been considerable advances in the use of PRP in therapeutic processes in recent years in tissue regeneration therapy. PRP is very promising for diabetic foot wounds as it enables healing, and reduces infection rates and exudates; in addition, it reduces amputation rates.

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Conflicts of interest

There are no conflicts of interest.

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Evaluation of near total lower lip reconstruction using mcgregor musculomucocutaneous cheek rotational flap

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Introduction
The goals of lower lip reconstruction are maintenance of adequate oral stoma, restoration of oral competence, to maintain speech, to preserve sensation, to provide both skin cover and oral lining and to produce an aesthetically satisfying result. A number of local flaps are available for reconstruction of lip defects, although free flaps may also be used for more extensive defects. Local flaps achieve better aesthetic and functional results compared with free flaps. In this study, we evaluate the near total lower lip reconstruction using single-stage McGregor musculomucocutaneous cheek rotational flap.

Aim
The aim of this study was to evaluate the near total lower lip reconstruction using McGregor musculomucocutaneous cheek rotational flap.

Patients and methods
This prospective study was performed at the Plastic Surgery Unit, Fayoum University Hospital, in the period from October 2015 to April 2017. Eight patients with squamous cell carcinoma at the lower lip excised with safety margin ranging from 0.5 to 1 cm in each side, leaving defects more than 2/3 of the length of the lower lip, were included in this study. Reconstruction was done in all patients using McGregor musculomucocutaneous flap.

Results
The mean age of the patients was 61.4 years (range: 55–70 years). Five patients were male and three patients were female. In all patients the angles of the mouth were symmetrical with preservation of the anatomic proportions of the lip, except in two patients there were some mucosal folds at the rotation point at the commissure. In all patients, the philtrum had a normal shape and position. The oral mobility was good in all patients, which was evaluated by facial expressions and sound formations.

Conclusion
Although more number of cases are required to build up our conclusion, according to our results on this low number of patients McGregor musculomucocutaneous cheek rotational flap is considered a good option for near total lower lip reconstruction with good functional and aesthetic outcomes.

Keywords:
lower lip, McGregor musculomucocutaneous, near total, rotational flap

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1110-1121

Introduction

The insufficiency of the remained lip tissue causes great difficulty in reconstruction of extensive lower lip defects resulting from the excision of malignant lesions, especially squamous cell carcinoma.

The goals of lower lip reconstruction are maintenance of adequate oral stoma, restoration of oral competence, to maintain speech, to preserve sensation, to provide both skin cover and oral lining and to produce an aesthetically satisfying result [1].

A number of techniques have been described, and the choice depends on the extent of the defect in addition to the surgeon's experience.

A number of local flaps are available for reconstruction of lip defects, although free flaps may also be used for more extensive defects.

Local flaps achieve better aesthetic and functional results compared with free flaps [2].

In this study, we evaluate the near total lower lip reconstruction using single-stage McGregor musculomucocutaneous cheek rotational flap.

Patients and methods

This prospective study was performed at the Plastic Surgery Unit, Fayoum University Hospital, in the period from October 2015 to April 2017. Ethical approval and patients consents: Were obtained.

Eight patients with squamous cell carcinoma at the lower lip excised with safety margin ranging from 0.5 to 1 cm in each side, leaving defects more than 2/3 of the length of the lower lip, were included in this study.

Reconstruction was done in all patients using McGregor musculomucocutaneous cheek rotational flap, which was based on the superior labial artery running just deep into the mucosa.

Supraomohyoid block neck dissection was performed in five patients.

In all patients, preoperative incisional biopsy was performed to prove the diagnosis. Computed tomography scan neck, chest and abdomen were performed to exclude metastasis.

Surgical technique

The skin is marked in a rectangular fan shape that extends laterally from the defect and around the nasolabial fold where the arc of the fan is completed and back cut is designed.

The width of the rectangular flap is equal to the vertical height of the lip defect and the vertical length of the flap is equal to the width of the defect plus the width of the flap itself.

The flap is based on the superior labial artery running just deep into the mucosa.

From the bottom of the lip defect the incision extended laterally along the full thickness of the flap, upward vertically, medially and then the back cut downward vertically up to few millimetres of the vermilion border of the remaining upper lip. The flap was rotated into place and mucosa, muscle and skin were sutured separately.

The donor site was closed directly and the skin and mucosa of the flap were sutured together to create the new vermilion.

Follow-up periods ranged from 9 months up to 1 year postoperative.

Results

The mean age of the patients was 61.4 years (range: 55–70 years). Five patients were male and three patients were female.

All eight patients had a squamous cell carcinoma at the lower lip excised with safety margin ranging from 0.5 to 1 cm on each side, leaving defects more than 2/3 of the length of the lower lip.

Reconstruction was done in all patients using McGregor musculomucocutaneous cheek rotational flap.

In all patients the flaps survived completely.

No recurrence of the tumour was noticed in the follow-up period in all patients.

The vermilion and vermilion–cutaneous white border were reconstructed and established in all patients with good satisfactory shape.

In all patients the angles of the mouth were symmetrical with preservation of the anatomic proportions of the lip, except in two patients there were some mucosal folds at the rotation point at the commissure.

In all patients the philtrum had a normal shape and position.

The oral mobility was good in all patients, which was evaluated by facial expressions and sound formations.

In all patients there was no microstomia with an adequate oral access.

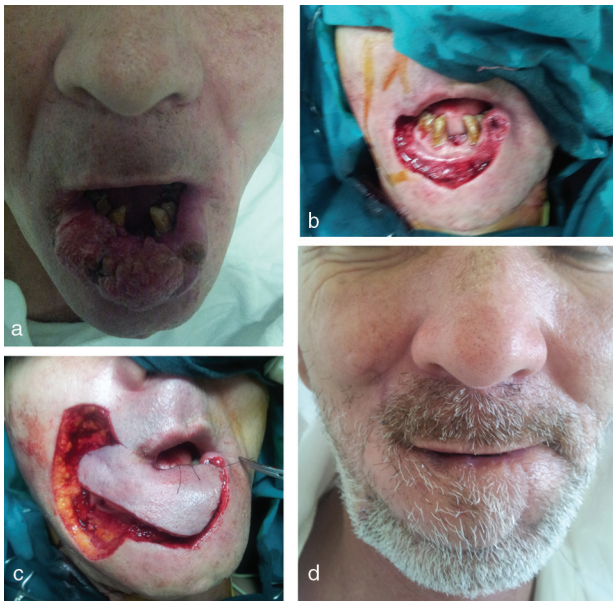
The oral continence to food, fluids and air was good in all patients.

The patients' satisfaction ranged from 60 to 100%: in three patients it was from 60 to 80%, and in five patients it was from 80 to 100% (Figs. 1 and 2).

Discussion

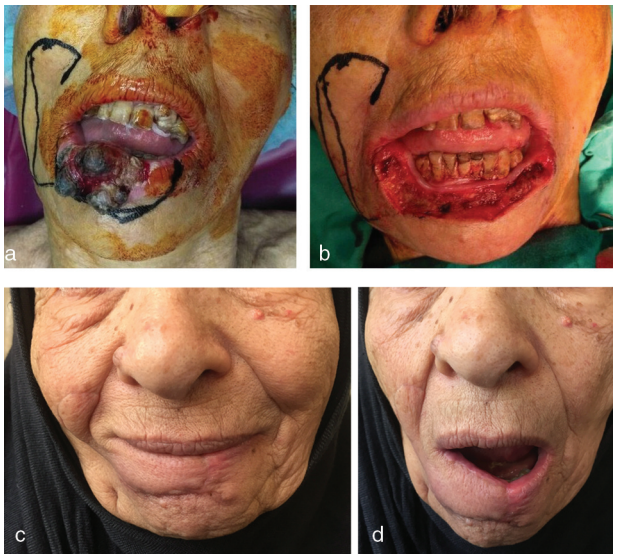
Many surgical techniques for reconstruction of the extensive lower lip defects have been described, each of them having its own advantages and disadvantages. Most of these techniques restore lip continuity, but compromise mouth opening (cause microstomia) or sphincter function, or cause significant perioral scarring and poor aesthetic outcome [3].

Figure 1



(a) Preoperative picture of squamous cell carcinoma at the lower lip; (b) intraoperative picture of the defect; (c) flap inset to the defect; (d) 6 months postoperative picture.

Figure 2



(a) Preoperative picture of squamous cell carcinoma at the lower lip; (b) intraoperative picture of the defect; (c) 6 months postoperative picture; (d) 6 months postoperative picture.

The local flaps that are used for extensive lower lip defects (>two-thirds) are mainly Karapandzic flap, the Gillies fan flap, McGregor and Nakajima flap and the Webster–Bernard flap.

The Karapandzic flap can achieve a functional lip with preserved competence and sensation, but results in narrowing of the mouth especially when reconstructing large defects and necessitating another setting of commissuroplasty [4].

The Gillies fan flap is another option to reconstruct massive lower lip defect, but the angle of the mouth is distorted and the lower lip is shortened [5].

The Webster–Bernard procedure can produce good lip reconstruction but involves a large amount of perioral tissue loss, resulting in a tight lower lip and significant perioral scarring with contour deformity [6].

The Fujimori nasolabial 'gate flaps' can achieve lip reconstruction with good functional and cosmetic results, but retouch operations are often necessary [7].Free flaps are suitable for reconstruction of the total lower lip owing to more soft tissue availability; however, there is risk of donor site morbidity, and the operative time is longer and the aesthetic appearance is less satisfactory because the flaps lack the harmony of the face. Furthermore, it is difficult to create a functional oral sphincter leading to oral incompetence [8].

In this study, we evaluated the functional and the aesthetic outcome of the McGregor musculomucocutaneous cheek rotational flap, which is a rectangular modification of the Gillis fan flap.

In all patients the flaps survived completely. The vermilion and vermilion–cutaneous white border were reconstructed and established in all patients with good satisfactory shape.

In all patients the angles of the mouth were symmetrical with preservation of the anatomic proportions of the lip, except in two patients there were some mucosal folds at the rotation point at the commissure.

In all patients the philtrum had a normal shape and position. The oral mobility was good in all patients, which was evaluated by facial expressions and sound formations.

In all patients there was no microstomia with an adequate oral access.

The oral continence to food, fluids and air was good in all patients.

The patient satisfaction ranged from 60 to 100%: for three patients it was from 60 to 80% and for five patients it was from 80 to 100%.

Conclusion

Although more number of cases are required to build up our conclusion, according to our results on this low

number of patients McGregor musculomucocutaneous cheek rotational flap is considered a good option for near total lower lip reconstruction with good functional and aesthetic outcome.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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Assessment of the efficacy and oncological safety of sentinel lymph node biopsy in node-negative breast cancer using methylene blue dye

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Background
Sentinel lymph node (SLN) biopsy in patients with breast cancer with clinically negative axillary nodes is an innovative technique in the management of the axilla. SLN biopsy has been performed using different techniques including injection of patent blue dye, radioactive colloid, and recently methylene blue dye. The aim of this study was to assess the safety and efficacy of methylene blue dye as a mapping agent for SLN biopsy in clinically axillary node-negative breast carcinoma.
Patients and methods
Between January 2014 and October 2016, 50 female patients with established diagnosis of breast carcinoma by tru-cut biopsy and clinically negative ipsilateral axillary lymph nodes were included in the study. All the patients were operated upon in Ain Shams University hospitals. After induction of anesthesia, 3–5 ml of sterile 1% methylene blue was infiltrated into the subareolar tissue on the affected side. The lymph nodes receiving the blue dye were excised as the SLN. Excised specimen with the axillary tissue was sent for histopathological examination. The presence or absence of metastasis in SLN and axillary lymph nodes was compared. Statistical analysis was carried out to know sensitivity, specificity, and accuracy of SLN biopsy in breast cancer.
Results
The incidence of breast cancer was highest at 41–50 years. Of our 50 cases, SLN was identified in 44 cases using methylene blue dye. The identification rate was 88%. None of the patients had negative SLN but positive axillary lymph nodes (false negative), and in six cases, SLNs were involved only but not the rest of the axilla (false positive). The sensitivity, specificity, positive predictive value, and negative predictive value were 100, 85.7, 25, and 100%, respectively.
Conclusion
This study confirms the safety and efficacy of methylene blue dye as a mapping agent for SLN biopsy in axillary node-negative breast cancer.

Keywords:
breast cancer, methylene blue dye, sentinel lymph node biopsy

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1110-1121

Introduction

Breast carcinoma is the most common cancer of women worldwide, including 23% of all female cancers [1]. Approximately one in nine women will have breast cancer during her lifetime. Breast cancer is the commonest cause of deaths owing to cancer in females throughout the world [2].

The incidence of breast cancer is increasing. This increase in incidence may be because of screening, self-examination, and awareness. Staging is very important for management of all patients with cancer, and breast cancer is not an exception. Staging of axilla in breast cancer is the single most important prognostic factor for selection of appropriate adjuvant therapy, locoregional recurrence, and long-term survival. Exact staging of axillary lymph nodes can be obtained in two ways: directly by axillary lymph node dissection (ALND) or indirectly by sentinel lymph node biopsy (SLNB). The ALND is drastic and associated with debilitating complications of the ipsilateral arm like lymphedema, seroma, paresthesia, etc.; whereas, SLNB is less drastic and devoid of aforementioned complications [3–5].

SLN biopsy by radio-colloid method was first reported by Krag *et al.* [6] and by blue dye method by Giuliano *et al.* [7]. Combined use of radioactive colloid and blue dye injection is considered as gold standard for axillary SLNB in breast cancer, with 97% accuracy rate [8–10], but this combined usage does not attain an adequately

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higher detection rate to defend the cost [11]. However, some researchers have been using blue dye only for identification of SLN with good reliability [12]. The positive results found by using methylene blue dye and by isosulfan blue dye were 99 and 97%, respectively [13,14]. Moreover, another similar study for methylene blue dye was done, showing the sensitivity and specificity of 85.7 and 71.4%, respectively [15]. Therefore, the efficiency of detecting SLN by methylene blue is as good as isosulfan blue with cost-effectiveness and is equal to ALND in breast cancer, but there is difference between the percentages of positive results in different studies [15].

For adopting SLNB technique, it is a well-recognized accepted fact that a multidisciplinary team, which includes surgery, nuclear medicine, and surgical pathology departments, is required to work in close cooperation. Each of these disciplines plays a crucial role in achieving success, and the surgeon cannot embark upon a successful SLNB program without cooperation from other disciplines.

In this study, we had chosen the subareolar technique in detection of sentinel lymph nodes (SLNs) using methylene blue dye only, together with the assessment of its accuracy, efficacy, and oncological safety in clinically node-negative patients.

Patients and methods

Between January 2014 and October 2016, a series of 50 consecutive female patients presenting with breast cancer proven with true-cut biopsy, and clinically node-negative axilla, were included in this prospective study. Patients with palpable axillary lymph nodes, distant metastasis, previous breast cancer surgery, neoadjuvant treatment, inflammatory breast cancer, pregnant females, male patients, and patients unwilling to participate in the study were excluded. Local ethical committee approval was given for the study, and written informed consent was obtained from all participants. This study was performed in Ain Shams University hospitals in Cairo, Egypt.

All patients underwent bilateral sono-mammographic examination, routine preoperative investigation, (complete blood count, prothrombin time and concentration, renal function test, and liver function test), and ECG for assessment for surgical fitness. Metastatic workup was done, including chest radio graphy, abdomen and pelvis ultrasonography, and isotope bone scan, to exclude presence of distant metastasis.

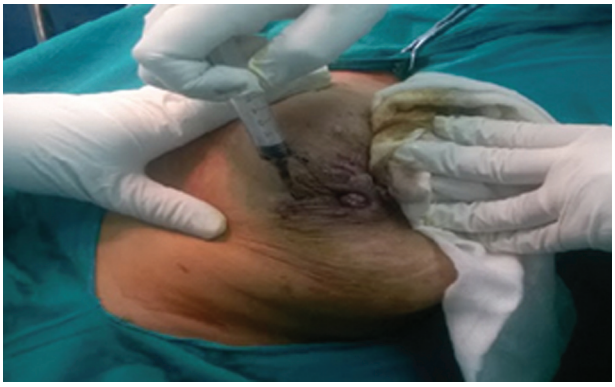
The procedure is carried out under general anesthesia with the patient supine on the operating table and the arm abducted at 90° from the body. After draping, 5 ml of 1% methylene blue dye was injected in the subareolar region, divided in three injections times (Fig. 1). Massage was done for 10–15 min in a clockwise direction. A useful anatomical landmark is made to place the incision 1 cm below the hairline of the axilla. Skin and subcutaneous tissue were dissected followed by dissection of clavipectoral fascia to enter the axilla, and blue-stained lymphatics were identified. Following the stained lymphatics, identification of the blue colored node(s) is made, which presented mainly below the pectoralis minor muscle (Fig. 2). These nodes, together with perilymphatic tissue, were dissected and were labeled separately, and then, planned procedure, either modified radical mastectomy (MRM) (Fig. 3) or wide local excision (WLE), was performed. The breast tissue or excised mass along with the remaining axillary lymph nodes were histopathologically examined separately from sentinel lymph nodes. The presence or absence of metastasis in SLN and axillary lymph nodes was compared. Statistical analysis was carried out to know sensitivity, specificity, and accuracy of SLN.

Results

Age of the study group

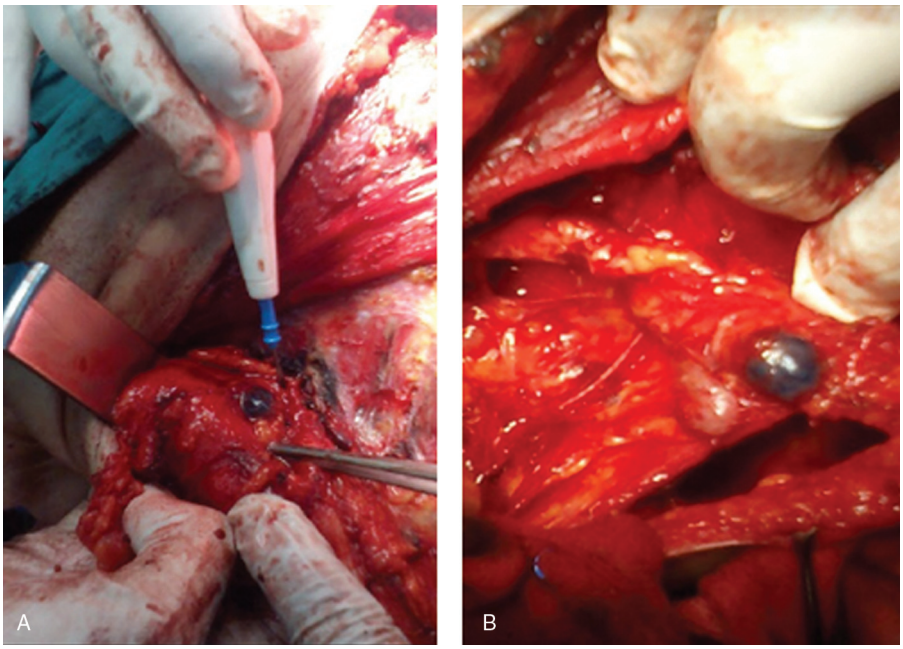
The age of the 50 female patients included in the study ranged between 30 and 70 years, with a mean age of 45.7±1.0 years. A total of 13 (26%) patients were between the age of 30 and 40 years. Patients between the ages of 41 and 50 years represented the highest percentage with 18 (36%) cases, followed by patients between the age of 51 and 60 years, with 12 (24%) cases, and finally, those older than 60 years, with seven (14%) cases (Table 1 and Fig. 4).

Figure 1



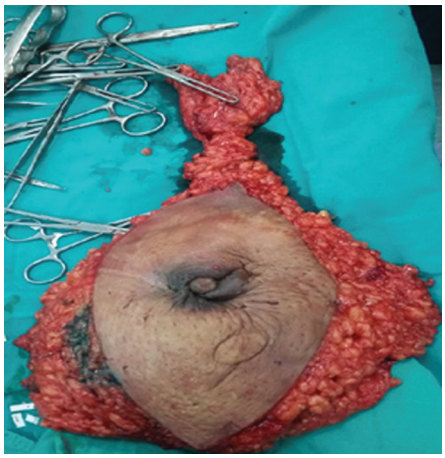
Injection of methylene blue dye in the subareolar region.

Figure 2



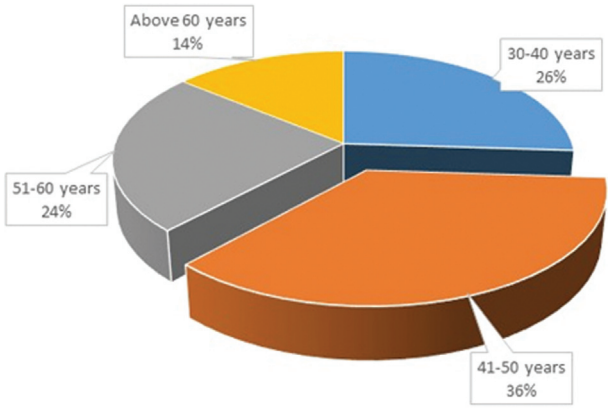
(a,b) Identification and dissection of sentinel lymph node in the axilla stained with methylene blue dye.

Figure 3



Modified radical mastectomy specimen together with remaining axillary specimen after dissection of sentinel lymph node.

Figure 4



Age of the study group.

Table 1 Age of the study group

Age groups	*n* (%)
30–40 years	13 (26)
41–50 years	18 (36)
51–60 years	12 (24)
>60 years	7 (14)

Table 2 Stage of tumor among the study group

Size of the tumor	*n* (%)
<2 cm (stage I) (T1, N0, M0)	3 (6)
>2–4 cm (stage IIA) (T2, N0, M0)	38 (76)
>4–5.5 cm (stage IIB) (T3, N0, M0)	9 (18)

Size and stage of the tumor

In our study, the size of the tumor ranged between 1.5 and 5.5 cm, with a mean size of 3.4 cm. A total of 38 (76%) patients had tumor size ranging from 2 to 4 cm (T2N0M0) and nine (18%) patients had tumor size ranging from 4 to 5.5 cm (T3N0M0), and finally, three (6%) patients presented with tumor less than 2 cm (T1N0M0). None of the patients had palpable axillary lymph nodes or distant metastasis (Table 2 and Fig. 5).

Site of the tumor

The outer upper quadrant was the most common site in 29 (58%) patients, the lower outer quadrant was involved in 14 (28%) patients, the upper inner quadrant in five (10%) patients, and central lesion in

two (4%) patients (Table 3). A total of 30 (60%) patients presented with left-sided breast cancer, and the rest (20 patients) presented with right-sided breast cancer (40%) (Fig. 6).

Detection of sentinel lymph node(s)

The detected SLNs were identified in 44 (88%) of 50 patients. The number of SLNs was as follows: one lymph node detected in 16 (32%) patients, two lymph nodes in 19 (38%) patients, and three lymph nodes in nine (18%) patients (Table 4).

In 47 (94%) patients, SLN biopsies were found in level I alone, and in three (6%) patients, SLN biopsies were found in both levels I and II.

Comparison between axillary and sentinel lymph nodes

When status of axillary lymph node was compared with SLNs, the result was as follow: 36 (81.8%) of the 44 patients with identified SLN showed negative result for metastasis. In this group, we found that none of them showed axillary metastasis.

In eight (18.2%) of the 44 SLNs cases, metastasis was found in the nodes. Of these eight cases, two (25%) cases contained metastasis in the remainder axillary lymph nodes whereas in the other six (75%) cases, the results of the axillary lymph nodes were negative (Table 5).

Table 3 Site of the tumor among the study group

Site of the tumor	*n* (%)
Outer upper quadrant	29 (58)
Outer lower quadrant	14 (28)
Inner upper quadrant	5 (10)
Central lesion	2 (4)

Table 4 Sentinel lymph nodes detected among the study group

Sentinel LN	*n* (%)
1	16 (32)
2	19 (38)
3	9 (18)
Negative	6 (12)

The relation between axillary and SLNs is statistically significant (Fig. 7).

Result of lymph node localization

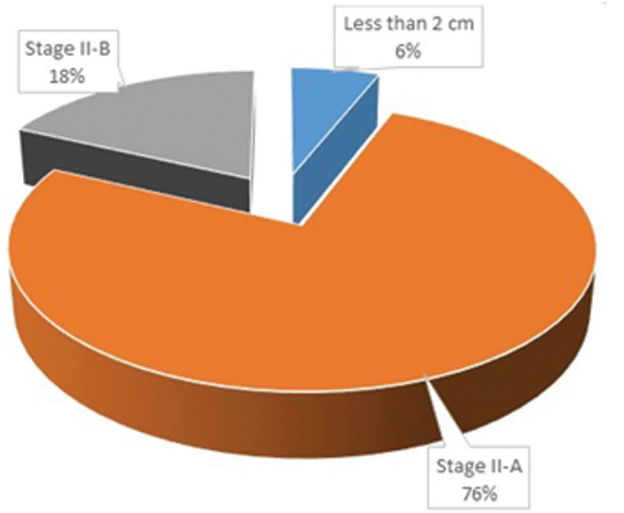
The identification rate for lymph node localization was 44/50 (88%).

Failure rate of the technique was 6/50 (12%).

Sensitivity statistics

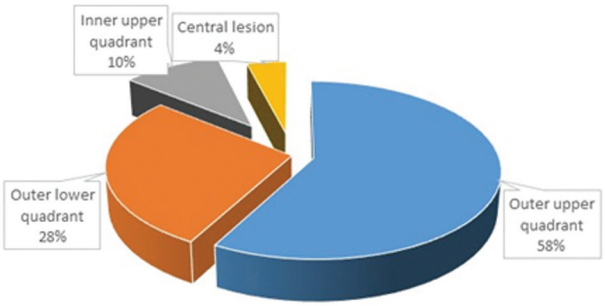
The number of true-positive cases (positive sentinel and positive axillary) was 2.

Figure 5



Stage of tumor among the study group.

Figure 6



Site of the tumor among the study group.

Table 5 Axillary and sentinel lymph node metastasis

Sentinel LN	Axillary metastasis [*n* (%)]	No axillary metastasis [*n* (%)]	χ^2	*P* value
Present sentinel LN				
Positive metastasis	2 (25)	6 (75)	11.44	0.003 (S)
Negative metastasis	0	36 (100)		
Absent sentinel LN	0	8 (100)		

The number of true-negative cases (negative sentinel and negative axillary) was 36.
The number of false-positive cases (positive sentinel and negative axillary) was 6.
The number of false-negative cases (negative sentinel and positive axillary) was 0.
Sensitivity=2/(2+0)=100%.
Specificity=36/(36+6)=85.7%.
Positive predictive value=2/(2+6)=25%.
Negative predictive value=36/(36+0)=100%.
Accuracy=(sensitivity+specifitiy)/2=92.9%.

Operation done for the patients

Overall, 16 (32%) patients underwent MRM, whereas 34 (68%) underwent wide local excision.

Histological type

Histological type showed that 47 (94%) patients had invasive ductal carcinoma, whereas three (6%) patients had invasive lobular carcinoma.

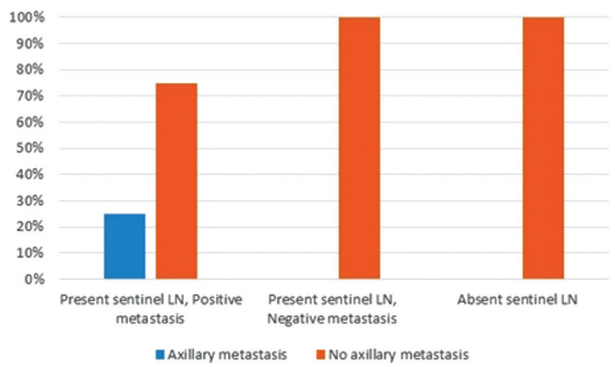
Postoperative morbidity

Postoperative morbidity results showed that three (6%) patients developed seroma, one (2%) patient developed hematoma, and one (2%) patient developed infection and necrosis. The remaining 45 (90%) patients had no postoperative complications. No complications related to the use of the dye, such as cutaneous and urine staining or allergic reactions, occurred in any of our patients (Table 6).

Discussion

Management and staging of breast cancer according to axillary nodal status has been the subject of intense debate and controversy [16]. The study of NSABP B-04, which randomized patients with clinically uninvolved axillary nodes to radical mastectomy, total mastectomy plus radiotherapy, or total mastectomy alone, demonstrated that axillary treatment with either dissection or regional radiotherapy reduced axillary recurrence rates from 18.6 to 1–2%. However, there was no benefit to axillary treatment in terms of distant disease-free survival [16,17].

Figure 7



Axillary and sentinel lymph node metastasis.

Sentinel lymph node dissection (SLND) alone is widely accepted as an axillary management for women with clinically node-negative breast cancer. SLND makes axillary procedure more conservative, less morbid, and improves the quality of life, with reduction in pain, lymphedema, and shoulder stiffness [18].

In this study, we conducted a validation study on the accuracy of SLND using methylene blue dye technique alone in patients with nodal negative breast cancer, using a simple, available, and cheap technique.

In our study, we did not expose our patients to oncological risk because we completed ALND after detection of SLN.

In this study, we excluded patients who received neoadjuvant chemotherapy because this produces an inflammatory response and fibrosis. Therefore, it is not surprising that identification and dissection of sentinel nodes is a more difficult procedure after neoadjuvant chemotherapy [19], and the sentinel lymph node biopsy identification rate is too low for routine use, and that the false-negative rate is also too high [20].

By contrast, there are those who believe that the advantages to the patient in reducing an unnecessary axillary clearance is such that SLNB has a definite role after neoadjuvant chemotherapy [21].

Moreover, we excluded node-positive patients (clinically and radiologically) because positive nodes may be blocked, and it prohibits accurate mapping leading to a false-negative result. This agrees with the studies performed by Lyman *et al.* [22] and Hoar and Stonelake [23].

In contrast, some authors report that clinically positive axilla is subject to false-positive result, so SLNB deserves wider consideration as an alternative to ALND in clinically positive patients [24,25].

Table 6 Postoperative morbidity

Postoperative	*n* (%)
Seroma	3 (6)
Hematoma	1 (2)
Infection and necrosis	1 (2)
None	45 (90)

Inflammatory breast cancer was also excluded. The false-negative rate for patients with inflammatory breast cancer is unacceptably high, hence SLNB is not recommended in such situation until more data are available [26].

Pregnant women with breast cancer were excluded because vital dyes should not be administered to pregnant women [26].

In our study, we excluded male breast cancer cases because of the rarity and no sufficient previous studies about drawback of SLNB in breast cancer in men. However, there are studies that encourage SLNB in men [27].

In our study, we found that among the series of 50 patients, the number of patients between ages of 30 and 40 years was 13 (26%), the number of patients between age of 41–50 years – which was the highest – was 18 (36%), the number of patients between the age of 51–60 years was 12 (24%), and finally, the number of patients older than 60 years was seven (14%). This was a similar figure to the study performed by Mahadevan *et al*. [28], where the highest number of breast cancer cases fell in the age group of 41–50 years (33.1%), followed by 31–40 years (27.8%) and 51–60 years (20.4%).

In our study, 38 (76%) patients were staged as IIA (T2 N0 M0) with a tumor size of 2–4 cm, and nine (18%) patients as stage IIB (T3 N0 M0) with a tumor size of 4–5.5 cm, and finally three (6%) patients as stage I (T1 N0 M0) with a tumor size less than 2 cm. This pattern coincides with the pattern in the study by Ravichandran *et al.* [29] where 151 patients had stage I, 315 patients had stage II, and excluded patients with higher stages of breast cancer.

We found that the outer upper quadrant was the most common site in 29 (58%) patients, the lower outer quadrant in 14 (28%) patients, the upper inner quadrant in five (10%) patients, and central lesion in two (4%) patients. A total of 30 patients presented with left-sided breast cancer (60%), and the rest (20 patients) presented with right-sided breast cancer (40%).

Moreover, Wilting and Hagedorn reported in their study that left-oriented breast cancer (especially upper outer quadrant) showed 45.8% positivity, having a 10% lead over the right orientation, and this was in consonance with the report by Tulinius and colleagues. Wilting and Hagedorn showed that the left side of the body is prone to carcinomas, especially breast cancer (5–10%) [30,31].

Regarding the site of the dye injection, we favored the subareolar injection, as it can access the subareolar lymphatic plexus of Sappey, drainage is independent of tumor size, requires less amount of the dye, and increases identification rate as compared with other methods of injection as demonstrated by McMasters *et al.* [32], D'Eredita *et al.* [33], and Povoski *et al.* [34].

In our study, SLNs were identified in 44 (88%) patients. The number of SLNs was as follows: one lymph node detected in 16 (32%) patients, two lymph nodes in 19 (38%) patients, and three lymph nodes in nine (18%) patients. The mean number of identified lymph nodes in our study was 1.6, and this finding matched with other studies such as Montumora *et al*. [35], Cox *et al*. [36], and Padmanabh *et al*. [37], where the mean number of identified lymph nodes was 1.8, 1.9, and 1.6, respectively.

In 47 (94%) patients, SLN biopsies were found in level I alone, and in three (6%) patients, SLN biopsies were found in both levels I and II. This matches with SLN report by Arima *et al*. [38], who postulated that axillary nodes with breast cancer have a relatively low rate of involvement of level II or level III nodes in the absence of involved level I nodes (called skip metastases), and there is a 2–4% rate of skip metastases above axillary levels I and II.

In our study, we did not find skip metastasis mostly owing to small number of patients (50) and detected SLN in 39 patients. This matches with an Indian study done by Padmanabh *et al*. [37], in which the number of patients was 35.

Overall, 34 (68%) of our patients underwent WLE and ALND, whereas 16 (32%) underwent modified radical mastectomy. Most patients underwent MRM upon their wishes, and two patients had multicentric lesions and two patients showed multiple positive margins after WLE.

Time needed for WLE ranged from 65 to 90 min, including frozen section of the mass and SLN examinations. On the contrary, time needed for MRM ranged from 60 to 105 min.

Drains after surgery were left for 48–72 h for observation of reactionary hemorrhage. The mean

amount of seroma in the first day was 250 cm^3, second day was 150 cm^3, and third day was 50 cm^3.

Postoperative morbidity showed that three (6%) patients developed seroma. These patients were treated conservatively by continuous aspiration under US guidance and coverage of antibiotics. Seroma subsided in 10–15 days. Moreover, one (2%) patient developed hematoma. This patient was treated conservatively, and hematoma subsided within 13 days. Another patient (2%) developed infection and necrosis. This patient underwent debridement of necrotic tissue after 1 week of conservative management, and the wound healed within 10 days. The remaining 45 (90%) patients had no postoperative complications.

The technique of SLNB, as any surgical manoeuver, is not devoid of complications related to technique as mentioned before or complications related to dye such as cutaneous staining, staining of urine, and allergic reaction, which was not reported in any case in our study.

Histological examination showed that 47 (94%) patients had invasive ductal carcinoma, whereas three (6%) patients had invasive lobular carcinoma. This was in agreement with Vahdaninia and Montazeri [40] who found that more than three-quarters (77.5%) of patients were diagnosed with ductal carcinoma and 41.7% of tumors were moderately and well-differentiated.

When we compared status of axillary lymph node with SLNs, the result was as follow: 36 (81.8%) patients of the 44 patients with identified SLN were negative for metastasis, and none of them showed axillary metastasis. In the rest of eight (18.2%) cases, metastasis was found. Of these eight cases, two cases contained metastasis in the remainder axillary lymph nodes (25%) whereas in the other six cases, the axillary lymph nodes were negative (75%). Moreover, Fraile *et al*. [41] reported that 1–15% of patients with negative SLNB had nodal metastasis in the same region, and the false-negative rate of SLNB has improved over time and is probably under 5% now in most experienced group [42].

In our study, SLNs were not identified in six cases, with a failure rate of 12%. This failure corresponded to many factors as following:

First, there is a well-documented learning curve of operator to SLNB. Successful identification of SLNB is directly related to surgeon experience [19]. In this study, we cannot identify 5/6 in the first 25 cases with percentage of 83.3% of failed cases. To decrease the failure rate that related to learning curve, we should take into consideration the multidisciplinary approach between the surgeon, the radiologist, the pathologist, and nursing acquiring the knowledge and skills to enable successful technique. In UK, a structured training programme called NEW START has been developed to standardize technique. This programme includes training of surgeon on five cases followed by performing a series of 25 cases of SLNB and immediate ALND. The aim is to identify SLNB with high rate and more importantly a low false-negative rate [19]. The American Society of Breast Surgeons [43] recommends that surgeons must perform at least 20 SLNB procedures before doing it therapeutically.Second cause is a metastatic lymph node causing a blockage to the lymphatic flow, which was found in four (66.6%) of six cases. To avoid this, careful palpation and an efficient ultrasonic examination should be provided [44].

Third cause is the age of the cases. We found that all six cases were older than 55 years [39].

The technique of SLNB can be applied in most of Egyptian hospitals that could not provide the supplies for SLNB mapping using Tc99m dye and gamma camera as a safe, cheap, reliable, and cost-effectiveness technique.

In our study, SLN was identified in 44 cases using methylene blue dye. The identification rate was 88%. None of the patients had negative SLN but had positive axillary lymph nodes (false negative), and in six cases SLN were involved only but not the rest of the axilla (false positive). The sensitivity, specificity, positive predictive value, and negative predictive value were 100, 85.7, 25, and 100%, respectively, and the overall efficacy was 92.9%.

These results should be compared with the study done by Mukherr and colleagues in 2014, where the identification rate was 88.9%. The sensitivity, specificity, positive predictive value, negative predictive value, and efficacy were 81.8, 100, 100,86, and 90.9%, respectively [45].

Our results are also comparable with the study performed by Chintamani *et al.* [46] where SLN identification rate was 100%, the sensitivity of SLNB was 86.6%, and the accuracy was 93.3%.

Our results showed that the technique of SLNB using methylene blue dye alone is reliable to detect the state of axillary lymph node, so we can avoid an unnecessary lymph node dissection in nodal negative breast cancer and its associated complications.

The technique of SLNB preserves a functioning limb, especially in developing countries as Egypt, where the women in rural area do their work manually.

Conclusion and recommendations

SLNB using methylene blue dye is a suitable, cheap, safe, and accurate technique in staging of the axilla and an alternative to in early stages of breast cancer. Moreover, it is associated with less morbidity.

Our breast surgeons should be trained on this simple technique to achieve high accuracy and lower false negative rate, and our institutes involved in breast cancer surgery should encourage this method because of its advantages regarding safety, feasibility, and economic advantages.

There are still many unanswered questions about SLND that should be answered in on-going trials.

(1) The first one is accuracy of SLNB in large and multifocal tumors.
(2) The second one is accuracy of SLNB after neoadjuvant chemotherapy.
(3) Role of SLNB in nodal positive patients.
(4) Overall disease-free survival.
(5) Role of SLNB in recurrent breast cancer and in male patients.

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Conflicts of interest
None declared.

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Donut mammoplasty in management of gynecomastia: general surgeon experience

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Background
Gynecomastia is benign enlargement of the male breast. Although treatment is not indicated in most cases, esthetic reconstructive surgery is commonly performed for psychological reasons. This clinical study discusses the outcomes of the surgical management of gynecomastia by subcutaneous mastectomy using the donut mastopexy technique in different grades of gynecomastia and assesses the morbidity and complication rates associated with the procedure.
Materials and methods
From January 2013 till January 2017, we operated on 20 patients with bilateral idiopathic grades 1, 2, and 3 gynecomastia by subcutaneous mastectomy using the donut mastopexy technique. Exposure was excellent with the circumareolar incision. Patients were followed for at least 6 months.
Results
Excised specimens were weighed and sent for histopathological examination. The mean weight of the resected specimen was 92±44 g (range: 38–280 g). One patient showed bilateral atypical hyperplasia on histopathological examination. All patients achieved good esthetic contour of the chest. Circumareolar scars were satisfactory for all patients. No wound infection, hematoma, seroma formation, or nipple–areola complex necrosis was seen in any of the patients Areolar sensation was diminished in one (5%) patient and recovered within 6 months postoperatively. The main disadvantage of the technique was the mild residual skin redundancy, which was noted in eight patients with grade 3 gynecomastia.
Conclusion
Donut mastopexy technique is indicated for grades 1, 2, and 3 gynecomastia. Circumareolar incision provides perfect exposure. It is considered to be less invasive, has minimal scarring, has low complication rates, and had good esthetic outcome. Moreover, it is oncologically safe through histopathological examination of excised specimens to discover pathological abnormalities and hidden malignancy.

Keywords:
circumareolar incision, donut mammoplasty, gynecomastia

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Introduction

Gynecomastia is a physiologic or pathological enlargement of the male breast [1]. Physiologic gynecomastia has three distinct age peaks. The first peak is within the first few weeks of neonatal life. The second occurs during puberty and the final peak is in older adulthood, usually after the age of 50 years [2]. Gynecomastia may be seen in 40–65% of adult males [3].

Pathologic gynecomastia can occur at any time when an imbalance develops in the androgen–estrogen plasma levels. This may be attributable to increased estrogen, decreased androgen, receptor defects, or an altered sensitivity of the breast to estrogen [4]. However, in most cases of gynecomastia, a cause cannot be identified, and the problem usually is idiopathic [5,6].

Careful evaluation of the affected patient still is essential before it is assumed that the gynecomastia is idiopathic and benign. A detailed history, thorough physical examination, and laboratory assessment should be performed to rule out any drug administration, neoplasm, urologic disorder, hormonal imbalance, liver disease, or malnutrition [7]. Gynecomastia does not require specific therapy except for the rare cases with disabling pain and tenderness [8]. Most patients request treatment for psychological reasons. The goal in treating these patients is resection of the abnormal tissue that restores the normal male

breast contour and minimizes scarring or residual deformity of the breast and nipple–areola complex [8,9].

Regarding surgery, no single technique is appropriate for all grades of gynecomastia [10] Several classifications are used for gynecomastia to define the choice of surgical technique [8,9,11,12]. Among these, Simon's classification, based on breast size and degree of skin redundancy, is commonly used. This classification divides gynecomastia into three grades: grade 1 (small enlargement, no skin excess), grade 2A (moderate enlargement, no skin excess), grade 2B (moderate enlargement with extra skin), and grade 3 (marked enlargement with extra skin) [9].

Surgery is planned depending on the grade and histopathology of gynecomastia. Webster's intra-areolar incision, periareolar or circumareolar incisions, Letterman's technique, and suction-assisted lipectomy are commonly used in the treatment of grades 1 and 2A gynecomastia [7,8,11]. Superiorly or inferiorly based pedicle areolar flaps and free nipple techniques are preferred for grades 2B and 3 gynecomastia [8].

The circumareolar donut approach is a relatively new technique that provides excellent exposure and postoperative scars in the treatment of grades 1 and 2 gynecomastia [13].

This study extends the role of the circumareolar donut approach in management of all grades of the gynecomastia including grade 3 and the clinical results of the technique.

Materials and methods

Between January 2013 and January 2017, we performed subcutaneous mastectomy using the donut mastopexy approach on 20 patients with gynecomastia. The mean patient age was 28.9±14 years (range: 22–75 years). The psychological embarrassment about feminine appearance was the major indication for surgery in 18 (90%) patients and tenderness in two (10%) patients.

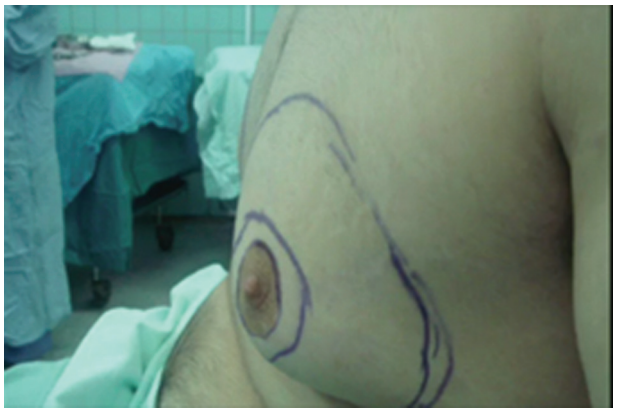
Two patients had grade 1 gynecomastia, four had grade 2A gynecomastia, six had grade 2B gynecomastia, and eight had grade 3 gynecomastia according to Simon's criteria. Lesions were bilateral in all patients. All the patients received a diagnosis of idiopathic gynecomastia after detailed history, physical examination, and laboratory evaluation. A detailed informed consent was signed by all of the patients.

Operations were performed under general anesthesia in all patients. Patients were followed up for at least 6 months.

Surgical technique

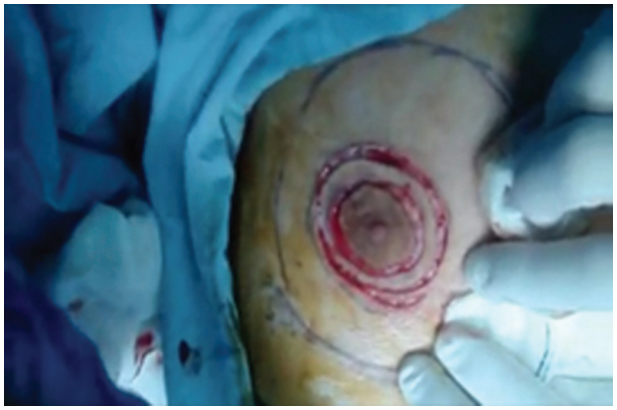
Preoperative markings were made with the patient in a upright position. First, the midsternal line and the breast mold to be excised were marked. The circumareolar incision at the junction of the areola and skin was marked 4 cm in diameter, including the nipple and areola complex, and a second concentric circle (or even eccentric if the areola needs a lift) is marked outside the circumference of the original areola (width of 1–2 cm). Their medial limit is 10–12 cm from the midsternal line (Fig. 1). Circumareolar skin incisions were made (Fig. 2). The ring of skin between them is de-epithelialized, leaving intact dermis and hence the dermal vascular plexus to nourish the nipple and areola (Fig. 3). A hemicircumferential incision from 3 to 9 o'clock position is made along the outer edge of the de-epithelialized ring, through dermis and subcutaneous

Figure 1



Preoperative marking.

