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Table of contents

Original articles

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Elevated serum bilirubin as a preoperative specific predictor for complicated appendicitis in children

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Objective
The aim of the study was to evaluate the diagnostic yield of preoperative high serum total bilirubin (TB) for cases of appendicitis in conjunction with clinical and other laboratory findings.

Patients and methods
The current study included 417 children presenting with right iliac fossa pain. All patients underwent clinical examination and gave blood sample on admission for estimation of serum TB and C-reactive protein (CRP) and total leukocytic count (TLC) and underwent surgical exploration and management according to operative findings.

Results
Surgical exploration defined 134 cases of complicated appendicitis (CA), 219 cases of simple appendicitis, and 64 cases of noninflamed appendix. Mean preoperative TLC and serum CRP showed high sensitivity (88.7 and 83.6%, respectively) for detection of acute appendicitis (AA), despite the lower specificity of CRP for diagnosis (57.8%), whereas the specificity rate of elevated TLC was 71.9%. For discrimination between simple appendicitis and CA, elevated serum CRP showed higher specificity compared with elevated TLC (70.3 vs. 65.8%) despite the higher sensitivity of elevated TLC compared with elevated serum CRP (91.8 vs. 80.6%). Serum TB showed the highest specificity rate for defining cases of AA and CA (79.7 and 86.3%, respectively) despite the low sensitivity for both. Receiver operating characteristic curve analysis defined the severity of rebound tenderness in the form of significant, sensitive, and elevated TLC as the most significant specific predictor for AA. Serum TB greater than 1 mg/dl was the most significant specific predictor for the diagnosis of CA.

Conclusion
Combined estimation of TLC and serum CRP and TB improves the diagnostic yield by combining the high sensitivity of TLC and CRP with the high specificity of TB, allowing early detection of cases that could develop CA and enabling better decision for patient discharge.

Keywords:
appendicitis, C-reactive protein, preoperative serum total bilirubin, total leukocytic count

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Introduction

Appendicitis represents one of the most common causes of abdominal pain among patients referred to the emergency department, and appendicectomy is one of the most frequent surgical interventions reported in hospitals, with worldwide prevalence. However, the diagnosis of appendicitis may be elusive and fraught with pitfalls because of the absence of a pathognomonic sign or symptom, the poor predictive value of associated laboratory testing, and its varied presentation at diagnosis [1–4].

The rate of negative appendicectomy still imposes a burden on health service resources, and, despite the extraordinary advances in modern radiography imaging and diagnostic laboratory investigations, the accurate diagnosis of acute appendicitis (AA) remains an enigmatic challenge. Although there are various diagnostic aids for appendicitis, no single test can reduce the rate of negative appendicectomy to zero [5–7].

The role of inflammatory markers for diagnosis of AA or for anticipation of the presence of complications is still a matter of debate. Sengupta *et al.* [8] suggested that patients experiencing lower abdominal pain, with normal white cell count and C-reactive protein (CRP) values, are unlikely to have AA and can be safely sent home. In contrast, Monneuse *et al.* [9] documented that the diagnosis of AA cannot be excluded when the patient presents with isolated rebound tenderness in the right lower quadrant even without fever and biological inflammatory signs. Vaughan-Shaw *et al.* [10] found that appendicitis in the presence of normal inflammatory markers is not uncommon and disagreed with the view of Sengupta *et al.* [8], who suggested that patients with normal white cell count and CRP are unlikely to have appendicitis, and recommended that clinicians be wary of normal inflammatory markers in patients with a high clinical suspicion of appendicitis.

The development of jaundice in sepsis is well recognized and has been associated with a variety

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of causative bacteria, with Gram-negative bacteria being most commonly implicated. Jaundice has been associated with appendicitis and studies have shown hyperbilirubinemia to be a useful predictor of appendiceal perforation [11,12]. However, these studies did not focus on the value of bilirubin as a marker for AA. Thus, the current prospective study aimed to evaluate the diagnostic yield of preoperative high serum total bilirubin (TB) for cases of appendicitis in conjunction with clinical and other laboratory findings.

Patients and methods

The current prospective study was conducted at Departments of General Surgery and Pediatrics, Al-Jafel Hospital (KSA) from July 2007 to October 2013. After obtaining approval from the local ethical committee for the study protocol and after obtaining fully informed written parents' consent, all patients presenting to the emergency department with right iliac fossa (RIF) pain were included in the study. Demographic and disease-related data were obtained from all patients. All of them underwent clinical examination for evaluation of other associated symptoms: temperature at the time of admission for categorization of patients according to a temperature cutoff point of 38.5°C; occurrence of vomiting, dysuria, diarrhea or bowel disturbances; clinical signs including the presence and severity of rebound tenderness, which was graded as light, moderate, or severe rebound tenderness; and presence of pain radiation and/or muscle guarding. All patients gave blood samples on admission to the emergency department for estimation of serum CRP and TB, for total leukocytic count (TLC), and for determination of the percentage of polymorphonuclear leukocytes. All laboratory investigations were conducted at the hospital laboratory. Thereafter, all patients underwent surgical exploration and management according to operative findings. Excised specimens were examined histopathologically for defining the extent of inflammation if present.

Statistical analysis

The obtained data were presented as mean ± SD, ranges, numbers, and ratios. The sensitivity and specificity of the estimated parameters as predictors were evaluated using the receiver operating characteristic (ROC) curve analysis judged by the area under the curve (AUC) compared with the null hypothesis that AUC = 0.05. Regression analysis (stepwise method) was used for stratification of the studied parameters as specific predictors. Statistical analysis was conducted using the SPSS (version 15, 2006; SPSS Inc., Chicago, Illinois, USA) for Windows statistical package. A *P* value less than 0.05 was considered statistically significant.

Results

The current study included 417 patients, 188 (45.1%) boys and 229 (54.9%) girls, presenting to the emergency department with pain in the RIF since a mean duration of 10.4 ± 3.1 h (range 2–18 h). The mean age of the enrolled patients was 10.7 ± 3 years (range 5–15 years); however, the majority of patients (246 patients; 59%) were older than 10 years. Vomiting was the most common presenting symptom other than pain and was reported in 139 (33.3%) patients, whereas 85 (20.4%) patients had dysuria and 55 (13.2%) patients had diarrhea. A total of 163 (39.1%) patients had temperature higher than 38.5°C. All patients had rebound tenderness of varying severity; 136 (32.6%) patients had light and 123 (29.5%) patients had medium rebound tenderness, whereas 158 (37.9%) patients had strong rebound tenderness with muscle guarding. Pain radiation was documented by 189 (45.3%) patients (Table 1).

Thirty patients had an appendicular mass that could not be mobilized and was drained for a second

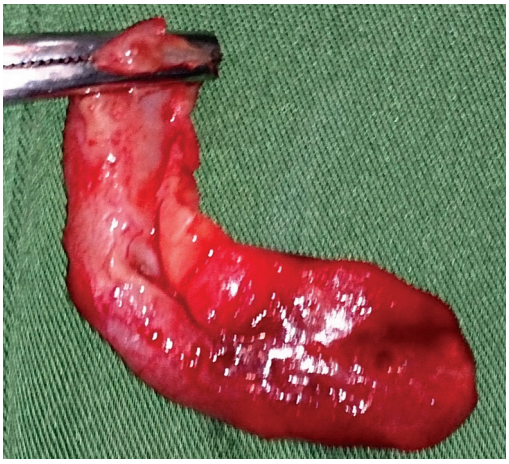
Table 1 Demographic and disease-related data

Data	Findings
Age (years)	
Strata	
<10	
N (%)	171 (41)
Mean	7.4 ± 1.2 (5–10)
>10	
N (%)	246 (59)
Mean	13 ± 1.2 (11–15)
Total	10.7 ± 3 (5–15)
Sex	
Males	188 (45.1)
Females	229 (54.9)
Duration of disease (h)	10.4 ± 3.1 (2–18)
Other presenting symptoms	
Vomiting	139 (33.3)
Diarrhea	55 (13.2)
Dysuria	85 (20.4)
Clinical signs	
Temperature (°C)	
<38.5	254 (60.9)
>38.5	163 (39.1)
Rebound tenderness	
Light	136 (32.6)
Medium	123 (29.5)
Strong	158 (37.9)
Pain radiation	189 (45.3)

Data are presented as mean ± SD and numbers; ranges and percentage are given in parenthesis.

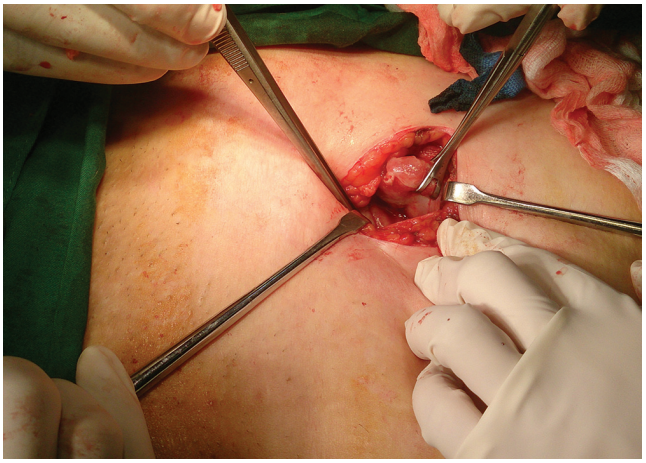
setting later on. Another 56 patients had a localized appendicular abscess that was drained; the appendix was found to have a thick edematous fragile wall but with a healthy base, thus allowing appendicectomy, and the stump was covered by an omental patch and the wound was drained. Forty cases had a localized appendicular abscess that was drained, but unfortunately exploration of its contents was not possible and appendicectomy was hazardous and thus postponed. Eight cases had generalized peritonitis, which was drained after peritoneal toilet, and appendicectomy was postponed. These 134 cases were collectively considered as complicated appendicitis (CA) (Figs. 1–3). The remaining 283 cases had a smooth intraoperative course with an uneventful outcome (Fig. 4). Histopathological examination of excised specimens (n = 339) revealed a noninflamed appendix in 64 (15.3%) patients (negative outcome).

Figure 1



Excised appendix with gangrenous spots in its tip.

Figure 3

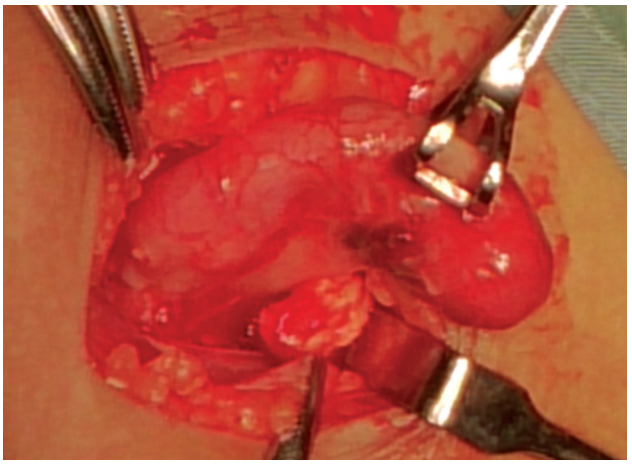


The appendix could not be delivered out of the wound and was bluntly dissected; the appendix had a healthy base and thus facilitated in-situ appendectomy.

Eighty-seven specimens showed inflammation with cellular infiltrate extending through the full thickness of the wall, and 132 specimens showed inflammation with cellular infiltrate not extending through the full thickness of the wall; these 219 cases were collectively considered as simple appendicitis (SA). Fifty-six specimens showed inflammation with cellular infiltrate extending through the full thickness of the wall, with endarteritis obliterans in the mesoappendiceal vessels with necrotic spots and minor perforations in some specimens. These specimens were considered as CA (Table 2).

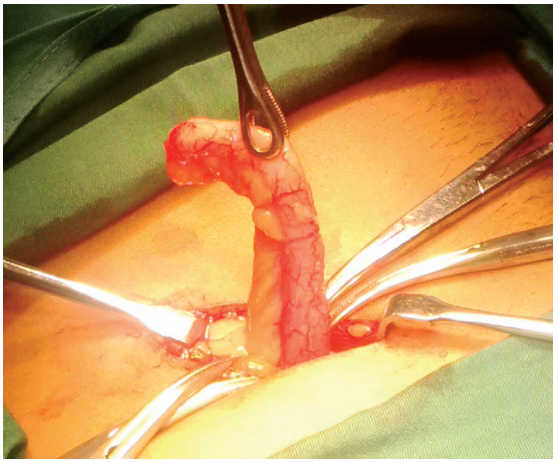
The mean preoperative TLC was 11.5 ± 2.6 (range 4.3–17.3 × 10^3 cells/ml); 87 (20.9%) patients had TLC less than 10 000 cells/ml, 282 (67.6%) had TLC in the range of 10 000–14 900 cells/ml, and 48 (11.5%) had

Figure 2



Appendix delivered out of the wound; the appendix was edematous with multiple spots of perforated gangrenous sites on the mesenteric side near the tip. The appendix appeared congested with a thickened inflamed mesoappendix.

Figure 4



The appendix was delivered out of the wound and appeared mildly inflamed with a normal-appearing mesoappendix.

TLC greater than 15 000 cells/ml (Fig. 5). The mean preoperative serum CRP level was 21.1±13 (range 4–63 g/l); 95 (22.7%) patients had a mean serum CRP less than 10 g/l, 298 (71.5%) patients had a serum CRP level in the range of 10–49 g/l, and 24 (5.8%) patients had a mean serum CRP level greater than or equal to 50 mg/l (Fig. 6). The mean preoperative serum TB was 1.32 ± 0.55 (range 0.54–2.31 mg/dl); 162 (38.8%) patients had a mean serum TB less than 1 mg/dl and 255 (61.2%) patients had a mean serum TB greater than 1 mg/dl (Table 3 and Fig. 7).

Evaluation of the test validity characteristics of the estimated laboratory parameters for exclusion of AA among patients presenting with RIF pain showed high sensitivity and

Table 2 Operative findings and histopathological diagnosis

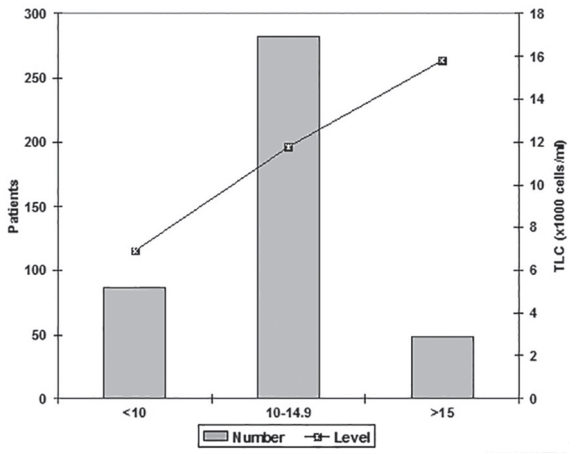
Data	*N* (%)
Negative appendicectomy (noninflamed appendix)	64 (15.3)
Simple appendicitis	
Full-thickness inflammatory infiltrate	87 (20.9)
Partial-thickness inflammatory infiltrate	132 (31.7)
Complicated appendicitis	
Mass	30 (7.2)
Localized abscess including resectable appendix	56 (13.4)
Localized abscess including unresectable appendix	40 (9.6)
Generalized peritonitis	8 (1.9)

Table 3 Laboratory data of the studied patients

Parameters	Frequency [*n* (%)]	Value
TLC (10^3 cells/ml)		
Strata		
<10	87 (20.9)	6.9 ± 0.9 (4.3–8.9)
10–14.9	282 (67.6)	11.8 ± 1.6 (10.3–14.9)
>15	48 (11.5)	15.8 ± 0.6 (15.2–17.3)
Total	417 (100)	11.5 ± 2.6 (4.3–17.3)
PNL%		
Strata		
70–84%	162 (38.8)	11 ± 3 (5.1–17.3)
85%	255 (61.2)	9.3 ± 2.5 (4.3–12.9)
Total	417 (100)	
Serum CRP (g/l)		
Strata		
<10	95 (22.7)	6.9 ± 1.1 (4–9)
10–49	298 (71.5)	22 ± 8.6 (12–49)
≥50	24 (5.8)	56.8 ± 3.1 (52–63)
Total	417 (100)	21.1 ± 13 (4–63)
Serum TB (mg/dl)		
Strata		
<1	162 (38.8)	0.72 ± 0.08 (0.54–0.98)
>1	255 (61.2)	1.7 ± 0.34 (1.08–2.31)
Total	417 (100)	1.32 ± 0.55 (0.54–2.31)

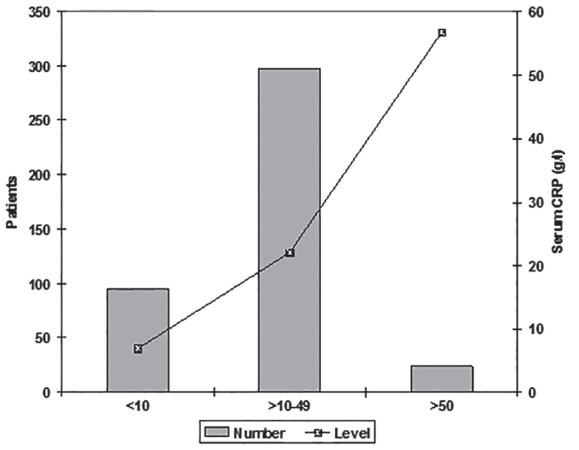
Data are presented as mean ± SD and numbers; ranges and percentages are given in parenthesis; CRP, C-reactive protein; PNL%, percentage of polymorphonuclear leukocytes; TB, total bilirubin; TLC, total leukocytic count.

Figure 5



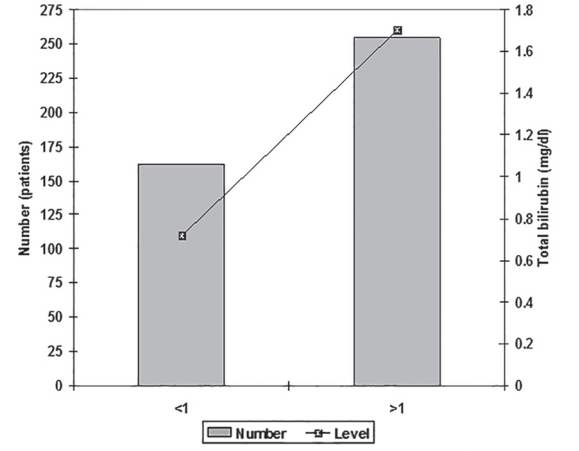
Patients' distribution according to total leukocytic count (TLC) category and mean count for each category.

Figure 6



Patients' distribution according to serum C-reactive protein (CRP) category and the mean level for each category.

Figure 7



Patients' distribution according to serum total bilirubin level and the mean level for each category.

positive predictive value for TLC and for estimation of serum CRP, whereas serum TB and TLC showed a high specificity (Fig. 8). For defining cases with probable CA, TLC showed the highest sensitivity and serum TB showed the highest specificity (Table 4 and Fig. 9).

The ROC curve analysis of the estimated laboratory parameters and clinical data defined severity of rebound tenderness as a significant (P = 0.019) sensitive predictor with AUC of 0.408 for the presence of AA, whereas occurrence of vomiting was a nonsignificant predictor for AA. Concerning laboratory data, elevated TLC was the most significant (P = 0.0003) specific predictor for AA, with AUC of 0.803, followed by high serum CRP, with AUC of 0.741, and serum TB greater than 1 mg/dl, with AUC of 0.707 (Fig. 10). For diagnosis of CA, all clinical data were nonsignificant sensitive predictors, whereas serum TB more than 1 mg/dl was found to be the most significant (P = 0.0001) specific predictor, with AUC of 0.805, followed by elevated TLC, with AUC of 0.788, and high serum CRP, with AUC of 0.755 (Table 5 and Fig. 11).

Regression analysis of the estimated laboratory parameters and clinical data defined TLC as a significant predictor for the presence of AA in three models, high serum CRP in two models, and serum TB more than 1 mg/dl in one model, whereas clinical data were nonsignificant predictors in the three models and were excluded. For diagnosis of CA, serum TB more than 1 mg/dl was the most significant predictor in four models, followed by elevated TLC in three models, elevated serum CRP in two models, and severity of rebound tenderness in one model, whereas the presence of fever and occurrence of vomiting were nonsignificant predictors in the three models and were excluded (Table 6).

Discussion

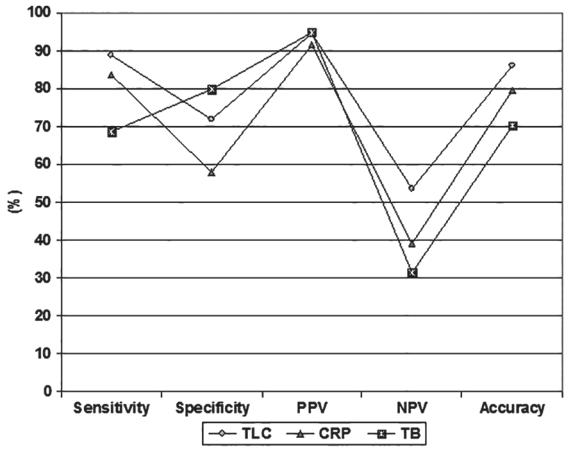
The current study detected significantly higher serum TB in patients with CA compared with those with uncomplicated SA, with significantly higher serum TB

Table 4 Test validity characters for estimated laboratory parameters

	Patients' distribution				Test validity characters (%)				
	T+	T−	F+	F−	Sensitivity	Specificity	PPV	NPV	Accuracy
Exclusion of AA (n = 417)									
TLC	313	46	18	40	88.7	71.9	94.6	53.5	86.1
CRP	295	37	27	58	83.6	57.8	91.6	38.9	79.6
TB	242	51	13	111	68.6	79.7	94.9	31.5	70.3
Defining CA (n = 353)									
TLC	123	144	75	11	91.8	65.8	62.1	92.9	75.6
CRP	108	154	65	26	80.6	70.3	62.4	85.6	74.2
TB	100	189	30	34	74.6	86.3	76.9	84.8	81.9

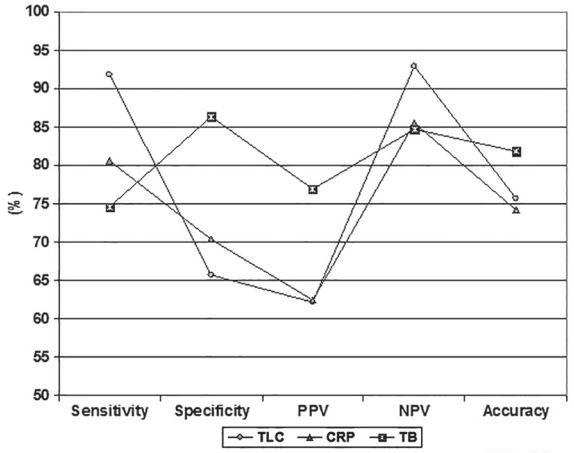
AA, acute appendicitis; CA, complicated appendicitis; CRP, C-reactive protein; F-, false negative; F+, false positive; NPV, negative predictive value; PPV, positive predictive value; T, true negative; T+, true positive; TB, total bilirubin; TLC, total leukocytic count.

Figure 8



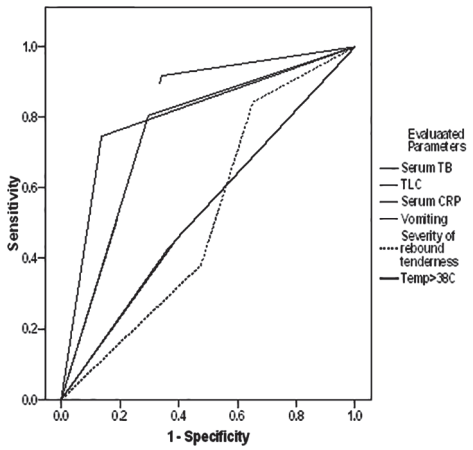
Test validity characteristics of estimated laboratory parameters for exclusion of acute appendicitis among patients with right iliac fossa pain. CRP, C-reactive protein; NPV, negative predictive value; PPV, positive predictive value; TB, total bilirubin; TLC, total leukocytic count.

