The Egyptian Journal of Surgery

The official organ of the Egyptian Society of Surgeons

Vol. (34), No. (1), January 2015

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Egyptian Journal of Surgery - Published Quarterly
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Last updated September 2014

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The Egyptian Journal of Surgery is published four times a year; in January, April, July and October. The annual subscription fees are as follows: Members of ESS: L.E. 100
Institutions: L.E.100
Issues will be mailed to subscribers only.

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Risk factors for post-ERCP pancreatitis: a prospective multicenter study in upper Egypt

Mohammed A. Omar[a], Ahmed E. Ahmed[a], Omar A. Said[a], Hussein El-Amin[b]

[a]Department of General Surgery, Faculty of Medicine, Sohag University, Sohag
[b]Department of Internal Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Mohammed A. Omar, MD, Department of General Surgery, Faculty of Medicine, Sohag University, 82511 Sohag, Egypt
Tel: (002) 0965228628; fax: (002)0934602963; e-mail: elqefty@yahoo.com

Received 27 May 2014
Accepted 02 September 2014

The Egyptian Journal of Surgery
2015, 34:1–10

Background and study aims
Endoscopic retrograde cholangiopancreatography (ERCP) has become widely available for diagnosis and treatment of pancreatic and biliary diseases. Pancreatitis is the most common and serious complication to occur after ERCP resulting in substantial morbidity and occasional mortality. The aim of this study was to evaluate the potential patient and procedure-related risk factors for postendoscopic retrograde cholangiopancreatography pancreatitis (PEP) in a prospective multicenter study.

Patients and methods
Consecutive ERCP procedures were prospectively studied at five centers (two universities, three private). Data were collected on patient characteristics and endoscopic techniques before the procedure, at the time of procedure, and 24–72 h after discharge. PEP was diagnosed and its severity graded according to consensus criteria.

Results
Pancreatitis occurred after 104 (8.9%) of 1162 consecutive ERCP procedures and was graded mild in 66 (63.5%), moderate in 30 (28.8%), and severe in eight (7.7%) cases. On univariate analysis, 11 of 18 evaluated variables were found to be significantly associated with PEP. On multivariate analysis, significant risk factors with adjusted odds ratio (OR) were: difficult cannulation (OR: 10.2), previous PEP (OR: 8.1), previous pancreatitis (OR: 7.9), at least two pancreatic duct injections (OR: 3.1), pancreatic duct cannulation (OR: 2.7), difficult stone extraction (OR: 2.2), and precut sphincterotomy (OR: 1.2).

Conclusion
Technique-related risk factors are probably more numerous and potent than patient-related ones in determining high-risk predictors for PEP.

Keywords:
endoscopic retrograde cholangiopancreatography, pancreatitis, risk factors

Egyptian J Surgery 34:1–10

1110-1121

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is one of the most complex endoscopic procedures [1]. The reported incidence of ERCP-specific complications ranges from 5 to 40%, depending on the complexity of the procedure, the underlying diagnosis, and the patient comorbidities [2,3].

Acute pancreatitis remains the most common and serious complication after ERCP with reported incidence ranging from 1.3 to 15.1% in most prospective series, resulting in substantial morbidity and occasional mortality [4–10]. Post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) is defined as acute pancreatitis that has developed de novo following ERCP [9,11]. The mechanisms that lead to PEP are complex and not fully understood. Rather than having a single pathogenesis, PEP is believed to be multifactorial, involving a combination of chemical, hydrostatic, enzymatic, mechanical, microbiologic, and thermal factors [12].

Several technical and patient-related risk factors for PEP, which act independently or together, have been identified [6,13,14]. The most previous studies of PEP have focused primarily on procedural and technical factors. However, it is equally plausible that patient characteristics also account for susceptibility or resistance to PEP [12]. The reported risk factors vary widely from study to study and these discrepancies may be attributable to differences in criteria used for diagnosis, differences in patient populations, indications, endoscopic techniques, endoscopic expertise, methods of data collection, and the use of preventative techniques such as placement of pancreatic stents [15–17]. More important, the use of univariate analysis to identify risk factors for PEP may produce misleading results because of inability to sort out confounding variables [18–22]. Recent studies have used multivariate analysis as a tool to identify and quantify the effect of multiple potentially confounding risk factors [2,4–7,23–26].

One of the most important steps to prevent PEP is to avoid the procedure altogether whenever possible, especially in patients who are thought to be at high-risk for this complication. Hence, awareness of

 DOI: 10.4103/1110-1121.153364

the risk factors for PEP is essential for the recognition of high-risk cases in which ERCP should be avoided if possible or in which protective endoscopic or pharmacologic interventions should be considered [27].

Aim of the work

The primary goal of this study was a comprehensive, prospective evaluation of risk factors for post-ERCP pancreatitis. To maximize the generalizability of the findings, groups in private practice as well as tertiary referral centers were included. This research attempted to evaluate the commonest postulated risk factors for PEP including patient and procedure-related variables, to generate a multivariate model that could identify the most important determinants of PEP for improving the safety of ERCP.

Patients and methods

This was a prospective, multicenter study conducted at five centers in Upper Egypt (three private practices, two universities-affiliated teaching hospitals). Of the 1162 consecutive patients scheduled to undergo ERCP, 712 (61.3%) were women and 450 (38.7%) were men, with a mean (± SD) age of 44.8 (± 13.9) years.

Patients were excluded for any of the following reasons:

(a) Age less than 18 years,
(b) Pregnancy,
(c) Mental disability,
(d) Patients with contraindication to ERCP (coagulopathy, history of contrast dye anaphylaxis, severe cardiopulmonary disease, recent myocardial infarction),
(e) Acute pancreatitis, cholangitis, or hyperamylasemia at the time of the procedure,
(f) Certain structural abnormalities of the upper gastrointestinal tract, which increase the risk of the procedure or renders it technically difficult or impossible, for example esophageal stricture,
(g) Planned biliary stent removal or exchange without planned ductal cannulation,
(h) Need for emergent ERCP within 12 h, or
(i) Prophylactic antibiotics. Ethical committee approval and informed written consent were taken before conducting the study at all participating centers.

All ERCP procedures were performed by high-volume endoscopists (who perform more than two sphincterotomies per week [33]. The data were collected during and after the procedure by the resident doctors who are not involved in the direct patient care and from the hospital reference sheets. All patients were admitted to the hospital at least for 24 h following the procedure to detect early complications. All patients were monitored at least for 6 h in the postoperative recovery room after the procedure to detect early symptoms and signs of pancreatitis then transferred to the inpatient department where they continue to be looked after by the resident for the rest of the 24 h until they can be discharged. Measurement of serum amylase was performed by sampling of blood at 4 h post-ERCP; if the 4 h amylase level was normal or less than three-fold increase, we repeat it on the next day before discharge. Abdominal ultrasonography was routinely performed in all patients suffering from pancreatic-like pain lasting at least 24 h for early detection of PEP. In cases of doubt of developing PEP, abdominal CT scan was performed. If complications arose, patients stayed in the hospital until they recovered.

Definitions

Bile duct diameter was the measured maximal duct diameter within 2 cm of the papilla adjusted for X-ray magnification. If any stricture was present, bile duct diameter was measured proximal to the stricture [9,11]. Cannulation time was measured between the time when the papillotome was advanced out of the endoscope channel, in front of the papilla, and the time when successful deep cannulation was evidenced by injection of contrast [11]. Total procedure time was measured between the time when the endoscope was advanced in the mouth and the time when the endoscope was advanced out from the mouth [11]. The number of pancreatic duct contrast injections was the total number of times when any volume of contrast was injected into the pancreatic duct [11]. Pancreatic cannulation was defined as deep cannulation of the pancreatic duct with any device [8]. Successful cannulation was defined as free and deep instrumentation of the biliary tree. A cannulation attempt was defined as sustained contact between the cannulating device and the papilla for at least 5 s [28]. Difficulty of cannulation was determined on the basis of the number of attempts on the major papilla with a cannulation instrument before final: easy (one to five attempts); moderate (six to 15 attempts); and difficult (>15 attempts) [9]. Difficulty of stone extraction was classified into three degrees: easy (Grade 0), stone extraction with no resistance; moderate (Grade 1), stone extraction with some resistance; difficult (Grade 2), stone extraction after lithotripsy or failed stone extraction.

The generally accepted criteria for the diagnosis of PEP were proposed in 1991 during a consensus workshop [13]. These criteria include the new onset

of pancreatic-type abdominal pain associated with at least a three-fold increase in serum amylase or lipase occurring within 24 h after an ERCP, and the pain symptoms need to be severe enough to require admission to the hospital or to extend the length of stay of patients who are already hospitalized [17]. Amylase values have been found to peak between 90 min and 4 h post-ERCP [29]. The serum amylase level measured 4 h after the procedure is the most reliable predictor of PEP [30,31]. We therefore used the 4 h amylase level as the most accurate amylase value for predicting subsequent pancreatitis. The severity of pancreatitis was classified on the basis of the length of hospital stay (2–3 days = mild; 4–10 days = moderate; >10 days or complications as hemorrhagic pancreatitis, pancreatic necrosis, pancreatic pseudocyst, or a need for percutaneous drainage or surgery = severe) [9,13]. Hyperamylasemia was defined as an increase of serum amylase to greater than the upper limit of normal [32].

Statistical analysis

The primary outcome analyzed was development of PEP. Analysis of risk factors was performed as follows: 18 potentially relevant risk factors were assessed by univariate analysis with the χ^2-test for categorical variables and simple logistic regression for continuous variables. A two-tailed *P* value of less than 0.05 was considered significant. Significant univariate predictors were then included in a forward stepwise multiple logistic regression model to identify the most important risk factors for pancreatitis. Goodness-of-fit for the final multivariate model was assessed by the two-log likelihood criterion.

Results

This was a descriptive single-arm prospective study that included 1162 patients subjected for ERCP between June 2009 and June 2013 (Table 1). ERCP was carried out to all patients (1162); cannulation of the papilla of Vater was successful in 1124 patients (96.7%) and failed in 38 patients (3.3%), 20 cases after trials of standard cannulation and 18 cases after precut sphincterotomy (Table 2).

The patient-related risk factors that were evaluated for PEP are: age, sex, previous pancreatitis, previous PEP, previous cholecystectomy, previous sphincterotomy, total serum bilirubin, common bile duct (CBD) diameter, and nature of the disease. The technique-related risk factors that were evaluated for PEP are: total procedure time, cannulation time, degree of difficulty of cannulation, number of pancreatic duct cannulation, number of pancreatic duct injection, biliary sphincterotomy, precut sphincterotomy, balloon dilatation, and degree of difficulty of stone extraction.

Table 1 Indications for endoscopic retrograde cholangiopancreatography

Indications	*n* (%)
Choledocholithiasis	802 (69)
Cholangiocarcinoma	104 (9)
Benign biliary stricture	82 (7)
Cancer head of pancreas	74 (6.4)
Ampullary tumor	42 (3.6)
Suspected SOD	32 (2.8)
Postoperative biliary leakage	18 (1.5)
Choledochocele	8 (0.7)

Table 2 Causes of failed cannulation

Causes	*n* (%)
Small and stenosed papilla	20 (1.7)
Duodenal diverticulum	10 (0.9)
Ampullary tumor	8 (0.7)

Serum amylase level was estimated 4 h after ERCP, and accordingly patients were divided into three groups:

(a) Patients with no hyperamylasemia (normal serum amylase level),
(b) Patients with hyperamylasemia (serum amylase level less than three times the upper limit of normal=asymptomatic hyperamylasemia), and
(c) Patients with hyperamylasemia (serum amylase level equal to or greater than three times the upper limit of normal = acute pancreatitis).

Upon studying patients after ERCP, 290 patients (25%) had no hyperamylasemia, 768 patients (66.1%) had asymptomatic hyperamylasemia, and 104 patients (8.9%) had acute pancreatitis [Assiut University Hospital 54 patients (9.1%), Sohag University Hospital 22 patients (8.2%), and the private centers: 10 (8.5%), 9 (8.7%), 9 (11%)]. All patients with an increase of serum amylase of three folds or more had epigastric pain radiating to the back persistent for 24 h (acute pancreatitis).

Upon studying patients with PEP according to the length of hospital stay, PEP was mild in 66 patients (63.5%), moderate in 30 patients (28.8%), and severe in eight patients (7.7%). Pancreatitis-related median hospital stay was 2.9, 9.5, and 17.5 days for mild, moderate, and severe disease, respectively. The PEP-related mortality rate was 1.9% (two cases) due to severe acute pancreatitis. No deaths were reported for mild or moderate pancreatitis.

Univariate analysis

Of 18 evaluated risk factors for PEP, 11 risk factors were found to be significantly associated with

PEP: four patient-related risk factors (age, female sex, previous pancreatitis, and previous PEP) and seven procedure-related risk factors (difficult stone extraction, difficult cannulation, pancreatic duct cannulation, ≥2 pancreatic duct contrast injections, precut sphincterotomy, cannulation time, and total procedure time) (Tables 3 and 4).

Multivariate analysis

The variables found to be significant in univariate analyses were taken as candidate explanatory variables in a multivariate logistic regression analysis to identify those risk factors associated with an increased risk for PEP in a multivariate setting and to estimate their independent contributions adjusted for the effects of each of the other factors. Seven risk factors were identified to be independently associated with pancreatitis; two were patient-related risk factors and five were procedure-related risk factors (Table 5).

Discussion

Acute pancreatitis remains the most common and serious complication after ERCP. Awareness of the risk factors for PEP is essential for the recognition of high-risk cases in which ERCP should be avoided if possible or in which protective endoscopic or pharmacologic interventions should be considered. Risk factors for developing PEP have been assessed in various studies and include patient and procedure-related risk factors [6].

Both PEP and asymptomatic hyperamylasemia occur because of injury to the pancreatic tissue induced by ERCP techniques, but the reason why some patients eventually develop pancreatitis and other asymptomatic hyperamylasemia remains unknown. The underlying mechanisms of the two vastly different clinical courses may include two respects: one may be attributable to the difference in the severity of the injury to the pancreas and the other to the difference in the magnitude of inflammatory response to the injury to pancreas. Asymptomatic hyperamylasemia is associated with mild injury to pancreas, perhaps without inflammatory response to pancreas. Pancreatitis may be associated with more severe injury to pancreas, meanwhile with inflammatory response to pancreas [33].

Post-ERCP hyperamylasemia was reported by many authors to be extremely common reaching up to 70% [3,6,7,15,34]. The finding of post-ERCP hyperamylasemia is attributed to maneuvers used during ERCP as manipulation of the papilla during difficult cannulation, pancreatic duct cannulation or

Table 3 Univariate analysis of risk factors for postendoscopic retrograde cholangiopancreatography pancreatitis

Variable	Pancreatitis [*n* (%)]		*P* value
	Yes	No	
Patient-related risk factors			
Significant			
Age (years)			
≤60	92 (10)	832 (90)	0.02
>60	12 (5)	226 (95)	
Sex			
Male	22 (4.9)	428 (95.1)	0.003
Female	82 (11.5)	630 (88.5)	
Previous pancreatitis			
Yes	24 (38.7)	38 (61.3)	<0.0001
No	80 (7.3)	1020 (92.7)	
Previous PEP			
Yes	10 (38.5)	16 (61.5)	<0.0001
No	94 (8.3)	1042 (91.7)	
Nonsignificant			
Previous cholecystectomy			
Yes	14 (10.1)	124 (89.9)	0.86
No	90 (8.8)	934 (91.2)	
Previous sphincterectomy			
Yes	8 (8.3)	88 (91.7)	0.55
No	96 (9)	970 (91)	
Total serum bilirubin (mg/dl)			
≤7	54 (9.9)	494 (90.1)	0.47
>7	50 (8.1)	564 (91.9)	
CBD diameter (mm)			
<5	2 (11.1)	16 (88.9)	
5–10	40 (11.2)	318 (88.8)	0.97
>10	62 (7.9)	724 (92.1)	0.74
Nature of the disease			
Benign	86 (9.1)	856 (90.9)	0.64
Malignant	18 (8.2)	202 (91.8)	
Procedure-related risk factors			
Significant			
Difficulty of cannulation			
Easy (Grade I)	26 (4.8)	314 (95.2)	
Moderate (Grade II)	46 (9.3)	448 (90.7)	0.01
Difficult (Grade III)	32 (25)	96 (75)	<0.001
Cannulation time (min)			
≤5	44 (7.1)	378 (92.9)	0.01
>5	60 (11.1)	480 (88.9)	
Total procedure time (min)			
≤30	46 (6.4)	672 (93.6)	0.006
>30	58 (13.1)	286 (86.9)	
Pancreatic duct cannulation			
Zero time	56 (5.9)	892 (94.1)	<0.0001
≥one time	48 (22.4)	166 (77.6)	
Pancreatic duct injection			
<2 injections	74 (6.9)	996 (93.1)	<0.0001
≥2 injections	30 (32.6)	62 (67.4)	
Difficulty of stone extraction			
Easy (Grade 0)	2 (1.6)	122 (98.4)	
Moderate (Grade 1)	34 (6.1)	520 (93.9)	0.04
Difficult (Grade 2)	30 (24.2)	94 (75.8)	<0.0001
Precut sphincterotomy			
Yes	24 (18.5)	106 (81.5)	0.02
No	80 (7.8)	934 (92.2)	
Nonsignificant			
Biliary sphincterotomy			
Yes	76 (8.1)	866 (91.9)	0.14
No	28 (14)	172 (86)	
Balloon sphincteroplasty			
Yes	4 (5.7)	66 (94.3)	0.46
No	100 (9.2)	938 (90.8)	

PEP, postendoscopic retrograde cholangiopancreatography pancreatitis.

Table 4 Pancreatitis rates in with respect to the number of attempts at cannulation with and without precutting

Variable	Cannulation attempts ≤15 (%)	Cannulation attempts>15 (%)	Total (%)	*P* value
Standard cannulation	60/954 (6.3)	20/78 (25.6)	80/1032 (7.8)	<0.0001
Precut cannulation	12/88 (13.6)	12/42 (28.6)	24/130 (18.5)	<0.01
Total	72/1042 (6.9)	32/120 (26.7)	104/1162 (8.95)	<0.0001

Table 5 Multivariate logistic regression analysis of factors that predict postendoscopic retrograde cholangiopancreatography pancreatitis

Characteristics	Odds ratio (95% CI)	*P* value
Previous PEP	8.1 (1.01–98.50)	0.004
Previous pancreatitis	7.9 (2.83–58.72)	0.01
Difficult cannulation		
Moderate vs. easy	3.1 (1.07–21.26)	0.04
Difficult vs. easy	10.2 (2.44–77.26)	0.004
≥2 pancreatic duct injections	3.1 (1.64–5.75)	0.0001
Pancreatic duct cannulation	2.7 (1.43–5.17)	0.0051
Difficult stone extraction	2.2 (1.49–4.24)	0.0001
Precut	1.2 (1.11–2.26)	0.01

CI, confidence interval; OR, odds ratio; PEP, postendoscopic retrograde cholangiopancreatography pancreatitis.

injection, precut sphincterotomy, balloon dilatation, and extraction of large stones. The mechanical trauma to the papilla or pancreatic sphincter during instrumentation may cause transient obstruction of outflow of pancreatic juice. In addition, subjecting the pancreatic duct to a sudden increase in pressure may be the cause of post-ERCP hyperamylasemia. Passage of common bile duct stones is also known to cause hyperamylasemia [35].

All patients who had increase in serum amylase at least three times the upper normal limit developed clinical symptoms of acute pancreatitis lasting at least 24 h. None of patients developing increase in amylase level less than three times the upper normal limit had clinically relevant acute pancreatitis. These results are in agreement with the previous authors who found out that increased amylase level at least three times the upper normal limit is predictive of acute pancreatitis [3,34,36].

The incidence of PEP ranged from 1.3 to 15.1% in most prospective series [11]. Higher rates reach up to 40% reported in certain series [3,6,7]. In our study, the incidences of PEP are still largely in agreement and comparable with the previous reports and agreed with the internationally acceptable norms; it was 8.9% of the cases (mild = 63.5%, moderate = 28.8%, and severe = 7.7%).

Younger age was associated with a high risk for pancreatitis only in the univariate analysis. This result is consistent with multiple studies showing that younger age was found to be a significant risk factor by univariate analysis but not by multivariate model [6,9,37]. There was an inverse relationship between the age and the occurrence of PEP (the younger the patient, the higher the percentage of pancreatitis). Younger age was first identified as an independent risk factor for PEP in a multicenter study in 1996 [4], and subsequently confirmed in four other multivariate analyses [23,38–40]. The higher risk may be explained by the progressive decline in pancreatic exocrine function with aging that may protect older patients from pancreatic injury [41]. In contrast, one recent study revealed that age of 60 years or less is not associated with any clinically significant risk for PEP [11]. Another study reported that age less than 25 years was a high risk factor for PEP [30]. In addition, Nishino *et al.*'s [42] study concluded that one of the patient-related risk factors was age more than 65 years.

Female sex was a significant risk factor for PEP in univariate but not in multivariate analysis, and this result is in agreement with a large multicenter study [9]. Our study disagrees with the studies reporting that female individuals appear to be at higher risk for developing postprocedural pancreatitis compared with male individuals in both univariate and multivariate analysis [6,11,14,25,43,44]. However, most previous studies have demonstrated a higher risk in patients with sphincter of Oddi dysfunction (SOD) [8,12,38], a condition that occurs primarily in women [45]. In contrast, Testoni *et al.* [37] revealed that female sex was not associated with any clinically significant risk for PEP.

Past history of pancreatitis was a highly significant risk factor for PEP, and these findings are consistent with several recent multivariate risk factor studies [2,5,14,46]. Our analysis showed that the risk in such patients was increased eight-fold [odds ratio (OR): 7.9]. In contrast, our results are inconsistent with the studies by Freeman *et al.* [4], Freeman *et al.* [6], Friedland *et al.* [47], and Testoni *et al.* [37], which revealed that history of previous pancreatitis is only a significant risk factor by univariate analysis. In addition, history of previous PEP was found to be a highly significant factor for PEP with eight-fold risk (OR: 8.1), and these findings are consistent with several multivariate risk factors studies [2,6,7,9,14,37,47]. In contrast, a recent multivariate study revealed that history of PEP was not a significant risk factor for PEP [11]. The previous two findings suggest that certain individuals have a 'reactive'

pancreas that places them at particular risk beyond that conferred by other definable risk factors [48].

History of previous cholecystectomy was found to be insignificant risk factor for PEP. This result is in agreement with a recent multivariate study [11]. In contrast, the results obtained by Freeman *et al.* [6] and Cheng *et al.* [9] showed that prior cholecystectomy is a significant risk factor for PEP in univariate but not in multivariate analysis. In addition, history of previous sphincterotomy was found to be insignificant risk factor for PEP. This result is in agreement with two multivariate studies [6,9].

No relationship was found between total serum bilirubin level and the rate of occurrence of pancreatitis after ERCP. Similarly, most studies agreed that hyperbilirubinemia is not a risk factor for pancreatitis [11]. Some studies showed that normal bilirubin level at the time of ERCP would independently increase the risk for PEP [6,7,44,46]; another one showed that normal bilirubin was not associated with any clinically significant risk for PEP [37]. None of the patients included in our study had normal serum bilirubin level at the time of the procedure.

Common bile duct diameter was insignificant risk factor for PEP. This result is in agreement with most studies that have found no independent influence of duct size on the risk for PEP [2,4,6,9,11,23,26,37–39]. In contrast, many early studies suggested small CBD diameter as a risk factor for pancreatitis [5,18,20,40]. The original descriptions of small CBD diameter as a risk factor came from centers with a preponderance of patients with sphincter dysfunction, most of whom also had nondilated bile ducts. Perhaps, small bile duct diameter has appeared to be important because it was a surrogate marker for absence of elevated serum bilirubin, presence of SOD, or female sex [6].

No significant difference was found between benign and malignant nature of the disease with respect to PEP. This result is in agreement with the only study comparing the relationship of nature of the disease and PEP [49]. The higher incidence of pancreatitis in patients with benign obstructive jaundice in comparison with patients with malignant obstructive jaundice may be attributed to gallstones (the commonest indication in patients with benign obstructive jaundice), which increases the risk for pancreatitis. Proposed mechanisms include reflux of noxious bile into the pancreatic duct from transient obstruction of the ampulla during gallstone passage and pancreatic ductal hypertension from either a stone impacted at the ampulla or ampullary trauma caused by stone passage [50]. In addition, patients with pancreatic malignancy appear to be at decreased risk for PEP, likely because of chronic obstruction of the pancreatic duct along with atrophy of the upstream pancreatic parenchyma [51].

Standard sphincterotomy was insignificant risk factor for PEP. This result is consistent with the previous data confirming that the performance of biliary sphincterotomy does not appear to add significant independent risk for pancreatitis after ERCP [2,6,7,9,26]. In certain circumstances, biliary sphincterotomy may be protective; pancreatitis occurred in four of 24 patients (17%) who had plastic biliary stents placed for hilar strictures without a sphincterotomy versus none (0%) of 59 in whom a sphincterotomy was performed, suggesting that a fulcrum effect of the proximal stricture on the large-caliber biliary stent, pushing it against the pancreatic duct orifice in the intact papilla, led to the increase in frequency of pancreatitis and that this could be precluded by biliary sphincterotomy [52].

Precut sphincterotomy was a barely significant (OR: 1.2) risk factor for PEP. There is controversy in the literature regarding the relationship of precut sphincterotomy with the occurrence of pancreatitis and other complications [53–57]. Many authors reported that precut sphincterotomy was an independent risk factor for PEP [4,5,7,11,14,37,58]. It has been controversial whether higher rates of complications and pancreatitis after precut sphincterotomy are because of the precut itself, the antecedent repeated cannulation attempts, the indication for the procedure (most risky with SOD in the absence of pancreatic stenting), other anatomic factors such as small papillas, or the thermal injury to the pancreatic sphincter causing edema and duct obstruction [59,60].

Our study also confirmed that early precut was safer than either delayed precut or multiple attempts at cannulating the papilla (6.9 vs. 25.6 and 28.6%), supporting the concept that, in expert hands, precut might be preferable to repeated cannulation attempts, especially in patients at high risk for postprocedure pancreatitis. This result is compatible with two recent meta-analyses; the first showed that PEP developed in 2.5% of patients randomized to early needle-knife sphincterotomy compared with 5.3% of patients who underwent persistent cannulation attempts before needle-knife sphincterotomy [61] and the second concluded that early needle-knife sphincterotomy significantly reduced the rate of PEP from 5.4 to 2.5% [62]. In addition, a recent retrospective study demonstrated that the rate of PEP was lower when this technique was performed with less than 10 cannulation attempts compared with 10 or more cannulation attempts without precutting [63].

In contrast, in many series from tertiary referral centers, the complication rate for precut sphincterotomy was no different than that for standard sphincterotomy [9,53,54,56,64–67], suggesting that risk for precut sphincterotomy is highly operator-dependent. In addition, this result disagree with the result of Freeman *et al.* [6] who concluded that precut access was associated with higher univariate but no independent risk for pancreatitis; however, most of these procedures were performed by a few highly experienced endoscopists and often included placement of a pancreatic stent.

Balloon dilatation of the CBD orifice for stone extraction was insignificant risk factor for PEP. This result was consistent with several studies that have demonstrated that balloon dilatation of the distal CBD and ampulla can be a well-tolerated and effective technique for the removal of biliary stones without increasing the rate of PEP [68–74]. In contrast, other studies showed that balloon dilatation has been associated with a markedly increased risk for PEP [6,75–77].

The duration of the whole procedure and the cannulation time were significant risk factors for pancreatitis in univariate but not in multivariate analysis, and this result is compatible with those obtained by two large studies [11,47]. Average ERCP and cannulation times were reported as 18 and 4 min by Penaloza-Ramirez *et al.* [78], and similar average durations of 16.5 and 3 min were determined by Sabri *et al.* [79]. Our results revealed that average ERCP and cannulation times were 28 and 5 min, and this disagreement may be explained by trainees' participation.

Difficult cannulation was the highest significant independent risk factor for PEP. More than 15 attempts at cannulating the Vater's papilla increased the risk for pancreatitis about 10-folds (OR: 10.2); interestingly, the risk rate showed a linear progression either between five or less attempts and six to 15 attempts (OR: 3.1) or between six to 15 and greater than 15 attempts (OR: 10.2). PEP had inverse relationship with the difficulty of cannulation (the higher the difficulty of cannulation, the higher the incidence of pancreatitis). Pancreatitis occurred in 4.8% of cannulation rated as easy, 9.3% of those considered to be moderately difficult, and 25% of cases when cannulation was considered difficult. The high incidence of pancreatitis after repeated attempts at cannulating, independently of pancreatic duct contrast injection, confirms that papillary edema-related and sphincter hypertension-related impairment of pancreatic drainage resulting from the extent of manipulation and repeated trauma of the papilla using guide wires and cannulation devices, rather than hydrostatic ductal and contrast agent injury, is a major factor. The fact that difficult cannulation did not reach significance as a risk factor in a study where prophylactic pancreatic stents were frequently used further confirms this [9]. These data also suggest that alternative techniques, such as precut sphincterotomy, should be adopted in cases with difficult cannulation, rather than insisting with multiple attempts, and confirm the preventive role of early precut in reducing the risk for pancreatitis, as in another study [80].

The difficulty of cannulation is not easily quantifiable and interactions with time for cannulation, method of cannulation, and number of pancreatic duct injections may occur [9]. Most studies came to similar results, namely difficulty in cannulation, which can produce papillary trauma, proved to be an independent risk factor for procedural complications and this risk should increase with the number of failed cannulations [2,4,6,9,26,37]. Although the difficulty of cannulation was all judged by the number of cannulation attempts in previous studies, the cutoff numbers vary widely, with six attempts in two studies, eight attempts in one study, and 20 attempts in another study [2,4,6,9].

Pancreatic duct cannulation was a significant risk factor in both univariate and multivariate analyses (OR: 2.7). This is most probably due to manipulation of pancreatic duct and pancreatic sphincter leading to subsequent spasm of pancreatic duct and obstruction of the flow of pancreatic enzymes. In addition, injury to the pancreatic duct and pancreatic parenchyma may cause premature activation of pancreatic enzymes leading to autodigestion of the pancreas. This finding agrees with that reported by Freeman *et al.* [6] stating that pancreatic duct deep cannulation is significantly associated with the risk for PEP.

Pancreatic duct injection (≥2) was an independent risk factor for PEP with a three-fold increase in risk (OR: 3.1), and this result is compatible with most previous reports [4,6,9,14,43,47,81]. In contrast, Wang *et al.* [11] concluded that pancreatic duct injection was significant only by univariate but not by multivariate analysis. They explained their result by the frequent use of guide wires cannulation that minimizes the unintentional injections into the pancreatic duct [11].

Difficult stone extraction was a significant risk factor by both univariate and multivariate analyses (OR: 2.6). PEP had inverse relationship with the degree of difficulty of stone extraction (the higher the difficulty of stone extraction, the higher the incidence of pancreatitis). In our study, pancreatitis occurred in 1.6% of extraction rated as easy, 6.1% of those considered to be moderately difficult, and 24.2% of cases when

extraction was considered difficult. This result may be explained by repeated trauma during trial of extraction and prolonged cannulation and procedure time.

Trainee participation has been previously evaluated in three large multicenter studies, and the result showed that it was not a significant risk factor for PEP [6,9,37]. In another report, the complications of ERCP performed solely by attending physician were not significantly different from those performed by fellows under the supervision of attending endoscopists [2]. Similarly, in our series, trainee participation did not increase the risk for PEP in univariate or multivariate analysis.