Figure 2



Incision of two concentric circles.

tissue, to gain access to the breast (Fig. 4). The breast tissue is dissected and freed from the pectoral fascia. An adequate thickness under the nipple was left to avoid areolar retraction or ischemia. Removing proper amount from each side was done to obtain symmetricity. No breast tissue was left over the prepectoral surface. A suction drain was brought out through the anterior axillary line incision and a purse–string suture (Fig. 5) to the outer dermal circle adjusted to 4-cm areolar diameter with 3/0 polydioxanone (PDS) and skin closure by 4/0 Monocryl subcuticular sutures were done. A light dressing was applied postoperatively.

Results

Excised specimens were weighed and sent for histopathological examination. The mean weight of the resected specimen was 92±44 g (range: 38–280 g). One patient showed bilateral atypical hyperplasia on histopathological examination.

The method described yields excellent shape, symmetry, and minimal unapparent scars. Areolar sensation was diminished in one (5%) patient and recovered within 6 months postoperatively. Good chest contour was achieved, and good patient satisfaction rate were noted in all patients (Figs 6–8).

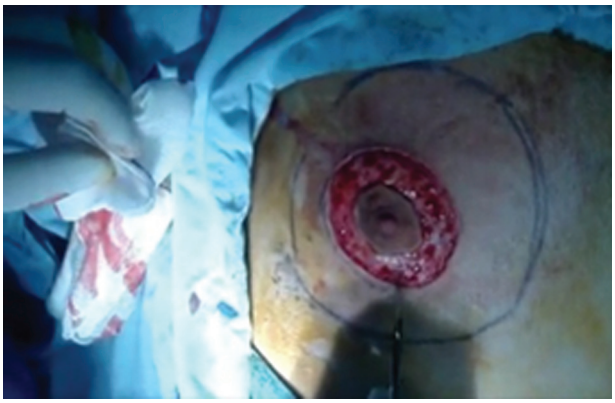
There were no major complications such as infection, hematoma, seroma, or nipple–areola complex necrosis. The main disadvantage of the technique was the mild residual skin redundancy, which was noted in eight patients with grade 3 gynecomastia. This redundancy, however, was never severe enough to require a secondary procedure and improved after 6 months of follow-up. Moreover, all patients were satisfied with the final result.

Discussion

Various incisions and techniques have been described for the treatment of gynecomastia. Among these, Webster's intra-areolar, periareolar, and circumareolar incisions are the most commonly applied.

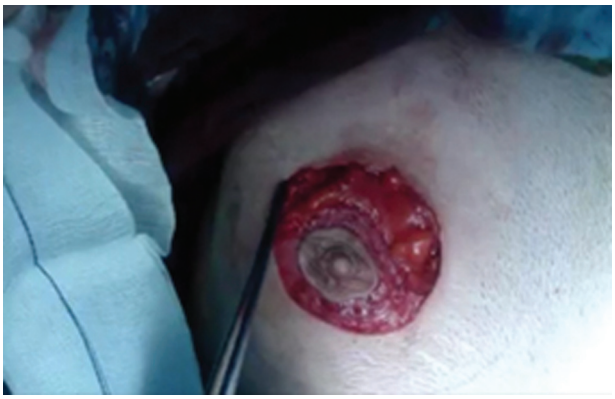
The donut mastopexy using the circumareolar incision is a relatively new technique [8]. It provides excellent results not only for grades 1 and 2 cases but also for

Figure 3



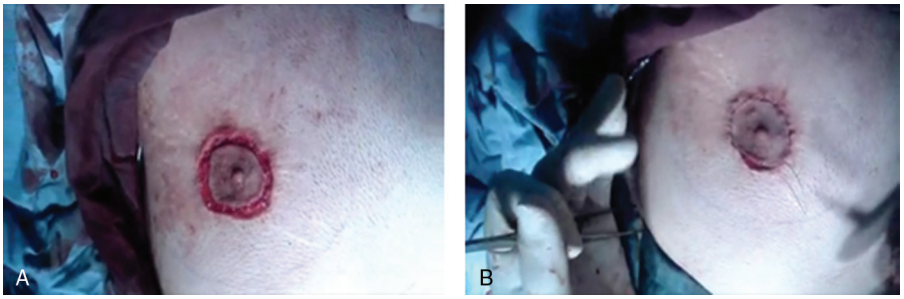
Donut de-epithelialization.

Figure 4



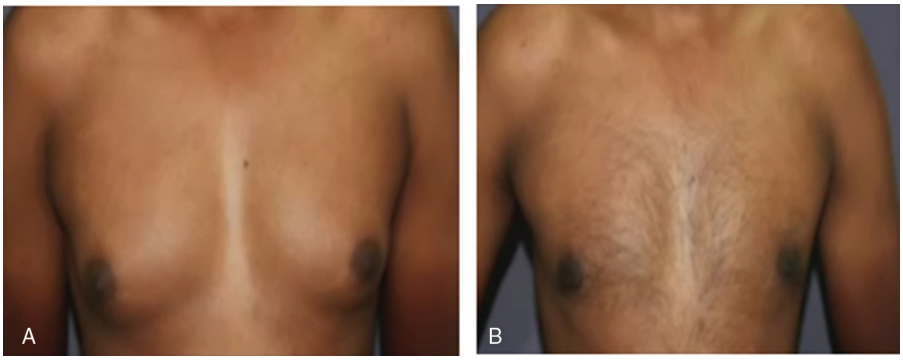
Access for resection.

Figure 5



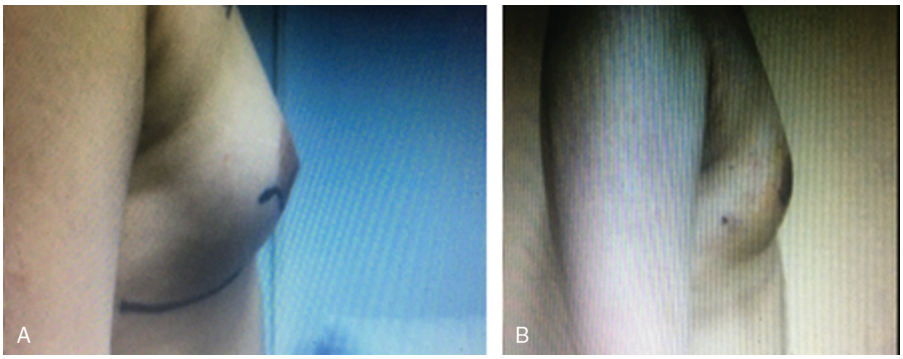
Wound closure through a purse–string and subcuticular fashion.

Figure 6



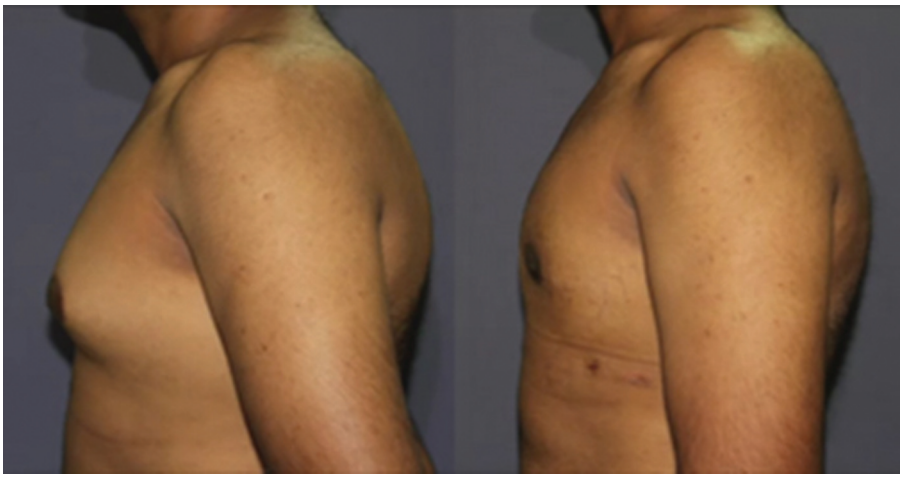
(a) Preoperative view and (b) postoperative view after 6 months.

Figure 7



(a) Preoperative view and (b) postoperative view after 6 months.

Figure 8



(a) Preoperative view and (b) postoperative view after 6 months.

grade 2B gynecomastia because the technique allows skin excision and areola reduction [13,14].

In our study, we extended the role of donut mastopexy technique to include patients with grade 3 gynecomastia with severe skin redundancy and the need for areolar lift.

Surgical exposure with the circumareolar incision is excellent, and the risk for postoperative hematoma formation is minimal. It should be noted that in cases with redundant skin, simultaneous medialization and cranialization of the nipple–areola complex completing the semicircular incision to a periareolar de-epthelialization were useful.

This is comparable with study by Aslan *et al.* [15] who suggested a modified surgical access that uses a W-shaped periareolar–transareolar–perithelial incision to provide wide exposure of the resection area and to facilitate nipple–areolar reduction in advanced stages.

En bloc resection of the breast tissue through avascular planes offers several advantages, such as the perioperative blood loss is minimal; hemostasis is easy; and the risk for leaving residual breast tissue, which may lead to a persistent gynecomastic appearance, is less.

The major concern with the exclusive use of liposuction is the lack of histopathological analysis of the resected tissue. Even though it is technically possible to submit tissue pieces from liposuction to a histopathological analysis [16], this has been performed only rarely, and the results are difficult to interpret owing to tissue damage and consistency.

The histopathologic finding in the present study was one patient with bilateral atypical ductal hyperplasia, which is accompanied by increased rate of associated neoplasia [17]. Bilateral atypical ductal hyperplasia in gynecomastia specimens has been described by other authors [18]. Nevertheless, it is important to emphasize that there is no convincing evidence linking gynecomastia with increased incidence of male breast cancer [19].

In contrast to gynecomastia, breast cancer in men has a peak at 71 years, and it usually presents as a painless lump or nipple retraction [19]. However, this does not eliminate the need for a histological examination of the resected tissue [20–23]. Voulliaume *et al.* [20] report a case in which a patient received liposuction for 'gynecomastia', which later proved to be established case of male breast cancer. They point out the problem of dissemination of malignant cells into healthy tissue during the liposuction procedure [20]. Other authors have also described that breast enlargement in young men is not always benign gynecomastia: malignant tumors such as breast carcinoma may be present in the midst of florid gynecomastia, even in a young patient [21]. DeBree *et al.* [22] describe a 22-year-old man initially diagnosed with unilateral gynecomastia, in which histological analysis revealed an invasive ductal carcinoma of the breast. In a recent publication, Staerkle *et al.* [23] report on synchronous bilateral ductal carcinoma *in situ* in a young man presenting with bilateral gynecomastia. Wadie *et al.* [24] describe a case of a 16-year-old boy with bilateral gynecomastia, in which the histological workup revealed a ductal carcinoma *in situ*.

These data emphasize the need for a histological analysis because gynecomastia may be harboring a neoplasia. Liposuction as an exclusive procedure should be limited to cases of pure pseudogynecomastia, in which preoperative assessment shows the presence of an isolated lipohypertrophy with no sign of glandular enlargement.

In our study, no wound infection, hematoma, seroma formation, or nipple–areola complex necrosis was seen in any of the patients. Areolar sensation was diminished in one (5%) patient and recovered within 6 months postoperatively. The main disadvantage of the technique was the mild residual skin redundancy, which was noted in eight patients with grade 3 gynecomastia. This redundancy, however, was never severe enough to require a secondary procedure and improved after 6 months of follow-up. All patients were satisfied with the final result.Numerous techniques to treat grade III gynecomastia have been described. Rai [25] recommends two stages for postweight problems with significant ptosis, whereas Ward and Khalid [10] technique ends with a periareolar scar and transverse medial and lateral extension. Presented study reveals lower complication rate than Courtiss [26] who reviewed 101 patients who underwent subcutaneous mastectomy for gynecomastia.

Our results should also be comparable with the series by Steele *et al.* [27] in 2002, where the most frequent complication of subcutaneous mastectomy was postoperative bleeding and hematoma or seroma formation. This finding is consistent with the results of other series that have described an overall complication rate of up to 28% in all patients [27,28].

Conclusion

The subcutaneous mastectomy using donut mastopexy technique is indicated for grades 1, 2, and 3 gynecomastia. Circumareolar incision provides perfect exposure. It is considered to be less invasive, produces minimal scarring with a low complication rates, and shows good esthetic outcome. It also could be considered oncologically safe through histopathological examination of excised specimens to discover pathological abnormalities and hidden malignancy.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Laparoscopic cholecystectomy for management of acute calculous cholecystitis within and after 3 days of symptom beginning: a retrospective study

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Objective
The aim of this study was to evaluate the competency and safety of surgical management of acute calculous cholecystitis (ACC) through laparoscopic cholecystectomy (LC) within and after 72 h of symptom onset. We are reviewing our experience by comparing the outcomes of both ways to carry out an ideal therapeutic strategy used for ACC.

Background
ACC is a very frequent surgical insult. The timing of surgery in the management of such condition is a subject of controversy among all surgeons. In this study, we tried to share in solving this conflict to implement the optimal timing of LC for ACC.

Patients and methods
The study includes 100 patients with ACC, divided according to the timing of LC into group E (50 patients), operated within 72 h of symptom onset and group L (50 patients), operated beyond 72 h of symptom onset. Patients in both groups monitored since admission, during operations, and along the postoperative (PO) period. The data collected include demographic data, clinical data, duration of symptoms before surgery, coexisting disease, laboratory and image results, operative data, PO complications, the length of stay in ICU and the total length of hospitalization.

Results
Fever and Murphy's sign were significantly greater in the early LC group. Initial total bilirubin and blood urea nitrogen are significantly higher (P=0.032 and 0.004, respectively) among the late LC group. The operative time and mean total hospital stay are significantly higher (P=0.005 and 0.010, respectively) in the late LC group compared with the early LC group. The rates of PO bile leakage and port-site infections were higher among patients of late LC group.

Conclusion
Emergent LC is a safe and reliable procedure for ACC within 72 h of symptom onset. Regarding the PO outcomes, financial costs and length of hospital stay, it is more helpful than LC beyond 72 h.

Keywords:
acute calculous cholecystitis, early laparoscopic cholecystectomy, laparoscopic cholecystectomy, late laparoscopic cholecystectomy

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Introduction

Gallstone disease has a prevalence stuck between 10 and 15%, and around 35% of patients develop problems or frequent symptoms in their life [1]. In 20% of cholelithiasis patients, acute calculous cholecystitis (ACC) occur with a wide discrepancy in severity [2]. Despite the high frequency of ACC, still, there is a significant controversy regarding its diagnosis and management [2]. Conservative treatment for ACC was followed by delayed cholecystectomy associated with numerous events [3]. About 20–26% of patients does not respond to medical treatment or develop prompt complications throughout the first admission and necessitate a pressing and technically challenging cholecystectomy [4]. If patients discharged home without operation after ACC, 15–30% were readmitted with recurrent manifestations and underwent an unplanned emergency cholecystectomy; the possibility of gallstone-related events include biliary colic in 70%, biliary tract obstruction occurs in 24%, and pancreatitis in 6% (4). At the times of delayed operation, dense fibrotic adhesions at Calot's triangle make interval laparoscopic cholecystectomy (LC) enormously difficult and risky [5].

According to Tokyo Guidelines 2013 (TG13), stated by the Japanese Society of Hepato-Biliary-Pancreatic

Surgery, the ideal management for ACC is early LC, mainly before 72 h of the symptom onset [6]. Conversely, surgical management for AC after 72 h of onset of symptoms is debatable. Due to the greater operative difficulty for delayed AC, surgery has been advised in an elective setting after 6–8 weeks or more; otherwise, LC can be performed carefully by a professional laparoscopic team [7]. A recent study has shown that emergent LC should be the first choice therapy for AC in patients who are fit for operative intervention; however, there are no report about the time of symptom onset [3]. Till now, few studies have compared the outcomes of LC implemented within and after 72 h of symptom onset [8]. In our present study, we try to evaluate the surgical outcomes of LC for ACC within and after 72 h of symptom onset.

Patients and methods

The current study completed at the General Surgery Department, Banha University Hospital in Egypt and King Saud Hospital in Saudi Arabia since January 2015 till May 2017. The present study includes 100 patients with ACC. After approval of the study protocol by the ethics committee and fully informed written patients' consent was obtained for participation in the study. Patients hospitalized through the emergency unit to the General Surgery Department, High-Dependency Unit or ICU according to the seriousness of patients' general condition at the time of admission.

Patients were admitted for clinical, laboratory, and radiological evaluation. Patients were examined generally besides local abdominal examination. Laboratory tests such as complete blood count, C-reactive protein, blood sugar, kidney function tests, liver enzymes, total and direct bilirubin, alkaline phosphatase and serum amylase were done. Diagnostic imaging was done by means of abdominal ultrasonography and/or computed tomography scans. Magnetic resonance cholangiopancreatography (MRCP) was carried out in selected cases to exclude common bile duct (CBD) stones subsequent to diagnosing ACC.

Preoperative endoscopic retrograde cholangio-pancreatography (ERCP) was done in two patients in group E and five patients in group L due to CBD stone and/or dilatation as revealed by preoperative MRCP. During ERCP, sphincterotomy was done, ballooning of CBD, stone/s extracted, washing of CBD, then leaves a stent for 3 months. In both groups, LC was implemented 1 or 2 days following ERCP.

Diagnosis of AC built on the occurrence of no less than two of the subsequent criteria: an acute pain in the upper abdomen besides the Murphy's sign, high core body temperature (>37.5°C) besides white blood cells (WBC) count more than 10×10^9/l and ultrasonography findings of gallstones as well as thick gallbladder (GB) wall (>4 mm), pericholecystic fluid and positive Murphy's sign on ultrasound probe.

Exclusion criteria in our present study were: patients with no gallstones, former upper abdominal operations, patients who underwent open cholecystectomy, age less than 18 years and more than 70 years, American Society of Anesthesiology (ASA) score more than IV, BMI greater than 35 kg/m^2, low-performance status, participation in an additional drug or device study and inability to offer informed consent. Also, we excluded patients with GB perforation or Mirizzi syndrome (preferred to do open cholecystectomy), patients with GB tumors or cholangitis (typically, to be managed conservatively first) and patients without complete data.

According to TG13 [9], the severity assessment of ACC graded, grade I (mild): AC with mild gallbladder (GB) inflammation with no organ dysfunction in a healthy patient; grade II (moderate): AC with one of the subsequent disorders: WBC count more than 18×10^9/l, tender mass in the right hypochondrium, onset of symptoms more than 72 h, biliary peritonitis, pericholecystic abscess, liver abscess, gangrenous GB or emphysematous GB; and grade III (severe): AC associated with dysfunctions in one of the subsequent systems/organs: neurological deterioration (diminished level of consciousness), cardiovascular impairment (hypotension necessitating dopamine 5 μg/kg/m or any dose of dobutamine); renal impairment (creatinine >2.0 mg/dl, oliguria), respiratory failure (PaO_2/FiO_2 ratio <300), bone marrow dysfunction (platelet count $<100\times10^9$/l), and hepatic function deterioration (international normalized ratio>1.5).

Preoperative assessment and preparation

On admission, all patients received intravenous broad-spectrum antibiotic as soon as the diagnosis of ACC was established. When clinically indicated, a urinary catheter and nasogastric tube were inserted. Our surgical unit's attitudes and practice of timing for cholecystectomy for patients suffering from the ACC was somewhat variable, some units tend to perform LC routinely within 72 h of symptom onset (hospital admission) unless there was a

contraindication for surgery, whereas other units tend to manage ACC conservatively and an appointment given to patients for interval LC within 6–8 weeks after discharge. In the later units, early LC is basically done upon patient's own request, when conservative medical management become unsuccessful (within or after 72 h) and when there is GB gangrene or perforation on the imaging studies.

Surgical procedure: laparoscopic cholecystectomy for acute calculous cholecystitis

Operations implemented by competent and experienced surgeons. Under general anesthesia, pneumoperitoneum created through 1.2 cm incision at the inferior aspect of the umbilicus, using blind puncture with a Veress needle, insufflation of CO_2 commenced up to 15 mmHg pressure. Four ports technique was used: 10 mm umbilical for a 0° scope, 10 mm three fingerbreadths inferior to the xiphoid process for working instruments, 5 mm on the right subcostal margin along the midclavicular line for a grasper, and 5 mm on the right subcostal margin along the anterior axillary line for retraction instruments. The patient's position adjusted to be in a reverse Trendelenburg with the left side down to permit colon and small bowel to drop away from the GB area. Since the GB was frequently distended, the fluid inside it aspired when necessary to allow better grasping. To produce a critical view of safety, the Calot's triangle dissected using a bipolar sealing device or ultrasonic dissection to isolate the cystic artery and cystic duct separately. At that time, both were clipped and divided. The GB separated from its bed with ultrasonic dissection or a monopolar electrocautery hook. To escape CBD injury, a retrograde cholecystectomy accomplished if there were dense adhesions at Calot's triangle. At the end of surgery, GB removed through the subxiphoidal incision, which was widened if needed. Hemostasis of the GB bed, saline lavage was done and then an abdominal drain was placed if indicated and the incisions closed. Conversion to open procedure accomplished through a long right subcostal incision when facing operative difficulties.

Data sheets for patients generated comprised: (a) demographic data; age, sex, BMI, ASA score, coexisting disease, and duration of symptoms up to surgery; (b) clinical data, such as core body temperature, Murphy's sign, and a palpable abdominal mass; (c) laboratory tests such as WBC count, blood urea nitrogen (BUN), international normalized ratio, total/direct bilirubin, alkaline phosphatase, amylase, aspartate transaminase, and alanine transaminase; (d) preoperative radiological findings, including ultrasonography/MRCP as well as ERCP; (e) operative data included the duration of operation, intraoperative bleeding and rate for conversion from LC to open cholecystectomy; (f) postoperative (PO) notes of concern documented regarding PO complications and length of stay. For statistical analysis, the gathered data entered into a database in the form of variables.

Patients categorized according to the timing of LC into two groups. Group E, including 50 patients who underwent LC within 72 h of symptom onset and group L, including 50 patients who underwent LC after 72 h of symptom onset. The analysis of the collected data was planned to compare between both patient groups.

Postoperative care

(1) Most patients shifted postoperatively to ordinary ward beds under close monitoring. However, some patients who were haemodynamically unstable were shifted to ICU.
(2) Patients managed with current enhanced recovery after surgery protocols.
(3) Patients encouraged for quick ambulation.
(4) Close observation of pulmonary function and SpO_2 monitoring.
(5) The intravenous antibiotic was continued for 24 h after surgery.
(6) Deep vein thrombosis (DVT) prophylactic measures (mechanical and chemical) applied according to protocols.
(7) On the first PO day, urine catheter was removed, oral fluid and soft fat-free diet were allowed.
(8) Drains were removed on the second PO day or when it became minimal (<50 ml in 24 h).
(9) Patients discharged home by the second PO day with advice to keep on a fat-free diet for 3 months at least.
(10) Outpatient clinic follow-up every week after discharge and sustained until patients became fully improved and had no more PO complaints.

Statistical analysis

Data presented as mean±SD, ranges, numbers, and ratios. Results were analyzed using Wilcoxon's ranked test for unrelated data (Z-test) and χ^2-test for numerical data. Statistical analysis conducted using the SPSS (version 21) for Windows statistical package (IBM Corp., Armonk, NY, USA). The P value less than 0.05 was considered as statistically significant.

Results

The study contained 100 patients with ACC, divided into two equal groups (50 patients in each group) according to the timing between the symptom onset and LC. Group E, for LC within 72 h and group L, for LC beyond 72 h of symptom onset.

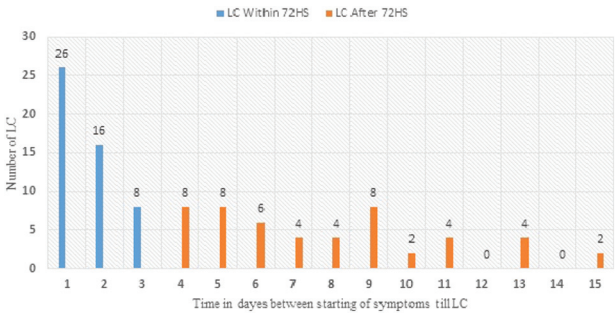
No difference regarding age, sex, ASA score or BMI between patients of both groups. Basic findings of clinical examination and medical history were nearly similar as well among both groups. However, the mean core body temperature and the positive Murphy's sign were significantly greater in group E compared with group L. Preoperative demographic and clinical data are clearly mentioned in Table 1.

In the early LC group, more than 50% of operations were performed within 24 h of symptom onset, whereas 32 and 16% of LC were done in the second and third days, respectively. On the other hand, 52% of LC in the delayed group were done between the fourth and seventh days of symptom onset and the remaining 48% were implemented in the subsequent week (Fig. 1).

Initial preoperative serum total bilirubin and BUN were significantly higher among patients of group L than patients of group E (P=0.032 and 0.004, respectively). However, there were no significant differences between both groups regarding other initial laboratory or radiological investigations. Preoperative ERCP was done in two patients in group E and five patients in group L. Preoperative laboratory and radiological data are summarized in Table 2.

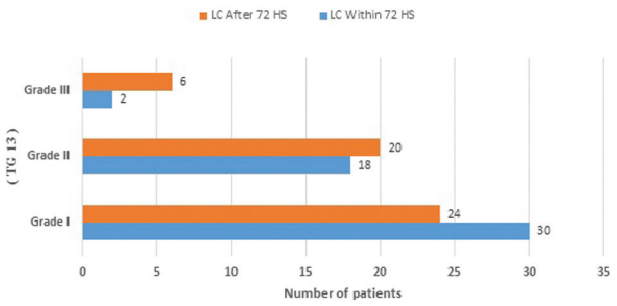
According to Tokyo Severity Grading (TG13) of ACC, GB was mildly inflamed in around 50% of patients in both groups. However, in 40% of group E and 36% of group L, the GB was moderately inflamed. A little percentage of patients in both groups suffered severe ACC, 4% in group E and 12% in group L (Fig. 2).

Figure 1



Distribution of cases, according to the time between starting of symptoms till laparoscopic cholecystectomy. LC, laparoscopic cholecystectomy.

Figure 2



Distribution of patients, according to Tokyo severity grading (TG13). LC, laparoscopic cholecystectomy.

Table 1 Patients' demographic and preoperative clinical data

Data	Group E	Group L	*P* value
N=100 [*n* (%)]	50 (50)	50 (50)	
Age (years)	40.44±13.66 (23–65)	41.2±13.96 (20–64)	0.689
Sex			
Males	22 (44)	20 (40)	NS
Females	28 (56)	24 (60)	NS
BMI (kg/m^2)	31.36±2.64 (26–35)	31.08±2.19 (28–35)	0.719
ASA score	1.72±0.74 (1–3)	1.96±0.73 (1–3)	0.440
Fever	38.25±0.63 (37.5–39.8)	37.46±0.47 (37.7–38.5)	0.016
Palpable tender mass	8 (16)	18(36)	0.002
Murphy's sign (+)	48 (96)	42 (84)	0.018
Coexisting disease[a]			
Diabetes mellitus	10 (20)	12 (24)	NS
Ischemic heart disease	2 (4)	4 (8)	NS
Hypertension	5 (10)	6 (12)	NS
COPD	3 (6)	4 (8)	NS
Renal impairment	1 (2)	3 (6)	NS

Data are presented as mean±SD and numbers; ranges and percentages are in parentheses. ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease. [a]Some cases had more than one coexisting disease.

In both groups, the majority of patients passed the operations smoothly without major intraoperative complications. The operative time in the delayed LC group was significantly higher (P=0.005) compared with the early LC group; however, there was a no significant difference between both groups regarding intraoperative complications, conversion rate, drain insertion rate, or ICU admission days. The mean total hospital stay was significantly higher (P=0.010) between patients of delayed LC group compared with the early LC group (Table 3).

Two patients of each group experienced PO bleeding (coming through the abdominal drain) ranging between 150 and 440 ml over the first 3 PO days and bleeding was managed conservatively. One patient from the delayed group suffered PO biliary leakage through the drain ranged between 10 and 110 ml/day over the first 5 PO days. On the sixth PO day, bile leakage stopped completely, abdominal ultrasonography was done and revealed no free fluid in Morison's pouch and laboratory results were normal, then the drain was removed. Hospital-acquired respiratory tract infection was recorded in two patients of group E and three patients of group L. In spite of applying DVT prophylactic measures, one patient of the late LC group suffered PO DVT in her left leg on the fourth PO day and managed with a therapeutic dose of subcutaneous clexane (Fig. 3).

Discussion

The most common infectious disease of the GB is the ACC. It is initiated by three chief mechanisms: cystic duct obstruction by gallstones, lysolecithin release, or ascending bacterial infection [9]. Formerly, the ideal time intended for LC for patients with ACC was 6–8 weeks after clinical improvement of acute inflammatory attack to permit the improvement of the acute phase reaction of the GB [10]. Conversely, in recent years, numerous studies have verified that early LC for ACC is harmless with morbidity and

Table 2 Patients' preoperative laboratory and radiological data

Data (NR)	Group E	Group L	*P* value
WBCs (4–11×10^9/l)	18.67±5.64 (12.9–34.2×10^9/l)	15.73±3.52 (11.5–2.6×10^9/l)	0.632
ALT (0–41 U/l)	42.69±14.8 (23–88)	60.52±27.2 (26–142)	0.053
AST (0–40 U/l)	38.72±24.5 (12–92)	42.28±24.1 (16–135)	0.262
Total bilirubin (<1.4 mg/dl)	1.76±0.74 (1–3.4)	1.9±1.1 (1–5.2)	0.032
Direct bilirubin (<0.2 mg/dl)	1.18±0.82 (0.1–2.8)	1.7±1.05 (0.3–4.5)	0.280
ALP (40–130 U/l)	90.9±68.7 (41–320)	116.9±85.4 (30–412)	0.492
Amylase (28–100 U/l)	127.9±97.6 (30–425)	126.8±117.4 (30–512)	0.423
BUN (10–20 mg/dl)	17.08±6.34 (10–31)	19.36±6.10 (11–31)	0.004
INR (0.8–1.1)	1.12±0.16 (1.1–1.5)	1.26±0.24 (1–1.9)	0.183
MRCP/ultrasonography findings			
Gallstones	50 (100)	50 (100)	
Thick-wall gallbladder	42 (84)	44 (88)	0.846
Pericholecystic fluid	34 (68)	30 (60)	0.840
CBD dilatation	4 (8)	8 (16)	0.676
Preoperative ERCP	4 (8)	10 (20)	0.002

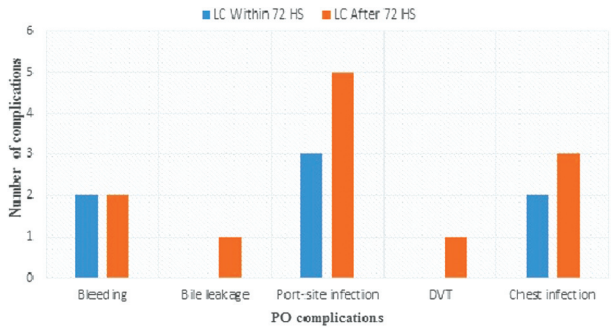
Data are presented as mean±SD and numbers; ranges and percentages are in parentheses. ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; BUN, blood urea nitrogen; CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; INR, international normalized ratio; MRCP, magnetic resonance cholangiopancreatography; NR, normal range; WBC, white blood cells.

Table 3 Operative and postoperative data

Data	Group E (*n*=50)	Group L (*n*=50)	*P* value
Operative time (min)	85.1±25.08 (45–125)	110.4±21.4 (75–160)	0.005
Intraoperative complications			
Blood loss	83.8±8.9 (10–210)	90.4±46.3 (20–200)	0.026
Biliary tract injury	0.0	1 (2)	NS
Conversion to an open procedure	1 (2)	3 (6)	0.739
Drain			
n (%)	29 (58)	35 (70)	0.764
Duration	1.48±2.9 (1–4)	1.84±0.3 (1–5)	0.001
ICU admission (days)	0.36±0.9 (1–3)	0.56±1.6 (1–4)	0.831
Total hospital stay (days)	5.24±1.66 (3–10)	9.6±3.69 (6–21)	0.010

Data are presented as mean±SD and numbers; ranges and percentages are in parentheses.

Figure 3



Postoperative 30 days complications. PO, postoperative.

mortality resembling those of LC in a delayed elective setting [11]. Ohta *et al.* [12], in a retrospective study, compared four timing groups of LC for management of ACC (within 72 h, 4–14 days, 3–6 weeks, and after 6 weeks subsequent to symptom onset), they found that the ideal timing is less than or equal to 72 h, compared with LC implemented later. According to the TG13 which is summarized by Yamashita *et al.* [6], management of ACC depend on the severity of the disease. Early LC soon after admission (within 72 h) for grade I (mild) and grade II (moderate) ACC. However, for grade III (severe) ACC, urgent management of system/organ dysfunction and GB drainage for control of severe local inflammation followed by delayed elective LC [6].

There is no doubt that the reduction of operative times and amounts of blood loss would participate in patient safety and improves the overall outcomes. In our study, operative time and the total amount of intraoperative blood loss were significantly higher (P=0.005 and 0.026, respectively) in the delayed LC group compared with the early LC group. Besides, the conversion rate and intraoperative complications in the delayed LC group were higher than the early LC group. This confirms the more safety of early LC for ACC (within 72 h) than beyond 72 h of symptom onset. The shorter operative time in early LC can be explained by the truth that inflammation accompanying AC makes an edematous plane nearby the GB, thus smoothing its dissection during operation. While in delayed operations, progress of the inflammation, and hence organization of the firm adhesions, result in scarring and contraction, making the GB cemented with the adjacent structures with distortion of normal anatomy leading to operative difficulty and inability to generate a critical view of safety. These findings go with Shunsuke *et al.* [13], who concluded from their study in comparison of early LC and late LC, that late LC was accompanied with longer operation time, more blood loss, more biliary injury, and greater conversion rate compared with early LC. However, their patients who underwent late LC had satisfactory surgical outcomes [13]. On the other hand, Alper *et al.* [14] found that although the operative time in early LC can be longer, there was no significant difference between the early and delayed LC groups regarding rates for conversion to open cholecystectomy and operation time. Also, the incidence of serious intraoperative complications was analogous to the delayed LC. However, they concluded that early LC still looks more advantageous than late intervention [14].

In our study, there were no noteworthy differences regarding the PO morbidities in both groups. However, the total PO complications (hemorrhage, bile leak, chest infections, DVT, and surgical site infections) were higher in the delayed LC group compared with early LC group (12 vs 7, respectively). On the reverse, Zafar *et al.* [15] found that PO complications were more frequent with early LC than delayed LC and they attributed this to the initially significant greater body temperatures and serum levels of conjugated bilirubin in the early LC group which were the only significant preoperative differences between both patient groups in their study. On the other hand, de Mestral *et al.* [16] agree with us in the same results and found that PO complications were significantly higher among patients of emergent early LC compared with late LC group.

In our present work, we found that the total hospital stay was significantly lower in early LC than delayed LC (P=0010). By the way, the short hospitalization will affect positively on the patient's PO quality of life (QOL). This goes with Zhu *et al.* [8] who mentioned that a recent survey assessing surgical approaches for management of acute cholecystitis (AC), total hospital stay was established to be shorter for a group of patients who underwent early (emergency) cholecystectomy at the time of the first admission compared with patients who had delayed elective cholecystectomy. Similar to the results of our present study and the above clinical studies, Samraj *et al.* [17] found that duration of hospital stay was significantly shorter and management-related costs were lesser with early LC compared with delayed LC for ACC. Along with the clinical studies, the meta-analyses of randomized clinical trials in the literature revealed that early LC (24–72 h of disease onset) offers advantages over delayed LC (beyond 72 h of disease onset) in the form of lesser total hospital stay, lower conversion rates, and fewer PO complications [18]. Siddiqui *et al.* [19] analyzed four clinical studies

comprising 375 patients of ACC who were managed at different periods following disease onset and found a shorter hospital stay in early LC. In a best-evidence subject that investigated 92 papers (retrospective cohort studies, meta-analyses, prospective controlled study, and randomized control trials), it was established that early LC for ACC is advantageous regarding the length of hospital stay without rises in morbidity or mortality [18]. Some recent studies have investigated the financial costs of early compared with delayed LC in the management of ACC. Masayuki *et al.* [20] mentioned that early LC is less pricey with superior outcomes regarding the QOL. An additional study from Canada established the better patient QOL and considerable cost savings with early LC. In our present study, due to a shorter duration of total hospital stay and near absence of conservative treatment in early LC, we conclude that management-related expenses were lesser in the early LC group [21]. According to Ansaloni *et al.* [22], the Scientific Board of the 2nd World Congress of the World Society of Emergency Surgery on August 2013, depending on the evidence involved in the guidelines, it can be specified that early LC is the best management method for ACC. However, the surgical therapy of ACC is limited to patients who are in good condition for urgent surgery. In cases of patients not fit for urgent LC (grade III according to TG13), World Society of Emergency Surgery agree with TG13 in management procedures which have been mentioned before [22].

We cannot deny that the current study had some restrictions regarding the small sample size and cost analysis was not based on a systematic decision model. However, the results of this study should offer a source for large-scale clinical studies and additional cost analysis matching early versus delayed LC for ACC, which is one of the most common procedures in surgical practice.

Conclusion

Emergent LC is a safe and a reliable management procedure for ACC within 72 h of symptoms onset. It was established that it is more advantageous than delayed LC (beyond 72 h) in terms of patient safety, financial costs, and length of hospital stay without rises in morbidity or mortality.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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Combined radiofrequency ablation and truncal foam sclerotherapy for greater saphenous vein incompetence can reduce recurrence and complications of radiofrequency ablation

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Objective
Although radiofrequency ablation (RFA) has been established as an effective method for the treatment of lower limb varicose veins with a good outcome, in all interventions, there were complications and recurrence, because of which in this study we are modifying our technique to reduce the rate of complications and recurrence that we faced in our previous work.
Patients and methods
A total of 74 patients (86 lower limbs) with greater saphenous vein (GSV) incompetence were randomized to two treatment groups; the first group was treated by RFA with duplex guided perforator injection and the second group was treated by RFA with duplex guided perforator injection plus below knee truncal sclerotherapy of incompetent GSV. Groups were followed up for 12 months and compared demographically; venous clinical severity scores (VCSS), need for sclerotherapy during follow-up and postintervention complications including recanalization and recurrence were determined.
Results
There was no statistically significant difference between both groups as regards demographic criteria, VCSS preoperatively, paresthesia around the medial malleolus and recurrence of varicose veins during the follow-up period. There was significant difference between both groups as regards GSV recanalization with a *P* value of 0.046; also there were significant difference between four different time periods of VCSS (preintervention, 3, 6 and 12 months postintervention) by pairwise comparison of the two groups. A significant difference was found between the two groups in the need for postintervention sclerotherapy all over 12 months with a *P* value of 0.038.
Conclusion
The addition of below knee truncal sclerotherapy to the above knee RFA of GSV can reduce the rate of recanalization, recurrence of varicose veins, and decrease the need for postintervention sclerotherapy without risk of increase in the total number of complications.

Keywords:
radiofrequency, sclerotherapy, varicose veins

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Introduction

Lower limb varicose veins management has changed rapidly in the recent years, with replacement of the conventional surgery by newer endovenous methods [1].

Durability of any vascular procedure, especially if it costs too much and how to make it live longer is a vital issue and important goal [2].

The natural history and the fate of untreated below knee greater saphenous vein (GSV) is important in understanding the ongoing chronic venous disease [3].

There is a close association between saphenous nerve and GSV throughout its course particularly several centimeters below the knee to the medial malleolus. Several branches of the nerve cross directly over the vein and are liable for injuries during any manipulation over the vein [4].

Paresthesia and numbness around the medial malleolus due to nerve damage following below

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knee radiofrequency ablation (RFA) and other varicose vein surgery are the most common causes of legal dispute and litigation [5].

Patients and methods

The study was conducted in Zagazig University Hospitals and at a private center during the period from August 2014 to August 2016 on 74 patients with GSV incompetence; patients were randomly divided into two groups; the first group was treated by RFA with duplex guided perforator injection (DGPI) and the second group by RFA with DGPI plus below knee truncal sclerotherapy (BKTS) of incompetent GSV. Patients with any of the following criteria were excluded: acute deep vein thrombosis, arterial disease of the lower limbs, lesser saphenous vein incompetence, superficial thrombophlebitis, thrombophilia, pregnancy, or are allergic to polidocanol.

The degree of venous insufficiency and severity of the disease was assessed by clinical examination, duplex ultrasound, and venous clinical severity score (VCSS).

All steps of the intervention, including type of anesthesia and possible complications which might be acquired were discussed carefully with all patients and written consents were obtained from all patients which were approved by the Institutional Review Board.

Under spinal anesthesia, GSV puncture above the medial malleolus under duplex guidance was made, using guidewire then 7 or 5 French sheath was inserted into the GSV. Normal saline injection inside the sheath with duplex ultrasound observation of its flow inside the vein was done for confirmation of the site of the sheath inside the vein. The ClosureFast (VNUS Medical Technologies Inc., San Jose, California, USA) was advanced through the sheath to 1.5 cm below SFJ. Under duplex guidance tumescent fluid (500 ml normal saline plus 1 ml adrenaline) was injected into the saphenous compartment in a subfascial location using spinal needle by multiple punctures along the course of the vein, in order to compress GSV and to decrease the incidence of local complications. In Trendelenburg position the catheter ablates a 7 cm segment of the GSV vein for 20 s per cycle. Two cycles were applied to the first segment, whereas the last segment was that just above the knee confirmed by the position of the tip of the catheter under duplex guidance, then the catheter was removed and polidocanol foam was injected from the sheath into the below segment of GSV in the second group followed by duplex guided foam injection of incompetent perforators in both groups.

The polidocanol foam was produced by the Tessari method [6] (double-syringe system) which involves the mixing of polidocanol 3% with room air in a ratio of 1 : 4 in two syringes linked through a three-way connector. A completion duplex ultrasound was done in both groups from SFJ downward to assess vein closure and fullness of below knee segment by foam in the second group and to measure immediate technical success rates. Follow-up duplex ultrasound at 3, 6, 12 months postintervention was conducted with reporting all cases of recanalization with return of venous flow in a previously obliterated venous segment or whole GSV recanalization and recurrence of varicosities related to previously treated venous segment.

Statistical analysis

Statistical package for the social sciences software (SPSS for Windows, version 17.0; SPSS Inc., Chicago, Illinois, USA) was used for data analysis.

Patients with bilateral lower limbs were treated as one for data analyzed by subject, but were included in the SPSS data analysis by one limb for each side separately. *P* values less than 0.5 were considered statistically significant.

Results

A total of 74 patients with 86 limbs, the first group included 38 patients and the second group included 36 patients with 43 limbs in each group; the first group included 25 (65.7%) women and was treated by RFA with DGPI and the second group included 22 (61.1%) women and was treated similarly as the first one plus BKTS of incompetent GSV. There was no statistically significant difference between both groups as regards demographic criteria as noticed in Table 1.

VCSS scores in both groups before the procedure (VCSS0), at 3 months (VCSS3), 6 months (VCSS6), and 12 months (VCSS12) after the procedure are shown in Table 2, whereas the comparison between both groups in the mean VCSS at the different time periods was shown in Fig. 1, for example, VCSS0 was 5.09±1.65 for the first group and 5.30±1.87 for the second group with a *P* value of 0.408.

As regards the different VCSS values in both groups during follow-up, there was no statistically significant

Table 1 Demographic criteria of all treated limbs in both groups

	First group [*n* (%)]	Second group [*n* (%)]	*P* value
Age (mean±SD) (years)	32.76±8.5	33.06±8.5	0.891[a]
Sex			
Female	27 (63)	28 (65)	0.018[b]
Male	16 (37)	15 (35)	0.032[b]
Side			
Unilateral	38 (88.3)	36 (83.7)	0.054[b]
Bilateral	5 (11.7)	7 (16.3)	0.333[b]
GSV diameter (mean±SD) (mm)	8.80±1.70	8.68±1.63	0.128[a]
Height (mean±SD) (cm)	168±6.6	171±5.9	0.917[a]
Weight (mean±SD) (kg)	76.16±6.7	78.43±7.6	0.474[a]
BMI (mean±SD)	26.64±2.02	26.44±2.18	0.832[a]
Diabetes mellitus	4 (9.3)	7 (16.2)	0.260[c]
Smoking	5 (11.6)	4 (9.3)	0.500[c]
Hypertension	6 (13.9)	8 (18.6)	0.386[c]
IHD	3 (6.9)	1 (2.3)	0.308[c]
Venous ulcer	9 (20.9)	7 (16.2)	0.400[c]

IHD, ischemic heart disease; GSV, greater saphenous vein; [a]Independent sample *t*-test; [b]χ^2-test; [c]Fisher's exact test.

difference between RFA group and RFA plus BKTS group as noticed in Table 3.

The significance was between the four different time periods of VCSS, so a pairwise comparison was made to identify what period of VCSS caused this difference, which is clearly shown in Table 4, that VCSS0 causes the difference between the four follow-up time periods; also there was a statistically significant difference between VCSS3 and VCSS12, which means there is significant improvement in patient symptoms over the follow-up periods.