Figure 9



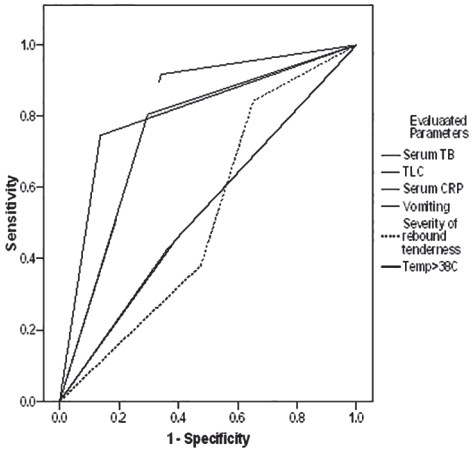
Test validity characteristics of estimated laboratory parameters for diagnosis of complicated appendicitis among patients with right iliac fossa pain. CRP, C-reactive protein; NPV, negative predictive value; PPV, positive predictive value; TB, total bilirubin; TLC, total leukocytic count.

Figure 10



Receiver operating characteristic curve analysis of clinical and laboratory data for exclusion of acute appendicitis in the studied patients. CRP, C-reactive protein; TB, total bilirubin; TLC, total leukocytic count.

Figure 11



Receiver operating characteristic curve analysis of clinical and laboratory data for the diagnosis of complicated appendicitis in the studied patients. CRP, C-reactive protein; TB, total bilirubin; TLC, total leukocytic count.

Table 5 Receiver operating characteristic curve analysis of clinical and laboratory data for exclusion of acute appendicitis and diagnosis of complicated appendicitis in the studied patients

Data	AUC	SE	Significance	95% CI	
				Lower	Upper
For exclusion of acute appendicitis					
Clinical data					
Occurrence of vomiting	0.448	0.040	0.183	0.370	0.526
Severity of rebound tenderness	0.408	0.039	0.019	0.331	0.484
Temperature >38.5°C	0.428	0.042	0.065	0.345	0.510
Laboratory data					
Serum TB	0.707	0.039	0.0009	0.631	0.783
TLC	0.803	0.035	0.0003	0.735	0.870
Serum CRP	0.741	0.033	0.0007	0.677	0.805
For diagnosis of complicated appendicitis					
Clinical data					
Occurrence of vomiting	0.532	0.032	0.308	0.470	0.595
Severity of rebound tenderness	0.519	0.031	0.545	0.459	0.580
Temperature >38.5°C	0.531	0.032	0.324	0.469	0.593
Laboratory data					
Serum TB	0.805	0.026	0.0001	0.754	0.855
TLC	0.788	0.024	0.0006	0.740	0.836
Serum CRP	0.755	0.027	0.0008	0.702	0.807

AUC, area under curve; CI, confidence interval; CRP, C-reactive protein; TB, total bilirubin; TLC, total leukocytic count; Significance: $P > 0.05$, nonsignificant; $P < 0.05$, significant.

Table 6 Regression analysis of clinical and laboratory data for exclusion of acute appendicitis and diagnosis of complicated appendicitis in the studied patients

Data	β	*t*	Significance
For exclusion of acute appendicitis			
Model 1			
TLC	0.464	12.196	0.0002
Serum CRP	0.272	7.239	0.0008
Serum TB	0.232	6.102	0.0009
Model 2			
TLC	0.505	12.935	0.0002
Serum CRP	0.298	7.935	0.0008
Model 3			
TLC	0.539	13.048	0.0001
For diagnosis of complicated appendicitis			
Model 1			
Serum TB	0.431	12.014	0.0002
TLC	0.357	9.945	0.0005
Serum CRP	0.283	7.947	0.0008
Severity of rebound tenderness	0.082	2.459	0.014
Model 2			
Serum TB	0.430	11.918	0.0003
TLC	0.359	9.937	0.0005
Serum CRP	0.278	7.765	0.0008
Model 3			
Serum TB	0.489	12.810	0.0002
TLC	0.418	10.936	0.0004
Model 4			
Serum TB	0.613	14.536	0.00009

β, standardized coefficient; CRP, C-reactive protein; *t*, unpaired *t*-test; TB, total bilirubin; TLC, total leukocytic count; Significance: $P > 0.05$, nonsignificant; $P < 0.05$, significant.

levels in those with SA compared with those with a noninflamed appendix. Moreover, the serum bilirubin level showed high predictability for CA among patients with AA, with high AUC on the ROC curve analysis. Regression analysis showed that elevated serum

TB was the most significant predictor in all studied statistical models, despite the low sensitivity. Moreover, low serum TB showed statistically high sensitivity as a screening test for exclusion of AA in susceptible cases of RIF pain, despite the low specificity.

These data indicate the ability of at-admission serum TB for stratification of cases of acute RIF pain and could discriminate between cases free of appendicitis and those with AA and between cases with complicated and those with SA. In line with these data, Emmanuel *et al.* [13] reported that mean TB levels were higher in patients with SA compared with those with a noninflamed appendix, with more patients with SA having hyperbilirubinemia on admission (30 vs. 12%), and that hyperbilirubinemia showed specificity of 88% and positive predictive value of 91% for AA and specificity of 70% for perforation or gangrene.

Giordano *et al.* [14] documented that hyperbilirubinemia had a sensitivity of 0.49, specificity of 0.82, positive and negative likelihood ratios of 2.51 and 0.58, and ROC curve analysis for AUC of 0.73 as a predictor of perforation in AA and concluded that patients with hyperbilirubinemia combined with symptoms and signs consistent with severe AA should be considered for early appendectomy. Burcharth *et al.* [15] reported that serum TB was significantly higher in patients with appendiceal perforation compared with patients with appendicitis without perforation and that elevated serum TB had a sensitivity ranging from 38 to 77% and a specificity ranging from 70 to 87% in predicting appendiceal perforation. They concluded that elevated serum TB has low sensitivity but higher specificity for determining the risk of perforation in appendicitis.

As regards TLC and CRP, both markers showed high sensitivity (88.7 and 83.6%, respectively) for detection of AA among cases of RIF pain despite the lower specificity of CRP for diagnosis (57.8%); the specificity rate for elevated TLC was 71.9%. For discrimination between SA and CA, elevated serum CRP showed higher specificity compared with elevated TLC (70.3 vs. 65.8%) despite the higher sensitivity of elevated TLC compared with elevated serum CRP (91.8 vs. 80.6%).

These findings are in agreement with those of Sand *et al.* [16], who found the specificity of hyperbilirubinemia for appendiceal perforation to be 86 versus 55 and 35% for TLC and CRP, respectively, whereas the sensitivity was 70% for hyperbilirubinemia compared with 81% for TLC and 96% for CRP. They concluded that patients with hyperbilirubinemia and clinical symptoms of appendicitis should be identified as having a higher probability of appendiceal perforation compared with those with normal bilirubin levels. Käser *et al.* [17] found hyperbilirubinemia to be a statistically significant marker of perforation in AA despite documenting that CRP is superior to TB for anticipation of perforation in AA.

Atahan *et al.* [18] found that assessment of preoperative TB is useful for the differential diagnosis of perforated versus suppurative AA, whereas WBC assessment is effective for diagnosing the presence versus absence of appendicitis. They concluded that symptom duration, WBC, and TB should be used as independent parameters in the early diagnosis of appendix perforation. Noh *et al.* [19] found WBC, CRP, and TB levels to be significantly higher in CA and the most sensitive markers for diagnosing CA were WBC followed by CRP, whereas bilirubin levels showed the highest specificity at 74.8%.

D'Souza *et al.* [20] reported that hyperbilirubinemia was significantly associated with appendicitis versus RIF pain of other etiologies and with perforated appendicitis versus SA and that bilirubin had a higher specificity (0.96%) compared with WBC (0.71%) and CRP (0.62%), but a lower sensitivity (0.27 vs. 0.68 and 0.82%, respectively), for the presence of appendicitis and a higher specificity (0.82%) than both WBC (0.34%) and CRP (0.21%), but a lower sensitivity, for perforated appendix. McGowan *et al.* [21] also found that the sensitivity and specificity of CRP were 78.57 and 63.01%, respectively, and that for bilirubin were 62.96 and 88.31%.

The reported increased serum levels of TB up to the level of hyperbilirubinemia indicated hepatic derangement, which could be attributed to the possibility of sepsis-induced hepatic dysfunction. Multiple studies tried to explore the underlying pathogenetic mechanisms for such an assumption; Deutschman *et al.* [22] using an animal model of cecal ligation and double puncture to induce severe sepsis simulating fecal peritonitis and intestinal gangrene found that cecal ligation and puncture induced cholestasis, steatosis, and hepatocellular injury in interleukin-6 (IL-6) –/– but not IL-6 +/+ mice and concluded that the absence of IL-6 is an important determinant of hepatic dysfunction and mortality in sepsis. Schonhoff *et al.* [23] reported that during sepsis-induced cholestasis there is a decrease in sodium-taurocholate cotransporting polypeptide-dependent uptake of bile acids and an increase in nitric oxide levels in hepatocytes. Bhogal *et al.* [24] documented that infections cause systemic and intrahepatic increase in proinflammatory cytokines, which result in impaired bile flow, and several other mediators of impairment in bile flow have been identified under conditions of

sepsis, such as increased nitric oxide production and decreased aquaporin channels. Recknagel *et al.* [25] also documented that polymicrobial sepsis produces profound hepatocellular dysfunction in the absence of traditional cytokine-mediated mechanisms of cellular injury and this questions the central role of cytokines and the ensuing oxidative stress as key molecular events in mediating liver dysfunction.

It could be concluded that no single laboratory parameter has the efficacy for discrimination between cases of AA; however, combined estimation of TLC and serum CRP and TB improves the diagnostic yield by combining the high sensitivity of TLC and CRP with the high specificity of TB, allowing early detection of cases that could develop CA and enabling better decision making for patient discharge or motivating further investigations in patients free of appendicitis.

Acknowledgements

Conflicts of interest

None declared.

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Preperitoneal versus Lichtenstein tension-free hernioplasty for the treatment of bilateral inguinal hernia

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Background
Inguinal hernia is one of the most common diseases in the surgical setting. Bilateral inguinal hernia is present in 12% of patients and its treatment has been debated for long, sequential or simultaneous repair especially after tension-free repairs. We carried out this study to compare the Stoppa procedure with bilateral Lichtenstein hernioplasty for the treatment of bilateral inguinal hernia.

Materials and Methods
The study included 40 patients with bilateral inguinal hernias who were allocated randomly to two groups. Group A included 20 patients who were operated by bilateral Lichtenstein hernioplasty. Group B also included 20 patients who were operated by Stoppa repair. Recording of preoperative data (age, sex, BMI, comorbidity, smoking, and type of hernia), operative data (operative time and operative complications) and postoperative data (complications, pain, hospital stay, return to normal daily activities, chronic groin pain, and recurrence) was performed for each patient in the study. Patients were assessed at 7 days, and 1, 6, and 12 months after the procedure at the outpatient clinic.

Results
All patients were men. There was no statistically significant difference between both groups in preoperative data. The Stoppa procedure took a significantly shorter time than bilateral Lichtenstein repair; the mean operative time for Stoppa and bilateral Lichtenstein was 39.0 ± 5.15 and 62.25 ± 7.95 min, respectively. Postoperative pain scoring using the visual analogue score at 12 h postoperatively was significantly lower with the use of the Stoppa procedure than bilateral Lichtenstein repair, but there was no statistically significant difference between both groups in postoperative pain scoring at 24 h and 7 days postoperatively. No significant difference was detected between both groups in operative complications, postoperative complications, hospital stay, return to normal daily activities, and chronic groin pain. No recurrence was detected in any of the patients after 1 year of follow-up.

Conclusion
Bilateral inguinal hernias can be repaired simultaneously in the same setting safely and effectively without an increase in morbidity or recurrence rate. The Stoppa procedure can be a good alternative to bilateral Lichtenstein repair for the treatment of bilateral inguinal hernia, with comparable outcome.

Keywords:
bilateral, hernia repair, inguinal hernia, Lichtenstein, Stoppa

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Introduction

Inguinal hernia is one of the most frequently performed operations in general surgery [1,2]. It occurs in ~1.5% of the general population [3]. Most inguinal hernias are unilateral and at the right side and only 12% of patients have bilateral inguinal hernias [4]. Simultaneous or sequential repair of bilateral hernias is still debatable [5,6]. For many years, it was believed that simultaneous repair of bilateral inguinal hernias could not be done because this approach may result in a high recurrence rate [7]. This idea is now being questioned with the emergence of the 'tension-free' techniques. Authors have described about 80 operative techniques for inguinal hernia repair since Bassini reported his procedure in 1887 [8]. Surgeons continue to search for the optimum repair method with the least recurrence and least complications. The development of tension-free repairs made a huge breakthrough in hernia surgery. Placement of a mesh is required in all types of tension-free repair; the mesh may be placed through an open anterior, open posterior, or laparoscopic route. Multiple tension-free techniques are available now, which include the open anterior approach (onlay Lichtenstein patch, plug and patch), the open posterior approach (Stoppa, Kugel), and the closed posterior approach (laparoscopic) [8]. Simultaneous repair of bilateral inguinal hernias may have the advantages of patient satisfaction and lower costs because the patient is subjected to only one hospital admission, one anesthesia, and only one period of recovery is required [9]. This debate on the management of bilateral inguinal hernias led us to carry out our

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present study with the aim of comparing the Stoppa procedure with Lichtenstein tension-free hernioplasty for the management of bilateral inguinal hernia in terms of operative time, intraoperative complications, postoperative complications, postoperative pain, hospital stay, return to normal daily activities, chronic groin pain, and recurrence.

Study design

This is a prospective, randomized, controlled trial. The design involved 40 male patients with bilateral inguinal hernia scheduled for simultaneous repair of their bilateral hernias at the Department of Surgery, Medical Research Institute Hospital, Alexandria University. Patients were considered eligible after evaluation of clinical history, a thorough physical examination, blood chemistry, and radiological evaluation (ultrasonography of the abdomen and pelvis). Patients included in the study were divided into two groups: group A (underwent bilateral Lichtenstein tension-free hernioplasty) and group B (underwent Stoppa repair); patients with recurrent inguinal hernias and those undergoing emergency hernia repairs were excluded.

Ethics

A specific informed consent form approved by our Institution's Ethics Committee had to be signed by the candidates before inclusion in the trial; this form included detailed information about the surgery, the expected complications, and possible recurrence.

Endpoints

Primary endpoint

To evaluate the incidence of recurrence and chronic groin pain in the two groups of patients.

Secondary endpoints

(a) Perioperative parameters (operative time, intraoperative, and postoperative complications),
(b) Hospital stay,
(c) Postoperative pain scoring,
(d) Timing of return to normal daily activity, and
(e) Follow-up details.

Randomization method

Eligible patients were randomized into two groups: group A (underwent bilateral Lichtenstein tension-free hernioplasty) and group B (underwent Stoppa repair) using sealed opaque envelopes containing computer-generated random numbers. The randomization was performed 1 week before surgery during the preoperative assessment.

Surgical technique

Spinal anesthesia was used routinely for all patients. Immediately preoperatively, every patient received 2 g cefatriaxone.

Lichtenstein tension-free hernioplasty [10]

A skin incision was made parallel to the inguinal ligament extending from about 1/2 inch above and lateral to the pubic tubercle to just below and medial to the anterior superior iliac spine. The indirect hernia sac was dissected, ligated, and sectioned using Vicryl 0 (Ethicon; Johnson & Johnson International, Sint-Stevens-Woluwe, Belgium). The large direct sacs were invaginated and plicated using Vicryl 2/0 (Ethicon; Johnson & Johnson International). A heavy prolene mesh of 6 × 11 cm (PMH, prolene mesh, polypropylene nonabsorbable synthetic mesh 6 × 11 cm, Ethicon; Johnson & Johnson International) was used in all cases. The mesh was fixed in place using interrupted polypropylene 2/0 (Ethicon Sutures, Cincinnati, Ohio, USA). The mesh was fixed to the inguinal ligament and the conjoint tendon starting from the pubic tubercle extending beyond the orifice of the internal ring.

Stoppa procedure

The technique developed by Stoppa was used, with some modifications [11–14]. For all patients, a pfenestiel incision was used as a standard, followed by vertical separation of both recti to enter the preperitoneal space. Blunt dissection of the preperitoneal space was performed. Dissection involved the retropubic space of Retzius, and reached the rectus abdominis muscle and epigastric vessels laterally, extending to the retroinguinal space. The spermatic cord and gonadal vessels were visualized. The superior pubic ramus, the obturator foramen, and iliac vessels were exposed. Direct hernias were identified and reduced. Large sacs were removed and ligated with a purse-string suture. Indirect sacs were divided, the proximal peritoneum was sutured, and the distal peritoneum was left in place attached to the cord. If indirect hernia was sliding, dissection of the sac from the cord structures was performed. Parietalization of the spermatic cord and gonadal vessels was performed by dissection of their peritoneal attachment. A prolene mesh (PMH, prolene mesh, polypropylene nonabsorbable synthetic mesh 30×30 cm; Ethicon; Johnson & Johnson International) was placed in the preperitoneal space. Fixation of the mesh was not required as the intra-abdominal pressure forces the mesh to lay flat between the peritoneum and the fascial layers.

Postoperative course

Operative data of each patient were recorded with a focus on operative time and intraoperative

complications. Postoperative data recording included assessment of postoperative pain, postoperative complications, hospital stay, time of returning to normal daily activities, chronic groin pain, and recurrence. For each patient, postoperative pain was assessed at 12, 24 h, and 7 days postoperatively using the visual analogue scale [15].

Follow-up

All patients were followed at 7 days, and 1, 6, and 12 months after the operation at the outpatient clinic for assessment complications, pain, return to normal daily activities, chronic groin pain, and recurrence.

Statistical considerations

Statistical analysis was carried out using the statistical package for the social sciences, version 20 software (SPSS Inc., Chicago, Illinois, USA). Significance level was set at $\alpha = 0.05$. Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, SD, and median. Comparison between different groups in terms of categorical variables was performed using the χ^2-test. When more than 20% of the cells had an expected count lower than 5, correction for χ^2 was performed using the Fisher's Exact test or Monte Carlo correction. For normally distributed data, comparisons between two independent population were performed using an independent *t*-test; comparisons between different periods using analysis of variance with repeated measures and post-hoc test were performed using Bonferroni adjustment. For abnormally distributed data, comparisons between two independent populations were performed using the Mann–Whitney test.

Results

The present study included 40 male patients with bilateral inguinal hernias who were allocated randomly to two groups. Group A included 20 patients who were operated by bilateral Lichtenstein tension-free hernioplasty. Group B also included 20 patients who were operated by Stoppa repair. All patients in the present study were men. There was no statistically significant difference between both groups in preoperative data (age, BMI, comorbidities, smoking, and type of hernia) (Table 1).

The operative time was significantly shorter in group B patients; it ranged between 30 and 50 min, with a mean of 39.0 ± 5.15 min, whereas in group A, it ranged between 50 and 75 min, with a mean of 62.25 ± 7.95 min, as shown in Table 2. There were no intraoperative complications (vascular or visceral injury) in either group.

Postoperative pain scoring measured by the visual analogue scale at 12 h postoperatively was significantly lower in group B patients, but there was no statistically significant difference between both groups in pain at 24 h and 7 days postoperatively (Table 3).

There was no statistically significant difference between both groups in postoperative complications, postoperative hospital stay, return to normal daily activities, and chronic groin pain (Table 2). No recurrence occurred in any patient after 1 year of follow-up in either group.

Discussion

For many years, it was believed that simultaneous repair of bilateral inguinal hernias should not be

Table 1 Preoperative assessment of both groups

Preoperative data	Group A (*n* = 20)	Group B (*n* = 20)	Test of significance	*P*-value
Age				
Minimum–maximum	20.0–62.0	22.0–62.0	$t = 0.569$	0.573
Mean ± SD	47.95 ± 9.0	49.60 ± 9.35		
BMI				
Minimum–maximum	25.0–38.20	25.20–37.40	$t = 0.596$	0.555
Mean ± SD	29.40 ± 3.97	30.14 ± 3.88		
Type of hernia [*n* (%)]				
Direct	18 (90)	17 (85)	$\chi^2 = 1.447$	$P_{MC} = 1.000$
Indirect	1 (5)	1 (5)		
Combined (bilateral)	1 (5)	1 (5)		
Direct (unilateral)+combined (unilateral)	0 (0)	1 (5)		
Comorbidities [*n* (%)]				
Hypertension	2 (10)	3 (15)	$\chi^2 = 0.709$	$P_{MC} = 1.000$
Diabetes	3 (15)	2 (10)		
COPD	3 (15)	2 (10)		
Smoking [*n* (%)]	5 (25)	6 (30)	$\chi^2 = 0.125$	0.723

MC, monte carlo test; *t*, Student *t*-test; COPD, chronic obstructive pulmonary disease.

Table 2 Operative and postoperative parameters

Perioperative parameters	Group A (n = 20)	Group B (n = 20)	Test of significance	P-value
Operation time (min)				
Minimum–maximum	50.0–75.0	30.0–50.0	t = 11.310*	<0.001*
Mean ± SD	62.25 ± 7.95	39.0 ± 5.15		
Postoperative complications [n (%)]				
Wound seroma and hematoma	4 (20)	1 (5)	χ^2 = 3.544	P_{MC} = 0.571
Urine retention	1 (5)	2 (10)		
Wound infection	1 (5)	0 (0)		
Scrotal hematoma	1 (5)	1 (5)		
Chronic groin pain [n (%)]				
Absent	17 (85)	18 (90)	χ^2 = 0.229	P_{FE} = 1.000
Present	3 (15)	2 (10)		
Postoperative hospital stay (days)				
Minimum–maximum	1.0–3.0	1.0–2.0	Z = 0.622	0.534
Mean ± SD	1.15 ± 0.49	1.05 ± 0.22		
Median	1.0	1.0		
Return to work (days)				
Minimum–maximum	12.0–22.0	13.0–23.0	t = 0.119	0.906
Mean ± SD	16.90 ± 2.53	17.0 ± 2.79		

FE, fisher exact test; MC, monte carlo test; t, student t-test; Z, Mann–Whitney test, *Statistically significant at $P \leq 0.05$.

Table 3 Postoperative pain in both groups

Groups	Postoperative pain		
	12 h	24 h	7 days
Group A			
Minimum–maximum	5.0–9.0	2.0–7.0	0.0–4.0
Mean ± SD	6.95 ± 1.10	4.60 ± 1.35	1.75 ± 1.16
Significance between stages		<0.001*	<0.001*
Group B			
Minimum–maximum	5.0–8.0	3.0–6.0	1.0–3.0
Mean ± SD	6.25 ± 0.97	4.35 ± 0.99	1.70 ± 0.66
Significance between stages		<0.001*	<0.001*
t	2.139*	0.667	0.167
P-value	0.039*	0.509	0.868

ANOVA, analysis of variance; t, student t-test, significance between stages was performed using stands for adjusted bonferroni P-values for ANOVA with repeated measures for comparison between 12 h for stage, *Statistically significant at $P \leq 0.05$.

performed because this approach would cause increased postoperative complications (pain, wound complications, and recurrences) [16]. Today, it is known that the simultaneous repair of bilateral hernia is safe and effective.

The European Hernia Society elaborated guidelines for the treatment of bilateral inguinal hernias and recommended a one-stage procedure (Lichtenstein or laparoscopic) [17]. The Stoppa procedure can be another alternative for bilateral inguinal hernia treatment, but only for the surgeons familiar with it [18,19]. This led us to carry out this study to compare the Stoppa procedure with bilateral Lichtenstein hernioplasty for the treatment of bilateral inguinal hernias.