Data from this study can be used by the clinician to decide whether or not to recommend ERCP for an individual patient. Intraoperative laparoscopic cholangiography, MRCP, and EUS all have accuracy rates rivaling that of ERCP and are becoming widely available. These techniques may be preferable to ERCP for patients with equivocal evidence of biliary obstruction, especially those at high risk for PEP. If pathologic obstruction such as a stone is definitely identified by one of these methods, then conventional ERCP is indicated. If no pathologic obstruction is found, then ERCP should be avoided altogether or direct referral to a center with extensive experience with manometric and pancreatic therapeutic ERCP should be considered. These data can be used by the endoscopist to decide how an ERCP will be performed. In high-risk patients, prolonged efforts at cannulation and the use of high-risk maneuvers such as precut sphincterotomy should be avoided. The current data may also be useful with respect to studies on the use of pharmacologic agents to reduce PEP. Until a cost-effective agent that prevents post-ERCP pancreatitis is found, the primary hope for reducing the burden of morbidity from ERCP lies in knowledge of the risk factors and the understanding that this knowledge will be used in deciding whether an ERCP is necessary, and, if so, how best to perform the procedure.

Conclusion

Multivariate analysis indicates that technique-related risk factors are probably more numerous and potent than patient-related ones in the risk for PEP. All patients should be followed by 4 h serum amylase after ERCP for early identification of patients with PEP for early and adequate management. The most important risk factors for PEP are difficult cannulation, previous history of pancreatitis and PEP, pancreatic duct cannulation and injections, difficult stone extraction, and precut sphincterotomy.

Acknowledgements

Conflicts of interest

None declared.

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Use of laparoscopy in the management of abdominal trauma: a center experience

Morsi Mohamed, Wael Mansy, Yahia Zakaria

Department of General Surgery, Zagazig University, Zagazig, Egypt

Correspondence to Morsi Mohamed, MD, Department of General Surgery, Zagazig University, Zagazig, Egypt
Tel: 01224900185;
e-mail: drmorsi@yahoo.com

Received 19 July 2014
Accepted 18 September 2014

The Egyptian Journal of Surgery
2015, 34:11–16

Background
The role of laparoscopy in diagnosis as well as therapeutic interventions has increased markedly in the last few years. In trauma, it has become a viable alternative for the diagnosis of intra-abdominal injury following penetrating and blunt trauma. The number of negative and/or nontherapeutic laparotomies performed has decreased since the use of laparoscopy in diagnosis and management.

Patients and methods
Sixty-five patients with abdominal trauma (21 blunt trauma, 44 penetrating trauma) were treated by the Trauma Team at the Emergency Unit of Zagazig University from November 2011 to August 2014 using laparoscopy for diagnosis. All patients underwent a physical examination, ultrasound, and computed tomography (abdomen and pelvis). Laparoscopy was used in the management of these patients through three trocars: one for 30° scope and two working trocars.

Results
In our series, we avoided laparotomy in 81.5% (53/65) of cases. Therapeutic laparoscopy was effective in 15 patients: six patients with stomach penetrations, four with liver lacerations, three with diaphragmatic injuries, and two with splenic lacerations.

Conclusion
Laparoscopy can be performed safely and effectively in stable patients with abdominal trauma.

Keywords:
abdominal trauma, blunt injury, laparoscopy, penetrating injury

Egyptian J Surgery 34:11–16

1110-1121

Introduction

In the last 30 years, penetrating abdominal injuries have been managed by operative exploration irrespective of the hemodynamic condition of the patient. The majority of clinicians would choose the surgical option for the management of patients with hemodynamic instability [1].

Sometimes, the choice between surgical and conservative management is difficult. This is consistent with cases with injury to the diaphragm or intestines, which cannot be detected by imaging techniques. Thus, this gives rise to a need for other modalities to aid the diagnosis and even management of such cases [2].

To avoid such oversights, indications for exploratory laparotomy have traditionally been generous, to extent that up to 41% of exploratory laparotomies turned out to be non-therapeutic and could be avoided with laparoscopy [2].

Since the early 1990s, the application of laparoscopy in general surgery has increased. Thus, it will not be surprising to expand its use in trauma management and diagnosis [3].

Here, in our study, we show that laparoscopy can be used safely in the management of stable patients with abdominal trauma and can reduce the rate of negative and nontherapeutic laparotomies in patients with both penetrating abdominal trauma (PT) and blunt abdominal trauma (BT).

Patients and methods

Sixty-five patients with abdominal trauma, 21 with BT and 44 with PT, were treated in the Trauma Unit of Zagazig University from November 2011 to August 2014.

We analyzed outcome measures including mechanisms of injury, radiological findings, operative procedures, and injuries that were treated.

In addition, postoperative outcomes including length of stay, complications, and mortalities were assessed.

All patients underwent physical examinations, ultrasonography, computed tomography (CT) (abdomen and pelvis) to assess the presence of free fluid and organ injuries.

According to our protocols, laparoscopy is considered only in patients who are hemodynamically stable. All patients with abdominal gunshot wounds were

 DOI: 10.4103/1110-1121.153365

excluded from our series and underwent immediate surgical exploration.

For patients with other PT without obvious anterior fascia injury, a local wound exploration is performed in the Trauma Unit.

In cases of obvious penetration of the anterior fascia or if it is determined or suspected during the initial exploration or presence of free fluid as a radiological findings, an immediate operative exploration is mandatory.

In patients with blunt abdominal trauma, the presence of unexplained free fluid on the abdominal CT, or patients showing deterioration under conservative management (abdominal pain, fever, leukocytosis, abdominal tenderness and rigidity, decreased hemoglobin levels) are typically evaluated by a laparoscopic exploration.

Laparoscopic exploration is performed with a patient in a supine position with both arms abducted if possible. The first access is achieved using a 10 mm trocar at the umbilicus (30° scope) for the videoscopic set; pneumoperitoneum should be slowly and if the blood pressure decreases or respiratory pressure suddenly increases, the gas pressure should be reduced. Two further trocars of 5–10 mm are introduced on both sides at the level of umbilicus at the mid-clavicular line.

The abdomen is explored systematically, all solid organs and hollow viscus are explored, and even the most hidden parts of the diaphragm can be assessed much better by laparoscopy than with an open technique. The presence of significant hemoperitoneum or succus entericus requires open exploration (Figs. 1–5).

Laparoscopy was classified as negative if there was no injury, as nontherapeutic if there was an injury but did not require a surgical intervention, therapeutic if an injury was identified and repaired, and positive if there was an injury that required conversion to open exploration for repair.

Results

Sixty-five patients (21 BT and 44 PT) who underwent a laparoscopic procedure were identified and reviewed; the characteristics and outcomes of patients undergoing laparoscopy on the basis of the mechanism of injury are shown in Table 1.

Blunt trauma

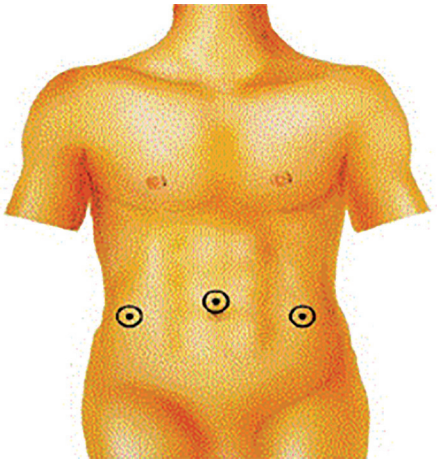
Laparoscopy was used for the evaluation of blunt abdominal injury in 21 patients. Ultrasound findings included free fluid in the pelvis; abdominal CT findings included free fluid in the abdomen in all patients, with suspected injuries in eight patients.

No significant injuries were identified in four patients upon an initial laparoscopic survey.

Nontherapeutic procedures were performed in nine patients; intraoperative findings in these patients included two minor splenic lacerations and hematomas, three minor liver lacerations, two nonexpanding retroperitoneal hematomas, and two with small mesenteric hematoma. No further interventions were performed in the above-mentioned 13 patients.

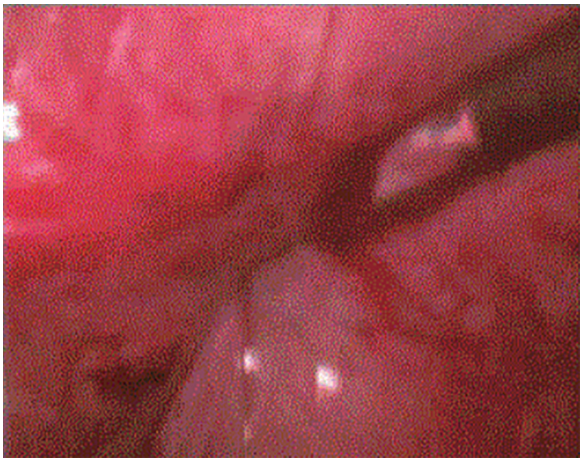
Laparoscopic intervention was performed in three patients; one presented with liver laceration under conservative management. The patient's condition deteriorated after 1 week. He presented with acute abdomen, fever, tachycardia, anemia, and leukocytosis.

Figure 1



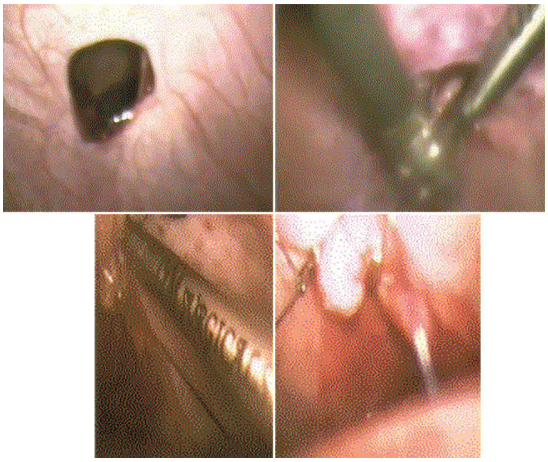
Trocar site.

Figure 2



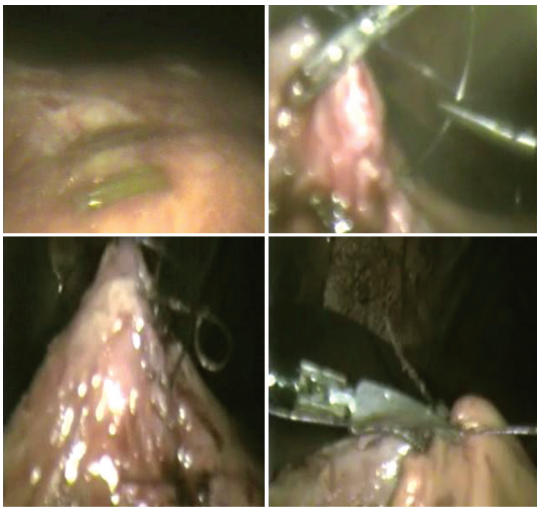
Liver penetration.

Figure 3



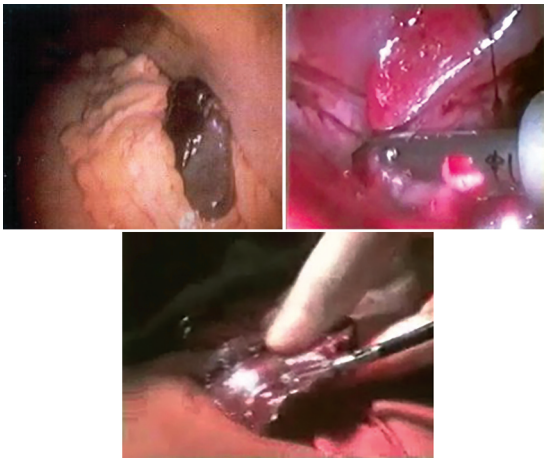
Diaphragmatic tear.

Figure 4



Stomach penetration.

Figure 5



Splenic laceration and laparoscopic splenectomy [1].

Table 1 Patients' characteristics according to the mechanisms of injury

Patient characteristics	Mechanisms of injury	
	Blunt trauma	Penetrating trauma
Number	21	44
Age (years)	25–45	18–30
Male	16	36
Female	5	8
Negative laparoscopy	4	14
Nontherapeutic laparoscopy	9	11
Therapeutic laparoscopy	3	12
Conversion to exploration	5	7
Length of hospital stay	6 ± 4.8	2 ± 2.5
Morbidity	3	1
Mortality	0	0

During laparoscopy we found a big cavity at the right lobe at the site of laceration filled with necrotic materials and hematomas, the necrotic tissue inside was removed, coagulation of the bleeding points, clip ligation of suspected biliary small ducts or bleeding vessels and irrigation and drainage of the cavity then putting a drain inside it.

The other two patients presented with splenic laceration and subcapsular hematoma that was diagnosed with CT, and were under conservative treatment until their condition deteriorated. Diagnostic laparoscopy was performed, which indicated internal hemorrhage because of rupture of subcapsular hematoma; laparoscopic splenectomy was performed using a Harmonic scalpel.

In the other five patients, a laparotomy was performed following injury identification on diagnostic laparoscopy. These patients were under conservative management until their condition deteriorated. Two patients presented with large splenic lacerations that required urgent open splenectomy. Three patients underwent bowel repair or resection because of bowel perforation.

Complications in patients undergoing laparoscopy without conversion to laparotomy were minor and limited to postoperative chest infection in one patient; there were no intraoperative complications during laparoscopy. In patients who required a laparotomy, minor complications were encountered in the form of paralytic ileus in one patient and wound infection in another. The average length of hospital stay was 6 ± 4.8 days for all BT patients.

Penetrating trauma

Forty-four patients underwent a laparoscopic evaluation in the setting of PT (Table 2). Diagnostic laparoscopy ruled out an intraperitoneal injury (negative laparoscopy) in 14 patients, including four patients with no peritoneal penetration.

Table 2 Laparoscopic evaluation and management of patients with penetrating trauma

Findings at laparoscopy	Numbers	Finding at laparotomy	Surgical procedure
No injury	14		Diagnostic laparoscopy
Liver laceration	9		Nontherapeutic laparoscopy (*n* = 6) Therapeutic laparoscopic (*n* = 3)
Stomach	6		Laparoscopic repair
Retroperitoneal hematoma	3		Nontherapeutic laparoscopy
mesenteric hematoma	2		Nontherapeutic laparoscopy
Diaphragmatic injury	3		Laparoscopic repair
Bowel injury	5	3 colonic perforation2 small bowel perforation	Open repairOpen repair
Hemoperitoneum	2	Mesenteric artery injury	Open suture ligation

Nontherapeutic laparoscopy was performed in 11 patients: six presented with minor liver lacerations, two with mesenteric hematoma, and three with retroperitoneal hematoma related to the descending colon with no significant colonic injury.

Therapeutic laparoscopy was performed in 12 patients: three liver lacerations needed biosurgical materials (gel foam), three diaphragmatic injuries needed repair, and six stomach perforation required repair. Seven patients had injuries identified at laparoscopy that necessitated conversion to open exploration (Table 2).

No complications were encountered in patients undergoing laparoscopy without conversion to open exploration. Among patients who required a laparotomy, a minor complication was encountered in the form of wound infection in one patient. The average length of hospital stay was 2 ± 2.5 days for all PT patients.

Laparoscopy in BT and PT was negative in 19 and 31.8%, respectively, and was nontherapeutic in 42.8 and 25%, respectively. Also, 15 patients were managed with laparoscopy (three cases with BT and 12 cases with PT). Overall, because of the use of laparoscopy, laparotomy was avoided in (53/65) 81.5% of the patients in this study.

Discussion

The application of laparoscopy has increased considerably with technical advances and constantly increasing experience with its use in the management of acute surgery cases including trauma surgery. New algorithms have been developed by many trauma centers worldwide for the management of BT and PT to aid the fast and effective diagnosis of visceral injuries [2].

In the earliest work on laparoscopy in abdominal trauma, Gazzangia *et al.* (1976) [4] evaluated 37 patients; in 14 of these patients, laparotomy was avoided because of a negative diagnostic laparoscopy (DL). There were no false-negative investigations. They concluded that the use of diagnostic laparoscopy in abdominal trauma was useful to decrease the rate of negative laparotomy [5].

In the largest study on laparoscopy in PT, Ivatury's group (Zantut *et al.*, 1997) [6] reported a multicenter retrospective study of 510 hemodynamically stable patients who underwent DL for PT. The inclusion criterion for the study was a hemodynamically stable patient who had penetration of the anterior fascia by a stab wound or a gunshot wound with a possible intraperitoneal injury. Negative or nontherapeutic laparotomy was avoided in 303 (59.4%) patients, of whom 26 patients received a therapeutic laparoscopic intervention [5].

Here, in our institute, because of the increase in the rate of PT, we have incorporated laparoscopy into our management algorithm for PT to detect missed injuries and prevent potential morbidity and mortality (Fig. 5).

The usual diagnostic procedures, diagnostic peritoneal lavage, sonography, and even CT, all have their strengths and weaknesses and none of them are 100% reliable. For this reason, exploratory laparotomy is often performed in the case of stab wounds, but with a high morbidity percentage that reaches up to 40% [7]. Therefore, the main benefits of laparoscopy are that it can reduce the rate of nontherapeutic and negative laparotomies, identify diaphragmatic injuries accurately, and even, in some cases, provide a therapeutic option [2].

Trauma laparotomy remains the gold standard for the evaluation of intra-abdominal injury. However, complications following negative or nontherapeutic laparotomy can be as high as 20% [8,9]. Consequently, it is advantageous to avoid a negative laparotomy, provided that a reliable and accurate alternative diagnostic procedure is available. In Kaban *et al.* [10] laparoscopy resulted in sensitivity for abdominal injury exceeding 90%, with a specificity of 100%. Furthermore, it proved to be a safe modality without direct operative or

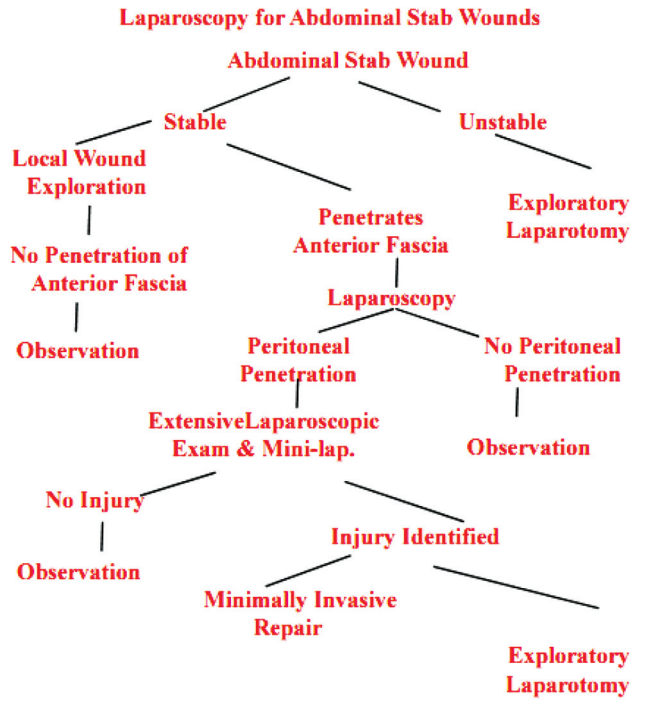
postoperative morbidity [10]. In our study, laparoscopy prevented 53 laparotomies in 65 patients (Algorithm 1).

Chol and Lim (2003) [11] performed a laparoscopic evaluation of 78 hemodynamically stable patients who had already undergone CT showing significant injuries. Nearly two-thirds of the patients were BT victims. This group reported no missed injuries, no mortality, and an 83% success rate in their ability to provide definitive surgical treatments ranging from gastrorrhaphy to small bowel resection to pancreatectomy. Although these results are exciting, data from different institutions show higher complication rates and missed injury rates and a narrower range of therapeutic interventions [12,13].

In our experience of BT, laparoscopy was beneficial especially in hemodynamic stable patients; nearly two-thirds of our patients benefited from diagnostic laparoscopy in avoiding unnecessary laparotomy and postoperative morbidity. Therapeutic laparoscopy was used in one patient who presented with infected liver lacerations and two patients with splenic laceration. Conversion to laparotomy was performed in five patients because of large splenic lacerations in two patients and three patients with small bowel injuries required resection and anastomosis.

A 10-year review of laparoscopic intervention from the University of Tennessee showed that the main utility of minimally invasive techniques was as usage of laparoscopy in management of abdominal trauma was effective to avoid negative laparotomy findings. Although some minor injuries were repaired laparoscopically, they were limited to diaphragm repair, repair of serosal tears and coagulation of omental haemorrhage [14]. Nevertheless, a review of the published literature shows an increasing number of case reports showing successful therapeutic interventions in abdominal trauma [15]. This trend will continue to grow as surgeons' comfort with minimally invasive techniques improves and technology becomes more convenient and advanced.

Algorithm 1



Algorithm for the management of penetrating abdominal trauma [1].

In our experience with PT, the use of laparoscopy as a diagnostic and therapeutic tool led to avoidance of an open surgery in more than 80% (37/44) of patients. Negative and nontherapeutic laparoscopies were performed in 25 patients and therapeutic laparoscopy was performed in 12 patients: six patients with gastrostomy at the anterior wall required laparoscopic closure, three patients with diaphragmatic penetration at the right copula of the diaphragm were managed by laparoscopic suturing, and 3 cases presented with bleeding liver laceration management laparoscopy by biotechnology coagulation materials as surge-cell. However, conversion to laparotomy was needed in seven cases (two cases with transverse colon perforation needed open repair with proximal colostomy and one with sigmoid perforation needed colostomy and Hartman, two cases with small bowel perforation needed open repair in one case and resection anastomosis in two cases, and two cases with hemoperitoneum because of mesenteric vessel injury required open ligation).

Potential risks when trauma patients undergo laparoscopy include air embolism, elevation of intracerebral pressure with head injuries, and tension pneumothorax when the diaphragm is injured. Small numbers of such complications were reported in the 1990s, and they now seem to be preventable if suitable measures are adopted [16].

In our study, the hospital stay and rate of postoperative complications were high in patients with BT than PT. In cases without conversion to laparotomy, we found one case with chest infection and in patients with conversion to laparotomy, we found two patients with wound infection and one patient with paralytic ileus. However, overall, the rate of hospital stay and postoperative complications was low in comparison with patients managed by laparotomy.

Minimally invasive surgery has become a useful tool in the management of trauma. Laparoscopy can detect and repair injuries to the hollow viscus and diaphragm and exclude the risks of nontherapeutic laparotomy.

Further advantages are reduced morbidity, shortened hospital stay, and lower cost. In the future, there may be exciting advancements for this field of surgery through innovative developments [2].

Conclusion

The routine use of laparoscopy can achieve a sensitivity of 90–100% in abdominal trauma. This can reduce the number of unnecessary laparotomies and the related morbidity.

Acknowledgements

Conflicts of interest

None declared.

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Postmastectomy seroma: how much is it affected by serum levels of IL-6 and CRP and how much is it reduced by intravenous hydrocortisone injection?

Ahmed Talha[a], Rabie Ramadan[a], Shreif Abdelhamid[b], Salwa Hamdi[c]

[a]Departments of Surgery, [b]Anesthesia, [c]Chemical Pathology, Medical Research Institute, Alexandria University, Alexandria, Egypt

Correspondence to Ahmed Talha, MD, MRCS, Department of Surgery, Medical Research Institute, Alexandria University, 165, Alhorreya Avenue, Hadara, 21561 Alexandria, Egypt
Tel: +20 342 82331; fax: +20 342 83719;
e-mail: ahmedtalha047@yahoo.com

Received 24 August 2014
Accepted 08 September 2014

The Egyptian Journal of Surgery
2015, 34:17–21

Background
Seroma is extremely common after breast surgery, and this could be because of the inflammatory response during wound healing. Several factors such as interleukin-6 (IL-6) and C-reactive protein (CRP) have been detected in the seroma fluid that support this assumption; therefore, inhibition of the inflammatory response by using hydrocortisone might decrease seroma formation. We aimed to evaluate the effect of adding hydrocortisone to the anesthetic regimen in the perioperative serum level of IL-6 and CRP and consequently in postmastectomy seroma formation.

Patients and methods
The study included female patients with primary operable breast cancer who were randomly allocated to two groups; each included 40 patients. Patients in group I received general anesthesia with hydrocortisone, and patients in group II received general anesthesia without hydrocortisone. Venous samples were collected for measuring IL-6 serum levels before surgery, 6 h after the end of the procedure, and 24 h after the procedure and for measuring CRP serum levels before surgery and 24 h after the procedure. All patients were followed up postoperatively for registration of the total drainage volume until drain removal, timing of drain removal, incidence of seroma formation, and management of seroma.

Results
Patients in group I had a lower total drainage volume ($P = 0.001$), had the drain removed earlier ($P = 0.009$), and had a lower incidence of postmastectomy seroma formation ($P = 0.005$). Postoperative serum levels of IL-6 and CRP showed a significant decrease in group I compared with group II.

Conclusion
Postmastectomy seroma is likely a proinflammatory process and can be reduced by giving intravenous hydrocortisone on induction of anesthesia and 2 h later, which significantly decreases the inflammatory mediators (IL-6 and CRP) that significantly reduce the incidence of seroma.

Keywords:
C-reactive protein, hydrocortisone, interleukin-6, mastectomy, postmastectomy seroma

Egyptian J Surgery 34:17–21

1110-1121

Introduction

Breast cancer is the most common site-specific cancer in women; it accounts for 33% of all female cancers and is responsible for 20% of cancer-related death in women [1,2]. Seroma is extremely common after breast surgery, secondary to the rich lymphatic drainage of the breast and possibly the low fibrinogen levels and net fibrinolytic activity within lymphatic fluid collections [3]. Seroma, which is formed under the skin flaps of mastectomy wounds, impairs the healing process; that is why drains are usually left in place for 1–3 weeks, when the skin flaps heal and adhere to the chest wall, as evidenced by diminished drain output [4]. Seroma collections that develop after drain removal can be managed by percutaneous aspiration, which is usually well tolerated because the mastectomy and axillary incisions tend to be insensate; these procedures can be repeated as frequently as needed to ensure that the skin flaps are densely adherent to the chest wall; however, in rare cases when the seroma continues to recur, a Seroma-Cath may be considered [3,4]. Various methods, ranging from shoulder immobilization [5], perioperative use of tranexamic acid [6], prolonged suction drainage [7], and flap fixation [8,9], have been advocated with varying degrees of success in the prevention of seroma formation after mastectomy. Seroma formation is most likely the result of the inflammatory response due to wound healing; several factors have been detected in seroma fluid that support this assumption. These factors are high levels of IgG, leukocytes, granulocytes, proteinases, proteinase inhibitors, and different kinds of cytokines (tPA, uPA, uPAR, PAI-1, PAI-2, IL-6, IL-1) [10,11]. Moreover, interleukin-6 (IL-6) stimulates the liver secretion of C-reactive protein (CRP), which is now considered to be an

 DOI: 10.4103/1110-1121.153366

important biomarker for proinflammatory status [12]. The use of hydrocortisone significantly decreased the inflammatory response in patients undergoing bilateral total knee replacement as measured by IL-6 production [10]. On the basis of this, an inhibition of the inflammatory response might result in a decrease in seroma formation, and perhaps improve the quality of life after mastectomy. Steroids inhibit the inflammatory response — for example, by inhibition of the cytokine function [10]. In this study, we aimed to evaluate the role of adding hydrocortisone to the anesthetic regimen in perioperative serum level of IL-6 and CRP and consequently in postmastectomy seroma formation.

Patients and methods

Patient selection

The study included female patients with primary operable breast cancer who were admitted to the hospital of the Medical Research Institute, University of Alexandria, Egypt, during the period from February 2013 to June 2014 and scheduled for a modified radical mastectomy. Patients with endocrine or metabolic disorders, diabetes, morbid obesity (BMI >40 kg/m^2 or 35 kg/m^2 with comorbidity), history of central nervous system diseases, who were under current or recent medication affecting the sympathetic response or hormonal secretion, such as carbamazepin, phenytoin, phenobarbital, rifampicin, salicylats, and ciclosporin, patients with distant metastasis, and patients who received previous anticancer treatment were excluded from the study. Institutional Research Committee approved the protocol before the study started. The study was explained to prospective patients and written informed consent was obtained before study entry.

Study protocol

All patients included in this study underwent complete history taking, full clinical examination, and laboratory and radiological investigations to exclude the presence of distant metastasis. Patients were randomly allocated to one of the two study groups; patients in group I received general anesthesia after insertion of an intravenous line, and standard monitors were attached. Preoxygenation was followed by induction with fentanyl 1 μg/kg, propofol 2 mg/kg, and cisatracurium 0.15 mg/kg. Two minutes later, an endotracheal tube was inserted and maintenance was ensured with isoflurane in oxygen. A dosage of 100 mg of hydrocortisone was administered at induction, followed by a second dose given 2 h later to patients in this group. Patients in group II received standard general anesthesia similarly to group I but without hydrocortisone and served as the control group. Venous samples were collected peripherally from an antecubital vein of the arm contralateral to the side of surgery using a small cannula.

For each patient, peripheral blood samples were collected for the following procedures: for measuring IL-6, the samples were collected at three time points — before surgery, 6 h after the end of the procedure, and 24 h after the procedure; for measuring CRP serum levels, samples were collected before the surgery and 24 h after the procedure. Serum and plasma samples were isolated from whole blood by centrifugation according to standard protocols. IL-6 was measured in serum samples by enzyme linked immunosorbent assay using an AviBion Human IL-6 ELISA Kit (Orgenium Laboratories, Helsinki, Finland) [13]. The CRP values were determined by turbidimetric immunoassay on an Olympus AU 400 autoanalyzer (Olympus, Hamburg, Germany) using Olympus Diagnostic reagents [14]. The detection interval for CRP was 0.08–160.0 mg/l, and the reference interval of serum CRP value was less than 1 mg/l [15] ghazals

Surgery was performed for all patients using the same technique irrespective of their randomization. The dissection of mastectomy flaps was performed with diathermy and the dissection of the axillary part as a sharp dissection. The incidence of intraoperative bleeding and the duration of surgery were registered. All patients underwent insertion of a closed suction drain. The drain was maintained on negative suction and removed when the daily drainage volume was below 30 ml. Compression dressing was applied for 48 h, and early arm exercises were advised for all patients. All patients were followed up postoperatively for registration of the total drainage volume until drain removal, for timing of drain removal, for the incidence of seroma formation, and for the management of seroma.

Statistical analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 20.0 (SPSS Inc., Chicago, IL, USA) for analyzing the collected data. Qualitative data were described using number and percentage. Comparison between different groups with respect to categorical variables was made using the χ^2-test. Quantitative data were described using mean and SD for normally distributed data. Comparison between two independent populations was made using the independent *t*-test, and for more than two populations the *F*-test (analysis of variance) was used. Significance of the obtained results was judged at the 5% level.

Results

The study included 80 female patients who were randomly allocated to two groups; each included 40 patients. Patients in group I received general anesthesia with hydrocortisone, whereas patients in group II received general anesthesia without hydrocortisone. As regards the distribution of the studied patients based on age, tumor stage, and duration of surgery, no significant differences were observed between the two groups but there was a significantly lower total drainage volume in group I and the drain was removed earlier. As regards the incidence of postmastectomy seroma, only two patients had postmastectomy seroma in group I, whereas eight patients had postmastectomy seroma in group II, with a significant difference between the two groups (Table 1). Neither significant major intraoperative bleeding nor significant difference in wound infection rate and wound healing delay has been registered in either group.

Table 1 Distribution of the studied patients with respect to age, tumor staging, and perioperative data

Patient's data	Group I (n = 40)	Group II (n = 40)	P-value
Age	49.1 ± 10.2	48.0 ± 9.1	0.398
Tumor stage [n (%)]			
IIA	11 (27.5)	13 (32.5)	0.231
IIB	10 (25)	14 (35)	0.107
IIIA	12 (30)	11 (27.5)	0.521
IIIB	7 (17.5)	4 (10)	0.311
Duration of surgery	107.0 ± 11.3	104.8 ± 11.7	0.325
Total drainage volume	665.0 ± 107.5	871.4 ± 82.7	0.001*
Timing of redivac removal	9.5 ± 1.7	12.8 ± 2.0	0.009*
Incidence of seroma formation [n (%)]	2 (5)	8 (20)	0.005*

*Significant at $P \leq 0.05$.

As regards IL-6 and CRP serum levels, there was no significant difference between the two groups preoperatively (the baseline value), but postoperatively a significant decrease was observed in group I compared with group II (Table 2).