There were 12 (27.9%) patients from the first group and five (11.6%) patients from the second group who required sclerotherapy over the 12 months period of follow-up for treatment of residual varicosities postintervention showing statistically significant difference between both the groups with a *P* value of 0.038 as shown in Fig. 2.

Primary GSV closure was achieved in all patients of both study groups. During the follow-up period, there were 11 (25.5%) cases of recanalization in the first group and four (9.3%) cases in the second group with a *P* value of 0.046 as described in Fig. 3) But as regards recurrence there were seven (16.2%) cases in the first group and three (6.9%) cases in the second group with a *P* value of 0.163 by the Kaplan–Meier test as described in Fig. 4. Recanalization was not associated with recurrent varicose veins in four cases of RFA group and one case in RFA plus BKTS group. Mean and median

Table 2 Venous clinical severity score in both groups before radiofrequency ablation, at 3, 6, and 12 months follow-up time

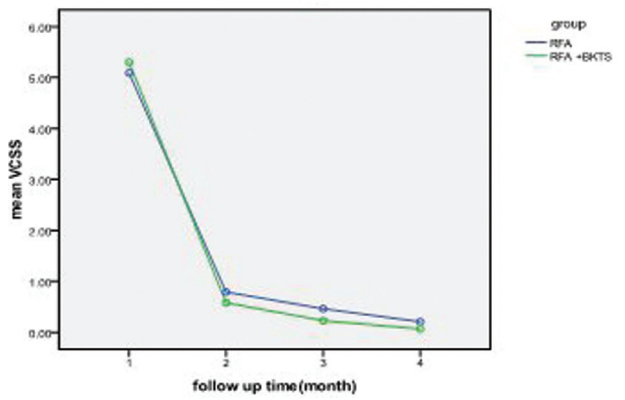
	Before radiofrequency						At 3 months follow-up						At 6 months follow-up						At 12 months follow-up					
	Mild		Moderate		Sever		Mild		Moderate		Sever		Mild		Moderate		Sever		Mild		Moderate		Sever	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Pain	13	14	2019	15	10	14	6	7	4	2	–	–	5	3	2	1	–	–	3	1	–	–	–	–
Varicose veins	24	27	–	16	–	–	10	11	3	1	–	–	6	3	–	–	–	–	5	2	–	–	–	–
Venous edema	17	26	3	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Pigmentations	15	13	–	2	–	–	8	7	1	–	–	–	5	2	–	–	–	–	1	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Induration	–	–	2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
No of active ulcers	7	5	–	2	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Ulcer duration	9	7	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Ulcer size	9	7	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Compression	4	1		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

A, RFA and DGPI groups; B, RFA and DGPI+BKTS groups; BKTS, below knee truncal sclerotherapy; DGPI, duplex guided perforator injection; RFA, radiofrequency ablation.

for recanalization and recurrence are discussed in Tables 5 and 6.

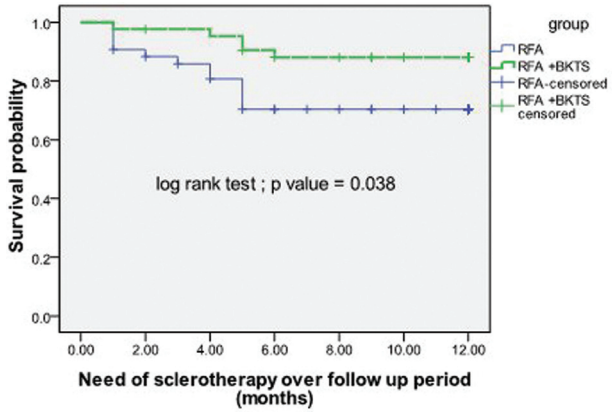
The pattern of recanalization in the first group was two (4.6%) cases with opened stump into the femoral vein due to tributary vein insertion, four (9.3%) cases with recanalization in the middle segment of the GSV, and five (11.6%) cases of whole GSV recanalization, whereas the pattern of recanalization in the second group was one (2.3%) case of groin recanalization due to undiagnosed anterior accessory saphenous vein and three (6.9%) cases with recanalization in the middle segment of GSV due to attachment to incompetent perforators and no cases of below knee or whole GSV recanalization.

Figure 1



Comparison between both groups in the mean VCSS at the different time periods.

Figure 2



Comparison between both groups in the need of sclerotherapy over follow up periods.

Table 3 Testing the relation between different values of venous clinical severity score together and the difference between the two study groups

Sources	Time	Type III sum of squares	df	Mean square	*F*	Significance	Partial η^2
Time	Linear	1034.626	1	1034.626	596.718	0.000	0.877
	Quadratic	397.965	1	397.965	306.329	0.000	0.785
	Cubic	70.409	1	70.409	75.819	0.000	0.474
Time×group	Linear	1.230	1	1.230	0.710	0.402	0.008
	Quadratic	1.407	1	1.407	1.083	0.301	0.013
	Cubic	0.084	1	0.084	0.090	0.765	0.001
Error (time)	Linear	145.644	84	1.734			
	Quadratic	109.128	84	1.299			
	Cubic	78.007	84	0.929			

Time: four VCSS values (VCSS0, VCSS3, VCSS6, and VCSS12); Groups: RFA and RFA plus BKTS; BKTS, below knee truncal sclerotherapy; RFA, radiofrequency ablation; VCSS, venous clinical severity score.

Table 4 Pairwise comparison between four different venous clinical severity score values represented by time

Time (I)	Time (J)	Mean difference (I–J)	SE	Significance[a]	95% confidence interval for difference	
					Lower bound	Upper bound
1	2	4.512	0.220	0.000	3.917	5.106
	3	4.849	0.218	0.000	4.258	5.439
	4	5.058	0.200	0.000	4.517	5.600
2	1	4.512	0.220	0.000	5.106	3.917
	3	0.337	0.148	0.149	0.061	0.736
	4	0.547	0.130	0.000	0.196	0.897
3	1	4.849	0.218	0.000	5.439	4.258
	2	0.337	0.148	0.149	0.736	0.061
	4	0.209	0.097	0.203	0.053	0.472
4	1	5.058	0.200	0.000	5.600	4.517
	2	0.547	0.130	0.000	0.897	0.196
	3	0.209	0.097	0.203	0.472	0.053

Time 1: VCSS0; time 2: VCSS3; time 3: VCSS6; time 4: VCSS12; VCSS, venous clinical severity score.

Paresthesia around the medial malleolus due to saphenous nerve damage was observed in two (4.6%) patients in the first group and in five (11.6%) patients in the second group with a *P* value 0.433 by Fisher's exact test. This paresthesia was temporary in the two patients of the first group and four patients of the second group and was permanent after 6 months in only one patient of the second group.

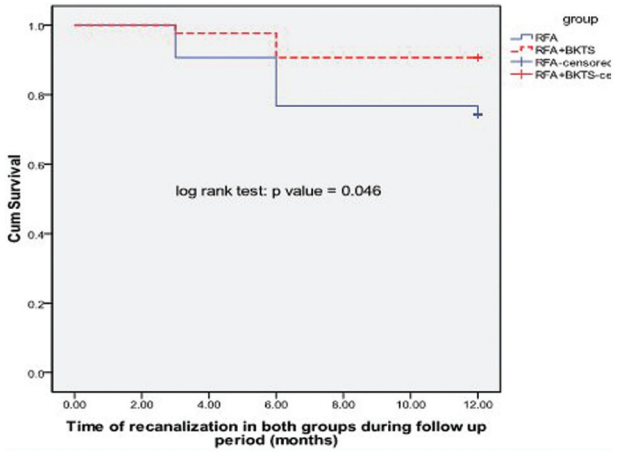
Discussion

To solve the problem of the durability of any varicose veins procedure as regards recurrence after a short time in our community so we were aiming to perform below knee GSV sclerotherapy not to achieve thrombosis of the vein *per se*, which may recanalize, but with almost transformation of the vein into a fibrous cord.

We discussed before in our previous work [7] that 15 (12.8%) cases had postoperative phlebitis which dropped to four (9.3%) cases among the first group plus three (6.9%) cases among the second group with a total number (7/86=8.1%) in the present study. As regards paresthesia, it was permanently affecting four (3.4%) cases in our previous study, dropped to only one case in the radiofrequency (RF) and truncal sclerotherapy group in the present study.

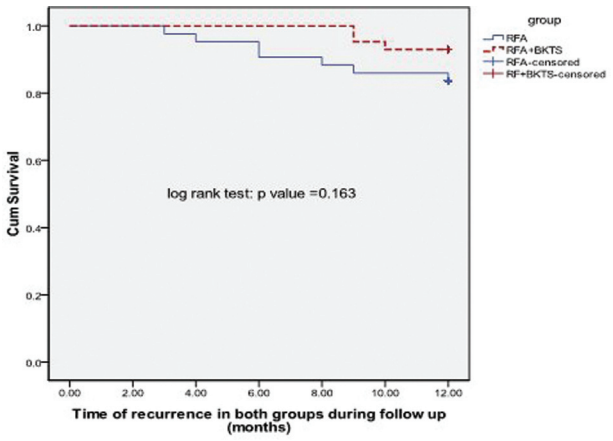
Shoab *et al.* [8] have stated that retreatment was required in below the knee branches in 46% of patients requiring additional treatment after initial endovenous laser ablation which meant that the reason for offering reintervention in those patients was reflux in residual below the knee segment of GSV with the potential risk for continued venous hypertension and recurrence of symptoms. So when we are facing a whole segment below the knee and although all incompetent perforators related were duplex guided injected, soon it may provide new

Figure 3



Recanalization in both groups during follow up periods.

Figure 4



Recurrence in both groups during follow up periods.

Table 5 Mean and median of recanalization in both groups

Groups	Mean[a]				Median			
			95% confidence interval				95% confidence interval	
	Estimate	SE	Lower bound	Upper bound	Estimate	SE	Lower bound	Upper bound
RF	10.326	0.500	9.346	11.305	–	–	–	–
RF+truncal sclerotherapy	11.372	0.305	10.774	11.970	–	–	–	–
Overall	10.849	0.298	10.264	11.434	–	–	–	–

RF, radiofrequency; [a]Estimation is limited to the largest survival time if it is censored.

Table 6 Mean and median for recurrence in both groups

Groups	Mean[a]				Median			
			95% confidence interval				95% confidence interval	
	Estimate	SE	Lower bound	Upper bound	Estimate	SE	Lower bound	Upper bound
RF	11.163	0.366	10.446	11.879	–	–	–	–
RF+truncal sclerotherapy	11.814	0.105	11.608	12.020	–	–	–	–
Overall	11.488	0.190	11.115	11.862	–	–	–	–

RF, radiofrequency; [a]Estimation is limited to the largest survival time if it is censored.

varicosities with increase in the venous pressure after a period of time or it may be itself a source of patient dissatisfaction after RF and incompetent perforators injection.

Chan *et al.* [9] reported that, 22 of 54 (40.7%) patients in the endovenous laser group required sclerotherapy within 6 months of the original surgery for the management of residual varicosities, which represents a higher rate of postendovenous intervention need for sclerotherapy than encountered in our study.

The statistically significant difference among both groups in freedom from postintervention sclerotherapy with a *P* value 0.038 in favor of RFA plus BKTS group reflects the lower rate of recanalization and although there was no statistically significant difference between both groups over 12-month follow-up as regards the recurrent cases, the number of recurrent cases may be increased over the longer follow-up periods than in our study timeframe especially with significant increased rate of recanalization in RFA with the DGPI group than the second group.

Although the number of patients affected by paresthesia in our study was higher in RFA plus BKTS group which may be attributed to the proximity to saphenous nerve during injection and the use of 7 French sheath in the early cases which was replaced by 5 French sheath, yet there was no statistically significant difference between both the groups.

Jin *et al.* [10] have stated that although there was occlusion failure or recanalization in a segment or whole GSV, there was significant reduction of the saphenous vein diameter and absence of venous reflux was noticed, which may explain symptomatic improvements in some cases

Not all cases of recanalization were associated with recurrence in our study; there were four (9.3%) in the RFA group and one (2.3%) case in the RFA plus BKTS group without recurrence of varicose veins or venous ulceration, which means that there were great benefits from ablation and sclerotherapy with elimination of annoying symptoms in all patients. Even those with recurrence had no ulcers and were managed by single sessions of duplex guided sclerotherapy.

Although there was no statistically significant difference between both groups as regards recurrence along 12 months follow-up, the total number of recurrent cases was lower in RF and in the truncal sclerotherapy group with no cases of below knee recurrence.

Cases of groin recurrence in both groups represent disease progression which may be due to increased venous pressure with recent reflux along the anterior or posterior accessory saphenous veins. Cases with recurrence in the thigh and who had recanalization in the GSV segment might had primarily thrombotic occlusion and subjected to enhanced recanalization caused by recent perforator incompetence not injected before.

As regards a series of complications which were reported by other studies [11,12], life-threatening pulmonary embolism, deep venous thrombosis, transient visual disturbance, anaphylactic shock were not encountered in our study

Conclusion

This study although has some limitations as regards the small sample size, relatively short period of follow-up, still give promising results of reduced recurrence rates and increased sclerotherapy survival-free periods without increase in the total number of complications.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Retrograde approach for complex lower limb arterial occlusions

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Introduction
Despite the advancement of endovascular technology, there are complex lesions which cannot be passed through antegrade approach, a retrograde approach to cross the complex lesion was first described by Iyer and colleagues, and it was used in cases where antegrade approach failed to cross the lesion. This promising technique had good results and was done through surgical incision and direct arterial puncture.
Patients and methods
A registry of retrograde approach has been maintained since March 2014, when the first transposterior tibial retrograde recanalization was performed at our institution till March 2016. Thirty-six patients were selected from the registry with age range from 49 to 85 (65.14), male pateints were 21 (58.3%) and female patients were 15 (41.7%). Patients were Rutherford class 4 (six patients), 5 (21 patients) and 6 (nine patients).
Results
After retrograde angioplasty a Kaplan–Meier curve for patency was 77.7% (28 of 36), 63.8% (23 of 36) and 47.2% (17 of 36) at 6, 12 and 24 months, respectively. Limb salvage rates were 97.2, 80.6, and 66.4% at 6, 12, and 24 months, respectively.
Conclusion
Retrograde approach is a safe and effective way to pass a complex lesion and it provides an alternative way to surgery with less complications and faster recovery.

Keywords:
complex lesions, peripheral arterial diseases, retrograde approach

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Introduction

Although clinical success is higher with endovascular intervention for critical limb ischemia (CLI); yet complex, calcified and total obstructing lesions present in some patients are challenging [1]. Endovascular treatment offers multiple strategies to achieve technical and clinical success [2].

Ferraresi *et al*. [2] described the first attempt to below the knee (BTK) arterial lesions which was done through an antegrade common femoral arterial access; either intraluminal or subintimal techniques. The first attempt to cross a chronic total occlusion (CTO) was made by intraluminal approach and when failed they used a subintimal approach which could be successful.

The failure rate associated with antegrade approach to cross the CTO was high; up to 25% in superficial femoral artery (SFA) lesions and 20–40% for infrapopliteal lesions [3–6]. A re-entry device can be used to cross the CTO in case of subintimal passage of a wire but these devices are not always available and costly. Hence, a new and alternative approach (i.e. retrograde approach) emerged allowing for better treatment option for these complex lesions.

The first retrograde approach was described by Iyer *et al*. [7], this promising technique had good results and was done through surgical incision and direct arterial puncture [8–13] which was possible through all BTK arterial levels from the popliteal artery to foot arteries [6].

This technique requires training and has a learning curve. So it was used in difficult cases in which other approaches fail [14].

Patients and methods

We present our experience with the retrograde approach in the last 2 years. A retrospective review of a prospectively maintained database of patients with 150 limbs undergoing endovascular treatment for CLI from March 2014 to March 2016. Patients who failed the conventional antegrade approach underwent retrograde approach to cross the lesion were identified and the data was collected and analyzed, the study also was approved by our institution review board.

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The grading of the ischemia severity was according to Rutherford classification. Although the Rutherford classification [15] remains the standard method it needs to be revised in CLI patients; because, a broad range of foot lesions are incorporated into a single category (category 5).

Indications of retrograde approach

We used retrograde approach when antegrade access failed to cross the lesion, or if there was a difficulty of antegrade femoral access due to SFA flush lesions, groin scars or infections.

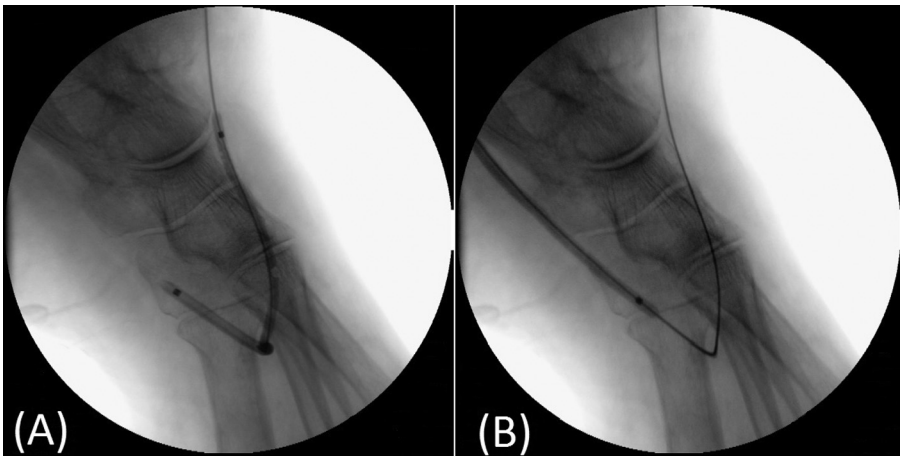
The techniques of retrograde approaches

All patients underwent full medical therapy and all had a trial of antegrade approach to cross the CTO. There were three techniques used for the retrograde approach the first is pedal-plantar loop technique which involves the passage of a wire from the Anterior tibial artery (ATA) to Posterior tibial artery (PTA) (or vice versa) through the pedal arch of the foot (Fig. 1).

The second is the transcollateral approach which uses a collateral artery suitable for guide wire passage to recanalize the tibials or foot arteries (Fig. 2).

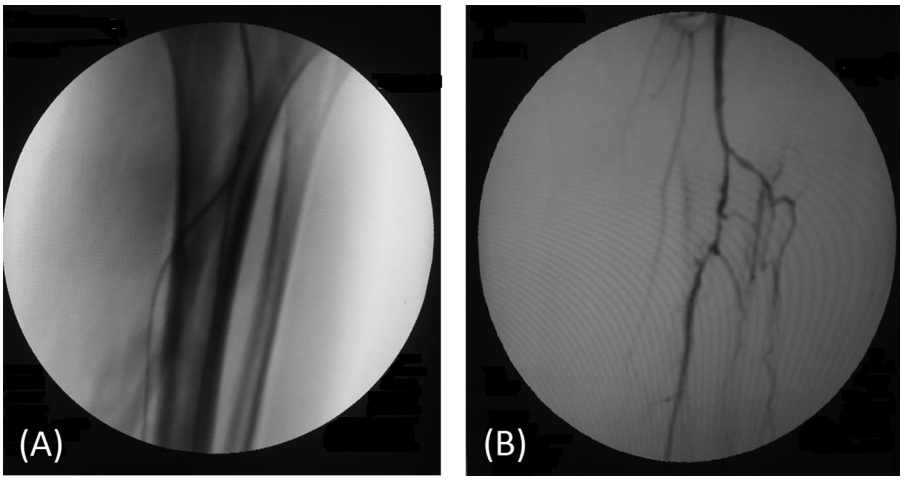
The third is the retrograde percutaneous access which is done by direct puncture of a distal patent artery followed by passage of the wire in a retrograde direction then dilatation of the CTO followed by the standard antegrade angioplasty (Fig. 3).

Figure 1



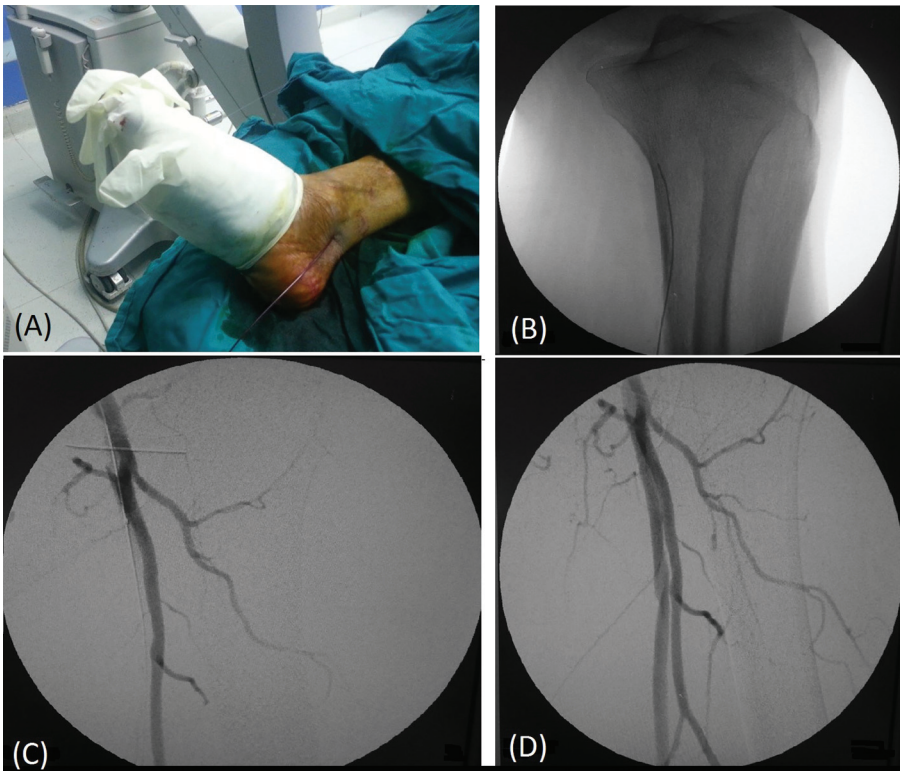
A representation of pedal-plantar loop technique (a) a balloon over the wire used to dilate the plantar arch. (b) Balloon over the wire passed into the posterior tibial artery through the plantar arch from the anterior tibial artery.

Figure 2



A representation of transcollateral artery approach (a) wire passes through suitable collateral from the peroneal into the posterior tibial artery upward into the popliteal artery. (b) The popliteal artery after dilatation with the balloon.

Figure 3



Direct puncture of the posterior tibial artery to cross the chronic total occlusion followed by standard antegrade approach.

Guidance for access

Historically, Iyer *et al*. [7] described surgical incision (cutdown) as the first technique used but currently less invasive methods are used.

Two methods are now used for arterial access, the first one is fluoroscopy which is now widely used as it does not need extra instruments thus it is easy to use, also it can be done even without contrast in case of severe calcification. But, it has several drawbacks such as multiple punctures trials which might increase the risk of local complications, extra contrast will be used during the puncture trials. Also, the patient will move his foot due to pain so the road-mapping is difficult.

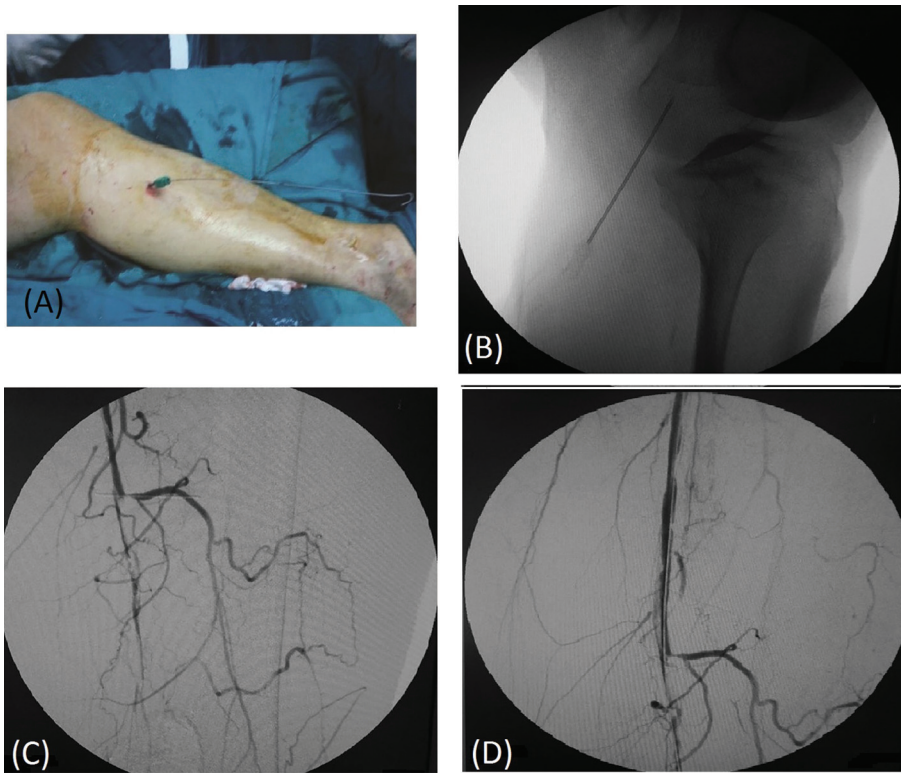
The second method used for retrograde approach arterial access is ultrasound guidance which gives a real time visualization of the arteries, less punctures so this would decrease pain and foot movement, no use of contrast and radiation exposure is decreased leading to less local complications and higher success rates. Access can be done in a few minutes as the learning curve is short.

We used different sites to access the artery using the retrograde approach; this was either transpedal access at any level of the leg (lower third, middle third or upper third), if there was a complex SFA, popliteal and tibioperonial occlusions and there was distal reconstitution of the tibial arteries, or by the distal SFA in patients with CTOs affecting the SFA in whom antegrade recanalization failed and the occluding lesion did not cross the level of the adductor canal (Fig. 4).

Percutaneous retrograde approach technique

(1) First the antegrade access was used with a 6-Fr ipsilateral (Radiofocus Introducer II; Terumo, Tokyo, Japan) or 6-Fr contralateral (Balkin; Cook, Bloomington, Indiana, USA) sheath or from a left brachial approach using a 5-Fr, 110-cm long sheath (Cook Inc., Bloomington, USA).
(2) After the placement of sheath 5000 U of Unfractionated heparin (UFH) given intravenously and additional 1000 U every 1 h for interventions that lasted longer than 1 h.
(3) The needle puncture of arteries in the retrograde approach is done either under fluoroscopic guidance or duplex guided (noncalcified vessels).
    (a) For the retrograde approach by the distal SFA, the C-arm was positioned into a contralateral oblique (30–45° for the right SFA (i.e. left oblique) and vice versa to facilitate puncture.
(4) The needle was introduced distal to the occlusion into the medial area of the thigh in a direct line with

Figure 4



An illustration of a retrograde superficial femoral artery approach. (a) Direct puncture through percutaneous approach. (b) Fluoroscopic position of the needle after puncture. (c) Passing the wire through the lesion. (d) Postdilatation angiogram.

the SFA. Oftentimes, contrast had to be injected through the antegrade sheath to visualize the distal SFA target.

(5) After arterial puncture, a guide wire was passed in the needle then a 5 or 6-Fr sheath was introduced.

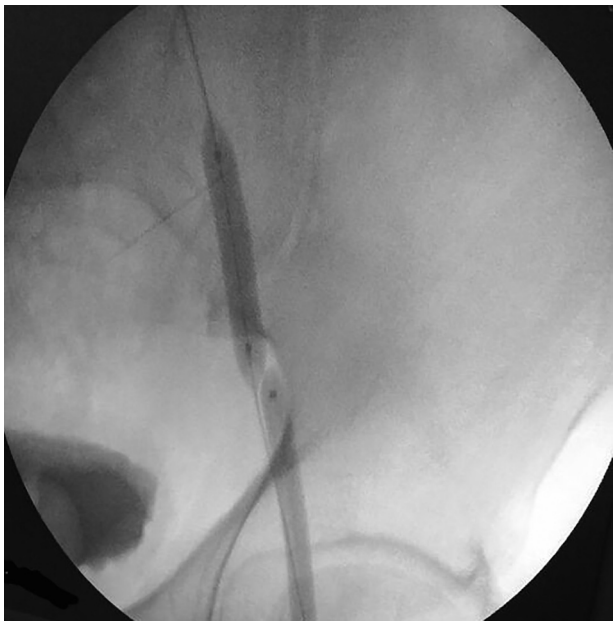
(6) If the wire cannot cross the lesion through the retrograde approach, a 'double-balloon' technique was used in which two balloons were used at the same time both in an antegrade and retrograde manner into the occlusion.

(7) The balloons were positioned with a 5 mm distance between their tips (no overlap) then the wires are retracted from the balloons followed by inflating the balloons for few seconds (Fig. 5).

(8) Balloons were inflated to break the dissection membrane separating the two balloons, then the balloons were pulled back for several centimeters, and another trial to pass the wire from both directions was reattempted.

   (a) The transpopliteal (face down) approach is the alternative [16] but it has many disadvantages: It has many drawbacks as the patient is put in a prone position, time-consuming and not convenient for both patient and interventionist and if the trial to pass the occlusion from a retrograde failed, no other access can be used in this prone patient [14].

Figure 5



Double balloon technique to break the fibrous cap in case of failure to pass the lesion through a retrograde approach only.

   (b) For pedal artery access if the ATA is the targeted vessel the C-arm was adjusted to an anteroposterior and cranial view with respect to the foot; if the PTA was the

artery to be punctured, the view was lateral to adjust the needle to the PTA.
After puncturing the tibial artery by the needle we use the sheath wire then the dilator to dilate the subcutaneous tissue especially when the artery is deep and also to exchange the wire then thread the wire upwards to cross the lesion and we prefer to continue the procedure sheathless by advancing the ballon over the wire (sheathless approach).

(c) After successful dilatation of the CTO we continue through the antegrade femoral sheath and sealing of the puncture site in the tibial artery by inflating balloon for 5 min and also with external compression.
(d) Antegrade administration of NTG 200 μg, prevent vasospasm in the retrograde approach.

Follow-up

After the procedure dual antiplatelet given with aspirin (150 mg/day) and cilostazol (100 mg twice/day) for 3 months and then lifelong daily aspirin thereafter.

Duplex ultrasound was done 1 day after the procedure to assess patency and detect the complications at puncture sites if present. Clinical follow-up took place every 1 month for at least 3 months (Tables 1–4).

A well maintained registry for patient with CLI was treated from March 2014 to March 2016, 150 limbs undergone angioplasty revascularization procedure of whom antegrade revascularization failed in 39 (26%) patients with complex CTOs.

Hence those 36 (21 males and 15 females) patients were suitable for retrograde approach, the success means the ability to cross the occlusion not only gaining an access. All lesions were CTO with a technical success rate of 92.3% (failed three cases); one case had a major amputation (below knee amputation), another case had femoroposterior tibial bypass by in-situ long saphenous vein using valvutom and one the third case was managed conservatively by medical treatment. The cause of failure was small tortious arteries (absence of sufficiently developed tibial vessels) in one case so that we could not get access and also the wire could not cross the lesion in two cases.

Many comorbidities in these patients was mainly diabetes mellitus in 75%, hypertension 61.1% and smoking 36.1% (Table 1). Postprocedure complications was bleeding, thrombosis, and vasospasm, all of which were managed successfully (Table 4); the occurrence of thrombi during the procedure was treated by infusion of urokinase at doses ranging from 25 000 to 200 000 IU. If vasospasm occurred, antegrade administration of nitroglycerine 200 μg was used which was an effective strategy to prevent vasospasm.

Considering that the below-the-ankle arteries were small and previous stenosis or occlusion existed, no treatment in case of bleeding was required.

Table 1 Patient characteristic, comorbidities and clinical condition (Rutherford classification)

Number of patients (*N*)	36
Age [mean (range)] (years)	65.14 (49–85)
Sex [*n* (%)]	
Male	21 (58.3)
Female	15 (41.7)
Medical comorbidities [*n* (%)]	
Smoking	13 (36.1)
CRF	6 (16.6)
Diabetes mellitus	27 (75)
Hypertension	22 (61.1)
IHD	7 (19.4)
Hyperlipidemia (*n*)	15 (41.7)
Clinical condition of treated limb [*n* (%)]	
Rutherford class 4	6 (16.7)
Rutherford class 5	21 (58.3)
Rutherford class 6	9 (25)

CRF, Chronic renal failure; IHD, ischemic heart disease.

Table 2 Outcomes

Overall outcome	*n* (%)
Technical failure	3 (7.6)
Death	2 (5.1)
Lost follow-up	3 (7.6)
Outcome of treated limb	
Wound healing	27(69.2)
Improved	4 (10.2)

Table 3 Access artery during retrograde approach

Superficial femoral artery [*n* (%)]	5 (13.8)
Tibioperoneal access [*n* (%)]	1 (2.7)
PTA [*n* (%)]	16 (44.4)
ATA [*n* (%)]	10 (27.7)
Peronieal access [*n* (%)]	4 (11.1)

Table 4 Incidence of postoperative complications

Complications	*N*=7 [*n* (%)]
Surgical site infection	0 (0)
Myocardial infarction	2 (28.5)
Deep vein thrombosis	0 (0)
Pulmonary embolism	0 (0)
Acute kidney injury	0 (0)
Unplanned readmission within 30 days	3 (43)
Postoperative groin hematoma that did not require readmission	2 (28.50)

A Kaplan–Meier curve was done to compare primary patency rates after retrograde angioplasty which was 77.7% (28 of 36), 63.8% (23 of 36) and 47.2% (17 of 36) at 6, 12 and 24 months, respectively. Limb salvage rates were 97.2, 80.6, and 66.4% at 6, 12, and 24 months, respectively (Fig. 6).

Discussion

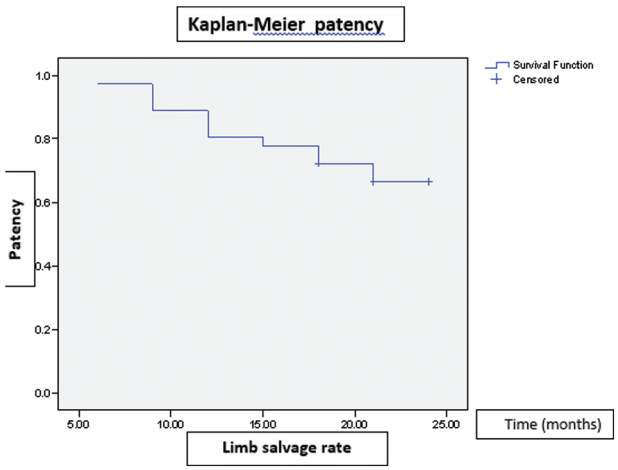
Previously antegrade approach was the only solution used to bypass a CTO affecting the lower limb arteries, with advances in technology a new method was used to cross the CTO requiring a subintimal passage of the wires with a re-entry device need to get back into the actual arterial lumen, these re-entry devices are not always available and costly to be used.

A newer technique emerged with a greater success rate of passing the CTO which proved effective as the CTO lesion cap was higher in density at its upper end than its lower end, also the wire will not enter side branches through a retrograde approach due to the direction of collaterals [17]. Also stronger wire push ability due to short distance between the puncture site and the occlusion and small size of access artery [18].

Retrograde pedal access can be used even without failure of antegrade approach and usually associated with shorter time of the procedure [19]. Lupattelli *et al.* [20] did not advice using the retrograde pedal access from the start to avoid serious access site complications.

In our study we used the retrograde approach to treat limb ischaemia and to avoid its complications we used this approach only as a backup method in case of failure of an antegrade access to cross the lesion or cannot be done due to flash CTO of SFA.

Figure 6



Kaplan–Meier patency curve for the retrograde approach.

This retrograde approach became possible with the availability of smaller catheters and balloons.

The use of sheath is well established in the femoral access, but in retrograde tibial is still controversial. Bazan *et al.* [17] and Yeh *et al.* [21] advised against the use of a sheath because of increased risk of local complications due to small tibial arteries diameter.

In contrast, other operators like Rutherford *et al.* [15] Montero-Baker *et al.* [22] preferred to use the sheath because it gives strong push ability, which would increase the success rate of passing the lesion, also with small (4 Fr microsheath or radial sheath) local access site complication become infrequent [21,23].

In our study we prefer sheathless approach because of its minimal complications and also due to less availability of microsheath in our hospital.

Thrombosis is usually high with retrograde access due to double access and the presence of CTO lesions compromising both the inflow and the outflow (especially during hemostasis of access site) [8].

So antithrombotic drugs should be used but no uniform regimens are established; most operators use UFH alone as we did with our cases, we gave the patients loading dose of 5000 UFH then 1000 µm every 1 h.

In spite of paucity of data. Kristić and Lukenda [24] tell that spasm of the radial artery access occurred with small artery, multiple attempt of punctures, diabetes mellitus and especially in females and young age. Despite the frequent occurrence of tibial and pedal arteries vasospasms no standardized protocols to prevent its occurrence [25].

Currently, nitroglycerine (NTG) is the commonly used agent to prevent arterial spasm. Walker and colleagues [19] give 200–400 NTG by the antegrade sheath and 1 : 1 mixed solution of 1% lidocaine and NTG subcutaneously at the retrograde puncture. In our cases we give 200 NTG routinely in all cases to avoid arterial spasm.

Hemostasis in retrograde access differ according to the technique used; in case surgical exposure was used fine stitches was needed. In percutaneous approach Werner *et al.* [26] used external compression for 5–10 min or intra-arterial balloon inflation for 10–15 min.

In our cases manual compression was effective for hemostasis in the ATA and PTA but not enough in

peroneal or tibioperonial access so we inflated the balloon for 5 min inside the artery at the retrograde puncture.

In a series of Walker *et al.* [18], he published 95% success of access puncture but crossing the occlusion was 87.2%. Failure of access was common in female, chronic renal failure (CRF) patients and small arteries.

In our study we had success rate in crossing the lesion of 92.3% (only three cases failed) which is very good as regard to the complexity of the lesions, diffuse disease and failure of the antegrade access in most cases.

With revascularization in CLI patency rate and limb salvage are the most important results and according to Romiti *et al.* [27] bypass surgery have higher patency than endovascular procedures but rates of limb salvage were similar.

According to many authors results of endovascular interventions using retrograde approach are similar to an antegrade approach [8,17,21,28].

The advantages and success rates of the pedal access approach for intervention and recanalization of BTK arteries for treatment of CLI overweighs that of the antegrade approach and can replace bypass surgery for tibial arteries which failed conventional antegrade approach [29].

In our study primary patency rates at 6, 12, and 24 months after retrograde angioplasty were 77.7% (28 of 36), 63.8% (23 of 36) and 47.2% (17 of 36), respectively. Limb salvage rates were 97.2%, 80.6%, and 66.4% at 6, 12, and 24 months, respectively. These results are comparable to the antegrade approach, thus this method can treat patients with complex lesions before shifting to any bypass surgery.

Some authors published a new technique using the first metatarsal artery which is connected to lateral plantar artery through the plantar arch and can be used to recanalize the tibial arteries [14,30,31]. We did not use this technique yet, but it may be tried in the next cases of failed retrograde approach.

Retrograde popliteal artery access need the patient to be prone so we need turn the patient [32] these maneuvers make the patient irritable and uncomfortable.

On the other hand, the operator needs to use the guide wire in the femoral and popliteal sheath in the same time which is difficult. Also popliteal access cannot be used in obese patients or those whom have cardiac, respiratory failure and severe rest pain. Popliteal access is also not used for patients with popliteal artery lesions [33]. So we did not use this technique in our study.

Conclusion

Retrograde approach can be used in failure of antegrade recanalization with the patient in the same supine position. Retrograde access for complex CTO disease has proven to be an easy and successful technique for treatment of patients with poor options or failed previous attempts. Interventionists should be encouraged to use this technique in their daily practices. This technique also preferred in cases when a re-entry device is not available.

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Conflicts of interest

There are no conflicts of interest.

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Management strategies of grade I, II, III blunt pancreatic injuries: our center's experience

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Background
Pancreatic injuries are rare among solid organ injuries. Blunt pancreatic injuries are classified according to the American Association for the Surgery of Trauma. According to the American Association for the Surgery of Trauma scale, grade I and II injuries are generally managed by conservative treatment, whereas grades III, IV, and V typically require surgical treatment. Traumatic pancreatic injuries are characterized by high morbidity and mortality rates.
Patient and methods
Grade I, II, II pancreatic injury patients were included in this study and grade IV patients were excluded together with the pediatric age group. Patients of this study were divided into operative groups, where surgical exploration with drainage and/or pancreatic resection or necrosectomy and continuous saline lavage was done with application of hemostatic sealant sheets over the raw surface of pancreas and conservative groups, where conservative measures were carried out.
Results
According to The American Association for the Surgery of Trauma (AAST) grade I, seven patients, grade II, eight patients grade III two patients, 10 patients underwent operative intervention, drainage and/or pancreatic resection with continuous saline lavage, and application of hemostatic sealant material when needed. One patient developed pancreatic pseudocyst. Seven patients underwent conservative measures, with two patients having developed pseudocyst and one patient developing pancreatic fistula.
Conclusion
Operative intervention of grade II, III injuries with application of continuous saline lavage, and application of hemostatic sealant material when needed helps to decrease complications.

Keywords:
blunt pancreatic, hemostatic sealant sheets, lavage

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Introduction

Pancreatic injuries are rare among solid organ injuries as compared with liver and spleen [1]; pancreatic injuries range from 0.2% [2,3] to 5% [4,5] in blunt abdominal trauma, and from 1 to 12% in penetrating abdominal trauma [1–6].

The common mechanisms of blunt pancreatic trauma are motor vehicle accidents (steering wheel and seat belt impact injuries) in adults, and impact due to bicycle handlebar injuries in children [7,8].

Other mechanisms include fall of heavy objects over the abdomen, fall from height, and direct blunt assault to the abdomen [7–10].

Classifications

The American Association for the Surgery of Trauma (AAST) scale for pancreatic injuries was introduced in 1990 [11], and this scale is the most used grading system [11,12] (Table 1).

The AAST scale emphasizes the importance of injury to the head and to Wirsung's duct. Because of its simplicity and correlation with treatment, this scale represents a valuable tool for the management of and decision-making related to pancreatic trauma. According to the AAST scale, grade I and II injuries (representing 60 and 20% of all pancreatic injuries, respectively) are generally managed by conservative treatment, whereas grades III, IV, and V typically require surgical treatment [12]. Other grading systems for pancreatic injuries include the Lucas and the Frey and Waddell classifications. Although these systems have been adopted in the past, they have more recently been nearly completely abandoned [11].

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Serious sequelae may follow if the magnitude of the pancreatic injury is underestimated or inappropriately treated [14,15].

Traumatic pancreatic injuries are characterized by high morbidity and mortality rates [1]. The morbidity rates range from 30 to 40%, and morbidity is primarily related to injuries to other associated organs. Major pancreatic-related complications include acute necrotic hemorrhagic pancreatitis (15%), pseudocysts (9%), abscesses (6%), and fistulas (4%) [1,16]. Early mortality is most commonly due to uncontrolled bleeding from large visceral veins in close proximity to the pancreas or major injuries to the nearby solid organs [16,17]. Late mortality is generally due to infection or multiple organ failure. Neglect of a major ductal injury with retroperitoneal extravasation of pancreatic enzymes predisposes to delayed local complications [17].

Patients and methods

Patient selection

This study was carried out in Zagazig University Hospital's Trauma Unit over a period of 3 years between June 2013 and June 2016. This work was approved by the IRB/Ethics Committee in Faculty of Medicine Zagazig University. Seventeen patients were diagnosed with pancreatic injury based on the computed tomography (CT) scan or surgical findings. Among the patients with abdominal trauma, patients with penetrating injury, duodenal injury, grade IV pancreatic or major duct injury, uremia, liver cell failure, advanced cardiac disease were excluded; immunocompromised and pediatric patients were also excluded.

Management strategy

The management guideline for trauma patients in our hospital entails resuscitation according to the Advanced Trauma Life Support measures, maintaining a blood pressure of above 90/60 with intravenous fluids, with or without blood transfusion, and/or medications support and dealing with the cases according to those priorities that patients with hemodynamic instability are dealt with. According to the cause, patients with severe solid organ injury, gas under diaphragm, peritonitis, and marked internal hemorrhage underwent surgical exploration; patients with pancreatic injury were managed according to the case. We applied continuous saline lavage and drainage of the peritoneal cavity for 1 week (Berger's lavage) and hemostatic synthetic sealant materials were applied to the surface of the pancreas when needed. Hemodynamically stable patients diagnosed by CT underwent conservative measures. All pancreatic injuries were graded using the AAST classification, based predominantly on CT imaging, or operative findings in patients diagnosed on abdominal exploration. Pancreatic injury grades are changed if intraoperative findings were inconsistent with CT imaging.

All patients underwent clinical, laboratory, and ultrasound of the abdomen; CT scan follow-up, and magnetic resonance cholangiopancreatography (if needed) were arranged for further evaluation.

Admission data, laboratory, and radiological investigations, management outcome, follow-up data for the following 6 months are collected and analyzed, with a detailed review of all medical records to determine the occurrence of late pancreas-specific complications.

Results

Of the 17 patients of this study, nine were diagnosed during abdominal exploration of hemodynamically unstable patients, and eight were diagnosed after CT examination in hemodynamically stable patients.

Demographic distribution and cause of injury

Thirteen male patients and four female patients, age ranged between 11 and 48 years, mean±SD age of 28.2±10.1 years, trauma caused by road traffic accident in 13 patients, fall from height in three patients and handlebar bicycle injury in one patient as shown in Table 2.