Malazgirt *et al*. [20] carried out a study on 45 patients with bilateral inguinal hernias (22 patients were operated by Stoppa and 23 patients were operated by bilateral Lichtenstein), and reported that Stoppa procedures took significantly shorter time than bilateral Lichtenstein repairs. They performed Stoppa repair under spinal anesthesia and Lichtenstein repair under either spinal or local anesthesia. In the present study, all procedures were performed under spinal anesthesia to avoid any bias in terms of postoperative pain scoring. Our results were comparable with those of Malazgirt *et al*. [20] in the operative time as the Stoppa procedure took a significantly shorter time than bilateral Lichtenstein repair. Gustavo *et al*. [21] carried out a study to evaluate simultaneous bilateral inguinal hernia repair by the Lichtenstein technique and reported a mean operative time of 113 ± 19.33 min, which was significantly longer than the mean operative time of bilateral Lichtenstein repair in the present study (62.25 ± 7.95 min). Gustavo *et al*. [21] did not exclude recurrent and complicated hernias; this may be an explanation for the prolonged operative time found in their study. Fernandez-Lobato *et al*. [22] carried out a large-scale study to evaluate Stoppa repair in bilateral inguinal hernia that involved 210 patients who underwent surgery for bilateral inguinal hernia from January 1995 to December 2003. They recorded that the operative time decreased significantly from 105 min in the first year to less than 61 min in 2001, with 73% of the cases operated in less than 60 min (P < 0.0001) and 62% in 2003. Stoppa *et al*. [13] described a mean operative time of 51 min. This duration is also shorter than that required in the bilateral Lichtenstein technique [13,23]. In the present study, the mean operative time for Stoppa repair was

39.0 ± 5.15 min, which is about 10 min less than what was reported by Stoppa because Stoppa and colleagues focused their study on complex and recurrent hernias and we excluded these cases from our study.

In our study, there was no significant difference between both groups in postoperative hospital stay, which was in agreement with the study by Malazgirt *et al.* [20]. Sasso *et al.* [21] reported a mean postoperative hospital stay of 1.55 ± 0.83 days for bilateral Lichtenstein repair (most of their patients were admitted for 1 day). Miller *et al.* [4] reported a mean hospital stay of 6.4 days and Serpell *et al.* [24] reported a hospital stay ranging from 2 to 12 days for bilateral Lichtenstein repair. We could not find a proper explanation for the relatively long postoperative hospital stay after bilateral Lichtenstein repair in these two studies [4,24]. Our results for postoperative hospital stay following bilateral Lichtenstein (1.15 ± 0.49 days) was close to that reported in the literature (1.3 ± 0.3 days) [25]. Fernandez-Lobato *et al.* [22] reported that the mean postoperative hospital stay following Stoppa repair was 1.2 days in 2003 during their study; this result was close to that of our study (1.05 ± 0.22 days). Carmen *et al.* [26], in their study of complex and recurrent bilateral inguinal hernias, reported a longer hospital stay following the Stoppa procedure (mean: 3 ± 0.3 days); this actually may have been because of associated comorbidities.

Malazgirt *et al.* [20] reported that there was no significant difference between bilateral Lichtenstein repair and Stoppa repair in the incidence of postoperative complications. A meta-analysis was carried out by Li *et al.* [27]. This meta-analysis pooled the effects of outcomes of a total of 2860 patients enrolled into 10 randomized-controlled trials and two comparative studies for comparison between preperitoneal and Lichtenstein repair for unilateral inguinal hernia and recorded that there was no significant difference between both groups in postoperative complications. Our results were comparable with those of Malazgirt *et al.* [20] and Junsheng *et al.* [27] as we did not find any significant difference between both groups in postoperative complications.

In the present study, there was no significant difference between both groups in return to normal daily activities; the mean was 16.90 ± 2.53 and 17.0 ± 2.79 days for group A and group B, respectively. Our results were close to those of Malazgirt *et al.* [20], who reported that the time required for return to normal daily activities was 18, 17, and 15 days following Stoppa, Lichtenstein under spinal anesthesia, and Lichtenstein under local anesthesia, respectively.

Malazgirt *et al.* [20] did not find any significant difference between both groups in immediate postoperative pain and chronic groin pain. In the study by Gustavo *et al.* [21], chronic groin pain occurred in only 3% of cases of bilateral Lichtenstein repair; this was much less than our results and the results of Malazgirt *et al.* [20] of 15 and 13.04%, respectively. Unilateral inguinal hernia repair by the Lichtenstein technique may lead to chronic groin pain in about 20–30% of patients [28]. The same results were reported by Solorzano *et al.* [29]. This high percentage of chronic groin pain following Lichtenstein hernia repair may be because of consideration of discomfort as a type of pain, whereas in our study, we recorded only patients with precise pain. Carmen *et al.* [26] reported that the incidence of chronic groin pain following bilateral Stoppa was 6.25%; in our study and the Malazgirt *et al.* [20] study, it was 10 and 9.09%, respectively. Junsheng *et al.* [27], in their meta-analysis, failed to find any significant difference between Lichtenstein and preperitoneal repair of inguinal hernia in postoperative chronic groin pain. In the present study, postoperative pain scoring at 12 h was significantly lower with the Stoppa procedure than bilateral Lichtenstein repair, but there was no significant difference between both groups in pain scoring at 24 h and 7days postoperatively. Both groups in our study were comparable with in chronic groin pain.

Malazgirt *et al.* [20] reported one recurrent case after Stoppa (1/22 patient) and no recurrence after bilateral Lichtenstein repair. Gustavo *et al.* [21] reported one recurrent case out of 59 patients operated by bilateral Lichtenstein repair after 2 years of follow-up. Kark *et al.* [30] observed less than 1% recurrence after Lichtenstein repair in 199 patients. Amid *et al.* [7] reported 0.1% recurrence in 1000 individuals and Hidalgo *et al.* [31] found no hernia recurrences in a total of 55 patients after Lichtenstein repair. The result of our study on recurrence following Lichtenstein was in agreement with other studies [7,20,21,30,31] as we did not find any recurrence after 1 year of follow-up. Fernandez-Lobato *et al.* [22] reported three cases of recurrence out of 210 patients following Stoppa repair for bilateral inguinal hernias. Two recurrences occurred in the first 30 cases and one recurrence in the remaining 140 cases. The total recurrence rate was 3/210 patients (1.4%) and 3/420 hernias (0.7%) (P<0.001). They reported that recurrence in all cases was because of the use of a small mesh, which did not cover the inguinal area correctly. After a mean follow-up of 24 months, Carmen *et al.* [26] reported a recurrence rate of 1% (1 of 124) per inguinal hernia repaired or 2% (1 of 64) per patient following Stoppa repair. In the present study, there was no recurrence following Stoppa repair after 1 year of follow-up. Our results of recurrence

following Stoppa repair were similar to those of other studies [22,26].

Conclusion

Simultaneous repair of bilateral inguinal hernia is safe and effective, without an increase in morbidity or the recurrence rate. The Stoppa procedure could be a good alternative to bilateral Lichtenstein repair for the treatment of bilateral inguinal hernia, with comparable operative and postoperative complications.

Acknowledgements

Conflicts of interest

There is no conflicts of interest.

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Tension-free primary closure compared with modified Limberg flap for pilonidal sinus disease: a prospective balanced randomized study

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Background
Pilonidal sinus disease (PSD) is a common disease that affects the patient's quality of life. We analyzed the outcome of the tension-free primary closure (TF 1ry) in comparison with the modified Limberg flap (MLF) technique.

Patients and methods
A total of 120 patients suffering PSD were assigned to one of two equal groups by closed envelope balanced randomization. Group I represents TF 1ry method and group II represents MLF.

Results
There were 102 (85%) male patients and 18 (15%) female patients elected for surgery. The mean follow-up period was 43.5 ± 3.4 months. There were no statistically significant differences between the two groups regarding patients' demographic data, clinical presentation, immediate postoperative complications, and disease recurrences. The operative time, blood loss, hospital stay, surgeon's performance scale, wound hypothesia, wound cosmoses score, patient satisfaction score, and patient quality of life (bodily pain and social functioning) were better in the TF 1ry group. The MLF group had better clinical results regarding frequency of seroma formation and time to drain removal.

Conclusion
Flap techniques are effective and efficient for PSD. TF 1ry closure can be tailored for female PSD patients and a junior surgeon. MLF can be tailored for male PSD patients and a senior surgeon.

Keywords:
Limberg flap, pilonidal sinus, primary closure

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Introduction

Pilonidal sinus disease (PSD) is a common and well-recognized entity. Hodge in 1880 suggested the term pilonidal disease [1]. It typically affects young male patients after puberty [2]. Absence of the exact etiology explains the diversity of treatment lines [3] and failure of treatment options [4]. Radical treatment has been wide excision of the chronic tracts with or without closure. Higher morbidity rate has been reported with primary closure due to tissue tension [5,6].

The main problem is the high rate of recurrence, which can diminish the patient's quality of life (QoL) [7]. Hence, the ideal operation should minimize PSD recurrences and financial cost (patient–community), should have short hospital stay, should cause minimal pain, should be associated with a low patient and procedure morbidity rates, and should be simple for surgeons [8].

Flap techniques reduced PSD recurrences and wound morbidity due to 'tension-free' healing site. Modified Limberg flap (MLF) technique is a simple modification of classic Limberg flap to eliminate midline maceration and reduce recurrence rate [9,10]. Tension-free primary closure (TF 1ry) has been suggested to avoid wound dehiscence, wound infection, and recurrence [4,11,12].

In this study, sufficient sample size was enrolled, and objective scoring systems were performed for procedures, patients, and surgeons.

The aim of study was to compare TF 1ry versus MLF technique regarding recurrence as a primary outcome measure. The secondary outcome measures included:

(a) Patient-related factors: postoperative pain scores (patient inconvenience), time to sit on toilet and walk pain free (patient financial cost), the QoL, and satisfaction;
(b) Procedure-related factors: operative time, blood loss, immediate postoperative complication, hospital stay (community financial cost), and wound morbidities; and
(c) Surgeon-related factor: surgeon performance.

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Patients and methods

This study was a prospective randomized single-blinded clinical trial. Local ethics committee approval was obtained. A total of 165 patients with PSD were referred to Mansoura General and Colorectal Surgery Units between March 2006 and September 2012. Forty-five patients were excluded from the study (15 patients were medically unfit and 30 had pilonidal abscess). The remainder patients (120) were enrolled in the study. They were assessed by documentation of clinical symptoms and their duration, full discussion of pain, satisfaction, and the QoL scores. Patients were prepared by overnight evacuation enema and operative site shaving on the day of surgery. Perioperative antibiotics 'ampicillin–sulbactam' were used. All patients received spinal anesthesia, except if sinus tracts were too high, general anesthesia was used. Patients were operated upon using the prone Jack knife position. Patients were randomized at operation room using sealed envelope into two equal groups.

Group I patients (tension-free primary closure)

It included 60 patients with a mean age of 27 ± 6.8 years. All of them were subjected to TF 1ry [13]. Excision of the sinus tract with elliptical skin incision was performed followed by 3 cm lateral subcutaneous tissue release. Suction drain was inserted. Flaps closure was achieved by 0 vicryl sutures including the presacral fascia and subcutaneous tissue by 3/0 vicryl sutures. Skin closure was performed with 3/0 polypropylene sutures or skin staples (Fig. 1).

Group II patients (modified Limberg flap)

It included 60 patients with a mean age of 28 ± 7.6 years. All of them were subjected to excision of the sinus tract and reconstruction with MLF technique [14]. A rhombus-shaped area of excision was mapped with a skin marker; its lower angle is not in the midline but 2 cm lateral to the anal canal to avoid any midline remnants below the flap. All sinus tracts were excised en-block deep until the presacral fascia in the midline and the gluteal muscles laterally. Rhomboid flap was then fashioned from the other buttock incorporating skin, subcutaneous fat, and gluteal fascia and stitched in place over a suction drain (Fig. 2). Drains were removed when outcoming serous fluid volume was below 20 ml/day. Sutures were removed on 10th postoperative day.

Follow-up visits were performed every week for 1 month, monthly for the first year then every 3 months. Operative time, blood loss, hospital stay, immediate postoperative complications, wound morbidities in the form of maceration (soft, white, and wet skin), infection (cellulitis or purulent discharge from wound edge or drain), gaping (separation of all wound layers), seroma, time of drain removal, sit on toilet, and walk pain free (walk comfortably without pain or tension) were documented. The visual analog scale (VAS), which is a measurement instrument for subjective characteristics, was used to measure postoperative pain [15], patient satisfaction [16], surgeon performance [17], and wound cosmoses [18]. Patients completed two VASs; the first evaluated postoperative pain on first and seventh days and at second and fourth weeks postoperatively, and the second measured patient satisfaction at the third postoperative month. Surgeons similarly recorded two VASs; the first was for surgeon performance at the end of surgery in terms of anatomy, tissue planes, and patient characters, and the second was for wound cosmoses at third postoperative month.

Figure 1

Tension-free primary closure (immediately postoperative).

Figure 2

Modified Limberg flap technique after sutures removal.

At the third month, the QoL assessment was performed [19] using 'SF-36 short form' in which 36 items are coded, summed, and scored on to a scale from 0 to 100 [20]. It is a generic form for QoL study; all entity and usage rules are available at *http://www.qualitymetric.com* home page. Subsequent follow-up was performed to detect disease recurrence.

The statistical analysis of the data in this study was performed using the SPSS version 10 under Windows XP (SPSS incorporation, Chicago, USA). The tests used were the arithmetic mean value (average) and SD, frequency (percentage), Student's t-test (a $P < 0.05$ was considered significant), and the χ^2-test.

Results

There were 102 (85%) male patients and 18 (15%) female patients suffering from PSD elected for surgery. All patients were followed up longer than 12 months with a mean follow-up period of 43.5 ± 3.4 months (range 12–60 months). There were no statistically significant differences between the two groups regarding patients' demographic data and clinical presentation (Table 1). Operative data study revealed significant shorter operation time, less operative blood loss, and easier surgeon performance (Fig. 3) for group I patients. There were no significant differences between the two groups regarding immediate postoperative complications (Table 2). Pain scores (Table 3) were significantly higher in group II patients on first postoperative day, but later on the differences were insignificant. Study of the first month wound morbidities revealed significant advantage regarding time until drain removal and frequency of seroma formation in group II patients but with a significant longer hospital stay (Table 4). In addition, pairwise comparison of wound complications declared significantly higher frequency of hypothesia in group II patients (Table 5). At third month, the TF 1ry technique had a significant advantage regarding patient satisfaction and wound cosmoses (Fig. 4).

Study of third month postoperative QoL revealed a significant reduction in bodily pain and better social functioning in group I patients (Table 6). The recurrence rate in group I patients [two (3.33%) patients detected at the fifth and 10th postoperative month] was not found to differ significantly from that of group II patients [one (1.6%) patient detected at sixth postoperative month].

Discussion

PSD and its recurrence are caused by forces focused on the midline (tension = force/surface area) mainly

Table 1 Patients' demographic data and clinical presentation

Patients	Group I [*n* (%)]	Group II [*n* (%)]	*P* value
Age (mean ± SD) (years)	27 ± 6.8	28 ± 7.6	NS
Preoperative duration of PSD (mean ± SD) (months)	1.8 ± 1.1	1.6 ± 1.2	NS
Clinical presentation			
Discharge	52 (86.6)	50 (83.3)	NS
Pain	30 (50)	32 (53.3)	
Pruritus	20 (33.3)	19 (31.6)	
Bleeding	4 (6.6)	3 (5)	

PSD, pilonidal sinus disease.

Table 2 Immediate postoperative complications

Variables	Group I [*n* (%)]	Group II [*n* (%)]	*P* value
Urine retention	3 (5)	4 (6.6)	NS
Bleeding	0 (0)	1 (1.6)	NS
Constipation	3 (5)	2 (3.3)	NS

Table 3 Postoperative pain scores

Timing	Group I (mean ± SD)	Group II (mean ± SD)	*P* value
Postoperative first day	2.8 ± 1.2	4.2 ± 1.4	<0.001
Postoperative seventh day	2.1 ± 1.05	2.5 ± 1.01	NS
Postoperative second week	1.0 ± 0.4	0.9 ± 0.47	NS
Postoperative fourth week	0.10 ± 0.307	0.00 ± 0.00	NS

Table 4 Postoperative wound morbidities and hospital stay

Variables	Group I (mean ± SD)	Group II (mean ± SD)	*P* value
Time to drain removal (days)	10.2 ± 2.1	4.5 ± 2.4	<0.01
Seroma formation (*n*)	5 ± 8.4	1 ± 1.6	0.05
Time to sit on toilet (days)	8.1 ± 0.17	7.8 ± 0.3	NS
Time to walk pain free (days)	6.9 ± 0.016	5.9 ± 0.21	NS
Hospital stay (days)	1.85 ± 0.7	3.8 ± 1.6	<0.05

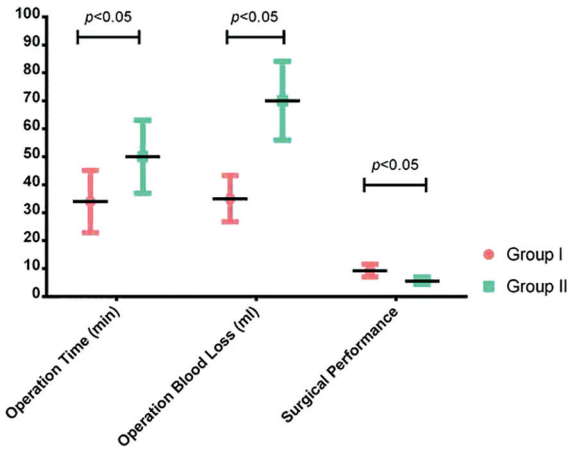
Table 5 Postoperative wound complications

Variables	Group I [*n* (%)]	Group II [*n* (%)]	*P* value
Infection	3 (5)	2 (3.3)	NS
Dehiscence	1 (1.6)	1 (1.6)	NS
Edema	2 (3.3)	1 (1.6)	NS
Maceration	1 (1.6)	0 (0)	NS
Hypothesia	2 (3.3)	6 (10)	<0.05

Table 6 Quality of life estimation

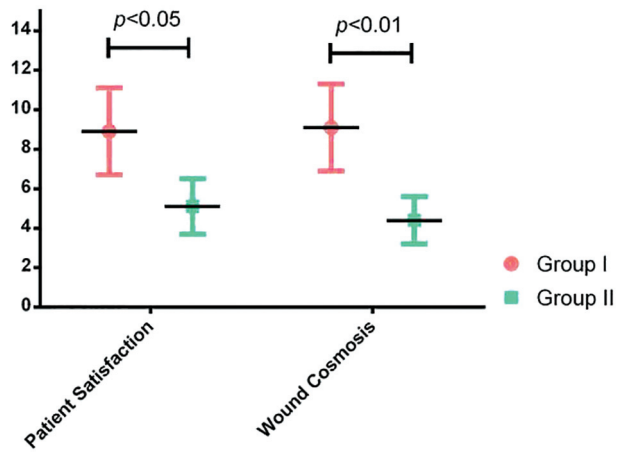
Variables	Group I (mean ± SD)	Group II (mean ± SD)	*P* value
Physical function	71.1 ± 11.7	73.4 ± 12.5	NS
Role of limitation of physical function	43.5 ± 15.1	41.9 ± 14.2	NS
Bodily pain	54.3 ± 6.3	61 ± 4.6	<0.001
Vitality and energy	74.5 ± 16.4	73.1 ± 17.4	NS
General health	73.1 ± 10.7	75.3 ± 14.3	NS
Emotional function	63.4 ± 5.3	66.2 ± 4.3	NS
Social functioning	59.6 ± 5.4	72 ± 8.7	<0.001
Role of limitation of emotional function	56.5 ± 13.7	55.4 ± 14.6	NS
Physical health perception	75.6 ± 11.7	77.3 ± 12.6	NS
Mental health perception	69.5 ± 6.4	57.5 ± 7.31	NS

Figure 3



Comparison between studied groups regarding operative time, operative blood loss, and surgeon performance.

Figure 4



Comparison between studied groups regarding patient satisfaction and wound cosmoses.

where the coccyx turns anteriorly [21]; vacuum effect created between the buttocks that attracts the anerobic bacteria, hair, and debris [22]; and friction movement of buttocks [23] in the presence of other risk factors such as adiposity, hirsuteness, and bad hygiene [24–27]. Thus, effective procedure will eliminate shearing forces, vacuum effect, and friction movement [26]. Both procedures had low recurrence rates with insignificant difference, in agreement with the study by Tavassoli *et al*. [27]. However, TF 1ry had shorter operative time and less blood loss, as reported by Muzi *et al.* [28], due to small defect and minimal dissection. Flap techniques achieved lower pain scores compared with direct primary closure due to tension-free construction as reported by Quinodoz *et al*. [29]. The relatively higher pain score on first day postoperatively in the MLF group is related mostly to more dissection and tension with net force. As pain (mild to moderate in this study) is the most critical point that exacerbates postoperative urine retention and constipation, their frequencies were infrequent in this study with minimal patient inconvenience. The less postoperative pain in TF 1ry closure patients and the infrequent immediate postoperative complications facilitated their early discharge, thus minimizing the financial cost to the community. This finding was similarly confirmed by the study by Muzi *et al.* [28]. Thus, regarding operative time, patient inconvenience (immediate postoperative pain, immediate postoperative complications), and financial cost to the community (hospital stay), TF 1ry closure is more advantageous than MLF. The case difficulty scale of surgeon was higher in MLF technique, being reserved for a senior surgeon, but the performance was better for TF1ry closure technique as it is simple to design and construct being reserved for junior surgeons. The MLF procedure keeps system under net force, as the recipient side is heavier (more dangling) than donor side [30]; meanwhile, the TF 1ry closure creates a TF midline healing site and keeps system in equilibrium as summation of force is zero [12]. Consequently, TF 1ry closure achieved less wound morbidity rate, which did not reach statistical significance.

Nearly, the flat natal cleft for the TF 1ry closure group and lateralized midline for the MLF group resulted in significant decrease in maceration rate, in agreement with the study by Akca *et al.* [11]. A high incidence of wound maceration (45.7%) was reported with the classic Limberg flap technique [4]; hence, both TF 1ry closure and MLF are efficient to reduce maceration.

The reduced maceration rate resulted in less wound infection as Akin *et al.* [10] and Muzi *et al.* [28] reported, compared with the higher incidence of wound infection for direct primary closure (21.8%) recorded by Zimmerman [31]. Generally, flap procedures achieve proper wound healing with less wound dehiscence, in agreement with the study by Mahdy [32]; hence, both TF 1ry closure and MLF techniques were equivalent regarding wound healing but MLF technique changed the anatomy of the gluteal region. The MLF had significantly shorter time until drain removal and less incidence of seroma formation, in agreement with the study by Erderm *et al.* [33]; this is related to more muscle exposure that deserves good absorptive power, and hence use of drains for MLF is controversial. The more dissection in MLF patients resulted in a significant higher rate of hypothesia (10%); this is comparable with the studies conducted by Akin *et al.* [10] and Soendenna *et al.* [34] who reported hypothesia in 8.9 and 9.5% of their patients, respectively. Patients after PSD surgery suffer wound

tenderness (sitting on hard chairs and time off work) that negatively affects the patient financial cost [35]. Holm and Hultén [36] found that 18% of their patients suffered pain during sitting on hard chairs. Moreover, time off work reported by Cihan *et al.* [4] was 28.6 ± 3.11 days for direct primary closure. The current study confirmed significantly shorter times to walk pain free and to sit on toilet for flap surgery. Thus, both techniques improve financial cost.

The patient satisfaction score was significantly higher for the TF 1ry closure group, which is similar to that reported by Akin *et al.* [10] and Tavassoli *et al.* [27], with positive community and patient costs, less disturbed anatomy, and minimal patient inconvenience being associated with better satisfaction. In PSD, the main problem is the high rate of morbidity and recurrence, which can greatly diminish the patient's QoL [3]. This study found TF 1ry closure advantageous in terms of bodily pain and social functioning, in agreement with the study by Ertan *et al.* [35]. The QoL drive is an important factor in decision making regarding PSD surgery modality.