The relation between the incidence of postmastectomy seroma and the changes in IL-6 and CRP serum levels preoperatively and postoperatively showed that, with a greater decrease in IL-6 and CRP serum levels in group I, the incidence of postmastectomy seroma became lower than that in group II, with a significant difference between the two groups (Table 3).

The two patients who developed seroma in group I required two to three aspirations, whereas in group II eight patients had seroma — five of them required multiple aspirations and three patients needed a second tube drainage.

Discussion

Seroma can infrequently occur after any surgical procedure and is the most prevalent postoperative sequel after breast surgery, with an incidence of 10–85%, leading to significant morbidity and discomfort and possibly delaying the adjuvant therapy [16]. Different causes of seroma have been proposed, such as the disruption of lymphatic drainage with fibrinolysis, or the surgical technique, especially the use of electrocautery versus

Table 2 IL-6 and CRP measurement preoperatively and postoperatively among the studied patients

Measurement time	IL-6		CRP	
	Group I	Group II	Group I	Group II
Preoperative				
Minimum–maximum	35–130	53–120	0.7–1.8	0.9–1.8
Mean ± SD	135.8 ± 29.8	88.0 ± 13.9	1.24 ± 0.31	1.21 ± 0.30
t-test	0.393		0.172	
P-value	0.696		0.864	
6 h Postoperative				
Minimum–maximum	80–200	100–280		
Mean ± SD	135.8 ± 29.8	158.1 ± 40.8		
t-test	2.453			
P-value	P = 0.017*			
24 h Postoperative				
Minimum–maximum	50–150	95–260	1.2–3.0	1.8–3.2
Mean ± SD	107.6 ± 21.9	147.7 ± 39.8	1.91 ± 0.43	2.23 ± 0.40
t-test	4.912		3.806	
P-value	<0.0001*		<0.0001*	
Significance (preoperative/6 h postoperative)	P < 0.0001*	P < 0.0001*		
Significance (preoperative/24 h postoperative)	P < 0.0001*	P < 0.0001*	P < 0.0001*	P < 0.0001*
Significance (postoperative 6 h/24 h postoperative)	P < 0.0001*	P < 0.0001*		

CRP, C-reactive protein; IL-6, interleukin-6. *Significant at $P \leq 0.05$.

Table 3 Relation between the changes in CRP and IL-6 from baseline to 24 h postoperatively and seroma formation

Group	Seroma formation	Mean change in IL-6	*P*-value	Mean change in CRP	*P*-value
Group I	With seroma, *n* = 2	37.3 ± 11.02	0.003*	1.21 ± 0.698	0.001*
	Without seroma, *n* = 38	25.6 ± 10.3		0.789 ± 1.01	
Group II	With seroma, *n* = 8	72.6 ± 15.2	0.0001*	2.22 ± 1.22	0.006*
	Without seroma, *n* = 32	52.6 ± 11.3		1.03 ± 1.09	
Significance of seroma between two groups regarding		0.0013*		0.005*	

CRP, C-reactive protein; IL-6, interleukin-6; *Significant at $P \leq 0.05$.

knife dissection [17,18]. Oertli *et al*. [6] concluded that tranexamic acid given perioperatively and postoperatively at a dose of 1 g three times daily in a randomized double-blind trial can produce a significant reduction in the mean postoperative drainage volume as well as in the incidence of seroma formation; however, this may need postoperative patient compliance, which is not always secured as the patient usually prefers to be on a reduced medication load postoperatively; therefore, in our work we administered hydrocortisone at 100 mg at induction, followed by a second dose 2 h later, with no additional postoperative medication load. The efficacy of shoulder immobilization has been investigated by Knight *et al*. [5]. Although seroma resulted in a delay in return to normal shoulder mobility, no patient sustained a long-term musculoskeletal dysfunction. Retention of the drain *in-situ* for a longer period seems to be a logical measure as the formed seroma usually subsides with aspiration [19]. Estes and Glover [7] concluded that the suction drain left *in-situ* for a prolonged period maintains physical contact between contiguous surfaces so as to facilitate adhesion. In our work the drain was removed when the daily volume was below 30 ml. Conveney *et al*. [8] and O'Dwyer *et al*. [9] demonstrated that both drainage and seroma formation were significantly less when dead space was obliterated by suturing the skin flaps to muscle. A similar flap tacking procedure was advocated by Chilson *et al*. [20] as having proven value in seroma prevention. Lindsey *et al*. [21] applied topical fibrin glue in the operative site in a Sprague–Dawley rat model and similarly decreased the incidence of seroma following mastectomy. A seroma was traditionally considered an accumulation of lymphatic fluid [16]. However, it has been demonstrated that a seroma is more than a mere accumulation of serum, probably an inflammatory response forming a part of the initial phase of wound healing [22]. McCaul *et al*. [23] concluded that fluid collection after breast cancer surgery and axillary clearance reflects the exudative phase of wound repair. Schulze *et al*. [24] demonstrated that it was possible to inhibit the inflammatory response with a single preoperative infusion of high-dose steroid in patients undergoing open resection of the colon. Recently, impressive achievements in seroma treatment were described by Taghizadeh *et al*. [25]. The single-dose methyl-prednisolone sodium succinate level was set at 125 mg on the basis of results obtained from previous head and neck surgery studies [26]. However, the inflammatory response after mastectomy is probably more pronounced than that seen following head and neck surgery, and it seems that the failure to report a significant effect could be ascribed to a very low dose of glucocorticoid, or to the fact that glucocorticoid was administered very soon after surgery. The inflammatory response to heart surgery with cardiopulmonary bypass is much more pronounced than that of other types of major surgery, which may be because of excessive activation of inflammatory mediators that promote postoperative atrial fibrillation [26]. Several reports on cardiac surgery document a prophylactic effect of 15–30 mg/kg hydrocortisone intravenously 1 h before surgery and up to 0.3 mg/kg intravenously every 6 h for 3 days [27–29]. This may be the right schedule of glucocorticoid administration for seroma prophylaxis. Taghizadeh *et al*. [25] have reported the therapeutic use of 80 mg of triamcinolone (Kenolog; E.R. Squibb, Middlesex, UK) in patients with seroma formation after autologous latissimus dorsi breast reconstruction. The glucocorticoid was injected into the cavity immediately after seroma aspiration. They demonstrated that a single dose significantly reduced the need for any further aspiration, the total number of aspirations, the total volume aspirated, and the total time to dryness. In our study, we used hydrocortisone 100 mg at induction, followed by a second dose 2 h later. Further studies are needed to evaluate prophylactic anti-inflammatory regimens against therapeutic regimens. A previous study has shown that a high preoperative single dose of glucocorticoid infusion (30 mg/kg methyl-prednisolone sodium succinate) inhibited the normal IL-6 and CRP response after colonic resection, and reduced plasma cascade system activation, the inflammatory response, and the immunofunction, but had no detrimental effect on wound healing [30]. Others [25] have argued that glucocorticoid suppresses the inflammatory process by the formation of a phospholipase inhibitor lipocortin, which diminishes the supply of arachidonic acid available for prostaglandin and leukotriene synthesis. This results in the inhibition of capillary permeability, edema, migration of leukocytes, later signs of capillary proliferation, and fibroblast and collagen deposition. One of the side effects of corticosteroid administration is the risk of infection and complicated wound healing. We found no differences between the groups with respect to wound infection,

epidermiolysis, wound necrosis, and wound hematoma despite the significant difference between the two groups with respect to the changes in the inflammatory mediators, which is in accordance with other studies [24,26]. The present study demonstrated a lower total drainage volume during the postoperative period in the hydrocortisone group compared with the control group, with a significant difference. The significant difference in the total drainage volume had a significant effect on postoperative seroma formation as there was a tendency toward lower seroma formation rate in the hydrocortisone group compared with the control group, with significant difference. We also found that the drain was removed earlier in the hydrocortisone group compared with the control group, with significant difference. In the study by Okholm and Axelsson [30], the case material comprised patients undergoing different types of axillary surgery. Two-thirds of the patients in each group underwent surgery with an axillary clearance of levels I and II and one-third in each group only with sentinel lymph node biopsy. This difference in the type of axillary surgery could perhaps influence their results. One could argue that a mastectomy with a sentinel lymph node biopsy would yield a smaller postoperative inflammatory response because of a smaller surgical trauma, and thereby less formation of seroma. They included patients with both types of axillary surgery in the case material. In our study, we avoid this potential confounder by standardization of the technique as all of our cases were submitted to modified radical mastectomy with level I and II axillary clearance.

Conclusion

Postmastectomy seroma is likely a proinflammatory process and can be reduced by administering intravenous hydrocortisone on the induction of anesthesia and 2 h later, which significantly decreases the inflammatory mediators (IL-6 and CRP) whose perioperative changes significantly affect the incidence of postmastectomy seroma.

Acknowledgements

Conflicts of interest

None declared.

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Outcome of laparoscopic diagnosis and treatment of intestinal malrotation in infants and young children

Yasser M. El Basatiny[a], Mohamed R. Abdella[b]

[a]Department of Laparoscopic Surgery, Al Iman General Hospital, Riyadh, Kingdom of Saudi Arabia, [b]Department of General Surgery, Faculty of Medicine, El Minia University, Minia, Egypt

Correspondence to Mohamed R. Abdella, MD, Department of General Surgery, Faculty of Medicine, El Minia University, Minia, 5255, Egypt
Tel: +20 966 509 030 521; fax: 4312799;
e-mail: mrabea177@gmail.com

Received 08 September 2014
Accepted 07 December 2014

The Egyptian Journal of Surgery
2015, 34:22–27

Objective
The aim of this study was to evaluate the safety and efficacy of laparoscopy in the diagnosis and treatment of intestinal malrotation in infants and young children.

Patients and methods
Diagnostic laparoscopy was performed on 27 infants and young children aged 4 months–5 years with suspected intestinal malrotation on clinical examination, imaging studies, or both. All patients with malrotation on exploration were treated with laparoscopic Ladd's procedure. After completion of laparoscopic Ladd's procedure, patients were followed up for 3–18 months.

Results
On diagnostic laparoscopy, seven patients (26%) with normal rotation, two patients (7.4%) with volvulus converted to open surgery, and 18 patients (66.6%) with malrotation only underwent laparoscopic Ladd's procedure. The rate of conversion to laparotomy was 18.5% in all patients and 11.1% in patients who underwent laparoscopic Ladd's. There was a significant association between presence of malrotation and preoperative presentation with bilious emesis. Sixteen patients completed laparoscopic Ladd's procedure for mlarotation with an average operative time of 46 ± 16 min, an average time to normal feeding of 2.7 ± 1 days, and an average postoperative hospital stay of 4.8 ± 2 days. There were no early postoperative complications, and there were no cases with late volvulus. Wound infection occurred in one patient who underwent open approach for volvulus and early adhesive small bowel obstruction in another patient who underwent open laparoscopic Ladd's.

Conclusion
Laparoscopy is a safe and effective method in the diagnosis and treatment of intestinal malrotation in infants and young children, with or without preoperative symptoms.

Keywords:
infants, intestinal malrotation, Ladd's procedure, laparoscopy

Egyptian J Surgery 34:22–27

1110-1121

Introduction

In embryological life, the rotation of the intestine occurs in counterclockwise direction at the level of the duodenum, as well as in the region of the small intestine loop and the cecum. Intestinal malrotation occurs when:

(a) The C-shaped duodenal loop is not rotated to the left,
(b) The mesentery of the small intestine has not become adherent to the posterior wall,
(c) The cecum is not located in the right iliac fossa,
(d) The retroperitoneal fixation of the ascending colon is missing, and
(e) The duodenum is constricted from the outside by the so-called Ladd's bands [1].

The incidence of intestinal malrotation is difficult to determine, but symptomatic intestinal malrotation has an incidence of about 1 in 6000 live births [2].

Malrotation can present at any age, although the classic presentation is in infants with bile vomiting due to duodenal obstruction (extrinsic because of Ladd's bands or by virtue of the twist of the volvulus) [3]. Early diagnosis of intestinal malrotation is of paramount importance to prevent the potentially devastating complications of this anomaly [4]. There is emerging literature to demonstrate the safety and efficacy of laparoscopy in the diagnosis and correction of malrotation in infants and children. Diagnostic laparoscopy is the procedure of choice when intestinal malrotation is suspected. If present, malrotation can be treated adequately with laparoscopic Ladd's procedure [5].

The aim of this study was to evaluate a personal experience with laparoscopy in the diagnosis and surgical treatment of intestinal malrotation in infants and young children in terms of its safety and efficacy.

Patients and methods

Study population

After approval of the study protocol by the Local Ethical Committee and obtaining written fully informed parents' consent. The study included 27 infants and young children who underwent diagnostic

 DOI: 10.4103/1110-1121.153367

laparoscopy for suspected intestinal malrotation and further treatment of proven disease on exploration, from January 2011 to December 2013 in Al Iman General Hospital, Riyadh, Kingdom of Saudi Arabia, and Al Jafel International Hospital, Riyadh, Kingdom of Saudi Arabia. The ages ranged from 4 months to 5 years. The laparoscopic evaluation was indicated on the basis of clinical evaluation in all patients and imaging studies with findings suspecting or confirming malrotation. In symptomatic patients, diagnosis was made within 24 h (eight patients) or less than 7 days (19 patients) of symptom onset. All patients were scheduled for laparoscopic exploration after clinical and/or radiological suggestion. The study excluded patients with preoperatively diagnosed congenital diaphragmatic hernia, gastroschisis, or omphalocele.

Operative technique

All procedures were performed with the patient positioned in a supine head up position. Three trocars of 5 mm diameter were used. A Veress needle was placed through an incision (5 mm) at the inferior umbilical fold, and the abdomen was insufflated to 8 mmHg with CO_2. Thereafter, the needle was replaced by the trocar that contained a camera (5 mm, 30°). The other two trocars were placed at the right and left mid to lower quadrants. Intraoperatively, malrotation was defined as the duodenojejunal junction and the cecum near the midline and the base of the mesentery less than 50% of the diameter of the abdomen, implying a greater risk of midgut volvulus [6]. The presence of Ladd's bands extending across the duodenum confirmed the diagnosis of malrotation. All patients with malrotation on exploration were treated with Ladd's procedure including division of adhesive bands, broadening of the intestinal mesentery, incidental appendectomy, and placement of the bowel in a nonrotated position.

To ensure that the malrotation is treated properly, the whole duodenum and the jejunum should lie on the right side; thus, it was important to free the duodenum in the distal direction and transect all bands. When the anterior mesentery has been widened enough, it is further incised distally and the adjacent bowel is further displaced to either side. Appendectomy was performed in all patients with malrotation using a standard technique, and then the appendix was mobilized using a mid-abdominal wall trocar. When malrotation was doubtful, visualization of the ligament of Treitz was carried out. When there was no malrotation, visualization of the ileocecal region was carried out to confirm whether it was normally fixed. If there was volvulus, difficult bowel orientation, intestinal ischemia, or other inaccessible diagnoses on laparoscopic exploration, conversion to open surgery was carried out.

Postoperative care and follow-up

A nasogastric tube was left behind until gastric retention had ceased. Hospital stay was related to recovery from the procedure and immediate procedure-related complications. The follow-up period for patients who underwent laparoscopic Ladd's procedure ranged from 3 to 18 months (average: 12 ± 4 months).

Statistical analysis

All statistical analyses were performed using SPSS, version 16 (SPSS Inc., Chicago, Illinois, USA). Quantitative numerical variables were presented as mean ± SD and were compared using Student's *t*-test. Qualitative and categorical variables were presented as number and percentage and were compared using the χ^2-test. Measurement of association between different variables and laparoscopic diagnosis of malrotation was performed by calculating odds ratio and its 95% confidence interval. All *P*-values were two sided, and data were considered statistically significant at *P*-value less than 0.05.

Results

At the time of diagnostic laparoscopy for suspected malrotation, there were 27 patients (16 male and 11 female) aged 4 months–4.5 years (14.85 ± 10 months; 1.23 ± 0.83 years) with suspected intestinal malrotation. There were 18 patients (66.7%) aged less than 1 year and nine patients (33.3%) aged more than 1 year. Preoperative symptoms suggesting malrotation were encountered in 19 patients (70%), and eight patients (30%) were asymptomatic. Of the 19 symptomatic patients, 10 patients had more than one symptom. The presenting symptoms include bilious emesis (11; 40.7%), abdominal pain (10; 37%), fever (four; 14.8%), and nonbilious emesis (two; 7.4%). The preoperative imaging studies were performed on 15 patients (55.5%) and not performed in 12 patients (44.5%). These studies include upper gastrointestinal (UGI) contrast series (11; 40.7%), ultrasonography (six; 22.2%), abdominal computed tomography (CT) scan (two; 7.4%), and barium enema (two; 7.4%). There were six patients who underwent more than one imaging study (Table 1).

On the initial diagnostic laparoscopy, there were seven patients (26%) with normal rotation, two patients (7.4%) with volvulus converted to open surgery, and 18 patients (66.6%) with malrotation only who underwent further laparoscopic Ladd's procedure, which was converted to open Ladd's procedure in two patients

(2/18; 11.1%) for further bowel orientation. There were no intraoperative complications during laparoscopic Ladd's procedure. Of the seven patients with normal rotation, six patients underwent diagnostic laparoscopy alone and one patient was converted to open surgery for other diagnoses (pyloric stenosis). Thus, conversion to laparotomy was indicated in five out of 27 patients who underwent initial laparoscopy (18.5%). The preoperative demographic characteristics and clinical presentation in 18 patients with malrotation were comparable to those in the nine patients with volvulus or no malrotation (Table 2). There was a statistically significant association between presence of malrotation and preoperative presentation with bilious emesis [odds ratio = 10 (95% confidence interval 1.02–97.5), $P = 0.02$].

As regards operative and postoperative outcome of 16 patients who completed laparoscopic Ladd's procedure for malrotation (Table 3), the operative time averaged 46 ± 16 min (range: 30–120 min). Normal feeding was started on postoperative day 1–5 (average: 2.7 ± 1 days), and postoperative hospital stay ranged from 3 to 7 days (average: 4.8 ± 2 days). There were no early postoperative complications in the 16 patients who completed laparoscopic Ladd's procedure; however, these complications occurred in two out of five patients who had been converted to open surgery because of malrotation or other diagnoses, including wound infection in one patient who underwent open approach for volvulus, and early adhesive small bowel obstruction in another patient who underwent open approach for malrotation. There were no cases with volvulus after Ladd's procedure during the follow-up period. There was no statistically significant influence of age at surgery and presence of preoperative symptoms on the outcome, after completion of laparoscopic Ladd's procedure in 16 patients (Table 4) and (Figs. 1 and 2).

Table 1 Demographic and clinical characteristics of 27 patients who underwent diagnostic laparoscopy for suspicion of malrotation

Variables	*N* (%)
Age	
Less than 1 year	13 (48)
More than 1 year	14 (52)
Sex	
Male	16 (59.3)
Female	11 (40.7)
Presence of clinical symptoms	19 (70)
Bilious emesis	11 (40.7)
Abdominal pain	10 (37)
Fever	4 (14.8)
Nonbilious emesis	2 (7.4)
Imaging studies	
Upper gastrointestinal series	11 (40.7)
Ultrasonography	6 (22.2)
CT scan	2 (7.4)
Barium enema	2 (7.4)

CT, computed tomography.

Table 2 Association of preoperative demographic and clinical characteristics with malrotation diagnosed on laparoscopy

Characteristics	Laparoscopic diagnosis (*n* = 27) [*n* (%)]		Odds ratio (95% CI)	*P*-value
	Malrotation (*n* = 18)	No malrotation (*n* = 9)		
Age				
Less than 1 year	14 (77.7)	4 (44.4)	2.5 (0.47–13.2)	0.08
More than 1 year	4 (20.3)	5 (55.6)		
Sex				
Male	11 (61.1)	5 (55.6)	1.25 (0.24–6.3)	0.78
Female	7 (38.9)	4 (44.4)		
Presence of symptoms				
Symptomatic	12 (66.7)	7 (77.8)	0.57 (0.09–3.6)	0.55
Asymptomatic	6 (33.3)	2 (22.2)		
Bilious emesis				
Present	10 (55.6)	1 (11.1)	10 (1.02–97.5)	0.02*
Absent	8 (44.4)	8 (88.9)		
Abdominal pain				
Present	6 (33.3)	4 (44.4)	0.62 (0.12–3.2)	0.57
Absent	12 (66.7)	5 (55.6)		
Fever				
Present	3 (16.7)	1 (11.1)	1.6 (0.14–18)	0.70
Absent	15 (83.3)	8 (88.9)		
Nonbilious emesis				
Present	1 (5.6)	1 (11.1)	0.47 (0.02–8.5)	0.60
Absent	17 (94.4)	8 (88.9)		

CI, confidence interval, *Significant difference.

Discussion

Intestinal malrotation results from a failure in the normal embryologic sequence of bowel rotation and fixation. Because its consequences are associated with volvulus leading to devastating intestinal necrosis, an increased awareness of this entity and an understanding of its varied presentation at different ages may reduce the time to diagnosis and improve patient outcome [7,8]. The present study included 27 infants and young children with suspected malrotation, and 18 of them had a confirmed diagnosis of malrotation on initial diagnostic laparoscopy, whose ages were less than 1 year in 77.7%. These findings are in agreement with the literature, which reports that 75–85% of patients are diagnosed by the age of 1 year [9].

In this study, preoperative clinical symptoms suggesting malrotation were reported in 70% of patients. The indication for initial laparoscopy was based not only on clinical symptoms but also on radiological suspicion. Moreover, the results of the present study show that presence of symptoms was not significantly associated

with the presence of malrotation on exploration and did not influence the outcome after laparoscopic correction. These findings were supported by the published data in previous studies, which recommend surgical management using Ladd's procedure for symptomatic or asymptomatic infants and children with malrotation because of the high risk of midgut volvulus, which can have devastating consequences at any age, increasing mortality related to malrotation [10,11].

The presence of bilious vomiting was the only preoperative sign that had a significant association with presence of malrotation on laparoscopic exploration. In the literature, pediatric patients with symptomatic malrotation of the intestine presented with bilious vomiting, which is the most common clinical presentation in neonates, whereas bilious vomiting, recurrent abdominal pain, and failure to thrive are the most common symptoms after the newborn period [12,13]. Moreover, a sudden onset of bilious vomiting in a previously healthy infant has been suggested as hallmark presentation of intestinal malrotation [9]. Thus, our findings also may urge that diagnosis of malrotation should always be kept in mind when assessing any infant or child with symptoms of vomiting and pain, particularly when the vomiting is bile-stained.

Preoperative imaging studies were performed in 55.5% of infants and young children with suspected malrotation, including UGI contrast series, ultrasonography, abdominal CT scan, and barium enema. The imaging studies may play a role in the preoperative diagnosis of malrotation due to nonspecific clinical findings in most cases. The goal of initial bowel imaging is the early detection or exclusion of malrotation to prevent volvulus and potentially life-threatening bowel ischemia. On a plain abdominal radiograph, malrotations may show a wide spectrum of appearances [14]; thus, other modalities such as UGI contrast series are preferred in stable patients with a documented accuracy greater than 80% [10]. Although it is true that the UGI series is the gold standard for the

Table 3 Operative and postoperative outcome of 16 patients who completed laparoscopic Ladd's procedure for malrotation

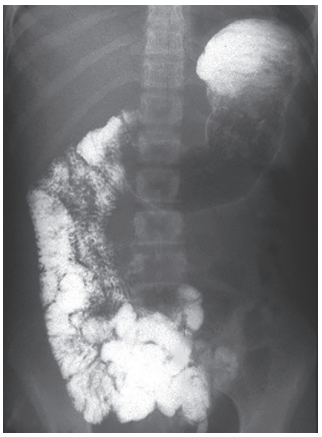
Outcome	Laparoscopic Ladd's procedure (n = 16)
Operative time (min)	46 ± 16
Time to normal feeding (days)	2.7 ± 1
Postoperative hospital stay (days)	4.8 ± 2
Conversion to open procedure	2 (11.1)
Postoperative complications	0 (0)

Data are expressed as mean ± SD, or number and percentage.

Table 4 Influence of age at surgery and presence of preoperative symptoms on outcome after completion of laparoscopic Ladd's procedure in 16 patients

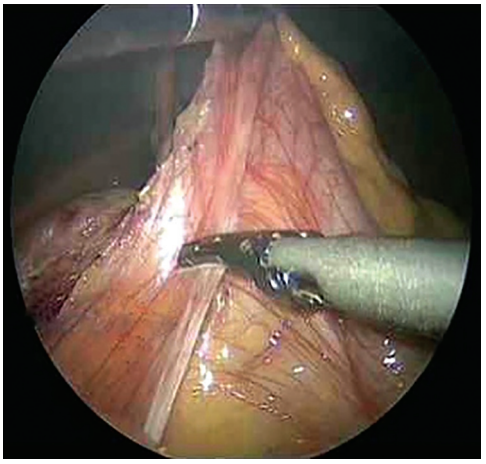
Outcome	Age			Symptoms		
	<1 year (n = 12)	>1 year (n = 4)	P-value	Present (n = 10)	Absent (n = 6)	P-value
Operative time (min)	44.4 ± 18.7	50 ± 18	0.60	49.5 ± 18.4	42.5 ± 18	0.47
Time to normal feeding (days)	2.8 ± 0.92	2.9 ± 1.2	0.86	2.9 ± 0.9	2.8 ± 1.1	0.90
Postoperative hospital stay (days)	4.6 ± 1	5.2 ± 1.7	0.39	5.1 ± 1.3	4.6 ± 1.3	0.55

Figure 1



Upper gastrointestinal contrast study in a 3-year-old child with intestinal malrotation. The duodenojejunal flexure and the small bowel lie to the right of the midline.

Figure 2



Laparoscopic view demonstrating dissection of Ladd's band in an infant with malrotation.

diagnosis of malrotation, it has both false positives and false negatives. Meticulous technique and an awareness of the variations of normal anatomy are critical to minimize errors in the performance and interpretation of this test [15].

Intestinal malrotation is currently treated using the Ladd's procedure. Many surgeons feel that this operation should be performed using the open approach to facilitate adhesion development, thus decreasing the risk for volvulus [16]. The results of the present study show that in the absence of volvulus, laparoscopic approach for malrotation can be safely used for infants and young children with a low rate of conversion to open approach if there is concern about uncorrected volvulus, proper bowel orientation, or true nonrotation. These findings are in agreement with those of other studies supporting the safety and efficacy of laparoscopic Ladd's procedure [5,16–19].

In our experience, there is an important rule to reduce the difficulty of laparoscopic Ladd's procedure that is based on freeing duodenum distally and transecting all bands before widening the mesentry and visualization of whole intestine. Reducing the difficulty of laparoscopic Ladd's might attribute to increased bowel orientation and hence may reduce the rate of conversion to open procedure. In the present study, the overall rate of conversion from initial diagnostic laparoscopy to laparotomy in infants and young children with suspected malrotation was 18.5%, and the rate of conversion from laparoscopic to open Ladd's procedure in patients with laparoscopy-diagnosed malrotation was 11.1%. This rate is within the literature-reported rate in the same age groups, which was 8.3% in the study by Stanfill *et al.* [19], 25% in the study by Hagendoorn *et al.* [5], and 33% in the study by Fraser *et al.* [16]. The variation in the conversion rate might be attributed to the variety of patient, surgeon, and technical factors.

In our study, the operative times, hospital stay, and clinical outcomes were acceptable. In our 16 patients with completed laparoscopic Ladd's procedure, operative time ranged from 30 to 120 min with an average of 46 min, return to normal feeding ranged from 1 to 5 days with an average of 2.7 days, hospital stay ranged from 3 to 7 days with an average of 4.8 days, and the mortality rate was 0%. These results are supported by published similar findings of studies investigating the role of laparoscopic Ladd's procedure in infants and children. In a study by Bass *et al.* [17], operative time averaged 58 min (35–20 min), feeding was started within 2 days after surgery, and hospital stay ranged from 2 to 4 days (average: 2.2 days) in the patients with isolated malrotation, with no complications. In the study by Draus *et al.* [18], operative time averaged 111 min (range, 77–176 min), hospital stay ranged from 3 to 5 days (average: 3.6 days), and all patients were discharged home on a regular diet, with no deaths. In the study by Hagendoorn *et al.* [5], the average operating time was 115 ± 7.8 min and the overall average hospital stay was 11 ± 2.0 days (range: 2–60 days). Several relatively long hospital stays were experienced by children with multiple congenital abnormalities requiring multidisciplinary care. We excluded such patients from our analysis.

In the present study, there was no postoperative complications in patients who completed laparoscopic Ladd's procedure, whereas wound infection and adhesive intestinal obstruction were reported in patients who were converted to open surgery. This finding highlights the potential advantage of laparoscopic over open approach in reducing the likelihood of complications from adhesions [18]. Moreover, despite the underestimate rate of adhesive small bowel obstruction because of limited surgical follow-up after open Ladd procedure reported in the literature, it may reach 15% [20].

From our experience, the successful role of laparoscopy in the diagnosis and treatment of suspected malrotation without preoperative suspicion of volvulus could be attributed to critical variables that include understanding of the anatomy, applying standard rules of laparoscopic management, surgical experience, and case selection, by which the surgeon can decrease the intraoperative laparoscopic complication rate. Moreover, identifying the potential factors for conversion preoperatively that mainly include other diagnoses rather than malrotation, may assist the surgeons in making decisions.

There are two main limitations of the present study: first is the small number of patients, which may be attributed to a low incidence of the disease; and second is the absence of a comparative analysis between laparoscopic and open procedures, which may be attributed to the prospective nature of the study and our trend during the study period to apply laparoscopy in all suspected cases of malrotation, whereas open procedure was not applied routinely for suspicion.

Conclusion

The findings of the present study reflect that laparoscopy is a safe and effective method in the diagnosis and correction of malrotation (Ladd's procedure) in infants and young children, with an acceptable rate of conversion to open Ladd's procedure, acceptable time

to normal feeding, and reduced stay in hospital after intervention.

Acknowledgements

Conflicts of interest

None declared.

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Evaluation of the versatility of superiorly based pedicled gastrocnemius myo- or myo-cutaneous flap, in upper leg defects after trauma or tumor excision: which is better?

Ayman M. Adbelmofeed[a], El-Sayed A. Abd El-Mabood[a], Refaat S. Salama[a], El Sayed M. Bayomy[b]

Departments of [a]General Surgery [b]Orthopedic Surgery, Benha University, Benha, Egypt

Correspondence to El-Sayed A. Abd El-Mabood, MD, 3a Elharameen Pharmacy Street, Beside Omar Ebn Elkattab Mosque, Benha-Quliobia, Egypt
Tel: 01065351802;
e-mail: elsayedafifi@yahoo.com

Received 22 September 2014
Accepted 12 October 2014

The Egyptian Journal of Surgery
2015, 34:28–34

Purposes
The current study aimed to focus on the versatility of the superiorly based pedicled gastrocnemius muscle flap or myocutaneous flap, either medial or lateral head, in upper-leg defects after trauma or tumor excision and the importance of these flaps to improve bone healing in trauma and to ensure an adequate safety margin in malignant tumors with minimal complications.

Patients and methods
A prospective, randomized trial was conducted on 27 patients suffering from upper-leg defects after trauma or tumor excision to compare postoperative outcomes, especially bone healing, using superiorly based pedicled gastrocnemius muscle flap covered by a split thierch skin graft [group A; 14 (51.8%)] against myocutaneous flap [group B, 13 (48.2%) cases], either medial or lateral head. Postoperative follow-up was for 6 months.

Results
Rapid healing of the tibial fracture was noticed in 8 (57.1%) cases in group A and in 8 (61.5%) cases in group B within 2 weeks after surgery, and there was no flap loss apart from partial skin loss, minor hematomas, or infections, all were noticed significantly more in group A [5 (35.7%), 6 (42.9%), and 4 (28.6%) cases, respectively], compared with group B [1 (8%), 2 (15.4%), and 1 (8%) cases, respectively; $P < 0.05$].

Conclusion
Both gastrocnemius myocutaneous and myocutaneous flaps for upper-leg reconstruction are considered as a reliable option to ensure a good safety margin in malignant tumor cases and to help bone healing in trauma cases, and myocutaneous flaps are safer, with no redo and lesser postoperative complications.