Anatomical site and grade of injury, associated injuries

Of the eight hemodynamically stable patients, diagnosed by CT we got grade I; three patients with isolated pancreatic injury, with mild contusion. Grade II: four patients, two patients with body and tail contusion one associated with splenic hematoma and the other left renal subcapsular hematoma; and two

Table 1 Pancreatic organ injury scale: American Association for the Surgery of Trauma [13]

Grades	Injury description
I	Hematoma – minor contusion without duct injuryLaceration – superficial laceration without duct injury
II	Hematoma – major contusion without duct injury or tissue lossLaceration – major laceration without duct injury or tissue loss
III	Laceration – distal transection or parenchymal injury with duct injury
IV	Laceration – proximal transection or parenchymal injury involving the ampulla
V	Laceration – massive disruption of the pancreatic head

patients with laceration and mild internal hemorrhage without duct injury. Grade III, one patient with complete transection of the body with splenic hematoma and subcapsular hematoma of the liver (Table 3). Four of the nine patients diagnosed on exploration we got grade I, four patients; grade II, four patients; and grade III, one patient with bodytail contusion and distal duct injury, tail injured in 11 patients and body in six patients as shown in Table 3.

The spleen was injured in four patients, small intestine in two patients, colon in one patient, mesenteric vessels in two patients, upper extremity injury in two patients, brain edema in one patient (Table 4).

Table 2 General considerations

Characteristics	Number of patients
Male/female	13/4
Age (years)	
Range	11 : 48
Mean±SD	28.2±10.1
Cause of injury	
Road traffic accident	13
Fall from height	3
Handlebar injury	1

Table 3 Anatomical site and grade of injury

Characteristics	Number of patients
Grade	
I	7
II	8
III	2
Site	
Body	6
Tail	11

Table 4 Associated injuries

Associated injured organs	*N*
Spleen	6
Liver	1
Small intestine	2
Colon	1
Mesenteric vessels	2
Kidney	1
Extremities	2
Central nervous system	1

Management of hemodynamically stable patients diagnosed with computed tomography

Those patients who underwent conservative measures, the hospital stay ranged between 8 and 35 days with mean of 20.6±11.92. Grade I patients (three) passed uneventful admission course, grade II patients (four) with peripancreatic fluid underwent ultrasound-guided aspiration, one resolved completely and three of them needed insertion of pigtail catheter, two of the three developed pseudocyst formation and one developed pancreatic fistula which entailed endoscopic sphincterotomy and pancreatic duct stenting.

Grade III patient with pancreatic transection underwent distal pancreatectomy and superficial pancreatic necrosectomy, and splenectomy. Synthetic hemostatic sealant sheets (collagen hemostatic patches) were placed on the entire pancreatic surface and at the distal end. Copious peritoneal washing with saline was done. A large irrigation tube was placed over the pancreas and two drainage tubes in the bed and in the pelvis. Abdomen was closed *en mass*. The patient was shifted to the ICU where continuous irrigation and drainage was done for 1 week. Follow-up in ICU showed no pancreatic-related complications.

Management of hemodynamically unstable patients diagnosed on laparotomy

After proper resuscitation according to the guidelines the patients underwent laparotomy. Splenectomy was done in four patients; alone in two patients grade I, and with distal pancreatectomy in one patient grade II where hemostatic sealant sheets was applied to the cut end of pancreas, and in one patient grade III together with superficial pancreatic necrosectomy and application of hemostatic sealant sheets to the surface of pancreas.

Small intestinal injuries were repaired in two cases, one of grade II and one of grade I, both of which were successful.

Transverse colon repair was done without diversion in one patient of grade I, who had an uneventful course.

Ligation of bleeding omental vessels were done in two patients of grade II; one of them developed a pseudocyst.

As a rule, in our study we inserted tube drains into the pelvis and peritoneal cavity irrigation tube was inserted over the pancreas, maintaining continuous saline lavage (Berger's lavage) in all patients for 1 week.

The hospital stay ranged between 9 and 42 days with mean of 23±12.13.

Morbidity and mortality

During the admission period, and follow up in the next 6 months, no mortalities occurred in the

Table 5 Management scheme and complication rate in all patients

Grade	Total number	Operative management				Nonoperative management				
		Drainage	Pancreatectomy	Complications		No intervention	Ultrasound-guided	Endoscopic	Complications	
				Fistula	Pseudocyst				Fistula	Pseudocyst
I	7	4	0	0	0	3	0	0	0	0
II	8	3	1	0	1	0	4	1	1	2
III	2	0	2	0	0	0	0	0	0	0

17 patients, but complications do exist; in the patients managed conservatively seven patients were detected: two cases of pancreatic pseudocyst managed by operative cystogastrostomy and one case of pancreatic fistula that needed stenting of pancreatic duct.

In the operated group (10 patients), one patient developed a pancreatic pseudocyst as shown in Table 5.

Discussion

The demographic distribution of the study patients agrees with most of the other studies [2,16], the cause of injury in our study is mostly due to road traffic accident, followed by falling from height and one case caused by bicycle handlebar injury; the differences between other studies may be due to case selection of this study as the early stages only were selected for this study.

Among the 17 patients we got grade distribution I, II, III as 8, 7, 2, respectively. The percentage of degrees of injury agrees with some studies [16,17]; if there is difference, it may be due to the study design for early grades. Tail is more injured in our study because the head injuries are more associated with major duct injury grade IV, which is excluded from the study.

Regarding patient management, the nonoperative management group showed average hospital stay and rate of complications as compared with other studies. Endoscopic sphincterotomy and stenting of pancreatic duct were used to manage pancreatic fistula and cystogastrostomy was done for the patients with pancreatic pseudocysts.

The operative management group (10 patients; four grade I, four grade II, and two grade III) showed average hospital stay time and a good rate of complications. In comparison to other studies especially in grade III patients [15], this is due to the use of continuous saline lavage as it helps in the dilution of the exudated pancreatic enzymes and facilitates drainage. The use of synthetic hemostatic sealant sheets in grade III patients helps decrease the exudation of pancreatic fluid in the peritoneal cavity.

Conclusion

Nonoperative management should be applied to noncomplicated grade I and II pancreatic injuries; operative management should be applied for the higher grades and for complicated grade I and II injuries, the use of continuous saline lavage and drainage of peritoneal cavity help decrease the rate of complications.

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Conflicts of interest

There are no conflicts of interest.

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Surgical management of gynecomastia: choice and outcome

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Background
Gynecomastia is defined as a male breast benign condition that is characterized by enlargement of the breast owing to glandular tissue proliferation. The cause of gynecomastia includes an imbalance between estrogen and testosterone levels in male breast tissue. The primary mechanism is production of more estrogen, reduction of production of androgen, and increased peripheral conversion to estrogen from estrogen precursors.
Patients and methods
A total of 35 male patients who presented with unilateral or bilateral gynecomastia (63 breasts) in the duration between June 2014 and June 2017 were assessed and surgically treated. All our patients were healthy except for one patient who had liver cirrhosis and two diabetic patients. Different surgical procedures were used to remove the excess skin and glandular tissue including lateral circumareolar incision, round block technique, reduction mammoplasty, liposuction, or combination of these procedures.
Results
The commonest procedure used was round block technique. A total of four cases had complications in the form of hematoma in one case, seroma in one case, skin infection in one case, and skin necrosis in another case.
Conclusion
Surgical correction of gynecomastia is the only hope for correction of gynecomastia in symptomatic patients.

Keywords:
gynecomastia, male breast, mammoplasty, round block

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Background

Gynecomastia is defined as a male breast benign condition that is characterized by enlargement of the breast owing to glandular tissue proliferation [1]. The cause of gynecomastia includes an imbalance between estrogen and testosterone in male breast tissue [2]. The primary mechanism is production of more estrogen, reduction of production of androgen, and increased peripheral conversion to estrogen from estrogen precursors [3]. Physiologic gynecomastia is the most common cause, which occurs mainly during the adolescent period. Overall, 85–90% of pubertal gynecomastia cases regress within 6 months to 2 years but some may persist till adulthood [4]. The condition may develop because of obesity, consumption of estrogens, anabolic steroids, or H2 blockers such as cimetidine [5]. Gynecomastia is characterized clinically by increase in the areolar diameter, breast swelling, deformation in the appearance of the male thorax, abnormal presence of an inframammary fold, skin ptosis with the nipple–areola complex sliding down to the height of the fold or even below it, and asymmetry [6]. Gynecomastia can be classified by different methods, but the most common is Simon's classification: grade 1, mild enlargement and no skin excess; grade 2a, moderate enlargement and no skin excess; grade 2b, moderate enlargement with excess skin; and grade 3, marked enlargement with more skin increase and severe ptosis [7]. If a cause is identified, its treatment may result in regression of gynecomastia. If gynecomastia is progressive and does not respond to other treatments, surgical therapy is indicated. There are multiple surgical procedures, including removal of the excessive glandular tissue and skin by subcutaneous mastectomy, breast reduction, liposuction, round block suture, or a combination of these techniques [6,8].

The aim of the work was to assess the different surgical techniques to treat nonregressing cases of gynecomastia.

Patients and methods

A total of 35 male patients who presented with unilateral or bilateral gynecomastia (63 breasts) in the duration between June 2014 and June 2017 were

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assessed and surgically treated. The study was approved by ethical committee of in Surgical department of Alexandria Faculty of Medicine. All our patients were healthy except for one patient who had liver cirrhosis and two diabetic patients.

Surgical procedures

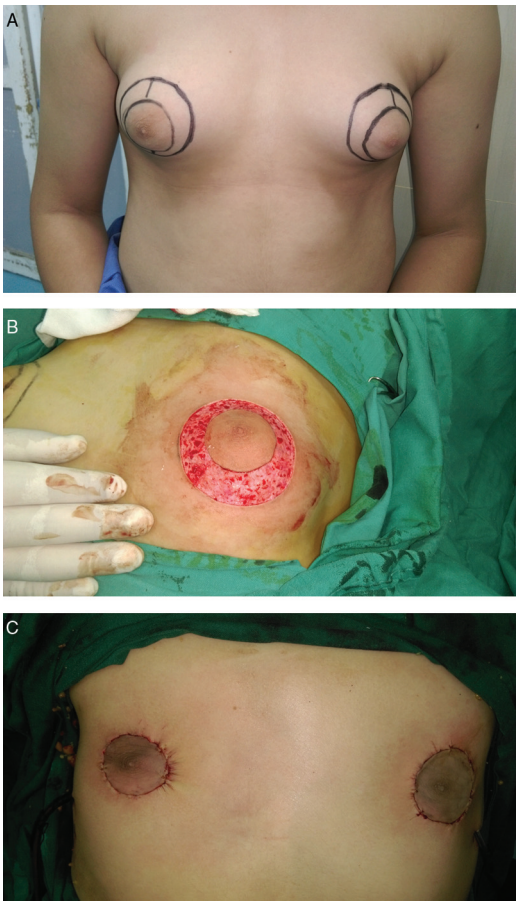
All patients were treated under general anesthesia. Concentric topography-type marks centered on the most prominent portion of the breast in the upright sitting position were made preoperatively. The inframammary fold, breast boundary, and planned incision sites were drawn on each breast. According to the grade of gynecomastia, a surgical procedure was done. For grade I, lateral circumareolar incision was done and the glandular disc was removed.

Round block technique (Fig. 1a–c) was the commonly used surgical procedure, and it involves de-epithelialization of the circumareolar skin according to the redundancy of skin followed by lateral incision between 6 and 12 o'clock position without reaching the midline. Dissection and excision of the glandular tissue was done through that incision with good hemostasis. Closure was done by approximation of the skin edges by absorbable suture material. We used to put suction drain after the procedure, which was removed on the third to sixth days according to the drained amount in 24 h.

Liposuction (Fig. 2a and b) was applied to cases where there was no increase in the glandular tissue but the fatty tissue.

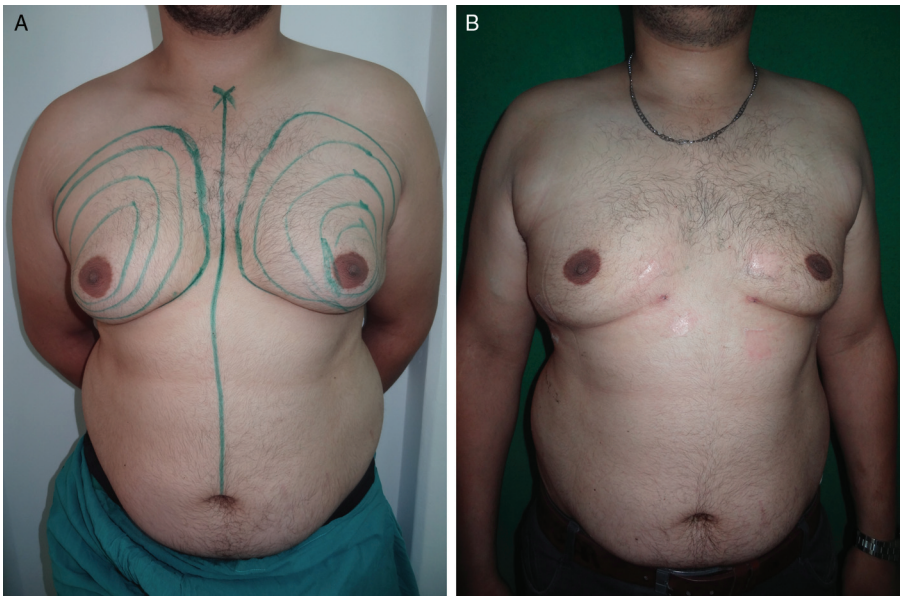
Superior pedicle reduction mammoplasty (Fig. 3a and b) was done to patients with grade III gynecomastia in whom the breast redundancy simulates the female breast.

Figure 1



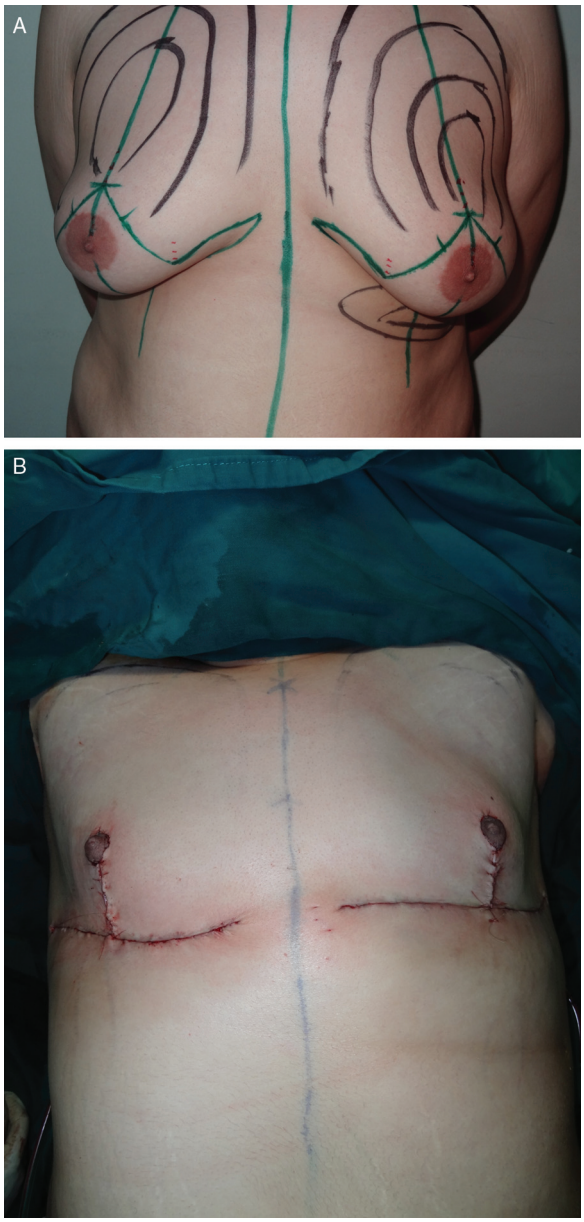
Round block technique for management of gynecomastia. A: Preoperative marking. B: Intraoperative de-epithelialization of peri-areolar skin. C: Immediate postoperative.

Figure 2



Liposuction for management of gynecomastia. A: Preoperative marking. B: Postoperative.

Figure 3



Superior pedicle reduction mammoplasty for management of gynecomastia. A: Preoperative marking. B: Immediate postoperative.

Combination of two procedures as liposuction and round block techniques may be needed in some cases with redundant skin and increased fat and glandular tissues (Fig. 4a–c).

Results

Most of our patients had bilateral gynecomastia (80%), most of them had grade II disease, and round block technique was the most commonly done surgical procedure (68.6%) (Table 1).

Postoperative complications were associated more with comorbid diseases. Complications were encountered in four cases in the form of seroma in one patient who was diagnosed to have liver cirrhosis. Diabetes mellitus was associated with wound infection in one case and skin necrosis in another patient. Hematoma was encountered in one patient after liposuction (Table 2).

Table 1 Distribution of the studied cases according to different parameters (*n*=35)

Age (years)	25.4±6.9
≤20	10 (28.6)
20–30	18 (51.4)
>30	7 (20.0)
Side	
Unilateral	7 (20.0)
Bilateral	28 (80.0)
Technique	
Lateral circumareolar	2 (5.7)
Liposuction	6 (17.1)
Round block	27 (77.1)
Liposuction and round block	3 (8.6)
Superior pedicle reduction mammoplasty	3 (8.6)
Comorbid disease	
No	32 (91.4)
HCV	1 (2.9)
DM	2 (5.7)
Complications	4 (11.4)
Pathology	
Primary	34 (97.1)
Secondary	1 (2.9)
Grades	
I	2 (5.7)
II	18 (51.4)
III	15 (42.9)

Qualitative data were described using number and percentage, whereas normally quantitative data were expressed in mean±SD. DM, diabetes mellitus; HCV, hepatitis C virus.

Discussion

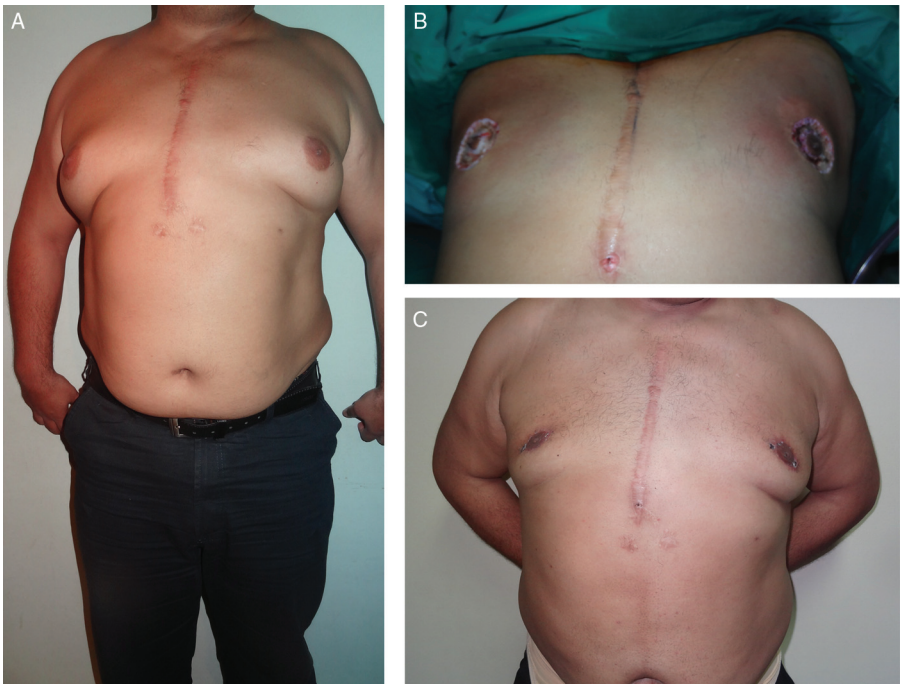
Gynecomastia is a benign breast disease that may affect men of all ages. It is caused by different degrees of proliferation of the glandular tissue, which differs from pseudogynecomastia in which there is an increase in the fatty tissues in obese men [9]. Most cases are caused by hormonal imbalance between estrogen and androgen, and this may occur with increased estrogen action or decreased androgen action [10–12]. Medical treatment of gynecomastia is controversial, and actually there is no consensus about the proper drug and its duration [13,14]. We performed different techniques for surgical management of symptomatic patients. The choice of the surgical procedure depended on the presence of excess skin and abundant glandular tissue. In symptomatic grade I cases, we adopted to do lateral circumareolar incision to remove the small

Table 2 Relation between complications and grade, technique, and comorbid disease

	Total	Complications		*P*
		No (*n*=31)	Yes (*n*=4)	
Grades				
I	2(5.7)	2 (6.5)	0 (0)	1.000
II	18 (51.4)	16 (51.6)	2 (50)	
III	15 (42.9)	13 (41.9)	2 (50)	
Technique				
Lateral circumareolar	2 (5.7)	2 (6.5)	0 (0)	1.000
Liposuction	6 (17.1)	5 (16.1)	1 (25)	0.546
Round block	27 (77.1)	24 (77.4)	3 (75)	1.000
Liposuction and Round block	3 (8.6)	3 (9.7)	0 (0)	1.000
Superior pedicle reduction mammoplasty	3 (8.6)	3 (9.7)	0 (0)	1.000
Comorbid disease				
No	32 (91.4)	31 (100)	1 (25)	0.001*
HCV	1 (2.9)	0 (0)	1 (25)	
DM	2 (5.7)	0 (0)	2 (50)	

Qualitative data were described using number and percentage. DM, diabetes mellitus; HCV, hepatitis C virus. *$P \leq 0.05$, statistically significant.

Figure 4



Combination of liposuction and round block techniques for management of gynecomastia. A: Preoperative picture. B: Intraoperative after liposuction and de-epithelialization of the peri-areolar skin. C: One week after surgery.

retroareolar glandular disc with minimal scarring and good cosmetic appearance. Other surgical procedures were used with excess skin. Excess skin was either de-epithelialized in round block technique, which was the procedure of choice for grade II gynecomastia, or removed in mammoplasty technique for cases with severe ptosis simulating female breast. These procedures enabled us to remove the excess skin and excess glandular tissue with little complication rate, which was related to comorbid diseases such as diabetes mellitus and liver cirrhosis. Liposuction alone was done in cases with excess fatty tissue.

Conclusion

The gold standard for correction of gynecomastia is surgical excision of the glandular tissue and excess skin. Different surgical procedures are available, all aiming at subcutaneous mastectomy with removal of the excess skin. Lateral circumareolar incision is indicated for grade I gynecomastia in which there is no need to

remove excess skin. For grade II, round block technique is optimum with de-epithelialization of the excess skin. In grade III, combined techniques are required, or reduction mammoplasty is done in severe cases.

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Conflicts of interest
There are no conflicts of interest.

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Combined liver resection and transarterial chemoembolization versus liver resection alone for the management of solitary large exophytic hepatocellular carcinoma with extrahepatic arterial supply: is two always better than one?

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Purpose
Does the control of extrahepatic arterial feeders with preoperative transarterial chemoembolization (TACE) in large exophytic hepatocellular carcinoma improve surgical and oncological outcomes compared with surgery alone?
Patients and methods
A total of 545 patients were assessed for eligibility, and 108 patients fulfilled the inclusion criteria and were assigned to either upfront surgery (group I) or surgery after TACE (group II).
Results
Patients in both groups had no significant difference with respect to age (P=0.573), sex (P=0.464), α-fetoprotein (P=0.313), American Society of Anesthesiologists score (P=0.820), and Child–Pugh score (P=0.577). The mean tumor size was comparable (9.8±2.2 cm in group I vs. 10.3±2.3 cm in group II, P=0.265). In group I, four patients underwent major hepatectomy, whereas 48 patients underwent minor hepatectomy. In group II, 54 patients underwent 121 TACE sessions with a mean of number of 2±0.8 session (range: 1–4 sessions). The mean interval between first TACE and surgery was 45±10.7 days (range: 12–72 days). Surgery after TACE had significantly higher rate of perihepatic adhesions (P=0.006), longer operative time ($P<0.0001$), increased blood loss (P=0.035), and longer hospital stay (P=0.020) compared with upfront surgery but with comparable outcomes regarding in-hospital and 30-day morbidity (P=0.819). After a mean follow-up of 14.3±5.9 months, both groups had similar disease-free survival, with none of the tumors in both groups showed local recurrence. There was no significant difference in the type, time of recurrence following resection, or the mean numbers of new (de-novo) tumors detected in both groups (2.22±1.60 and 2.54±1.69 in groups I and II, respectively).
Conclusion
In patients with solitary large exophytic hepatocellular carcinoma, combined hepatic resection plus TACE is associated with increased perihepatic adhesions, increased operative time, blood loss, and postoperative hospital stay compared with liver resection alone. Preoperative TACE has no additional oncological benefit, with no reduction in recurrence rate or improvement in disease-free survival.

Keywords:
exophytic hepatocellular carcinoma, extrahepatic feeders, large solitary hepatocellular carcinoma, neoadjuvant transarterial chemoembolization

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Introduction

Hepatic resection is currently recommended for solitary hepatocellular carcinoma (HCC) less than 5 cm in size in patients with well-preserved liver function without significant portal hypertension and major vascular or lymphatic invasion [1]. Published literature has reported outcomes of surgical resection for solitary large HCC (beyond 5 cm) to be similar to those of solitary small HCCs less than 5 cm [2]. Most HCC arises on top of liver cirrhosis with a poor hepatic functional reserve, and it is frequently multicentric; therefore, transarterial chemoembolization (TACE) has an established role mounting to first-line treatment of unresectable HCC, aiming at either palliation or improving survival [3–5]. Its role in management of resectable HCC is still controversial. The main rationale behind using TACE preoperatively as a neoadjuvant therapy in patients with resectable HCC is to decrease incidence of recurrence and improve disease-free survival. However, published literature contains numerous studies reporting

conflicting data, with some studies demonstrating improved survival with reduced recurrence rate [6–8], whereas others have failed to show any significant survival benefit [9–12] to the extent of reporting a reduction in long-term survival rates [12,13]. Therefore, it remains uncertain whether preoperative TACE has positive or negative effect on patients with resectable HCC, taking in consideration the wide spectrum of patients included under the term 'resectable HCC' regarding to size, number, location, growth pattern, multiplicity, Child score, and liver reserve.

An extrahepatic collateral pathway to the liver is established in various conditions [14–16]. It mainly develops after interruption of the hepatic artery by surgical ligation, arterial injury induced by repeat TACE, or placement of a catheter. Not infrequently, an extrahepatic blood supply to HCC also develops in the anatomic location of HCC, even when the hepatic artery is patent [15,17–21]. This is very commonly encountered in exophytic HCC [21,22]. Adhesion between the liver and other organs exaggerates the degree of extrahepatic collaterals [14–16,23]. Besides the surface location of the tumor as a prerequisite for the formation of the parasitic feeders, the size of the tumor when above 6 cm in maximum diameter has a high prevalence for such condition [21,22,24]. The presence of extrahepatic feeders may be of an oncological concern because of a chance of tumor spread to surrounding neighbor structures. Manipulation of the tumor during surgery before the control of those collaterals may increase the chance of tumor spread. Preoperative control of these collaterals through TACE may obviate this risk. For transcatheter management of HCC to be effective, these collaterals should be adequately embolized [15,17–20,25–30].

The aim of this study was to compare prospectively the surgical and oncological outcomes of combined hepatic resection and TACE versus surgical resection alone in the management of solitary large exophytic HCC with extrahepatic collateral arterial supply in Child A cirrhotic patients.

Patients and methods

The study was conducted at the Surgery Department, Main University Hospital, which is a 1000-bed teaching hospital and a tertiary referral center serving a community of four million people. The Ethics Committee and review board in our institute approved the study and treatment protocol. An informed consent was obtained from all patients who agreed to participate in the study.

Between January 2015 and July 2017, all patients with solitary HCC were assessed for eligibility. Inclusion criteria were patients with Child A cirrhosis presenting with solitary HCC equal or more than 7 cm, exhibiting an exophytic growth pattern with at least one extrahepatic collateral artery detected on initial dynamic abdominal computed tomography (CT) scan. Exclusion criteria were patients with an American Society of Anesthesiologists (ASA) score exceeding 3, a decompensated liver cirrhosis (Child B or C), esophageal varices grade greater than 2, a platelet count less than 80×10^9/l, previous upper abdominal surgeries, previous treatment for HCC with TACE or other intervention, occlusion of hepatic artery or celiac trunk, presence of portal vein thrombosis, macroscopic vascular invasion, and distant metastases.

A total of 545 consecutive patients were assessed for eligibility. Of them, 101 patients refused to participate in the study, whereas 336 patients did not fit to the inclusion criteria or had an exclusion criterion. Therefore, 108 patients were enrolled in the study. The diagnosis of HCC was based on the characteristic dynamic abdominal CT or MRI findings and elevation of the α-fetoprotein (AFP) level (>400 ng/ml). Biopsy was not performed to confirm the diagnosis of HCC. All patients with HCC were discussed at a weekly multidisciplinary team conference consisting of hepatopancreaticobiliary surgeons, hepatologists, interventional radiologists, and medical and radiation oncologists. After consent from each patient, 54 patients were assigned to group I (upfront surgery), and 54 patients to group II (surgery after TACE) using closed sealed envelopes that were opened in order when assignments were made. An independent observer managed patients' allocation in either group. The allocated treatment was performed within 96 h. The same experienced team of hepatobiliary surgeons and intervention radiologists performed all procedures in both groups.

The following clinical data and treatment outcome in the two groups was recorded and compared: clinicopathological factors including age, sex, BMI, ASA grade, hepatitis serology, and esophageal varices and preintervention laboratory data including AFP level, tumor size (recorded as the maximum diameter in at least one dimension), location, surgical margin status, microscopic vascular invasion, and histological grade as defined by Edmondson and Steiner [31].

All patients had dedicated dynamic abdominal CT study for assessment of number, extent, and size of the tumor with proper delineation of the hepatic and extrahepatic arterial collateral feeder to the tumor and exclusion of any macrovascular tumor invasion. The scans were read thoroughly as source two-dimensional images, maximum intensity projection images, and three-dimensional images. The origin and course of the main hepatic artery was identified, whether classical or replaced, as well as any accessory hepatic arteries. A thorough search for possible extrahepatic arterial feeders was performed, taking in consideration the hepatic segment involvement by the exophytic large HCC. The following arteries were well traced to identify possible feeder collateral arteries:

(1) The right inferior phrenic artery in exophytic HCC within segment VII/VIII, which would appear on CT as passing nearby or toward the lesion and could be rather prominent and dilated compared with the other side.
(2) The left gastric artery in exohytic HCC of segments II/III of the left lobe.
(3) The right renal or adrenal arteries in exophytic tumors of segments VI/VII.
(4) Near totally exophytic and contacting the omental fat, feeders from the gastroduodenal and superior mesenteric arcades are usually encountered and also from the gastroepiploic arteries.
(5) Intercostal and internal mammary parasitic feeders are less commonly found when the tumor is at the most anterosuperior portion of segments IVa/VIII or in contact with the right lateral thoracic/abdominal wall, respectively.
(6) Moreover, much more rare are the lumbar arteries and usually are seen giving feeding twigs in advanced cases.

Transarterial chemoembolization

TACE was done for all group II patients using the super selective technique. According to the findings, dynamic CT done before the procedure, and a selective angiogram of the celiac trunk was performed with subsequent cannulation of the hepatic artery after the subtraction angiogram of the main hepatic artery (to be sure that there is no double right and left hepatic supply to the mass). A super selective angiogram of the segmental hepatic artery giving the feeder to the HCC mass lesion was performed and looking for the blush of contrast staining the mass whether it is completely covering its volume or there is a defect of staining of the contrast blush within the mass. If this defect is evident, then we put in consideration that there will be more work to be done after managing the main hepatic feeder supplying the mass as there will be definitely another extrahepatic arterial feeder to manage. In some cases, the digital subtraction angiogram was supplemented with a contrast-enhanced cone-beam CT acquisition to verify all arterial feeding vessels in rotatory maximum intensity projection and three-dimensional pattern, as an option in the angiography device. We start first cannulating the subsegmental main arterial hepatic feeder in a super selective approach using hydrophilic microcatheter (Progreat; Terumo Medical Corportaion, Tokyo, Japan), and when satisfied by our location after testing with contrast, we inject the drug mixture of iodized oil (Lipiodol; Andret Gurbet, Paris, France) and 50 ml of doxorubicin hydrochloride emulsion. We inject first a diluted amount followed by a concentrated amount until evident arterial flow stasis occurs, then we inject absorbable gelatin sponge particles (0.5–1 mm; gelfoam) soaked in 2–3 ml of the contrast to block the artery. Thereafter, we perform another digital subtraction angiography to identify the site of the residual part of the lesion not having the radiopaque particle of the lipiodol mixture and that will be corresponding to the staining defect of contrast seen in the first subtraction angiogram done before drug mixture injection. According to the anatomical segment of the lesion and the location of the residual active part, the nearby parasitic feeder will be cannulated. A subraction angiogram will be performed till stasis of the drug mixture followed by blockage using gelfoam. We defined technical success as successful catheterization into the tumor-feeding branch of extrahepatic collaterals and delivery of TACE using injected particles. Follow-up dynamic triphasic CT was requested 1 month after the session to assess the efficacy of the treatment and to exclude any residual viable tumor. Another session of embolization was performed if viable tumor was identified. Complications related to collateral TACE were recorded and analyzed by laboratory tests and CT findings, in addition to post-TACE symptoms.

Hepatic resection

The same surgical team with at least 10 years of experience in liver resection performed all the surgical procedures in group I and group II under general anesthesia. CT volumetric assessment of the residual liver volume was ensured to be more than 40% in all patients. Anatomical hepatectomy based on inflowing vessels was used as a general method for the hepatic resection; however, nonanatomical resections were resorted to if anatomical resection would leave the patient with residual liver volume of less than 40%.

All patients were treated with curative intent aiming at achieving R0 resection. The surgical resection margins were planned at least 1–2 cm from the edge of the tumor. Parenchymal transection was performed using either Cavitron Ultrasonic Surgical Aspirator (CUSA) combined with harmonic scalpel or using radiofrequency-assisted technique. When necessary, the liver pedicle was intermittently clamped in cycles of 10–15 min with 3–5 min of reperfusion. Data recorded included operative and postoperative details (operative time, resection time, need for Pringle maneuver, amount of blood loss, transfusion requirement intraoperatively and postoperatively, ICU admission, duration of hospital stay, postoperative complications, and 30-day mortality). Specific complications were those related to the liver resection procedure or the underlying liver disease and included the following: bile leak, operative site hemorrhage, ascites (defined as clinically detectable or as abdominal drainage output, when present, of 500 ml or more per day), hepatic encephalopathy, jaundice, and variceal bleeding. Other complications were recorded as nonspecific complications.

Postintervention morbidity and mortality were defined as events occurring during the same hospital stay or within 3 months of allocated intervention and was graded following the Dindo–Clavien classification [32]. Postprocedure mortality was defined as any death within 30 days after the procedure was performed. Treatment-related death was defined when patients died directly owing to treatment-related complications that developed within 1 week of treatments.

Follow-up, survival, and recurrence

After discharge, patients were regularly scheduled for follow-up outpatient visit and monitored with a standard oncologic protocol, which included liver function tests, AFP, and liver imaging with triple-phasic multi-slice CT and/or MRI at 1 month and then every 3 months during the first 2 years and then every 6 months thereafter for any intrahepatic recurrence together with annual chest radiography, and CT scan, bone scan for distant metastasis.

Local recurrence was defined as recurrence at surgical resection bed after R0 resection was histopathologically proven or at the local site of previously embolized HCC. Intrahepatic distant recurrence was defined when new tumor growth that met the previously mentioned criteria for diagnosing HCC appeared remote from the previously managed HCC. Extrahepatic metastasis refers to any recurrence outside the liver. All recurrences were recorded in the database immediately after confirmation of the diagnosis, and the site, number, and size of recurrent tumors were documented.

Statistical analysis

The raw data were coded and entered into SPSS system files (SPSS package version 18; SPSS Inc., Chicago, Illinois, USA). Analysis and interpretation of data were conducted. The following statistical measures were used: descriptive statistics including frequency, distribution, mean, median, SD, and interquartile range were used to describe different characteristics. Kolmogorov–Smirnov test was used to examine the normality of data distribution. Univariate analyses including *t*-test, analysis of variance test, Mann–Whitney test and Kruskal–Wallis test and Tamhane post-hoc test were used to test the significance of results of quantitative variables. χ^2-test or its correction namely Monte–Carlo test and Fisher's exact test were used to test the significance of results of qualitative variables. The significance of the results was at the 5% level of significance.

Results

A total of 108 patients with exophytic solitary large HCC greater than 7 cm with at least one collateral extrahepatic arterial supply documented in preassessment dynamic abdominal CT scan were included in the study. Of them, 54 patients underwent surgical resection (upfront surgery group), whereas 54 patients underwent TACE (surgery after TACE group). The baseline demographic and clinicopathological characteristics of the two groups of patients are listed and compared in Table 1. There was no statistical significant difference between both groups with respect to age (P=0.573), sex (P=0.464), or preprocedure laboratory tests, including AST (P=0.282), total bilirubin (P=0.262), AFP (P=0.313), ASA score (P=0.820), and Child–Pugh score (P=0.577). TACE group had a significantly higher BMI (29.4±2.6 vs. 28.4±2.5, P=0.029) than surgery upfront group, whereas the latter had a significantly higher alanine aminotransferase levels than TACE group (P=0.007) as illustrated in Table 1. The most common cause of cirrhosis in both groups was hepatitis C virus infection (90 and 94% in surgery upfront and TACE group, respectively, P=0.508). The mean tumor size in surgery upfront group was 9.8±2.2 (range: 7.2–15.6 cm) versus 10.3±2.3 (range: 7.0–15.5 cm) in surgery after TACE group, with no significant difference (P=0.265).

In surgery upfront group, all patients underwent hepatic resection as shown in Table 2. Major hepatectomy was performed in six patients, whereas 48 patients underwent

Table 1 Baseline demographic and clinicopathological characteristics of the patients in the two groups

Personal characteristics	Upfront surgery group (*n*=54) [*n* (%)]	Surgery after TACE group (*n*=54) [*n* (%)]	Significance
Age (years)			
Minimum–maximum	39.0–64.0	28.0–65.0	*t*=0.565
Mean±SD	52.4±6.5	51.7±7.4	*P*=0.573
Sex			
Male	25 (46.3)	21 (38.9)	χ^2=0.536
Female	29 (53.7)	33 (61.1)	*P*=0.464
BMI			
Minimum–maximum	22.0–34.0	23.0–36.0	*t*=2.206
Mean±SD	28.4±2.5	29.4±2.6	*P*=0.029*
ASA score			
II	44 (81.5)	45 (83.4)	χ^2=0.052
III	10 (18.5)	9 (16.6)	*P*=0.820
Cause of cirrhosis			
HCV	48 (88.2)	51 (94.4)	^{FE}P=0.508
Unknown	6 (11.1)	3 (5.6)	
Previous laparotomy			
No	47 (87.1)	50 (92.6)	χ^2=1.299
Yes	7 (12.9)	4 (7.4)	*P*=0.254
Bilirubin			
Minimum–maximum	0.6–1.2	0.7–1.2	*Z*=1.121
Median (Q1–Q3)	0.9 (0.8–1.0)	0.9 (0.8–1.1)	*P*=0.262
AST			
Minimum–maximum	58–178	45–125	*Z*=1.075
Median (Q1–Q3)	0.9 (0.8–0.9)	0.9 (0.7–0.9)	*P*=0.282
ALT			
Minimum–maximum	67–150	64–150	*Z*=2.680
Median (Q1–Q3)	99 (88–115)	88 (76–100)	*P*=0.007*
AFP			
Minimum–maximum	38–3880	38–3400	*Z*=1.009
Median (Q1–Q3)	670 (417–865)	600 (370–780)	*P*=0.313
Child score			
A5	33 (61.1)	36 (66.7)	χ^2=0.312
A6	21 (38.9)	18 (33.3)	*P*=0.577
Tumor size (cm)	7.2–15.6	7.0–15.5	*t*=1.120
Minimum–maximum	9.8±2.2	10.3±2.3	*P*=0.265
Median (Q1–Q3)	7.2–15.6	7.0–15.5	*t*=1.120

ASA, American Society of Anesthesiologists; AFP, α-fetoprotein; ALT, alanine transaminase; AST, aspartate transaminase ; ^{FE}P, Fisher's exact test; HCV, hepatitis C virus; TACE, transarterial chemoembolization. *$P \leq 0.05$, significant.

minor hepatectomy. In spite of the large size of HCCs, major hepatectomies constitutes only 11.1% of all hepatetcomies performed. Curative intent of resection was achieved through final histopathological examination of free resection margin (R0) in all patients with a mean of 1.7±0.5 cm (range: 0.7–3 cm). However, microvascular invasion was detected in 64.8% of tumors resected. The operative time ranged from 110 to 340 min (median: 162 min), with mean blood loss of 607.3 ±386.4 ml (range: 100–1600 ml). Overall, 12 (22.2%) patients required blood transfusion, and 21 (38.9%) patients stayed at least 1 day in ICU with median total postoperative hospital stay of 5 days (range: 3–7 days) as shown in Table 3.

In surgery after TACE group, 54 patients underwent 121 TACE sessions with a mean of number of 2±0.8 session (range: 1–4 sessions). After the initial session of TACE, no patients in TACE group achieved the technical success of full control of hepatic and extrahepatic feeders. The mean interval between first TACE and surgery was 45±10.7 days (range: 12–72 days). The most common complications were owing TACE toxicity itself manifested as fever, sense of fatigue, and right hypochondrial pain, with seldom anorexia nausea/vomiting. A number of complications were encountered during control of extrahepatic collaterals as shown in Table 4.

The comparison of surgical parameters and outcomes of surgery upfront group with surgery after TACE groups are illustrated in Table 2. Patients undergoing surgical resection after TACE experienced significantly higher rate of perihepatic adhesions (*P*=0.006) than upfront

Table 2 Operative characteristics of the studied patients subjected to upfront surgery and surgery after transarterial chemoembolization

Operative characteristics	Upfront surgery (*n*=54) [*n* (%)]	Surgery after TACE (*n*=54) [*n* (%)]	Significance
Type of hepatectomy			
Monosegmentectomy	6 (11.1)	5 (9.3)	χ^2=0.747
Nonanatomical	26 (48.2)	28 (51.9)	^{MC}P=0.949
Bisegmentectomy	10 (18.5)	8 (14.8)	
Right/left hepatectomy	6 (11.1)	5 (9.3)	
Left lateral segmentectomy	6 (11.1)	8 (14.8)	
Perihepatic adhesions			
No	37 (68.5)	23 (42.6)	χ^2=7.617
Yes	17 (31.5)	31 (57.4)	*P*=0.006*
Operative time (min)			
Minimum–maximum	110–340	123–350	*Z*=3.788
Median (Q1–Q3)	162.0 (145.8–180.0)	190.0 (170.0–230.0)	*P*<0.0001*
Blood loss (ml)			
Minimum–maximum	100–1600	190–1800	*t*=2.133
Mean±SD	607.3±386.4	763.7±368.5	*P*=0.035*
Intraoperative transfusion			
No	42 (77.8)	35 (64.8)	χ^2=2.570
Yes	12 (22.2)	19 (35.2)	*P*=0.109
Clamping			
No	51 (94.4)	50 (92.6)	^{FE}P=0.679
Yes	3 (5.6)	4 (7.4)	
Associated procedures			
No	48 (88.9)	45 (83.3)	χ^2=1.150
Yes	6 (11.1)	9 (16.7)	*P*=0.284
Cholecystectomy	6 (11.1)	7 (13.0)	
Hernia repair	0 (0.0)	2 (3.7)	
Histological grade			
Well differentiated	24 (44.4)	25 (46.3)	χ^2=0.046
Moderate differentiated	23 (42.6)	23 (42.6)	*P*=1.0
Poor differentiated	7 (13)	6 (11.1)	
Microvascular invasion			
No	19 (35.2)	20 (37.0)	χ^2=0.068
Yes	35 (64.8)	34 (63.0)	*P*=0.795
Resection margin			
Minimum–maximum	0.7–3.0	0.7–3.0	*t*=2.991
Mean±SD	1.7±0.5	2.0±0.6	*P*=0.003*

^{FE}P, Fisher's exact test; ^{MC}P, Monte–Carlo corrected *P* value; TACE, transarterial chemoembolization; *Z*, Mann–Whitney test. *$P \leq 0.05$, significant.

surgery group (31 vs. 17 patients, respectively). These adhesions were vascular, resulting in adhesion of embolized tumor to the surrounding structures and organs including stomach, colon, omentum, diaphragm, and gallbladder according to its respective location. Dissection of those adhesions resulted in significantly longer operative time in those patients ($P<0.0001$) with median of 190 min (range: 123–350 min) compared with 162 min (range: 110–340 min) in surgery upfront group. Consequently, a significantly higher mean amount of blood loss was recorded in those patients (763.7±368.5 vs. 607.3±386.4 ml, $P=0.035$) compared with surgery upfront group; however, this did not result in an increase rate of blood transfusion ($P=0.109$). Interestingly, there was no significant difference between the two surgery groups regarding the type and extent of surgical resection with similar rates of nonanatomical, major and minor anatomical hepatectomies ($^{MC}P=0.949$).