Conclusion

Flap techniques are effective and efficient for PSD. TF 1ry closure can be tailored for female PSD patients and a junior surgeon. MLF can be tailored for male PSD patients and a senior surgeon.

Acknowledgements

Conflicts of interest

None declared.

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Subtotal cholecystectomy in difficult laparoscopic cholecystectomies: is it safe?

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Purpose
Laparoscopic cholecystectomy is now accepted as the 'gold standard' procedure for cholecystectomy. However, this procedure can be dangerous in cases of unclear anatomy at the Callot's triangle. A significant proportion of patients with unclear anatomy are still converted to 'open' to complete the procedure. The other option is subtotal cholecystectomy rather than open conversion. Our purpose was to study the safety of laparoscopic subtotal cholecystectomy in cases where the clear identification of the anatomical land marks in Callot's triangle is difficult.

Materials and methods
Patients who underwent laparoscopic subtotal cholecystectomy between January 2011 and December 2011 were evaluated prospectively. These patients underwent subtotal cholecystectomy without isolation of the duct or artery, as this was judged to be hazardous, and the Hartmann pouch was transacted, stones were evacuated and the gall bladder remnant was closed by endoscopic sutures and a subhepatic drain left *in situ*.

Results
Laparoscopic subtotal cholecystectomy was performed in 30 elective procedures among 30 patients, male patients 18 (60%) and female patients 12 (40%). Their mean age was 52.6 years ± 12.65 SD. The mean operative time was 92 min ± 20 SD, and the mean hospital stay was 72.43 h ± 22 SD. We encountered one conversion into open and two patients who developed intra-abdominal collection. No mortalities were recorded.

Conclusion
Subtotal cholecystectomy is a safe procedure in cases where there is no clear identification of the structures in Callot's triangle. However, it is not a substitute for conversion into open, if deemed required.

Keywords:
bile leakage, difficult cholecystectomy, subtotal cholecystectomy

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Introduction

Laparoscopic cholecystectomy is introduced as a treatment option for symptomatic gall bladder disease in 1987 and it is now the gold standard treatment for symptomatic gall bladder disease [1].

About 60 000 cholecystectomies are performed every year in the UK, and it is performed in both elective and emergency situations. The rate of conversion from laparoscopic to open ranges between 5 and 10% [2].

The step of paramount importance in cholecystectomy is the clear identification of the cystic duct and artery, which in some situations can be difficult especially in presence of dense adhesions or severely inflamed gall bladder, increasing the risk for common bile duct (CBD) injury. Despite that, the incidence of common bile duct injury in laparoscopic cholecystectomy is 0.25–0.5% [3].

The traditional response to encountering a difficult laparoscopic cholecystectomy procedure is to perform conversion to an open procedure but the open conversion has its drawbacks; it definitely prolongs hospital stay and the patient will lose all the privileges of laparoscopic surgery [4,5].

Hence, the aim of our study was to assess the safety of laparoscopic subtotal cholecystectomy in difficult cholecystectomies.

Materials and methods

Our study was a prospective study that recruited 30 patients who underwent laparoscopic subtotal cholecystectomy in Ain Shams University Hospitals between January 2011 and December 2011. All our patients signed an informed consent and IRB approval was obtained and all the data were kept on a password protected computer.

Inclusion criteria

Patients with symptomatic gall bladder disease who underwent laparoscopic cholecystectomy and in whom identification of the Callot's triangle is difficult.

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Exclusion criteria

Patients with acute cholecystitis.

Preoperatively, all patients underwent the following:

(1) Ultrasound scan.
(2) Liver function tests.
(3) Total bilirubin and direct bilirubin estimation.

Technique

(1) All our patients were operated upon under general anaesthesia.
(2) Prophylactic dose of second-generation cephalosporin was given with induction.
(3) All patients were placed in the supine position with the surgeon on the left hand side of the patient opposite to the monitor and the cameraman on his left hand side.
(4) Pneumoperitoneum was created by open method through an infraumbilical incision. In addition, a 10-mm port was inserted and a 30°, 10 mm camera was used.
(5) The other three ports were inserted under complete visualization after infiltration of the peritoneum with local anaesthetic: 10-mm port in the epigastrium, 5-mm port in the right hypochondrium and a 5-mm port in the right iliac fossa.
(6) The fundus of the gall bladder was pushed cranially with a grasper through the right iliac fossa port and a counter traction was achieved by pulling the Hartmann's pouch caudally using a grasper through the right hypochondrium port.
(7) Dissection of the Callot's triangle was commenced using a diathermy mounted on a hook/maryland grasper. When we felt that further dissection is hazardous because of anatomical uncertainty, we started antegrade dissection.
(8) The fundus was pulled caudally using the grasper in the right hypochondrium port and a counter traction achieved by pushing the tip of the liver cranially using the grasper in the right iliac fossa port. In addition, dissection between the liver and the gall bladder was commenced.
(9) We continued dissection until it is not safe to proceed furthermore because of unclear anatomical landmarks in Callot's triangle; at this point the gall bladder was grasped from its middle part squeezing all the stones to the fundus using a noncrushing endoscopic clamp.
(10) The gall bladder was opened using a diathermy mounted on hook, and direct diathermy was applied to the edges to minimize bleeding. The gall bladder was retrieved from the epigastric port.
(11) Suction and irrigation of the opened gall bladder and removal of any stones were performed.
(12) Continuous suturing of the gall bladder was performed, using vicryl 2/0 stitches; only single layer was applied.
(13) Careful haemostasis of the liver bed and suction of the subhepatic space and subdiaphragmatic spaces were performed.
(14) Wide bore-free drainage tube was placed in the subhepatic region and brought out through the right iliac fossa port site.
(15) Inspection of the ports was performed from inside before removal to check for haemostasis, and all ports were removed under vision.
(16) Fascial defects were closed using 2/0 vicryl mounted on a J needle.
(17) Skin was closed using 3/0 monocryl.

Postoperative care

(1) Early mobilization was encouraged.
(2) Patients are allowed to eat and drink once tolerated.
(3) Single dose of antibiotics.
(4) Drains were removed if draining was less than 50 ml in 24 h.

The following parameters were recorded: intraoperative complications including bile duct injury and bowel injury and postoperative complications such as bile leakage, ligated ducts, the operative time and hospital stay.

Results

Our study recruited 30 patients, male patients 18 (60%) and female patients 12 (40%). Their mean age was 52.6 years ± 12.65 SD. The mean operative time was 92 min ± 20 SD, and the mean hospital stay was 72.43 h ± 22 SD.

Intraoperative and postoperative complications

	n
Duodenal injury	0
Bile duct injury	0
Intra-abdominal collection and bile leakage	2
Missed stone	0
Wound infection	0
Conversion to open	1

Discussion

Our study recruited 30 patients with difficult cholecystectomy and 18 (60%) patients were men. When searched through the literature, we found that different authors such as Vivek *et al.* [6] in 2014 and Nachnani and Supe [7] in 2005 studied the preoperative

predictors for a difficult cholecystectomy and male sex is believed to be one of the preoperative predictors that increases the likelihood of difficult cholecystectomy.

Careful identification of the structures in the Callot's triangle is the main step to perform cholecystectomy, either open or laparoscopic. In addition, despite careful dissection and identification of those structures, there is always an incidence of injury to the bile ducts. At the early beginning's of laparoscopic cholecystectomy it was believed that the incidence of bile duct injury is higher that during open cholecystectomy but this has been challenged by many authors and the incidence of bile duct injury during laparoscopic cholecystectomy is just 0.5% now [8,11–13].

In our study, we did not encounter any bile duct injuries, although there were difficult cholecystectomies, and this could be attributed to the fact that we performed a subtotal cholecystectomy. Hence, our dissection usually stopped away from Callot's triangle and this is in agreement with the results published by other authors who studied the subtotal cholecystectomy as an alternative approach in difficult cholecystectomy [14].

However, the incidence of bile duct injuries in total cholecystectomies performed for difficult cholecystectomies is higher; it is up to 3.4% [14,15].

We encountered two cases with bile leakage and intra-abdominal collection, which were managed conservatively, and Davis *et al.* [16] in 2012 showed the same results.

This is relatively higher than the incidence of bile leakage after standard laparoscopic cholecystectomy, which is less than 1% [17]. The value of an intra-abdominal drain in prevention of postoperative collection in standard cholecystectomies was studied thoroughly and most of the authors believe that there is no value of an intra-abdominal drain in preventing intraperitoneal collection [18–20]. However, we did not find enough literature to support this in cases of difficult cholecystectomies; hence, we considered that opening the gall bladder for stone extraction will contaminate the field, and hence we placed drains in all our cases. This did not prevent collection but our sample was not big enough to challenge the value of an intra-abdominal drain in such cases. We converted only one patient into open cholecystectomy; however, we are not adopting this technique as an absolute substitute for conversion to open. It is not appropriate to compare our rate of conversion to the rate of conversion during standard laparoscopic cholecystectomy because we did not include patients who underwent standard cholecystectomy in our study. In addition, we cannot use our data to comment on reduction of rate of conversion, but many authors cross-examined this point in their work and concluded that using this technique in difficult cholecystectomies will reduce the need to conversion [21–24].

We did not encounter any mortalities and no intestinal injury was encountered, in comparison with the incidence of bowel injury in standard cholecystectomy, which is less than 1% [17]. Operative time and hospital stay were longer than the usual operative time for laparoscopic cholecystectomy but this was expected [25,26].

Conclusion

Subtotal cholecystectomy is a safe procedure in cases where there is no clear identification of the structures in Callot's triangle. However, it is not a substitute for conversion into open, if deemed required.

Acknowledgements

Conflicts of interest

None declared.

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How much is the axillary nodal status in breast cancer affected by neoadjuvant chemotherapy? An Alexandria medical research institute hospital experience

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Background
The multidisciplinary approach, including surgery, chemotherapy, endocrine therapy, and radiation therapy, has become the standard treatment for primary breast cancer patients. The status of axillary lymph nodes (AxLNs) remains the most important prognostic factor. The number of lymph nodes retrieved in axillary lymph node dissection (ALND) varies considerably. Removal of at least 10 AxLNs is generally considered as an adequate ALND for reliable lymph node staging. Several authors have reported a significantly lower AxLN count in patients undergoing ALND after the completion of neoadjuvant chemotherapy (NAC) compared with patients who underwent surgical resection first.

Objective
Our aim was to evaluate the effect of NAC on the axillary nodal status in breast cancer patients regarding the number of AxLNs retrieved at ALND and to compare the degree of response to NAC relative to the primary tumor's nodal status in the both studied groups.

Patients and methods
In this retrospective study, we reviewed the records of all patients with invasive breast cancer who were admitted to the Department of Surgery, Medical Research Institute hospital, Alexandria, during the period between August 2013 and July 2014 and were scheduled for ALND. Cases were categorized into two groups: group I included patients who received NAC and were then subjected to surgery, whereas group II included patients who were subjected to surgery without NAC. Data collected from both groups included patient demographics and clinicopathological characteristics.

Results
The study included 237 female patients who were allocated to one of the two groups: group I (GI) included 93 patients (39.2%), whereas group II (GII) included 144 patients (60.8%). There was no statistically significant difference between the two groups regarding the age, the tumor grade, and the tumor type. However, significant differences were seen in a variety of baseline criteria between the two groups; patients who received NAC had larger tumors (T) ($P = 0.001$), a higher lymph node (*N*) classification ($P = 0.002$), and a higher overall disease stage ($P = 0.0001$) compared with patients who underwent surgical resection first. After NAC in GI, AxLNs were significantly more responsive to NAC relative to the primary tumor ($P = 0.003$). The number of AxLNs harvested during ALND revealed a significantly lower LNY in patients who underwent NAC in comparison with patients who did not, with a median total number of nine nodes in GI compared with 14 axillary nodes in GII ($P = 0.0001$). The number of positive AxLNs was higher in patients who underwent surgical resection first, with a statistically significant difference ($P = 0.006$).

Conclusion
NAC is a significant independent parameter for a reduced AxLN number retrieved by ALND. Also, we can conclude that AxLNs are significantly more responsive to NAC relative to the primary tumor either clinically or pathologically.

Keywords:
axillary lymph node, axillary lymph nodes dissection, breast cancer, lymph node status, neoadjuvant chemotherapy

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Introduction

Breast cancer is the most frequent malignant tumor in women worldwide. The incidence and mortality rates among women vary among countries, but are steadily increasing worldwide [1]. In Egypt, breast cancer is the most common cancer among women, representing 33.5% of the total number of cases, with 18660 new cases diagnosed in 2012. It is also the leading cause of cancer-related mortality, accounting for 29.1% of the total with 6546 deaths [2]. These estimates are confirmed in many regional Egyptian cancer registries [3,4]. The axillary nodal status remains the most important prognostic factor for patients with breast cancer. Clinical assessment and imaging

modalities are not always reliable. Axillary lymph node dissection (ALND) is routinely performed for patients with lymph node-positive breast cancer for purposes of staging and regional control. However, the optimal management of the axilla remains uncertain [5]. The number of nodes retrieved during axillary dissection has been demonstrated to have a significant impact not only on regional nodal failure, but also on local failure [6]. Current guidelines suggest that at least 10 nodes should be examined for reliable lymph node staging [7]. The role of the percent of positive lymph nodes in predicting distant metastasis and survival was recently demonstrated in several institutional series. These studies showed consistently that the percentage of positive lymph nodes is a significant independent prognostic indicator of survival in women with lymph node-positive breast carcinoma [8–10]. The multidisciplinary approach, including surgery, chemotherapy, endocrine therapy, and radiation therapy, has become the standard treatment for primary breast cancer patients [11]. When it first emerged in the late 1970s, the use of neoadjuvant chemotherapy (NAC) was limited primarily to women with inoperable locally advanced breast cancer to enable surgical resection [12]. Many other trials followed in the past two decades studying the role of induction chemotherapy [13]. Currently, NAC followed by surgery is the treatment of choice for patients with inflammatory breast cancer or locally advanced breast cancer [14,15]. Recently, this approach was also recommended for primary operable breast cancer [16]. NAC has been compared with standard, postoperative adjuvant chemotherapy, with the dual goals of improving survival and facilitating local therapies. Large randomized trials proved that preoperative chemotherapy has at least the same survival benefit as postoperative chemotherapy [17]. Several authors have reported a significantly lower AxLN count in patients who underwent ALND after the completion of NAC compared with patients who underwent surgical resection first without any prior chemotherapy [18,19]. In this study, we aimed to evaluate the effect of NAC on the axillary nodal status in breast cancer regarding the number of AxLNs retrieved at ALND and the degree of response to NAC relative to the primary tumor.

Patients and methods

This retrospective review was conducted on all patients with pathologically proven nonmetastatic invasive breast cancer, who were admitted to the department of Surgery, the hospital of Medical Research Institute, University of Alexandria, during the period between August 2013 and July 2014. These patients were scheduled for ALND as a part of modified radical mastectomy or conservative breast surgery with or without reconstruction. Patients who underwent sentinel lymph node biopsy, who had bilateral breast cancer, who had primary inflammatory carcinoma, who were operated upon by a surgeon lower than senior residents, and patients with level III ALND were excluded. Cases were categorized into two groups: GI included patients who received NAC and were then subjected to surgery, whereas GII included patients who were subjected to surgery without NAC. Patients were examined by a multidisciplinary team to confirm the diagnosis of breast cancer and to evaluate the clinical stage of the disease at presentation (GI, GII) and the response after four cycles of chemotherapy (GI). The tumor size and the nodal status before and after NAC were measured routinely by ultrasound. Data collected from both groups included patients' characteristics, diagnostic methods, the type of surgery, tumor characteristics such as the histological subtype, the tumor grade, the total number of AxLNs identified in pathologic specimens, the number of positive AxLNs, lymphovascular invasion, estrogen and progesterone receptors, the human epidermal growth factor receptor 2 (Her-2) status, and treatment details. Patients in the former group were treated as per the institutional protocols during that time, which included anthracycline-based therapy with or without the addition of taxanes. After four cycles of NAC in GI, only responding patients underwent surgery, whereas patients with a partial response, no response, or progressive disease underwent additional cycles of non-cross-resistant chemotherapy. The standard surgical technique at our institution is to perform level I and II ALND. Pathologic processing of ALND specimens at our institution has been consistent throughout the study period and is comprised of sharp dissection of all lymph node tissue from the surrounding fat. No fat-dissolving techniques are used. All lymph node tissues are then examined histologically.

Statistical analysis

Data were analyzed using the statistical package for social sciences (SPSS ver.20; SPSS Inc., Chicago, Illinois, USA). Quantitative data were described using the mean and SD, whereas qualitative data were described using the number and percent. For comparing quantitative variables between the two groups, we used the independent sample *t*-test. We used the Monte Carlo significance test if >2 × 2 categories and more than 20% of the cells had an expected cell count less than 5. In all statistical tests, a level of significance of 0.05 was used; statistical significance was set at P less than 0.05.

Results

This study included 237 female patients who were allocated to one of the two groups: GI received NAC and was then subjected to surgery and included 93 patients (39.2%), whereas GII was subjected to surgery without NAC and included 144 patients (60.8%). On comparing the two groups, there was no statistically significant difference between them regarding patients' age (P = 0.196). In contrast, there was a statistically significant difference in the other standard prognostic factors between the two groups. As treatment decisions regarding NAC are routinely based on the tumor size, clinical nodal involvement, and the overall disease stage, patients who received NAC had larger tumors (T) (P = 0.001), a higher lymph node (N) classification (P = 0.002), and a higher overall disease stage (P = 0.0001) than patients who underwent surgical resection first (GII). The distribution of the studied patients according to age and intial tumor characteristics are summarized in Table 1.

After NAC in GI, we registered both the tumor stage and the nodal stage to assess the degree of response of AxLNs (the nodal stage) and the primary tumor (the tumor stage) to NAC, which revealed that axillary AxLNs (the nodal stage) were significantly more responsive to NAC relative to the primary tumor (the tumor stage) (P = 0.003) as shown in Table 2.

Regarding the data collected from postoperative pathological reports, there were no statistically significant differences between the two groups regarding the tumor grade and the tumor histological subtype. In contrast, the number of AxLNs harvested during ALND revealed a significantly lower LNY in patients who underwent NAC in comparison with patients who did not receive NAC. The median total number of nodes was 9 in GI compared with 14 axillary nodes in GII; these results were highly statistically significant (P = 0.0001). The number of positive AxLNs was higher in patients who underwent surgical resection first, with a statistically significant difference (P = 0.006) as shown in Table 3.

Discussion

In our practice, we have noticed that NAC in breast cancer can downstage AxLNs more than the primary tumor, and also, the number of retrieved lymph nodes in ALND in patients who received NAC is usually lower than that in patients who underwent surgical resection first, but both former points were just observations and the literatures showed debates about them.

According to Erbes *et al.* [20], NAC reduces the number of AxLNs retrieved by ALND significantly, whereas Boughey *et al.* [21] concluded that the number of AxLNs recovered at ALND does not appear to be affected by NAC and may even be higher than in patients who underwent surgical resection first. Also Sinn *et al.* [22] concluded that NAC could result in a downstaging of positive AxLNs, but the potential

Table 1 Distribution of the studied patients according to age and tumor characteristics before neoadjuvant chemotherapy in group I and before surgery in group II

Item	Group I (N = 93)	Group II (N = 144)	P
Age (years)			0.196**
Range	32–53	30–50	
Mean ± SD	43.250 ± 7.46835	40.4500 ± 5.89804	
Tumor stage [N (%)]			
T0	0 (0)	20 (13.9)	0.001*
T1	6 (6.5)	38 (26.4)	
T2	28 (30)	68 (47.2)	
T3	42 (45.2)	18 (12.5)	
T4	17 (18.3)	0 (0)	
Nodal stage [N (%)]			
N0	8 (8.6)	19 (13.2)	0.002*
N1	16 (17.2)	76 (52.8)	
N2	45 (48.4)	38 (26.4)	
N3	24 (25.8)	11 (7.6)	
Overall disease stage			0.0001*
Stage I	0 (0%)	7 (5%)	
Stage II	23 (24.7%)	88 (61%)	
IIA	12	59	
IIB	11	29	
Stage III	66 (71%)	49 (34%)	
IIIA	47	25	
IIIB	4	6	
IIIC	15	18	
Stage IV	4 (4.3%)	0 (0%)	

*The Monte Carlo test; **The t-test.

Table 2 Distribution of patients in group I according to the degree of response of the axillary lymphadenopathy (nodal stage) to neoadjuvant chemotherapy relative to the primary tumor (tumor stage)

Item	Group I (before NAC) (N = 93) [N (%)]	Group I (after NAC) (N = 93) [N (%)]
Tumor stage		
T0	0 (0)	5 (5.4)
T1	6 (6.5)	17 (18.3)
T2	28 (30)	29 (31.2)
T3	42 (45.2)	31 (33.3)
T4	17 (18.3)	11 (11.8)
Nodal stage		
N0	8 (8.6)	23 (24.8)
N1	16 (17.2)	39 (41.9)
N2	45 (48.4)	22 (23.6)
N3	24 (25.8)	9 (9.7)
P	0.003*	

NAC, neoadjuvant chemotherapy; *The t-test.

Table 3 Distribution of postoperative pathological parameters in the two studied groups

Item	Group I (*N* = 93) [*N* (%)]	Group II (*N* = 144) [*N* (%)]	*P*
Tumor grade			
1	27 (29)	24 (16.7)	0.165*
2	45 (48.4)	72 (50)	
3	21 (22.6)	48 (33.3)	
Tumor histological subtype			
Invasive ductal	58 (62.4)	96 (66.7)	1.000*
Invasive lobular	21 (22.6)	29 (20.1)	
Other	14 (15)	19 (13.2)	
Number of AxLNs			
Median	9	14	0.0001**
Positive			
<4	29 (31.8)	26 (18)	0.006**
≥4	64 (68.2)	118 (82)	

AxLNs, axillary lymph nodes; *The Monte Carlo test; **The Pearson χ^2-test.

influence of chemotherapy on the LNY and their morphology and detectability is still unclear.

To resolve this conflict, we conducted this research work. We retrospectively reviewed all patients with breast cancers who were admitted to the Department of Surgery, Alexandria Medical Research Institute Hospital, during the period between August 2013 and July 2014 and were scheduled for ALND. Patients who underwent sentinel lymph node biopsies, who were operated upon by surgeons lower than senior residents, and patients with level III ALND, who had bilateral or inflammatory breast cancer, were excluded to avoid selection bias. Cases were categorized into two groups: GI included patients who received NAC and were then subjected to surgery, whereas GII included patients who were subjected to surgery without NAC. We examined 237 patients who were allocated to one of the two groups: GI included 93 patients (39.2%), whereas GII included 144 patients (60.8%).

The findings of this study demonstrated that the number of AxLNs recovered after completion of NAC was lower than in patients who underwent surgical resection first, which is similar to the results of Belanger *et al.* [18] and Neuman *et al.* [19], but in contrast to the results of Boughey *et al.* [21], Straver *et al.* [23], Petrick *et al.* [24], Patel *et al.* [25], and Cil *et al.* [26] who concluded that the number of AxLNs recovered at ALND does not appear to be affected by NAC and may even be higher than in patients who underwent surgical resection. Boughey *et al.* [21] explained the slightly higher average number of lymph nodes found after the completion of NAC by a subconscious decision to perform a more aggressive surgical approach in these locally advanced cases, a subconscious effort to conduct a more comprehensive search for lymph nodes in the resected specimen by the pathologists, or due to a statistically higher lymph node stage and a higher number of positive lymph nodes in the neoadjuvant group.