Keywords:
gastrocnemius flaps, malignancy, tibial defect, trauma

Egyptian J Surgery 34:28–34

1110-1121

Introduction

All major trauma centers around the world have developed standard operative procedures for the management of open fractures of the lower extremity. In order to reduce the risk of nonunion and osteomyelitis, early vascularized soft tissue coverage is mandatory in these injuries [1–3].

Muscle flaps have gained wide popularity in this context since their first use by Ger [4]. Muscle flaps are also suitable for the coverage of open joint and exposed orthopedic implants. Muscle flaps provide good vascularity to the defect area of either soft tissues and/or bone by their excellent intrinsic blood supply and provide a good bulk that fills these defects and provides a good healthy vascular bed for skin grafting if needed [4,5].

Early cover has been found to reduce the incidence of complications [6]. The gastrocnemius muscle flap is the workhorse of all muscle flaps for soft tissue coverage around the knee [7].

These type I muscle flaps have a unique and independent vascular anatomy; one pedicle (sural artery) at the level of the knee joint situated close to its origin provides blood supply to the heads of the gastrocnemius muscle. These vessels arise from the popliteal artery above the level of the knee joint. Each vessel courses a few centimeters with its venae comitantes before entering the anterior aspect of the proximal muscle belly with the innervating branches of the tibial nerve [8,9].

The fact that the size of the muscle belly, its location in the dissection field, and its transfer does not impair the function of the limb adversely make it an ideal flap to cover wounds in the region [10].

The aims of limb sparing for either open comminuted tibial fracture or malignant tumors in the upper one-third of the leg are improvement of survival,

 DOI: 10.4103/1110-1121.153368

achievement of adequate negative margins in malignant tumors, and improvement in the quality of life functionally and esthetically. When a bone is exposed either by trauma or by tumor excision, it is mandatory to cover these defects by bulky vascular tissue such as muscle flaps to decrease the incidence of osteomyelitis due to bone exposure in trauma cases and to resist radiotherapy postoperatively if needed in malignant tumor cases [11].

The unique vascularization of the gastrocnemius muscle (one pedicle to each head), the bulk of the muscle belly, and its presence in the operative field after that do not affect the function of the limb [12].

Vascular anatomy

There is only one vasculonervous pedicle for each muscular head (Mathes and Nahai type I) [5], composed of a sural artery (formerly a gastrocnemius artery) and one or two veins. In a certain number of cases, a secondary sural artery is present [6–8]. This pedicle is protected within the popliteal fossa with little risk of injuries. It has a mean length of 4 cm with extremes varying from 2 to 5 cm. The diameter of the sural arteries is 2–2.5 mm on average, and that of the veins is 3–5 mm [9–11]. In most cases, the sural artery terminates in two branches, occasionally three or even four, having a longitudinal course, in the muscle axis just below its deep aspect and a terminal vascular distribution [9,11].

These arteries give rise to the perforating branches destined to the cutaneous plane; some anastomose with the vascular system of the opposite gastrocnemius; some anastomose with the vascular system of the soleus [11,12]. Finally, around the distal aponeurosis of the muscle, there is a thin network of numerous blood vessels destined to the cutaneous plane [13]. These vascular characteristics are the basis of several applications on which we will elaborate later on. It is possible to safely harvest a skin paddle overlying the muscle [3].

The additional advantage is being able to raise the skin length/width ratio of the leg, which should not exceed 1/1 [9] or even 1.5/1 [14]. Therefore, a medial gastrocnemius (GM) flap harvested with the superjacent cutaneous plane shows a skin ratio of 3.5/1 (8–30 cm). During the elevation of a myocutaneous flap, the delicate distal perifascial vascularization should be preserved. It is possible to divide the muscle into two sections longitudinally according to the needs [15,16]. According to Jepegnanam *et al.* [17], the anastomosis between the medial and the lateral gastrocnemius (GL) muscles allows one to harvest a gastrocnemius that is vascularized by them. The large caliber of blood vessels is compatible with the creation of a 'local free flap' [7,18,19].

Patients and methods

Approval by the local ethical committee of Benha university and fully informed written consent from patients was obtained. This study included 27 patients with an exposed upper one-third of the tibia, who were fit for surgery, from Benha University during the period between July 2011 and August 2014, so as to allow 6 months' follow-up period for the last case operated on. All patients presenting were admitted at the General Surgery ward for clinical evaluation and laboratory assessment.

Patients included in this study were suffering from trauma (20; 74.1% of the cases, with an age range of 21–40 years) or malignant soft tissue tumor (7; 25.9% of the cases, with an age above 45 years). All were fit for surgery with good general condition. However, patients who were suffering from diabetes mellitus, peripheral arterial ischemia, or hypercoagulation disorders, those maintained on immunosuppressive therapy or corticosteroids, and patients with a traumatic crushed gastrocnemius muscle, tumor invading this muscle, or previous muscle harvesting were excluded from this study.

Operative procedures

In all cases of trauma, emergency operative procedures were performed, which included debridment and bone fixation by an external fixator; because all cases were associated with Gustilo type III fracture tibia, further debridment and preparation of wound for coverage were performed.

A swab culture of the wound was sent in all cases and any overt infection was treated first, and then flap coverage was provided 1–4 weeks after the trauma. The seven tumor cases included three cases of soft tissue sarcoma of the upper third of the leg and four cases of squamous cell carcinoma on top of old scars in the upper third of the leg proved by the preoperative pathology; preoperative evaluation of the tumor extent was achieved by a computed tomography scan; a metastatic work up was also performed intraoperatively, with a wide local excision of the tumor to achieve safety margins guided by the intraoperative pathology.

Harvesting techniques

After general or spinal anesthesia, the preoperative localization of the muscle to be harvested in an upright

position, with and without muscular contractions, gives a good indication of the amount of muscle mass available, which varies from one patient to another; the localization in the posterior median groove at the upper part of the leg of the subcutaneous adipose tissue containing the lesser saphenous vein and the medial sural cutaneous nerve (formerly, the sural nerve and vein), elements that are preserved, allow the division of the two gastrocnemius muscles. The division of the gastrocnemius and the soleus is easy to perform, and often characterized by the presence of the plantaris muscle within them. The GM muscle is longer, thicker, and more movable than the lateral muscle, has a better arc of rotation, which allows it to cover the proximal 1/3 of the leg, the knee at the medial and the lateral levels, and the medial distal femur. Its arc of rotation can be improved by being passed under the gracilis and the semitendinosus tendons. Finally, preservation of the aponeurosis of the leg during the dissection enables one to raise a medial saphenous flap at the same time or later on [20].

Open fracture of the proximal third of the tibia is; a. stabilized by external fixation; b. Elevation of a medial gastrocnemius flap; c. The flap is turned over the exposed tibia; d. Result at the end of the surgery; Longitudinal division of the soft tissue of the medial gastrocnemius (GM) or of the lateral gastrocnemius (GL) according to Francel *et al*. [11], when a tunnel has to be created within the muscle, if the skin is cicatricial, it is preferable to discard it and to use the muscle as a thin skin graft in order to prevent the loss of the flap caused by compression; when a myocutaneous flap is elevated, the 'soaping,' which may damage the perforators, should be avoided using stitches fixing the muscle to the dermis and a careful manipulation of the flap; the cutaneous plane overlying the GM can be elevated up to 5 cm from the medial malleolus [3,21,22].

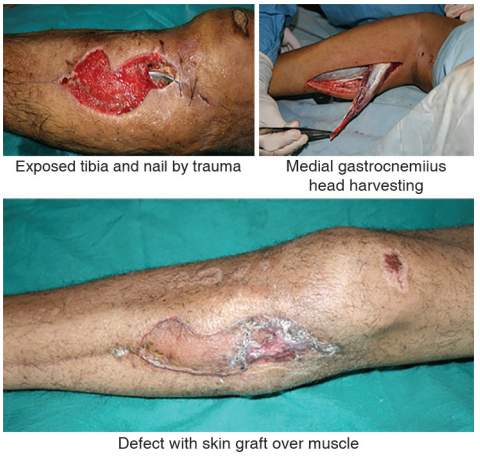
In this way, the medial myocutaneous gastrocnemius enables to cover the proximal 2/3 of the leg; there are numerous thin and long blood vessels coursing distally on the aponeurosis of the gastrocnemius muscles, beyond the muscular body and which superficially run toward the skin in several locations. This perifascial vascularization will have to be preserved during the elevation of the myocutaneous flap: it is recommended to immobilize the limb when raising an innervated flap to avoid applying tension to the sutures; the pure muscular flap will be grafted as a thin skin graft, expanded or not according to the size, in the same step as the creation of the flap, or for cosmetic reasons, within 8–15 days after the phase of granulation [21,23].

The gastrocnemius is a reliable flap in the cover of the leg skin loss. However, the distal 1/3 usually remains beyond the amount of coverage it can achieve. Numerous more procedures that will be described and some tips and tricks that can be applied to the muscular flap [group A: 14 (51.8%) cases] or to the myocutaneous unit [group B: 13 (48.2%) cases] enable significant improvement in its mobility and its arc of rotation, possibly even allowing for the cover of the whole leg segment. For the GM flap (better used for large defects, being more bulky), the incision was made 2–3 cm behind the medial border of the tibia from the popliteal fossa to below the mid-calf level. The incision was deepened to the deep fascia, and the medial head of the gastrocnemius was identified and separated from the underlying soleus muscle. The distal end of the muscle was divided sharply from the Achilles tendon taking care to include the portion of the tendinous material with the muscle belly as this improved suture holding; it was then divided and separated from the GL at the midline raphae. Care was taken to avoid injury to the small nerve and the short saphenous vein; the muscle was then tunneled anteriorly to cover the defect and fixed by suturing, and muscles were covered by the thierch skin graft (group A) if not taken as a myocutaneous flap (group B). However, if taken as a myocutaneous flap, the skin graft needed to cover the donor area, the skin paddle taken with the muscle ranged from 5 to 7 cm in width and 10 to 15 cm in length. In the GL flap (better used only for small defects being less bulky), the common peroneal nerve must be positively identified and safe-guarded; the rest of the procedure was completed as on the medial side. The wound was closed over the suction drain, and then supported with a splint [21–23] (Figs. 1–4).

Outcome items

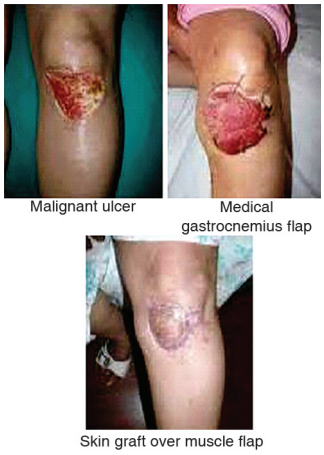
The limb was immobilized for 1 week; the flap was checked at the third postoperative day for infection

Figure 1



The traumatic defect was covered with a gastrocnemius muscle flap, which was covered by a thierch graft at the defect area, and the donor area was covered primarily.

Figure 2



A malignant ulcer (squamous cell carcinoma) in the upper leg was excised, leaving a large defect that was covered with a gastrocnemius muscle flap, with the overlying thierch graft at the defect area, and the donor area was covered primarily.

or necrosis, and the patient was followed up as an inpatient for 1 week and as an outpatient monthly for 6 months to assess the functional outcome, that is any disability or effect on the bulk of the cuff was recorded. Follow-up of bone fractures was conducted by an orthopedic surgeon by serial radiographic scanning.

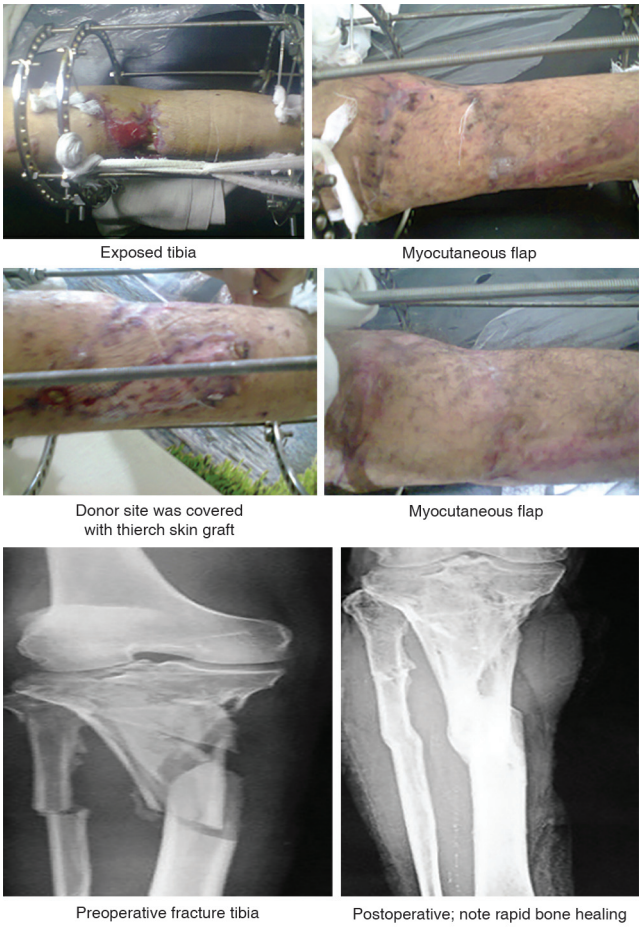
Statistical analysis

Analysis of the data was performed using SPSS, version 16 (Bristol University, Bristol, UK). Qualitative data are presented as numbers and percentages and were compared between groups. *P*-value greater than 0.05 was considered insignificant, *P*-value less than 0.05 was considered statistically significant, whereas *P*-value less than 0.01 was considered statistically highly significant.

Results

A prospective, randomized trial was conducted to focus on the versatility of the superiorly based pedicled gastrocnemius muscle flap [group A; 14 (51.8%) patients] or the myocutaneous flap [group B; 13 (48.2%) patients], either medial or lateral head, in upper-leg defects after trauma or tumor excision and the importance of these flaps to improve bone healing in trauma and to ensure an adequate safety margin in malignant tumors with minimal complications. Regarding the sex distribution, there were 4 (14.8%) female and 23 (85.2%) male patients. Patients included in this study were suffering from either trauma [20 (74.1%) cases with an age range of 21–40 years] or malignant soft tissue tumor [7 (25.9%) cases with age above 45 years]. None of the patients were lost to follow-up, and data collection was complete (Table 1 and Graph 1).

Figure 3



A traumatic fractured upper tibia was fixed by an external fixator and there was an overlying traumatic defect that was covered with a myocutaneous flap, and the donor area was covered with a thierch graft. Note the rapid healing within 2 weeks.

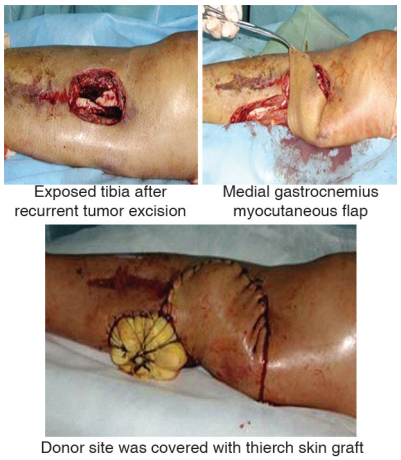
Table 1 Distribution of cases

Preoperative parameters	*N* (%)
Types of flap used	
Group A; muscle flap	14 (51.8)
Group B; myocutaneous flap	13 (48.2)
Indications	
Trauma	20 (74.1)
Tumors of upper one-third leg	7 (25.9)
Soft tissue sarcoma	2
Squamous cell carcinoma	5
Age (years)	
Between; 21 and 40 years old; trauma	20 (74.1)
Above; 45 years old; tumors	7 (25.9)
Sex	
Female	4 (14.8)
Male	23 (85.2)

All trauma patients had emergency debridment and bone fixation by an external fixator (Fig. 2), which consisted of preparation of the wound for coverage, and excision with an adequate safety margin in all patients suffering from malignancy; the flap was then applied with a means operative time of 2 ± 0.9

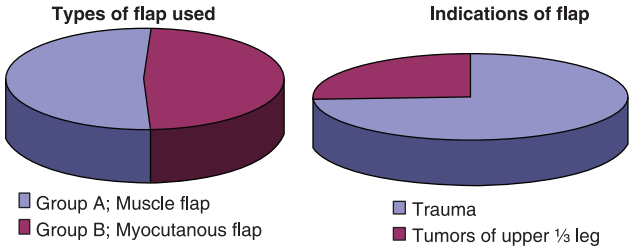
(range:1.5–3 h). The mean blood loss was 540 ± 115 (range: 400–900 ml). Most patients (22; 71.5%) required blood transfusion, with a mean number of units used being 1.8 ± 0.7 (range: 1–3 U) (Table 2). No intraoperative complications or mortality was recorded.

Figure 4



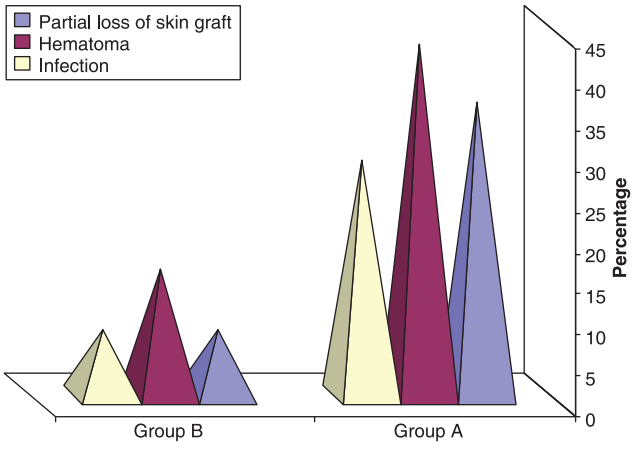
Fibrosarcoma in the upper leg was excised, leaving a large defect that was covered with a gastrocnemius myocutaneous flap, and the donor area was covered with a thierch skin graft.

Graph 1



Distribution of cases.

Graph 2



Inpatient complications

Regarding inpatient complications, no flap loss was recorded in any of the procedures. Minor complications such as partial loss of skin graft was noticed in group A in 5 (35.7%) cases at the defect area; these cases were treated conservatively and healed by secondary intension, except 2/5 (40%) cases that needed another thierch graft at the defect area; however, partial loss of the skin graft was noticed only in one case (8%) in group B at the donor area, which was treated conservatively. Also, a small hematoma was noticed in 6 (42.9%) cases in group A compared with only 2 (15.4%) cases in group B. All these cases were treated conservatively and ended with good results. Infection was encountered in trauma cases only: 4 (28.6%) patients in group A, three cases at recipient sites and one case in the donor area, and one case in group B at the donor site; the infection was controlled by appropriate antibiotics according to the culture and the sensitivity (Table 3 and Graph 2).

Regarding bone healing in cases of traumatic tibial fracture or bone defects due to tumor excision for an adequate safety margin, the results were nearly similar in both groups, that is rapid healing of fracture occurred in 8 (57.1%) cases in group A and another 8 (61.5%) cases in group B within 2 weeks after surgery as compared with the preoperative healing period (Table 4 and Graph 3). This was monitored by a serial radiography (Fig. 3). Finally, overall wound healing was noticed in 9 (64.3%) cases in group A and 12 (92.3%)

Table 2 Operative data

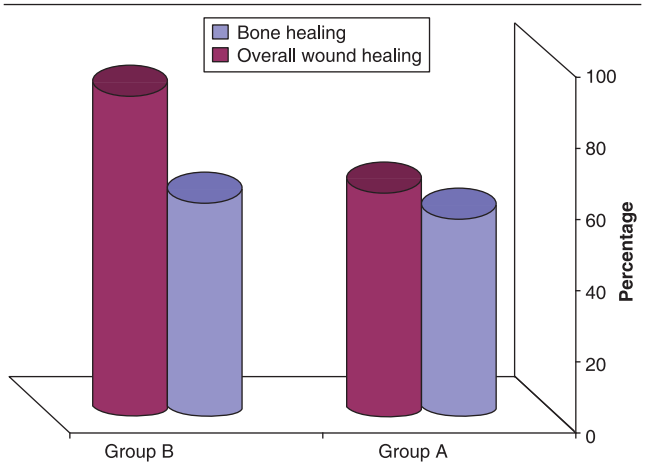
Operative time (h)	*N* (%)
Strata	
<1.5	11 (40.8)
1.5–2	9 (33.3)
2–3	7 (25.9)
Total	2 ± 0.9 (1.5–3)
Blood loss (ml)	540 ± 115 (400–900)
Replacement of red cells (U)	
Strata	
1	4 (14.8)
2	16 (59.3)
3	2 (7.4)
Total	1.8 ± 0.7 (1–3)

Data are presented as means ± SD and number; ranges and percentages are within parentheses.

Table 3 Inpatient complications

Inpatient complications	*N* (%)		*P*-value
	Group A; muscle flap (*N* = 14 cases)	Group B; myocutaneous flap (*N* = 13 cases)	
Partial loss of skin graft	5 (35.7)	1 (8)	0.022
Hematoma	6 (42.9)	2 (15.4)	0.036
Infection	4 (28.6)	1 (8)	0.028

Graph 3



Healing after 2 weeks

Table 4 Healing after 2 weeks

Healing after 2 weeks	*N* (%)		*P*-value
	Group A; muscle flap (*N* = 14 cases)	Group B; myocutaneous flap (*N* = 13 cases)	
Bone healing	8 (57.1)	8 (61.5)	0.11
Overall wound healing	9 (64.3)	12 (92.3)	0.14

cases in group B; regarding the functional outcome, no disability was recorded, with complete functions of the lower limb and minimal effect on the bulk of the cuff.

Discussion

Management of compound fractures of tibia Gustilo type III, with involvement of the knee joint, present a difficult problem to orthopedic and plastic surgeons. Reconstructive procedure is frequently required to cover the exposed bones or joints to obliterate the dead space and help eradicate infection [4].

Early cover has been found to reduce the incidence of complications [6]. The gastrocnemius muscle flap is the workhorse of all muscle flaps for soft tissue coverage around the knee [7].

The gastrocnemius muscle flap, described by Ger [13] as a muscle flap, is used in cases of exposed defects of the proximal tibia [14].

The lateral head of the muscle, compared with the medial, is used more rarely in reconstructive surgery [15]. The reasons for its restricted use are the size, the limited arc of rotation, and the potential risk of peroneal nerve palsy of the muscle, which might be caused by the surgical procedure itself. [16] The medial head of the gastrocnemius muscle, which is the part most often used, meets all requirements needed for a successful wound coverage [17].

This study was conducted to focus on the versatility of the superiorly based pedicled gastrocnemius muscle flap [group A: 14 (51.8%) patients] or the myocutaneous flap [group B: 13 (48.2%) patients], either medial or lateral head, in upper-leg defects after trauma or tumor excision; no intraoperative mortality was recorded, with a mean operative time of about 2 h and a blood loss of about 540 ± 115 ml. Throughout the first 2-week follow-up period; there was no flap loss apart from partial skin loss, minor hematomas, or infections. All were noticed significantly more in group A [5 (35.7%), 6 (42.9%), and 4 (28.6%) cases, respectively] compared with group B [1 (8%), 2 (15.4%), 1 (8%) cases, respectively; $P < 0.05$]. This finding concurs with that reported previously in the literature concerning the applicability of the gastrconemius myocutaneous flap for the reconstruction of upper-leg defects, irrespective the etiology of the defect. Han *et al.* [18] used the gastrconemius myocutaneous segment obtained by intramuscular dissection of the vascular pedicle for the reconstruction of composite and three-dimensional knee defects, and found that the flap survived completely, wound healing progressed smoothly without infection, hematoma or seroma, and patients were satisfied with their esthetic outcomes.

There are disadvantages associated with the application of the gastrconemius flap, such as deformation of the donor area, [18] but this study revealed that no major complications occurred in the donor areas apart from wound infection, which was controlled with appropriate antibiotic treatment. The advantages of the gastrocnemius flap favor its use as this surgical technique is relatively easy to perform and requires lesser time than free tissue transfers. Furthermore, the gastrocnemius flap provides better tissue coverage and greater stability to the knee joint.

Regarding bone healing in cases of traumatic tibial fracture or bone defects due to tumor excision for an adequate safety margin, the results were nearly similar in both groups, that is rapid healing of the fracture occurred in 8 (57.1%) cases in group A and another 8 (61.5%) cases in group B within 2 weeks after surgery as compared with the healing in the preoperative period. This was monitored by a serial radiography, and overall wound healing was noticed in 9 (64.3%) cases in group A and 12 (92.3%) cases in group B; regarding the functional outcome, no disability was recorded, with complete functions of the lower limb and minimal effect on the bulk of the cuff. This finding is supported by the study conducted by Liu *et al.* [19], who studied

65 patients who underwent resection of proximal tibial osteosarcoma and reconstruction of the bone defect by prosthesis: 35 cases underwent medial gastrconemius muscle flap transposition to reconstruct the soft tissues and the other 30 did not and reported a significantly lower rate of local complications, with a significantly higher functional outcome in the group with gastrconemius muscle flap transposition. Liu *et al*. [19] first explained that this good bone healing occurred because myogenic progenitors of the MyoD lineage contribute to bone repair, giving new perspectives for the treatment of fracture nonunion through the optimization of myogenic progenitor proliferation, migration, and differentiation. This eventually helps ensure a good safety margin in malignant tumor cases and helps bone healing in trauma cases.

Also, Park *et al*. [10] used an extended medial gastrconemius muscle flap including a tendinous portion of the Achilles and a saphenous neurocutaneous flap for coverage in a patient who had multiple fractures with open comminuted patellar fractures that were initially managed, but unfortunately, the fractured patella and the overlying soft tissue became totally infected with wide necrosis, requiring complete debridement of the dead tissue with removal of the patella and its tendon, leaving a large bone and a soft tissue defect on the knee joint; at 12 months postoperatively, he showed complete extension, 135° of flexion, and grade IV knee extensor power, and was able to ambulate without a walking aid.

These findings are also supported by numerous other studies conducted to isolate progenitor cells from muscles for the purpose of bone tissue engineering; these approaches often utilize ex-vivo gene therapy approaches, where the forced expression of osteogenic bone morphogenetic proteins in cultured myoblasts can lead to new bone formation after their subsequent implantation into experimental animals [20].

Hence, muscle flaps in bone fractures not only bring blood supply, but also give the fracture myokines and progenitor cells, which differentiate into osteocytes; this fact supports the concept that muscles act as a 'secondary periosteum', which is able to contribute osteoprogenitors when the periosteum itself is damaged [21].

Conclusion

We conclude that both gastrocnemius myocutaneous and myocutaneous flaps for upper-leg reconstruction are considered as a reliable option to ensure a good safety margin in malignant tumor cases and to help bone healing in trauma cases; myocutaneous flaps are safer, with no redo and lesser postoperative complications.

Acknowledgements

Conflicts of interest

None declared.

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Cyclo-oxygenase-2 and vascular endothelial growth factor expression in colorectal cancer patients

Mohammed S. Hedaya[a], Ahmed Hazem Helmy[a], Houssin Ezzat[a], Olfat Hammam[b]

[a]Departments of General Surgery, [b]Pathology, Theodore Bilharz Research Institute, Giza, Egypt

Correspondence to Mohammed S. Hedaya, MD, Department of General Surgery, Theodore Bilharz Research Institute, Giza 11571, Egypt
e-mail: hedayamoh@yahoo.com

Received 23 September 2014
Accepted 03 October 2014

The Egyptian Journal of Surgery
2015, 34:35–40

Introduction
Colonic neoplastic lesions represent a common health problem in Egypt. Colorectal carcinoma (CRC) is one of the common malignancies among Egyptians. There is considerable interest in the involvement of cyclooxygenase-2 (COX-2) in colon carcinogenesis and its progression. Vascular endothelial growth factor (VEGF) is a well-characterized tumor angiogenesis factor which has a role in the development, progression and risk of metastases of CRC
The aim of the present study was to explore the correlation between COX-2 and VEGF colon tissue expression profile in colorectal cancer patients with a special emphasis on clinicopathological features.
Patients and methods
This study was carried out on 40 patients with colorectal cancer (CRC). CT and Colonoscopy were mandatory for staging and grading. CRC classification, grading and staging was done following the American Joint Committee on Cancer (AJCC) staging system.
Results
Contralateral site control biopsies were totally negative for both biomarkers in the CRC patients. COX-2 & VEGF were over expresed intensly in the advanced stage and grade of the postive expression in the CRC samples obtaind during surgery.
Conclusion
The over-expression of COX-2 and VEGF in colorectal cancer suggests the role of both of them as a risk biomarker particularly in patients with advanced stage and grade.

Keywords:
colorectal carcinoma, cyclo-oxygenase-2, vascular endothelial growth factor

Egyptian J Surgery 34:35–40

1110-1121

Introduction

There is considerable interest in the involvement of cyclo-oxygenase-2 (COX-2) in colon carcinogenesis and its progression. This was initiated by clinical observations in which patients who had taken NSAIDs were associated with a 30–50% reduction in colorectal cancer (CRC) risk [1,2]. COX-2, which leads to the synthesis of prostaglandins, is one of the known targets of NSAIDs and it has been reported that tumor cells overexpressing COX-2 stimulate angiogenesis, inhibit apoptosis, and increase the metastatic potential by producing prostaglandins in colon cancer cell lines [3,4].

Although NSAIDs act through COX-2 to inhibit colon cancer growth, there also appears to be COX-2-independent actions for NSAIDs. COX-2 selective inhibitors can be the core drugs for the prevention and treatment of colon cancer [5,6].

The vascular endothelial growth factor (VEGF) expression in colon cancer tissues has not been clearly studied.

VEGF is a well-characterized tumor angiogenesis factor that has a role in the development and progression of CRC and in its risk for metastases [7].

The aim of the present study was to explore the correlation between COX-2 and VEGF colon tissue expression profile in CRC patients with special emphasis on clinicopathological features.

Patients and methods

This study was carried out on 40 patients with CRC at the Theodor Bilharze research Institute after obtaining the approval of IRB. All patients were subjected to history taking and clinical examination. Computed tomography and colonoscopy were mandatory for staging and grading. During colonoscopy two biopsies were obtained from each patient: one from the lesion for diagnosis and the other from the contralateral normal side to serve as a control. All patients were subjected to elective hemicolectomy according to the site and extent of the lesion. All biopsies and surgical specimens were investigated with immunohistochemical analysis for anti-COX-2 and anti-VEGF. Serial sections were

 DOI: 10.4103/1110-1121.153369

cut from paraffin blocks and stained with hematoxylin and eosin for routine histological examination. CRC classification, grading, and staging were carried out following the American Joint Committee on Cancer AJCC staging system.

Immunohistochemical procedures

Four-micrometer-thick tissue sections were cut from the paraffin blocks (containing both tumor and benign tissues), mounted on charged poly-l-lysine-coated slides, and subjected to immunohistochemical analysis using the avidin–biotin detection system, following the manufacturer's instructions. The antibody used was a mouse anti-human COX-2 monoclonal antibody (Dako Cytomation Norden A/S, Glostrup, Denmark; dilution 1: 50). Immunohistochemical analysis was carried out using an automatic immunostainer (Ventana Bench Mark XT; Ventana Inc., Tucson, Arizona, USA). In each analysis, positive controls consisting of CRC samples previously shown to stain with this antibody were used. Tris-buffered saline in place of the primary antibody was used as a negative control.

Interpretation of immunohistochemical staining

Cells were considered positive for COX-2 when distinct yellow to brown staining was identified in the cytoplasm and occasionally in the nuclear envelope. The extent and intensity of the staining were recorded on a scale from 0 to +++; +++ implied strong staining that was maximally intense throughout the specimen, and 0 implied negative staining. When dichotomized for statistical risk assessment (odds ratio), negative (–) and weak (+) staining was defined as low expression, whereas moderate (++) and intense (+++) staining was included in the high expression category.

Statistical analysis

Continuous variables are expressed as number and percentage. Statistical comparisons were made with the Pearson χ^2-test. Statistical significance was defined by a P value less than 0.05.