Using Clavien–Dindo classification to evaluate and compare the postoperative complications after liver resection in surgery upfront group versus surgery after TACE revealed comparable outcomes regarding in-hospital and 30-day morbidity ($P=0.819$). There were no differences in the perioperative morbidity and mortality rates for the two groups. In the surgery upfront group, 24 patients had a total of 43 complications, including bleeding ($n=2$), bile leak ($n=2$), ascites requiring treatment ($n=13$), hyperbilirubinemia ($n=4$), mild pleural effusion ($n=9$), wound infection ($n=3$), hematoma ($n=1$), chest

Table 3 Postoperative data, complications, and pattern of recurrence encountered among the studied patients subjected to upfront surgery and surgery after transarterial chemoembolization

Postoperative data and complications	Upfront surgery (*n*=54) [*n* (%)]	Surgery after TACE (*n*=54) [*n* (%)]	Significance
ICU stay			
No	33 (61.1)	29 (53.7)	χ^2=0.666
Yes	21 (38.9)	25 (46.3)	*P*=0.415
Duration of hospital stay (days)			
Minimum–maximum	3–7	3–9	*Z*=2.335
Median (Q1–Q3)	5 (4–5)	5 (4–6)	*P*=0.020*
Overall complications			
No	28 (53.8)	23 (42.5)	χ^2=1.810
Yes	24 (46.1)	31 (57.4)	*P*=0.178
Clavien–Dindo classification			
No complications	28 (53.8)	23 (42.6)	χ^2=1.612
Grade I	4 (7.7)	5 (9.3)	^{MC}P=0.819
Grade II	15 (28.8)	20 (37.0)	
Grade IIIa	1 (1.9)	2 (3.7)	
Grade IIIb	4 (7.7)	4 (7.4)	
Occurrence of bleeding			
No	50 (96.2)	51 (94.4)	^{FE}P=1.0
Yes	2 (3.8)	3 (5.6)	
Ascites			
No	39 (75.0)	36 (66.7)	χ^2=0.889
Yes	13 (25.0)	18 (33.3)	*P*=0.346
Liver failure			
No	52 (100.0)	53 (98.1)	^{FE}P=1.0
Yes	0 (0.0)	1 (1.9)	
Jaundice			
No	48 (92.3)	49 (90.7)	^{FE}P=1.0
Yes	4 (7.7)	5 (9.3)	
Encephalopathy			
No	52 (100.0)	53 (98.1)	^{FE}P=1.0
Yes	0 (0.0)	1 (1.9)	
Wound			
No	49 (94.2)	51 (94.4)	^{FE}P=1.0
Yes	3 (5.8)	3 (5.6)	
Chest			
No	47 (90.4)	48 (88.9)	χ^2=0.064
Yes	5 (9.6)	6 (11.1)	*P*=0.801
Bile leak			
No	50 (96.2)	51 (94.4)	^{FE}P=1.0
Yes	2 (3.8)	3 (5.6)	
Hematoma			
No	51 (98.1)	53 (98.1)	^{FE}P=1.0
Yes	1 (1.9)	1 (1.9)	
Pleural effusion			
No	43 (82.7)	43 (79.6)	χ^2=0.162
Yes	9 (17.3)	11 (20.4)	*P*=0.687
Incisional hernia			
No	48 (92.3)	50 (92.6)	^{FE}P=1.0
Yes	4 (7.7)	4 (7.4)	
30 days readmission			
No	52 (96.3)	50 (92.6)	^{FE}P=0.363
Yes	2 (3.7)	4 (7.4)	
Overall recurrence			
No	32 (59.2)	29 (53.7)	χ^2=0.446
Yes	22 (40.7)	25 (46.3)	*P*=0.504
Intrahepatic recurrence	22 (40.7)	25 (46.3)	*P*=0.504
Extrahepatic recurrence	5 (9.3)	3 (10.3)	^{FE}P=1.0
Time of recurrence			
<6 months	5/22 (22.7)	5/25 (20)	*P*=0.558
<12 months	9/22 (40.9)	14/25 (56)	*P*=0.286

^{FE}P, Fisher's exact test; TACE, transarterial chemoembolization; *Z*, Mann–Whitney test. *$P \leq 0.05$, significant.

Table 4 Complications after transarterial chemoembolization of extrahepatic collateral feeder to hepatocellular carcinoma in group II

	Number of TACE	Complications	*n* (%)
RIPA	34	Shoulder pain	32 (94)
		Pleural effusion	30 (88)
		Basal lung atelectasis	12 (35)
LIPA	9	Shoulder pain	6 (67)
		Pleural effusion	3 (33)
RGA	8	No	0 (0)
LGA	9	No	0 (0)
OA	16	Abdominal pain	10 (63)
AA	6	No	0 (0)
MCA	5	No	0 (0)
RIMA	4	Cutaneous pain, itching and skin discoloration	1 (25)
RICA	2	Itching, skin necrosis	1 (50)
LA	13	Paraplegia	1 (7.7)
CA	15	Acute cholecystitis	3 (20)
		Perforation	1 (6.6)
Total	121		

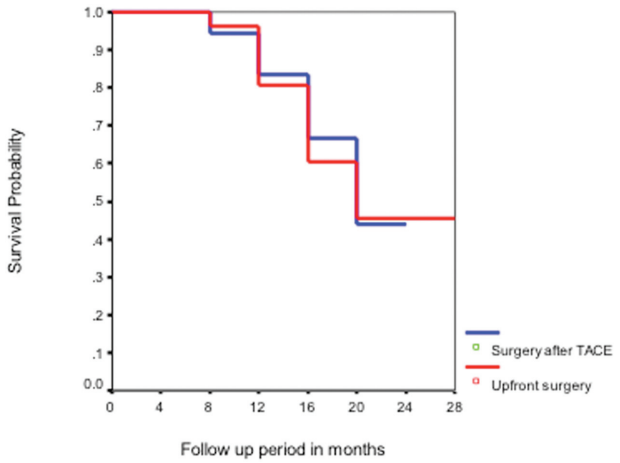
AA, adrenal artery; CA, cystic artery; LA, lumbar artery; LGA, left gastric artery; LIPA, left inferior phrenic artery; MCA, middle colic artery; OA, omental artery; RGA, right gastric artery; RICA, right intercostal artery; RIMA, right internal mammary artery; RIPA, right inferior phrenic artery; TACE, transarterial chemoembolization.

infection (*n*=5), and incisional hernia (*n*=4). In the surgery after TACE group, 31 patients had 56 complications, including bleeding (*n*=3), bile leak (*n*=3), ascites requiring treatment (*n*=18), hyperbilirubinemia (*n*=5), chest infection (*n*=6), hematoma (*n*=1), liver failure (*n*=1), pleural effusion (*n*=11),

encephalopathy (n=1), wound infection (n=3), and incisional hernia (n=4). Overall, 25/54 (46.3%) of patients in surgery after TACE required at least 1 day ICU stay compared with only 21/54 (38.9%) patients in upfront surgery group (P=0.217). Overall, upfront surgery group showed a statistically significant shorter duration of postoperative hospital stay compared with surgery after TACE subgroup (P=0.020). All cases in both groups achieved R0 resection on final histopathology, with no significant difference in incidence of microvascular invasion (P=0.795); however, patients who underwent surgery after TACE had statistically significant wider resection margin (2.0±0.6 vs. 1.7±0.5 mm) compared with surgery upfront group (P=0.003).

After a mean follow-up of 14.3±5.9 months (range: 2–24 months), none of the tumors in both groups showed local recurrence. No significant differences in the disease-free survival were noted between the upfront surgery and surgery after TACE groups (P=0.516) as shown in Fig. 1. During the follow-up period, 22 (40.7%) patients in surgery upfront group developed intrahepatic distant recurrence in comparison with 25 (46.3%) patients in the surgery after TACE group. There was no significant difference between the mean numbers of new (de-novo) tumors detected in surgery upfront (2.22±1.60) or surgery after TACE group (2.54±1.69; P=0.492). Moreover, the two groups showed no significant difference regarding type, and time of recurrence within 6 months or 1 year following resection (Table 4). None of the de-novo tumors had re-resection in either group. In the surgery upfront group, retreatment was performed in 22 patients, including RFA in 15 patients and TACE in seven. In the surgery after TACE group, recurrent tumors were treated by RFA (n=17) and TACE (n=5), whereas three patients could not be treated further because of poor liver function.

Figure 1



Kaplan–Meier plot showing the Disease free survival patterns for patients who were treated by either upfront surgery (blue line) or surgery after TACE (red line).

Discussion

The major drawback after curative hepatic resection of HCC is the high incidence of recurrence. The cumulative 5-year recurrence rate reported in literature is 75–100% [33]. Recurrence after curative resection is believed to originate through intrahepatic spread of the primary tumor or from de-novo multicenteric recurrence. Recurrences are usually classified into either intrahepatic (solitary or multiple) and extrahepatic recurrence [34] and according to time into early (<1 year) or late (>1 year) [35]. It was believed that early recurrences appeared to originate mainly from intrahepatic metastases, whereas late recurrences were likely to arise from a multicentric origin. The principle behind neoadjuvant TACE for resectable HCC is to decrease the tumor load by inducing necrosis to decrease the chance of metastases from the tumor after curative resection. For neoadjuvant TACE to fulfill its role, it should succeed in preventing extrahepatic metastases and decrease rate of early intrahepatic recurrence. In our study, this was not achieved, and no significant difference was observed in the pattern of recurrence or the recurrence time between the two groups. The control of extrahepatic collaterals with preoperative TACE did not have any oncological advantage in improving disease-free survival or reducing the recurrence rates, which might suggest that spillage of tumor cells during surgical manipulation might not be the main cause for HCC recurrence.

Published literature investigating clinical outcomes of surgery versus TACE for solitary large HCC yielded controversial results [2,36,37]. For resectable HCC, Zhang *et al.* [8] reported an improved disease-free survival after hepatctomy in patients having preoperative TACE in contrast to a retrospective study by Choi *et al.* [11] who reported that preoperative TACE did not significantly improve DFS or recurrence patterns after curative resection of HCC. In our study, and in accordance with the latter, there was no statistical significant difference between surgery alone (surgery upfront group) and resection after TACE in terms of the incidence (P=0.679) and type of recurrence, whether intrahepatic (P=0.679) or extrahepatic (^{FE}P=1.0). In agreement with published studies [9–12], preoperative

TACE did not improve the disease-free survival after curative resection of large exophytic HCC, and there was no clear added benefit of control of extrahepatic collaterals preoperatively.

In this study, upfront surgery group achieved 100% technical success with R0 resection in all cases, with no 30-day mortality. In spite of the large size of HCCs included in our study (mean: 9.8±2.2 cm, range: 7.2–15.6 cm), major liver resections were needed in only 11.1% of cases owing to the exophytic pattern of growth of those tumors. Technical difficulties were encountered in TACE group considering the wide spectrum of extrahepatic collateral arteries, and the selective angiography of individual collateral vessels was tedious, time consuming, and not possible to tackle all collateral feeders in one session of TACE. This interfered with effective control of the tumor. None of our patients in TACE group achieved full control of hepatic and extrahepatic feeders in a single session (mean: 2±0.8 session, range: 1–4 sessions). Failure of complete tumor control resulted from failure of control of extrahepatic feeders with the appearance of new feeders, which were technically impossible to embolize safely. As the number of TACE sessions increased, the cumulative probability of the development of de-novo extrahepatic collateral arteries also increased, owing to the neovascularity induced by ischemia together with hepatic artery attenuation resulting from repeated cannulation in sequential TACE procedures that potentially stimulate the development of parasitic supply to the peripheral zone of the corresponding liver parenchymal segment. These findings highlight the importance of the exophytic pattern of growth in large HCCs and its effect on the development of extrahepatic collateral feeders.

All of our HCCs were technically resectable, and patients who had liver resection after TACE showed a significant technical difficulty in the form of increased perihepatic adhesions (P=0.006*), which were vascular and led to a significant increase in the operative time and blood loss compared with those who had liver resection alone in (resection group). This finding is in agreement with a study by Luo *et al.* [38] who also demonstrated longer operative times (P<0.0001), more blood loss (763.7±368.5 vs. 607.3±386.4, P=0.035), and more postoperative abdominal drainage on comparing patients who had had received LR alone with those who had received TACE. Although abdominal drainage showed an increase in patients who underwent preoperative TACE, it did not reach a statistical significant value in our study. Patients who had surgery after TACE had a statistical significant longer duration of postoperative hospital stay compared with upfront surgery group. Interestingly, patients who underwent surgical resection after TACE did not show any significant difference regarding the type or extent of surgical resection compared with upfront surgery group, with similar rates of nonanatomical, major and minor anatomical hepatectomies (P=0.949) with no change of resection plan after TACE compared with pre-TACE findings. Preoperative TACE did not result in parenchymal-sparing strategy among those patients, with no patients showing a shift from major hepatetcomy plan to more limited resection plan after TACE. So overall, preoperative TACE among this subgroup of patients increased surgical difficulty and risk, added no benefit in decreasing the amount of liver parenchyma resected or decreasing the rate of major hepatectomies, and delayed the curative surgery. In addition, in 16.8% of cases, repeated TACE contributed to worsening of the biochemical parameters of those patients beyond accepted criteria for further management of the tumor.

Selective catherterization of collateral vessels with microcatheters is mandatory with placement of the catheter tip as close as possible to the specific feeder supplying the tumor to reduce the risk of embolizing nontarget branches which can lead to a number of complications depending on the embolized artery. The experience of the operator is mandatory to prevent embolic material from refluxing into nontarget branches and lowering vascular access complications, especially intimal injury, and arterial spasm might lead to technical failure with subsequent failure of tumor control. In our study, shoulder pain was common (91%) with embolization of the right inferior phrenic artery together with pleural effusion and basal lung atelectasis. Cutaneous itching associated with reddish skin patches of different color grades mounting to skin necrosis occurred with embolization of intercostal and internal mammary artery or lumbar artery. Abdominal pains occurred in 53% of cases with embolization of omental branches. Unfortunately, one case developed paraplegia owing to accidental embolization of spinal branch from lumbar artery. Acute cholecystitis occurred in 20% of cases with one progressing to gallbladder perforation in a diabetic patient resulting from cystic artery embolization.

Classical TACE is based on the fact that exclusively the hepatic artery supplies HCCs. In clinical practice, HCCs supplied by extrahepatic collateral arteries are frequently encountered even when the hepatic artery is patent [29,39]. The development of extrahepatic arterial supply for HCC is governed by tumor

location, patency of hepatic artery, exophytic growth pattern, multiple sessions of TACE, and direct contact or invasion into other organs. The combined effect of exophytic growth pattern with anatomic locations of HCCs adjacent to the bare area, suspensory ligaments, and diaphragm might lead to a higher incidence of diaphragmatic blood supplies, including the inferior phrenic, internal mammary, and intercostal arteries. In our patients, the tumor location and adherence to near by organ determined the origin of the parasitic feeder. The presence and development of those collateral arteries further complexes the embolization procedure with the necessity of controlling those feeders. It is essential to try to determine first whether parasitic or collateral blood supply is present. The preassessment dynamic abdominal CT scan had a critical role in selection of our patients, and the results were confirmed during angiography performed in TACE group patients, where all patients had at least one collateral extrahepatic arterial feeder. In the view of our results, detection of those vessels at early stage should be a predictor of lower incidence of technical success than conventional TACE with a higher number of sessions needed for tumor control and increased incidence of complications.

There is no clear treatment strategy for solitary large HCC (>5 cm) in the Barcelona clinic liver cancer guidelines [40]. The biological behavior of these single large tumors that grow over time without becoming multinodular needs further characterization and may hint toward a more benign course. Up till now, there is no consensus regarding the size limit for solitary HCC undergoing surgical resection with a curative intent. In view of our results, in patients with solitary large HCC showing an exophytic growth pattern, hepatic resection should be the first line of treatment if the liver condition and volumetric assessment permits. TACE may be useful in the setting of downsizing to transplant accepted criteria. Expected outcome of TACE in term of technical success is low, and it requires multiple sessions to achieve adequate tumor control. It should be carefully evaluated, with the benefits weighted against the potential risks and complications anticipated during embolizing the collateral arteries.

Conclusion

In Child A cirrhotic patients with solitary large exophytic HCC with extrahepatic blood supply, combined hepatic resection plus TACE is associated with increased perihepatic adhesions, increased operative time, blood loss, and postoperative hospital stay compared with liver resection alone. Upfront surgical resection should be considered as a first-line therapy in those patients, as preoperative TACE does not have additional oncological benefit with no reduction in recurrence rate or improvement in disease-free survival.

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Conflicts of interest

There are no conflicts of interest.

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Nitinol stent implantation for femoropopliteal lesions: 12-month results

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Objective
To evaluate the 1-year efficacy and safety of the self-expanding nitinol stent in treatment of intermediate femoropopliteal lesions.
Patients and methods
This prospective study included patients with symptomatic (Rutherford grade 2–5) 5–15 cm femoropopliteal artery lesion between July 2014 and July 2016. Study end points were primary patency rate, improvement of Rutherford clinical criteria and ankle brachial indices, major adverse events (MAE), target lesion revascularization, and stent fracture.
Results
The study enrolled 45 patients. Technical success rate 100%. A total of 45 stents were implanted in 45 patients. A single stent was used for each lesion. The primary patency rate at 1 year was 75.5%. The mean Rutherford clinical criteria decreased from 3.84±0.85 at baseline to 0.71±0.84 at 1 year ($P<0.001$). Compared with baseline, a significant improvement in ankle brachial indices was found at 12-month (0.93±0.16; $P<0.0001$) follow-up visits. No MAE were present at 30 days. At 12 months, there was one MAE case that showed target vessel revascularization using angioplasty. Target lesion revascularization at 12 month was 8.9%. Stent fracture at 12 months was 4.4%. All stent fractures were type 1 fracture.
Conclusion
The outcome of the study demonstrates that the self-expanding nitinol stent is effective and safe device for treating intermediate femoropopliteal arterial lesions.

Keywords:
femoropopliteal artery lesion, nitinol stent, peripheral artery disease

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Introduction

Peripheral artery disease (PAD) is common, affecting between 8 and 12 million USA residents [1]. The lower limb is the most common site of PAD [2]. Femoropopliteal segment is the most common site for peripheral arterial atherosclerotic disease [3,4].

Endovascular treatment is commonly performed as an initial treatment of choice for PAD [5]. Endovascular therapy is established as the first-line strategy for femoropopliteal obstructive disease [6].

The femoropopliteal arterial segment is a particularly challenging location for implantation of a permanent endoprosthesis owing to the extreme mechanical forces exerted on these arteries during the activities of daily living [7].

Nitinol stent implantation after balloon angioplasty has been used for the treatment of longer and more complex lesions than in lesions treated with PTA alone [5].

Newer nitinol stents with enhanced flexibility have been developed for femoropopliteal use and may be associated with a reduced rate of stent fracture and improved long-term patency [7].

The aim of this study was to evaluate the 1-year efficacy and safety of the self-expanding (SE) nitinol stent in the treatment of intermediate femoropopliteal lesions.

Patients and methods

This prospective study was carried out in Vascular Surgery Department, Sohag Faculty of Medicine, following approval by the Scientific Ethics Commitee. The study included a series of 45 patients between July 2014 and July 2016.

Patient selection

Eligible participants had the following inclusion criteria:

A documented symptomatic (Rutherford grade 2–5) de-novo occlusion or 50% at least de-novo or restenotic

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stenosis in the superficial femoral artery (SFA) and proximal popliteal arteries with reference vessel diameters of 4–7 mm of an adult patient. The target lesion had to be located with its most distal point maximally 3 cm proximal to the knee joint. Lesion lengths had to be 5–15 cm, with a minimum of one patent runoff vessel present. Treatment of both legs was possible. The patient provides a written informed consent before enrolment in the study.

Patients were excluded if they had the following:

Significant stenosis (50%) or occlusion of the inflow tract (proximal ipsilateral, iliofemoral, or aortic lesions).
Previous stenting or bypass surgery of the target vessel.
No patent runoff vessel.
Aortic/iliac/popliteal aneurysms.
Acute thrombosis in the index vessel.
Venous thrombosis or thrombophlebitis.
Complications of arterial access site in legs within 30 days before the study procedure.
Life expectancy of less than 12 months.
Not completed our follow-up protocol.
Other factors making follow-up impossible.

Preprocedural assessment

All eligible patients underwent a baseline clinical examination with Rutherford clinical category, ankle brachial indices (ABI) measurement, duplex ultrasound examination, and computed tomography angiography.

Preprocedural medication

Patients received clopidogrel (75 mg/day) for at least 3 days before the intervention, otherwise loading dose of 300 mg was given immediately before the procedure.

Procedure

Under local anesthesia, 6-Fr sheath was placed by an antegrade ipsilateral approach or cross-over technique via retrograde contralateral femoral approach. Intravenous bolus of 5000 IU of heparin was administered. The lesions were crossed endoluminally or subintimally with 0.035-inch Glidwire (Terumo Medical Corporation, Somerset, UK) together with 4 or 5-Fr multipurpose diagnostic catheter. Then, the lesions were dilated using an optimally sized balloon. Lastly, nitinol stent deployment was carried out. The stents used for this study were complete SE SFA stent (Medtronic Vascular, Santa Rosa, California, USA). The deployed stents were 1 cm proximally and distally from the target lesion, and the stent sizes were selected to be 1–2 mm larger than the diameter of the reference vessel. Following stent deployment, postdilation was performed according to the physician's discretion. Completion angiography was done to verify technical success of the procedure.

At the end of the procedure, manual compression at the puncture site of the femoral artery was done for inducing hemostasis.

Postprocedural medication

The patients were given aspirin 75 mg/day and clopidogrel 75 mg/day for 3 months.

Follow-up

All patients were evaluated at discharge, 1, 3, 6, and 12 months following intervention by Rutherford categorization, ABI, and duplex scanning. Plain radiograph in straight and bent knee configurations was done for all patients at 12 months to asses stent fracture.

Definitions

Technical success was defined as the ability to implant the stent with angiographic evidence of less than 30% final residual stenosis.

Primary patency refferred to uninterrupted patency with no procedures performed on or at the margins of the treated segment as documented by a peak systolic velocity ratio (PSVR) of more than 2.0 on duplex.

Major adverse events (MAEs) were defined as device-related and/or procedure-related death (or any death occurring through 30 days), as well as target limb loss and target vessel revascularization.

Clinically driven target lesion revascularization (TLR) was defined as procedures (angioplasty or bypass surgery) for ischemic symptoms referable to the target lesion as demonstrated by a decrease in the Rutherford scale by at least one category or at least 0.15 decrease in ankle brachial index (ABI)/toe brachial index (TBI).

End points

The effectiveness end points were as follows:

(1) Primary patency at 1 year.
(2) Clinical improvement that is evident by improvement of Rutherford clinical criteriaby at least one category and ABI by at least 0.15 increase in ABI reading at 12 months.

The safety end points were as follows:

(1) The MAE at 30 days and 1 year.

(2) TLR at 30 days and 1 year.
(3) Stent fracture (assessed by radiography in straight and bent knee configurations) at 12 months.

Statistically analysis

Data are presented as mean±SD for continuous variables and as counts (percentages) for categorical variables. IBM SPSS, (version 19: IBM Coporation, Somer, NY, USA) was used to measures change over time using test for repeated measures. *P* value was considered significant if less than 0.05. The primary patency rates were estimated using Kaplan–Meier method.

Results

Between July 2014 and July 2016, 45 patients with SFA and proximal popliteal artery lesions met the inclusion criteria and were enrolled in the current series.

The baseline characteristics of the study patients

The baseline characteristics of the study patients are shown in Table 1. The mean age of the study population was 67.3±9.3 years. There were 31 (68.9%) men and 14 (31.1%) women.

Baseline vascular risk factors

Vascular risk factors were prevalent. History of smoking was reported in 29 (64.4%) patients, 25 (86.2%) of which were still current smoker. Eighteen (40%) patients had arterial hypertension. Diabetes mellitus was present in 28 (62.2%), hypercholesterolemia in 19 (42.2%), renal insufficiency in four (8.9%), and cerebrovascular stroke in three (6.7%) patients (Table 1).

The preintervention symptoms assessment according to Rutherford clinical category of the limbs

A total of nine (20%) patients had a walking distance 100–250 m (Rutherford category 2), seven (15.5%) patients had a limited walking distance less than 100 m (Rutherford category 3), 13 (28.9%) had rest pain (Rutherford category 4), and 16 (35.5%) had nonhealing arterial ulcers (Rutherford category 5) (Table 1).

Angiographic findings of the study patients

Angiographic findings of the study patients are summarized in Table 1, with 13 (28.9%) cases involving the proximal SFA, 15 (33.3%) cases involving the mid-SFA, 11 (24.4%) cases involving the distal SFA, and six (13.3%) distal SFA lesion extended to proximal popliteal lesion. The lesion length ranged from 8 to 15 cm. Occlusions were present in 53.3% of patients. Calcification was present in 60% of patients.

Procedural results

Technical success was achieved in all 45 patients, and 45 complete SE stents were used to treat the 45 lesions. A single stent was used for each lesion.

Effectiveness assessment

The primary patency rate at the 1 month was 93.3%, at 3 months was 88.9%, at 6 months was 80%, and 12 months was 75.5%. The primary patency rates were estimated using Kaplan–Meier method (Fig. 1).

Clinical improvement determination

It was estimated through improvement of Rutherford class by at least one category, which was 91.1% at 12 month, and through the improvement of ABI by at least 0.15 increase in ABI reading at 12 month, which was seen in 86%.

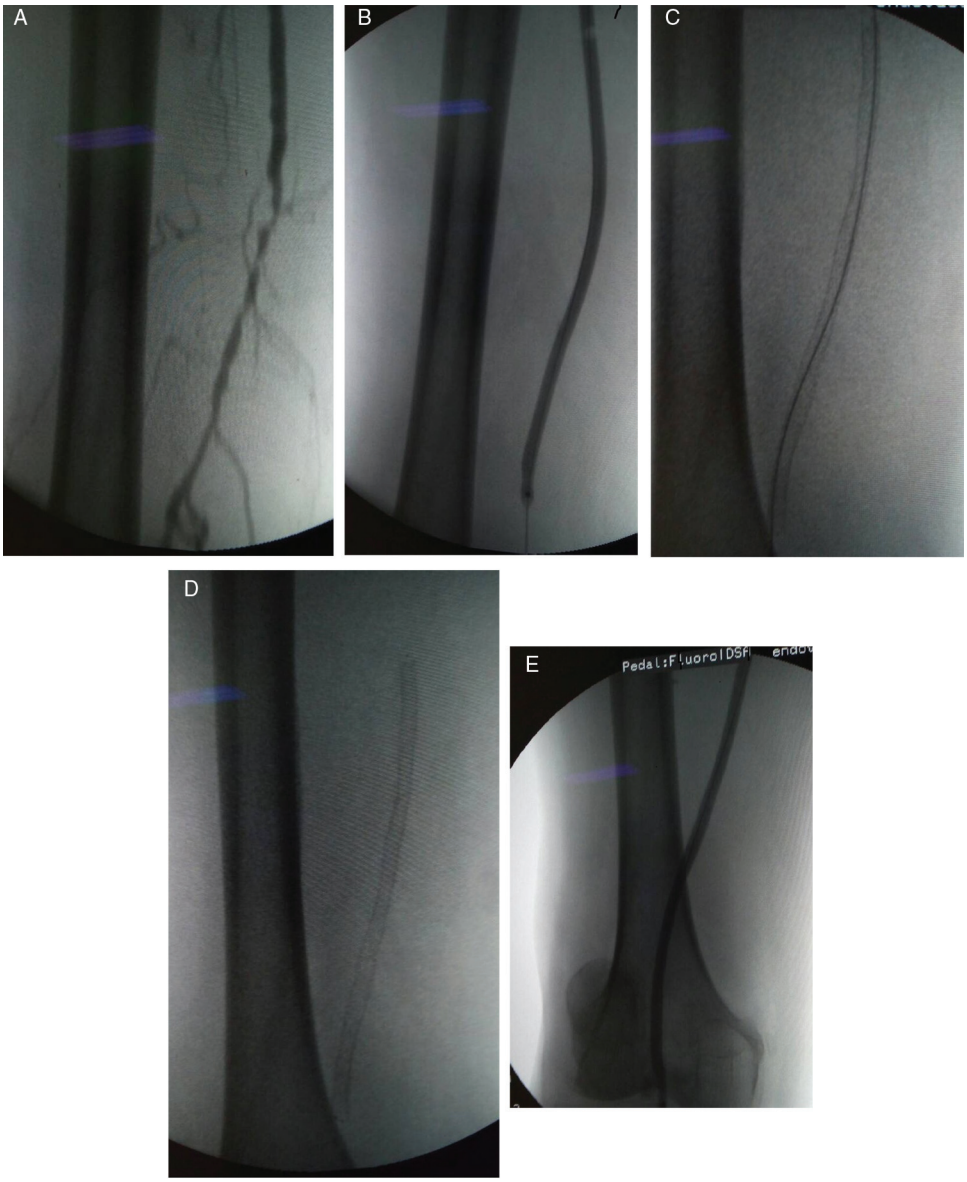
Changes in ABI and Rutherford clinical criteria are summarized in Table 2. Compared with baseline, a significant improvement in ABI was found at the 1-month (0.98±0.12; $P<0.0001$), 3-month (0.97±0.14; $P<0.0001$), 6-month, (0.94±0.15; $P<0.0001$), and 12-month (0.93±0.16; $P<0.0001$) follow-up visits. The mean Rutherford clinical criteria decreased from 3.84±0.85 at baseline to 0.71±0.84 at 1 year ($P<0.001$).

Table 1 The baseline characteristics of the study patients

Total number of patients	45
Demographic characteristics of patients	
Age	67.3±9.3
Males	31 (68.9)
Females	14 (31.1)
Baseline vascular risk factors	
Smoking	29 (64.4)
Hypertension	18 (40)
Diabetes mellitus	28 (62.2)
Hypercholesterolemia	19 (42.2)
Chronic renal failure	4 (8.9)
Cerebrovascular stroke	3 (6.7)
Clinical category of limbs (*N*=45)[a]	
Rutherford criteria+ 2	9 (20)
Rutherford criteria+ 3	7 (15.5)
Rutherford criteria+ 4	13 (28.9)
Rutherford criteria+ 5	16 (35.5)
Angiographic finding of the study patients (*N*=45)	
Proximal SFA lesion	13 (28.9)
Middle SFA lesion	15 (33.3)
Distal SFA lesion	11 (24.4)
Distal SFA lesion extended to proximal popliteal lesion	6 (13.3)
Occlusion [*n*/*N* (%)]	34/45 (75.5)
Calcification [*n*/*N* (%)]	27/45 (60)

Data expressed as the mean±SD value or *n* (%) of patients. SFA, superficial femoral artery. [a]Rutherford classification reference [8].

Figure 1



Kaplan–Meier estimates of primary patency rate.

Safety assessment

The safety assessment measures are summarized in Table 3.

Major adverse events

There were no deaths and limb amputation over 30 days.

There were no deaths and limb amputation over 1 year, but there was one case that showed target vessel revascularization using angioplasty.

Target lesion revascularization

TLR at 12 month was 8.9%. Angioplasty was used for revascularization of three cases, and bypass surgery was used for revascularization of the fourth one.

Stent fractures

Analysis of straight and bent-knee radiographs indicated that there were two (4.4%) stent fractures at 12 months. All stents fractures were type 1 fracture.

Discussion

Endovascular technology has revolutionized the treatment of lower extremity arterial disease over the past decades [9,10].

Stents are commonly used for treatment of femoral and popliteal occlusive disease, particularly for longer lesions [5].

Implantation of nitinol stents into the femoropopliteal segment has become a widely used technique, resulting

Table 2 Changes in ankle brachial indices and Rutherford clinical criteria from baseline to 12 months

	Changes in ankle brachial indices					*P* value
	Baseline	1 Month	3 Months	6 Months	12 Months	
Mean±SD	0.51±0.13	0.98±0.12	0.97±0.14	0.94±0.15	0.93±0.16	<0.0001
	Changes in Rutherford clinical criteria					*P* value
	Baseline	1 Month	3 Months	6 Months	12 Months	
Mean±SD	3.84±0.85	0.33±0.60	0.53±0.82	0.64±0.83	0.71±0.84	<0.0001

Table 3 Safety assessment

Safety assessment	
Major adverse events [*n*/*N* (%)]	1/45 (2.2)
Death	
Through 30 days	0
Through 1 year	0
Limb amputations	
Through 30 days	0
Through 1 year	0
Target vessel revascularization	
Through 30 days	0
Through 1 year	1
Angioplasty	
Target lesion revascularization [*n*/*N* (%)]	4/45 (8.9)
Through 30 days	0
Through 1 year	4
Angioplasty	3
Bypass graft	1
Stent fracture [*n*/*N* (%)]	2/45 (4.4)

in improved clinical outcome over other percutaneous procedures [11].

This article describes our experience on the primary stenting using nitinol stents for treating symptomatic patients with moderate length (5–15 cm) femoropopliteal atherosclerotic lesions. Occlusions were present in 75.5% of patients. Calcification was present in 60% of patients.

The technical success rate (<30% final residual stenosis) in the current study is 100%. The technical success rate in the current study compares favorably with the results in the MISAGO clinical trial, which is similar to our study in dealing with moderate femoropopliteal lesions. Schulte *et al.* [12] reported in MISAGO clinical trial that the technical success rate was 100%. MISAGO clinical trial enrolled implantation of 81 stents in five centers across Europe. Average lesion length was 85± 50 mm, and 64% of the lesions were totally occluded. The technical success rate in the current study is more than that reported in other literature studies [7,13] dealing with similar moderate femoropopliteal lesion length. Larid *et al.* [7] reported in a study, which including 196 patients from 28 centers, dealing with complete SE nitinol stents for obstructive lesions of the SFA or PPA with lesion length of 4–14 cm, acute lesion success rate (<30% residual stenosis) of 90.4%. This may be explained by the presence of moderate to severe calcifications in 91% of lesions. Larid *et al.* [13] reported in RESILENT randomized trial that the acute lesion success rate (<30% residual stenosis) was 95.8% for the stent group. The stent group includes 134 nitinol stents that were used for moderate length lesions (5–17 cm) in the SFA and proximal popliteal lesions.

The 12-month primary patency rate of the current study is 75.5%, which is comparable to the results in the studies by Sabeti *et al.* [14], Larid *et al.* [7,13], Rocha-Singh *et al.* [15], Bosiers *et al.* [16], and Werner *et al.* [11]. All these seven studies are similar in dealing with nitinol stent implantation for moderate femoropopliteal lesions, except for the study by Bosiers *et al.* [16], which dealt with moderate superficial femoral artery lesion only.

Sabeti *et al.* [14] reported that the primary patency rate after 52 nitinol stents implantation for moderate femoropopliteal lesion length 30–100 mm was 75% at 12 months. Overall, 54% of the lesions were occlusions. Primary patency was defined as PSVR more than 2.4.

Larid *et al.* [7] reported that the primary patency rate was 72.6% at 12 months. Primary patency was defined as PSVR more than 2.0. Use of the lower duplex PSVR threshold for restenosis would have no doubt resulted in a lower patency rate.

Rocha-Singh *et al.* [15] reported in meta-analysis study dealing with nitinol stents implantation performed for femoropopliteal lesions a primary patency rate of 72.8% for lesions 43.7–76.8 mm and 69.1% for lesions 76.8–112.3 mm. Primary patency was defined as PSVR more than 2.0 for five studies and 2.5 for one study. Nearly two-thirds of patients had mild to severe calcifications.

Bosiers *et al.* [16] reported in DURABILITY 1 study that the rates for freedom from more than 50% restenosis (defined as PSVR ≥2.5 or angiographic

evidence of more than 50 stenosis) at 12 months were 72.2%. DURABILITY 1 study enrolled 161 stents which were implanted in 151 patients with 10–15 cm superficial femoral artery lesions. Occlusions were present in 40% of patients. Moderately calcified lesions were present in a third of the subjects.

Larid *et al.* [13] reported that the primary patency rate was 81.3% at 12 months in the stent group. Patency definition in this study was based on PSVR of at least 2.5 by duplex or freedom from restenosis more than 50% by arteriography. The stent group includes 134 nitinol stents that were used for moderate length lesions (5–17 cm) in the SFA and proximal popliteal lesions. Occlusions were present in (26/153) of lesions. Moderate and sever calcified lesions were present in (39/153) of lesions.

Werner *et al.* [11] reported in a multicenter nonrandomized SUMMIT study a primary patency rate (defined as PSVR ≥2.5) of 85.1% at 1 year. The SUMMIT study enrolled 100 patients with 9–15 cm femoropopliteal lesions that were treated with EPIC SE nitinol stents. Almost half of the lesions had moderate to severe calcifications.

Matsumura *et al.* [5] reported in Durability II study that the duplex ultrasound patency (defined as PSVR >2.0) rate was 67.7% in evaluable patients at 1 year. Durability II study included 287 patients with more than 4 cm and less than 18 cm SFA and proximal popliteal artery lesions, which were treated with Protégé EverFlex nitinol stent. Occluded lesions were 48.1%, and severely calcified lesions were 43%.

Clinical improvement in the current study was evident by significant improvement of ABI and Rutherford category after stent placement. Compared with baseline, a significant improvement in ABI was found at the 12-month (0.93±0.16; $P<0.0001$) follow-up visits. The mean Rutherford clinical criteria decreased from 3.84±0.85 at baseline to 0.71±0.84 at 1 year ($P<0.001$).

Freedom from TLR after 1 year was 91.1% in the current study. Freedom from TLR after 1 year in the current study lies within the range reported in Werner *et al.* [11] (92.3%), Larid *et al.* [7] (90.8%), Rocha-Sing *et al.* [15] (86.9%), Matsumura *et al.* [5] (86.8%), and Bosiers *et al.* [16] (79.1%).

Stent fracture rate in the current study was 4.4% at 1 year. All the stent fractures were type 1 fracture. Our 4.4% 1-year stent fracture rate falls in between the rates reported in Bosiers *et al.* [16] (7.7%), Larid *et al.* [7] (4.6%), Larid *et al.* [13] (3.1%), Schulte *et al.* [12] (1.7%), Matsumura *et al.* [5] (0.4%), and Werner *et al.* [11] (0%).

Limitations

Limitation included lesion length up to 150 mm only, so for lesions up to 150 mm in length, so the conclusion in this study is limited to this lesion length. Further studies are needed to be done in the future to evaluate nitinol stent for longer SFA lesions more than 150 mm. In addition, the patency rate definition (PSVR >2) may be oversensitive measurement for diagnosis of stenosis, which had a direct effect on the patency rate in this study, especially with presence of other studies that have suggested that a PSVR of more than 2.4 may accurately reflect more than 50% stenosis [17].

Conclusion

The outcome of the study demonstrates that SE nitinol stent is an effective and safe device for treating intermediate femoropopliteal arterial lesions. The results provide additional support for the use of nitinol stents in intermediate femoropopliteal arterial lesions.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Hybrid revascularization techniques in the management of multiple level peripheral vascular disease

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Objective
Extensive multilevel atherosclerotic disease is common in patients with ischemia of the lower extremities. It is frequently associated with multiple medical comorbidities, resulting from disease in distant vascular territories and making these patients the high-risk group for extensive open surgical procedures. The purpose of this study is to evaluate the feasibility and efficacy of simultaneous, combined endovascular, and open lower extremity arterial reconstruction.

Patients and methods
A case series study with retrospective analysis of prospectively collected nonrandomized data.

Results
Thirty-five patients with multilevel ischemic peripheral vascular disease underwent hybrid procedures during the period from September 2014 to September 2016 with 100% technical success rate. Inflow endovascular procedure was performed in 48.57% and outflow in 37.14% of the cases. For five (14.28%) patients, both inflow and outflow percutaneous transluminal angioplasty were performed together with an open surgical revascularization. The open surgical procedures were a femoral procedure in the groin (34.3%) or with a bypass (65.7%). Patients are maintained on clopidogrel 75 mg daily for at least 6 weeks after hybrid interventions. Thereafter, lifelong aspirin therapy can be substituted for clopidogrel. The mean duration of the operation for all hybrid procedures was 290±110 min (range: 60–580 min). It was longest in procedures where an inflow percutaneous transluminal angioplasty (±stenting) and distal bypass were combined (279 min).

Conclusion
Hybrid revascularization procedures for the treatment of multilevel vascular disease in the fragile vascular patient population seem to be as good as with open revascularization, but with less morbidity and shorter intensive care and hospital stay.

Keywords:
hybrid, peripheral, revascularization

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Introduction

Extensive multilevel atherosclerotic disease is common in patients with ischemia of the lower extremities. It is frequently associated with multiple medical comorbidities, resulting from disease in distant vascular territories and making these patients high risk for extensive open surgical procedures. The mainstay of treatment for peripheral arterial disease has been arterial bypass surgery, but recent advanced endovascular interventions have challenged surgery as the first-line treatment [1].

The Trans-Atlantic Inter-Society Consensus (TASC) classification suggests the choices for first-line therapy and predicts successful intervention after endovascular or open surgical therapy mainly according to the site of the lesion and its length [2].

However, peripheral arterial disease usually affects multiple levels of the iliac femoral, popliteal, tibial, and peroneal arteries, especially in patients with critical limb ischemia. The anatomic variables, combined with patient-specific comorbidities, make the therapeutic decisions more complex. This difficulty in making the therapeutic decisions is made easier by using hybrid reconstruction techniques [3].

This study was performed to assess the efficacy of hybrid techniques for lower limb arterial revascularization in patients with critical lower limb ischemia.

Aim

The aim of this study was to evaluate the feasibility and efficacy of hybrid revascularization techniques in the management of multilevel peripheral vascular diseases.

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Patients and methods

This is a case series study with retrospective analysis of prospectively collected nonrandomized data. The study was conducted on patients from the Vascular Surgery Department of Menoufia University Hospital. It was done retrospectively on a 24-month period (September 2014–September 2016).

The patients who had been selected for this study had their hybrid revascularization techniques according to the localization and morphology of the arterial lesions, disease stage, comorbidities, and risk factors.

All patients had preoperative, clinical, and paraclinical evaluation, including their risk factors and medical comorbidities, followed by an imagistic diagnostic procedure: Doppler ultrasound and contrast-enhanced computed tomography angiography.

The Rutherford classification was used to determine the clinical category of the patients [4].

These procedures were performed in the hybrid operating room, equipped with a Ziehm Vision® FD Imaging Co. (Nuremberg, Germany) Hybrid Edition and a moveable radiolucent surgical table.

The procedures were performed under local or regional (i.e. spinal and epidural) anesthesia. All patients were administered preoperative prophylactic cefepime intravenously. Typically, we begin the hybrid procedure with surgical exposure of the vessels. Unfractionated heparin is given intravenously (1 mg/kg) before vessel clamping. An additional dose of heparin is administered (usually half of the first dose) at 90 min after the first dose if the revascularization takes longer. The ipsilateral femoral bifurcation was exposed through a longitudinal inguinal incision. The open arterial reconstruction was followed by upward or downward endovascular revascularization in all patients; the latter was performed under continuous blood flow. The sheath was placed through a direct puncture of the prosthetic material (patch or graft).

The following three techniques were applied in this study.

Common femoral artery (CFA) endarterectomy/patch angioplasty with proximal ipsilateral iliac artery angioplasty and stenting or distal endovascular intervention.

Femoropopliteal bypass with proximal ipsilateral iliac artery stenting or infrapopliteal (distal) endovascular intervention.

Femoropopliteal bypass with proximal ipsilateral iliac artery stenting and infrapopliteal (distal) endovascular intervention.

Reconstruction of the CFA and bifurcation is typically completed using a patch (synthetic) or an interposition synthetic graft, depending on the length of the treated segment.

The mean follow-up was 15±8.3 months (median: 15 months; range: 0–24 months) and had the following endpoints: primary and secondary patency, initial technical success, complication rate, morbidity and mortality associated to each technical procedure, symptomatology improvement, and limb-salvage rate.

Patients are maintained on clopidogrel 75 mg daily for at least 6 weeks after hybrid interventions. Thereafter, lifelong aspirin therapy can be substituted for clopidogrel.

Analysis of the operative indications as well as the risk factors with influence on the post-therapeutic outcome was also done. All patients in the study gave written consent for their respective procedures. The study had full approval from the respective Hospital Ethics Committee. Technical success was defined as residual stenosis of less than 30% as demonstrated on intraoperative arteriography. Hemodynamic success was defined as an increase in the ankle-brachial pressure index by more than 0.1.

Clinical improvement was defined as an upward shift by at least one clinical Rutherford category, except when actual tissue loss existed, in which case there should be moving up of at least two categories. Perioperative morbidity and mortality included complications and death occurring within 30 days from surgical intervention. In this study, patency refers to the status of the reconstructed arterial segments. Patients with rest pain or tissue loss (Rutherford category 4 or 5) were used to determine the limb-salvage rates.

Statistical analysis

The data were evaluated via descriptive statistics (mean, median, and SD) and compared with the χ^2 or Fisher's test for the categorical data and the Student's t test for the continuous variables. Lesion severity and clinical results were evaluated in relationship to the clinical and preprocedural and postprocedural angiographic variables. The statistical

analysis was performed with the SAS software (SAS Institute, Cary, North Carolina, USA). A *P*-value of less than 0.05 was considered statistically significant.

Results

This study included a total of 35 patients with multilevel peripheral vascular disease. The median age was 65±13.2 years (range: 49–78 years). Of the patients, 25 (71.4%) were men and 10 (28.6%) were women, and their underlying risk factors were hypertension in 27 (77.1%) patients, diabetes mellitus in 30 (85.7%) patients, dyslipidemia in 14 (40%) patients, coronary artery disease in 14 (40%) patients, a history of cerebrovascular disease in eight (22.8%) patients, with 100% technical success rate in 35 procedures done. Inflow endovascular procedure was performed in 17 (48.57%) and outflow in 13 (37.14%) of the cases. For five (14.28%) patients, both inflow and outflow percutaneous transluminal angioplasty (PTA) were performed together with an open surgical revascularization. The open surgical procedures were a CFA endarterectomy/patch angioplasty in 12 (34.3%) or with a femoropopliteal bypass in 23 (65.7%). The mean duration of the operation for all hybrid procedures was 290±110 min (range: 60–580 min). It was longest in procedures where an inflow PTA (±stenting) and distal bypass were combined (279 min) (Tables 1–5).