In contrast, Belanger *et al.* [18] suggested that the lower number of AxLNs after NAC may be secondary to the fibrosis of lymphatics caused by NAC; this explanation is similar to the findings of recently published studies that also reported chemotherapy-induced changes in lymph nodes, including lymphoid depletion [27–29], and this may affect the pathologist's ability to find AxLNs within the dissection specimen as NAC could cause fibrosis of lymphatics, resulting in smaller atrophic AxLNs that are more challenging to identify macroscopically [26]. Results of the current study support this theory.

In our study; the number of positive lymph nodes was lower in the patients undergoing NAC, and this may support our findings regarding the downstaging effect of NAC on AxLNs not only clinically (as shown in our results in Table 2) but also pathologically. this finding is still in contrast to the results of Boughey *et al.* [21], who concluded that the number of positive lymph nodes was higher in the patients who underwent NAC, reflecting the more advanced stage of disease in these patients. Regarding surgeons' training as a factor, some reports concluded that the surgeon's level of training appears to impact the number of AxLNs resected [24,30]. To avoid this bias, patients who were operated upon by surgeons lower than senior residents were excluded from the study to fulfill a satisfactory level of training for adequate axillary dissection.

Some previous studies have indicated that the number of AxLNs found correlates inversely with the patient's age, with younger patients having more lymph nodes excised than older patients [24,26,31], whereas other studies have not found this association [11]. We did not notice this as there was no statistically significant difference between the two groups regarding age (P = 0.196), and this supports our results of NAC as the strongest independent variable for a diminished lymph node number.

Conclusion and recommendations

Our study identified NAC as a significant independent parameter for a reduced LNY number retrieved by ALND.

Existing recommendations for a minimum removal of 10 lymph nodes by ALND are clearly compromised by the clinically already established concept of NAC. Consequently, the lymph node count of less than 10 by ALND after NAC is not indicative of insufficient axillary staging.

Our study concluded that axillary AxLNs (nodal stage) are significantly more responsive to NAC relative to the primary tumor (tumor stage) both clinically (TNM staging) and pathologically (the number of positive LNYs). Therefore, guideline recommendations for the future should consider these points.

Because of the short period of the study and the low number of patients studied, larger scale, longer period, and multicentric surveys for the documentation of our finding are needed.

One of the major limitations of this study is that this study is retrospective in design, and therefore, it is potentially biased by which patients underwent NAC and which patients underwent surgical resection first. In addition, the pathologic processing of ALND specimens varied between pathologists, and so we recommend conducting prospective studies to unify the inclusion and exclusion criteria and the surgical, pathological, and oncological parameters.

Acknowledgements

Conflicts of interest

None declared.

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Improving lymph node harvest in colorectal cancer by intra-arterial injection of methylene blue: a randomized trial

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Background
Prognosis in colorectal carcinoma is related to the state of lymph node involvement. Myriad studies demonstrate that both survival and prognosis are significantly influenced by the number of lymph nodes harvested, particularly in node-negative disease.

Aim
The aim of this study was to evaluate the usefulness of injecting methylene blue into the main artery/arteries of resected colorectal specimens in terms of the total number of lymph nodes identified.

Patients and methods
The study included 54 patients randomly divided into two groups: group 1 (26 patients), in which resected specimens of colorectal carcinoma were injected with methylene blue, and group 2, in which no injection was carried out.

Results
The total number of lymph nodes per patient in group 1 was 19.5 (17–39) [median (range)] and that in group 2 was 16.5 (8–19). The difference was statistically highly significant ($P < 0.001$). We also noticed that the best improvement in lymph nodes harvest was among the very small and small lymph nodes.

Conclusion
Methylene blue injection into the main artery/arteries is an effective and simple method for improving the lymph node harvest in resected specimens of colorectal carcinoma.

Keywords:
colorectal carcinoma, lymph nodes harvest, methylene blue injection

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Introduction

Prognosis in colorectal carcinoma is clearly related to the degree of tumor infiltration through the bowel wall and the presence or absence of lymph node involvement. These two factors are the basis of the staging systems established for this disease. Today, almost 80 years after Dukes published his pioneer classification, all attempts to improve his proposal are mostly based on refinements of these two data [1].

Many authors have advocated that a minimum of 12 lymph nodes are required for accurate colorectal cancer staging [2–4].

Most studies suggest that node positivity rates increase with increased nodal harvest [5–8].

In other words, the higher the number of lymph nodes we examine, the higher the number of positive lymph nodes we find [9].

Myriad studies demonstrate that both survival and prognosis are significantly influenced by the number of lymph nodes harvested, particularly in node-negative disease [10–12].

In addition, the current paradigm of neoadjuvant chemoradiation for the treatment of rectal cancer complicates this issue because radiation is known to result in a decrease in the number of assessable lymph nodes [13].

Hence, the concept of improving lymph node identification to facilitate further pathological assessment was introduced.

Immunohistochemical staining and fat clearance methods using alcohol, acetone, and other substances seem to be efficient techniques for upgrading lymph node identification [14–16].

However, these methods are time-consuming, need additional equipment and expertise, and entail the use of hazardous materials [14].

Methylene blue injection is found to be superior to other dyes because of higher availability and affordability [17,18].

This method was originally introduced by Märkl *et al*. [19]. They injected the superior rectal artery with methylene blue solution to improve lymph node harvest in rectal carcinoma [19].

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In this study we carried the technique one step ahead by injecting methylene blue into the inferior mesenteric artery, right colic artery, and middle colic and/or left colic artery in colorectal carcinoma cases, rather than in rectal carcinoma cases only.

Patients and methods

This study was carried out between August 2011 and August 2014 in Menoufia University Hospital (Shibin Alkom, Egypt). The study included 54 consecutive patients who had undergone surgeries for colorectal carcinoma with a curative intent, both laparoscopic and open.

The patients were randomly divided into two groups: group 1, in which specimens were injected with methylene blue, and group 2, in which no injection was carried out. In group one, at the end of surgery and after removal of the specimen, the surgeon cannulated the main artery (arteries) with a 20-G plastic cannula and injected 15 ml of methylene blue dye (Merck, Darmstadt, Germany) (50 mg methylene blue in 5 ml distilled water, diluted in 10 ml 0.9% NaCl solution). The artery was then ligated and the specimen sent for histopathological evaluation following standard techniques (i.e. no special handling was done by the pathologist). Group 2 represented the control group, in which patients were operated upon by the same surgeons and the specimens were processed in the same way as group 1 and examined by the same pathologist.

Both groups were compared for age, sex, weight, total number of lymph nodes recovered, number of lymph nodes with malignant deposits, and the size of lymph nodes (≤1 mm, between 1 and 5 mm, and >5 mm). We recorded whether the patients received radiotherapy, the type and length of each specimen, and the TNM stage of each tumor.

Statistical analysis

Results were statistically analyzed using statistical package SPSS (version 16; SPSS Inc., Chicago, Illinois, USA). Student's *t*-test and the Mann–Whitney test were used for quantitative variables. The χ^2 and *Z* tests were used for qualitative variables. *P* values less than 0.05 were considered significant.

Results

Twenty-six patients were assigned to group 1 (injection group) and 28 patients to group 2 (no injection group). Table 1 shows a summary of the findings from both groups. Both groups were homogenous with regard to age, grade, sex, length, prior chemoradiotherapy, and type of resection. None of our cases had undergone a total colectomy. In group 1, we encountered no case with a lymph node count less than 12; however, in group 2 all three cases who had received prior radiotherapy had a lymph node count of less than 12.

Discussion

Insufficient lymph node harvest is commonly attributed to an incomplete resection by the surgeon. Moreover, it is an indication for expensive chemotherapy with known side effects [20].

Table 1 The findings in the two groups

Point of comparison	Group one (*n* = 26)	Group two (*n* = 28)	*P*-value
Age (mean ± SD) (years)	55.26 ± 9.06	57.42 ± 6.61	0.319
Sex			
Male	14 (53.8)	15 (53.8)	–
Female	12 (46.2)	13 (46.4)	
Weight (mean ± SD) (kg)	76 ± 11.73	74 ± 12.54	0.228
Localization			
Rectal	12 (46.2)	13 (46.4)	0.796
Right colon	5 (19.2)	6 (21.4)	0.890
Transverse colon	2 (7.7)	3 (10.7)	0.928
Left colon	7 (26.9)	6 (21.4)	0.877
Grade			
I	2 (7.7)	2 (7.1)	0.662
II	10 (38.5)	11 (39.3)	0.826
III	12 (46.2)	13 (46.4)	0.796
IV	2 (7.7)	2 (7.1)	0.662
Prior chemoradiotherapy	4 (15.4)	3 (10.7)	0.913
Length of specimen (mean ± SD) (cm)	23.48 ± 6.19	22.52 ± 7.30	0.605
TN stage			
T1	0 (0.0)	0 (0.0)	–
T2	4 (15.4)	3 (10.7)	0.913
T3	17 (53.4)	20 (71.4)	0.277
T4	5 (19.2)	5 (17.9)	0.819
N0	14 (53.8)	12 (42.9)	0.597
N1	7 (26.9)	10 (35.7)	0.687
N2	5 (19.2)	6 (21.4)	0.890
Total number of lymph nodes recovered/patient [median (range)]	19.5 (17–39)	16.5 (8–19)	<0.001 (S)
Number of positive nodes/patient [median (range)]	6.40 (2–12)	3 (2–10)	0.043 (S)
Lymph node ratio	6/23 = 26	4/14 = 28.5	0.829
Size of lymph nodes (mm)			
<1	5 (1–8)	2.5 (1–3)	<0.001 (S)
Between 1 and 5	15 (11–22)	8 (3–11)	<0.001 (S)
>5	6 (3–8)	6 (3–8)	0.349

S, significant.

It is demonstrated that the total number of resected lymph nodes in colorectal cancer surgeries is an independent prognostic factor, as it is used as an indicator of the quality of surgery itself [10].

It is understood that the accuracy of lymph node status assessment increases with an increase in the number of lymph nodes examined [3,21,22], and most studies suggest that node positivity rates increase with increased nodal harvest [2].

Methylene blue (methylthioninium chloride) when injected intra-arterially stains the arteries and capillaries, and, because the lymph nodes harbor a higher content of vessels in relation to the surrounding fat, they stain deeper than the surrounding fat and become easily identified [23].

It is not entirely clear how the solution passes into the lymph nodes when injected into the specimens, but the most likely mechanism could be the increase in interstitial pressure caused by the injection and therefore induced lymphatic flow [24]. That is why we injected the specimens with methylene blue just after ligation of the pedicle(s) of the specimen.

Methylene blue solution is often found to be superior to other dyes because of its relative safety, higher availability, and affordability [25].

In our study, the total number of lymph nodes recovered per patient was significantly higher in the methylene blue group compared with the control group ($P < 0.001$) (Table 1). Both groups were homogenous regarding other factors that could have affected the lymph node harvest (e.g. grade, length of specimen, age, prior chemoradiotherapy, type of resection) (Table 1).

The American Society of Anesthesiologists stated that grade, older age of the patient, and neoadjuvant radiotherapy are commonly found to be the main factors associated with a low lymph node harvest. Moreover, transverse colectomy and abdominoperineal resection are the methods of surgery associated with the poorest lymph node harvest in the histopathological examination of the surgical specimens [26]. Patients with higher BMI usually have a bigger mesocolon with a larger number of lymph nodes.

We noticed significant improvement in the identification of smaller lymph nodes: that is, less than 1 mm and between 1 and 5 mm Table 1. This is in accordance with other studies [23].

This could be explained by the improved visual identification of smaller lymph nodes when using methylene blue because smaller lymph nodes are more likely to be mistaken for fat lobules if not stained. Overlooking small-sized lymph nodes is dangerous as lymph node size is not a reliable marker for lymph node metastases [27]; that is, very small and small lymph nodes may contain metastases and large lymph nodes may be free and the enlarged size may be due to an immune response rather than due to metastases. Large lymph nodes in stage I/II disease might indicate a favorable outcome [27].

Better identification of smaller lymph nodes is a good point in favor of the use of methylene blue.

Upstaging of colorectal cancer with improved nodal harvest is a controversial issue. Some authors claim that collecting and examining more lymph nodes will lead to upstaging of cases because of better identification of metastases that would otherwise be missed [28]. Others deny this [29].

Extensive studies were carried out on the lymph node ratio [30–32] (i.e. the ratio between the number of positive lymph nodes resected and the total number of lymph nodes harvested) being a better prognostic factor than the mere presence of positive lymph nodes.

In our study, we noticed that the total number of lymph nodes harvested increased significantly with the use of methylene blue; yet simultaneously the number of positive lymph nodes per patient also increased from four to six. Thus, the lymph node ratio did not differ significantly ($P > 0.05$) (Table 1). Also, the treatment plans in three of our patients were changed with the finding of additional lymph nodes.

Preoperative use of chemoradiotherapy is known to reduce the number of lymph nodes identified in the specimens [33,34]. In a recent study, complete absence of recovered lymph nodes in resected specimens after neoadjuvant chemoradiation was observed in 7.6% of specimens [35]. Thus, the use of methylene blue in such cases is more clearly indicated [36].

We also noticed significant improvement in the number of lymph nodes with deposits identified in the methylene blue group compared with the control group (Table 1). This can be attributed to the larger number of lymph nodes examined, but further study may be needed to evaluate the hypothesis that blue staining of lymph nodes makes the identification of micrometastases easier. Recently, Markl *et al.* [20] studied this hypothesis and concluded that identification of lymph node metastases was not improved using methylene blue.

Conclusion

We recommend the routine use of methylene blue intra-arterial injection in colorectal cancer, especially in patients treated with neoadjuvant therapy.

Acknowledgements

Conflicts of interest

None declared.

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Two-port retrograde laparoscopic appendicectomy for complicated pediatric appendicitis using a single Hem-O-Lock clip for the closure of the appendicular stump

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Objective
The aim of this study was to assess the safety and the technical feasibility of retrograde laparoscopic appendicectomy for the pediatric population with complicated appendicitis (gangrenous, perforated, or forming mass) and to evaluate the security and advantages of closing the appendicular stump with a single Hem-O-Lock polymer clip.

Materials and Methods
This is a prospective review of 82 pediatric patients presenting with acute appendicitis, of whom 50 patients were selected, according to computed tomographic abdomen and pelvis, to have a complicated appendicitis. All the data were collected and interventions were performed in Zagazig University Hospitals during the period from December 2012 to August 2014. All cases were operated by two-port retrograde appendicectomy using single Hem-O-Lock polymer clips to close the appendicular stump. The age, the sex of the patients, and complications were evaluated. Treatment complications and outcomes were recorded for all cases.

Results
Four of the 50 patients (8%) had postoperative complications; four patients developed intra-abdominal abscess postoperatively: two of them underwent laparoscopic drainage during the same admission and the other two patients were readmitted after 1 and 2 weeks, respectively, when one of them underwent ultrasound-guided drainage and the other one improved within 48 h by medical treatment. No other complications were noted apart from one case that converted to open surgery due to a large cecal mass with a gangrenous cecal wall. The cases of postoperative abscess occurred early during our initial experience, with laparoscopic appendectomy for complicated cases.

Conclusion
Retrograde appendicectomy allows easy access to operate complicated appendicitis. The use of two ports adds an advantage to the procedure by decreasing postoperative pain. The use of a single polymer clip is as secure as two clips for the closure of the appendicular stump even for a complicated appendix.

Keywords:
laparoscopic appendicectomy, polymer clips

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Introduction

Acute appendicitis was and still is one of the most common pediatric surgical emergencies. Laparoscopic appendectomy, first performed by Semm in 1983, has become increasingly popular over the years. Children are more prone than adults to present with complicated appendicitis, especially perforation [1]. Laparoscopic appendectomy has become an accepted management modality in complicated pediatric appendicitis (CPA) as well as in uncomplicated cases [2].

The proper management technique of CPA (appendicular mass, gangrenous or perforated) had been more controversial [3]. However, in cases of complicated appendicitis, the anatomy can be obscure, and the operative time can be significantly prolonged. Laparoscopy in complicated cases of acute appendicitis can be a challenging and technically demanding procedure that requires more than basic laparoscopic skills, and requires the use of special techniques to access the complicated appendix as most complicated cases have a hidden appendix, especially the tip [4].

There are several methods for the ligation of the appendicular stump during laparoscopic appendicectomy. Many studies have shown the safety and the cost of different devices in different situations. Each technique has its own potential advantages and disadvantages. Endo-GIA staplers are expensive instruments. Titanium clips may be slipped from their primary position. A Hem-O-Lock clip is a nonabsorbable polymer clip with a lock-engagement feature and teeth within the jaws, which may provide greater security [5].

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Laparoscopic appendicectomy using a single polymeric clip to close the appendicular stump in children is a safe, feasible, and inexpensive method [6]. The use of a single clip for the closure of the appendicular stump can be used as the standard procedure in laparoscopic appendectomy whenever possible as its secure jaw favors it over single endoloop application and there is no difference in the safety in case of two-clip application [7].

Materials and Methods

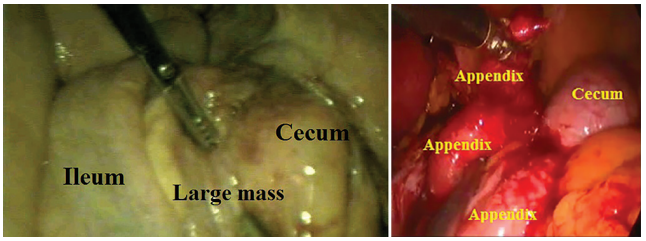
Between December 2012 and August 2014, 82 Pediatric patients presenting to our university hospital in the Emergency Room Department and/or referred from other hospitals with complicated acute appendicitis were identified from our prospectively collected data [clinical examination, fever, elevated total leukocyte count, pelviabdominal ultrasound by a senior staff, and finally the most diagnostic results are obtained from the computed tomographic (CT) abdomen and pelvis. Only pediatric population with suspected complication exposed to CT, as patients with classic appendicitis are not exposed to CT and not included in our study 50 consecutive patients from a total of 82 patients presented and diagnosed with complicated acute appendicitis were treated laparoscopically.

Pediatric patients constituted 11 cases with an appendicular mass (Fig. 1a), nine cases with an appendicular abscess (Fig. 2), five cases with a gangrenous appendix (Fig. 3a), 21 cases with a perforated appendix at the tip, and four cases perforated near the base (Fig. 4).

Laparoscopic appendicectomy was performed with the patient under general anesthesia; the abdomen was dripped and prepped in the ordinary manner with insufflation of CO_2 pneumoperitoneum. The insufflation pressure was controlled automatically and kept below 12 mmHg. Foley's catheter was inserted after the induction of anesthesia to empty the bladder. It was mandatory because the Foley catheter is helpful in decompressing the bladder, thereby maximizing the viewing field and improving the working space and allowing the demarcation of the dome of the bladder. A monitor was positioned to the right of the patient.

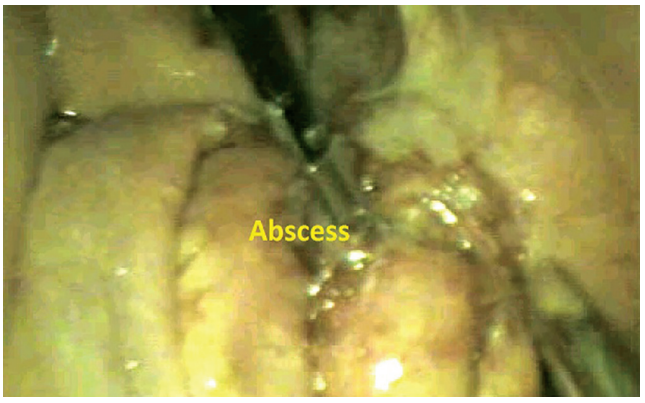
A two-port was used; the first or the optical trocar was a 10 ml trocar used for the camera, using a safety port, a thorough look with the scope done for the abdomen with more focus on the pelvis. Once the procedure is started and the laparoscope has been inserted, steep Trendelenburg positioning allows proper placement of the remaining trocar. The other trocar was inserted under complete vision. It was a 10 mm trocar for the introduction of the clip applier at the left midclavicular line.

Figure 1



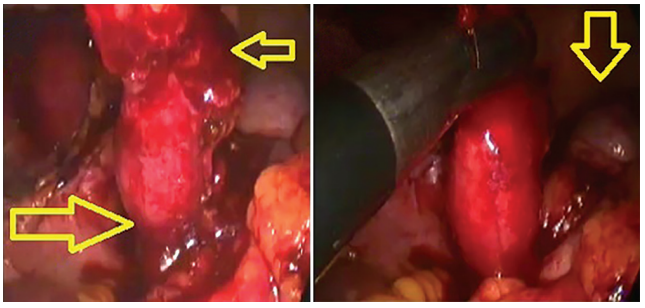
A large appendicular mass.

Figure 2



An appendicular abscess.

Figure 3



A gangrenous appendix.

After all of the trocars have been placed, placing the patient left side down aids gravity in relocating the small bowel away from the appendiceal/cecal field of vision.

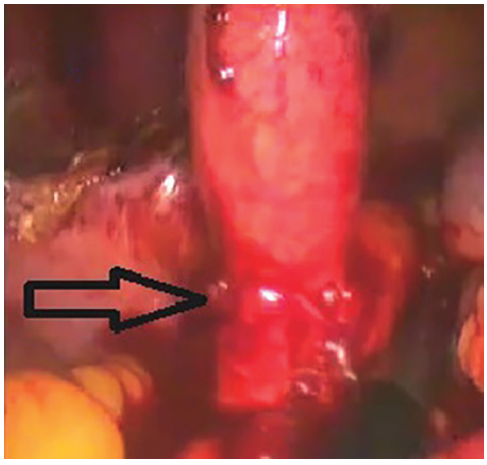
In recent and past cases, disposable equipment was used, whereas in early cases, the equipment was nondisposable.

The appendix was identified. Any part of the appendicular shaft was stayed by a nontraumatic grasper and pushed to the abdominal wall at the Mcburney point detected by pressing from the outside,

and a 2/0 proline suture on a straight needle or a curved rounded needle was passed from the abdominal wall to the appendix to the abdominal wall again and tied extracorporeally, the gangrenous appendix cases were the most difficult cases for staying. Reorientation and thorough exploration of the pelvis was performed to demarcate the extension of the appendicular mass or the retroperitoneal abscess.

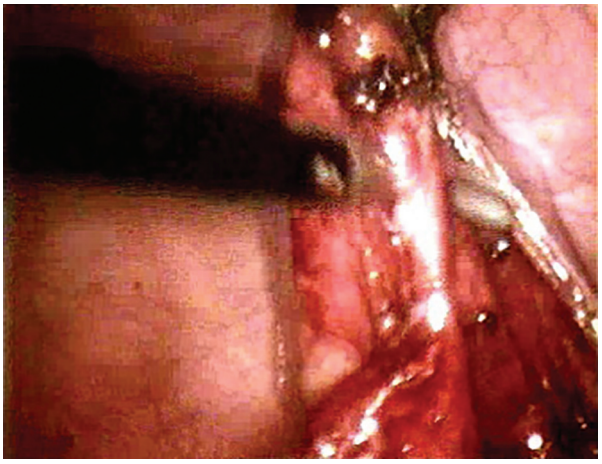
The appendix was freed, dissection of appendicular vessels was performed (Figs. 5 and 6), but dissection was difficult due to disturbed anatomy. The vessels were difficulty dissected after a window was created in the mesoappendix beside and adherent to the base; a clip applier was introduced and a single Hem-O-Lock polymer clip (L, XL clips) was fired at the appendicular base (Figs. 7–9), and another titanium clip or a polymer clip was applied distally.

Figure 4



Perforation near the base of the appendix.