Results

The mean age of the patients was 52 years (range: 24–69 years). The associations between COX-2 and VEGF expression and clinicopathological features showed no significant differences with respect to sex, age, or tumor location. There were 22 male patients and 18 female patients; 26 patients were older than 50 years and 14 patients were younger than 50 years; and 11 patients had tumor located on the right side and 29 patients had tumor on the left side.

Clinical data of the patients with CRC, whose tissue samples were used in this study, are summarized in Table 1.

The COX-2 immunoexpression in epithelial cells and specimens is shown in Table 2. All control biopsies were negative for COX-2 expression (100%). Positive COX-2 immunoexpression showed significant increase in all surgical specimens compared with control biopsies (Figs. 1 and 2). An overall 67.5% of patients showed marked COX-2 immunoexpression with statistically significant difference ($P < 0.01$) from the rest of the patients, who showed moderate COX-2 immunoexpression (32.5%) (Table 2).

VEGF-positive immunoreactivity was detected as diffuse cytoplasmic brownish color within the epithelial cells. All control biopsies were negative for VEGF immunoreactivity. The extent of VEGF expression among the cases is shown in Table 2. CRC samples showed a higher percentage of positive cases for VEGF compared with control biopsies ($P < 0.01$) (Figs. 3 and 4).

As regards the intensity of COX-2 immunoexpression, 21 samples (75%) presented with strong COX-2 intensity, which was statistically significantly different from seven (25%) samples that presented with moderate intensity and none (0%) with mild intensity ($P < 0.01$ and $P < 0.01$, respectively). The number of samples with strong intensity (75%) was statistically significantly higher compared with controls ($P < 0.01$) (Figs 1 and 2). However, 75% of cases in the CRC group were intensely positive for VEGF, and the rest of the cases were mildly positive for VEGF (25%) with no statistically significant difference between them (Table 3).

However, tumor stage and distant metastasis were significantly associated with COX-2 expression, with

Table 1 Clinical data of the patients with colorectal cancer

Variables	Patients
Number	40
Men/women	22/18
Mean age (range) (years)	52 (24–69)
Tumor localization[a]	
Left colon	11
Right colon	29
Tumor stage (Dukes)	
A	5
B	15
C	20
Differentiation grade	
Well	6
Moderate	24
Poor	10

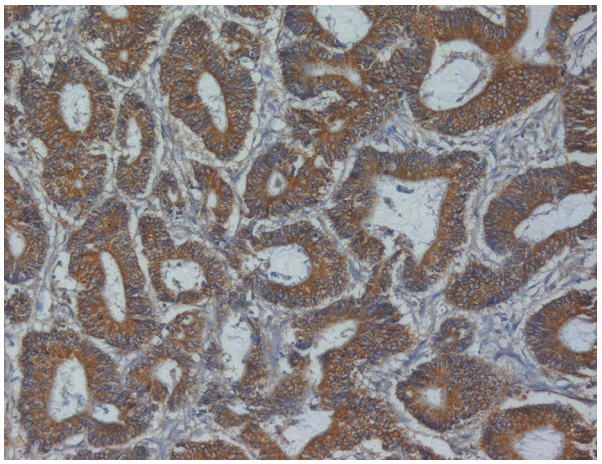
[a]Left-sided colon: descending colon, rectum and sigmoid; right-sided colon: cecum, ascending and transverse colon.

Table 2 COX-2 and VEGF immunoexpression in epithelial cells in both control and colorectal cancer patients

Pathological diagnosis	Range of COX-2[b] staining [*n* (%)]		Range of VEGF[c] staining [*n* (%)]	
	51–75 (%)	76–100 (%)	<10 (%)	>10 (%)
Control (*n* = 40)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CRC (*n* = 40)COX-2-positive cases 28/70%[a]VEGF-positivecases 30/75%[a]	11 (32.5)*	17 (67.5)*	10 (25)	30 (75)**

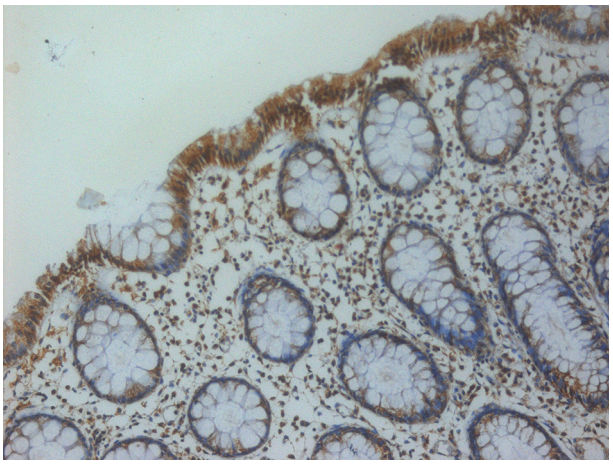
COX-2, cyclo-oxygenase-2; CRC, colorectal cancer; VEGF, vascular endothelial growth factor. [b]Range of COX-2 staining 1–25% and 26–50% equal zero for all control biopsies and CRC samples. [c]Range of VEGF<10% is considered negative for all control biopsies and CRC samples. [a]$P < 0.01$ compared with the control group, Pearson χ^2. *$P < 0.01$ compared with 26–50%, 51–75% expression respectively in the same group, Pearson χ^2. **$P < 0.01$ compared with the control group, Pearson χ^2.

Figure 1



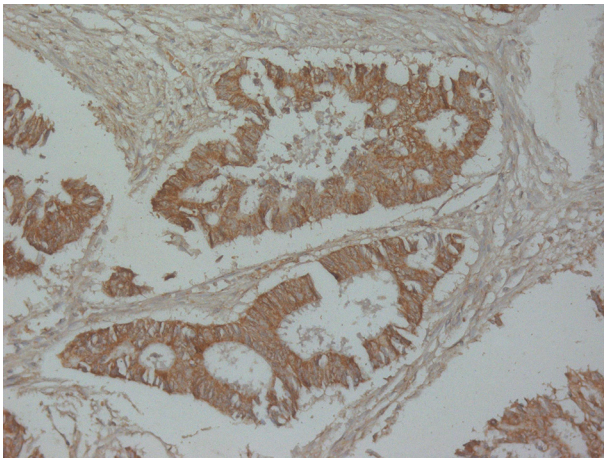
Colonic adenocarcinoma sample positive for COX-2 (IHC ×200). COX-2, cyclo-oxygenase-2.

Figure 2



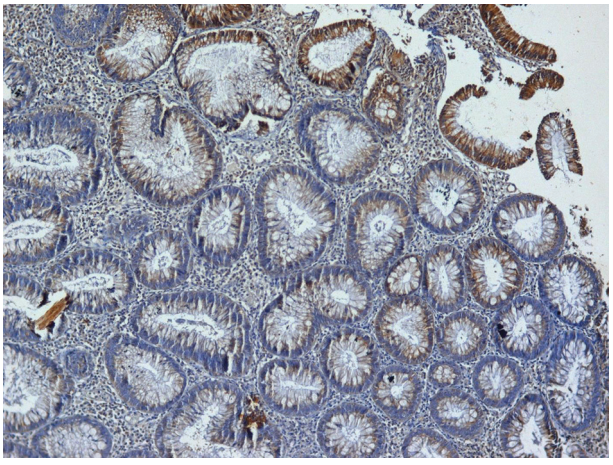
Control colonic Bx negative for COX-2 (IHC ×200). COX-2, cyclo-oxygenase-2.

Figure 3



Colonic adenocarcinoma sample positive for VEGF (IHC ×200). VEGF, vascular endothelial growth factor.

Figure 4



Control colonic Bx negative for VEGF (IHC ×200). VEGF, vascular endothelial growth factor.

higher expression being more common in advanced tumors. The percentage of Dukes C patients with positive immunoreactivity for COX-2 was statistically significantly higher compared with patients of Dukes A ($P < 0.01$) and Dukes B ($P < 0.01$). All patients with Dukes A showed moderate COX-2 immunoexpression (100%). An overall 71.4% of Dukes B patients had intense COX-2 immunoexpression, 28.6% had moderate COX-2 immunoexpression, and none (0%) had mild COX-2 expression. The results were statistically significantly different ($P < 0.01$). All patients with Dukes C showed intense COX-2 immunoexpression (100%) (Table 4).

The percentage of Dukes C patients positive for VEGF was statistically significantly higher

compared with Dukes A patients ($P < 0.01$). The percentage of Dukes B patients positive for VEGF was also statistically significantly higher compared with Dukes A patients ($P < 0.05$). All positive patients with Dukes A showed moderate VEGF immunoexpression (100%). All positive patients with Dukes B showed moderate VEGF immunoexpression (100%). All positive patients with Dukes C showed intense VEGF immunoexpression (100%) (Table 4).

Patients with poorly differentiated adenocarcinoma (GIII) showed significant increase in positive COX-2 immunoexpression compared with patients with well-differentiated adenocarcinoma (GI) and moderately differentiated adenocarcinoma (GII) ($P < 0.01$ and $P < 0.01$, respectively). Patients with moderately differentiated adenocarcinoma (GII) showed significant increase in positive COX-2 immunoexpression compared with patients with well-differentiated adenocarcinoma (GI) ($P < 0.01$). An overall 66.7% of patients with well-differentiated adenocarcinoma (GI) showed moderate COX-2 immunoexpression compared with the rest of the patients with intense COX-2 immunoexpression (33.3%), with statistically significant difference between them ($P < 0.01$). All patients (100%) with poorly differentiated adenocarcinoma (GIII) showed intense COX-2 immunoexpression (Table 5).

Three of six patients with well-differentiated adenocarcinoma (GI) were positive for VEGF immunoexpression (50%), 17 of 24 patients with moderately differentiated adenocarcinoma (GII) were positive for VEGF immunoexpression (70.8%), and 10 of 10 patients with poorly differentiated adenocarcinoma (GIII) were positive for VEGF immunoexpression (100%).

Table 3 Intensity of COX-2 and VEGF immunoexpression in epithelial cells in positive CRC patients

Pathological diagnosis	Intensity of COX-2 staining [*n* (%)]		Intensity of VEGF staining [*n* (%)]	
	(++) Moderate	(+++) Strong	(++) Moderate	(+++) Strong
Control ($n = 40$)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CRC ($n = 40$) COX-2-positive cases 28/70% [a]VEGF-positive cases 30/75%a	7 (25)	21 (75)*	10 (33.3)	20 (66.7)

(+) Mild intensity of COX-2 and VEGF staining equal to zero for all control biopsies and CRC samples. COX-2, cyclo-oxygenase-2; CRC, colorectal cancer; VEGF, vascular endothelial growth factor; [a]$P < 0.01$ compared with the control group, Pearson χ^2. *$P < 0.01$ compared with the control group, Pearson χ^2.

Table 4 COX-2 and VEGF immunoexpression intensity in positive CRC patients in correlation with Dukes stage

Stages of adenocarcinoma	Range of COX-2[d] staining [*n* (%)]		Range of VEGF[e] staining [*n* (%)]
	51–75 (%)	76–100 (%)	>10
Duke A (5) COX-2-positive cases 1/20%VEGF-positive cases 1/20%	1 (100)	0 (0.0)*	1 (20)*
Duke B (15) COX-2-positive cases 7/43.3% [c]VEGF-positive cases 9/60%[c]	2 (28.6)	5 (71.4)*	9 (60)*
Duke C (20) COX-2-positive cases 20/100% [a,b]VEGF-positive cases 20/100%[a,b]	0 (0.0)	20 (100)*	20 (100)*

COX-2, cyclo-oxygenase-2; CRC, colorectal cancer; VEGF, vascular endothelial growth factor; [d]Range of COX-2 staining 1–25% and 26–50% equal zero for all control biopsies and CRC samples. [e]Range of VEGF <10% is considered negative for all control biopsies and CRC samples. [a,b]$P < 0.01$ compared with Dukes stage A, B, Pearson χ^2. [c]$P < 0.01$ compared with Dukes stage A, Pearson χ^2. *$P < 0.01$ compared with 51–75% COX-2 expression in the same group, Pearson χ^2. *$P < 0.01$ compared with <10% VEGF expression in the same group, Pearson χ^2.

Table 5 Immunoexpression intensity of COX-2 and VEGF in positive CRC cases in relation to their pathological grades

Histopathological grade of adenocarcinoma	Range of COX-2[d] staining [*n* (%)]		Range of VEGF[e] staining [*n* (%)]
	51–75 (%)	76–100 (%)	51–75 (%)
Well-differentiated GI ($n = 6$) COX-2-positive cases 3/50%VEGF-positive cases 3/50%	2 (66.7)	1 (33.3)*	3 (50)
Moderately differentiated GII ($n = 24$) COX-2-positive cases 15/62.5%[c]VEGF-positive cases 17/70.8%[c]	5 (33.3)	10 (66.6)*	17 (70.8)
Poorly differentiated GIII ($n = 10$) COX-2-positive cases 10/100%[a,b]VEGF-positive cases 10/100%[a,b]	0 (0.0)	10 (100)*	10 (100)

COX-2, cyclo-oxygenase-2; CRC, colorectal cancer; VEGF, vascular endothelial growth factor; [d]Range of COX-2 staining 1–25% and 26–50% equal zero for all control biopsies and CRC samples. [e]Range of VEGF <10% is considered negative for all control biopsies and CRC samples. [a,b]$P < 0.01$ compared with GI and GII, respectively, Pearson χ^2. [c]$P < 0.01$ compared with GI, Pearson χ^2. *$P < 0.01$ compared with 51–75% COX-2 expression in the same group, Pearson χ^2.

The percentage of poorly differentiated CRC patients with positive VEGF immunoexpression was statistically significantly higher compared with well-differentiated patients ($P < 0.01$). The percentage of moderately differentiated CRC patients with positive VEGF immunoexpression was also statistically significantly higher compared with well-differentiated patients ($P < 0.05$).

All positive cases of well-differentiated adenocarcinoma showed moderate VEGF immunoexpression. All positive cases of moderately and poorly differentiated adenocarcinoma showed intense VEGF immunoexpression (Table 5).

Discussion

Colonic neoplastic lesions represent a common health problem in Egypt. Colorectal carcinoma is one of the most common malignancies among Egyptians. Studies have shown that CRC patients under 30 years of age represent more than 20% of the total CRC patients [8,9].

COX-2 is an enzyme involved in the conversion of arachidonic acid to prostaglandins H2, the precursor of other prostaglandins and thromboxanes. These compounds are pivotal in the regulation of cell proliferation, angiogenesis, and the response of the human immune system to malignant tumor cells [10,11].

An important aspect in the measurement of COX-2 and VEGF expression is standardization. Standardization against control from the same patient will yield more accurate results compared with the use of a separate control group. To achieve this we obtained control biopsies from the healthy contralateral side during colonoscopy instead of from the safety margin area in the obtained pathological samples. In our study, all control biopsies with completely normal mucosa were negative for COX-2 immunoexpression, which was in agreement with previous studies [12].

We found that 70% of cases with CRC specimens were positive for COX-2 immunoexpression. This is in agreement with a study conducted by Joo *et al.* [13], which found that 62.6% of CRC patients exhibited markedly more intense positive COX-2 immunostaining compared with control colon cells.

In addition, this study showed that only 28 patients of the CRC group were positive for COX-2; and 10.7% were well-differentiated (GI), 53.5% were moderately differentiated (GII), and 35.8% were poorly differentiated (GIII). Among CRC patients with COX-2-positive immunoreactivity, 3.5% were in Dukes stage A, 25% were in Dukes stage B, and 71.5% were in Dukes stage C. These findings were in agreement with those of Sheehan and colleagues, who demonstrated that the extent of COX-2 expression in colorectal tumor epithelial cells is related to survival. He also showed a relationship between COX-2 staining and advancing Dukes tumor stage; his explanation was that colon cancer cells expressing COX-2 are more invasive, possibly because of the enhanced expression of metalloproteinase-2 [14].

The role of angiogenesis in the development and progression of human cancers has been widely studied. However, a more complete knowledge of this phenomenon is obviously required. As angiogenesis is associated with a higher risk for metastases in various types of cancer, we are interested in understanding the genetic regulation of the angiogenesis process. VEGF is a well-characterized angiogenesis factor and is known to play a crucial role in tumor angiogenesis. Moreover, a relationship between VEGF and tumor progression has recently been reported in different kinds of human cancers, including colon cancer [15,16].

In our study, 30 of 40 patients (75%) with CRC showed intense VEGF immunoexpression in the cell membrane and adjacent cytoplasm of the malignant epithelial cells. This is in agreement with a study conducted by Ochs *et al.* [17], in which 72 of 109 CRC patients (66%) were positive for VEGF immunoexpression.

In our study, 10% of CRC patients positive for VEGF had well-differentiated adenocarcinoma (GI), 56.7% of CRC patients positive for VEGF had moderately differentiated adenocarcinoma (GII), and 33.3% of CRC patients positive for VEGF had poorly differentiated adenocarcinoma (GIII). In CRC patients with VEGF immunoreactivity, 3.3% were in Dukes stage A, 30% were in Dukes stage B, and 66.7% were in Dukes stage C. These findings are in agreement with those of others, in which VEGF expression correlated significantly with stage and grade [18,19].

Conclusion

COX-2 and VEGF expression seems to provide useful prognostic information in patients with CRC. The overexpression of COX-2 and VEGF in CRC suggests the role of both as a risk biomarker particularly in patients with advanced stage and grade. Attention should be focused on these biomarker inhibitors as potential promising chemopreventive drugs against CRC.

Acknowledgements

Conflicts of interest

None declared.

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Laparoscopic sleeve gastrectomy versus laparoscopic gastric greater curvature plication: a prospective randomized comparative study

Mohamed M. Abouzeid[a], Osama Taha[b]

[a]Department of General Surgery, Ain Shams University, Cairo, [b]Department of Plastic Surgery, Assiut University, Assiut, Egypt

Correspondence to Mohamed M. Abouzeid, MD, MRCS, 64 Nakla El Motaee St, Heliopolis, Cairo, 11736, Egypt
Tel: +20 100 662 9170/+20 111 228 8844;
e-mail: abouzeid2000@hotmail.com

Received 26 September 2014
Accepted 08 October 2014

The Egyptian Journal of Surgery
2015, 34:41–47

Background
Laparoscopic sleeve gastrectomy (LSG) involves resection of a significant portion of the stomach. Laparoscopic greater curvature plication (LGCP) is a relatively new alternative procedure similar to LSG, but without the need for gastric resection.

Patients and methods
Fifty patients fulfilled the National Institutes of Health criteria and were assigned randomly to receive either LGCP ($n = 25$) [16 women and nine men; mean age 32.1 years (19–49 years) and mean BMI 47.8 kg/m^2 (42–57 kg/m^2)] or LSG ($n = 25$) [18 women and seven men; mean age 34.8 years (18–58 years) and mean BMI 46.8 kg/m^2 (41–55 kg/m^2)] by a block randomization method. Patients were studied in terms of postoperative weight loss, changes in hypertension, HbA1c, and postoperative complications.

Results
All procedures were completed laparoscopically. Follow-up was 24 months. The mean hospital stay was 36 h (range 24–144 h) for both groups. No intraoperative complications occurred. Postoperatively, one case of minor leak was detected after LSG and two cases of stenosis following LGCP. All patients experienced postoperative excess weight loss and improvement in HbA1c. The improvement was significantly better in the LSG group in terms of the change in BMI (mean 14.45 compared with 10.35 in LGCP) and change in HbA1c (mean 1.2 compared with 0.5 in LGCP); the change in hypertension was not statistically significant.

Conclusion
LGCP is feasible, safe, and effective, but has an inferior weight-loss effect and is less effective in diabetes compared to LSG for morbidly obese patients with BMI above 40 kg/m^2.

Keywords:
greater curvature placation, laparoscopic bariatric surgery, laparoscopic sleeve gastrectomy, morbid obesity, restrictive procedure

Egyptian J Surgery 34:41–47

1110-1121

Introduction

Obesity is a major health problem affecting over 1.7 billion individuals worldwide, and although it was considered a disease of the western world, it seems to have expanded to the developing world, especially in urban settings [1]. Since 1997, the WHO has recognized it as a global epidemic, and in 2005, over 400 million obese adults were recorded. Conservative measures, such as dieting and physical exercise, have proven inadequate, as has treatment with medications [2]. There is considerable evidence in the literature on the long-term positive impact of bariatric surgery as a primary therapy for the treatment of obesity and its comorbidities. Significant debate remains as to which patients are optimal candidates for which procedures [3]. Traditionally, the primary mechanisms through which bariatric surgery achieves its outcomes are believed to be the mechanical restriction of food intake, reduction in the absorption of ingested foods, or a combination of both [4]. Adjustable gastric banding and vertical sleeve gastrectomy (VSG) are restrictive approaches used commonly in bariatric practice. Although these procedures have proven to be good therapeutic options for some patients, they are not without significant complications, such as erosion or slippage of the gastric band or gastric leaks in VSG. Leaks in VSG pose a particularly difficult challenge when they occur near the angle of His, potentially generating severe clinical conditions that require reoperation, and may even cause death [5,6]. Laparoscopic sleeve (VSG) gastrectomy was first described in 1999 as part of the biliopancreatic diversion duodenal switch procedure [7]. Subsequently, laparoscopic sleeve gastrectomy (LSG) has been performed as a stand-alone procedure [8].

Laparoscopic greater curvature plication (LGCP) is a new restrictive technique that was first reported by Wilkinson in 1981 [9]. It reduces the gastric volume successfully by plication of the greater curvature and has the advantage of a reversible restrictive procedure without the use of foreign materials or gastrectomy.

 DOI: 10.4103/1110-1121.153370

The aim of the present study was to investigate LGCP, which is a new restrictive bariatric surgical technique in comparison with the more performed LSG in terms of postoperative weight loss, changes in hypertension and HbA1c, and postoperative complications.

Patients and methods

The study was carried out in Ain Shams University hospitals and Assiut University hospitals under the supervision of the authors following the same protocol in the period from August 2011 to January 2014. All patients provided signed informed consent and the study was approved by the hospital's ethics committee.

Fifty patients fulfilled the National Institutes of Health criteria [10] and were assigned randomly to receive either LGCP ($n = 25$) or LSG ($n = 25$) by a block randomization method. Patients with BMI more than 60 kg/m^2 were not encouraged to participate in the study. This study was carried out on 25 patients who underwent LSG [18 women and seven men, mean age 34.8 years (18–58 years) and mean BMI 46.8 kg/m^2 (41 kg/m^{2}55)], and 25 patients who underwent LGCP [16 women and nine men, mean age 32.1 years (19–49 years) and mean BMI 47.8 kg/m^2 (42–57 kg/m^2)]. The two groups were studied in terms of postoperative weight loss, changes in hypertension and HbA1c, and postoperative complications. Follow-up was 24 months (Table 1).

All patients underwent a multidisciplinary evaluation (endocrinologist, cardiologist, psychologist, and nutritionist). Blood tests, abdominal ultrasonography, and upper endoscopy were performed preoperatively to establish a baseline.

All surgical procedures were performed under general anesthesia with the patient in a supine position. Prophylactic intravenous antibiotics and subcutaneous heparin were administered before induction of anesthesia. Closed pneumoperitoneum was achieved using a five-trocar port technique similar to that used in laparoscopic Nissen fundoplication.

Operative technique of laparoscopic sleeve gastrectomy

Trocar placement was as follows: one 12-mm optical trocar above and slightly to the left of the umbilicus for the 30° laparoscope; one 12 mm on the upper right quadrant for the surgeon's left hand and one 15 mm trocars for the surgeon's right hand were placed 5 cm subcostally; one 5- or 10-mm trocar on the upper left quadrant (ULQ) anterior axillary line 3–4 cm subcostally for the surgeon's assistant; and one 10-mm wound below the xiphoid appendices for liver retraction (Fig. 1).

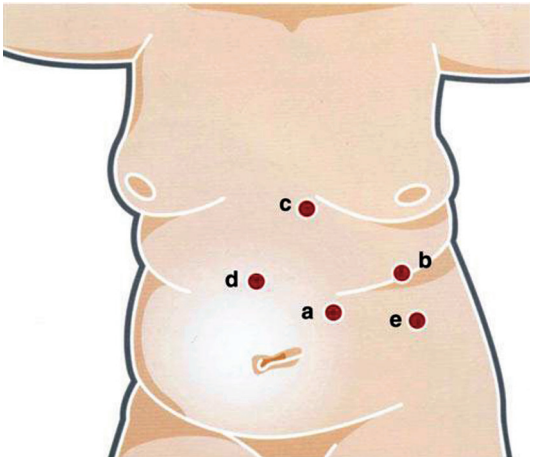
The procedure began with the dissection of the angle of His, followed by careful dissection of the gastric greater curvature using the Harmonic scalpel (Ethicon Endo-Surgery Inc., Cincinnati, Ohio, USA) or the LigaSure Vessel Ligation System (Covidien, USA). Starting from the antrum 7 cm from the pylorus toward the left crus of the diaphragm and the angle of His, the omentum and the gastroepiploic vessels were dissected away from the greater curvature, followed by the short gastric vessels, the posterior gastric vein, and the posterior gastric attachments. The left side of the crus was prepared carefully, preserving the fat pad (Fig. 2).

Then, a 36 Fr bougie was passed into the stomach with its tip positioned in the pylorus. The bougie was used to calibrate the size of the sleeve. The stomach was first transected tangentially from the greater curve toward the lesser curve using a Endo GIA™ stapler 7 cm proximal to the pylorus. Once the bougie was reached, all subsequent stapler firings were cephalad, parallel to the bougie (Fig. 3), until the angle of His was identified and transected. The specimen was then

Table 1 Comparison between two the study groups in personal data

Personal data	LPSG [*N* (%)]	LGP [*N* (%)]	*P*	Significance
Sex				
Male	7 (28.0)	9 (36.0)	0.544	NS
Female	18 (72.0)	16 (64.0)		
Age				
Mean ± SD	34.8 ± 11.3	32.1 ± 8.8	0.348	NS
Range	18–58	19–49		

Figure 1



Trocar position. a, 12 mm above the umbilicus slightly to the left; b, 15 mm in upper left quadrant (ULQ); c, 10 mm wound below xiphoid; d, 12 mm in the upper right quadrant (URQ); e, 5 or 10 mm on the ULQ at the anterior axillary line.

extracted through the 15-mm port site. Finally, we leak tested the entire staple line using methylene blue. Intra-abdominal drain was inserted and removed 24 h postoperatively; patients were discharged as soon as they could consume a liquid diet and could tolerate pain, provided they were vitally stable, and received a prescription of a daily proton-pump inhibitor for 90 days. During the first 6 postoperative months, all patients were treated with multivitamins.

The postoperative diet was prescribed as follows: a customized liquid diet for 10 days, followed by a progressive return to solid foods in a stepwise manner, with the dietary restrictions removed at 4–6 weeks, depending on patient acceptance. Follow-up visits for the assessment of safety and weight loss were scheduled for 1 week and at 1, 3, 6, 12, 18, and 24 months in the postoperative period, with assessment of hemoglobin, liver enzymes, serum creatinine, iron, vitamin B_{12}, and calcium blood levels. Upper endoscopy was performed optionally.

Plication surgical procedure

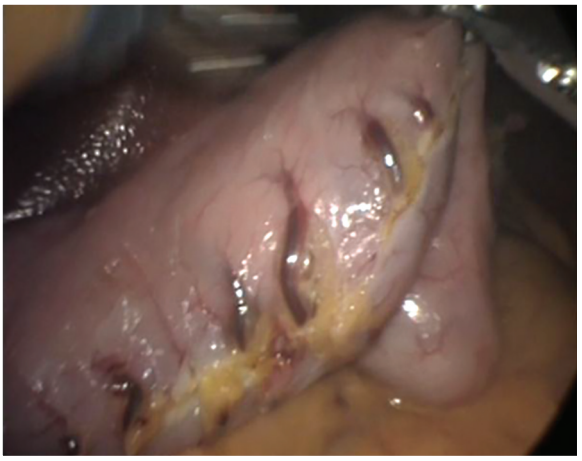
Trocar placement was as follows: one 12-mm optical trocar above and slightly to the left of the umbilicus for the 30° laparoscope; one 12-mm trocar in the ULQ for passing the needle, for suturing, and for the surgeon's right hand; one 5-mm trocar also in the ULQ at the anterior axillary line for the surgeon's assistant; one 10-mm wound below the xiphoid appendices for liver retraction; and one 5-mm trocar in the URQ for the surgeon's left hand (Fig. 4).

We followed the same steps for dissection of the greater curve as in sleeve gastrectomy, also beginning 7 cm proximal to the pylorus till the angle of His. Posterior gastric adhesions were also dissected to allow optimal freedom to create and size the invagination properly.

The next step was to initiate gastric plication by invaginating the greater curvature over a 36 Fr bougie and applying a first row of extramucosal continuous stitches of nonabsorbable sutures 2-0 Ethibond (Ethicon Inc., Somerville, New Jersey, USA) or 2-0 Prolene (Ethicon Inc.). This row guided a subsequent row created with extramucosal running suture lines. The reduction resulted in a stomach shaped like a large sleeve gastrectomy (Figs. 5–8).

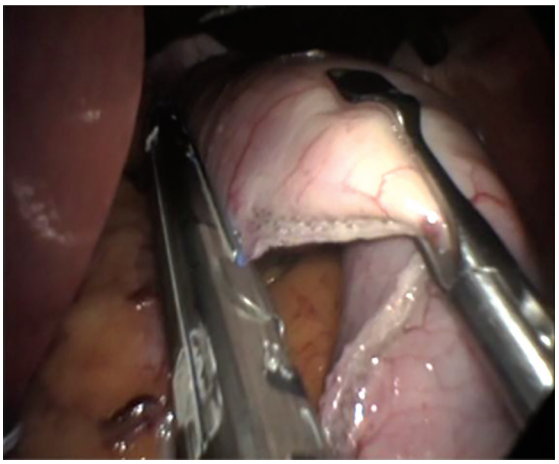
Leak tests were performed with methylene blue in all cases, which was injected under pressure to ensure that there was no out-pouching in the plicated stomach. No drains were placed. On the first postoperative day, nausea, vomiting, and sialorreia were reported by all patients; these symptoms resolved on treatment with ondasetron and the anti spasmodic hyoscine. The rest

Figure 2



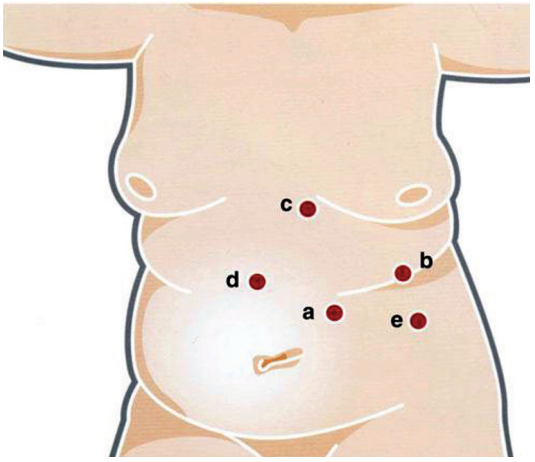
Dissected greater curve and bougie introduction.

Figure 3



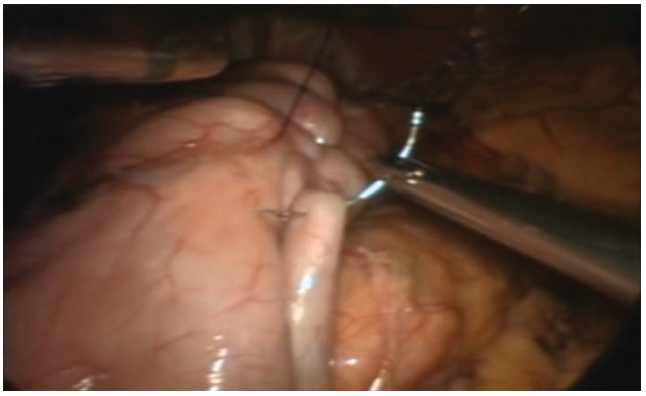
Dividing the stomach parallel to the bougie.