Table 1 Patients' demographic and clinical data

Variables	*N* [*n* (%)]
Age [mean±SD (range)] (years)	65±13.2 (49–78)
Sex (male/female)	25/10
Comorbidity	
Hypertension	27 (77.1)
Diabetes	30 (85.7)
Dyslipidemia	14 (40)
Coronary artery disease	14 (40)
Cerebrovascular disease	8 (22.8)

Table 2 Anatomical characteristics of the lesions and the type of procedure done

Lesions	*N*	Procedure
Iliac artery stenosis/ obstruction with localized CFA lersion	4	Iliac angioplasty and senting with CFA endartectomy and Patch graft
Iliac artery stenosis/ obstruction with SFA occlusion	9	Iliac angioplasty and senting with femoropopliteal bypass graft
Localized CFA lesion with infragenicular lesions	7	CFA endartectomy and patch graft with infragenicular angioplasty
SFA occlusion with infragenicular lesions	10	Femoropopliteal bypass with infragenicular angioplasty
Localized CFA lesion with inflow and outflow lesions	1	Iliac angioplasty and senting with CFA endartectomy and patch graft with infragenicular angioplasty
SFA occlusion with inflow and outflow lesions	4	Iliac angioplasty and senting with femoropopliteal bypass graft with infragenicular angioplasty

CFA, common femoral artery.; SFA, superficial femoral artery.

Overall technical success was achieved in 35 (100%) of 35 cases. Before discharge, the ABI increased significantly from 0.42±0.19 to 0.80±0.24 (*P*=0.007). Out of the 30 diabetic patients, three had incompressible arteries, which excluded them from mean ankle-brachial pressure index calculations.

The clinical status improved greatly (+3 Rutherford categories) in 24 (68.5%) patients; there was a moderate improvement (+2 Rutherford categories) in seven (20%) patients, and two (5.7%) patients had no clinical improvement. No mortality occurred in our study. Minor infections occurred in four patients in our study. All of them are managed early by proper antibiotics and wound care. The length of hospital stay in our study was (4.8±7.0 days) (Table 6).

The mean follow-up was 15±8.3 months (median: 15 months; range: 0–24 months). Loss of primary patency occurred in seven patients between 0 and 24 months, three of which were related to abnormalities detected in the endovascular-treated segments (42.85%) and three related to the bypass, one was related to the endarterectomized segment. In the seven patients who needed interventions for maintaining patency, one had PTA of infrapopliteal restenosis, and one needed angioplasty of the endarterectomized

Table 3 Technical success and mortality

	n (%)
Technical success	35 (100)
Mortality	0 (00)

Table 4 Clinical improvement according to ankle-brachial pressure index

	Preoperative (min)	Postoperative (min)	*P*-value
Ankle-brachial pressure index	0.42±0.19	0.8±0.024	0.007

Table 5 Clinical improvement according to Rutherford categories

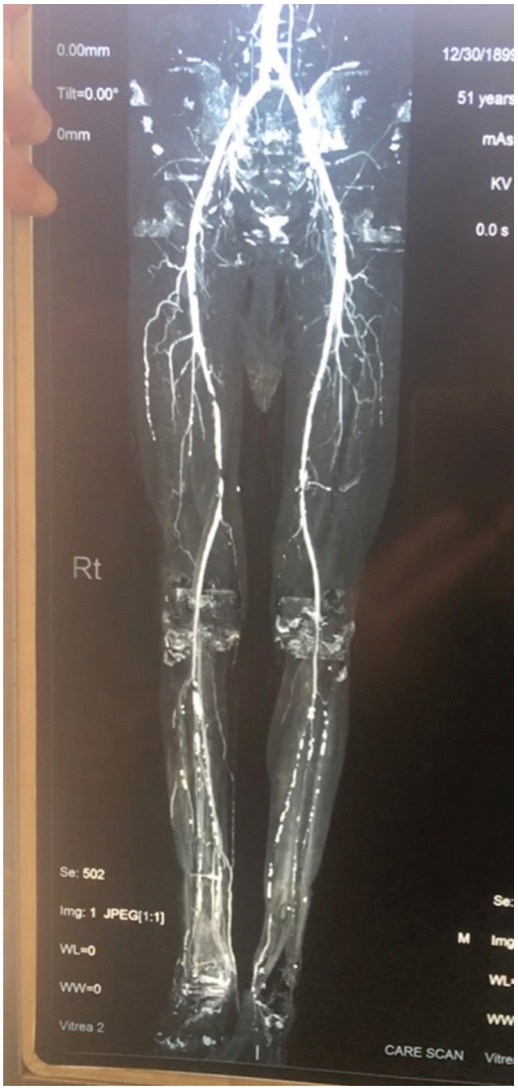
Rutherford categories	*n* (%)
+3 Rutherford categories	24 (68.5)
+2 Rutherford categories	7 (20)
No improvement	4 (11.5)

Table 6 Primary failures and their management

Initial procedure	Failure	*N*	Reintervension
CFA endarterectomy with inflow stenting	CIA occlusion	1	PTA and restensting
Bypass with infragenicular outflow angioplasty	Infragenicular stenosis	2	PTA
Bypass with infragenicular angioplasty	Graft thrombosis	2	Bypass graft thrombectomy
CFA endarterectomy with outflow angioplasty	Endraterectomy restonosis	1	PTA of endarterectomized segment

CIA, common iliac artery; CFA, common femoral artery; PTA, percutaneous transluminal angioplasty.

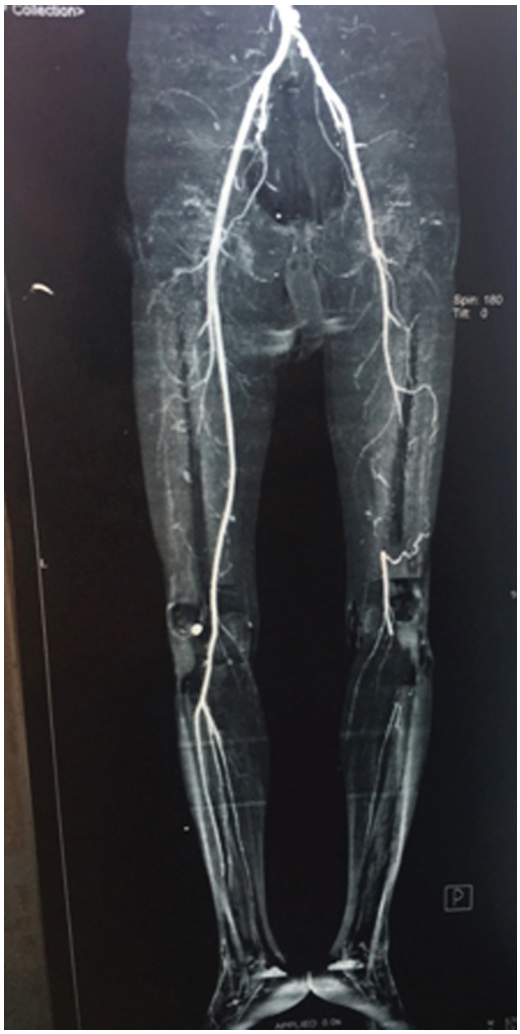
Figure 1



Femoral–popliteal bypass with infragenicular angioplasty.

segment. Two had bypass graft thrombectomies and revisions, one had iliac thrombolysis and restenting and one had been treated conservatively; the secondary patency rate was 100% during the follow-up period (Figs 1–12).

Figure 2



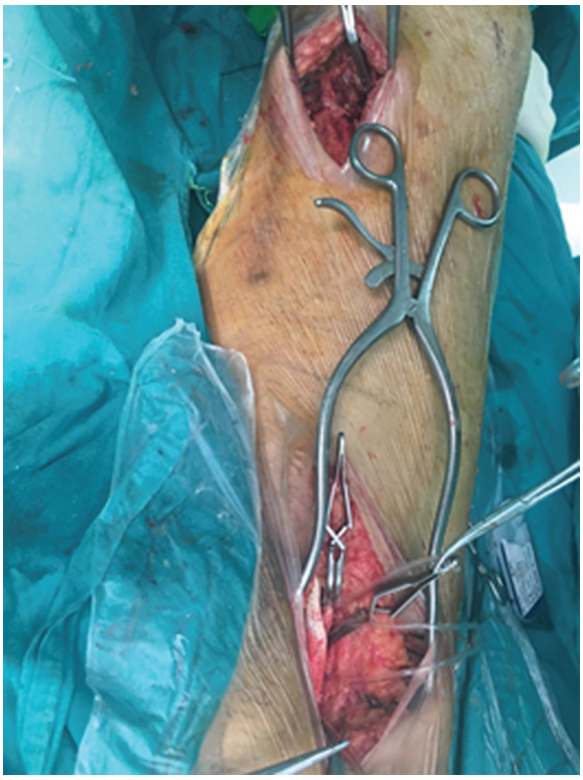
Femoral obstruction with inflow and outflow lesions.

Discussion

Treatment of multilevel ischemic peripheral vascular disease is often a difficult exercise. Conventional open surgical management of such lesions required extensive revascularization and lengthy procedure, commonly associated with significant morbidity and mortality. Endovascular interventions should be preferred for the elderly, high-risk patients, but in practice we often encountered situations in which it was difficult to proceed with angioplasty solely because of simultaneous calcifications and stenosis of the multilevel arteries [4].

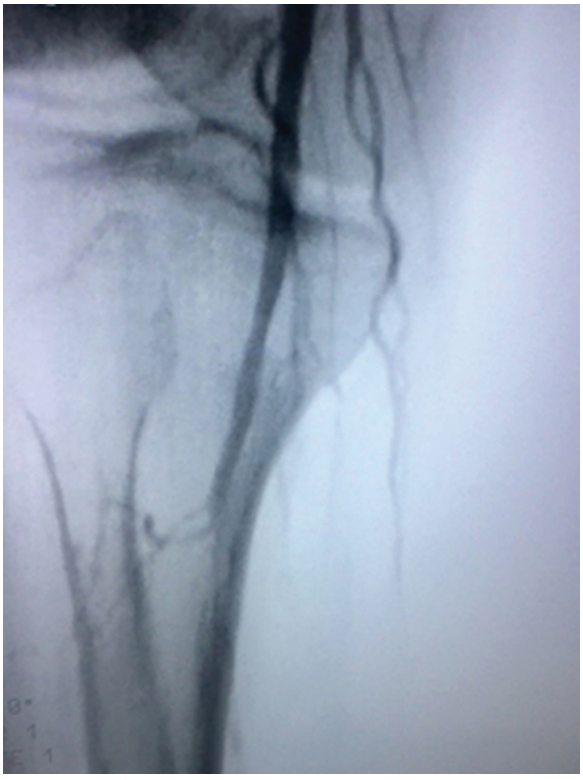
This difficulty in making the therapeutic decisions are made easier by using hybrid reconstruction techniques in which endovascular treatment used for inflow and outflow lesions or both in combination with open surgery for the intermediate lesions, during a single session [5].

Figure 3



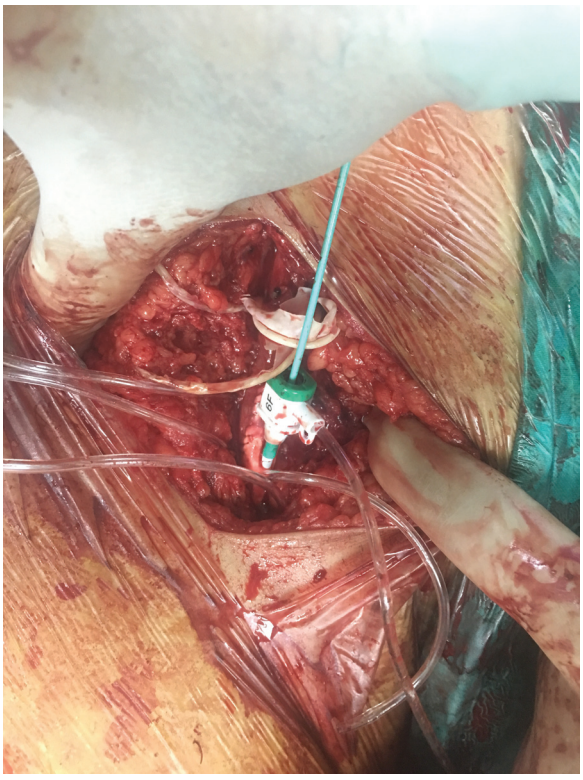
Femoral–popliteal bypass graft.

Figure 4



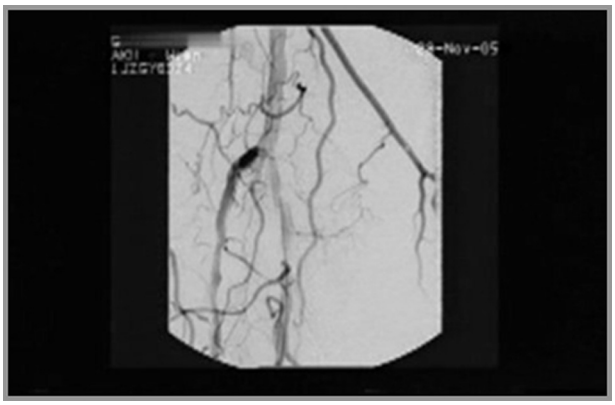
Infragenicular lesion after femoral endarterectomy.

Figure 5



Infragenicular angioplasty.

Figure 6

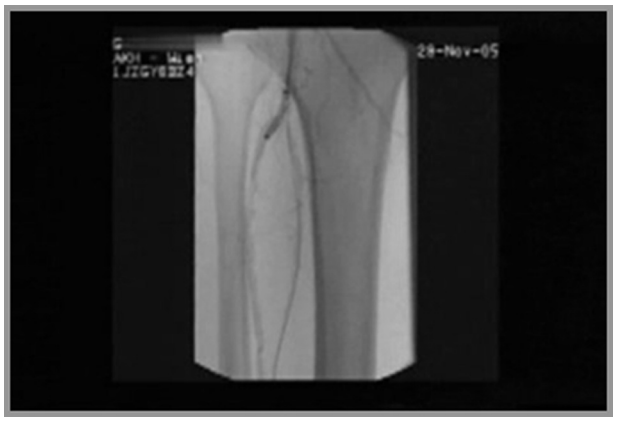


Pretransluminal angioplasty stenosis in the ostium and proximal segment of anterior tibial artery and another stenosis in the distal segment of anterior tibial artery/high-grade stenosis in the tibioperoneal trunk.

In our study, immediate technical and hemodynamic success rates were 100 and 94.4%, respectively, and those were achieved, confirming the immediate efficacy of this combined approach, matched with Dosluoglu *et al.* [6] who reported that the hybrid procedure for the infrainguinal vessel was comparable to the bypass procedure, with a technical successful rate of 92% and a limb salvage rate of 91% at 5 years. The hybrid procedures shorten the length of the operation.

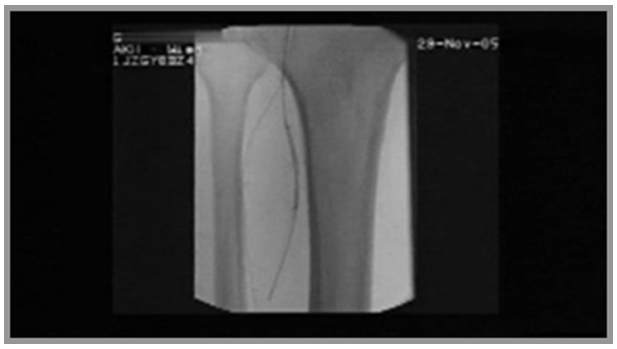
The mean duration of the operation for all hybrid procedures was 290±110 min (range: 60–580 min). It was longest in procedures where an inflow PTA

Figure 7



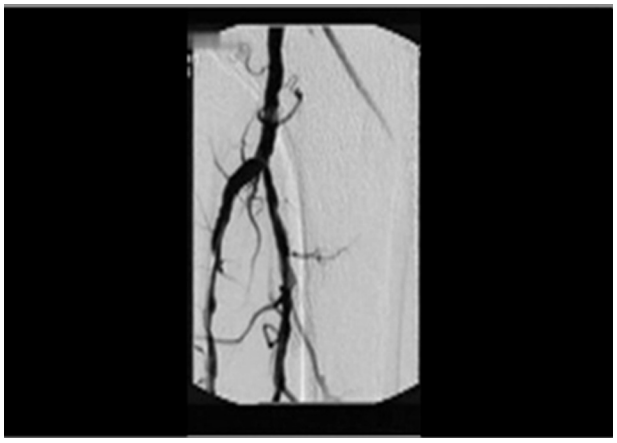
Balloon in the proximal segment of anterior tibial artery.

Figure 8



Balloon in the tibioperoneal trunk.

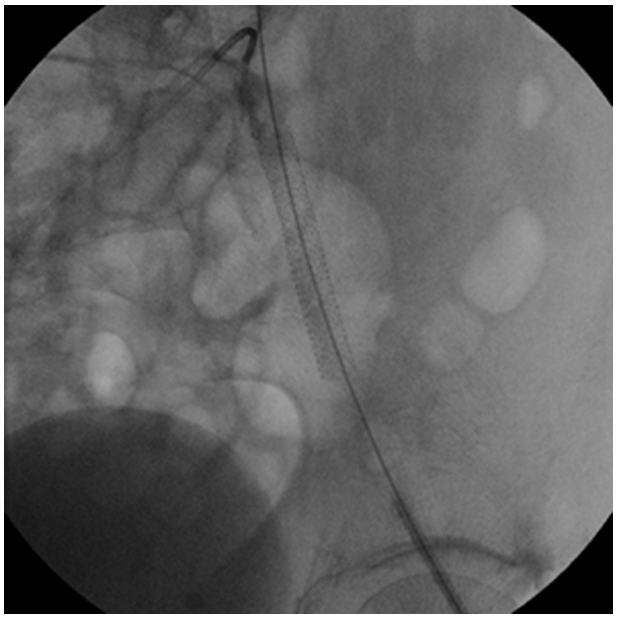
Figure 9



Post-transluminal angioplasty in the proximal segment of anterior tibial artery and tibioperoneal trunk.

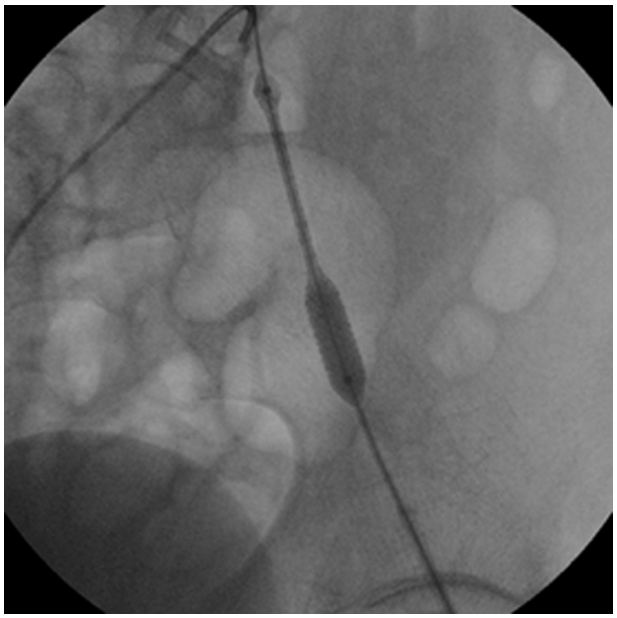
(±stenting) and distal bypass were combined (279 min), reduced the hospital cost, and decreased the length of hospital stay. The length of hospital stay in our study was 4.8±7.0 days, these results were compatible with Schneider PA.

Figure 10



Iliac guidewire.

Figure 11

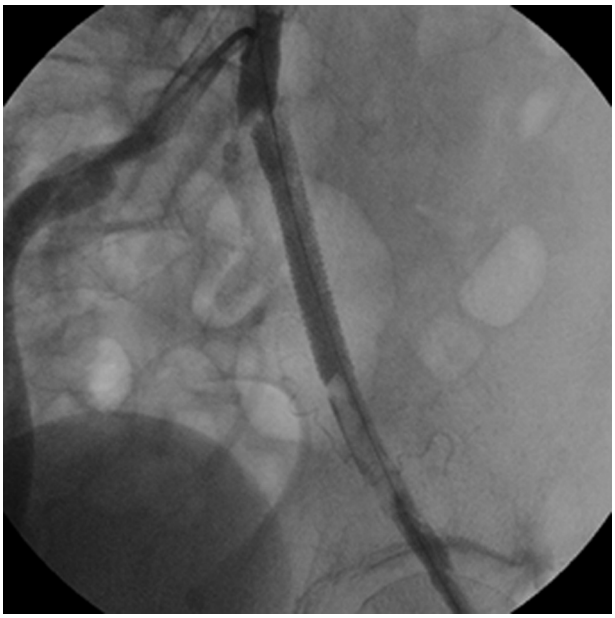


Iliac ballooning.

Iliac angioplasty and stenting in association with infrainguinal bypasses: timing and techniques.

When we perform an infrapopliteal bypass, it is necessary to secure a sufficient length of vein grafts. The hybrid procedure permits vascular surgeons to use shorter bypass grafts. The hybrid procedure allowed us to obtain a primary patency rate of 78.78%, a secondary patency rate of 100%, an amputation-free survival rate of 100%, and a freedom from secondary intervention rate of 78.8% during the follow-up period.

Figure 12



Iliac stent.

We obtained results were comparable to or better than those reported in several previous studies, and these results justify our hybrid treatment [7–9].Schrijver *et al.* [10] reported that the primary patency, secondary patency, limb salvage, and patient survival rates were 56.8, 62.7, 78.2, and 48.6%, respectively, at 5 years.

Cotroneo *et al.* [11] followed up 44 patients (24 with claudication and 20 with critical limb ischemia) after hybrid procedures and reported 2-year primary and secondary patency rates of 79.1 and 86.1%, respectively. Nishibe *et al.* [12] reported a 3-year experience with hybrid procedure for multifocal peripheral TASC D lesions. The primary patency rates were 94, 70, and 70% at 6, 12, and 24 months, respectively.

Our study also matched with the open surgery literature, as regards primary and secondary patency of Norgren [13], van Den Berg [14], McQuade [15], Neville [16], Reed [17]. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II).

Zero mortality in these study groups demonstrates the minimally invasive character and superiority of the hybrid techniques for the elderly patients with high operative risk.

Conclusion

Hybrid revascularization procedures for the treatment of multilevel vascular disease have the following benefits:

(1) Complete revascularization of the ischemic limb occurs in a single session.
(2) Open surgery can immediately repair inadequate endovascular results and *vice versa*.
(3) Puncture complications related to angioplasty are eliminated.
(4) Potential infectious complications of long open intervention or two separate interventions are minimized.
(5) Lower the anesthetic complication risks especially in high-risk patients.
(6) Hospital stay is shortened and possibly cheaper.
(7) Primary patency and secondary patency have the same results as in open surgery.
(8) This technique helps the vascular surgeons to have an upper hand in the treatment of their patients.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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Effect of biliary stenting for unextractable choledocholithiasis

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Introduction
Large choledocholithiasis is associated with higher rates of failed extraction with conventional endoscopic techniques. Alternative methods such as electrohydraulic lithotripsy and extracorporeal shock wave lithotripsy, laser lithotripsy, and dissolving solutions can remove 90% of difficult common bile stones. However, these methods are indicated only in special situations and require experience and additional equipment that may not be available in every center.
Aim
The aim of this study was to investigate the efficacy of biliary stenting in the treatment of endoscopically unextractable common bile duct (CBD) stones.
Patients and methods
A total of 46 patients with endoscopically unextractable CBD stones underwent placement of a plastic biliary stent. After 6 months, a second endoscopic retrograde cholangiopancreatography (ERCP) was performed and endoscopic stone removal was again attempted. Differences in stone size and CBD diameter before and after biliary stenting were compared. The complete stone removal rate after treatment was determined.
Results
The second ERCP procedure showed that the bile stone disappeared in 11 (23.91%) patients. Decreased stone size with complete stone removal was achieved in 29 (63.04%) patients. No significant changes were observed in the sizes of CBD stones and stone extraction eventually failed in six (13.04%) patients. Thus, in a total of 40 (87%) patients with unextractable stones, successful stone extraction was performed during the second ERCP.
Conclusion
Temporary biliary stenting has an established place in the management of large CBD stones and can facilitate stone extraction by a basket or a balloon catheter in the second ERCP.

Keywords:
biliary stenting, common bile duct stone, endoscopic retrograde cholangiopancreatography

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Introduction

Common bile duct (CBD) stones are found in ~7–12% patients who undergo cholecystectomy for symptomatic cholelithiasis and are the most common reasons for endoscopic retrograde cholangiopancreatography (ERCP) in the pericholecystectomy setting [1].

They vary in size from rather small (~1–2 mm) to very large (>3 cm). ERCP with endoscopic sphincterotomy and basket or balloon extraction are well-established therapeutic techniques for the treatment of choledocholithiasis [2].

Biliary stenting may be used as a temporizing measure to maintain biliary drainage when extraction techniques have failed to remove CBD stones completely, particularly in frail, elderly, and high-risk patients [3]. Importantly, the short-term use of biliary stenting has been shown to be associated with a reduction in stone size or fragmentation and serves as a bridge treatment to secondary intervention, thereby leading to successful stone removal at follow-up ERCP [4].

Although several studies have reported that therapeutic ERCP plus stent placement is safe and effective for the elderly, there are still some conflicting results on the effectiveness and safety of this technique in patients with difficult CBD stones. The data are still limited on whether biliary stenting can decrease the size of large CBD stones [5].

Although success rates of removal of CBDs are 85–90%, the large (≥15 mm) calculi, the shortness (≤36 mm) and narrow angle (≤135°C) of distal CBD, impacted calculi, and anatomical difficulties are factors that contribute toward the failure of endoscopic stone extraction during

ERCP [6]. These are known as 'difficult common bile stones' and cannot be removed using standard methods. Alternative methods such as electrohydraulic lithotripsy and extracorporeal shock wave lithotripsy, laser lithotripsy, and dissolving solutions can remove 90% of them. However, these methods are indicated only in special situations and require experience and additional equipment that may not be available in every center. Furthermore, these techniques are not without cost, morbidity, mortality, and significant reduction in quality of life [7].

Many authors have found that stenting, in addition to providing biliary drainage, also has a very positive effect on the size or fragmentation of large or multiple bile duct stones, with a very high percentage of clearance of stones [8].

In this study, we aimed to investigate the efficacy of biliary stenting on the treatment of difficult CBD stones. We attempted to answer the question of whether a transient biliary stenting plays a role in the reduction or fragmentation of large CBD stones.

Patients and methods

This randomized study was carried out at the Department of General Surgery, Aswan University Hospital, Egypt. From October 2015 to January 2017, 46 patients with CBD stones refractory to conventional endoscopic removal, including basket extraction and balloon sweeping, underwent endoscopic placement of a straight plastic biliary stent. Patients stented for other etiologies such as malignant tumors and benign biliary strictures were not included in the analysis. A difficult CBD stone was defined as a large and impacted CBD stone that could not be removed endoscopically, either by basket or by balloon extraction. Extracorporeal or intracorporeal lithotripsy was not used for stone removal in this study (Fig. 1).

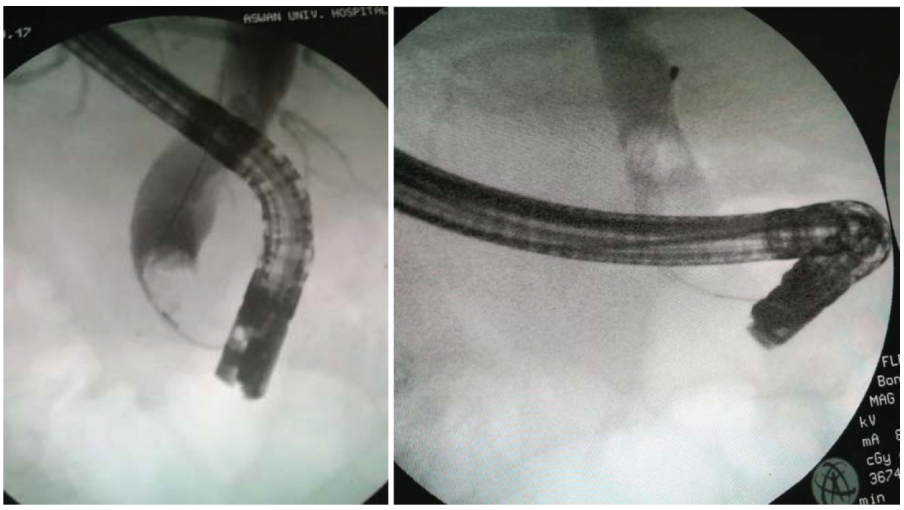
ERCP was performed to all patients under general anesthesia. Endoscopic sphincterotomy was performed in every patient, and basket and balloon extraction was attempted, but failed. In 46 patients, plastic stents were placed for temporary biliary drainage before further endoscopic attempts at duct clearance. The plastic stents were placed extending the proximal end above the stones and with the distal stent end in the duodenum (Fig. 2).

Information on age, sex, comorbidities, number of CBD stones, the largest diameter of the stone, diameter of CBD, and stent sizes was recorded.

After 6 months, a second ERCP was performed. CBD diameter, and CBD stone size and number were measured again for comparison with the values at the initial ERCP. Endoscopic stone removal was attempted again using conventional endoscopic procedures. No oral dissolution agent or associated medications for bile duct stone were prescribed to any patient.

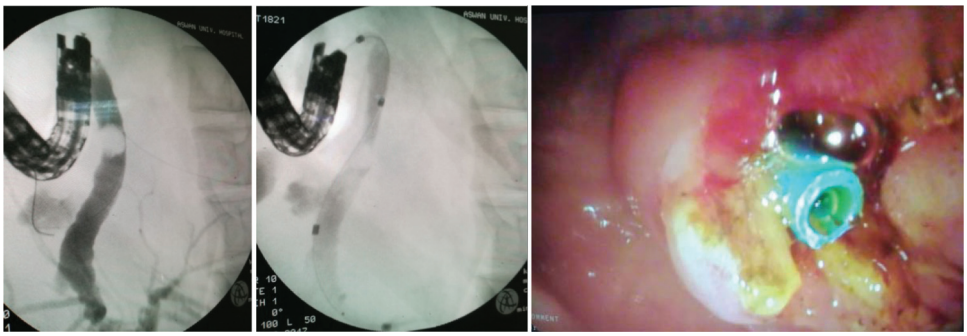
Outcomes were the rate of spontaneous stone passage and the rate of stone extraction after the endoscopic insertion of a biliary stent in patients with unextractable CBD stones. Other factors (e.g. age, sex, the diameter of the largest stone, stone multiplicity, length of the

Figure 1



Cholangiogram showing a large and impacted common bile duct stone that could not be removed endoscopically by basket.

Figure 2



Cholangiogram showing stenting for a large common bile duct stone.

stent, stent diameter, and follow-up period) that may affect the success of stone removal after stent insertion were also investigated.

Statistical analysis

Data were analyzed using the SPSS 23 data program. Stone sizes, diameters of CBDs, stone indices, and differences were analyzed using the Mann–Whitney *U*-test. Receiver operating characteristic curve analysis was carried out to determine the specificity and sensitivity, whereas the χ^2-test, Fisher's exact test, and univariate and multivariate analyses were used for determination of other data. Values of *P* less than 0.05 were considered statistically significant.

Results

The patients included 11 men and 35 women. The characteristics of the patients, clinical presentations, and concomitant chronic diseases are shown in Table 1.

Endoscopic placement of a biliary plastic stent was successful in all patients. After 6 months of stenting, the second ERCP procedure yielded the following:

(1) The bile stone disappeared in 11 (23.91%) patients.
(2) Decreased stone size with complete stone removal was achieved using only the basket and retrieval balloon catheter, without other additional procedures, in 29 (63.04%) patients (Fig. 3).
(3) No significant changes in the sizes of CBD stones were observed, and the stone extraction eventually failed in six (13.04%) patients, who later underwent elective surgery for CBD exploration and surgical removal of the retained stones.

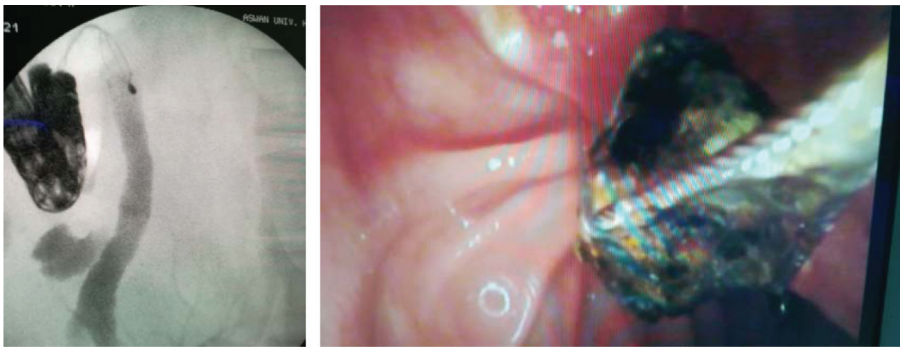
In terms of the complications of ERCP, only four patients developed complications in the form of recurrent cholangitis because of an occluded plastic stent (in three patients) and acute post-ERCP pancreatitis (in one patient). Post-ERCP pancreatitis was completely resolved under conservative medical treatment. Therapeutic ERCP and exchange of the occluded plastic stent were carried out for the treatment of patients with recurrent

Table 1 Characteristics of patients according to procedure

Characteristics	*N*=46 [median (minimum–maximum)]
Age (years)	56.0 (33.0–79.0)
Sex [*n* (%)]	
Male	11 (23.91)
Female	35 (76.08)
Proportion of abnormal LFTs [*n* (%)]	42 (91.30)
Diameter of CBD (mm)	19 (12–29)
Diameter of stones (mm)	18 (10–29)
Number of stones [*n* (%)]	
Single	31 (67.39)
Multiple	15 (32.60)
Length of stent (cm)	7 (5–12)
Stent diameter (Fr)	10 (7–10)
Duodenal diverticulum [*n* (%)]	7 (15.21)
Previous cholecystectomy [*n* (%)]	9 (19.56)
Comorbidity [*n* (%)]	
Ischemic heart disease	1 (2.17)
Liver cirrhosis	2 (4.34)
Hypertension	4 (8.69)
Diabetes mellitus	7 (15.21)
Hepatitis	4 (8.69)
Chronic renal insufficiency	3 (6.52)
Pulmonary disease	2 (4.34)
At presentation [*n* (%)]	
Cholangitis	8 (17.39)
Pancreatitis	2 (4.34)
Post-ERCP complications [*n* (%)]	3 (6.52)

CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; LFT, liver function test.

Figure 3



Cholangiogram showing decreased stone size with complete stone removal that was achieved using only the basket after 6 months of biliary stenting.

Table 2 Common bile duct stone size changes after biliary plastic stenting in 46 patients

Items	Managed by stenting [*n* (%)]	Initial size of the stones [median (minimum–maximum)] (mm)	Stones' size poststenting [median (minimum–maximum)] (mm)	*P* value
Complete disappearance of stone	11 (23.91)	14 (10–17)	0.0	<0.000***
Decreased stone size	29 (63.04)	19 (10–28)	9 (6–13)	<0.001**
Unchanged stones	6 (13.04)	26 (23–29)	26 (23–29)	1

cholangitis before the scheduled stent exchange (Tables 2 and 3).

Discussion

Choledocholithiasis is one of the most common gastrointestinal diseases encountered in clinical therapeutic endoscopy practice. Primary stones are softer than secondary stones, and this difference may increase the chance of endoscopic success in primary calculi [9].

Periampullary diverticula are observed in 15.21% of the patients undergoing duodenoscopy. In patients undergoing ERCP, there are still some conflicting results on whether or not periampullary diverticula affect successful biliary cannulation. However, recent publications support the theory that periampullary diverticula do not decrease the rate of successful endoscopic treatment [10].

It has been reported that the impacted CBD stones and stone sizes are predictive of endoscopic treatment that leads to potential difficulty in bile duct clearance [11]. When assessed according to the success of the treatment, patients with successful endoscopic clearance had fewer percentages of impacted stones than the unsuccessful group, although this was not considered as a factor that affects the treatment success in our study because of the small number of cases.

When CBD stones cannot be removed with conventional endoscopic methods, a temporary biliary stenting may be inserted to prevent impaction and to provide a bridge for surgical treatment. It has been reported that this method, in addition to providing biliary drainage, also reduces stone size by stent-stone friction force. Mechanical friction between the stone and the plastic stent may cause fragmentation. Because the plastic stent is easily mobile with body movements and gut peristalsis, this friction is more than expected. It is believed that the mechanical grinding of the stones against the biliary stents increases stone fragmentation, reduces the size of the biliary stones, and creates space around and between the stones, potentially facilitating extraction during the second ERCP session. In addition, the powerful stenting drainage could improve the solubility of bile and prevent calcium bilirubinate from precipitating in the bile duct [12].

In a study carried out by Chan *et al.* [13] plastic biliary stents were deployed in 46 patients whose CBD stones could not be extracted during the first ERCP session. However, during the next ERCP session, in 28 (60.9%) of these patients, successful removal of their stones was achieved. This is in agreement with the present study, which indicated that 29 (63.04%) patients showed decreased stone size with complete stone removal during the next ERCP session.

In the present study, we observed that leaving the stent inside the CBD for an average of 6 months resulted in the complete disappearance of stone in 11 (23.91%) of 46 patients. Katsinelos *et al.* [14] reported that CBD

Table 3 Comparison of the characteristics of patients according to the outcome of the study treatment

Characteristics	Successful stone removal (*n*=40) [median (minimum–maximum)]	Unsuccessful stone removal (*n*=6) [median (minimum–maximum)]	*P* value
Age (years)	49 (33–62)	58 (44–79)	<0.04*
Sex [*n* (%)]			
Male	9 (22.5)	4 (66.67)	<0.000***
Female	31 (77.5)	2 (33.33)	
Proportion of abnormal LFTs	36 (90.0)	6 (100)	0.683 (NS)
Diameter of CBD (mm)	17 (12–24)	22 (16–29)	<0.001**
Diameter of stones (mm)	19 (10–28)	26 (23–29)	<0.02*
Number of stones [*n* (%)]			
Single	27 (67.5)	4 (66.67)	0.647 (NS)
Multiple	13 (32.5)	2 (33.33)	
Length of stent (cm)	7 (5–12)	7 (5–10)	0.362 (NS)
Stent diameter (Fr)	10 (8.5–10)	10 (7–10)	0.895 (NS)
Duodenal diverticulum	5 (12.5)	2 (33.33)	<003*
Previous cholecystectomy	9 (22.5)	0	<0.02*
Comorbidity [*n* (%)]			
Ischemic heart disease	1 (2.50)	0	<0.04*
Liver cirrhosis	2 (5.0)	0	
Hypertension	3 (7.50)	1 (16.67)	
Diabetes mellitus	5 (12.50)	2 (33.33)	
Hepatitis	3 (7.50)	1 (16.67)	
Renal insufficiency	2 (5.0)	1 (16.67)	
Pulmonary disease	2 (5.0)	0	
Post-ERCP complications [*n* (%)]			
Cholangitis	2 (5.0)	1 (16.67)	<0.01*
Pancreatitis	1 (2.50)	0	
Impacted stones	5 (12.5)	2 (33.33)	<0.000***

ERCP, endoscopic retrograde cholangiopancreatography; LFT, liver function test.

stones of 11 (44%) of 25 patients were completely removed not in the first, but in the second ERCP procedure. In another study, plastic biliary stents were deployed in 40 patients, and 65 days later, no stones were found in 37 (93%) of 40 patients [15].

Similar to the studies reported by Jain *et al.* [15], we removed the CBD stones of 40 (86.95%) of 46 patients successfully in the next ERCP session.

In our study, a decrease in stone size was observed in 29 (63.04%) patients. When the findings were grouped according to the results of endoscopic treatment, the reduction in the size of the stones and fragmentation was higher in the successful endoscopic treatment group ($P<0.05$).

Also in agreement with our study, Krishnan *et al.* [16] and Aslan *et al.* [7] also found a significant reduction in stone size ($P<0.011$ and 0.001, respectively).

Lauri *et al.* [17] reported that stones with less than10 mm diameter can be removed by conventional endoscopic methods. However, stone extraction is possible in only 12% of patients when the stone diameter exceeds 15 mm and the chances of successful endoscopic therapy decrease with stone diameters of at least 18 mm. The receiver operating characteristic curve analysis in our study showed that the chance of success of endoscopic therapy may increase in patients with CBD stones with diameters less than 22 mm.

The brown pigment stones were more prominent in the successful endoscopic stone treatment group according to previous stenting. This is in agreement with Li *et al.* [18], who showed that brown pigment stones are soft and are characterized as easily crushed, in contrast to black pigment stones and cholesterol stones, which are often hard and more difficult to reduce in size. Because of these particular features, the brown pigment stones disintegrate easily after the temporary placement of a plastic stent.

In the present study, there were no significance differences ($P>0.05$) in stent diameter in relation to successful stone removal. This is in agreement with Ye *et al.* [3], who reported no significant stent occlusion for both a 10 Fr stent and a 6–7 Fr stent. Also, even if stent occlusion occurs, stents may still

maintain continuous drainage of the bile duct by a 'wicking' phenomenon, with bile flowing around and between the stents. The other reasons considered in selecting 7 and 8.5 Fr stents were ease of operation and reduced trauma to the bile duct, particularly for elderly, fragile patients. It is known that the plastic stent clog after 3 to 4 months, but the bile duct patency is maintained by passing around the stent. However, it seems to be promising that larger stents (i.e. 10 Fr) may improve outcomes.

Hui *et al.* [19] reported cholangitis in 63.2% of their patients after ERCP. Early complications, including bleeding and pancreatitis, and late complications (mostly cholangitis) were reported in 28 and 34% of patients, respectively, in another study by Ye *et al.* [3]. In a study of 83 patients by Ang *et al.* [20], plastic biliary stenting caused cholangitis, biliary pancreatitis, obstructive jaundice, and biliary colic in 71, 3.6, 21.4, and 3.6% of patients, respectively, during a mean follow-up duration of 19 months (range: 1–103 months).

In the present study, three (6.5%) patients had cholangitis after ERCP: two (5.0%) patients In successful stone removal group and one (16.67) patient in unsuccessful stone removal group with significance difference ($P<0.01$). This is in agreement with Consolo *et al.* [21], who reported that the most significant drawback of a biliary endoprosthesis is the risk of recurrent cholangitis, which is reported in 3.5–40% of patients.

The current study did have some limitations similar to those in the other studies that included a limited number of patients. A multicenter study for a larger population should be carried out in the future.

Conclusion

These data suggested that for CBD stones, which are considered to be difficult to remove, temporary biliary stenting within an average of 6 months has an established role in the management of large and multiple CBD stones and will facilitate stone extraction by a basket or a balloon catheter in the second ERCP procedure. It is a minimally invasive and effective method for stone removal in all patients with unextractable CBD stones irrespective of whether they are fit for surgery or not. Endoscopic placement of a biliary stent also functions as a bridge for surgery.

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Conflicts of interest
There are no conflicts of interest.

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Outcome of obstetric anal sphincter injuries repair techniques

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Objective
The objective was to compare outcomes of primary end-to-end repair versus overlap repair of the external anal sphincter following obstetric anal sphincter injuries.
Materials and methods
This study was carried on 30 patients with obstetric anal sphincter injuries in the Department of General Surgery, Zagazig University Hospitals, during the period from May 2015 to June 2017. The patients divided into two groups: group A was managed primarily with end-to-end repair technique of external anal sphincter and group B was managed using overlap repair technique.
Results
The age of the studied patients in group A ranged from 25 to 56 years, with mean of 30.8±9.9 years, and in group B, it ranged from 23 to 59 years, with mean of 31.5±8.2 years. Group A has shorter operative time and less intraoperative bleeding, with no difference between both the groups regarding fecal incontinence, flatus incontinence, dyspareunia, and perineal pain.
Conclusion
Obstetric anal sphincter damage and related fecal incontinence are common and can cause long-term sequelae if not detected and corrected. End-to-end repair is a simple operation that has shorter operative time and less intraoperative bleeding; however, there was no significant difference between both the groups regarding fecal incontinence, flatus incontinence, perineal pain, and dyspareunia. Early sphincter repair by a skilled surgeon minimizes the associated morbidity.

Keywords:
end-to-end repair, fecal incontinence, overlap repair

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Introduction

The most common cause of sphincter lesions is obstetric trauma. Overall, 1–4% of deliveries result in lesions of the sphincter complex or of the pelvic floor [1–4].

The main risk factors include fetus weight, surgical median incision of the perineum performed to ease childbirth (episiotomy), the use of forceps, and breech presentation [5–7].

Perineal tears are classified into four grades depending on severity of extension. First-degree and second-degree tears involve the vaginal epithelium and perineal muscles, respectively, whereas third-degree and fourth-degree tears involve obstetric anal sphincter injuries (OASIS). Third-degree perineal tears involve injury to the anal sphincter and are subdivided into grade 3a, less than 50% of external anal sphincter (EAS) thickness torn; grade 3b, more than 50% of EAS thickness torn; and grade 3c, both EAS and IAS torn. Fourth-degree tears involve the anal sphincter as well as the anorectal epithelium [8]. Furthermore, anal incontinence caused by sphincter injury has been reported to be associated with very high cumulative costs for health services [9].