Figure 6



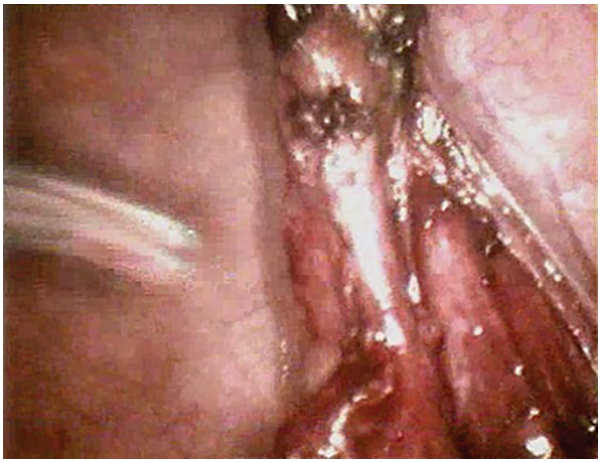
Dissection of appendicular vessels.

For cases with perforation at the base, the polymer clip was applied more proximally. Six out of the nine cases with appendicular abscess necessitated opening the peritoneal reflection or tolds line to access the pus.

One case necessitated transfixing the base of the appendicular stump. The appendix was transected between the proximal polymer and the distal titanium clip or the distal polymer clip over a piece of gauze (Figs. 10 and 11); the mesoappendix was then divided using bipolar diathermy (Fig. 12) or an endoloop. The stay suture dislodged and the freed appendix was placed in sterile gauze and removed with the 10 mm port.

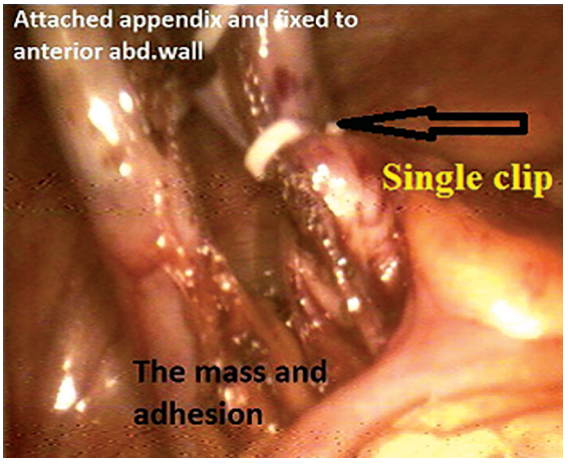
The 10 mm port was reinserted, peritoneal lavage and suction was completed, and hemostasis was secured. Patients had a Jackson-Pratt drain placed in the pelvis after the completion of the appendectomy.

Figure 5



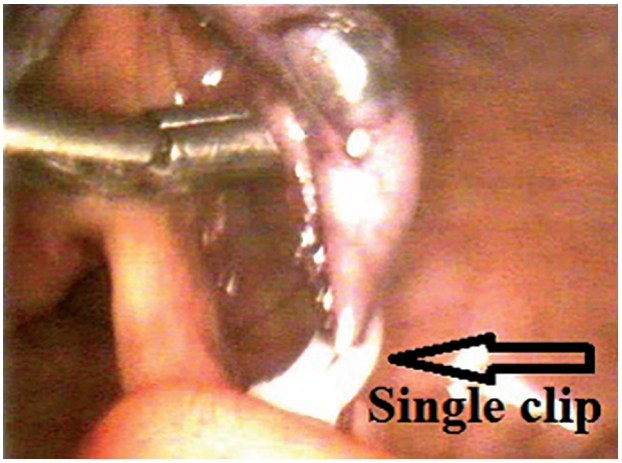
Dissection of appendicular vessels, while the appendix stayed to the abdominal wall.

Figure 7



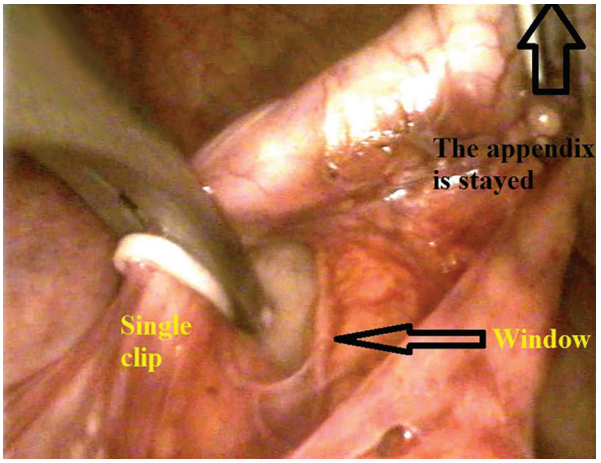
A single clip applied at the base, while the appendix stayed and the tip forming mass and hidden.

Figure 8



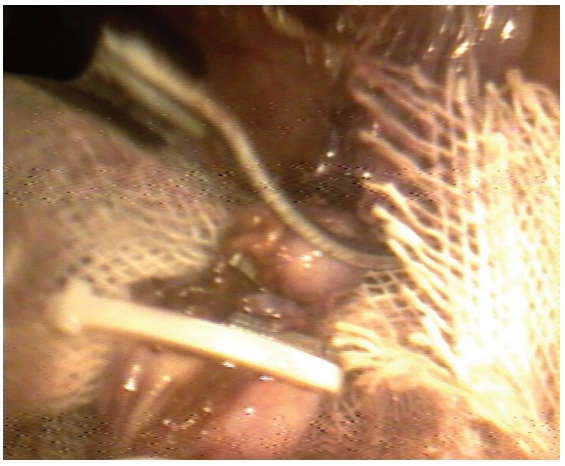
Single clip.

Figure 9



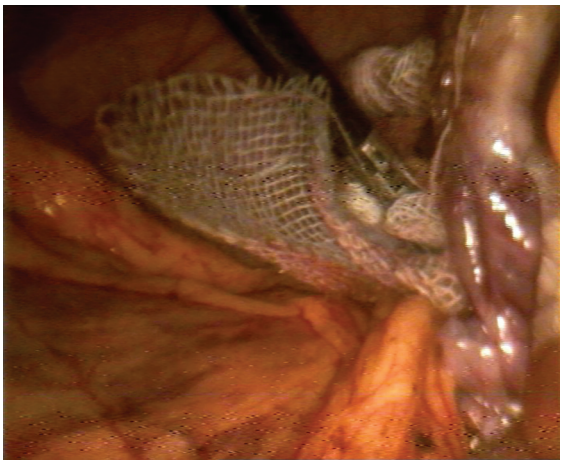
Single clip.

Figure 10



Cutting above the single clip over a piece of gauze.

Figure 11



Cutting above the single clip over a piece of gauze to remove the appendix within it.

Figure 12

Division of the mesoappendix with bipolar.

The insufflated gas was released and the skin edges were approximated with absorbable sutures. Postoperative analgesia and perioperative intravenous antibiotics were administered using third generation cephalosporin. An oral diet (diet as tolerated) was resumed usually within 12 h, and the drain was removed after 24 h.

Statistical analysis

Categorical qualitative variables were expressed as absolute frequencies (n) and relative frequencies (%). The 95% confidence interval for rates were calculated to interfere with the rate of occurrence in the population. All statistics were performed using SPSS, 22.0 for windows (SPSS Inc., Chicago, Illinois, USA) and MedCalc, 13 for windows (MedCalc Software bvba, Ostend, Belgium).

Results

A total of 82 patients were diagnosed with complicated acute appendicitis. The diagnosis of complicated appendicitis in all patients was based on clinical and confirmed by CT findings. About 50 patients (60.9%) with a positive CT scan underwent two-port laparoscopy. Thirty-two patients (39.1%) with vague symptoms and negative CT imaging were observed and underwent classic laparoscopic appendicectomy.

Pediatric patients constituted 21 cases with a perforated appendix at the tip, four cases perforated near the base, 11 cases with an appendicular mass, nine cases with an appendicular abscess, and five cases with a gangrenous appendix (Table 1).

Forty-two (84%) male and eight (16%) female patients underwent surgery. Patients' age ranged from 9 to 16 years (mean 13.5 years). All appendectomies were completed laparoscopically, except two patients. One patient with an appendicular mass, unhealthy base, and a gangrenous cecal wall was converted to open surgery and we proceeded for right hemicolectomy. The other patient had previous transverse suprapubic incision for intussusceptions and very difficult adhesiolysis, and so we converted the laparoscopic approach to open surgery.

All patients were operated using one proximal clip for the stump, except one patient, who required an extra transfixation suture below the single proximal polymer clip, and this was due to defective clips at the time of operation, explained by slippage of three clips after locking into the jaw of the clip applier and failed reinsertion of two of them; the last clip was inserted and secured with transfixation. This also occurred in the early cases.

Four of the 50 patients (8%) had postoperative complications. Four patients (8%) developed intra-abdominal abscess (IAA) postoperatively: two of them underwent laparoscopic drainage during the same admission, and the other two patients were readmitted after 1 and 2 weeks, respectively, and one of them underwent ultrasound-guided drainage and the other one improved within 48 h with the use of invanz intravenously and metrinidazole rectally (Table 2).

No other complications were noted. None of these patients were readmitted for port-site complication. The postoperative abscess occurred early during our initial experience with laparoscopic appendectomy, and it was the first case of CPA performed laparoscopically. The postoperative course of all patients was uneventful, except for the patients who developed postoperative IAA.

Table 1 The type of complication and the number of patients

Complications	*n* (%)	95% CI (%)
Perforated tip	21 (42)	26–64.2
Perforated near base	4 (8)	2.1–20.4
Appendicular mass	11 (22)	10.9–39.3
Appendicular abscess	9 (18)	8.2–34.1
Gangrenous appendix	5 (10)	3.2–23.3

CI, confidence interval.

Table 2 Postoperative complications (intra-abdominal abscess) and the timing of management

Timing of intervension for post operative complication	First admission	Second admission after 1 week	Second admission after 2 weeks
n (%)	2 (2.8)	1 (1.4)	1 (1.4)
95% CI (%)	0.3–10.3	0.3–7.9	0.3–7.9
Method of management	Laparoscopic drainage	Underwent US-guided drainage	Improved within 48 h with the use of invanz intravenously and metronidazole rectally.

CI, confidence interval; US, ultrasound.

All patients were discharged from the hospital within 2 days, except for the four patients with abscesses and the case of right hemicolectomy, which necessitated the patient to stay up to 6 days postoperatively. All patients were followed for at least 30 days in the outpatient clinic by the attending physician and resident doctors.

Discussion

In our study, we excluded this technique for noncomplicated cases; hence, we added CT pelvis to confirm our diagnosis. Many other studies have emphasized the role of CT and other scores to avoid operation or performing a negative appendicectomy [8]. It has been suggested in the past that laparoscopic appendectomy for CPA in children is not a safe procedure and should be avoided [9]. Our recent findings suggest that laparoscopy can be a main therapeutic procedure instead of open appendicitis in these complicated cases. Taylor [10] recommended only the open approach in cases with appendiceal masses if diagnosed well by ultrasound. This was not supported in our current study in which most of the cases with appendiceal masses were successfully treated laparoscopically, except one case. Most cases were diagnosed preoperatively on the basis of CT of the abdomen and the pelvis.

Recent guidelines recommended immediate surgery for an appendicular mass by open surgery against the laparoscopic approach, and using a single incision adds

more advantage to the laparoscopic approach [11], which is in agreement with our study, but we used two ports instead of the single port. Early operation, in contrast, has the benefit of being curative in the index admission and ensures early return to work and higher compliance [12]. The previous concept that surgery is difficult in a state where the inflamed appendix is buried deep in the mass and the bowel loops are friable is no more a valid argument at present, due to the improvement in anesthesia, the electrosurgical unit, and antibiotics [13].

In retrospective studies, the incidence of postoperative IAA formation after laparoscopy in children with CPA varies anywhere between 5.8 and 41%, and in our study, it was 8%, but our study was for complicated cases; the improvement in the percentage was supported by the use of the two-port technique and the accepted method of dissection by the retrograde approach, In another recent study conducted and reported by Arash et al. [14], comparing laparoscopy with open appendectomy for CPA, no IAA occurred after laparoscopic appendicectomy for uncomplicated appendicitis. In other studies, the overall infection rate including port-site infection and IAA was 2.54% in uncomplicated cases and it was 7.32% in complicated cases [15]. A study conducted by Nasher [16] revealed results similar to our results, and he used a technique considered to be the same as our approach.

A study similar to our study conducted by Partecke [6], from January 2009 to December 2009, included 82 patients in the prospective, nonrandomized trial; a single Hem-O-Lock MLX polymeric clip was applied. The data collected included the age, the sex, the number of clips used, complications, and the preoperative white blood count and C-reactive protein. He found a lower incidence of postoperative IAAs and surgical site infection, and he attributed his results to both the laparoscopy and the single polymer clip used. It is partially similar to our study, but we used a larger number of patients over a larger period of time.

In the Mariadason series [17], six of their 37 patients having severe right lower abdominal pain were subsequently found to have abscesses, and they reported that the disadvantage of the conservative management is the chance of misdiagnosis by conditions such as intussusception, and cancer cecum may be treated conservatively by mistake, adding considerable morbidity.

Walz et al. [18] conducted a study and documented that all study patients with complicated appendicitis had drains placed in the abdomen for drainage. A high degree of suspicion and the use of imaging helps in the diagnosis and the early treatment of postoperative IAA. In a recent study, it was suggested that the placement of drains in the right lower quadrant might be beneficial in patients with complicated appendicitis, especially perforated appendicitis and localized abscess cavities. In that study, 80% of the patients with CPA had an uneventful laparoscopic appendectomy. All these patients had drains placed in the right lower quadrant. In our study, we treated about 96% of the patients with laparoscopy, but we inserted the drain in only the left midclavicular port despite being less dependent, but patients did not need extra incision.

In our study, the use of a polymer clip was a must as we operated on complicated cases, and securing the stump was of utmost importance, and because the safety of the single clip was proved in our study, future cases will be subjected to the same technique. Our study on single clip usage was in complete agreement with other international studies, [19]with nearly the same number of patients, but a shorter period of study. Our findings compared favorably with others in terms of the safety and the feasibility.

Conclusion and recommendations

Laparoscopic appendectomy seems to be a safe alternative for the treatment of complicated appendicitis in children. The use of two ports added an advantage for the procedure by decreasing postoperative pain, decreasing the hospital stay, decreasing the incidence of port-site complications, and providing better cosmoses. Placement of drains is a must. Complicated appendicitis should not be considered as a contraindication for laparoscopy. Retrograde appendicectomy facilitated the treatment of complicated appendicitis, especially for appendicular mass and perforated appendix, and yield the best results, especially with the use of polymer clips that ensure secure closure of the stump even in a perforated appendicitis.

Endoscopic staplers are expensive instruments. Titanium clips may be slipped from their primary position or cut through edematous tissue. A Hem-O-Lock clip is a nonabsorbable polymer clip with a lock-engagement feature and teeth within the jaws; the jaw provides considerable safety to apply only one proximal clips, which ensures complete lumen closure that is as strong as with two clips, but it is more advantageous than using two clips in being less time consuming and less costly, all of which may provide greater security. Using polymeric clips to close the appendicular stump in children

is a safe, feasible, and inexpensive method. We, as well as many others, have also adopted the Hem-O-Lock for laparoscopic appendicectomy. As the safety of the single clip was proved in our study, we recommend that future cases be subjected to the same technique.

Acknowledgements

Conflicts of interest

None declared.

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Carotid endarterectomy in Iraq: a single-center experience

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Background
Carotid endarterectomy (CEA) refers to surgical removal of carotid atheroma. It was first reported in 1956 and eventually became widely accepted as an effective operation for stroke prevention. Herein, we present the experience of a single Iraqi center in CEA.

Patients and methods
We conducted a retrospective study of 21 patients with significant symptomatic carotid stenosis that was surgically managed in Ibn-Alnafees Hospital, Baghdad, over the period 2009–2014. Workup consisted of duplex ultrasonography and computed tomography angiography of the carotid arteries. General anesthesia, a standard technique, and routine carotid shunts were used, followed by patch closure, mostly a venous patch. Aspirin and antiplatelets were given postoperatively to patients who underwent a venous patch; otherwise, warfarin was prescribed.

Results
There were 20 male patients. Ages ranged between 37 and 82 years, with a mean of 60.3 ± 12.2 years. One-third of the patients ($n = 7$) were in the seventh decade. Six of 12 patients had jobs consistent with a low economic status. Smoking, hypertension, and diabetes mellitus were the main risk factors. Most patients had hemiparesis ($n = 17$, 81%). All patients had significant carotid stenosis (moderate to severe). Twenty-two operations were performed (one patient underwent two operations). Left-sided operations were more frequent (14/8) ($P < 0.05$), as well as venous patches (20/2 Gore-Tex) ($P < 0.05$). There was no incidence of stroke, but cervical hematomas ($n = 22$), tongue deviation ($n = 2$), and hyperperfusion syndrome ($n = 2$) were seen, all of which resolved spontaneously; one case of mortality was reported (4.8%), in a 73-year-old-man.

Conclusion
Although this study is the first on CEA in Iraq with a small number of patients, the results compare favorably with the published literature.

Keywords:
atherosclerosis, carotid endarterectomy, carotid stenosis, stroke, transient ischemic attacks

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Introduction

Michael E. De Bakey is credited with performing the first successful carotid endarterectomy (CEA) in 1953 at the Methodist Hospital in Houston, Texas [1], but unfortunately he did not report the procedure until 1959 [2].

The first published report of CEA for atheromatous disease is by Yousif D. Al-Naaman, a pioneer cardiovascular Iraqi surgeon, and his colleagues Denton A. Cooley and Charles A. Carton from the USA, which was published in 1956 [2,3]. Their patient was a 71-year-old white man with nonhemispheric symptoms in whom angiography revealed a preocclusive lesion of the distal common carotid artery just proximal to the bifurcation. An in-dwelling arterial shunt was used, and the procedure was uncomplicated [2,3].

Eastcott and colleagues are given credit for popularizing carotid intervention for symptomatic atheromatous disease. On 7 May 1954, Anna Tuckwell, a 66-year-old woman, underwent operation in St. Mary's Hospital for atheromatous obstruction of the left internal carotid artery (ICA). Eastcott elected to excise the diseased segment and reconstruct the vessel with end-to-end anastomosis between the distal common and ICAs. Mrs Tuckwell survived an additional 20 years without further neurological events [2]. Hence, Eastcott's procedure was not strictly an endarterectomy as we now understand it [4] but a carotid arterectomy [2–4].

CEA eventually became a widely accepted operation after clinical trials conducted in Europe and America (1991–1995) and conclusively showed its benefit in preventing stroke [4–7]. CEA is now the most commonly performed peripheral arterial surgery in the USA [8]with nearly 140 000 operations performed in 2003 [4].

Symptomatic carotid stenosis has a high risk for stroke within the next 2 days. Therefore, National Institute for Health and Clinical Excellence (NICE) guidelines recommend that symptomatic patients with moderate

to severe (50–99%) stenosis should undergo 'urgent' endarterectomy as soon as possible and preferably within 2 weeks to get maximum benefit from the operation [4,8].

In asymptomatic patients, the incidence of stroke, including fatal stroke, is 1–2% per year [4]. Surgeons are divided over whether asymptomatic patients should be treated with medication alone or should undergo surgery. Current surgical best practice restricts surgery for asymptomatic carotid stenosis to patients with at least 70% stenosis, provided that surgery is performed with 3% or less risk for perioperative complications [4].

CEA cannot be performed when there is a complete ICA occlusion, a previous ipsilateral stroke with heavy sequelae, or when the patient is considered unfit for surgery because of comorbidities [4,5].

As more and more vascular and neurosurgeons began to perform endarterectomy, it soon became clear that it was the most effective strategy for partially occlusive lesions rather than for total occlusions, in which restoration of flow was possible in only 40% of cases and in many of which operation was contraindicated because of the clinical presence of acute profound strokes, with operative mortality being reported to range from 20 to 60% [5]. It was gradually realized that the principal role of CEA was one of stroke prevention in patients with transient ischemic attacks (TIAs), mild deficits, and asymptomatic stenoses, rather than treatment for completed or profound strokes, as in the early days of endarterectomy [1,5].

Lyons C. (1959) [cited in 1] stated that a patient who slips into a coma with a vascular accident should not be explored. Similarly, De Bakey (1959) had reported the case of three patients with severe cerebral arterial insufficiency who had presented with coma and paralysis preoperatively and had died from irreversible ischemic brain damage despite restoration of circulation [1]. On the other hand, Crawford (1959) [cited in 1] had operated successfully upon patients in a coma and had them regain consciousness on the operating table when the restoration had been completed.

Although the first case report of a successful CEA for atherosclerotic carotid artery stenosis was partly authored by a vascular surgeon from Iraq (Al-Naaman YD, 1956) [2,3,5], it is unclear to us why this operation was not widely practiced in Iraq. A search on the net revealed no single publication on CEA from Iraq apart from that aforementioned. Literature review showed that this operation had witnessed a rise and fall in its popularity in the USA, Canada, and Europe in the 1980s, based on published outcomes from clinical studies [5,8]. The high stroke and/or mortality rates from the operation reported by some published studies induced fear and reluctance in neurologists to refer their patients with symptoms and signs of carotid artery stenosis, resulting in reduced popularity of the technique; however, the good surgical outcome from the technique compared with medical therapy in other studies led to a surge in its demand [5,8]. The operation's acceptance by the neurological community was slow and awaited controlled clinical trials [5,6]. In most Arab countries, results of CEA for carotid stenosis were not assessed before 2009 [7]. Neurologists in Iraq might have been reluctant to take the (risky) surgical route and preferred to treat their patients conservatively. Similarly, vascular surgeons could have had the same attitude. However, the multiple clinical trials of the early 1990s that showed superior results of CEA over medical treatment [5,6] definitely changed the attitude of both neurologists and surgeons in Iraq towards surgery.

Recently and particularly in the last few years some young Iraqi surgeons have begun to perform this procedure in some centers in Baghdad, Sulaimaniyah and Mosul (personal communication); unfortunately, no one has published his experience yet. Therefore, the present series may be the first study of CEA from Iraq.

Patients and methods

This is a retrospective study of 21 patients with symptoms and signs of carotid stenosis referred to the Department of Thoracic and Vascular Surgery, Ibn-Alnafees Teaching Hospital, Baghdad, Iraq, over a 5-year period (2009–2014) who underwent CEA. Informed consent was obtained from the patients before enrollment in the study. An informed written consent in accordance with the hospital Ethical Committee was also obtained.

The patients in this study were seen by a team of neurologists and a vascular surgeon. Detailed history was obtained from every patient with respect to chief complaints, such as unilateral body weakness, limb paresthesia, slurred speech, decreased visual acuity etc. Risk factors such as smoking, hypertension, diabetes mellitus (DM), hyperlipidemia, and alcohol use, as well as details of drugs used by the patient, were also noted. A thorough physical examination was carried for evidence of neurological deficits, carotid bruit, and features of atherosclerosis elsewhere in the body, such as ischemic heart disease, abdominal aortic aneurysm, and peripheral arterial disease.

Duplex ultrasonography, color Doppler, and computed tomography (CT) angiography of the carotid arteries

were used to evaluate the severity of carotid stenosis. Other investigations included chest radiography, ECG, and echocardiography to assess cardiopulmonary status, and blood biochemistry and serum virology tests. Symptomatic patients with moderate (50–69%) to severe (>70%) carotid stenosis were chosen for surgery.

Preoperative measures included a thorough medical checkup, fitness for general anesthesia (GA), and blood preparation; a written high-risk consent form was signed by each patient. Smoking patients were asked to quit smoking for at least 2 weeks before surgery. Aspirin and antiplatelets were stopped 3 days preoperatively. Antihypertensive and statin medications were continued, and diabetic patients receiving oral hypoglycemic drugs were switched to soluble insulin until the fifth postoperative day.

All operations were performed under GA and by the same surgeon. Because of nonavailability of intraoperative electroencephalography (EEG) or transcranial Doppler ultrasonography of cerebral blood flow, intraluminal carotid shunts were used routinely to provide cerebral protection during ICA clamping. The standard surgical procedure of CEA was employed [4,5]. Unfractionated heparin (5000 IU) intravenously was given just before arterial clamping and the patients were switched to LMWH 6000 IU twice daily subcutaneously for 5 postoperative days. The arteriotomy was closed mostly by a venous and occasionally by a prosthetic patch. A tube drain was used after securing the hemostasis.