Figure 4



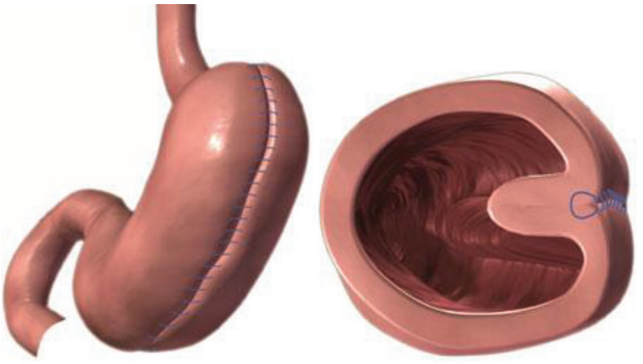
Trocar position. a, 12 mm above the umbilicus slightly to the left; b, 12 mm in upper left quadrant (ULQ); c, 10 mm below xiphoid; d, 5 mm in the URQ; e, 5 mm on the ULQ at the axillary line.

Figure 5



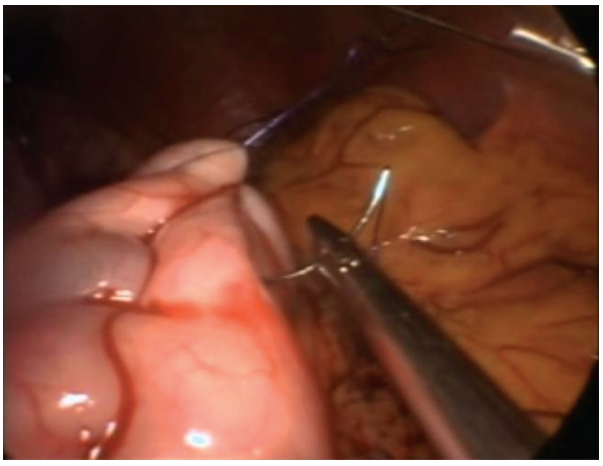
First row of extramucosal continuous stitches of nonabsorbable sutures.

Figure 6



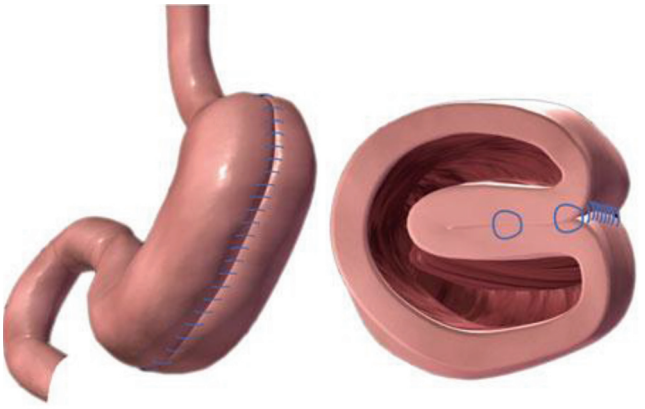
Computerized drawing of the initial fold generated by first initial suture line.

Figure 7



Intraoperative pictures of the final suture line with running nonabsorbable suture.

Figure 8



Computerized drawing of the final aspect of laparoscopic greater curvature plication procedure.

of the postoperative follow-up protocol was the same as for sleeve gastrectomy.

Results

All procedures were completed laparoscopically. Follow-up was 24 months. There was no statistically significant difference in hospital stay for LSG and for LGCP and the mean length was 36 h (range 24–144 h) for both groups. The mean operative time was 44 min (32–70 min) for LSG and 48 min (36–68 min) for LGCP, with no statistically significant difference between both. Postoperatively, one patient developed a minor leak after sleeve gastrectomy treated by endoscopic stenting and two patients developed stenosis following gastric placation; the first patient was treated by a second look after 3 days and removal of the second row of stitches at the stenotic area and the second patient presented after 2 months from the surgery and was treated by endoscopic dilatation (Fig. 9 and Table 2).

Table 2 Comparison between two the study groups in terms of postoperative leak and stenosis

Complication	LSG [*N* (%)]	LGCP [*N* (%)]	*P*	Significance
Leak				
Yes	1 (4.0)	0 (0.0)	1.00*	NS
No	24 (96.0)	25 (100.0)		
Stenosis				
Yes	0 (0.0)	2 (8.0)	0.490*	NS
No	25 (100.0)	23 (92.0)		

LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy; *X2 test.

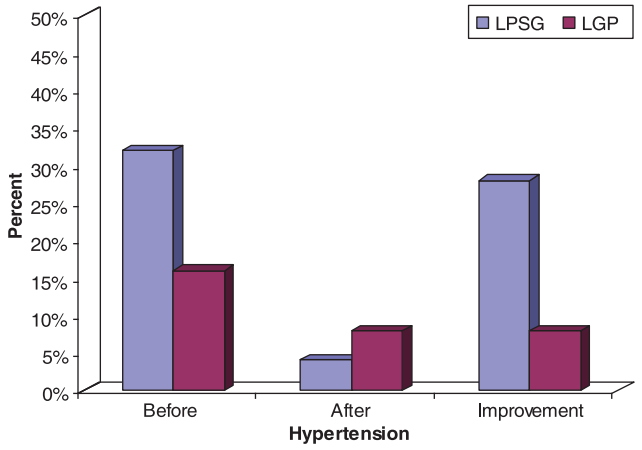
In terms of hypertension, there were no statistically significant changes in both groups, attributable to the small number of hypertensive patients in each group, but in the hypertensive group, seven out of eight patients (87.5%) improved after LSG whereas two out of four (50%) patients improved after LGCP (Fig. 10 and Table 3).

All patients experienced postoperative excess weight loss and improvement in HbA1c, but the improvement was significantly better for sleeve gastrectomy in terms of the change in BMI (mean 14.45 compared with 10.35 in gastric plication) and change in HbA1c (mean 1.2 compared with 0.5 in gastric placation). No weight regain in any patient was recorded until the end of the study (Figs. 11–13 and Tables 4–8).

Discussion

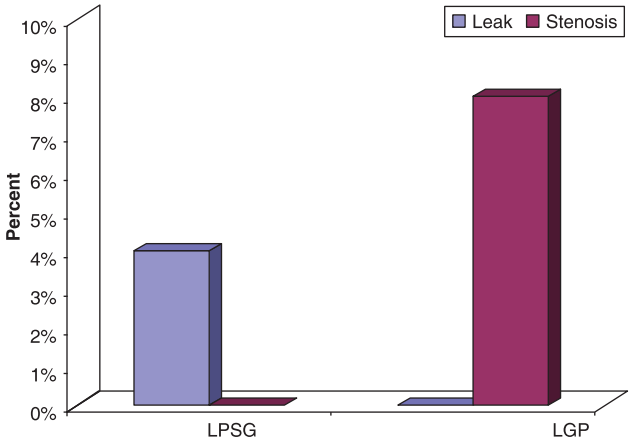
LSG is a procedure used initially as the first stage of a definitive bariatric treatment known as the duodenal switch [11]. Vertical gastrectomy of the greater curvature is performed, resulting in a tubular stomach with the purpose of restricting food intake. As a primary bariatric procedure, medium-term results have been shown to be adequate (>60% exsess weight loss (EWL)), with improvements in comorbidities such as type 2 diabetes mellitus, hypertension, and obstructive sleep apnea in more than 65% of cases [12]. These promising results are associated with some complications, however, such as esophagitis, stenosis, fistulas, and gastric leaks near the angle of His. These leaks and fistulas are reported in nearly 1% of cases [6,13]. LGCP is notably similar to a LSG in that it generates a gastric tube by means of eliminating the greater curvature, but does so without gastric resection. It is likely that LGCP considerably reduces the possibility for gastric leaks. Talebpour and Amoli [14] reported one case of a gastric leak associated with a more aggressive version of LGCP, which the authors attributed to excessive vomiting in the early postoperative period. In two separate

Figure 9



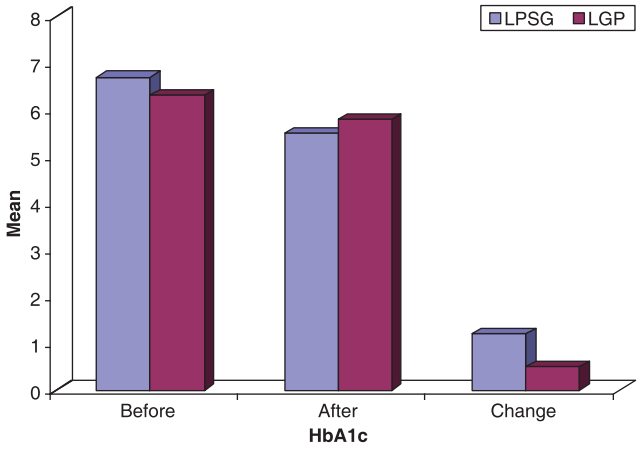
Comparison between two study groups in terms of postoperative leak and stenosis. LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy.

Figure 10



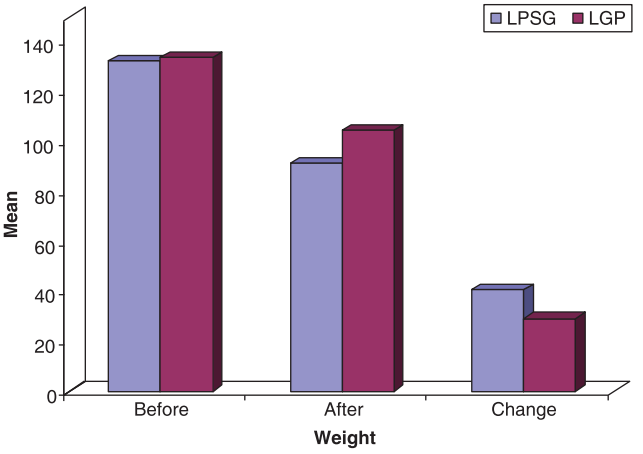
Comparison between two study groups in terms of hypertension before, after and its change after operation. LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy.

Figure 11



Comparison between two study groups in terms of HbA1c before, after and its change after operation. LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy.

Figure 12

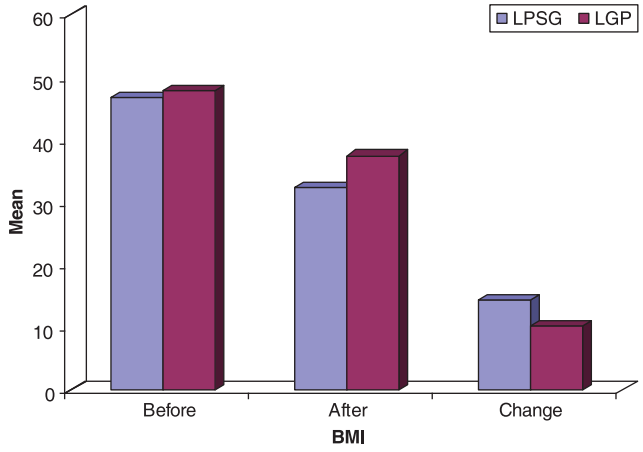


Comparison between two study groups in terms of weight before, after and its change after operation. LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy.

papers, Fusco *et al.* [15,16] reported efficacy in gastric plication procedures, as measured by changes in the weight progression of rats. In one paper, Fusco and colleagues reported an increased effect from placation of the greater curvature compared with plication of the anterior surface. These results are in agreement with initial clinical reports by Brethauer *et al.* [17], who reported increased weight loss in patients receiving LGCP compared with plication of the anterior surface.

In the present study, we also aimed to explore the efficacy of the new LGCP procedure, which has

Figure 13



Comparison between two study groups in terms of BMI before, after and its change after operation. LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy.

Table 3 Comparison between two the study groups in terms of hypertension before and after, and change after the operation

HTN	LSG [*N* (%)]	LGCP [*N* (%)]	*P*	Significance
HTN before				
Yes	8 (32.0)	4 (16.0)	0.158[a]	NS
No	17 (68.0)	21 (84.0)		
HTN after				
Yes	1 (4.0)	2 (8.0)	1.00[b]	NS
No	24 (96.0)	23 (92.0)		
HTN change				
Improvement	7 (28.0)	2 (8.0)	0.138[b]	NS
No change	18 (72.0)	23 (92.0)		

HTN, hypertension; LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy, [a]χ^2-Test, [b]Fisher's exact test.

Table 4 Comparison between HbA1c, weight, and BMI before and after a laparoscopic sleeve gastrectomy operation

	Before LSG (mean ± SD)	After LSG (mean ± SD)	*P*	Significance
HbA1c	6.7 ± 1.5	5.5 ± 0.8	0.0001	HS
Weight	132.3 ± 13.4	91.4 ± 9.6	0.0001	HS
BMI	46.8 ± 3.7	32.3 ± 2.9	0.0001	HS

HS, highly significant; LSG, laparoscopic sleeve gastrectomy, Paired *t*-test.

Table 5 Comparison between HbA1c, weight, and BMI before and after a laparoscopic greater curvature plication operation

	Before LGCP (mean ± SD)	After LGCP (mean ± SD)	*P*	Significance
HbA1c	6.3 ± 1.6	5.8 ± 1.2	0.0001	HS
Weight	133.9 ± 13.0	104.7 ± 8.9	0.0001	HS
BMI	47.8 ± 3.8	37.5 ± 3.7	0.001	HS

LGCP, laparoscopic greater curvature plication; HS, highly significant, Paired *t*-test.

Table 6 Comparison between two the study groups in terms of HbA1c before and after, and change after the operation

HbA1c	LSG			LGCP			*P*	Significance
	Mean ± SD	Minimum	Maximum	Mean ± SD	Minimum	Maximum		
HbA1c before	6.7 ± 1.5	4.0	9.2	6.3 ± 1.6	4.0	9.0	0.348	NS
HbA1c after	5.5 ± 0.8	4.0	7.0	5.8 ± 1.2	4.0	8.2	0.417	NS
HbA1c change	1.2 ± 0.9	0.0	3.2	0.5 ± 0.7	0.0	2.1	0.006	HS

HS, highly significant; LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy, Student's *t*-test.

Table 7 Comparison between the two study groups in terms of weight before and after, and change after the operation

Weight (kg)	LSG			LGCP			*P*[a]	Significance
	Mean ± SD	Minimum	Maximum	Mean ± SD	Minimum	Maximum		
Weight before	132.32 ± 13.35	165.00	105.00	133.92 ± 12.95	165.00	110.00	0.669	NS
Weight after	91.40 ± 9.57	110.00	70.00	104.68 ± 8.94	122.00	87.00	0.0001	HS
Weight change	40.92 ± 9.41	70.00	29.00	29.24 ± 8.42	49.00	9.00	0.0001	HS

HS, highly significant; LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy, [a]Student's *t*-test.

Table 8 Comparison between the two study groups in terms of BMI before and after, and change after the operation

BMI	LSG			LGCP			*P*[a]	Significance
	Mean ± SD	Minimum	Maximum	Mean ± SD	Minimum	Maximum		
BMI before	46.76 ± 3.66	40.60	55.25	47.80 ± 3.77	42.13	57.50	0.328	NS
BMI after	32.31 ± 2.86	26.23	37.72	37.45 ± 3.67	30.46	46.00	0.0001	HS
BMI change	14.45 ± 2.97	8.80	23.12	10.35 ± 2.60	3.50	15.20	0.0001	HS

HS, highly significant; LGCP, laparoscopic greater curvature plication; LSG, laparoscopic sleeve gastrectomy, [a]Student's *t*-test.

gained more popularity during the last 3 years; the change in BMI after LGCP was 10.35 kg/m^2 (45.4% EWL) compared with LSG, which was 14.45 kg/m^2 (66.4% EWL) after 1 year; thus, the result was significantly better with sleeve gastrectomy. There has been no record of weight regain in any patient until the end of the study. Both groups showed improvement in hypertension and HbA1c, but the improvement in HbA1c was significantly better with sleeve gastrectomy (the mean change was 1.2 compared with 0.5 in gastric placation). The effect of LGCP was inferior and may not be sustained compared with LSG. Silecchia *et al*. [12] have described type 2 diabetes mellitus resolution in 69.2% and an improvement in 15.4% at 12 months and 76.9 and 15.4% at 18 months in morbidly obese patients after LSG.

Conclusion

The present trial shows that LGCP may be a feasible and safe procedure in the short term when used in morbidly obese patients; it has a positive effect in improving hypertension and diabetes mellitus in morbidly obese patients, but is inferior to other restrictive procedures such as LSG and adjustable gastric banding. Longer follow-up and prospective comparative trials are needed to clarify whether it can be used as a stand-alone effective procedure for weight loss and resolution of comorbidities, especially in developing countries.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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Laparoscopic resection rectopexy versus laparoscopic mesh rectopexy for rectoanal intussusception

Sameh Hany, Saleh El-Awady, Sabry Ahmed, Mohamed Abo-Elkheir, Hosam Ghazy, Mohamed Farid

Department of General Surgery, Mansoura University, Mansoura, Egypt

Correspondence to Sameh Hany, MS, Department of General Surgery, Mansoura University, 35516 Mansoura, Egypt
Tel: +20 01006267150; fax: 050-2248-203; e-mail: sameh200@hotmail.com

Received 19 October 2014
Accepted 04 November 2014

The Egyptian Journal of Surgery
2015, 34:48–55

Background and aim
Rectoanal intussusception (RI) can be treated by laparoscopic rectopexy successfully following different techniques. This study aims to compare laparoscopic resection rectopexy with laparoscopic ventral mesh rectopexy in patients with RI.

Patients and methods
From February 2012 to February 2014, 28 patients with RI were admitted to the Colorectal Surgery Unit, Mansoura University. The patients were divided into two groups: the ventral mesh rectopexy group and the resection rectopexy group. Postoperative improvement in clinical symptoms, symptoms scores, anorectal manometry, and defecography were evaluated over 12 months.

Results
Eleven (39.3%) patients were male and 17 (60.7%) were female, with a mean age of 43.42 years. Improvement in obstructed defecation symptoms was observed in 22 (78.5%) patients overall: 85.7% in the resection rectopexy group and 71.4% in the ventral mesh rectopexy group (P = 0.648). The mean Wexner score dropped from 15.57 to 4.8 at 3 months (P = 0.0025). The mean operative time was 2.97 h in the resection rectopexy group versus 2.14 h in the ventral mesh rectopexy group (P = 0.0003). Minor morbidities were detected in five cases and no mortality was reported. Recurrence was diagnosed in six (21.4%) patients at 1 year.

Conclusion
Laparoscopic resection rectopexy is superior to ventral mesh rectopexy despite longer operative time, longer hospital stay, and higher risk of complications

Keywords:
rectoanal intussusception, resection rectopexy, ventral mesh rectopexy

Egyptian J Surgery 34:48–55

1110-1121

Introduction

Rectoanal intussusception (RI) is defined as the circumferential full thickness infolding of the midrectum during straining that extends into the anal canal, without reaching the anal orifice [1]. Patients most frequently present with constipation, excessive straining on defecation, a sensation of incomplete evacuation, and sometimes fecal incontinence (FI) [2].

The treatment of rectal intussusception associated with obstructed defecation (OD) remains challenging. Conservative management and biofeedback yield disappointing results. Surgical treatment is divided into transanal and abdominal approaches, with transanal approaches tending to have lower morbidity and abdominal approaches having lower recurrence rates [3].

Laparoscopic resection and mesh rectopexy have proven short-term benefits and economic savings compared with their open counterparts. Resection rectopexy has recurrence rates from 2 to 8%, but with additional morbidity of an anastomosis [4].

The current study aims to compare laparoscopic ventral mesh rectopexy with resection rectopexy as regards improvement in clinical symptoms, symptoms scores, and defecography and anorectal manometry. Operative time, hospital stay, postoperative complications, recurrence, and patients' quality of life were also evaluated.

Patients and methods

The present study is a prospective study conducted after approval of the local ethical committee of Mansoura University on 28 patients (17 women and 11 men) with a mean age of 43.42 years who underwent laparoscopic surgery for symptomatic RI in the Colorectal Surgery Unit, Mansoura University, between February 2012 and February 2014. Patients were divided into two equal groups: group I (n = 14) underwent lap ventral mesh rectopexy and group II (n = 14) underwent lap resection rectopexy.

The exclusion criteria were the following: being unfit for general anesthesia or having contraindications

 DOI: 10.4103/1110-1121.153371

for laparoscopic procedures; having other colorectal pathologies such as neoplasm, inflammatory bowel disease, or diverticular disease; having OD due to anismus or descending perineum syndrome; having colonic inertia; and having undergone abdominal procedures for RI or rectal prolapse previously.

All patients had symptoms of OD. Among them two patients had mixed symptoms of OD and FI, two patients had an additional complaint of bleeding per rectum, and three patients complained of mucus discharge.

The decision for operation was based on the fitness of the patients for long procedures and the length of the sigmoid colon, as patients who were fit for long procedures with redundant long sigmoid colon were chosen for laparoscopic resection rectopexy.

Preoperative workup included defecography with application of the Oxford grading system [5], anorectal manometry, endoanal ultrasound, and colon transit time and colonoscopy or barium enema.

Preoperative preparation

Patients were prepared 24 h preoperatively following standard methods for colonic preparation such as rectal enemas every 6 h, restriction of oral intake to clear fluids, and using stimulant laxatives once or twice.

All patients wore antiembolic stockings and received a prophylactic dose of low-molecular-weight heparin on the night of the operation. All patients received a single intravenous dose of third-generation cephalosporin and metronidazole at induction.

Written informed consent with respect to the nature of surgery was obtained from all patients.

Preoperative and postoperative questionnaires

All patients included in the study were personally interviewed and were asked to apply for Wexner constipation score [6] and Pescatori score for FI [7].

Quality of life was assessed by the Patient Assessment of Constipation-Quality of Life (PAC-QoL) questionnaire [8]. The PAC-Qol is a self-reported questionnaire composed of 28 items grouped into four subscales: physical discomfort, psychosocial discomfort, worries and concerns, and satisfaction.

Patient satisfaction was graded as follows: grade I – very good with almost no defecatory problems; grade II – good with some but not significant defecatory problems; grade III – fair with several defecatory problems; grade IV – poor with severe defecatory problems significantly affecting the quality of life [1].

Operative techniques

Laparoscopic ventral mesh rectopexy

The standardized, stepwise procedure includes the following:

After induction of general anesthesia, the patient is placed in a modified lithotomy position with careful padding of the lower extremities. Both arms are tucked and the patient is secured to the table. Using a four-port technique, the camera is placed at the umbilicus and 5-mm trocars are inserted in the left and right lower quadrants at the midaxillary lines. A 12-mm trocar is placed in the suprapubic region just to the right of the midline.

Steep Trendelenburg positioning is used to expose the pelvic organs, and the small bowel is retracted cephalad. Hysteropexy may be performed as needed for exposure. The rectosigmoid is retracted toward the spleen to expose the peritoneum. The right ureter is identified along the right pelvic sidewall.

The right side of the peritoneum is then incised at the level of the sacral promontory and the peritoneal dissection continues downward in the midpoint between the rectum and sidewall to the level of the pelvic floor. If a symptomatic rectocele is present, the dissection can be carried down to the perineal body and pubococcygeus muscles for additional support (Fig 1).

A polypropylene mesh measuring 6×11 cm is introduced though the 12-mm trocar site. We use a 2-0 polypropylene suture to secure the mesh to the pelvic floor muscle laterally and the anterior rectal wall using six to eight laparoscopic sutures, avoiding full-thickness rectal bites (Fig 2).

The sacral lateral anterior ligament is exposed at the sacral promontory and two laparoscopic tacks are used to secure the mesh to the sacrum. The rectum should not be placed under tension. The peritoneum is closed over the mesh and an intraperitoneal drain is inserted if needed (Fig 3).

Laparoscopic resection rectopexy [10]

The patient is in lithotomy position. The surgeon and first assistant stand on the right side of the patient with the monitor at the patient's left leg. The 10-mm camera trocar is inserted 2 cm cranial of the umbilicus via minilaparotomy. Two additional 10-mm trocars are inserted in the left and right lower quadrants,

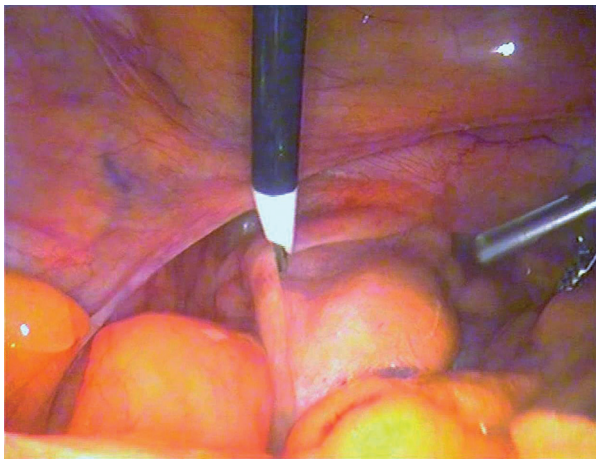
respectively. These two trocars should be positioned ~2 cm medial and distal to the anterior iliac spine to allow for good access to the small pelvis. A 5-mm trocar is inserted in a virtual semicircular line between the trocars in the midline and the right lower quadrant to guarantee proper triangulation.

The procedure starts with the mobilization of the left colon by dissecting the left paracolic gutter toward the splenic flexure on the plane of Gerotas' fascia in a lateral to medial manner. The ureter should always be identified but left untouched under the plane of Gerotas' fascia. The splenic flexure is generally left immobilized which allows for 'stretching' and elevation of the rectum.

We then change the level of dissection and open up the retrorectal space from the right side. Meticulous care is given to the preservation of the superior rectal artery to maintain excellent perfusion of the anastomosis, also preserving the hypogastric plexus and nerves. The mesorectum is then mobilized down to the pelvic floor (retrorectal dissection) under preservation of the lateral rectal ligaments and the branches of the hypogastric nerves. It is crucial to perform the mobilization to the pelvic floor to allow for sufficient straightening of the rectum. The aim of this straightening and lifting is to restore the pelvic anatomy and thus ameliorate the functional interaction of the components of the pelvic floor compartments.

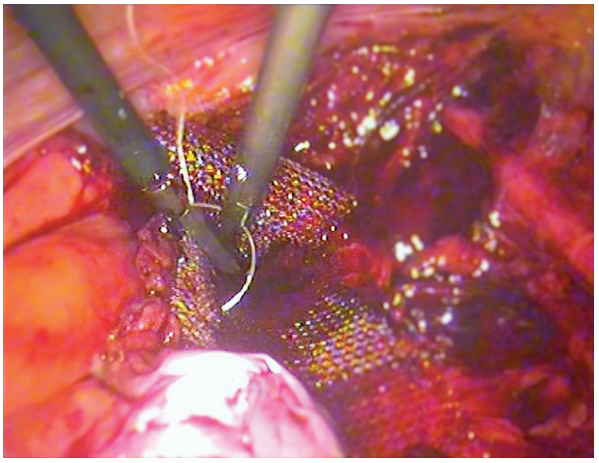
We then fenestrate the sigmoid mesentery and expose the mesentery by using an angulated retractor (Fig 4), elevating the sigmoid to the ventral abdominal wall. The mesentery is dissected close to the colonic wall

Figure 1



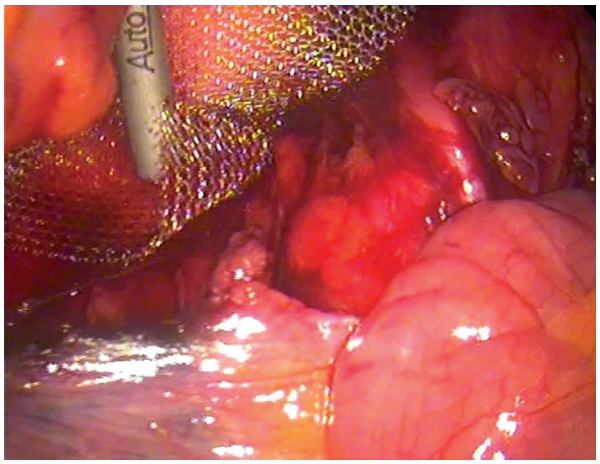
Starting anterior dissection with laparoscopic hook in ventral mesh rectopexy.

Figure 2



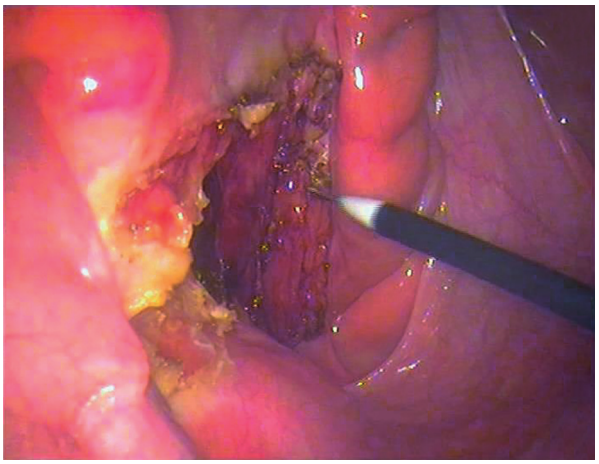
Suturing the polyprolene mesh to the anterior rectal wall with laparoscopic suture.

Figure 3



Fixing the polyprolene mesh to sacral promontory using a laparoscopic tacker.

Figure 4



Dissection of the sigmoid mesocolon to create a mesenteric window in laparoscopic resection rectopexy.

to preserve the superior rectal artery pedicle. The dissection is performed down to the upper third of the rectum; then the rectum is transected by a linear endostapler after rectal washout (Fig 5).

Finally, the incision of the left lower trocar is enlarged according to the diameter of the colon (3–5 cm) and the specimen extracted. The sigmoid colon is then resected, and the head of the stapler is inserted in the descending colon. A purse-string suture is tied.

The colon is replaced into the abdominal cavity, and the mini-laparotomy wound is closed.

Now, the circular stapling device is introduced into the rectum. The tip of the center rod is placed directly above or below the center of the endostapler suture line. After the stapler head has been connected to the center rod and the instrument has been approximated, the stapler is fired. It is important to slightly pull back the stapling device to achieve a wide anastomosis. A pneumatic test verifies the absence of any primary leakage.

The pexy is performed by three running sutures, creating an inverted 'Y'. The first suture closes the peritoneal defect anteriorly and fixates the rectum ventrally on the peritoneal edge to elevate the peritoneal reflection. This avoids a cul-de-sac phenomenon. The remaining running sutures fixate the mobilized and elevated rectum on the left and right lateral wall of the peritoneal edge. An intraperitoneal drain is put in all patients (Fig 6).

Postoperative care

Vital signs and output of drains and urinary catheter were measured and recorded. Third-generation cephalosporins and metronidazole were administered to all patients for 36 h postoperatively and proper pain management with analgesics was achieved as needed.

Early ambulation was advocated in all patients within 8 h of the procedure. Starting of oral fluid intake varied. For patients with ventral mesh rectopexy, oral fluid intake started as soon as bowel sounds were heard, whereas in patients who underwent resection rectopexy oral fluid intake was delayed until the fourth postoperative day.

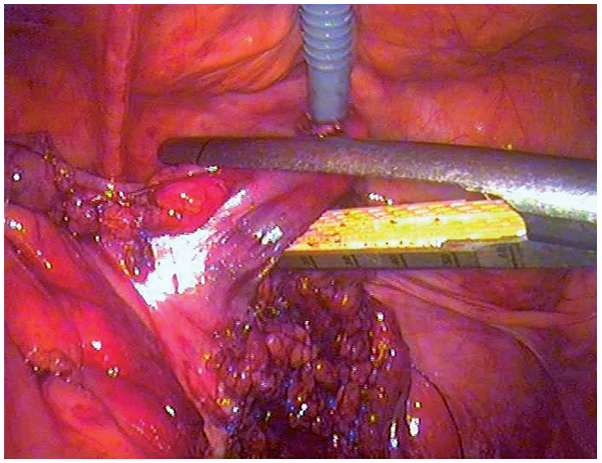
Follow up

Follow-up was conducted at 3 months, 6 months, and 1 year postoperatively and included postoperative symptoms review, Wexner constipation score, Pescatori continence score, clinical recurrence, postoperative manometry, defecography, and patient satisfaction.