Optimal timing for the repair is within 3–4 months following the trauma. However, the surgical procedures are often performed years later (even if the results are less effective) [1].

The most frequently performed surgical procedure for the treatment of obstetric lesions is direct anterior sphincter suture repair [10,11].

Anal sphincter repair can be performed using end-to-end technique, thereby facing the two flaps after resecting scar tissue, as well as through overlap technique, which is performed by overlaying the residual functional extremities [12].

In this study, we compare the outcome of primary end-to-end repair versus overlap repair in the EAS injuries.

Materials and methods

This was a prospective randomized study, and patients were simply randomized by closed envelop method. Between May 2015 and June 2017, of all surgically treated patients, 30 patients were selected with third-degree and fourth-degree anal sphincter injuries either early or late and were divided into two groups. The study was approved by the ZUH Institutional Review Board. In patients, we registered neither first degree, second degree, nor previously managed anal sphincter injury.

Group A contained 15 patients, and they were managed by primary end-to-end repair technique of EAS. Group B also contained 15 patients, and they were managed by overlap repair technique. The age of the patients in group A ranged from 25 to 56 years and in group B from 23 to 59 years. All patients were subjected to full clinical assessment for anal incontinence that includes flatus incontinence, passive soiling, and incontinence of liquid or solid stool.

Every patient was inspected for perineal body, vaginal epithelium tear, and episiotomy scar. Digital rectal examination was performed. Endoanal ultra sonography was done to identify anal sphincter complex and occult anal sphincter tear (an injury, which is clinically undetectable and recognizable just on endoanal ultrasonography). Anorectal manometry was performed to assess anal sphincter pressures, rectal sensation, rectoanal reflexes, and rectal compliance.

The techniques and possible complications were explained to the patient, and informed consent was obtained. Preoperative full bowel preparation and insertion of a Foley's catheter were applied. The analysis was conducted in June 2017, with follow-up period of 1 year (at 3, 6, and 12 months after operation) at surgery outpatient department to assess perineal pain, dyspareunia, flatus incontinence, and fecal incontinence.

Operative techniques

The surgery was performed under either spinal or general anesthesia. The patient is placed in a lithotomy position. The incision is made at the inferior margin level of the vagina. The rectovaginal cleavage that leads to the peritoneal floor leaves the EAS of the anus posteriorly and the vaginal flap anteriorly. The levator ani muscles are now visible laterally. Therefore, preanal sutures of the levator ani are obtained with two–three polypropylene sutures 2/0 located far behind on the muscles, to avoid tightening of the vagina and potential dyspareunia.

The anterior quadrant of the EAS, often sclerotic, is then dissected and detached from the internal sphincter. The scar is followed laterally until the identification of the residual muscles/extremities is performed, on which two traction sutures can be made.

When using end-to-end technique, to restore the anatomical continuity and functional EAS as well as to restore its tension, a few approximation interrupted sutures are needed (two or three polypropylene sutures 2/0 or 0/0, depending on the muscle fiber volume, which needs to be attached).

When using overlap technique, the sphincter extremities are dissected by ~3 cm, while carefully maintaining the neurovascular bundle intact. By crossing the two traction sutures, the sphincter extremities are exposed to ensure that they are sufficiently mobilized and to obtain an overlapping of at least 2 cm without tension.

After repairing the anal sphincter, the perineal body is reconstructed by suturing the perineal muscles. The vaginal mucosa and perineal skin are repaired in the usual fashion.

Results

In this study, age of the patients in group A ranged from 25 to 56 years, with a mean of 30.8±9.9 years, and in group B from 23 to 59 years, with a mean of 31.5± 8.2; no significant difference was found between both the groups regarding age (P=0.61).

In group A (end-to-end repair), 11 (73.3%) patients had 3b-degree tear, three (20%) 3c degree, and one (6.7%) fourth degree. In group B (overlap repair), 12 (80%) patients had 3b-degree tear, two (13.3%) 3c degree, and one (6.7%) fourth degree. It is obvious that 3b-degree anal sphincter injury is the most common in both groups (Table 1).

The mean operative time in the end-to-end group was 33.66±4.6 min (range: 20–60 min), and it was 45.4± 8.8 min (range: 30–80 min) in the overlap group, with the overlap technique indicating longer operative time.

Blood loss during end-to-end repair was ~100–300 ml, with mean of 200±20, and in overlap group, it was

~150–600 ml, with mean of 370±30. The overlap technique had more intraoperative bleeding (Table 2).

After 3 months, in group A, four patients of 15 experienced perineal pain, whereas in group B, three of 15 experienced perineal pain. After 6 months, two patients of 14 experienced perianal pain in group A whereas in group B, one of 14 experienced that pain. One patient was lost to follow-up in both groups. After 12 months, one patient of 13 experienced perineal pain in group A and one of 14 experienced perineal pain in group B. Another patient was lost to follow-up after 12 months in group A. No significant difference was found between both groups regarding perineal pain during follow-up (Table 3).

Regarding dyspareunia during follow-up, at 3 months, four patients in group A and five in group B experienced dyspareunia. At 6 months of follow-up, one patient in each group showed improvement of dyspareunia. At 12 months, two patients in group A and three patients in group B experienced no more dyspareunia. No significant difference was found between both groups regarding dyspareunia during follow-up (Table 4).

Of the 15 patients in group A, five experienced flatus incontinence after 3 months, and in group B, three patients of 15 experienced flatus incontinence. At 6 months of follow-up, four of 14 patients experienced flatus incontinence in group A, whereas in group B, three of 14 experienced flatus incontinence. One patient in each group experienced improvement of flatus incontinence. One patient in each group was lost to follow-up at 6 months. At 12 months of follow-up, three patients of 13 patients experienced flatus incontinence, whereas in group B, two of 14 patients experienced flatus incontinence. One patient in each group showed improvement of flatus incontinence, and one patient in group A was lost to follow-up. No significant difference was found between both groups regarding flatus incontinence at 3, 6, and 12 months of follow-up (Table 5).

Table 1 Degree of anal sphincter injury distribution in both groups

Degree of anal sphincter injury	Groups		Total	χ^2	*P*
	Group A: end to end	Group B: overlap			
3b degree	11 (73.3)	12 (80.0)	23 (76.6)	0.24	0.9
3c degree	3 (20.2)	2 (13.3)	5 (16.7)		
Fourth degree	1 (6.7)	1 (6.7)	2 (6.7)		
Total	15 (100.0)	15 (100.0)	30 (100.0)		

This table shows 3b-degree anal sphincter injury is the most common in both groups.

Table 2 Intraoperative bleeding in both groups

Bleeding	Groups		Total	χ^2	*P*
	Group A: end to end	Group B: overlap			
Yes					
Amount (ml)	100–300	150–600	1	1.03	0.3
Mean±SD	200±20	370±30	3.3%		

This table shows that overlap technique has more intraoperative bleeding.

Table 3 Perineal pain distribution in both groups at 3, 6, and 12 months

Perineal pain	Groups [*n*/*N* (%)]		Total [*n*/*N* (%)]	χ^2	*P*
	Group A: end to end	Group B: overlap			
3 months	4/15 (26.6)	3/15 (20.0)	6/30 (20.0)	0.14	0.9
6 months	2/14 (14.2)	1/14 (7.1)	3/28 (10.7)		
12 months	1/13 (7.7)	1/14 (7.1)	1/27 (3.7)		

This table shows no difference between both the groups regarding perineal pain.

Table 4 Dyspareunia distribution in both groups at 3, 6, and 12 months

Dyspareunia	Groups [*n*/*N* (%)]		Total [*n*/*N* (%)]	χ^2	*P*
	Group A: end to end	Group B: overlap			
3 months	4/15 (26.6)	5/15 (33.3)	9/30 (30.0)	0.03	0.9
6 months	3/14 (21.4)	4/14 (28.5)	7/28 (25.0)		
12 months	1/13 (7.7)	1/14 (7.1)	2/27 (7.4)		

This table shows no difference between both the groups regarding dyspareunia.

In group A, three of 15 patients experienced fecal incontinence after 3 months, and in group B, two of 15 patients experienced fecal incontinence. At 6 months of follow-up, one of 14 patients experienced fecal incontinence in group B. One patient in group B experienced improvement of fecal incontinence. One patient in each group was lost to follow-up at 6 months. At 12 months of follow-up, two out of 13 patients experienced fecal incontinence in group A. One patient in group A showed improvement of fecal incontinence, and one was lost to follow-up. No significant difference was found between both the groups regarding fecal incontinence (Table 6).

Discussion

Obstetric sphincter lesions can be detected immediately postpartum and are caused by third-degree laceration [13]. In ~40% of cases, continence disorders are detected as early as 6 months after delivery [5]. The compensation of the pelvic muscles frequently disguises sphincter function deficit; however, with time, abnormalities deviously evolve along with muscle weakening, most frequently during menopause, and are discovered years later [14,15].

OASIS can be associated with significant short-term and long-term consequences like pain, infection, and sexual dysfunction; they vary in severity and affect the quality of life of the patient. This may in turn result in considerable economic burden to healthcare providers and patients. It also has an implication on future deliveries. Although it can never be eliminated, it can be reduced by improving practice, training, and provision of high-quality multidisciplinary care to reduce long-term morbidity [16].

OASIS is the primary cause of fecal incontinence in women. These injuries may be clinically recognized as third-degree or fourth-degree tears or may be occult and diagnosed using ultrasound. Repair of injuries recognized at delivery by an experienced operator using a standard protocol, and either end-to-end approximation or overlap techniques of the external sphincter, has been proven to greatly improve the outcome for women by reducing symptoms of fecal incontinence and the persistence of sphincter defects seen on follow-up ultrasound [17].

In the present study, the age of the studied patients in group A ranged from 25 to 56 years old, with mean of 30.8±9.9 years, and in group B ranged from 23 to 59 years, with mean of 31.5±8.2 years. There was no significant difference regarding age in both groups.

Regarding the degree of anal sphincter injury distribution among groups, there was no significant difference between both groups as the 3b-degree anal sphincter injury is most common injury noticed in both groups (80.0% in overlap technique vs. 73.3% in the end-to-end technique).

Fernando found that 3b-degree anal sphincter injury is most common injury noticed in both groups (78.1% in overlap technique vs. 75% in the end-to-end technique) [18].

Moreover, in our study, there was a statistically significant difference regarding the operative time as cases managed using the end-to-end technique have shorter operative time, with mean of 33.66±4.6 min, than cases managed using the overlap technique, with mean of 45.4±8.8 min

Our result goes with the study by Fernando *et al.* [18] that found that there was a significant difference between both the groups regarding operative time,

Table 5 Flatus incontinence distribution in both groups at 3, 6, and 12 months

Flatus incontinence	Groups [*n*/*N* (%)]		Total [*n*/*N* (%)]	χ^2	*P*
	Group A: end to end	Group B: overlap			
3 months	5/15 (33.3)	3/15 (20.0)	8/30 (26.6)	0.04	1
6 months	4/14 (28.5)	3/14 (21.4)	7/28 (25)		
12 months	3/13 (23)	2/14 (14.2)	5/27 (18.5)		

This table shows no difference between both groups regarding flatus incontinence distribution at 3, 6, and 12 months.

Table 6 Fecal incontinence distribution in both groups at 3, 6, and 12 months

Fecal incontinence	Groups [*n*/*N* (%)]		Total [*n*/*N* (%)]	χ^2	*P*
	Group A: end to end	Group B: overlap			
3 months	3/15 (20.0)	2/15 (13.3)	7/30 (23.3)	0.23	0.9
6 months	3/14 (21.4)	1/14 (7.1)	4/28 (14.2)		
12 months	2/13 (15.3)	1/14 (7.1)	3/27 (11.1)		

This table shows no difference between both the groups regarding fecal incontinence.

with median 28 min (range: 15–55 min) in the end-to-end technique versus 38 min (range: 15–70 min) in the overlap technique.

Regarding intraoperative bleeding, the end-to-end technique has less intraoperative bleeding, with mean of 200±20 ml, than cases managed using the overlap technique, with mean of 370±30 ml (6.75%).

Fernando *et al*. [18] recorded that the median estimated blood loss in the overlap group was 260 ml (range: 100–600) compared with 100 ml (range: 100–450) in the end-to-end group.

Regarding perineal pain distribution among groups (Table 3), no difference between both the groups was observed at 3, 6, and 12 months.

Williams *et al*. [19] found that there was no statistically significant difference in the perineal pain between the two repair techniques. Fernando *et al*. [18] found that there was no significant difference in perineal pain from 6 weeks up to 6 months. However, at 12 months, a significant proportion of women in the end-to-end group reported perineal pain.

In our study, there was no difference between both the groups regarding dyspareunia distribution at 3, 6, and 12 months.Fernando *et al*. [18] and Rygh and Korner [20] found that there was no statistically significant difference in dyspareunia between the overlap and end-to-end groups.

In our study, that there was no difference between both the groups regarding flatus incontinence distribution at 3, 6, and 12 months.

Fernando *et al*. [18], Farrell *et al*. [21], and Rygh and Korner [20] found that at 6 months, there was a statistically significant difference in flatus incontinence, favoring the end-to-end group, but there were no differences in flatus incontinence between the two groups at any of the other time points.

Regarding fecal incontinence, no difference was found between both the groups in our study, and this was in agreement with Farrell *et al*. [21] and Rygh and Korner [20] who did not show a statistically significant difference the incidence of fecal incontinence between the two repair techniques.

Fernando *et al*. [18] found that a significant proportion of women in the overlap group reported an improvement in symptoms of fecal incontinence from 6 weeks to 12 months.

Considering the aspects evaluated in this study, there was no statistically significant difference between end-to-end repair and overlap repair techniques. However, a larger sample size may result in projection of more detailed comparison between the two techniques.

Conclusion

Obstetric anal sphincter damage and related fecal incontinence are common and can cause long-term sequelae if not detected and corrected. End-to-end repair is a simple operation that has shorter operative time and less intraoperative bleeding; however, no significant difference was observed between both the groups regarding fecal incontinence, flatus incontinence, perineal pain, and dyspareunia.

Early repair of injuries recognized at delivery by an experienced operator using a standard protocol minimizes the associated morbidity.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Living donor liver transplantation for hepatocellular carcinoma: Milan criteria versus University of California San Francisco

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Introduction
Hepatocellular carcinoma (HCC) is the most common primary liver cancer and most patients with HCC also suffer from coexisting cirrhosis. HCC recurrence is a major concern after liver transplant. The Milan criteria was accepted after a good 5 years survival but was criticized for being so restricted and this criticism promoted the appearance of more expanded criteria like the University of California San Francisco (UCSF). Our study compares the results of both Milan and UCSF criteria and the risk factors for recurrence.
Patients and methods
This study included 60 patients had living donor liver transplantation for HCC between January 2011 and December 2016 in Ain Shams Center for Organ Transplantation. They were divided into two groups. Group A: transplanted within the Milan criteria; and group B: transplanted while beyond Milan but within the UCSF criteria. Both groups are compared as regards the recurrence, survival, and risk factors for recurrence.
Results
There is no statistically significant difference between the two groups as regards the survival and recurrence. The 1 and 3 years survival were 86.5 and 71.9% for the Milan group and 81.7 and 61.4% in the group of patients beyond Milan (statistically nonsignificant, P=0.348). Seven (15.1%) patients from the Milan group had recurrence while in the beyond Milan group four (28.6%) patients had recurrence (statistically nonsignificant, P=0.258). There were no statistically significant difference in microvascular invasion (P=0.388), tumor grade (P=0.207), and α-fetoprotein (P=0.112) between both groups.
Conclusion
Milan criteria can be safely expanded to UCSF with comparable results if responding well to downstaging and with low α-fetoprotein.

Keywords:
beyond Milan criteria, hepatocellular carcinoma, living donor liver transplantation, Milan criteria

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Introduction

Hepatocellular carcinoma (HCC) constitute about 80–90% of all liver malignancies [1]. Although there are different modalities for HCC treatment, liver transplant is considered a superior modality as it does not only remove the tumor from the body, but also remove the whole diseased organ and provide the patient with a new liver specially in patients with liver cell failure. HCC recurrence is always a concern and prediction of the recurrence is always a challenge. The appearance of the Milan criteria was mainly to predict the outcome after liver transplant and to find the group of patients who will have a survival benefit from transplant with less recurrence rates. The Milan criteria was criticized by many literatures because of its selectivity as it being restricted to small group of patients. Many literatures showed that the Milan criteria can be safely expanded with comparable results but still the Milan criteria is widely used in many different center all over the world.

This study aims at assessment of the outcome of living donor liver transplantation (LDLT) for patients with HCC within the Milan criteria and beyond Milan criteria but within University of California San Francisco (UCSF).

Patients and methods

This is a retrosepctive study analyzing the clinical data from 60 consecutive adult patients who had LDLT between January 2011 to December 2016 for having HCC in Ain Shams Centre for Organ Transplantation. Our study included 60 patients who met our criteria and transplanted for HCC out of total 254 patients who were transplanted during the previously mentioned period of

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time. After approval by the ethical committee in Ain Shams university, Patients were divided in two groups; (group A) represents patients whom underwent liver transplantation for HCC within Milan's criteria.

The patients were divided in two groups: group A represents patients who underwent liver transplantation for HCC within the Milan criteria, while group B represents patients who underwent liver transplantation for HCC beyond the Milan criteria but within UCSF. Both groups were compared as regards the recurrence, survival (1 and 3 years survival), tumor grade, microvascular invasion, largest tumor size, and the total tumor burden (the total tumor diameter for patients with multiple tumor nodules was calculated as the sum of the maximal diameter of each lesion in centimeters).

The patients were followed up after transplantation with clinical, laboratory [liver function tests, α-fetoprotein (AFP), and lab for routine post-transplant follow-up, e.g. kidney function tests, etc.) and radiological [abdominal ultrasound every month and abdominal triphasic computed tomography (CT) every 6 months]. If CT scan showed hepatic focal lesion with HCC criteria or elevated AFP, metastatic work-up (i.e. CT chest and bone scan or total body positron emission tomography scan) was done.

Our inclusion criteria include patients with HCC without extra hepatic metastasis and no macrovascular invasion. Patients included in this study were either within the Milan criteria or beyond Milan but within UCSF with good response to downstaging (child A, early B) (most of group B patients) or test of time (child late B, C) patients. Downstaging was done for patients exceeding Milan but within the UCSF criteria. Bridging treatment [ablation or transarterial chemoembolization (TACE)] was done for patients within Milan if transplantation will be delayed for any reason.

We consider downstaging was successful when:

(1) The tumor size and number were stationary.
(2) AFP <decreasing to be less than 200.
(3) Adequate radiological response with no enhancement in 1 and 3 months follow-up imaging (triphasic CT or MRI).

Protocol of immunosuppression

The standard is a combination of the two drugs calcineurin inhibitors (CNIs) and steroids. High-dose intravenous corticosteroids are used in the immediate perioperative and postoperative period and then tapered accordingly. In patients without renal dysfunction post-transplantation, CNIs are the mainstay of therapy with the long-term goal of low levels of immunosuppression and minimization of medication. In patients with renal insufficiency, a combination of low-dose CNI therapy and Mycophenolic ascid (MFAs) or a switch to mammalian target of Rapamycin (mTOR) inhibitors to preserve graft function and prevent further renal deterioration. Patients are weaned off corticosteroids within 3 months, providing they do not have evidence of autoimmune disease or recurrent episodes of rejection.

Results

The Milan group had 46 patients, 44 were men and two patients were women and the beyond Milan group had 14 patients, 13 men and one women patient. There is no statistically significant difference between the two groups as regards the sex distribution. Also the age was nearly comparable. The Milan group mean age was 53 years, ranging between 38 and 66 years, while in the beyond Milan group the mean age was 51 years with a range between 30 and 60 years. There is no statistically significant difference between the two groups as regards age (Table 1).

As regards the model for end-stage liver disease score, the mean model for end-stage liver disease for the Milan group was 16.98 and for the beyond Milan was 15.86 (statistically nonsignificant, P=0.152).

The etiology of the liver disease was mainly due to hepatitis C cirrhosis in both groups 95.7 and 92.9 for the Milan and beyond Milan. Each group has one case of cryptogenic cirrhosis and one case in the Milan group had hepatitis B virus infection (statistically nonsignificant, P=0.575).

As regards the liver functions, the Milan group had four (8.7%, child A) cases, and 15 (32.6, child B) cases, and 27 (58.7%, child C) cases and for the beyond Milan group there were six (42.9%, child A) cases, and five (35.7%, child B) cases, and three (21.4%) cases were child C (statistically significant, P=0.005).

Survival

We compared the 1 and 3 years survival for both groups and we did not find statistically significant difference in survival between the two groups (P=0.348). The overall 1 and 3 years survival were 88.2 and 69.5% with a mean survival of 44.9 months for the whole group. The 1 and 3 years survival were 86.5% and versus 85.7% and 61.4% with a mean survival of 37.3 months for patients within the UCSF and beyond Milan (Fig. 1, Tables 2 and 3).

Table 1 Preoperative data

	Milan group (*n*=46) [*n* (%)]	Beyond Milan group (*n*=14) [*n* (%)]	Test value	*P* value	Significance
Sex					
Female	2 (4.3)	1 (7.1)	0.177[a]	0.674	NS
Male	44 (95.7)	13 (92.9)			
Age					
Mean±SD	53.09±6.50	51.07±9.07	0.922[b]	0.360	NS
Range	38–66	30–62			
MELD score					
Mean±SD	16.98±2.66	15.86±1.99	1.453[b]	0.152	NS
Range	12–21	13–19			
Child					
A	4 (8.7)	6 (42.9)	10.528[a]	0.005	HS
B	15 (32.6)	5 (35.7)			
C	27 (58.7)	3 (21.4)			
Etiology					
Cryptogenic	1 (2.2)	1 (7.1)	1.108[a]	0.575	NS
HBV	1 (2.2)	0 (0.0)			
HCV	44 (95.7)	13 (92.9)			

HBV, hepatitis B virus; HCV, hepatitis C virus; HS, highly significant; MELD, model for end-stage liver disease; S, significant; [a]χ^2-test; [b]Independent *t*-test; [c]Mann–Whitney test.

Table 2 Overall survival and mean survival for each group

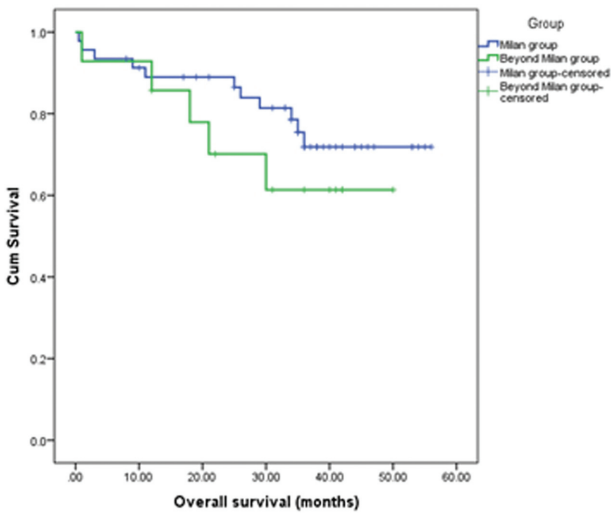
	Overall survival (months)		Log-rank test		1 year (%)	3 year (%)
	Mean	SE	χ^2	*P* value		
Milan group (*n*=46)	46.160	2.668	0.880	0.348	86.5	71.9
Beyond Milan group (*n*=14)	37.279	4.700			85.7	61.4
Overall survival (*n*=60)	44.945	2.431			88.2	69.5

Table 3 Hepatocellular carcinoma recurrence

	Milan group (*n*=46) [*n* (%)]	Beyond Milan group (*n*=14) [*n* (%)]	Test value	*P* value	Significance
HCC recurrence					
No recurrence	39 (84.8)	10 (71.4)	1.278	0.258	NS
Recurrence	7 (15.2)	4 (28.6)			

HCC, hepatocellular carcinoma.

Figure 1



Overall survival in months.

Recurrence

As regards recurrence, seven patients from the Milan group had recurrence with a recurrence rate of 15.1%, while for the beyond Milan group, four (28.6%) patients had recurrence with no statistically significant difference between the two groups (*P*=0.258).

Bridging and downstaging

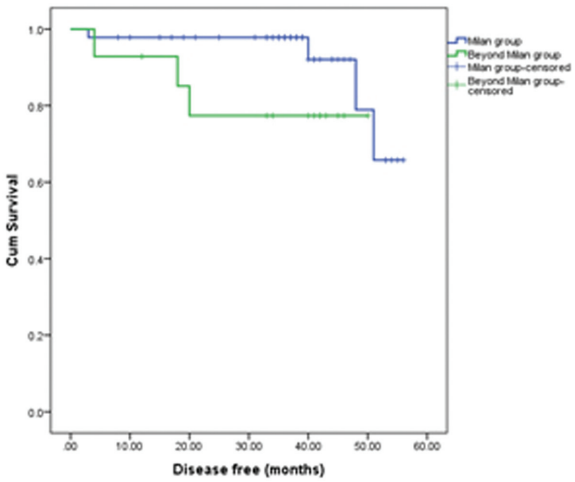
Only six patients from the Milan group needed intervention before transplant as a bridge to avoid tumor progression (Table 4). Two (4.3%) patients had TACE and four (8.7%) patients had radiofrequency ablation (RfA), while on the other hand in the beyond Milan group eight (51%) patients had TACE before transplant and two (14.3) patients had RfA and one (7.1) patient had microwave ablation (statistically highly significant, *P*<0.000) (Figs 2 and 3).

Table 4 Tumor characters, bridging, and downstaging in both groups

	Milan group (*n*=46) [*n* (%)]	Beyond Milan group (*n*=14) [*n* (%)]	Test value	*P* value	Significance
Bridging and downstaging					
N	40 (87.0)	3 (21.4)	28.002[a]	0.000	HS
Microwave	0 (0)	1 (7.1)			
RfA	4 (8.7)	2 (14.3)			
TACE	2 (4.3)	8 (57.1)			
Largest tumor size (cm)					
Mean±SD	2.73±0.90	4.39±0.85	6.119[b]	0.000	HS
Range	1.5–5	3.5–6			
Total tumor burden (cm)					
Mean±SD	3.60±1.15	6.82±1.05	9.339[b]	0.000	HS
Range	1.5–6	5.5–8.5			
AFP					
Median (IQR)	10.3 (4.61–76.6)	16.33 (10.8–46)	–1.590[c]	0.112	NS
Range	1.96–989	5.88–899			
Microvascular invasion					
No	32 (69.6)	8 (57.1%)	0.745[a]	0.388	NS
Yes	14 (30.4)	6 (42.9%)			
Tumor grade					
No	2 (4.3)	1 (7.1)	4.560[a]	0.207	NS
I	24 (52.2)	5 (35.7)			
II	18 (39.1)	5 (35.7)			
III	2 (4.3)	3 (21.4)			

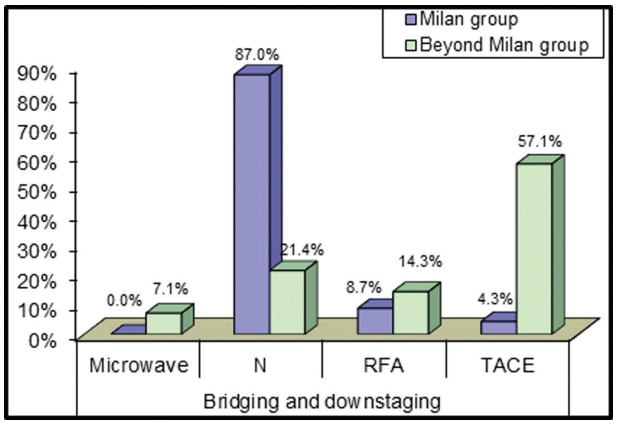
AFP, α-fetoprotein; HS, highly significant; IQR, interquartile range; RfA, radiofrequency ablation; S, significant; TACE, transarterial chemoembolization; [a]χ^2-test; [b]Independent *t*-test; [c]Mann–Whitney test.

Figure 2



Disease-free survival.

Figure 3



Bridging and downstaging (statistically highly significant, *P*=0.000).

Tumor character

In our study, the mean of the largest tumor size in the Milan group was 2.7±0.9 cm ranging between 1.5 and 5 cm, while the mean largest tumor size for the beyond Milan was 4.39± 0.85 cm ranging between 3.5 and 6 cm, which was highly significant (statistically highly significant, *P*<0.000) (Fig. 4).

Also the total tumor burden for the Milan group was 3.6 cm and for the beyond Milan was 6.82 cm which was highly significant (statistically highly significant, *P*<0.000) (Fig. 4).

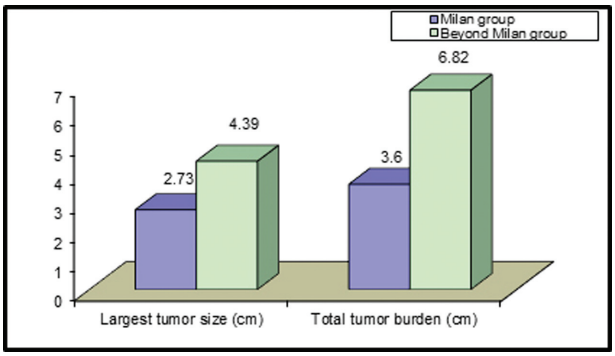
Microvascular invasion

Fourteen patients from the Milan group had microvascular invasion (MVI) which constitute 30% of the cases while in the beyond Milan group six (42.8%) patients showed MVI (statistically no significant, *P*=0.388).

Tumor grade

In our study, 52% of the patients in the Milan group had grade I (well-differentiated) tumor by pathology,

Figure 4



Largest tumor size and total tumor burden (statistically highly significant, *P*=0.000).

39% grade II, and 4.3% grade III and only two (4.3%) cases could not be assessed due to good ablation. For the other group of patients (beyond Milan group), five (35.7%) cases had grade I tumors, five (35.7%) cases had grade II, and three (21/4%) cases had grade III. Only one case could not be assessed due to severe tumor necrosis (statistically nonsignificant, *P*=0.207).

α-Fetoprotein

The median for AFP at the time of transplantation for the Milan group was 10.3, while for the beyond Milan group it was 16.33 (statistically nonsignificant, *P*=0.112).

Discussion

It is well known that HCC recurrence affects survival postliver transplantation; that is why the selection of a suitable candidate for liver transplant with HCC is crucial in order to avoid wasting of the resources especially at a time of marked organ shortage all over the world.

Following the Milan criteria the liver transplant showed good results for HCC patients with a 5-year survival of 79%, but was criticized for being so restrictive which promoted the appearance of many expanded criteria like UCSF, Tokyo criteria, Hangzhou criteria, and the up to seven criteria [2].

Tokyo criteria that involve the 5–5 rule (tumors not >5 cm and not >5 lesions) showed 3 years survival of 94% compared with 50% in patients outside the criteria [2]. The up to seven criteria by Mazaferro (the sum of the tumor number and the size of the largest tumor (in cm) was not larger than 7) showed that the 5-year survival was 71.25. Also the UCSF criteria showed that the 5-year survival was 64%, *P*=0.61 [3].

In this study, we compared the results of the LDLT for HCC patients who are within Milan and the beyond Milan but within the UCSF criteria as regards the survival, recurrence, and possible risk factors for recurrence. Our study showed that the survival is comparable in both groups. The 1 and 3 years survival was 86.5 and 71.9% for the Milan group, respectively, and 85.7 and 61.4% for the beyond Milan group. Although the 3 years survival in the beyond Milan group is slightly lower, it is not statistically significant with a *P* value of 0.348.

As regards the tumor size, it has been shown in any literature that the size of the tumor is an important preoperative variable and the Milan criteria is mainly dependent on the tumor size, but Ito *et al.* [4] have shown that there is no difference in survival in patients within and beyond Milan in his study (71% in patients within Milan compared with 64% in patients beyond Milan). In our study, the mean of the largest tumor size in the Milan group was 2.7 cm, ranging between 1.5 and 5 cm, while the mean largest tumor size for the beyond Milan was 4.39, ranging between 3.5 and 6 cm which was a highly significant difference between the two groups ($P<0.05$); also the total tumor burden for the Milan group was 3.6 cm and for the beyond Milan was 6.82 cm which was highly significant ($P<0.05$). There was no statistically significant difference as regards the difference between the two groups as regards the largest tumor size and total tumor burden and the overall survival and recurrence which confirm that the tumor size alone is not the only predictor for recurrence.

MVI has been shown in different studies that it is associated with high recurrence rates and poor survival. Unfortunately, it is a postoperative finding and cannot be assessed by the preoperative biopsy. Many studies are trying to find a preoperative marker for MVI.

Also the histologic grade is an important factor affecting recurrence and survival after liver transplant for HCC. Poorly differentiated tumors were previously considered as a contraindication for liver transplant. High-grade tumors have been correlated in some studies to increase the size of the tumor. A study by Mazaffero *et al.* [3] showed that the increase in tumor size and number together with the microvasular invasion goes in parallel relation with the high-grade tumors.

In our study, there is no statistically significant difference between the two groups as regards MVI and tumor grade. This finding may be explained by proper patient selection due to acceptance only for patients with HCC within the UCSF if responding

to downstaging or test of time. The absence of significant difference in MVI and grade between both groups may be the main cause of absence of significant difference in overall and recurrence-free survival.

AFP is an important marker for diagnosis and follow-up in patients with HCC. The high levels of AFP before transplant were correlated to poor prognosis and high recurrence rate. Also the AFP level is important to monitor the response after locoregional therapy and the persistent high levels of AFP after locoregional therapy may predict either inadequate treatment or distant metastasis. Unfortunately, AFP is not always high in recurrence. In a study done by Hsieh *et al.* [5], 23% of patients demonstrated normal AFP levels at the time of HCC recurrence. The AFP levels in these patients were initially high. Those patients with inconsistent AFP levels had a longer recurrence interval and worse recurrence-to-death survival rate than other patients in the study which may be because of the delay of the recurrence diagnosis [5].

In our study, the median for AFP at the time of transplantation for the Milan group was 10.3, while for the beyond Milan group it was 16.33. There was no statistically significant difference between the two groups as regards the AFP level.

Many authors have shown that downstaging can decrease recurrence rate and the dropout of the waiting list. Mazzaferro *et al.* [3] reported no dropouts in 50 patients within the Milan criteria treated with RFA. Some studies reported no dropouts in patients within Milan treated by TACE and a short waiting time (178 days), while others documented a probability of dropout of 15% at 6 months and 25% at 12 months. Cumulative results show that RFA achieves the highest rates of complete necrosis (12–55%) compared with TACE (22–29%). Complete necrosis is best achieved with percutaneous ablation in tumors less than 3 cm in diameter [3,6].

Only six patients from the Milan group needed intervention before transplant as a bridge to avoid tumor progression. Two (4.3%) patients needed TACE and four (8.7%) patients needed RfA, while on the other hand the beyond Milan group had eight (51%) patients who had TACE before transplant and two (14.3) patients had RfA and one (7.1%) patient had microwave ablation. The difference in selection were mostly related to tumor character (size, site, diffuse, or well localized, in relation to major vascular or biliary structure).

Conclusion

Although the Milan criteria were used as the standard criteria for the selection of patients with HCC eligible for LDLT, it seems to be too restrictive. The Milan criteria can be safely expanded to UCSF with comparable results if responding well to downstaging and with low AFP.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Role of ultrasound in diagnosis and management of inflammatory breast diseases

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Introduction
Inflammatory breast diseases are frequently encountered clinical complaints, and they range from benign to malignant forms, namely inflammatory breast carcinoma (IBC). It is crucial to differentiate IBC from other types of mastitis because there are major differences in its prognosis and treatment. Ultrasound (US) is one of the main diagnostic tools for discriminating benign and malignant mastitis. US-guided aspiration and core needle biopsy are the mainstay in diagnosis and management of inflammatory breast diseases.
Materials and methods
The study is a prospective study that included 48 patients referred to the Radiology Department, Women's Imaging Unit from the 'Surgical Breast Clinic', and surgical outpatient's clinics and wards in the period between January 2016 and July 2016. US examination was performed for all the cases by 8–12 MHz linear array transducer. Full field digital mammography was performed for 33/48 patients. US-guided core biopsies of the breast were performed in indicated cases. Drainage under US guidance and cytological assessment was performed also in certain cases.
Results
In all, 36/48 (75%) cases were finally diagnosed as benign mastitis, and 12/48 (25%) cases were finally diagnosed as malignant. Within the examined group, 40/48 (83.3%) cases underwent short-term first look follow-up US study after a course of antibiotic therapy: seven/40 (17.5%) patients showed complete resolution of the symptoms and the diagnosis of simple infectious mastitis was confirmed, whereas 33/40 (82.5%) patients showed no response to treatment.
Conclusion
US plays a specific role in diagnostic approach and management of inflammatory breast diseases. It is essential to discriminate benign from malignant etiologies as there are major differences in their prognosis and treatment options.

Keywords:
breast abscess, duct ectasia, inflammatory breast diseases, ultrasound

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Introduction

Breast involvement by inflammatory or noncurrent infectious diseases is not uncommon. 'Mastitis' is a frequently encountered complaint in clinical practice.

Although a significant problem especially among lactating women, there remains a paucity of scientific research into the anatomical, physiological, and pathological determinants of inflammatory breast disorders [1].

The radiological features of breast lesions caused by immunologic, reactive, and noncurrent infectious diseases often mimic those of malignancy, frequently constituting a diagnostic challenge even if the underlying disease is known [2] and usually require biopsy [1].

In general, 'Mastitis' is inflammation of the breast that may or may not be accompanied by infection. The term 'Mastitis' is often used synonymous with breast infection, but strictly speaking 'Mastitis' is inflammation of the breast irrespective of the cause [3].

Mastitis can be classified into three main types: the infectious, noninfectious, and malignant mastitis (MM) [4].

Infectious mastitis encompasses breast-specific and nonspecific forms of infections whether primary or complicating already present breast pathologies. This form of mastitis is more common during the child-bearing period especially during lactation. Patients in this group usually present with fulminant inflammatory manifestations and are usually treated with antibiotics,

hot fomentations, and various breast drainage procedures [4].

Noninfectious forms of mastitis encompasses another group of aseptic or chemical inflammatory breast disorders that do not necessarily occur during lactation, and thus do not usually present with fulminant inflammatory signs and do not usually resolve with antibiotics. Microbial infection may trigger some forms as periductal mastitis or complicate others as diabetic Mastopathy [4].

The third group of mastitis, which is the most serious form of mastitis, is MM usually accompanying the inflammatory breast carcinoma (IBC) or the very rare form of malignant breast abscess [4].

Any nonlactating female patient presenting with inflammatory breast symptoms that fail to respond to antibiotic therapy should be advised to go for both a mammography and ultrasound (US) examination immediately followed by a punch biopsy from the skin and aspiration from the subdermal lymphatics to exclude any possibility of IBC [4].

Materials and methods

The study is a prospective study that included 48 patients referred to the Radiology Department, Women's Imaging Unit from the 'Surgical Breast Clinic' and Surgical outpatient's clinics and wards in the period between January 2016 and July 2016. The study was approved by the Editorial Review Board of the Radiology Department of Kasr el Aini, Cairo University Hospitals.

Inclusion criteria were patients presenting with clinical signs of mastitis including redness, hotness, and focal or diffuse swelling of the breast with or without generalized constitutional symptoms with or without palpable breast masses.

Patients presenting with other sole mammary manifestations, for example, palpable mass lesions or nipple discharge, were not included in the study. According to the imaging findings recorded with US they were classified into benign and malignant forms of mastitis. Reference standard of diagnosis was histopathology after core or surgical biopsy, as well as follow-up studies for lesions for typical signs of simple mastitis. Histopathology results were then correlated with the imaging findings of US.

Methods

All patients were subjected to complete medical history and full clinical examination by their referring physicians. Cases were obliged to supply these data at the time of imaging.

Ultrasonography

USexamination was performed for all the cases by 8–12 MHz linear array transducer (General Electric Company, Easton Turnpike, Fairfield, Connecticut, United States). US reports should confirm (positive finding) or exclude (negative finding) the presence of the following:

(1) Echogenic edematous fat lobules.
(2) Interstitial edema.
(3) Ill-defined collections.
(4) Retroareolar duct system dilatation.
(5) Thickened skin (>2 mm) and its measurement.
(6) Masses and it confirm their cystic or solid nature.
(7) Abscess cavities.
(8) Fistulous tracts.
(9) Lymph node enlargement and its status.

US follow-up after a course of antibiotic therapy was performed for indicated cases to ensure condition amelioration.

Mammography

Full Field Digital Mammography was performed for 33/48 patients using GE Senograph 2000 Machine. Standard craniocaudal and mediolateral oblique views were obtained, with the axilla included in the latter.

Exclusion criteria: lactating and young patients were excluded as mammogram was not feasible for these patients.

US-guided core biopsies of the breast were performed in indicated cases using 14 G needle.

Drainage under US guidance and cytological assessment was performed also in certain cases.

Results

The study population included 48 patients with clinical symptoms and signs of mastitis.

Demographic data

Ages of these patients ranged from 22 to 73 years (mean age: 39.7±12.8), as shown in Table 1.

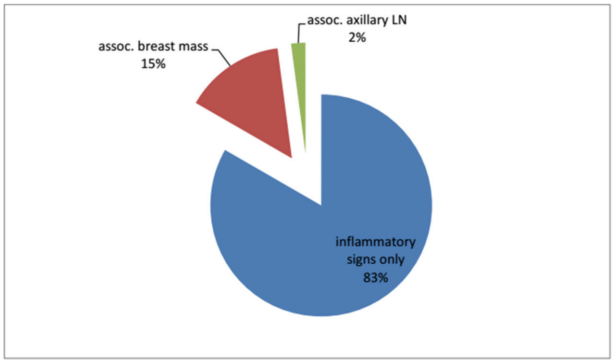
All patients presented with clinical signs of mastitis (pain, redness, hotness, and swelling). They were the

Table 1 Age of the studied group

Characteristics	Patient group (*n*=48)
Age (years)	
Range	22–73
Mean±SD	39.7±12.8

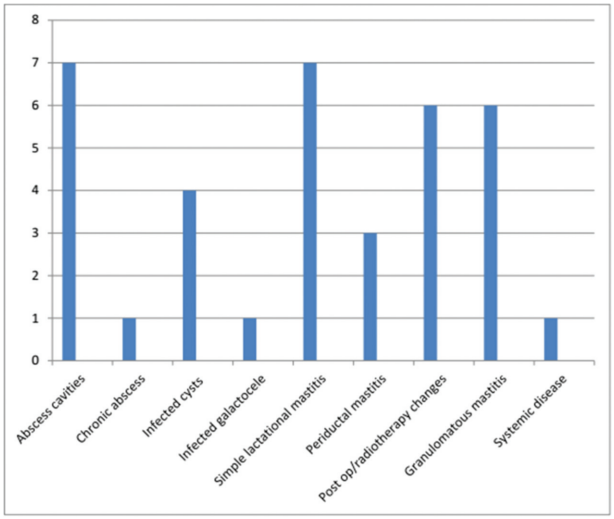
Lactating women comprised 20.8% (*n*=10/48).

Figure 1



Frequency of different clinical presentations. LN, lymph nodes.

Figure 2



Distribution of cases of benign mastitis included in the study.

sole signs in 40 (83.3%) patients. Seven (14.6%) patients had an additional palpable intramammary mass and another one (2.08%) patient had a palpable axillary mass, as represented in Fig. 1.

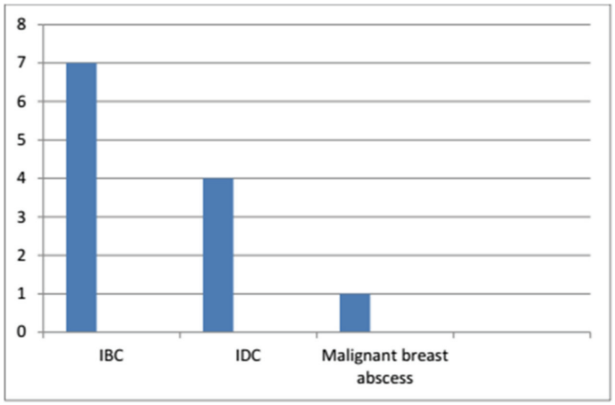
The study included one (*n*=1) pregnant female patient.

Final diagnosis

Final diagnosis was reached either by performing a short-term follow-up study or after revision of core biopsy/surgical specimens or cytology of fluid aspirates.

In all, 36/48 (75%) cases were finally diagnosed as benign mastitis, including the following:

Figure 3



Distribution of cases of malignant mastitis included in the study. IBC, inflammatory breast carcinoma.

Table 2 Response of the patients to antibiotic therapy

Characteristics	Patient group (*n*=48) [*n* (%)]
Antibiotic (positive)	40 (83.3)
Response	7 (17.5)
No response	33 (82.5)

(1) Abscess cavities (*n*=7).
(2) Chronic abscess (*n*=1).
(3) Infected cysts (*n*=4).
(4) Infected galactoceles (*n*=1).
(5) Simple lactational mastitis with or without abscess formation (*n*=7).
(6) Active Periductal mastitis (*n*=3).
(7) Postoperative/radiotherapy changes (*n*=6).
(8) Granulomatous mastitis (*n*=6).
(9) Systemic disease (*n*=1).

This is represented in Fig. 2.

In addition, 12/48 (25%) cases were finally diagnosed as malignant, as represented in Fig. 3, including the following:

(1) IBC (*n*=7).
(2) Invasive ductal carcinoma (*n*=4).
(3) Malignant breast abscess (*n*=1).