The patients were carefully evaluated for any evidence of cranial nerve injuries and stroke, as well as for cervical hematoma. The tube drain was removed when the volume of drainage fell below 50 ml/day. The same preoperative medications were resumed, besides warfarin therapy for prosthetic patch receivers only. The patients were discharged home once they were stable, usually within 5 days after surgery. The late outcome of all patients in this series was assessed by frequent clinical and Doppler US exam during their visits to the consultation clinic.

Statistical analysis was performed using the *Z*-test for two population proportions and the *t*-test for two dependent means.

Results

There were 21 patients in this study (male, *n* = 20 and female, *n* = 1). The male to female ratio was 20: 1. This difference was statistically significant ($P < 0.05$). The youngest patient was a 37-year-old man and the oldest was an 82-year-old man. The mean age was 60.3 ± 12.2 years.

Table 1 shows the age and sex distribution. Most patients were in the seventh decade of life (*n* = 7, 33.3%).

The jobs of nine patients were not documented in the medical files; the jobs held by the remaining 12 are shown in Table 2. Of these 12, six had jobs consistent with a low economic status (worker, *n* = 3; farmer, *n* = 2; and housewife, *n* = 1).

The risk factors are shown in Table 3. Smoking topped the list, whereas alcohol consumption was the least prevalent. Hypertension and DM were also frequently observed. However, hyperlipidemia was not documented.

Table 1 Age and sex distribution

Age (years)	Male (*n*)	Female (*n*)	Total [*n* (%)]
30–40	1	0	1
41–50	4	0	4
51–60	4	1	5
61–70	7	0	7
71–80	3	0	3
81–90	1	0	1
Total	20 (95.2)	1 (4.8)	21 (100)

Table 2 Jobs versus sex and age of the patients

Jobs	Male		Female		Total
	<40 years	>40 years	<40 years	>40 years	
Housewife	0	0	0	1	1
University professor	0	1	0	0	1
Teacher	0	1	0	0	1
Officer	0	1	0	0	1
Engineer	1	0	0	0	1
Lawyer	0	1	0	0	1
Merchant	0	1	0	0	1
Worker	0	3	0	0	3
Farmer	0	2	0	0	2
Unmentioned	0	9	0	0	9
Total	1	19	0	1	21

Table 3 Risk factors versus age of the patients

Risk factors	Age <40 years	Age >40 years	Total
Smoking	1	19	20
Hypertension	0	12	12
DM	0	11	11
Alcohol consumption	0	2	2
Undocumented	0	2	2
Total	1	46	47[a]

DM, diabetes mellitus; [a]Some patients had more than one risk factor.

Table 4 shows the clinical characteristics of the patients. The vast majority had unilateral body weakness (n = 17, 81%). Other neurological deficits occurred less frequently.

The workup of the patients in this study was based on carotid Doppler and CT carotid angiography, which revealed significant carotid stenosis (moderate to severe).

Table 5 shows the performed operative procedures. The total number of operations was 22. Left-sided operations were significantly more frequent than right-sided ones (P < 0.05). Venous patches were used more frequently than prosthetic patches to close the arteriotomy (P < 0.05).

Complications on the basis of the side of operation are shown in Table 6. Both cervical hematoma and death were significantly higher on the left side (P < 0.05), whereas tongue deviation and cerebral hyperperfusion were significantly higher on the right (P < 0.05).

The patients are being regularly followed up by the operating surgeon and are doing well.

Table 4 Clinical characteristics

Symptoms and signs	*n*	Symptoms and signs	*n*
Unilateral body weakness	17	Associated operations for atherosclerotic disease elsewhere in the body before or after CEA	5 [aorto-bifemoral bypass graft (n = 2) CABG (n = 2) Femoropopliteal bypass (n = 1)]
Right-sided	9	Decreased visual acuity	1
Left-sided	8	Amaurosis fugax	1
Slurred speech	3	Carotid bruit	1 (the remaining 20 patients had no mention of carotid bruit)
Limb paresthesia	3	Ptosis	1

CABG, coronary artery bypass graft; CEA, carotid endarterectomy.

Table 5 Operative procedures

Side of CEA	Type of patch[a]		
	Venous	Gore-Tex	Total
Right	8	0	8
Left	12	2	14
Total	20	2	22[b]

CEA, carotid endarterectomy; [a]The result was significant at P < 0.05; [b]One patient had bilateral CEA; The result was significant at P < 0.05.

Table 6 Complications versus side of surgery

Type of complication	Side of surgery	
	Right [*n* (%)]	Left [*n* (%)]
Transient tongue deviation	1 (12.5)	1 (7.1) (the result was significant at P < 0.05)
Stroke	0 (0)	0 (0)
Mild to moderate hematoma resolving spontaneously	8 (100)	14 (100) (the result is significant at P < 0.05)
Cerebral hyperperfusion	1 (12.5)	1 (7.1) (the result is significant at P < 0.05)
Re-exploration	0	0
Wound infection	0	0
Death (4.8%). The patient was a 73-year-old man who died 2 days after surgery. He developed deterioration of consciousness level and acute renal failure	0 (0)	1 (7.1) (the result is significant at P < 0.05)

Discussion

There is a definite relationship between carotid atherosclerosis and age. This is evident in previous as well as recent studies. With regard to age, Smyth GE (1956) [cited in 3] found the majority of carotid stenosis in the sixth and seventh decades, similar to our findings [seven cases (33.3%) in the seventh decade]. De Weerd *et al.* [9] likely noted an increasing prevalence with age. In the study by Willeit and Kiechl [10], the variable 'age' was without doubt the strongest and most consistent indicator of carotid atherosclerosis. In their opinion, the strong relation of age to carotid atherosclerosis is probably an indirect expression of the continuous exposure to various risk factors rather than the result of an intrinsic process of aging [10].

Only a few studies address the question 'to what extent does the prevalence of carotid atherosclerosis differ between the sexes' [10]. Smyth GE (1956) [cited in 3] observed that the condition was about twice as common in men as in women. De Weerd *et al.* [9] similarly observed that moderate carotid stenosis was more prevalent among men than among women. Willeit and Kiechl found a 2: 1 preponderance of men in the 40–59 age group. With advancing age, however, the differences, although still detectable, were found to decrease, which possibly reflects the loss of the protective premenopausal status [10]. In the present study, male patients were significantly more than female patients (male: female = 20: 1; P < 0.05). As that CEA also appeared to be more beneficial in men than in women, screening for asymptomatic carotid stenosis might be more worthwhile among men with reasonable life expectancy than among women [9].

Half of our patients (6/12) had jobs consistent with a low economic status. Socioeconomic status (SES) is significantly associated with cardiovascular morbidity and mortality [11]. There is a strong association between SES and atherosclerosis. This association is mediated by known atherosclerotic risk factors and

is evident in the early stages of atherosclerosis [12]. Compared with the lowest SES group, men with the highest SES had 14–29% less atherosclerotic progression [11], whereas men with poor education and low income had significantly greater progression of carotid atherosclerosis than did men with higher education and income [11]. The findings strengthen the contention that SES plays a significant role early in the atherosclerotic disease process and that reducing the burden of atherosclerotic vascular disease associated with lower SES will require approaches that focus on all stages of life [11].

Survivors of a TIA or stroke represent a population at increased risk for subsequent stroke. Approximately one-quarter of the 795 000 strokes that occur each year are recurrent events [13]. Control of the modifiable risk factors is, therefore, an important measure of preventing a second stroke. The most significant risk factor for stroke is hypertension [10]. A person with untreated hypertension is four times more likely to have a stroke than someone whose blood pressure falls within the healthy range [14]. High blood pressure occurs in 80% of patients with acute ischemic stroke [14]. Twelve of our patients (57.1%) were hypertensive. Diabetes is a clear risk factor for first stroke, but the data supporting diabetes as a risk factor for recurrent stroke are more sparse [13]. Prevalence of DM is 15–33% in patients with ischemic stroke [13]. In our study, 11 patients (52.4%) were diabetic. With regard to lipid profile, studies have shown an association of ischemic stroke risk with elevated levels of total cholesterol, low-density lipoprotein, triglycerides, and low levels of high-density lipoprotein [13]. Unfortunately, only one of our patients had a record of lipid profile. There is strong evidence that cigarette smoking is a major risk factor for ischemic stroke [13,15]. Almost all patients in this series were smokers. Likewise, there is strong evidence that chronic alcoholism and heavy drinking are risk factors for all stroke subtypes [14]. Two of our patients (9.5%) were alcoholics [13].

Patients with symptomatic carotid artery stenosis typically have either TIA or minor stroke, defined as a focal neurologic deficit affecting one side of the body, speech, or vision [4,5]. Asymptomatic patients have narrowing of their carotid arteries, but have not experienced a TIA or stroke [4,5]. The true prevalence of TIA is difficult to gauge because a large proportion of patients who experience a TIA fail to report it to a healthcare provider [9,13]. By conventional clinical definitions, the presence of focal neurological symptoms or signs lasting less than 24 h has been defined as a TIA [13]. A new tissue-based definition of TIA is as follows: a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction [13]. All of the patients in this series were symptomatic; two patients presented with amaurosis fugax (transient loss of vision in one eye), one had ptosis, three had slurred speech, three had limb paresthesia, and the majority (17/21) had unilateral hemiparesis. Although carotid artery bruit is an important physical finding in patients with carotid stenosis, it was recorded only once in this study. Irrespective of the detection of a carotid artery bruit in patients with possible vascular events, most authorities would still recommend imaging studies [16].

At a bare minimum, all stroke patients should undergo brain imaging with CT or MRI to distinguish between ischemic and hemorrhagic events, and both TIA and ischemic stroke patients should have an evaluation sufficient to exclude high-risk modifiable conditions such as carotid stenosis or atrial fibrillation as the cause of ischemic symptoms [13]. Accurate diagnosis of the degree of ICA stenosis is needed for decisions regarding optimal stroke prevention. Although controversy now exists over the most appropriate method of measuring carotid stenosis [5], many authors consider duplex ultrasound imaging as the method of choice for the evaluation of carotid atherosclerosis in clinical practice [14]. Not until 1937, however, when Moniz introduced an efficient method for carotid arteriography, was accurate diagnosis of carotid stenosis made possible, and since that time the disease is being recognized with increasing frequency [3]. Noninvasive magnetic resonance angiography is being proposed and used as a replacement for the gold standard, intra-arterial angiography [17]. CT angiography of the head and neck is readily available and can be part of the routine imaging of stroke patients [18]. The workup of all patients in this study was based on carotid Doppler and CT carotid angiography.

Methods to determine the adequacy of the cerebral circulation include the xenon method, temporary carotid occlusion under local anesthesia, determination of the stump pressure in the occluded distal ICA, EEG monitoring, transcranial Doppler monitoring, and sensory-evoked potential monitoring [5,15]. Unfortunately, none of these techniques was available in our study. Some surgeons believe that awake testing under locoregional anesthesia is the only reliable method of monitoring cerebral circulation [19].

The procedure may be performed under GA or local anesthesia [4,8]. The latter allows for direct monitoring of neurological status by intraoperative verbal contact and testing of grip strength. With GA, indirect methods of assessing cerebral perfusion must be used, such as EEG, transcranial Doppler analysis, and carotid artery stump pressure monitoring. At

present there is no reliable evidence to show any major difference in outcome between local anesthesia and GA [4]. Proponents of regional anesthesia claim many advantages over GA, such as ease of monitoring of cerebral perfusion, lower cardiovascular morbidity due to lower requirements for shunting, shorter hospital stay, and reduced overall costs [15].

The first author of this paper (Professor Taha AY) describes his observation of CEA that was performed in Guy's Hospital, London, UK (March 2009). The operation was performed on an awake patient under local anesthesia according to the patient's will. The patient was an 80-year-old lady with TIAs 2 weeks earlier. She had more than 70% carotid stenosis as shown by duplex ultrasonography. To detect any alteration in neurological function, verbal communication with the patient was maintained throughout the operation and she was repeatedly requested to squeeze a balloon that produced a sound to test her muscle power especially after clamping the ICA. Moreover, the blood flow and velocity in the cerebral artery were monitored by transcranial Doppler ultrasonography. A reduction in cerebral blood flow indicated the need for carotid shunting. The standard surgical technique for CEA was followed and a big atheroma was quickly removed. However, once the ICA artery was clamped, the cerebral blood flow reduced and a shunt was necessary. The patient recovered with no neurological deficit.

In the past, hypothermia, hypercarbia, and hypocarbia were used for cerebral protection [5]. Eastcott *et al.* [3] used cerebral hypothermia as a method of cerebral protection during the period of cross-clamping in their landmark case of carotid arterectomy and anastomosis of common carotid artery to ICA (1954) [3,6]. Soon thereafter, shunting replaced hypothermia [3,6]. The case described by Cooley and colleagues [3,5] is of interest in that an external shunt was used for cerebral protection, the first reported use of a shunt for CEA. Arterial flow was restored after 9 min of carotid clamping [3]. The shunt consisted of a polyvinyl tube with a 14-G needle at its lower end and a 16-G needle at its upper or internal carotid end. Additional cerebral protection was attempted by immersing the patient's head in crushed ice for 30 min. Despite this the patient suffered an operation-related stroke from which he recovered rapidly over the course of several weeks [5]. The use of a shunt is still under discussion. Some surgeons use it routinely [5], others use it selectively on the basis of an assessment of the collateral circulation, whereas some rarely or never use it [5]. Today the temporary shunt remains the most effective means of providing cerebral protection when judged necessary [4,5]. In our series, routine intraluminal shunting was elected as all of the operations were performed under GA and we lacked any facility for monitoring the cerebral function intraoperatively.

Controversy revolves around patching versus simple closure of the arteriotomy after CEA [5,20]. Thompson JE [5] believes that patching is useful for small arteries and reoperation but is probably not necessary as a routine maneuver [5]. Saad *et al.* [20] from Egypt used patching after endarterectomy in 45 patients with good results and therefore recommend it over simple closure. We share the same opinion and have applied this technique in all of our cases as it gives less incidence of postoperative thrombosis, stenosis, and recurrent stroke [20]. It has been suggested that the flow characteristics of patched carotid arteries may be superior to those of primary closed arteries in terms of preventing early thrombosis. Dirrenberger and Sundt [cited in 20] state that the endarterectomized artery is thrombogenic for the first several hours after CEA, during which time the carotid artery is most vulnerable to acute thrombosis. Others have attributed this improvement to widening of the artery with a corresponding reduction in the effect of intimal hyperplasia [20]. Opponents of carotid patching highlight the increased operative time of 15–20 min required for patch closure, risk of patch rupture, and false aneurysm formation [20].

The choice of patch material has also been a subject of debate [20]. Seabrook [cited in 20] states that the autogenous vein is superior to prosthetic materials because the luminal surface is less thrombogenic and more resistant to infection. Synthetic patch (PTFE) has the advantages of availability, resistance to aneurysmal formation, or patch rupture [20]. Opponents to synthetic patches fear bleeding through the patch material, intraluminal thrombosis, and infection [20]. In our study, venous patches were significantly more frequently used than prosthetic ones (20: 2) as we believe they are less thrombogenic and more resistant to infection.

The chief complication of CEA, apart from death, is the production or aggravation of stroke [5]. None of our patients had stroke after surgery. Hemorrhage of the wound bed is potentially life threatening, as swelling of the neck due to hematoma could compress the trachea. Although cervical hematoma developed in all of the patients in this series, it was mild and resolved spontaneously. Occasionally, the hypoglossal nerve can be damaged during surgery. Two patients in this study developed tongue deviation toward the side of the operation but both eventually resolved. Another rare but potentially serious complication is hyperperfusion syndrome because of the sudden increase in perfusion of the vasculature distal to stenosis [4]. Two of our

patients had this syndrome (one recovered while the second died on the second postoperative day). Thompson JE believes that results of the operation have progressively improved with proper selection of patients, arteriography performed by skilled radiologists, avoidance of surgery for those with acute profound and progressing strokes, meticulous operative techniques used by well-trained surgeons, and appropriate use of cerebral protection [5].

The surgical mortality of endarterectomy ranges from 1 to 2% to as much as 10% [4]. In a survey of 15 960 CEAs, Hertzer [cited in 5] found the overall average operative mortality rate to be 1.4%. Perioperative CEA risks for combined 30-day mortality and stroke risk should be less than 3% for asymptomatic patients and less than or equal to 6% for symptomatic patients [4,7]. Patients with multiple medical problems have a higher postoperative mortality rate [4,7]. In our series, we had a single incidence of mortality (4.8%), which was within the reported standard rate.

Fourteen of 22 (63.6%) operations in this series were left-sided. Similarly, Johnson and Walker (1951) [cited in 3] found that carotid stenosis was 6.5 times more common in the left carotid than in the right. The exact explanation for this finding is unknown and of great interest is the influence of the side of CEA on its outcome. Recent randomized controlled trials and observational studies have suggested that outcomes may be poorer in left-sided procedures [21]. Girard *et al.* [21] in a mixed method study that involved 7048 patients have demonstrated that left-sided surgery is an independent risk factor for increased rates of postoperative stroke or death after CEA. Surgeon-handedness and microemboli are two speculations that could explain this finding. Some surgeons anecdotally report that, for anatomic reasons, left-sided CEA is technically more difficult for a right-handed surgeon. If handedness is indeed found to be a contributing factor, there would be a need to develop modified surgical approaches that improve ergonomics for right-handed surgeons operating on left carotid arteries. Stork *et al.* [21] reported that left-sided CEA was associated with an increased risk for microembolic events detected intraoperatively. If microemboli from surgery account for the phenomenon, then consideration could be given to the use and evaluation of embolic capture devices similar to those being considered in the context of coronary artery procedures and during carotid artery stenting. Further research is definitely needed to clarify the underlying mechanism(s) and to determine whether these mechanisms can be modified [21].

In our study, all operations were performed by one surgeon who was right-handed. The single death occurred following a left-sided CEA. Both cervical hematoma and death were significantly higher on the left side ($P < 0.05$), whereas tongue deviation and cerebral hyperperfusion were significantly higher on the right side ($P < 0.05$).

This study has some limitations. Being a retrospective study, the documentation was not optimum. The number of patients enrolled in this study was small. Long-term follow-up was not available for all patients.

Conclusion

Although this study is the first on CEA in Iraq in which a small number of patients were enrolled, the results compare favorably with the published international literature (a 4.8% death rate that is lower than 6% for CEA in symptomatic carotid artery stenosis and a 0% incidence of stroke and persistent cranial nerve injuries).

Acknowledgements

Conflicts of interest

None declared.

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Subintimal angioplasty of chronic total superficial femoral artery occlusions in critical lower limb ischemia patients: the single center experience

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Objective
The aim of this article was to report our results of subintimal angioplasty (SIA) of long superficial femoral artery (SFA) occlusions and try to appreciate factors that affect patency following this type of intervention in critical lower limb ischemia (CLI) patients.

Patients and methods
The current series was conducted prospectively over a 1-year period. Forty cases, 40 limbs (mean age = 65.8 years old) with long SFA occlusion (>15 cm) and patent popliteal artery continuous with at least one leg artery runoff were included. Exclusion criteria were: renal impairment, nonatherosclerotic occlusions (thrombosis, dissection, or compression), short SFA occlusions (<15 cm), or non-SIA revascularization intervention. Results were considered successful with primary technical success combined with improving ischemic rest pain or healing wounds following minor amputations. Nonrecanalization or major amputations were considered failures. One-year patency and salvage rates were calculated. Factors that affected patency such as patent leg arteries and TASC grading were analyzed.

Results
Results were considered successful in 34 (85%) patients and failure was noticed in six (15%) cases. At the end of the first follow-up year, the primary patency rate was 75% and the salvage rate was 87.5%. The 1-year patency rate was higher in TASC C patients (85.7%) in comparison with TASC D cases (69.2%). The patency rate was 50% or less with one patent leg artery and 80% or more with two or three patent leg arteries.

Conclusion
SIA is a good alternative for recanalization of chronic long SFA total occlusions in CLI patients with acceptable 1-year patency rates. Number of patent leg arteries is an important determinant of durable procedures.

Keywords:
critical limb ischemia, subintimal angioplasty, total superficial femoral artery occlusion

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Introduction

During the last two decades major changes have taken place in the diagnostic and treatment techniques for peripheral arterial disease (PAD). In the past, the main treatments for PAD were thrombectomy, endarterectomy, and bypass surgery [1,2]. Today occlusions can be corrected by means of percutaneous transluminal angioplasty, subintimal angioplasty (SIA) [3], laser angioplasty [4], thrombolysis, and endovascular stenting [5].

Lower limb SIA is now a well-known technique which can achieve recanalization of long occluded arterial segments [6]. It has been proposed as an alternative to lower limb bypass procedures, especially in patients with critical lower limb ischemia (CLI) [7]. Much of the criticism about this technique is based on its patency rate compared with bypass procedures [8]. It is often stated that the ~50% [9] primary patency rate at 12 months postintervention is quite low compared with the almost 80–90% [10] rate for bypass procedures.

However, despite the relatively high reocclusion rate, SIA allows an exceptionally good limb salvage rate in patients with limb threatening ischemia [11].

Since the introduction of the technique of SIA which was first described by Bolia *et al.* [12] for the treatment of long occlusive lesions, the indications remain variable and controversial. Subintimal recanalization however, in some centers, is the procedure of choice even for fitter patients with severe PAD [13]. Advantages of this technique compared with surgical bypass are reduced morbidity and mortality, reduced anesthesia requirements and potential reduction in hospital length stay and cost [14]. In the current study, we report our results of SIA of long superficial femoral artery (SFA) occlusions and try to appreciate factors that affect patency following this type of intervention in CLI patients.

Patients and methods

The current series was conducted prospectively over a 1-year period. CLI patients with long SFA occlusions (>15 cm) and patent popliteal artery continuous with at least one leg artery as the distal runoff were included. CLI is defined according to the SVS/ICSVS reporting standards, with rest pain and/or tissue loss [15]. Forty cases, 40 limbs (mean age = 65.8 years old) were included for a limb salvage procedure. Our Institutional Review Board approved the informed consent that was given by all participants included in the current study.

Management strategy

Following clinical evaluation, all CLI patients presenting to our center performed multidetector computed tomography (MDCT) angiography serving TASC grading [16]. TASC C and D cases were potential candidates for our study. Trying endo-first is our treatment approach for CLI patients requiring a revascularization procedure.

During the same study period, 151 patients were excluded as a result of renal impairment, nonatherosclerotic occlusions (thrombosis, dissection, or compression), short SFA occlusions (<15 cm), or non-SIA revascularization procedures. In the current series, all included patients were pretreated with combined acetylsalicylic acid 100 mg and clopidogrel 75 mg daily. Clopidogrel was continued for at least 30 days after the intervention and aspirin was continued indefinitely.

The technique of SIA has been described by Bolia *et al.* [12] Contralateral retrograde femoral access was performed in all cases using a 6Fr introducer sheath that was replaced by a crossover 55 cm long sheath (BRITE TIP Interventional Sheath Introducer; Cordis Corporation, 430 Route 22 East Bridgewater, NJ 088071831, U.S.) positioned in the common femoral artery.

A 0.035-inch Stiff hydrophilic J tip wire (glide wire; Terumo) combined with a 4-Fr angled tip catheter (glidecatheter; Terumo Corporation 2-44-1 Hatagaya, Shibuya-Ku, Tokyo, Japan) approached the arterial occlusion. The wire was intentionally introduced into the subintimal plane guided by the angled catheter directed to the arterial wall. The wire/catheter combination is then advanced into the occlusion. Entry into the subintimal space is confirmed by injection of a small volume of dilute contrast medium and in addition the guide wire moves freely when the subintimal space has been entered.

When the catheter tip is 2 : 3 cm from the distal end of the occlusion, the J-wire is manipulated to form a large loop and the true arterial lumen re-entered by the forward pressure on the loop [17].