Statistical analysis

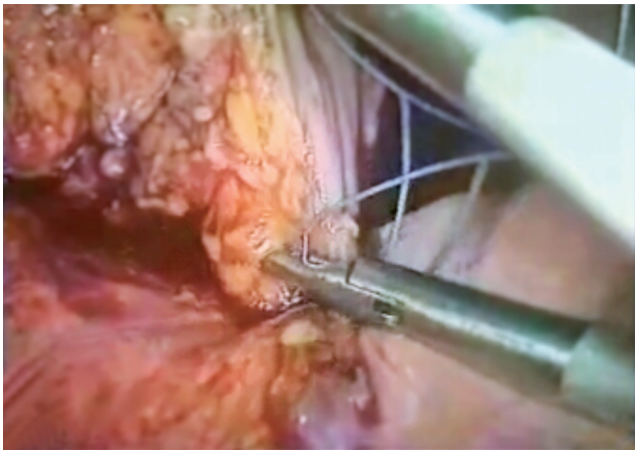
Data were analyzed using Excel and SPSS (Statistical Package for Social Science, Bristol University, UK) version 16 under Microsoft Windows. The description of data was in the form of mean ± SD for quantitative data and frequency and proportion for qualitative data. The analysis of data was carried out to test the statistically significant difference between groups. The Student *t*-test was used to compare quantitative data (mean ± SD) between two groups. *P* values less than 0.05 were considered significant. OD was considered if Wexner score was more than 5. Significant improvement in OD or FI was considered as a reduction in Wexner or Pescatori score of at least 25%.

Figure 5



Application of a linear stapler to the sigmoid colon in laparoscopic resection rectopexy.

Figure 6



Suturing the rectum after reanastomosis to lateral peritoneal folds in laparoscopic resection rectopexy.

Results

The demographic data of all patients are shown in Table 1. All patients had symptoms of OD mainly in the form of sense of outlet obstruction and straining. Two (7%) patients had mixed symptoms of OD and FI, two patients had an additional complaint of bleeding per rectum, and three patients complained of mucus discharge. Nine (32.14%) female patients were discovered to have anterior rectocele in association.

At 3 months postoperatively, 22 (78.5%) patients reported improvement as regards OD symptoms and six (21.5%) patients had persistent OD symptoms. Of the 22 patients whose condition improved, 16 patients were cured and six showed improvement but were not totally cured. Among the 22 patients who showed improvement, 12 patients were from the resection rectopexy group (85.7% of the group) and 10 patients were from the ventral mesh rectopexy group (71.4% of the group) (P = 0.648). No patient experienced worsening of OD. At 3 months postoperatively, the Wexner constipation score was significantly reduced (P = 0.0025) from a mean preoperative of 15.57 ± 2.3 to a mean postoperative of 4.8, which declined at 1 year postoperatively to 3.27 ± 1.58 [confidence interval (CI) = 95% at ± 0.59] (Table 2).

Two of the 28 patients with RI complained of mixed FI/OD preoperatively. At 3 months postoperatively, one (50%) patient showed improvement in FI and the other patient still complained of persistent FI. Among the two patients who had FI, the patient who did not show improvement was in the ventral mesh rectopexy group, and the patient whose condition had improved was in the resection rectopexy group. No patient experienced worsening or new onset of FI. The overall Pescatori score for incontinence decreased from a mean preoperative score of 0.32 to a mean postoperative score of 0.17 (P = 0.49). For the patients with FI, the score dropped from a mean of 4.5 preoperatively to a mean of 2.5 at 1 year postoperatively.

All patients had a visible RI during straining in the defecogram. According to the Oxford grading system, 11 (39.2%) patients were grade IV, 13 (46.5%) patients were grade III, two (7.14%) patients were grade II, and two (7.14%) patients were grade I (Table 3). Anterior rectocele less than 2 cm was detected in four (14.28%) patients and anterior rectocele more than 2 cm was detected in five (17.85%) patients; 22 (78.5%) patients showed no RI in the postoperative defecogram. Twelve (85.7%) patients of the resection rectopexy group and 10 (71.4%) patients of the ventral mesh rectopexy group had disappearance of RI in defecography at 3 months postoperatively. As for the nine patients who had coexisting anterior rectocele, the postoperative defecogram of six (66.6%) of them (five in the resection group and one in the ventral mesh group) did not reveal a rectocele, whereas three patients (one in the resection group and two in the ventral mesh group) were seen to have persistent rectocele.

The mean anal pressure during rest changed from 60.2 ± 13.3 mmHg preoperatively to 63.4 ± 11.7 mmHg at 3 months postoperatively (P = 0.655; CI = 95% at ±

Table 1 Demographic data of 28 patients

Patients	*n*	Mean age	Obstructed defecation [*n* (%)]	Fecal incontinence [*n* (%)]	Other symptoms	Mean Wexner score
Male	11	41.16	11 (100)	0 (0)	Bleeding/rectumMucus discharge	14.85 ± 3.13
Female	17	45.68	17 (100)	2 (11.76)	Bleeding/rectumMucus discharge	16.28 ± 1.47

Table 2 Epidemiology and postoperative symptom improvement in both groups

Patients	Laparoscopic ventral mesh rectopexy	Laparoscopic resection rectopexy	*P* value
Age	44.62	42.2	
Sex (female : male)	10 : 4	7 : 7	0.44
Duration of symptoms (years)	1.39	1.43	
Improvement in OD [*n* (%)]	10 (71.4)	12 (85.7)	0.648
Improvement in FI [*n* (%)]	0 (0)	1 (100)	1.00
Mean Wexner score			
Preoperative	15.48 ± 2.4	15.66 ± 2.2	0.863
Postoperative	4.27 ± 1.7	2.28 ± 1.46	0.0025
Mean Pescatori score			
Preoperative	0.35 ± 1.87	0.28 ± 1.39	0.911
Postoperative	0.35 ± 1.87	0	0.49

FI, fecal incontinence; OD, obstructed defecation.

4.33). The mean anal pressure during maximal squeeze dropped from 139.9 ± 25.2 mmHg preoperatively to 114.85 ± 6.4 mmHg at 3 months postoperatively (P = 0.244; CI = 95% at ± 2.37). RAIR was intact in all patients (Table 4).

The mean operative time in the ventral mesh rectopexy group was 2.14 h, whereas the mean operative time in the resection rectopexy group was 2.97 h (P = 0.0003). Conversion to open procedure was implemented in five (17.8%) patients (P = 1). Minor morbidity occurred in five (17.8%) patients but there were no mesh-related complications. One (3.5%) patient developed a major complication in the form of dehiscence of anastomosis and leakage. No female patients complained of sexual dysfunction and no male patient complained of ejaculatory or erectile difficulties postoperatively. There was no postoperative mortality.

Clinical recurrence was diagnosed in six (21.4%) patients at 3 months postoperatively (four patients after ventral mesh rectopexy and two patients after resection rectopexy). Two of the recurrent cases were of Oxford grade I, another two cases were of grade II, one case was of grade III, and one case was of grade IV.

Fifteen (53.57%) patients reported grade I satisfaction, seven (25%) patients reported grade II, six (21.4%) patients reported grade III, and two (7.14%) patients reported grade IV satisfaction. As for the quality of life assessed by PAC-QoL, 14 (50%) patients were in the excellent subscale, five (17.8%) patients in the good subscale, four (14.28%) patients in the fairly good subscale, and only three (10.7%) patients were in the poor subscale.

Discussion

RI presents with a spectrum of related complaints ranging from constipation to FI. The most common complaints are rectal pressure with constipation in mild and moderate intussusception, and straining at bowel movement with constant rectal pain in severe intussusception [11].

Doubts have been raised about the relationship of RI to external rectal prolapse and a possible shared common pathophysiology, which has brought focus on the effect of rectopexy surgery for RI [12].

The aim of surgery for rectal intussusception is to correct the anatomical defect, alleviate bowel dysfunction, and avoid functional sequelae. Abdominal rectopexy appears to be more effective than perineal procedures in controlling RI [13].

Laparoscopic ventral rectopexy became popular as a result of both impressive functional results in external rectal prolapse [14] and the advantages of a laparoscopic approach. Because it avoids posterior rectal mobilization and thus rectal denervation inertia, it improves OD symptoms in about 80% of patients without worsening or inducing new-onset constipation symptoms [15]. This is in distinct contrast to traditional posterior rectopexy for external rectal prolapse, after which about 50% of patients complain of new or worse constipation [16].

In our study we compared ventral mesh rectopexy and resection rectopexy for correction of RI. Choosing the laparoscopic approach as a minimally invasive approach had its advantages as it entails a smaller surgical incision; thus, there is less postoperative pain and better cosmetic appearance, with less incidence of postoperative ileus and wound complication [17].

The dominant symptom in all our patients was sense of outlet obstruction and straining similar to what was reported in another study on RI [18]. FI was a secondary complaint in 7.25% of patients, which might be attributed to widening of the anal canal, alteration of the sensory mechanisms and sphincter muscles, and also pudendal neuropathy resulting from long-standing, excessive straining to defecate [19]. Sometimes distention of the lower rectum by the intussusceptum activates the

Table 3 Oxford grading of rectoanal intussusception

Grades	Definition	Percentage (%)
I	High rectorectal	7.14
II	Low rectorectal	7.14
III	High rectoanal	46.5
IV	Low rectoanal	39.2

Table 4 Changes in mean anal pressure after both procedures

Manometric results	Laparoscopic ventral mesh rectopexy	Laparoscopic resection rectopexy	P value
Mean resting anal pressure			
Preoperative	58.7 ± 12.2	61.7 ± 14.4	0.557
Postoperative	62.4 ± 11.3	64.4 ± 12.1	0.655
Mean squeeze anal pressure			
Preoperative	137.5 ± 24.7	142.3 ± 25.56	0.617
Postoperative	113.4 ± 5.7	116.3 ± 7.1	0.244

rectoanal inhibitory reflex, resulting in relaxation of the internal anal sphincter and producing an overflow incontinence [20].

As for symptoms, 22 (78.5%) patients with OD showed improvement overall, with 16 patients reporting complete cure of symptoms. The improvement was higher in the resection rectopexy group (85.7%), similar to the result obtained in a recent study [21], compared with the ventral mesh rectopexy group (71.4%), but is less than the 86% seen in another study [12]. Two patients, both female, had mixed complaints of OD and FI; only one of them, from the resection rectopexy group, reported improvement (Table 2).

Defecography revealed RI in 100% of patients, with 46.5% of them in Oxford grade III. Postoperative defecography showed disappearance of RI in 22 (78.5%) patients overall, similar to Johnson's study [21]. Resection rectopexy showed better results than ventral mesh rectopexy (85.7 vs. 71.4%). Interestingly, the four cases showing recurrence in the ventral mesh rectopexy group were of Oxford grade I and grade II, which might imply that, the higher the intussusception, the lower the success rate of ventral mesh rectopexy.

Anterior rectocele was observed as an associated finding in almost one-third of the patients, all of whom were female. About two-third of these rectoceles disappeared postoperatively, mostly in the resection rectopexy group, which is concordant with the report of Laubert *et al*. [22] that the combination of sigmoid resection and rectopexy results in the highest rates of improvement in OD syndrome.

Mean resting and squeeze anal pressures were within the normal range, as observed by Christiansen *et al*. [23]. Postoperative anorectal manometry showed mild increase in the mean resting anal pressure in both groups and decrease in the mean squeeze anal pressure also in both groups; yet, both results were statistically insignificant (P = 0.592 and 0.162, respectively) (Table 4).

Comparison of the two groups revealed a longer mean operative time, more intraoperative blood loss, longer hospital stay, and a higher conversion to open procedure in the resection group (Table 5). One major operative complication was detected in the resection group with dehiscence of the anastomosis and leakage, which was detected in the third postoperative day and managed by laparotomy, peritoneal toilet, and end colostomy (Hartmann's procedure). Minor complications such as wound infection and urinary tract infection were detected and managed properly. No mortality was reported in the study.

In six patients (two males and four females) with persistent complaint, clinical recurrence was diagnosed by Digital Rectal Examination (DRE) in the outpatient clinic at 3 months' follow-up; four of these patients were in the ventral mesh group. All six patients showed persistent or recurrent RI in the postoperative defecography, correlating with the clinical findings.

The overall patient satisfaction graded from I to IV showed that more than half of the patients reported no defecatory problems (grade I), and 7.14% of them reported severe defecatory problems affecting their quality of life (grade IV)

Conclusion

Laparoscopic rectopexy is a unique approach for RI. Both the ventral mesh method and the resection method give excellent early functional outcomes such as improving OD symptoms and/or associated FI with minimal morbidity, due to the benefits of minimally invasive surgery.

While resection rectopexy proved to be superior as regards symptom improvement, with the lowest recurrence rate, it has its drawbacks, such as longer

Table 5 Operative data of both procedures

Data	Laparoscopic ventral mesh rectopexy	Laparoscopic resection rectopexy	*P* value
Number of patients (*n*)			
Male	4	7	0.44
Female	10	7	
Mean operative time (h)	2.14 ± 0.635	2.97 ± 0.371	0.0003
Average blood loss (ml)	143 ± 57.98	228.3 ± 129.61	0.033
Conversion	2	3	1
Complications			
Minor	2	3	0.648
Major	0	1	
Postoperative hospital stay (days)	2.4 ± 0.7	5.9 ± 0.99	0.0001
Recurrence	4	2	0.648

operative time and hospital stay, which increase both potential morbidity and healthcare costs. Ventral mesh rectopexy, although not as efficient as resection rectopexy in controlling the symptoms, proves to be safer, easier, and less time-consuming. Thus, the choice between the two procedures should be made carefully and tailored to each individual patient.

Acknowledgements

Conflicts of interest

None declared.

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Transabdominal gastroesophageal devascularization with versus without esophageal stapler transection in the control of variceal bleeding in cirrhotic patients

Wael E. Lotfy[a], Taha A. Biomy[a], Mohamed I. Abdelhamid[a], Sherif M. Galal[b], Mohamed M. Refaey[b]

Departments of [a]General Surgery, [b]Tropical Medicine, Faculty of Medicine, Zagazig University, Zagazig, Egypt

Correspondence to Wael E. Lotfy, MD, El Mohafza Tower, Behind Kasr El Thakafa, Zagazig-Sharkeia, Egypt
Tel: +20 552 345 187, +20 552 310 360; fax: +2055 2370600;
e-mails: waellotfy@hotmail.com, waellotfy@zu.edu.eg

Received 29 October 2014
Accepted 05 December 2014

The Egyptian Journal of Surgery
2015, 34:56–63

Aim
The aim of the study was to assess the efficacy and safety of adding esophageal transection to the devascularization operation in controlling variceal bleeding.

Patients and methods
A total of 115 patients with acute variceal bleeding who finally needed surgery were included in this study. They were divided into two groups: group I included 32 patients who underwent transabdominal gastroesophageal devascularization and esophageal transection and group II included 83 patients who underwent transabdominal gastroesophageal devascularization only. Survivors were followed up for at least 3 years by endoscopy to check for recurrence of esophageal varices.

Results
The incidence of early bleeding, residual varices, and recurrent varices was significantly lower in group I than in group II and there was no statistically significant difference in both early and late morbidity and mortality between the two groups.

Conclusion
Esophageal stapling is a safe and effective procedure for both short-term and long-term control of bleeding varices.

Keywords:
esophageal varices, gastro-esophageal devascularization, stapler transection

Egyptian J Surgery 34:56–63

1110-1121

Introduction

Acutely bleeding portal hypertension remains a medical and surgical challenge. Endoscopic treatment remains the mainstay for the initial control of actively bleeding esophagogastric varices. However, about 10–15% of patients fail to respond to emergency sclerotherapy, and this subgroup of patients has a particularly poor prognosis with high mortality rates [1].

Treatment options in such cases consist of transjugular intrahepatic portosystemic shunt, surgical shunting, devascularization procedures, and liver transplantation with variable success rates. However, transjugular intrahepatic portosystemic shunt and liver transplantation may not be readily available at all centers, and surgical shunting requires special expertise. Transabdominal gastroesophageal devascularization and esophageal transection (TAGEDET) is the most favored emergency procedure for the control of continued bleeding after failed endoscopic therapy [2–5].

The objective of this study was to compare the short-term and long-term results of the two surgical procedures, a modified devascularization procedure with stapler esophageal transection (group I) and a devascularization procedure without stapler transection (group II), to assess the efficacy and safety of esophageal transection.

Patients and methods

Between June 2008 and June 2011, all patients admitted to Zagazig University Hospitals with esophageal variceal bleeding who needed surgical intervention were enrolled in this study.

Inclusion criteria

(1) Patients above 18 years of age and below 70 years.
(2) All patients with bleeding esophageal varices due to portal hypertension diagnosed with endoscopy.
(3) Patients subjected to surgery either due to failure of endotherapy and pharmacotherapy to arrest bleeding or due to hypersplenism.
(4) Patients who consented to the operation and were willing to join this research work.

Exclusion criteria

(1) Age below 18 years and above 70 years.

 DOI: 10.4103/1110-1121.153372

(2) If the origin of bleeding was not variceal — for example, concomitant portal gastropathy, erosive gastroduodenitis, or peptic ulcer.
(3) If portal hypertension was not due to cirrhosis.
(4) If the patient was unfit for or refused surgery.
(5) Patients who responded to endotherapy and/or pharmacotherapy and were not candidates for surgery.
(6) Patients who were lost during the follow-up period.

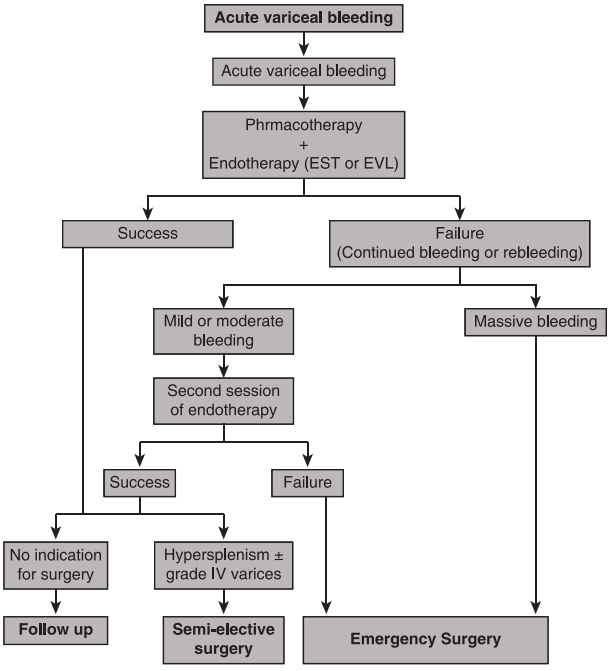
This research work was approved by the ethical committee of our Department of Surgery and Faculty of Medicine, Zagazig University.

Preoperative care

All patients were initially admitted to the emergency unit in our hospital (the hematemesis ward) where they were rapidly resuscitated with intravenous fluids, blood and plasma transfusion when needed, and infused with vasopressin at a rate of 0.1–0.4 U/min or somatostatin (sandostatin) at a rate of 50 μg/h. Gastric lavage was performed immediately to assess the amount of bleeding, to clean the stomach for endoscopy, and to lessen the incidence of encephalopathy. Once the patient was resuscitated, upper gastrointestinal (GI) endoscopy was performed to confirm the diagnosis of bleeding varices and to rule out any other cause. Then endotherapy, either endoscopic sclerotherapy or endoscopic variceal ligation, was performed in the same setting to arrest bleeding, and the patient was returned to the observation ward where conservative measures were continued and full laboratory and imaging investigations were ordered to evaluate organ functions, degree of anemia, risk of encephalopathy, and the stage of cirrhosis. Patients were classified according to Child–Pugh classification into Child A, B, or C.

Some patients continued to bleed or bled again after initial arrest of bleeding during this observation period. If the bleeding was massive, a Sengstaken–Blakemore tube was applied and kept inflated in place during transfer of the patient to our emergency unit of surgery where he or she was prepared for emergency surgery; if the bleeding was mild or moderate the patient underwent another trial of endotherapy, but if the procedure failed again he or she was transferred to emergency surgery.

Also, if pharmacotherapy and/or endoscopic therapy succeeded in arresting bleeding, but there was marked hypersplenism or grade IV varices with high risk of rebleeding, the patient was transferred to our Department of Surgery and prepared for semielective surgery. Again, patients who responded to pharmacotherapy/endotherapy and did not need surgical intervention were discharged from the hospital on regular sessions of endotherapy and were not included in this study. Our approach to manage cases of acute variceal bleeding is explained in the following algorithm:



Patients were classified into two groups:

Group I: Patients who underwent transabdominal gastroesophageal devascularization and esophageal transection (TAGEDET) when stapler was available and the intraoperative conditions were favorable for esophageal stapling (supple esophagus).

Group II: Patients who underwent transabdominal gastroesophageal devascularization (TAGED) only if marked edema and friability of the esophagus or fibrosis and adhesions around the abdominal esophagus interfered with esophageal stapling.

Thus, esophageal stapler transection was attempted whenever possible. If successful, the patient was placed in group I; otherwise, TAGED alone was performed and the patient was placed in group II.

Operative work

All patients were operated upon by the same surgical team following the same surgical principles and under the same facilities. All patients underwent TAGED, and in group I patients esophageal transection was added. TAGED was performed by complete

devascularization of the lesser curvature and most of the greater curvature of the stomach together with transhiatal devascularization of the lower 6–10 cm of the esophagus. This entails dissection–ligation of the left gastric, short gastric, left gastroepiploic veins, and all paraesophageal collaterals. In group I patients, esophageal stapler transection was added. After complete mobilization of the esophagus, the two vagal trunks, or at least the posterior one, were identified and preserved. Then a small anterior gastrotomy about 3–5 cm from the cardia was made and an end-to-end anastomotic circular stapler of size 25–29 mm (Ethicon) was introduced smoothly through the gastrotomy into the lower esophagus. After tying the lower esophagus over the anvil of the stapler and closing the device to the level of safety firing, the device was fired to transect and anastomose the esophagus about 2–3 cm above the cardia. After removal of the device the transected doughnut was assessed for completion, and the lower esophagus was reassessed for integrity of the anastomosis before closure of the gastrotomy in two layers. Pyloroplasty was not needed and was not performed as we wanted to preserve at least one vagal trunk. Splenectomy was routinely performed in all cases unless already splenectomized before. Liver biopsy was routinely obtained. Tube drains were left near the anastomosis and the laparotomies were closed over Jackson Pratt suction drains.

In one case, during digital dissection of the esophagus, perforation of the esophagus occurred and therefore we divided the esophagus above the perforation between two intestinal clamps; the lower segment of the esophagus, harboring the perforation, was removed and the cardia was closed in two layers and the distal end of the esophagus was closed around the anvil of the stapler using purse-string suture. Then, anastomosis between the esophagus and the fundus of the stomach was performed using the circular stapler.

Postoperative care

Postoperatively, all patients were immediately transferred to the ICU in our hospital where they were closely monitored. Full laboratory investigations were ordered in the second postoperative day (POD). Blood transfusion was resorted to only if hemoglobin fell below 8 g%. If early signs of encephalopathy developed, patients were put on an antiencephalopathy regimen (hepamerz intravenous infusion, aminoleban, etc.). Oral feeding was withheld for 3 days in group I, in which esophageal transection was performed, but allowed once intestinal motility was regained in group II. When survivors were surgically stable, they were transferred to the inpatient wards of the surgical department where they completed their postoperative regimen.

Patients who bled again were transferred back to the emergency unit of hematemesis, where conservative measures were resumed and patients were prepared to have an upper GI endoscopy to diagnose the source of rebleeding and managed accordingly.

All survivors underwent upper GI endoscopy before their discharge on the 21st POD or later. Esophageal varices detected at the discharge endoscopy session were regarded as residual varices.

Follow-up

Survivors were followed up in the outpatient clinic of our unit on regular visits every 3 months in the first year and then every year in the next 2 years. In each follow-up visit, the patient was examined clinically and fully investigated and an upper GI endoscopy was performed. Esophageal varices that appeared at the follow-up endoscopy but not detected at discharge were regarded as recurrent varices.

Statistical analysis

The patients' demographic and clinical data were expressed as frequencies for qualitative data. Quantitative data were summarized as mean, SD, and range. Group comparison between the devascularization procedure with/without esophageal transection with respect to rates of postoperative morbidity and mortality was made with Pearson's c^2-test, Fisher's exact test, and the unpaired Student t-test, as applicable on an intention-to-treat basis. A P value less than 0.05 was taken as significant.

Results

This study, including the minimum 3 years' follow-up period, extended from June 2008 to June 2014. Out of 3212 patients admitted to the emergency unit in Zagazig University Hospitals with acute variceal bleeding from June 2008 to June 2011, only 133 patients needed surgical intervention and were enrolled in this research. However, 18 patients were excluded later: two patients had associated severe portal gastropathy, three patients had associated peptic ulcerations, three patients were not cirrhotic (as proven on liver biopsy) and their portal hypertension was due to another cause, one patient died intraoperatively, and nine patients were lost during the follow-up period. Thus, only 115 patients were finally included in this study, comprising 86 men and 29 women, their ages ranging from 24 to 68 years, with a mean age of 47 ± 9.6 years. All patients were cirrhotic with hepatitis C virus-positive markers. The demographic, clinical, and investigative data are shown in Table 1.

After resuscitation, all patients underwent a session of endotherapy; 104 (90.4%) patients had endoscopic sclerotherapy and 11 (9.6%) patients had endoscopic variceal ligation (Photos 1 and 2). Bleeding stopped in 98 (85%) patients and these patients were transferred to semiselective surgery because of hypersplenism and/or grade IV varices with high risk of rebleeding. The remaining 17 (15%) patients either continued to bleed (three patients) or rebled after initial arrest of the bleeding (14 patients). Three of them had massive bleeding and were transferred to emergency surgery on a Sengstaken–Blakemore tube, and the remaining 14 patients underwent another trial of endotherapy. Five patients responded well and were transferred to semielective surgery, whereas nine patients had profuse bleeding and were transferred to emergency surgery. Thus, all patients underwent at least one session of endotherapy and finally we had 12 (10.4%) patients who required emergency surgery and 103 (89.6%) patients who underwent semiselective surgery. According to the surgical procedure, patients were divided into two groups:

Table 1 Demographic, clinical, and investigative data

Data	Group I (TAGEDET) (*N* = 32)	Group II (TAGED) (*n* = 83)	*P* value
Age (mean ± SD) (years)	48 ± 5.6	46 ± 6.1	0.42
Sex (male and female)	22–10	58–25	0.45
Comorbid disease			
Diabetes mellitus	3	5	0.39
Cardiac troubles	1	2	0.62
Renal troubles	0	1	0.72
Cerebrovascular disease	2	1	0.18
Stage of cirrhosis			
Child class A	14	25	0.18
Child class B	11	35	0.44
Child class C	8	22	0.88
Variceal bleeding episodes			
1–3	24	56	0.43
4–5	6	26	0.17
>5	2	1	0.18
Grade of varices			
Grade I and II	9	21	0.75
Grade III and IV	23	62	
Type of endotherapy			
EST	27	77	0.15
EVL	5	6	
Source of bleeding			
Esophageal varices	26	68	0.93
Gastric varices	6	15	
Time of surgery			
Emergency surgery	3	9	0.56
Semielective surgery	29	74	

EST, endoscopic sclerotherapy; EVL, endoscopic variceal ligation; TAGED, transabdominal gastroesophageal devascularization; TAGEDET, transabdominal gastroesophageal devascularization and esophageal transection.

Group I included 32 (27.8%) patients who underwent TAGEDET.

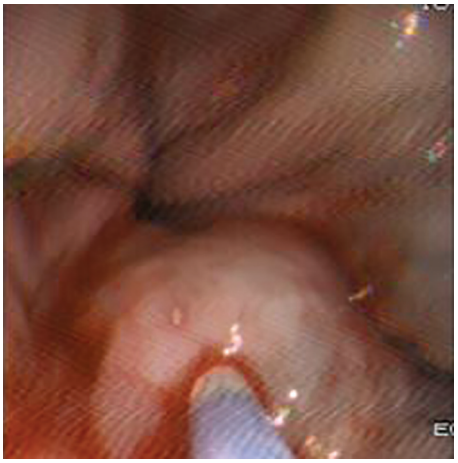
Group II included 83 (72.2%) patients who underwent TAGED only.

Although selection of patients for the two groups was not random and depended on the feasibility of the stapling procedure, statistical analysis of the demographic, clinical, and investigative data showed no significant differences between the two groups, thus ensuring that they were well-matched and amenable to comparative study.

Operative data

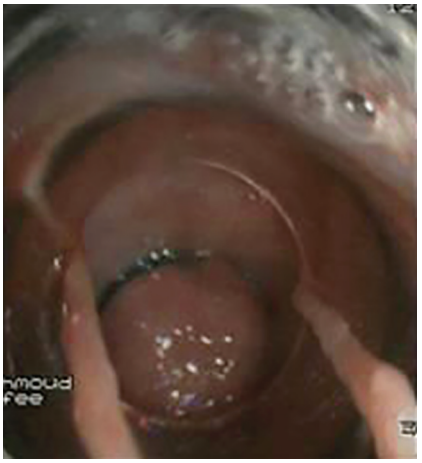
The mean operative time was 3.1 h (range 1.5–6 h). It was significantly longer in the emergency group than in the semiselective group. Also, it was significantly longer in group I than in group II (3.9 vs. 2.5 h). The

Photo 1



Endoscopic sclerotherapy (EST).

Photo 2



Endoscopic variceal ligation (EVL).

mean amount of perioperative blood and/or packed red blood cells transfusion was 3.2 U (range 1–10 U). Again, it was significantly larger in the emergency group than in the semielective group (4.2 vs. 2.1 U) but it showed no statistically significant difference between group I and group II. Splenectomy was routinely performed in all cases unless the patient had been splenectomized before (three cases). There was only one intraoperative mortality that occurred before completion of the procedure, which was excluded from the study (Table 2).

Early postoperative morbidity and mortality

Acute bleeding was controlled in all cases. The mean duration of ICU stay was 4.5 days (range 1–12 days). The mean duration of hospital stay was 32 ± 12 days (range 21–52 days). Hospital stay was statistically longer among emergency cases than among semiselective ones and in group I than in group II (Table 3).

Eighteen patients developed encephalopathy postoperatively. There was a statistically significantly higher incidence of encephalopathy among emergency cases than among semielective ones. Fifteen patients recovered well, whereas three patients developed hepatorenal syndrome and died within POD 6–18.

Early bleeding (within 30 days postoperatively) occurred in 15 (9.6%) patients: one (3.1%) patient in group I and 14 (16.8%) in group II. Endoscopy revealed the source of bleeding in each case (Photos 3 and 4): bleeding was from the anastomotic line in one case and from residual varices in the remaining cases. The bleeding anastomotic line responded to conservative measures, whereas

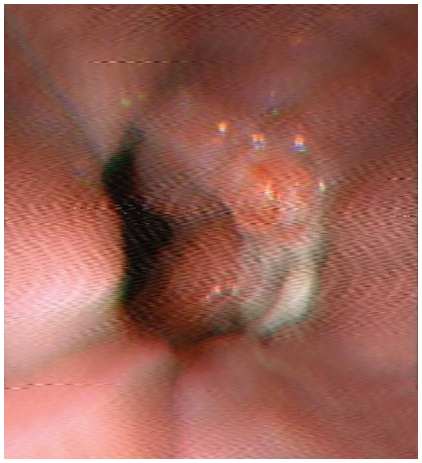
Table 2 Operative data of the patients

Data	Group I (*n* = 32)		Group II (*n* = 83)		Group I vs. group II (*P* value)	Emergency vs. elective (*P* value)
	Emergency (*n* = 3)	Elective (*n* = 29)	Emergency (*n* = 7)	Elective (*n* = 76)		
Operative time (mean ± SD) (h)	4.1 ± 1.2	3.8 ± 1.1	2.9 ± 0.9	2.1 ± 0.5	0.000	0.04
Blood transfusion (mean ± SD) (units/patient)	4.1 ± 1.1	2.1 ± 1.2	3.9 ± 0.9	1.9 ± 0.8	0.3	0.000
Splenectomy (number of patients)	3	28	6	75	0.62	0.24

Table 3 Early postoperative morbidity and mortality

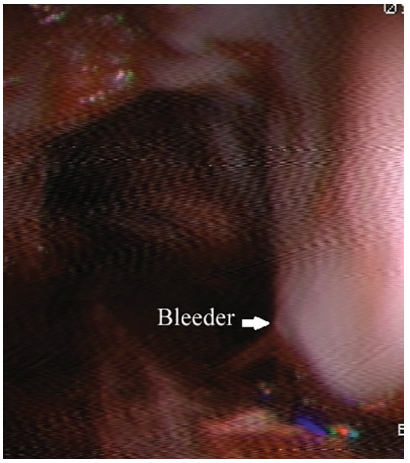
Early morbidity and mortality	Group I (*n* = 32)		Group II (*n* = 83)		Group I vs. group II (*P* value)	Emergency vs. semielective (*P* value)
	Emergency (*n* = 3)	Elective (*n* = 29)	Emergency (*n* = 9)	Elective (*n* = 74)		
Hospital stay (days)	44 ± 5.2	32 ± 6.1	38 ± 7.3	28 ± 4	0.000	0.000
Encephalopathy	2	4	6	6	0.57	0.000
Early bleeding	1	0	2	12	0.04	0.19
Subphrenic collection	1	0	1	3	0.68	0.02
Anastomotic leakage	0	1	0	0	—	—
Residual varices	1	0	3	15	0.01	0.097
Operative mortality	1	0	2	3	0.53	0.001

Photo 3



Bleeding from the staple line.