Ultrasound follow-up study

Within the examined group, 40/48 (83.3%) cases underwent short-term first look follow-up US study after a course of antibiotic therapy:

(1) A total of seven out of 40 (17.5%) patients showed complete resolution of the symptoms, and the diagnosis of simple IM was confirmed.
(2) In addition, 33 out of 40 (82.5%) patients showed no response to treatment.

This is shown in Table 2.

Core/surgical biopsy specimens and cytology of aspirates

Within the examined group, 17 out of 48 (35.4%) patients underwent core/surgical biopsy, whereas 19 out of 48 (39.6%) patients performed fine needle aspiration/drainage under US guidance, and cytological assessment of the aspirates was done, as shown in Table 3.

Descriptive and comparative analysis

Imaging findings identified on US were reported and their frequencies were calculated. The diagnoses (whether benign or MM) were postulated according to US. Findings were then correlated with the final diagnoses. In reference to this accuracy, measures were then calculated for US, namely sensitivity, specificity, and positive and negative predictive values.

(1) Cases that were diagnosed as benign inflammatory by US and proved to be benign inflammatory in the final diagnosis, either by aspiration cytology, histopathology, or follow-up, were considered as true negative cases.
(2) Cases that were diagnosed as malignant by US and proved to be malignant in the final diagnosis by histopathology were considered as true positive cases.
(3) Cases that were diagnosed as benign inflammatory by US and proved to be malignant in the final diagnosis by histopathology were considered as false negative cases.
(4) Cases that were diagnosed as malignant by US and proved to be benign inflammatory in the final diagnosis by aspiration cytology, histopathology, or follow-up were considered as false positive cases.

Ultrasonography

On US, signs of local or diffuse inflammatory changes were identified in all cases (48/48, 100%). These signs included echogenic edematous fat lobules that are delineated by dark interstitial edema lines.

Additional signs were also reported including:

(1) Ill-defined collections.
(2) Lymph node status.
(3) Skin thickness.
(4) Subdermal lymphatic layer thickness.
(5) Associated mass lesions.

Table 3 Frequency of core biopsy &and fine needle aspiration in cases included in the study

Characteristics	Patient group (*n*=48) [*n* (%)]
Core/surgical biopsy	
Fine needle	17 (35.4)
Aspiration/drainage	19 (39.6)

Ill-defined collections

The association between the final diagnosis and the presence or absence of ill-defined collection was studied.

(1) In benign inflammatory cases:
   (a) The presence of ill-defined collection was 21/22, 95.5%.
   (b) The absence of ill-defined collection was 15/26, 57.7%.
(2) In malignant cases:
   (a) The presence of ill-defined collection was 1/22, 4.5%.
   (b) The absence of ill-defined collection was 11/26, 42.3%.
(3) The presence of ill-defined collection (21/22, 95.5%) was higher in benign cases of mastitis than malignant cases (1/22, 4.5%).

Lymph nodes status

These results are shown in Tables 4 and 5 and Figs. 4 and 5.

(1) In benign inflammatory cases:
   (a) The presence of indeterminate axillary lymph nodes was 6/10, 60%.
   (b) The presence of nonspecific axillary lymph nodes was 29/30, 96.7%.
   (c) The presence of pathological axillary lymph nodes was 1/8, 12.5%.
(2) In malignant cases:
   (a) The presence of indeterminate axillary lymph nodes was 4/10, 40%.
   (b) The presence of nonspecific axillary lymph nodes was 1/30, 3.3%.
   (c) The presence of pathological axillary lymph nodes was 7/8, 87.5%.

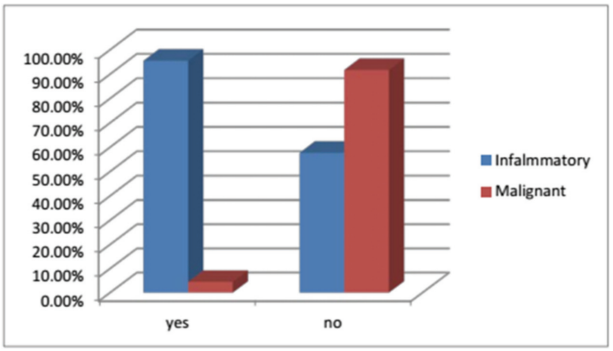
Table 4 Correlation between final diagnosis and the presence of ill-defined collection in the studied group

Final diagnosis	Collections [*n* (%)]	
	No (*n*=26)	Yes (*n*=22)
Inflammatory (*n*=36)	15 (57.7)	21 (95.5)
Malignant (*n*=12)	11 (42.3)	1 (4.5)

Table 5 Correlation between final diagnosis and the lymph node status

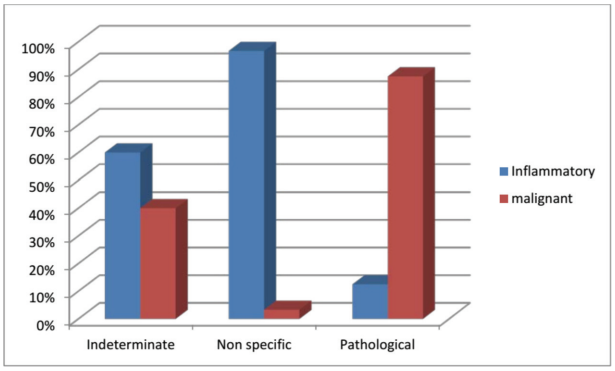
Final diagnosis	Indeterminate (*n*=10) [*n* (%)]	Nonspecific (*n*=30) [*n* (%)]	Pathological (*n*=8) [*n* (%)]
Inflammatory (*n*=36)	6 (60)	29 (96.7)	1 (12.5)
Malignant (*n*=12)	4 (40)	1 (3.3)	7 (87.5)

Figure 4



Frequency of ill-defined collections associated with benign and malignant mastitis cases.

Figure 5



Frequencies of the different lymph node status with benign and malignant mastitis cases.

(3) The presence of pathological axillary lymph nodes with prominent cortices and muffled hila was strongly indicative of a malignant pathology.
(4) Indeterminate axillary lymph nodes were a common association with severe benign mastitis. Resolution was the rule on follow-up US studies performed in 6/10 (60%) cases.

Skin and subdermal lymphatic thickening

A cut-off value of both skin thickness and subdermal lymphatic thickness was calculated with area under receiver operating characteristic (ROC) curve, sensitivity, and specificity as shown in Table 6 and Figs 6–8.

Associated mass lesions and abscess cavities

The correlation between the final diagnosis and associated mass lesions and abscess cavities is demonstrated in Table 7.

Final diagnosis

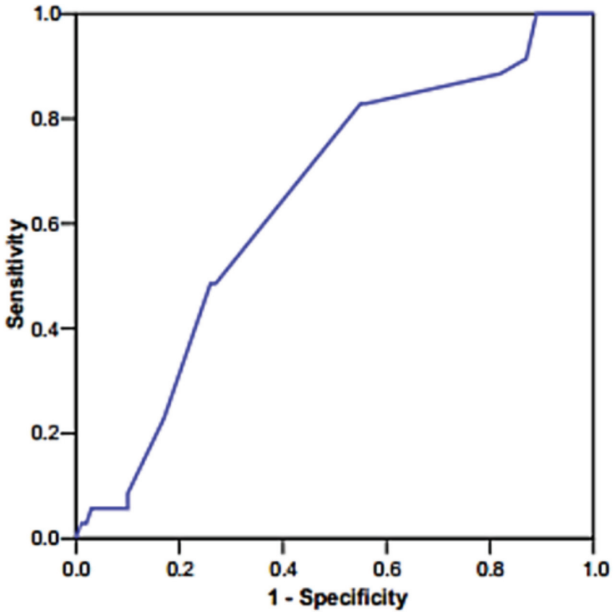
The association between the final diagnosis and US diagnosis is demonstrated in Table 8 and Fig. 9.

Table 6 Skin thickness and subdermal lymphatic studied parameters

	Cut-off value	Area under ROC curve	Sensitivity (%)	Specificity (%)
Thick skin	>3.5 mm	0.642	82.86	45
Subdermal lymph	>1 mm	0.920	80	94

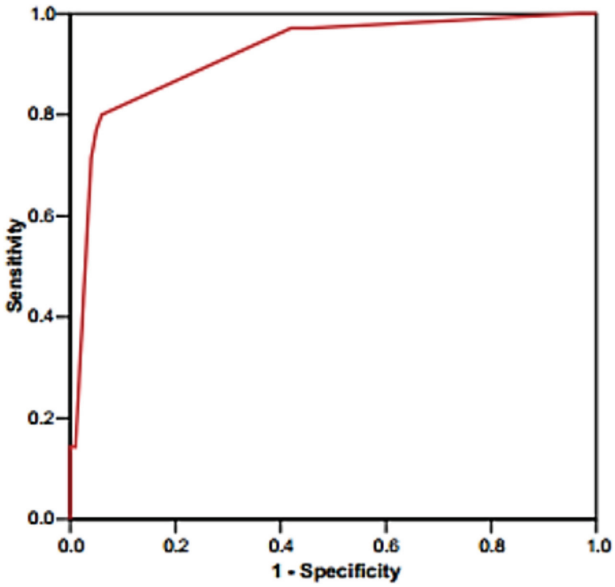
A cut-off value of skin thickness greater than or equal to 3.5 mm and subdermal lymphatic thickness greater than 1 mm were considered indicative of malignancy.

Figure 6



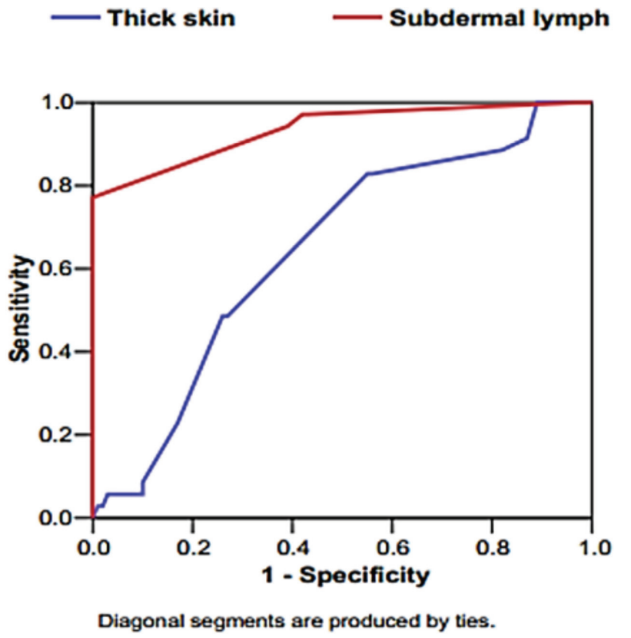
Receiver operating characteristic curve for thick skin.

Figure 7



Receiver operating characteristic curve for subdermal lymph thickness.

Figure 8



Receiver operating characteristic curves for both skin subdermal lymph thickness.

Table 7 Correlation between final diagnosis and associated lesions

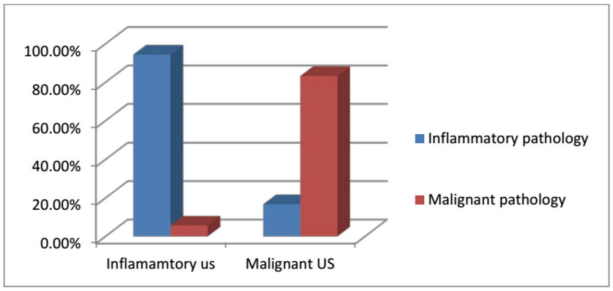
Final diagnosis	Associated [*n* (%)]	
	Mass lesions (*n*=4)	Abscess cavities (*n*=13)
Inflammatory (*n*=36)	1 (25)	12 (92.3)
Malignant (*n*=12)	3 (75)	1 (7.7)

Table 8 Association between final diagnosis and ultrasound in the studied group

Final diagnosis	US [*n* (%)]	
	Inflammatory (*n*=36)	Malignant (*n*=12)
Inflammatory (*n*=36)	34 (94.4)	2 (16.7)
Malignant (*n*=12)	2 (5.6)	10 (83.3)

US, ultrasound.

Figure 9



Association between final diagnosis and ultrasound in the studied group. US, ultrasound.

Mammography

In our study, mammography showed 87.5% sensitivity and 48% specificity in detection and characterization of inflammatory breast disorders. The low specificity is mainly attributed to the higher incidence of inflammatory breast disorders in young individuals where mammography is considered inappropriate and when performed is usually inconclusive.

Diagnostic indices:

$$\text{Sensitivity} = \frac{\text{number of true positive results (TP)}}{\text{number of true positive results (TP)} + \text{number of false negative results (FN)}} \times 100$$

The age of the patients included in the study ranged from 22 to 73 years (mean age: 39.7±12.8). Compared with only 1/33 (3.03%) false negative cases diagnosed by mammography, we had 13/33 (39.4%) false positive cases. False negative cases were cases that presented

Sensitivity for US=83.33%.

Sensitivity for mammography=87.5%.

$$\text{Specificity} = \frac{\text{number of true negative results (TN)}}{\text{number of true negative results (TN)} + \text{number of false positive results (FP)}} \times 100$$

with early IBC with early diffuse inflammatory signs and insignificantly enlarged axillary lymph nodes. False positive cases were mainly attributed to the relatively high number of chronic granulomatous mastitis cases and extensive aggressive forms of infective mastitis (13/33 39.4%) where the reactionary lymph nodes strongly resembled pathological lymph nodes that commonly associate with IBC.

Specificity for US=94.44%.

Specificity for Mammography=48%.

Positive predictive value=TP/(TP+FP)×100.

Positive predictive value for US=83.33%.

Positive predictive value for mammography=35%.

Discussion

The breast lesions caused by inflammatory disorders often clinically resemble a carcinoma; therefore, they constitute a diagnostic dilemma [2]. It is a challenge to distinguish acute mastitis from malignancy, especially form IBC, by clinical or imaging features [5].

These disorders range from benign up to malignant forms, namely IBC, which carries a grave prognosis. It is very important to distinguish IBC from other types of mastitis because there are major differences in its prognosis and treatment.

Inflammatory breast disorders were classified aiming to differentiate simple forms of mastitis from more complicated and malignant forms [4], where mastitis is classified into three main groups:

(1) Group 1: IM.
(2) Group 2: non-IM.
(3) Group 3: MM.

IM encompasses breast-specific and nonspecific forms of infections whether primary or complicating already present breast pathologies. This form of mastitis is more common during the child-bearing period especially during lactation. Patients in this group usually present with fulminant inflammatory manifestations and are usually treated with antibiotics, hot fomentations, and various breast drainage procedures [4].

Non-IM encompass another group of aseptic or chemical inflammatory breast disorders that do not necessarily occur during lactation, and thus do not usually present with fulminant inflammatory signs and do not usually resolve with antibiotics. Microbial infection may trigger some forms as periductal mastitis or complicate others as diabetic mastopathy [4].

The third group of mastitis, which is the most serious form of mastitis, is MM usually accompanying the IBC or the very rare form of malignant breast abscess [4].

In this study, we discussed the role of US in the evaluation of, and discrimination between, benign and malignant inflammatory breast disorders. Results were mainly compared with the final diagnosis, which was reached either by performing a short-term follow-up study or after revision of core biopsy/surgical specimens or cytology of fluid aspirates.

Total of 36/48 (75%) cases were finally diagnosed as benign mastitis, including:

(1) Abscess cavities (*n*=7).
(2) Chronic abscess (*n*=1).
(3) Infected cysts (*n*=4)
(4) Infected galactoceles (*n*=1).
(5) Simple lactational mastitis with or without abscess formation (*n*=7).
(6) Active periductal mastitis (*n*=3).
(7) Postoperative/radiotherapy changes (*n*=6).
(8) Granulomatous mastitis (*n*=6).
(9) Systemic disease (*n*=1).

Total of 12/48 (25%) cases were finally diagnosed as malignant, including:

(1) IBC (*n*=7).
(2) Invasive ductal carcinoma (*n*=4).
(3) Malignant breast abscess (*n*=1).

A few previous studies have reported various sonography and mammography features of mastitis. Described mammography findings are also vague and lack specificity. Mammography findings varied from ill-defined dense poorly demarcated areas of diffuse edema with extensive skin thickening to normal study.

Adding to this, patients with mastitis have painful, swollen, and dense breasts, and thus they cannot withstand adequate mammography compression. Therefore, mastitis patients are usually referred for an early US examination.

In our study, mammography showed 87.5% sensitivity and 48% specificity in detection and characterization of inflammatory breast disorders. The low specificity is mainly attributed to the higher incidence of inflammatory breast disorders in young individuals where mammography is considered inappropriate and when performed is usually inconclusive.

The age of the patients included in the study ranged from 22 to 73 years (mean age: 39.7±12.8). Compared with only 1/33 (3.03%) false negative cases diagnosed by mammography, we had 13/33 (39.4%) false positive cases. False negative cases were cases that presented with early IBC with early diffuse inflammatory signs and insignificantly enlarged axillary lymph nodes.

False positive cases were mainly attributed to the relatively high number of chronic granulomatous mastitis cases and extensive aggressive forms of infective mastitis (13/33, 39.4%) where the reactionary lymph nodes strongly resembled pathological lymph nodes that commonly associate IBC.

US was proven to be superior in the diagnosis of inflammatory breast disorders in previous studies [4]. By US, in addition to the general signs of mastitis, we have more discriminating signs that can differentiate between benign and malignant forms of mastitis, namely:

(1) The presence or absence of ill-defined collections, abscess cavities, and associated mass lesions.
(2) The lymph node status whether pathological, reactionary, or nonspecific.
(3) The presence or absence of significant skin thickening and dilated subdermal lymphatic layer.

The presence of ill-defined collection (21/22, 95.5%) was higher in benign infective mastitis cases than malignant cases (1/22, 4.5%). Its presence was a reliable sign in the exclusion of a malignant process.

Similar results were also reported by Kamal *et al.* [4], where ill-defined collections were not identified in MM.

In addition, Martins *et al.* [6] reported that the US findings of multiple irregular ill-defined collections with fingerlike aspects would suggest benign mastitis rather than carcinoma.

Globular axillary lymph nodes with prominent and thickened cortices and muffled hila are considered pathological.

Pathological lymph nodes (7/8, 87.5%) were higher in malignant cases. They were also identified in 1/8 (12.5%) benign mastitis cases that proved to be chronic nonspecific granulomatous mastitis after revision of biopsy specimens.

Bilgen *et al.* [7], in their study, diagnosed metastatic enlarged lymph nodes when they showed eccentric or absent hila and when the long to short axis ratio was less than 1.5.

Kamal *et al.* [4] found that lymph nodes with these criteria were higher in IBC, a sign that favored its diagnosis.

Associated abscess cavities confirmed the benign nature of mastitis (12/13, 92.3%), whereas the presence of associated mass lesions indicated a malignant nature (3/4, 75%).

Kamal *et al.* [4] found that the presence of abscess cavities in IM and the absence of masses are significant differentiating signs between infectious and MM. Kamal *et al.* [4] in 2009 deduced that US was superior to mammography in detection and measurement of skin thickening [4]. Wilson *et al.* [8] in 1982 reported that skin thickness should not exceed 2.5–3 mm; Robertson *et al.* [9] in 2010 confirmed the similar finding on mammography and MRI, and stated in addition that the thickness in patients with IBC frequently measures up to 13 mm.

In our study, a cut-off value of skin thickness greater than or equal to 3.5 mm was considered indicative of malignancy (area under ROC 0.668). A cut-off value of subdermal lymphatic thickness greater than or equal to 1 mm was also considered indicative of malignancy (area under ROC 0.920).

Out of the 48 cases included in the study, US results showed the following:

Two false negative (4.2%), two false positive (4.2%), 34 true negative (70.8%), and 10 true positive (20.8%) cases.

The calculated sensitivity and specificity of US are 83.33 and 94.44%, respectively.

The positive predictive value for US was 83.33% and the negative predictive value was 94.44%. US plays a fundamental role in the diagnostic workup of mastitis patients. An ideal US should ensure an accurate diagnosis, guide for interventional procedures whenever necessary, and should be used to monitor adequate management by short-term follow-up studies along the course of therapy. Kamal *et al.* [4] classified Mastitis patients management according to their US findings into three categories:

(1) Category 1: the patients were reassured and were given a short course of antibiotics and hot fomentations.
(2) Category 2: the patients were asked to come for a short-term follow-up study after completion of medical therapy or after performing ultrasound or operative intervention.
(3) Category 3: the patients were subjected to immediate interventional procedures. This classification depends

on US 'Diagnostic Workup' of mastitis cases passing through several sequential steps.

Mastitis is diagnosed on US examination when the following signs are encountered: interstitial edema lines that delineate the echogenic and edematous fat lobules with overlying focal or diffuse skin thickening. Next, other associated signs should be looked for.

If no other associated signs are seen, simple mastitis is diagnosed. The patient is assured and is asked to come for a short-term follow-up study after completing an antibiotic course. Complete resolution should be the rule. Nonresolution should raise the possibility of development of complications, infection by atypical organisms, or IBC. A biopsy should then be considered. If abscess cavities, infected cysts, or postoperative collections are encountered, they should be drained and followed up to ensure no re-collection. If pathological lymph nodes, dilated subdermal lymphatics, or mass lesions are encountered, we should directly resort to biopsy [10].

In our study, within the examined group, 40/48 (83.3%) cases underwent short-term first look follow-up US study after a course of antibiotic therapy:

In all, seven out of 40 (17.5%) patients showed complete resolution of the symptoms and the diagnosis of simple IM was confirmed, whereas 33 out of 40 (82.5%) patients showed no response to treatment.

Complete resolution is the rule after a short course of antibiotics if simple mastitis is the case.

When a patient is resistant to treatment, one of three conditions should be considered:

(1) The patient might have an unusual form of infection (e.g. granulomatous mastitis).
(2) She might have developed complications – for example, abscess cavity.
(3) She might have early malignant signs.

Therefore, US-guided diagnostic and therapeutic interventional procedures should then play a role.

In our study, within the examined group, 17/48 (35.4%) patients underwent core/surgical biopsy, whereas 19/48 (39.6%) patients performed fine needle aspiration/drainage under US guidance and cytological assessment of the aspirates was done.

US-guided biopsy is performed to evaluate suspicious mass lesions when present. Skin punch biopsies, axillary lymph node biopsy, and aspiration from the dilated subdermal lymphatic layer are performed to confirm the diagnosis of IBC. Abscess cavities, infected cysts, and postoperative collections are drained.

Treatment of breast abscesses is a difficult clinical problem. The surgical literature describes classic abscess treatment as that consisting of an incision over the point of maximal tenderness and digital disruption of abscess septa with the patient under general anesthesia. The abscess cavity is left open and packed with gauze, and there are subsequent dressing changes for up to 6 weeks during wound granulation.

Cosmetic results are often disappointing owing to scar formation. After the administration of antibiotics, abscess incision and drainage are still required because the abscess capsule prevents adequate contact between the antibiotic and the organisms. Even with this aggressive approach, the abscess recurrence rate is reported to be between 10 and 38% [11].

In our study, US has been shown to be useful in depicting abscesses in patients with mastitis and subsequently has been used to guide drainage. It is conceivable that US guidance may facilitate complete drainage of breast abscesses compared with blind aspiration because US enables visualization of multiple abscess loculations. It is possible that loculated abscess is the reason for recurrence after blind aspiration.

In all, six (46.2%) out of 13 patients diagnosed with breast abscess showed resolution of symptoms after US-guided complete aspiration.

In conclusion, US plays a specific role in diagnostic approach and management of inflammatory breast diseases. It is essential to discriminate benign from malignant etiologies as there are major differences in their prognosis and treatment options and the Ultrasound is so helpful in this discrimination, the U/S also act as a guide for interventional procedures whenever necessary and should be used to monitor adequate management by short term follow up studies along the course of therapy.

Summary and conclusion

Inflammatory breast disorders are a frequently encountered clinical complaints and can occur in healthy, nonlactating women of all ages.

They range from benign up to malignant forms and it remains a challenge to distinguish acute mastitis from malignancy, especially from IBC, by clinical or imaging features. It is very important to distinguish IBC from other types of mastitis because there are major differences in its prognosis and treatment

In our study, we verified the role of US in the diagnosis and management of inflammatory breast disorders, stressing on how to differentiate between benign and malignant etiologies.

Mammography plays a limited role in inflammatory breast disorders. It showed a low specificity. Mastitis usually hits patients at young ages where mammography examinations are usually not recommended.

Even at older ages, mammography findings described in mastitis are nonspecific.

On the other hand, ultrasonography plays a significant and important role in the diagnostic workup of inflammatory breast disorders. The following parameters were the crucial points of differentiation: (a) ill-defined collections, (b) skin thickening, (c) subdermal lymphatic thickness, (d) lymph nodes status and course of therapy.

In comparison, the sensitivity and specificity of mammography was 87.5 and 48%, respectively. The positive predictive value for mammography was 35% and the negative predictive value was 92.3%.

On the other hand, the calculated sensitivity and specificity of US was 83.33 and 94.44%, respectively. The positive predictive value for US was 83.33% and the negative predictive value was 94.44%.

To conclude, ill-defined collections, skin thickening, subdermal lymphatic thickness, and lymph nodes status are the crucial points of differentiation between benign and malignant etiologies of different inflammatory breast diseases.

US plays a specific role in diagnostic approach and management of inflammatory breast diseases. It is essential to discriminate benign from malignant etiologies as there are major differences in their prognosis and treatment options and the Ultrasound is so helpful in this discrimination, the U/S also act as a guide for interventional procedures whenever necessary and should be used to monitor adequate management by short term follow up studies along the course of therapy.

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Conflicts of interest
The authors have no commercial or other associations that might be a conflict of interest in relation to this article.

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Combined stab high ligation with retrograde laser ablation compared to endovenous laser ablation in the treatment of symptomatic great saphenous varicose veins

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Objective
To compare reflux recurrences and complications after combined stab high ligation and retrograde laser ablation (SHL/ablation) with endovenous laser ablation (EVLA) of the great saphenous vein (GSV) varicosity.
Patients and methods
This study was designed as a single-center, nonblinded, randomized controlled trial; patients with symptomatic primary GSV varicosity with an incompetent saphenofemoral junction (SFJ) were randomized into two groups: the first was treated by high ligation of GSV with SHL/ablation and the second group was treated by EVLA, both groups received laser therapy using 120 J/cm of 980 nm diode laser. Patients with bilateral GSV insufficiency were randomized separately for each leg. The primary outcome was anatomic success with complete obliteration of the GSV. Secondary outcomes were sonographically determined reflux and clinical recurrence in the treated area after 1 year.
Results
Between March 2014 and December 2016, 280 legs in 257 patients were treated by SHL/ablation (n=140) or EVLA (n=140). The mean age, preoperative complain, mean GSV diameter, and treated length were comparable in both groups. There were no significant differences in postoperative complications or pain experience during or after the procedure in both treatments. The procedure time was significantly longer in SHL/ablation group (88.5±9.8 min) than EVLA (66.5±11.76 min). Twelve months after procedures, SHL/ablation limbs had no recurrence of clinical complaints or venous reflux while EVLA limbs showed venous reflux in 17 (12.1%) limbs and recurrence of limb edema and heaviness in 15 (10.7%) limbs with significant difference between the two groups ($P< 0.05$).
Conclusion
Combined high ligation through stab incision with laser ablation of GSV significantly decreases the risk of venous reflux and clinical recurrence after treatment of GSV varicosities.

Keywords:
endovenous laser ablation, great saphenous vein, SFJ, varicose veins

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Introduction

Varicose vein disease is one of the most common health problems faced by vascular surgeons worldwide affecting up to 23% of adult population [1]. In Western countries, the reported prevalence of varicose veins ranges from 20% in men to more than 25% in women. The majority of patients with primary varicose veins have great saphenous vein (GSV) insufficiency [2].

Along with affecting the quality of life of patients, it also causes physical symptoms such as achiness, swelling, and itching, with further worsening of the condition leading to skin changes and ulcerations. Proper treatment of varicose veins does, however, abolish these symptoms and improve the quality of life of patients [3].

Over the past decades, the gold standard treatment of the insufficient great saphenous vein (GSV) has been high ligation and stripping (HL/S) combined with phlebectomies; the results of this procedure are long lasting and have been shown to improve disease specifically and general quality of life of the patients with primary varicosis. However, HL/S is often performed as a day-case or inpatient operation [4].

In the last two decades and with the advent of the 'endovenous revolution, thermal endovenous ablation (EVA) of the great saphenous vein (GSV) or small

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saphenous vein by laser [endovenous laser ablation (EVLA)] or radiofrequency (RFA) has progressively become the principal therapy for VVs in the USA. It has increased in volume by 450-fold during the last decade [5].

EVLA represents the most commonly applied method within randomized controlled trials. EVLA and HL/S are comparably effective concerning improvement of disease severity and quality of life. In terms of clinical recurrence and saphenofemoral refluxes, HLS is superior to EVLA 5 years after treatment [6].

EVLA has the advantage of less pain, faster recovery to normal activities, and can be carried out as day-case or in an office-based setting under local anesthesia with or without sedation. Although technical success of EVLA is close to 100%, post-EVLA complications such as postprocedural pain, ecchymosis, tenderness, and phlebitis are common. One of the more concerning side effects is deep venous thrombosis (DVT), which has been reported in up to 7.7% of cases [7].

To reduce the risk of thrombosis, proper positioning of the laser tip, with a general distance of 1.5–2 cm below the SFJ, is essential. However, extension of the thrombus of the GSV into the common femoral vein has been reported; this phenomenon is called endothermal heat-induced thrombosis (EHIT) [8].

The mechanism of EHIT formation is not fully understood. Superficial venous thrombus is expected following thermoablation, whether this is by thrombotic vessel occlusion or local vessel injury from direct thermal damage or steam bubbles. Thrombus may form in the deep veins or propagate from treated superficial veins to the deep veins [9]. Some authors have suggested that changing the treatment distance from 2 cm to greater than or equal to 2.5 cm peripheral to the deep venous junction may result in a diminished incidence of EHIT [10].

Another rare complication of EVLA, reported by many authors, is external iliac arteriovenous fistula due to improper positioning of laser fiber tip in GSV [11–13].

One of the primary causes of recurrences after EVLA that was observed was reflux from a venous tributary in close proximity of the SFJ. While underreported in the literature, the frequency observed suggests that this reason for recurrence will likely increase as more EVLA are being performed and the duration of follow-up increases. The current recommendation of termination of EVLA at 2 cm from the SFJ may contribute to this cause of recurrence and warrants further evaluation [14].

Patients and methods

Patient selection

This study was designed as a single-center, nonblinded, randomized controlled trial at the Department of Vascular Surgery, Menoufia University. Adult patients with a symptomatic primary GSV incompetence at least above the knee and with an incompetent SFJ were eligible to participate. The incompetence of the GSV was defined as a reflux of 500 ms or more at color duplex ultrasound. Medical history, physical examination, duplex ultrasound (DUS), and CEAP classification were documented for all patients.

Exclusion criteria were previous treatment of the ipsilateral GSV, deep venous thrombosis or incompetence, agenesis of the deep system, vascular malformations, ipsilateral small saphenous vein incompetence, arterial insufficiency (defined as an ankle brachial index$<$0.7), pregnancy, heart failure, allergy for lidocaine, immobility, use of anticoagulation, known thrombophilia associated with a high risk of thromboembolism, and inability to provide written informed consent to trial participation.

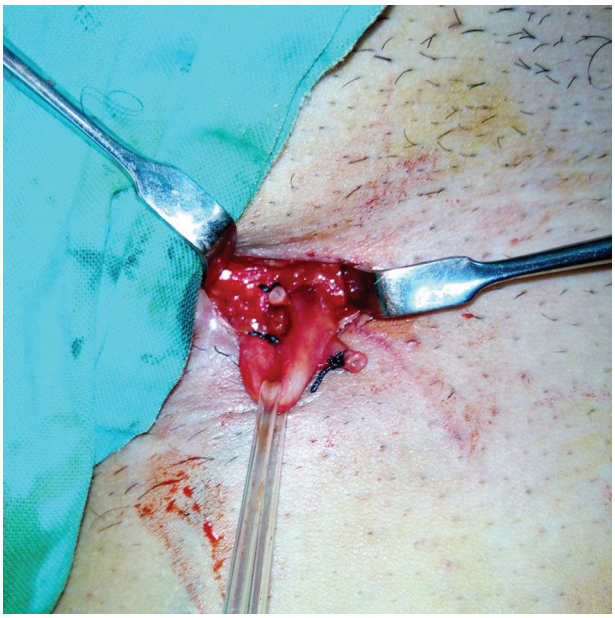
In this study, only the GSV in the thigh (from just below or above knee level) was treated. After written informed consent, eligible patients were randomized using a computerized list into two groups: the first group was treated by EVLA group; the second group was treated by stab high ligation with retrograde laser ablation (SHL/ablation) of the great saphenous vein group. Patients with bilateral GSV insufficiency were randomized separately for each leg.

Interventions

EVLA was performed under ultrasound guidance. In brief, venous access was obtained by puncturing the vein at the knee level, with a 16 or 18 G needle under ultrasound guidance; then a 0.35 guide wire was passed into the GSV up to the level of the SFJ. The needle was removed and a 5-inch introducer sheath was passed over the guide wire. Subsequently, the laser fiber was introduced after removing the guide wire. The laser fiber was positioned at 1.5–2 cm below the SFJ. About 250–500 ml of tumescent anesthetic solution was administered into the saphenous compartment under ultrasound guidance. Withdrawal of the laser fiber was performed in continuous mode, and it was attempted to deliver 100 J/cm.

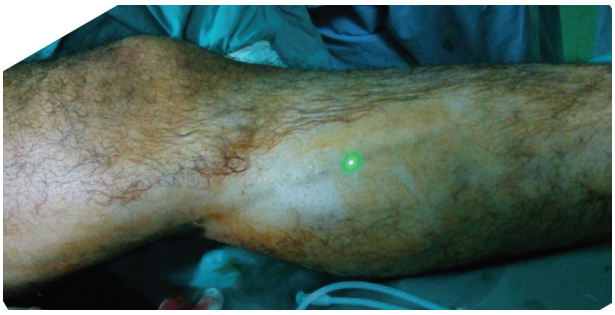
SHL/ablation was performed under tumescent anesthesia. An incision measuring 1 cm was performed at the site of premarked SFJ; ligation of all tributaries was followed

Figure 1



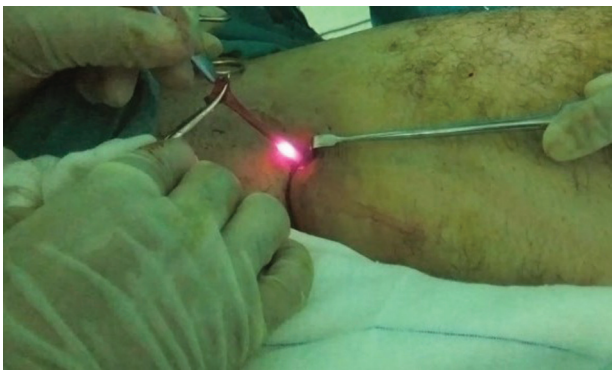
Saphenofemoral junction with ligated tributaries.

Figure 2



Laser fiber tip at the level of knee joint.

Figure 3



Proximal segment ablation.

by flush SFJ ligation (Fig. 1), after saphenofemoral disconnection, a 0.35 guide wire was passed into the GSV to the knee level. Then a 5-inch introducer sheath was passed over the guide wire. Subsequently, the laser fiber was introduced after removing the guide wire (Fig. 2). About 250–500 ml of tumescent anesthetic solution was administered into the saphenous compartment under ultrasound guidance. Withdrawal of the laser fiber was performed in continuous mode, and it was attempted to deliver 100 J/cm (Fig. 3). Ligation of proximal end of the GSV was performed after completion of ablation. The cribriform fascia, superficial fascia, and skin were closed.

Patients received laser therapy with a 980 nm diode laser (12 W; ARC Laser, Nuremberg, Germany), using a bare fiber in continuous mode under duplex guidance. The tumescent anesthetic solution included 500 ml saline, 25 ml 2% lidocaine, and 10 ml 8.4% sodium bicarbonate. Tumescent anesthetic solution was administered along the perivenous space of the GSV under duplex guidance with a 19 G needle.

After both treatments, an ambulatory compressive bandage was applied for 48 h, followed by therapeutic full-thigh compression stockings (20–30 mmHg) for 4 weeks. All patients were observed for at least 1 h after treatment. Patients were encouraged to mobilize and to resume their usual activities as soon as possible. All patients were discharged on the day of the procedure and NSAIDs were prescribed for pain to all the patients. The pain score was measured using a visual analog scale ranging from 0 (no pain) to 10 (most severe pain).

Delivered total energy, GSV diameter, treated GSV length, procedure time, energy in joules per length of GSV in centimeters, and delivered tumescent volume were recorded for each limb. The treated limbs were evaluated as separate treatment events.

Follow-up examinations

Patients were evaluated clinically and by DUSs on the first 48 h, first week, first month, 6 month, and 12 month after the procedure. The presence of flow in the previously ablated vein, symptoms of CVI, ecchymosis, skin burn, paresthesia, induration, swelling, hyperpigmentation, DVT, wound infection, and complaints related to EVLA were recorded as complication.

Outcomes

The primary outcome was anatomic success according to duplex ultrasound evaluation. This was defined as complete obliteration, without flow or reflux, of the GSV. Secondary outcomes were the sonographically determined reflux and clinical recurrence in the treated

area after 1 year; the type and frequency of complications of both treatments were reported.

Statistical analysis

Statistical analysis was performed using SPSS version 24.0. (IBM Corp., Armonk, New York, USA). Discrete variables were presented as numbers (counts) and percent. Continuous variables presented as mean and SD. Student's *t*-test was used for intergroup comparisons to test the significance of difference between two different variables. *P* value of less than 0.05 was considered statistically significant.

Results

Between March 2014 and December 2016, according to the eligibility criteria 280 legs in 257 patients were randomized to SHL/ablation (*n*=140) or EVLA (*n*=140).

Baseline patient characteristics are shown in Table 1. The two groups were comparable with regard to demographic characteristics, CEAP classification of the treated legs, GSV diameter, and complaints of chronic venous disease at randomization.

Technical success was achieved in all procedures of both groups; the mean length of treated GSV and procedure time were significantly longer in the SHL/ablation group; however, the amount of total energy delivered and the tumescent anesthetic volume were comparable in both groups as shown in Table 2. There were no significant differences in pain experience during or after the procedure in both treatments. The procedure time was significantly longer in the SHL/ablation group (88.5±9.8 min) than EVLA (66.5±11.76 min). Treated patients resumed their normal daily activities after few days with no significant difference between the two groups.

No major complications such as skin burn, deep vein thrombosis, persistent pain, persistent bruising, allergy, or anesthetic complications were encountered. Wound infection was seen in two patients after SHL/ablation and needed oral antibiotics to control. Other complications such as ecchymosis, hematoma, phlebitis, induration, hyperpigmentation, and transient paresthesia were higher in the EVLA group but with no significant statistical differences (Table 3).

Table 1 Baseline patient characteristics

	SHL/ablation (*n*=140)	EVLA (*n*=140)	*P* value
Male/female (*n*/*N*)	91/49	77/63	0.112
Age			0.62
Range (years)	17–48	18–51	
Mean±SD	31.22±6.88	30.8±7.3	
Diameter of GSV 2 cm from SFJ	1.34±0.28	1.39±0.24	0.1
Diameter of GSV at knee level	0.9±0.18	0.94±0.22	0.09
Preoperative complaints [*n* (%)]			
Pain	62 (44.2%)	56 (40%)	0.54
Heaviness	95 (67.8%)	81 (57.8%)	0.1
Calf cramps	31 (22.1%)	40 (28.5%)	0.27
Edema	42 (30%)	33 (23.5%)	0.28
Skin changes	7 (5%)	11 (7.8%)	0.45
Venous ulcer	5 (3.5%)	7 (5%)	0.76
CEAP classification			
C2	95 (67.8)	102 (72.8)	0.43
C3	42 (30)	33 (23.5)	0.28
C4	7 (5)	11(7.8)	0.45
C5	1	0	1
C6	5 (3.5)	7 (5)	0.76

EVLA, endovenous laser ablation; GSV, great saphenous vein; SHL/ablation, stab high ligation and retrograde laser ablation.

Table 2 Procedure data and results in both groups

	SHL/ablation (mean±SD)	EVLA (mean±SD)	*P* value
Length of treated vein	44.75±2.83	43.51±3.77	0.002
Total laser energy (J)	4853.3±375.9	4759.7 ±446.9	0.058
Laser energy (J/cm)	108.43±4.3	109.38±4	0.08
Procedure time	88.5±9.8	66.5±11.76	0.0001
Tumescent volume	400.5±30.1	392.1±43.4	0.06
Pain during procedure	3.8±1.13	3.7±1	0.43
Postoperative pain	4.2±0.89	4.35±0.91	0.16
Pain after 48 h	5.55±0.99	5.35±1.2	0.13
Pain after 7 days	3.51±0.88	3.32±0.95	0.08
Daily activity	4.91±1.2	5.11±1.2	0.16
Time needed for ulcer healing (days)	35–70 (52 ±13.5)	42–71 (54.1±11.2)	0.15

EVLA, endovenous laser ablation; SHL/ablation, stab high ligation and retrograde laser ablation.

Table 3 Postoperative complications

Postoperative complications	SHL/ablation [*n* (%)]	EVLA [*n* (%)]	*P* value
Skin burn	0	0	1
Ecchymosis	19 (13.5%)	25 (17.8%)	0.41
Hematoma	0	2 (1.4%)	0.49
Infection	2 (1.4%)	0	0.49
Phlebitis	2 (1.4%)	5 (3.5%)	0.44
Induration	22 (15.7%)	29 (20.7%)	0.35
Persistent pain	0	0	1
Hyperpigmentation	0	1	1
Thromboembolism	0	0	1
Allergy	0	0	1
Persistent bruising	0	0	1
Anesthetic complication	0	0	1
Sensory disturbance	0	3 (2.1%)	0.24

EVLA, endovenous laser ablation; SHL/ablation, stab high ligation and retrograde laser ablation.

Clinical and duplex examination of treated limbs 6 months after the procedure showed maintained obliteration of the GSV treated segment in both groups. Venous reflux was detected at SFJ to tributary veins in the femoral region in 17 (12.1%) limbs treated by EVLA; on the other hand, no reflux was detected in limbs treated by SHL/ablation ($P<0.05$). Twelve months after the procedures, recanalization of GSV was higher in limbs treated by EVLA [seven (5%) limbs] than limbs treated by SHL/ablation [two (1.4%) limb], but still was statistically insignificant ($P=0.17$). Limbs treated by SHL/ablation had no recurrence of clinical complaints or venous reflux; on the other hand, EVLA limbs showed persistence of venous reflux in the 17 (12.1%) limbs and recurrence of limb edema and heaviness in 15 (10.7%) limbs, with significant difference between the two groups ($P<0.05$).

Discussion

Surgery remained the standard treatment of varicose vein disease for centuries until its thrown had been threatened by EVA techniques, including laser ablation, during the last two decades. Being minimally invasive with less pain and earlier ambulation than surgery gave these procedures preference to vascular surgeons and patients.

However, these procedures are not complication free. Efforts had been made to minimize the incidence of recurrence, EHIT or even the rare arteriovenous (AV) fistula complications. In this study, the refluxing GSV was treated by classic EVLA procedure or by high ligation of GSV through stab incision combined with retrograde ablation of the vein; stab incision with minimal dissection was found to minimize the risk of wound infection to 1.4% of cases when compared with 6% of cases reported in the literature [15]. Insertion of the laser fiber retrogradely through the proximal cut end of GSV was found to be feasible and gives alternative to GSV access which in some cases may be difficult and needs a cut down to achieve.

There is some debate about the necessity of high ligation of GSV with EVA procedures; in this work, high ligation of GSV combined with laser ablation had a significant lower clinical and duplex-detected recurrence rate than EVLA (P?0.05). Flessenkämper *et al.* [16], compared EVLA with and without high ligation and surgery and reported that in EVLA without high ligation reflux developed in all side branches, not only in the anterior accessory GSV; on the other hand, there was no major difference between the clinical outcomes of the three therapeutic strategies after a median follow-up of 4 years. Disselhoff *et al.* [17] also concluded similar recurrent rates in EVLA with and without high ligation. Both studies of Flessenkämper *et al.* [16] and Disselhoff *et al.* [17] described neovascularization as an explanation for recurrence with high ligation. High ligation through stab wound with minimal dissection in our work may explain lower incidence of recurrence; this explanation is supported by the lower recurrence and recanalization rate of combined pinhole high ligation and EVLA published by other authors [18]. Packing up the role of high ligation in minimizing recurrence, Rass *et al.* [6], reported that even with different mechanisms of recurrence, high ligation and stripping is superior to EVLA with respect to long-term duplex and same site clinical recurrence.

Another advantage of high ligation is that it may ameliorate the debate about the proper distance between the laser fiber tip and SFJ. While some authors recommend decreasing this distance to decrease the rate of recurrence after EVLA [14], others advocate increasing this distance from 2 to 2.5 cm peripheral to the deep venous junction may result in diminished incidence of EHIT [10].

Conclusion

Combined high ligation through stab incision with laser ablation of GSV significantly decrease the risk of venous reflux and clinical recurrence after treatment of GSV varicosities

Recommendation

Combined stab high ligation with retrograde laser ablation can offer a minimally invasive ablative procedure for great saphenous varicose vein. Large-scale studies with a longer follow-up period may be needed before recommendation of the proper first-line treatment of varicose veins.

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Conflicts of interest

There are no conflicts of interest.

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