There was no need for re-entry devices in all cases of the current series. The return point was the first part of the popliteal artery in 29 (72.5%) cases and its second part in 11 (27.5%) patients. The catheter was then replaced with a 5-Fr 5 or 6 mm diameter balloon catheter (Wanda; Boston Scientific Manufacturing Company, Marlborough, MA, USA) inflated throughout the entire length of the subintimal passage at 10 : 12 atmospheres for 60 s (Fig 1). If there is a residual stenosis of greater than 30% then the dilatation is repeated using slightly higher pressures and if the problem persisted, stenting was performed.

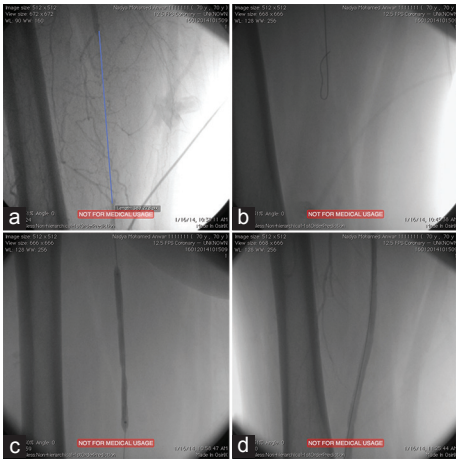
Appreciation of results and follow-up

Results were considered successful with primary technical success combined with improving ischemic rest pain or healing wounds following minor amputations. Nonrecanalization or major amputations were considered failures. All patients were followed up at regular intervals (3, 6, and 12 months) with clinical assessment, ABI measurements and duplex arterial mapping. One-year patency and salvage rates were calculated. Factors that affected patency such as patent leg arteries and TASC grading were analyzed.

Results

Forty cases were included in the current series for assessment of SIA of long SFA occlusions and factors affecting patency rates following this type of intervention.

Figure 1



(a) Long chronic superficial femoral artery (SFA) occlusion with return of the dye in the proximal popliteal (P1) artery. (b) Looping of the wire in the subintimal space. (c) Ballooning after traversing the lesion. (d) Final.

All included patients presented with rest pain (25%) or ischemic toe gangrene (75%). The current study included 27 (67.5%) men and 13 (32.5%) females. Twenty-eight (70%) patients were diabetic, 24 (60%) cases were hypertensive, and 22 (55%) patients were suffering from ischemic heart disease. Out of 40 included patients, 14 (35%) cases were of TASC C and 26 (65%) patients were of TASC D occlusions.

Following intervention, stenting was not deemed necessary in any of the current study cases. Results were considered successful in 34 (85%) patients and failure was noticed in six (15%) cases. At the end of the first follow-up year, the primary patency rate was 75% and the salvage rate was 87.5%. Further interventions were needed in seven (17.5%) cases. Table 1 shows types of performed procedures. We found that the three (7.5%) cases where thrombectomy was performed underwent major amputation of their ischemic limbs in the follow-up periods.

When analyzing factors affecting the patency rate in the current series with different variables, none of the factors predisposing to atherosclerosis was found to affect the SIA outcome in our study.

We found that the 1-year patency rate was higher in TASC C patients (85.7%) in comparison with TASC D cases (69.2%) (Table 2). Table 3 demonstrates the relation between the state of distal runoff presented as the number of patent leg arteries and the 1-year patency rate. We noticed that the patency rate was 50% or less with one patent leg artery and 80% or more with two or three patent leg arteries.

Table 1 Interventions following subintimal angioplasty performed in the current series

Procedure performed	Frequency [*n* (%)]
Thrombectomy	3 (7.5)
Bypass	2 (5)
Perforation, surgical repair	1 (2.5)
Amputation	1 (2.5)

Table 2 The relation between TASC II staging and the patency rate in the current series

Recanalized segment	TASC C [*n* (%)]	TASC D [*n* (%)]
Not patent	2 (14.3)	8 (30.8)
Patent	12 (85.7)	18 (69.2)

Discussion

With the improved endovascular armamentarium, introduction of new materials, better patient selection, and refined indications, it's necessary to continuously report results of specific promising interventions such as SIA that offer an important revascularization alternative for a subset of CLI patients.

The current single center, nonrandomized, prospective study included 40 CLI cases to report our results of SIA of long SFA occlusions. We reported 85% primary technical success in the current series. The technical success of SIA is generally high and varies between 78 and 90% in different reports [8,11,18]. According to the literature, infrapopliteal occlusions have a less favorable technical success rate when compared with the femoropopliteal occlusions [8,9,18].

The selection of patients suitable for SIA has to be defined clearly to avoid failures. Reekers and Bolia and Aleksynas and Kaupas found that arterial calcification was predictive of technical failure [6,19]. Bolia *et al.* [12] in addition, stated that the extensive calcification, recent (3 : 6 months) occlusions, and distal atherosclerotic disease should not be treated with subintimal recanalization. In the current study, we encountered failure in six cases. We could not return to the true lumen distal to the occlusion as a result of heavy calcification in three patients. In the other three cases, thrombosis developed in the recanalized segment.

The 1-year primary patency rate in our study was 75% and the salvage rate was 87.5%. London *et al.* [17] in their series reported a 1-year patency rate of 71% in three prospective studies. Florenes and colleagues [20,21] presented 12 month overall patency rates for SIA ranging from 53 to 70%. Lazaris *et al.* [22] reported a limb a salvage rate of 92% in their series of 46 CLI patients.

Variability in reporting patency rates among different studies is attributed to the different patients' characteristics, affected arterial segments and factors that could affect outcome and patency. In the current study, we report our results for a homogenous group of CLI patients with SFA lesions of more than 15 cm length and expected return points at the first or second part of the popliteal artery.

Table 3 The relation between the state of distal runoff and the 1-year patency rate

Recanalized segment	ATA [*n* (%)]	PTA [*n* (%)]	Peroneal artery [*n* (%)]	ATA and PTA [*n* (%)]	ATA and peroneal a [*n* (%)]	PTA and peroneal a [*n* (%)]	Patent 3 leg vessels [*n* (%)]
Not patent	3 (50)	4 (66.7)	1 (50)	0	0	2 (18.2)	0
Patent	3 (50)	2 (33.3)	1 (50)	2 (100)	4 (100)	9 (81.8)	9 (100)

ATA, anterior tibial artery; PTA, posterior tibial artery.

With regard to the possible factors that might determine the patency rate of SIA, we found that the number of patent crural vessels after the procedure was the most important. We noticed that the patency rate was 50% or less with one patent leg artery and 80% or more with two or three patent leg arteries.

Lazaris *et al.* [23] reported that patients with two or three patent runoff vessels after the angioplasty have a 81% 1-year patency compared with 25% with one patent runoff vessel. London *et al.* [17] reported a similar result in patients with only femoropopliteal occlusion treated by SIA. Similar results have also been reported by other investigators for percutaneous transluminal infrainguinal angioplasty [24,25].

We reported in the current study a 1-year patency rate of 85.7% in TASC C patients in comparison with 69.2% in TASC D cases. The length of the recanalized occluded arterial segment was also found to be related to the patency rate of SIA in the study conducted by Lazaris and colleagues. They found that for every 10 cm of recanalized occlusion there is about a 1.22 risk of reocclusion after the angioplasty [23]. Also, London *et al.* [17] considered that the risk of reocclusion of a femoropopliteal SIA increases by 1.73 for every 10 cm of occlusion length. Comparable results have also been reported by other investigators for percutaneous transluminal infrainguinal angioplasty [25].

Despite the fact that a small number of patients is considered our main study limitation, our results support the reported data that the number of runoff vessels and the length of occlusion are the main determinants of SIA patency. This knowledge could improve SIA patency rates, as a recanalization of more than one vessel is often achievable [23].

SIA is a good alternative for recanalization of chronic long SFA total occlusions in CLI patients with acceptable 1-year patency rates. Number of patent leg arteries is an important determinant for durable procedures.

Acknowledgements

Conflicts of interest

None declared.

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Evaluation of the role of endoanal ultrasonography in preoperative assessment of perianal fistula

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Background
Although anal fistula are encountered commonly in surgical practice and have been studied extensively, some complex forms still continue to represent a difficult surgical challenge for many surgeons. The corner stone and the main aim of treatment for an anal fistula is to permanently eliminate abscess formation and achieve healing at the same time preserving anal function and continence. Therefore, precise preoperative assessment of perianal fistulae is crucial to achieving optimal surgical results.

Patients and methods
In this prospective comparative study, 60 patients were enrolled during the period from December 2012 to June 2014. Endoanal ultrasonography (EAUS) (two-dimensional/three-dimensional) with or without H_2O_2 enhancement was used for the preoperative assessment of perianal fistulae and abscesses, and the degree of accuracy and its agreement with the surgical findings were estimated. Primary fistulous tract and its relation to the sphincter complex, side tracts, internal opening, and any associated sepsis were determined by EAUS; the reviewers were blinded to the findings of the assessment.

Results
In classification of the primary tract, there was agreement between EAUS and surgical findings in 47 of the 60 (78.3%) patients. In terms of the presence of an internal opening, the corresponding figures were 53 (88%) cases. In assessment of the secondary (side) tracts by EAUS, 55 (91.7%) patients were diagnosed accurately. In terms of the diagnosis of the presence or absence of abscess cavity or collection in the cases, EAUS diagnosed 53 (88.3%) patients accurately.

Conclusion
EAUS with its recent innovations of three-dimensional technique and H_2O_2 enhancement is an excellent modality when planning for fistula surgery, especially with experienced and well-trained operators.

Keywords:
endoanal ultrasonography, fistula, hydrogen peroxide, internal opening, primary tract

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Introduction

Inspection and digital examination with or without anesthesia are basic diagnostic methods. However, digital examination may fail to detect complex fistulae or to localize the internal opening. It is now well established that preoperative imaging modalities can alert the surgeon to fistula components that might otherwise be missed [1,2]. Among these modalities are fistulography and computed tomography, which have been disappointing and provide insufficient data for surgery planning; in addition, fistulography has been shown to be inaccurate in many instances. In recent years, MRI has emerged as the leading contender for the preoperative classification of fistula in ano. Endoanal ultrasonography (EAUS) is increasingly being used in the preoperative evaluation of anal fistulae. Initial EAUS evaluation was not satisfactory, [3] but the diagnostic accuracy of EAUS has improved with technical advancements in ultrasonography, including the use of hydrogen peroxide (H_2O_2) as a contrast agent and three-dimensional (3D) image reconstruction [4,5].

The image is no longer limited to the axial plane in 3D-EAUS. Instead, it is possible to cut across any part of the data set in the coronal, sagittal, or oblique plane. This property is expected to be useful in tracing the tract and internal opening [6].

The aim of this work is to evaluate the role of EAUS in the preoperative assessment of perianal fistulae and abscesses through its agreement with the surgical findings as a reference standard.

Patients and methods

This prospective comparative study included 60 patients who were enrolled from the Colorectal Unit,

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General Surgery Department, Kasr Al-Ainy Hospital, Faculty of Medicine, Cairo University, and from referrals from private clinics during the period from December 2012 to June 2014.The inclusion criteria were patients diagnosed with and having symptoms of any type of perianal fistula, whether it was high or low, recurrent or not. Patients with intolerable pain or those in acute pain, or those who could not tolerate or refused to undergo EAUS, and those who did not sign the consent form were excluded from the study. All patients signed a written informed consent before inclusion in the study. The age of the patients included ranged from 18 to 65 years (mean age 39 years); patients of both sexes were included (55 men and five women). Clinical assessment of history [age, occupation, presentation, history of anorectal diseases (e.g. anorectal abscess), history of previous anorectal surgery (e.g. abscess drainage or fistulotomy), …] and physical examination were performed in all patients to exclude patients who did not fulfill the criteria. A total of 60 patients who were suspected of having fistula in ano were subjected to routine labs and underwent a preoperative digital examination and 10-MHz anal endosonography (BK Medical US Scanner 1202; BK Medical, Herlev, Denmark). Primary fistulous tract and its relation to the sphincter complex, side tracts, internal opening, and any associated sepsis were determined by reviewers blinded to the findings of both assessments. The results obtained were compared with the intraoperative findings as a standard reference to assess the accuracy of each modality. Postoperative antibiotics, analgesics, and sitz baths were prescribed and follow-up was performed on a weekly basis until complete healing of the perianal wound. All scans were performed using the BK Medical Systems Flex Focus 1202 scanner and the BK 2052 probe (BK Medical), which is used in the Kasr Al-Ainy Colorectal Unit. The patient underwent an enema to clear the rectum and after a digital rectal examination, a rigid rotating probe with a 360° radius and an ultrasound frequency between 6 and 16 MHz was introduced into the rectum with the patient in a left lateral position. The probe was then slowly withdrawn so that the pelvic floor and subsequently the sphincter complex could be seen. The diameter of the probe is small enough to minimize any distortion of the anal canal. The ultrasound was performed systematically from the upper third to the lower third of the anal canal. Manual two-dimensional (2D)-EAUS was performed first to confirm the diagnosis, followed by computerized 0.2-mm sections along a 6-cm length, and then the 3D-EAUS image was subsequently reconstructed using specialized software provided by the manufacturer. 3D-EAUS was performed at a frequency of 13 MHz, which provides a focal range of 5–25 mm, an axial resolution of 0.3 mm, and a lateral resolution of 1.2 mm. When the diagnosis was unclear, examination was repeated while instilling diluted (3%) H_2O_2 from a 10 ml syringe into a flexible cannula (16–21 18 G cannula for intravenous injection made in Egypt) through the external opening. Only 44 out of 60 (73.3%) patients underwent H_2O_2-enhanced endosonography; the remaining 16 (26.7%) patients did not undergo H_2O_2-enhanced endosonography because of either closed external opening or intolerability of the patient to the dye (H_2O_2).

Two-dimensional ultrasonography

We evaluated the visualization of the internal fistula opening empty or with injection of H_2O_2. H_2O_2 was not injected if the external opening was closed or if the patient could not tolerate the injection, and was used selectively in those with acute sepsis. The primary fistulous tract was classified following a modified Parks classification [7] as:

(1) Not visualized.
(2) Intersphincteric: the tract crosses the intersphincteric space without crossing fibers of the external anal sphincter (EAS).
(3) Low transsphincteric: the tract crosses the EAS or both sphincters in the most distal two-thirds of the anal canal.
(4) High transsphincteric: the tract crosses both sphincters in the high third of the anal canal.
(5) Suprasphincteric: the tract crosses the intersphincteric space surrounding the upper edge of the puborectalis.
(6) Extrasphincteric: the tract is found to be outside the EAS. Other data obtained with this technique were the presence of secondary tracts (linear or circular) and the existence or not of perianal cavities and abscesses.

Three-dimensional ultrasonography

A 3D ultrasound was then performed without removing the probe, which allowed us to obtain sagittal and coronal images of the anal canal. We reassessed the site of the internal fistula opening, the primary tract of the fistula, and the possible secondary tracts and abscesses, corroborating and improving the information obtained from the 2D-EAUS. We classified the fistulae using the 3D-US according to their primary tract as follows:

(1) Not visualized.
(2) Intersphincteric: the tract crosses the intersphincteric space without crossing EAS fibers.
(3) Low transsphincteric: affects less than 66% of the EAS.
(4) High transsphincteric: affects 66% or more of the EAS.

(5) Suprasphincteric: the tract crosses the intersphincteric space surrounding the upper edge of the puborectalis.
(6) Extrasphincteric: the tract is found to be outside the EAS. Once the examination was completed, the images were recorded and could be carefully reviewed at any point to obtain the required information (Fig. 1).

Surgery

Fistula surgery was performed after investigations had been carried out, with an average time gap of 3–5 days; the surgeons involved were blinded to the EAUS findings.

Results

Demographic and descriptive data

The study was carried out on 60 patients.

Sex distribution

The study included 55 (91.7%) men and five (8.3%) women.

Age distribution

Age distribution is as shown in Table 1.

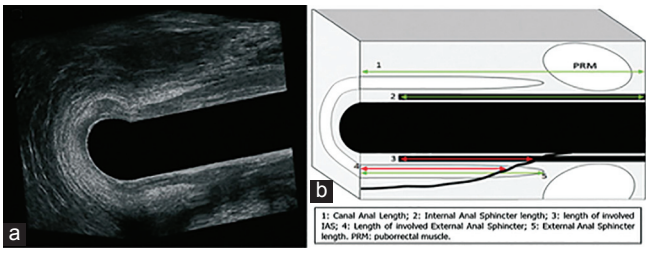
Clinical data

At the time of the study, all patients had perianal fistulae because of a cryptoglandular etiology, with no cases with Crohn's disease.

All types of fistulae were included, whether high or low, recurrent or nonrecurrent cases. The types of fistulae (according to surgical findings) were as follows: 26 (43.3%) patients had intersphincteric fistula, 18 (30%) patients had transsphincteric fistula, nine (15%) patients had suprasphincteric fistula, and seven (11.7%) patients had extrasphincteric fistula (Fig. 2).

Analysis of the results obtained from our study (2013–2014) indicated the following:

Figure 1



High posterior transphincteric fistula. (a) Three-dimensional endoanal ultrasonography (3D-EAUS) image of a sagittal section taken from the left. (b) Diagram of the 3D-EAUS measurements.

Internal opening

In terms of the diagnosis of the internal opening of the perianal fistula, our study showed that the EAUS had accurately diagnosed 53 (88.3%) cases out of 60, whereas seven (11.7%) cases were diagnosed inaccurately as shown in (Table 2).

Main (primary) tract

With respect to the diagnosis of the main (primary) tract, 47 (78.3%) cases were diagnosed accurately by the EAUS, whereas 13 (21.7%) cases were diagnosed inaccurately as shown in (Table 3).

Secondary (side) tracts

In terms of the diagnosis of the secondary (side) tracts by the EAUS, 55 (91.7%) cases were diagnosed accurately, whereas five (8.3%) cases were diagnosed inaccurately as shown in Table 4.

Table 1 Age distribution

	N	Minimum	Maximum	Mean	SD
Age	60	18	65	39.53	10.998

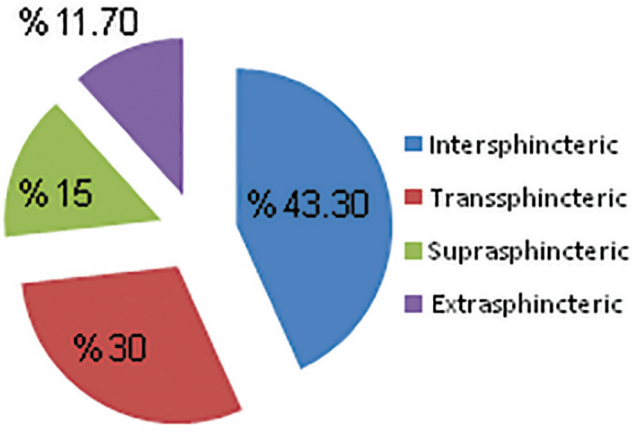
Table 2 Accuracy of endoanal ultrasonography in the detection of the internal opening

Valid	Frequency (%)
Inaccurate	7 (11.7)
Accurate	53 (88.3)
Total	60 (100)

Table 3 Accuracy of endoanal ultrasonography in the detection of the main tract

Valid	Frequency (%)
Inaccurate	13 (21.7)
Accurate	47 (78.3)
Total	60 (100)

Figure 2



Percentage of type of fistulae in the study.

Abscess cavity (collection)

With respect to the diagnosis of the presence or absence of abscess cavity or collection in the cases, the EAUS diagnosed 53 (88.3%) cases accurately and seven (11.7%) cases inaccurately as shown in Table 5.

Discussion

Different diagnostic methods are available for the preoperative evaluation of perianal fistulas. Accurate preoperative assessment of perianal fistulas is necessary for planning the most suitable surgical procedure and enables the surgeon to inform the patient of the type of surgery and its possible complications; it also decreases the rates of postoperative recurrence because of missed pathology. Currently, the main techniques used are EAUS and MRI. EAUS is a safe and economical technique that can also be used in patients who cannot undergo MRI because of claustrophobia, obesity, or metallic implants (such as pacemakers). Conventional EAUS has limited value in visualizing fistula tracts. EAUS combined with H_2O_2 as a contrast medium improves visualization and provides an accurate preoperative assessment of fistulas [8–10].

3D-EAUS is a new technique. 3D-EAUS enables axial images of the anal canal to be reconstructed in the coronal and sagittal planes. The use of 3D images provides more information on the anatomy of anorectal disorders [11].

In 2009, Kim and Park [6] published their study in the *World Journal of Gastroenterology* in which 61 patients were included in this prospective study to evaluate the effectiveness of 3D-EAUS in the assessment of anal fistulae with and without H_2O_2 enhancement; the results obtained were – as in our study – compared with the operative findings as the reference standard. The results of our study seem to be in agreement with the results of the study by Kim and Park to a large extent. In their study, the accuracy of 3D-EAUS in detecting the primary tract was 84% (in our study, it was 78.3%); the accuracy in detecting secondary tracts was 81.8% (in our study, it was 91.7%); and the accuracy in detecting localization of the internal opening was 84.2% (in our study, it was 88.3%) [6].

Table 4 Accuracy of endoanal ultrasonography in the detection of the secondary tract

Valid	Frequency (%)
Inaccurate	5 (8.3)
Accurate	55 (91.7)
Total	60 (100)

Table 5 Accuracy of endoanal ultrasonography in the detection of abscess cavity

Valid	Frequency (%)
Inaccurate	7 (11.7)
Accurate	53 (88.3)
Total	60 (100)

In agreement with our results, Ratto *et al.* [12] carried out a prospective study of 102 patients with primary cryptogenic anal fistula and reported an overall intraoperative concordance rate (with respect to preoperative EAUS) of 94% for the primary tract (78.3% in our study), 91% for the internal opening (88.3% in our study), 96% for the secondary tract (91.7% in our study), and 100% for abscess (88.3% in our study) [12].

Again, our results are very much in agreement with the results of Gustafsson *et al.*'s [13] study published in June 2001, in which 23 patients underwent preoperative 0.5-T body coil MRI and 10 MHz EAUS that included propping in six patients. The results of both techniques were compared against the surgical findings as a reference method [13].

In the classification of the primary tract in Gustafsson *et al.*'s [13] study, there was agreement between EAUS and surgical findings in 14 (61%) cases (in our study it was 78.3%). In terms of the localization of the internal opening, there was agreement in 17 (74%) cases in their study (in our study it was 88%), and in judging the presence of an extension or an abscess, there was agreement in 15 (65%) cases in their study (in our study it was 88.3%).

Finally, similar to any research or study carried out before, we acknowledge that our study may have some limitations. It did not include many patients with complex fistulae; because of low prevalence of high type fistulae or fistulae because of Crohn's disease, it was difficult to draw clear conclusions on how adequate EAUS was in detecting high type or complex fistula.

Another limitation of our study was the involvement of more than one colorectal surgeon in the surgeries of fistula, with different levels of experience and technical approaches, thus influencing the results of the present study. Most previous reports, similar to our study, have considered surgical results as the reference standard. However, surgery as a gold standard has been questioned as studies have shown that EAUS can detect fistula tracts that are not seen on surgical exploration [14].

In our study, we did not use H_2O_2 (as an enhancing agent in endosonography) in all cases because of technical difficulties or patient intolerability; thus, this may have biased our results to some extent.

Conclusion

EAUS combined with H_2O_2 and 3D technique enables greater visualization of perianal fistulas and therefore provides more information than conventional EAUS. Therefore, the EAUS may be considered the preferred examination technique in the study of anal fistulas, especially as EAUS is more economical and can be used in patients who cannot undergo MRI such as in obese patients or patients with metallic implants such as pacemakers or patients known to be claustrophobic.

Other advantages that make the EAUS the modality of choice are its rapidity (takes <10 min) and portability (can be performed in the operating room). Also, no radiation hazards are encountered with EAUS, as in computed tomography or conventional fistulography.

Acknowledgements

Conflicts of interest

None declared.

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