Photo 4



Bleeding from residual varices.

bleeding residual varices were endoscopically injected. Thirteen patients responded well and the bleeding stopped, whereas the remaining two patients continued to bleed and died. There was a statistically significantly higher incidence of early bleeding in group II than in group I.

There were five (4.3%) reported cases of subphrenic collections in the splenic bed in our series: four in group II and one in group I. They were managed conservatively. In two of them the collection disappeared under conservative measures and the other three needed ultrasound-guided drainage: two of them were cured and one needed surgical drainage; however, she died on the 29th POD from sepsis and hepatorenal failure. Subphrenic collection occurred more frequently in the emergency group than in the semielective patient group but there were no statistically significant differences between group I and group II regarding the incidence of subphrenic collection.

Discharge endoscopy picked up 19 (16.5%) cases of residual varices: one (3.1%) case in group I and 18 (21.6%) cases in group II. There was no significant difference in the incidence of residual varices between emergency and semielective groups, but there was a statistically higher incidence of residual varices in group II than in group I. All cases of residual varices were managed conservatively and discharged on regular visits for endoscopic follow-up.

Leakage from anastomosis, in group I, occurred only in one (3.1%) case, which was managed conservatively and stopped spontaneously.

The total number of early mortality cases (within 30 days postoperatively) was six (5.2%). Operative mortality was statistically higher in the emergency group (25%) than in the semielective group (2.9%), but it did not show statistically significant difference between group I (3.1%) and group II (6%).

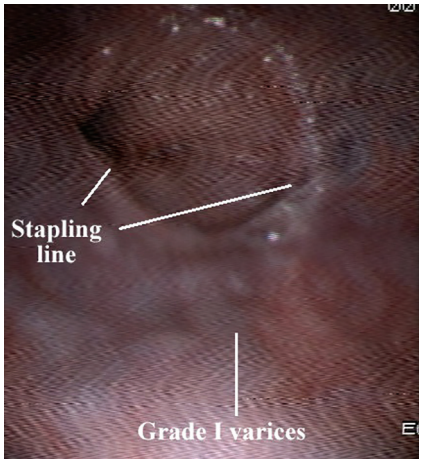
Late morbidity and mortality

The mean follow-up period was 4.2 ± 0.9 years; however, with respect to late results in this study, endoscopic examination showed recurrent varices in 22 (19.4%) cases: two (6.2%) cases in group I and 20 (24%) cases in group II (Photos 5 and 6). There was a statistically significantly higher incidence of recurrent varices in group II than in group I. All patients went on regular endoscopic follow-up. Only one patient needed resurgery and underwent fundectomy for his bleeding recurrent gastric varices. He recovered well postoperatively, but 4 months later we discovered a hepatocellular carcinoma on his computed tomographic scan and he died 5 months later (Tables 4 and 5).

Twenty-three (20%) patients developed liver cell failure with encephalopathy and ascites throughout the follow-up period. Five patients died in the first 3 years. Three other patients underwent liver transplantation: two patients survived and one patient died 1 month postoperatively.

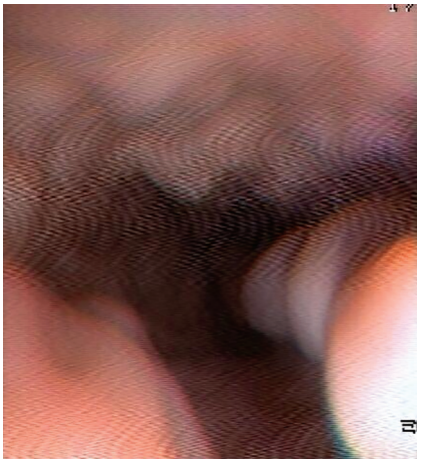
Three patients developed hepatocellular carcinoma during the first 3 years of follow-up and all died 6–11 months from the time of diagnosis. Fifteen patients showed hemorrhagic portal gastropathy at endoscopy and they were managed conservatively with proton pump inhibitors, inderal and others; three patients died of bleeding attacks complicated with shock and hepatorenal failure. There was no statistically significant

Photo 5



Recurrent varices 3 years after transabdominal gastroesophageal devascularization and esophageal transection (TAGEDET).

Photo 6



Recurrent varices 3 years after transabdominal gastroesophageal devascularization (TAGED).

Table 4 Late morbidity

Late morbidity	Group I (*n* = 32) [*n* (%)]	Group II (*n* = 83) [*n* (%)]	*P* value
Recurrent esophageal varices (at last endoscopy)			
Grade I and II	2 (6.2)	13 (15.6)	0.02
Grade III and IV	0 (0)	7 (8.4)	
Liver cell failure	4 (12.5)	11 (13.2)	0.59
Hepatocellular carcinoma	1 (3.1)	2 (6.2)	0.62
Portal gastropathy	5 (15.5)	10 (12)	0.4
Anastomotic stricture	2 (6.2)	—	—
Incisional hernia	11 (34.3)	26 (31.3)	0.75

Table 5 Risk factors for late mortality

Risk factors	Late mortality [*n* (%)]	*P* value
Child classification		
Child A (*n* = 39)	1 (5.1)	0.002
Child B (*n* = 46)	3 (10.8)	
Child C (*n* = 30)	8 (50)	
Timing of surgery		
Emergency (*n* = 12)	2 (16.6)	0.45
Semielective (*n* = 103)	10 (9.7)	
Type of operation		
TAGEDET (*n* = 32)	3 (9.3)	0.81
TAGED (*n* = 83)	9 (10.8)	

TAGED, transabdominal gastroesophageal devascularization; TAGEDET, transabdominal gastroesophageal devascularization and esophageal transection.

difference between the two groups regarding the incidence of both hepatocellular carcinoma and portal gastropathy.

Two patients developed stricture at the anastomosis in group I. Both of them underwent endoscopic dilatation and did well with repeated sessions.

Thirty-seven (32.1%) patients developed incisional hernia at the sites of laparotomies but only 23 (20%) patients underwent hernioplasty. It is worth mentioning that 57 (49.5%) patients had associated paraumbilical hernias and 29 (25%) patients had associated inguinal hernias on first presentation.

The late mortality from 30 days to 3 years postoperatively was represented by 12 (10.4%) patients. Mortality was statistically not affected by the time of surgery or the type of operation performed but it had a very strong correlation with Child classification of the patients (Table 5). The overall mortality, early and late postoperative mortality, was represented by 18 (15.6%) patients.

Discussion

Patients in whom endotherapy has failed will eventually resort to second-line salvage treatment in the form of surgery for immediate and long-term control of variceal bleeding. The modified Sugiura procedure is among the most favored emergency surgical procedures because of a low rate of encephalopathy and variceal rebleeding. Yet, controversies exist regarding its long-term results [6,7]. In this study, we tried to compare the short-term and long-term results of the two procedures, TAGEDET and TAGED.

There were no differences in demographic, clinical, and investigative data between the two groups; this ensures absence of bias in either group.

In our study, endotherapy together with pharmacotherapy achieved a success rate of about 85% in controlling bleeding varices, which correlates well with the figures recorded by many studies [1,8–13].

It was not surprising that operative time was longer in group I than in group II because of the extra time needed to apply the stapler and close the gastrotomy. Also the hospital stay is longer in group I because of the additional time required for the patients to return to a traditional diet after the stapling procedure and as we tried to delay the discharge endoscopy as needed to ensure sound healing of the staple line.

Encephalopathy, subphrenic collections, and subsequently early mortality were more common among emergency patients than among semielective ones. This may be attributed to many factors such as the injurious effect of the preoperative shock, the effect of the blood in the intestine, inadequacy of sterilization measures in the emergency unit, and the lack of good preoperative preparation of the patient under emergency conditions.

The incidence of early bleeding, residual varices, and recurrent varices was lower in group I than in group II. Moreover, residual and recurrent varices that occurred in group I were of grade I and II, which rarely bleed and are usually managed conservatively, a fact that proves that adding esophageal stapling to the devascularization procedure adds more control of the variceal bleeding both in the short and long term. This disagrees with the results of many studies [14–17] that concluded that esophageal stapler transection is not mandatory in the performance of the modified devascularization procedure and that residual intramural varices can be safely obliterated with combined endotherapy (1–2 sessions only) and propranolol.

The incidence of esophageal stapling-related complications was minimum. Leakage occurred in one (3.1%) case, and bleeding from the stapling line also occurred in one (3.1%) case; both stopped spontaneously on conservative measures. Anastomosis

stricture occurred in two (6.2%) cases and responded to endoscopic dilatation. These figures are lower than those recorded by many studies. Leakage from anastomosis was seen in 6–22% of cases [7,18–22], bleeding from the anastomosis line was as high as 50% [11,21], and stricture was seen in 10–28% of cases [19,22–24]. This may be due to the improvement in the quality of new generations of circular staplers and because of the greater experience of surgeons in the use of staplers.

There was no significant difference in the incidence of other morbidities such as encephalopathy, subphrenic abscess, incisional hernias, and portal gastropathy between group I and group II. Also, there was no significant difference in both early and late mortalities between the two groups. These previous data ensure the relative safety of the esophageal stapling procedure and its little impact on patients' morbidity and mortality.

Child classification of the patient appears to be the most important prognostic factor determining both early and late mortality.

Conclusion

Adding esophageal stapling to the devascularization operation improves both short-term and long-term control of bleeding varices without significant increase in morbidity and mortality.

Recommendation

We recommend repetition of this study on a larger number of patients in multiple surgical centers and gathering of data to conduct a meta-analytic study that can establish surgical guidelines for management of bleeding gastroesophageal varices, which are the nightmare of patients with portal hypertension.

Acknowledgements

Conflicts of interest

None declared.

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Single-incision transperineal repair of simple and recurrent rectovaginal fistula with a vital bulbocavernosus muscle flap

Tamer Youssef[a], Rafik Barakat[b], Mohamed Farid[c]

Departments of [a]Surgery, [b]Gynecology and Obstatrics, [c]General and Colorectal Surgery, Mansoura Faculty of Medicine, Mansoura University Hospital, Mansoura University, Mansoura, Egypt

Correspondance to Tamer Youssef, MD, Department of General and Endocrine Surgery, Mansoura Faculty of Medicine, Mansoura University Hospital, Mansoura University, Gomhoria st., Mansoura, Egypt
Tel: +20 050 2304344; fax: +20 050 2267016; e-mail: tamyousif@yahoo.com

Received 10 December 2014
Accepted 29 December 2014

The Egyptian Journal of Surgery
2015, 34:64–69

Background
Rectovaginal fistulas (RVFs) are abnormal epithelium-lined connections between the rectum and the vagina. RVFs may be simple or complex. This study analyzed the outcome of single-incision transperineal repair of simple RVFs with a vital bulbocavernosus muscle flap.

Patients and methods
A total of 11 consecutive patients with simple and recurrent RVFs were included and assigned to single-incision transperineal repair with a vital bulbocavernosus muscle flap. Postoperatively, patients were followed up at the outpatient clinic or through telephone interviews with specific questionnaires to collect information on the status of fecal control, flatus, or fecal leakage from the vagina, and on the quality of personal and social life. Functional results were evaluated after 6 months by means of anal manometry and a questionnaire reflecting the symptomatic results, Wexner Incontinence Score and the Female Sexual Functional Index.

Results
The mean hospital stay was 10.37 ± 1.12 days. The mean follow-up period was 8.81 ± 2.56 months. The results of mean anal pressure measurements postoperatively showed no significant differences compared with preoperative measurements. The results of preoperative and postoperative Wexner Incontinence scores and Female Sexual Function Indices showed high significant postoperative improvements in all patients ($P = 0.001$). By the time of the last follow-up, there was no recurrence of RVF, and all patients reported normal fecal continence and had returned to a normal life.

Conclusion
Although RVF is troublesome for surgeons, it can be cured using our procedure. It seems that this technique is both simple and effective, giving excellent anatomical and functional results without the need for a protecting stoma.

Keywords:
bulbocavernosus muscle flap, rectovaginal fistula, recurrent rectovaginal fistula

Egyptian J Surgery 34:64–69

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Introduction

Rectovaginal fistulas (RVFs) are abnormal epithelium-lined connections between the rectum and vagina, being uncommon and accounting for only 5% of anal rectal fistulas [1]. They can be quite bothersome to both the patient and the surgeon because of their irritating and embarrassing symptoms and high failure rate after repair. RVFs can be the result of congenital malformations or acquired etiologies. Acquired RVFs may be caused by prolonged labor, with necrosis of the rectovaginal septum, obstetric injury with a third-degree or fourth-degree perineal tear, or due to episiotomy [2]. Cryptoglandular anorectal abscesses and Bartholin gland infections may spontaneously drain causing a low RVF [3]. Inflammatory bowel disease, diverticular disease, tuberculosis, lymphogranuloma venereum, radiation therapy, and malignancy have also been reported [4].

RVFs are classified on the basis of location, size, and etiology into simple and complex fistulas, which affects the treatment plan and prognosis [5,6]. Simple RVFs consist of small or medium, low or mid-zonal fistulas secondary to infection or trauma [7]. RVFs are considered complex if they are large, high, recurrent, or caused by inflammatory bowel disease. Small-sized fistulas are less than 0.5 cm in diameter, medium-sized fistulas are 0.5–2.5 cm, and large-sized fistulas exceed 2.5 cm. Low and mid-zonal RVFs are located between the lower-third of the rectum and the lower-half of the vagina, whereas high fistulas occur between the middle-third of the rectum and the posterior vaginal fornix [8,9]. Low fistulas generally have healthy, well-vascularized surrounding tissue, which can be repaired with local perianal techniques [7].

To provide the best chance of successful repair, healthy, well-vascularized tissue needs to be introduced after resection of diseased tissue [8,9]. In simple RVFs, rectal advancement flaps (RAF) are the most popular transanal procedures among colorectal surgeons [10,11]. Two newer approaches have been introduced: one approach

involves the use of a bioprosthetic fistula plug made from porcine intestinal submucosa (Anal Fistula Plug; Cook Surgical Inc., Bloomington, Indiana, USA) [12]; the second recently popularized surgical treatment is coined ligation of intersphincteric fistula tract [13]. A bulbocavernosus flap is a versatile flap for repair of simple vaginal fistulas. An anteriorly based flap is good for urogenital fistulas and a posteriorly based flap for RVFs [10].

In complex RVFs, abdominal resection procedures or tissue interposition techniques are used. Tissue interposition using a perineal approach includes a labial fat pad, bulbocavernous muscle, and pedicled muscle flaps (rectus, sartorius, and gluteal muscles), as well as bioprosthetic materials [14].

In our research, a single-incision transperineal repair with a left posteriorly based bulbocavernosus muscle flap, through the same incision, was applied on 11 cases of simple RVF.

Patients and methods

The potential study population comprised 16 patients with RVFs referred to our General and Colorectal Surgery Unit, Mansoura University Hospital, from January 2010 to January 2012 with one or more of the following symptoms: passage of flatus or liquid or solid stool per vagina, a malodorous vaginal discharge, recurrent vaginitis, and or dyspareunia. Patients with Crohn's disease with active proctitis, malignant or radiation-related fistula, stricture of the anorectum, or an external sphincter defect were excluded from the study. A total of 11 patients fulfilled the study criteria. A detailed informed consent was obtained from all patients after approval from the local ethics committee.

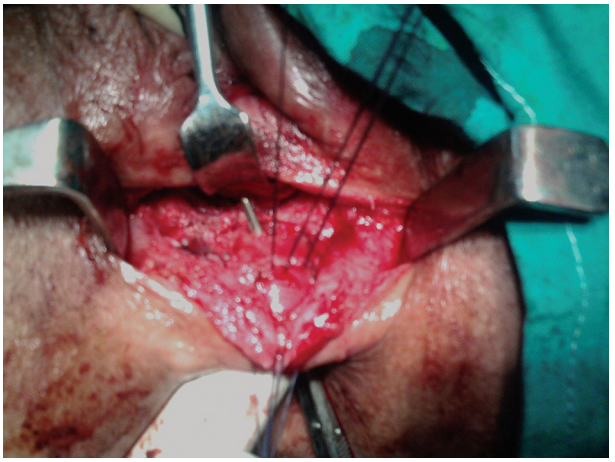
All patients were evaluated preoperatively by means of a clinical interview including the Wexner Incontinence Score (WIS) [15] and the Female Sexual Functional Index (FSFI) [16]. Anorectalmanometry using perfusion catheter systems (Synectics, Stockholm, Sweden) was performed on all patients for evaluating the mean anal resting pressure, mean anal squeezing pressure, and rectoanal inhibitory reflex.

Patients were given a mechanical bowel preparation the day before surgery, and an enema of sorbitol was administrated on the morning of the operation. The patient was placed in the lithotomy position under general anesthesia. Antibiotics in the form of third-generation cephalosporin and 500 mg of Metronidazole (Baxter, Deerfield, Illinois, USA) were given.

Submucosallidocain 5% in adrenalized saline at a ratio of 1 : 200 000 was injected around the fistula at the vaginal and rectal sides. Surgical excision of the fistula without the use of diathermy using scalpel number 15 was performed. Biopsies of rectal mucosa and the fistula margin were also obtained for pathological evaluation to exclude an underlying active IBD or malignancy. A transverse perineal incision was done with elevation of the posterior vaginal wall until the cervical uteri. Dissection of the internal sphincter fibers away from the external sphincter fibers was performed, allowing a tension-free rectal closure at the fistulous site (Fig. 1). Closure of the fistulous opening at the rectal side was done using Vicryl 3/0 sutures (Vicryl; Ethicon, Somerville, New Jersey, USA). This was followed by suturing of the rectovaginal septum to the internal sphincteric fibers using Vicryl 3/0 sutures (Fig. 2). The bulbocavernous muscle flap was harvested from the left side in all patients at its anterior part, preserving the posteroexternal vascular pedicle (Fig. 3), through the same incision, and sutured across the rectum to its counterpart on the other side (Fig. 4) using 2/0 Vicryl sutures. The vaginal flap was advanced at the fistula site and sutured to the perineal skin using Vicryl 3/0 sutures (Fig. 5). No suction drain was used. No covering stoma was done. Postoperatively, oral intake was restricted to intravenous fluids for 5 days, followed by clear oral fluids for another 5 days, with gradual return to food intake. Meanwhile, patients abstained from vaginal intercourse for 3 months.

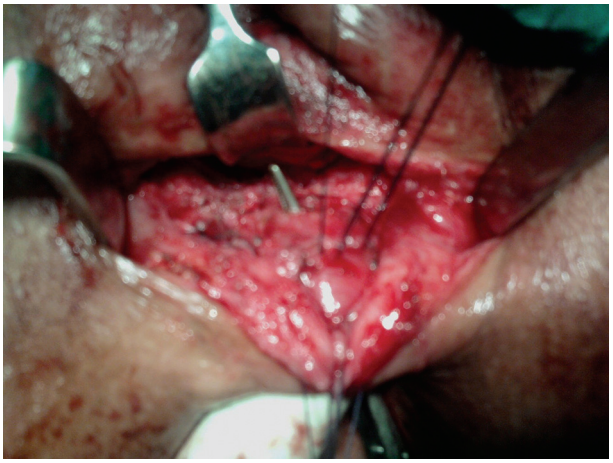
Postoperatively, patients were followed up at the outpatient clinic or through telephone interviews with specific questionnaires to collect information on the status of fecal control, flatus, or fecal leakage

Figure 1



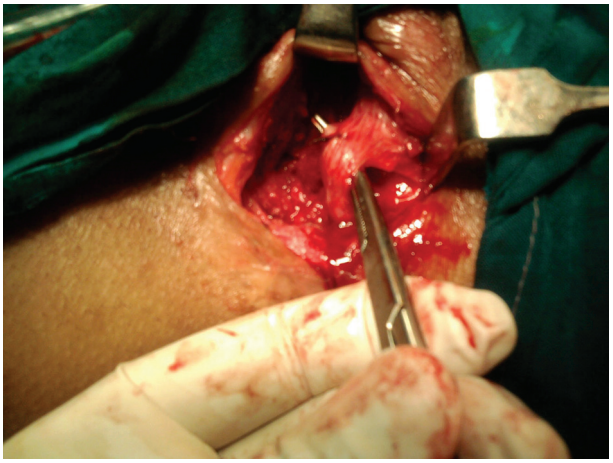
Dissection of internal sphincter fibers from external sphincter fibers.

Figure 2



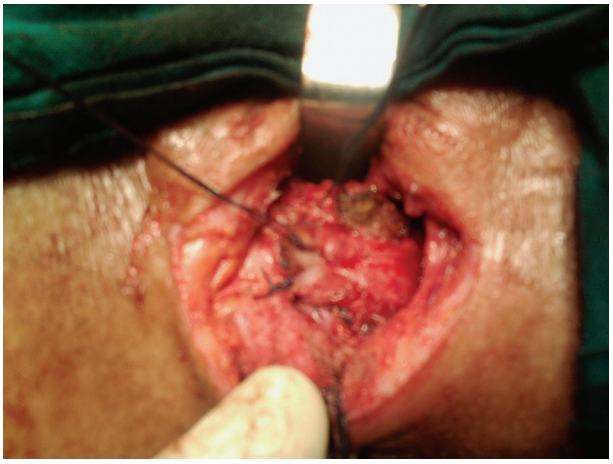
Suturing of internal sphincter fibers to the rectovaginal septum.

Figure 3



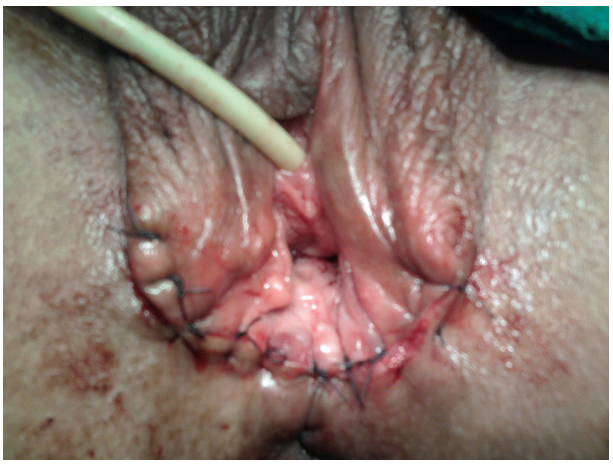
Preparation of the bulbocavernosus flap.

Figure 4



Posterior muscle repair.

Figure 5



Vaginal advancement flap.

from the vagina, and on the quality of personal and social life. The interview was scheduled twice a month for the first 3 months, followed by once a month for 6 months. Functional results were evaluated after 6 months by means of anal manometry and a questionnaire reflecting the symptomatic results, involving both the WIS and the FSFI.

Success was defined clinically by the absence of any vaginal passage of feces, flatus, or mucous discharge.

Statistical analysis

The statistical analysis of the data in this study was performed using SPSS version 10 under windows XP (SPSS incorporation, Chicago, USA). The tests used were the arithmetic mean (average) and standard deviation, and the Student *t*-test ($P < 0.05$ was considered significant).

Results

The mean age of the patients was 31.26 ± 3.927 years (range 26–40). The etiologies of RVFs are shown in Table 1. Two of the 11 patients underwent two trials for RVF surgical repair. All patients had symptoms of passage of flatus or liquid or solid stool through the vagina and/or signs of vaginitis. Openings of the fistula were all located above the anal sphincter and varied between 5 and 25 mm in diameter. The preoperative mean anal resting pressure, mean anal squeezing pressure, and rectoanal inhibitory reflex were normal in all patients.

Symptoms occurring after the surgery included discomfort in the anus in all patients, tenesmus without diarrhea in three patients, and sensation of incomplete defecation in two patients. Mean hospital stay was 10.36 ± 1.12 days (range 9–12). All symptoms

Table 1 Patient characteristics and follow-up data of 11 patients

Patient's number	Age (years)	Multiparous	Etiology	Stoma	Previous repair	Follow-up (months)
1	29	Yes	Prolonged labor	No	No	7
2	32	Yes	Iatrogenic injury during rectocele repair	No	No	9
3	28	Yes	Iatrogenic injury during episiotomy	No	No	6
4	33	Yes	Prolonged labor	No	No	9
5	27	Yes	Iatrogenic injury during rectocele repair	No	No	6
6	34	Yes	Prolonged labor	No	No	9
7	40	Yes	Prolonged labor	No	No	6
8	32	Yes	Iatrogenic injury during episiotomy	No	No	10
9	33	Yes	Failed previous RVF repair	No	2	14
10	26	No	Failed previous RVF repair	No	2	12
11	30	Yes	Prolonged labor	No	No	9

RVF, rectovaginal fistula.

spontaneously disappeared within 2 weeks after surgery. Wound swelling was seen in three patients on the third postoperative day, which was caused by hematoma in one patient and infection in two patients. However, there was no incision disruption and all surgical wounds healed within 21 days after surgery. No postoperative mortality was seen.

Mean follow-up was 8.81 ± 2.56 months (range 6–14). Patients were followed up in the clinic or by telephone interview with specific questionnaires to collect information on the status of fecal control, flatus or fecal leakage from the vagina, and the quality of personal and social life. The interview was scheduled twice a month for the first 3 months, followed by once a month for 6 months. Functional results were evaluated after 6 months by means of anal manometry and a questionnaire reflecting the symptomatic results involving both the WIS and the FSFI. Two patients complained of mild dyspareunia, which required no further surgical management.

The results of the mean postoperative anal pressure measurements showed no significant differences compared with preoperative measurements (Table 2). The results of preoperative and postoperative WIS showed high significant postoperative improvements in all patients (P = 0.001) (Table 3). The results of preoperative and postoperative female sexual function indices showed high significant postoperative improvements in all patients (P = 0.001) (Table 3). By the time of the last follow-up, there was no recurrence of RVF, and all patients reported normal fecal continence and had returned to a normal life.

Discussion

Fistulas between the rectum and vagina are generally debilitating and often resistant to repeated repair procedures. The management of RVFs depends on the size, location, and cause of the fistula, on anal sphincter function, on the overall health of the patient, as well as on the skill and judgment of the surgeon [2,5,6].

Various surgical procedures have been suggested for the repair of these fistulas, including fecal diversion, primary repair, endorectal advancement flap, transvaginal repair, coloanal sleeve anastomosis, and transposition flaps [17,18]. The relative rarity of this type of fistula makes prospective studies and randomized controlled trials difficult to carry out.

Careful preoperative assessment of the fistula, the surrounding tissue, and the anal sphincter, and exclusion of associated disease, is essential. Timing of repair is also of importance. The chances of success are increased if the surrounding tissue is in optimal condition – that is, not inflamed or infected. A rest period of 3–6 months is suggested by some authors [19].

More importantly, underlying disorders such as IBD or tumor should also be diagnosed at the same time because these conditions can lead to repeated failure of a correct surgical procedure. Therefore, biopsy of the mucosa from the rectum or from the margin of the fistula, pelvic CT, and colonoscopy should be considered compulsory before surgical repair [2,3].

Noble first described the use of a sliding flap for repair of an RVF in 1902, and in 1983 Farkas and Gingold [20] described the first case of a RAF for RVF in Crohn's disease. The advantages of the flap procedure are as follows: absence of a perineal wound and of keyhole deformity; no worsening of incontinence; no aggravation of patients' symptoms in case of failure; and lack of requirement of a stoma [21].

The reported success rate of the RAF technique to repair RVFs in different series ranges from 29% in a mixed group of patients with both simple and complex fistulas after varying numbers of previous repair attempts to as high as 88% in patients with simple fistulas who had

Table 2 Comparison between preoperative and postoperative motility studies changes in our patients

Variables	Preoperative	Postoperative	*P* value
MARP	62.45 ± 2.20	62.81 ± 2.13	Nonsignificant
MASP	121.45 ± 3.45	121.36 ± 2.83	Nonsignificant

MARP, mean anal resting pressure; MASP, mean anal squeezing pressure.

Table 3 Comparison between preoperative and postoperative Wexner Incontinence Score and Female Sexual Functional Index changes in our patients

Variables	Preoperative	Postoperative	*P* value
MARP	20	0.91 ± 1.45	0.0001
MASP	13.07 ± 2.33	27.08 ± 2.50	0.0001

MARP, mean anal resting pressure; MASP, mean anal squeezing pressure.

an advancement flap as their primary procedure [18]. The success rate decreases with repeated attempts at repair. Successful repair correlates with the number of previous repairs – that is, none, 88% success; one, 85% success; two, 55% success [22].

A RAF is preferred whenever feasible because the flap is created on the high-pressure anorectal side of the fistula rather than on the low-pressure vaginal side [23].

In our study, transperineal combined rectal and vaginal advancement flaps with an intervening vital bulbocavernosus muscle flap were accomplished. Its use is based on the hypothesis that the interposition of tissue between the sutures lines will result in enhanced blood supply to the devascularized epithelium, obliteration of dead space, and the interruption of suture lines along the length of the multilayer closure. Furthermore, the flap interposition prevents vaginal stenosis.

Certain basic principles should be followed, including excision of the epithelialized tract, complete closure of the rectal opening, inversion of the rectal edges, adequate tissue mobilization, hemostasis, and tension-free multilayer closure.

As the described fistulas were located in the lower-half of the vagina, we decided, in consultation with the patients and as per their request, not to perform a protecting stoma. If the fistula is located in the upper-third of the vagina it may be prudent or even essential to divert the fecal contents by means of a temporary ileostomy or colostomy.

Rates of healing reported after other procedures appear to be lower. The Musset technique obtained good initial results in 87–100% of patients but with the risk for anal incontinence owing to the sphincterotomy required for this procedure [8]. RAF alone, which avoids direct anal sphincter damage, resulted in a healing rate of 80% of patients [12]. Repairing fistulas in patients with Crohn's disease has a lower success rate, which ranges from 50 to 70% [13]. We have successfully cured all of our patients without any significant morbidity, apart from two patients who experienced mild dyspareunia, for whom further treatment was not needed. Neither fecal incontinence nor recurrence was found during the time of follow-up.

Our success can be attributed to the following reasons. The etiology of fistulas in our patients was relatively simple, which may have contributed to the excellent outcome in these patients. Interposing a healthy and well-vascularized tissue avoids direct apposition of two suture lines and introduces well-vascularized tissue to the area. Understanding the anatomy of the rectum, anus, and pelvic floor, and the meticulous dissections, without diathermy, for protecting the blood vessel of the pedicle, is essential for successful repair.

Conclusion

Although RVFs are problematic for surgeons, they can be cured using our procedure. Despite the small patient cohort in this series, this technique seems to be both simple and effective, giving excellent anatomical and functional results without the need for a protecting stoma.

Acknowledgements

Conflicts of interest

None declared.

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