Risk factors for intra-abdominal abscess following laparoscopic appendectomy for acute appendicitis: a retrospective cohort study on 2,076 patients

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Abstract

Background. Intra-abdominal abscesses (IAA) may develop after laparoscopic appendectomies (LA) for acute appendicitis. The identification of risk factors for postoperative IAA could lead to a decrease in the readmission rate and surgery redoes after LA for acute appendicitis. **Materials and methods.** We reviewed 2,076 patients managed via a LA for acute appendicitis between 2001 and 2017. Male gender accounted for 53.5% of patients. Mean age was 29.5 (SD $\pm$ 18.47) years. Thirty-seven patients (1.8%) developed a postoperative IAA. Comparison between groups was made via univariate and multivariate analyses. **Results.** Male gender ($p < 0.05$), ASA score ≥ 2 ($p < 0.05$), a gangrenous or perforated appendicitis ($p < 0.0001$), abscess or pelvic peritonitis ($p < 0.0001$), clipping the mesoappendix ($p < 0.0001$), appendix division by mechanical stapler ($p < 0.05$), and prolonged antibiotic therapy ($p < 0.01$) were significantly more frequent in the group of patients with IAA. In terms of multivariate analysis, only pelvic peritonitis ($p < 0.005$), a perforated appendicitis ($p < 0.05$), and clipping the mesoappendix ($p < 0.0001$) were independent predictive factors for postoperative IAA. **Conclusion.** Patients with peritonitis or a perforated appendicitis, and those who had their mesoappendix clipped showed a higher likelihood of developing an IAA. At-risk patients should be provided with careful follow-up for the early detection and management of this complication.

Background

Post-appendectomy intra-abdominal abscesses (IAA) are estimated to complicate up to 4.2% of acute non-perforated appendicitis cases and 6.7% to 28% of acute perforated appendicitis cases [1]. Laparoscopic appendectomy (LA) has been demonstrated to be safe and effective for acute appendicitis but, compared to open appendectomy (OA), an increased rate of IAAs has been reported [2,3]. IAA is a significant cause of morbidity that increases the length of the hospital stay and needs to be treated by prolonged antibiotic therapy, percutaneous drainage or even reoperation.

The etiology of this complication remains unclear. On the one hand, some authors speculate that the occurrence of postoperative IAA might be influenced by several factors, such as advanced appendicular disease, appendicular perforation, the type of technique used for the removal of the appendix and the lack of an adequate perioperative antibiotics' regimen [4]. On the other hand, there are suggestions that a large-volume intraoperative peritoneal lavage might increase the rate of post-appendectomy IAA [5-8]. Unfortunately, most of the studies investigating the risk factors for IAA are relatively small-sized, retrospective, and often report conflicting results. The aim of the present study was to discover what factors that might contribute to the onset of IAA in patients undergoing LA.

Methods

Data collection

We reviewed the data of a prospectively collected database of patients who underwent laparoscopic appendectomy for acute appendicitis during the period 2001-2017 at the Department of Emergency Surgery of Pisa University Hospital. The diagnosis of acute appendicitis was based on the clinical presentation, laboratory parameters, and imaging studies. An ultrasound scan was performed for all of the patients with suspected acute appendicitis. Computed tomography was required in those cases for which a discordance was noted between the clinical presentation and the ultrasound. For all patients, antibiotics were administered about 30 minutes before the surgical operation according to the international guidelines on antibiotic prophylaxis in general surgery. This study is compliant with the STROCSS criteria [9] and is in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The informed consent for this study was waived because of the retrospective nature.

Surgery

We adopted the policy of performing a laparoscopy for all comers. Laparoscopic surgery was accomplished with the patient supine in the Trendelenburg position, and the table rotated to the left 10°-15°. Pneumoperitoneum was established with CO₂ at 12 to 14 mmHg by placing a Veress needle in the umbilical area or by using a Hasson open technique for cases of previous surgical operations. A 5-mm trocar was inserted in the periumbilical region for the introduction of a 5-mm - 30° laparoscope. Then another 5-mm trocar was inserted in the suprapubic area, and a 12-mm trocar was inserted in the left iliac fossa for the removal of the appendix. Following a laparoscopic exploration of the whole abdominal cavity, including the identification of signs of acute appendicitis, the mesoappendix was transected with electrocautery or using clips (HEM-O-LOK® Ligation System, Teleflex, Inc., Morrisville, NC, USA). The base of the appendix was ligated with endoloops and divided or sectioned with a 45-mm laparoscopic articulating stapler in the case of a large or gangrenous/perforated appendicular base. The appendix was then removed with a bag. After the complete evacuation of abdominal collections, a peritoneal lavage with warm saline solution, followed by suctioning, was performed in all patients until a satisfactory peritoneal clearance was achieved. Antibiotics (amoxicillin/clavulanic acid or ciprofloxacin) were continued after surgery in cases of complicated acute appendicitis. In cases of severe and diffuse contamination of the peritoneal cavity, a piperacillin/tazobactam regimen of antibiotic therapy was given.

Follow-up and IAA diagnosis

After discharge, a follow-up program of outpatient visits or phone calls was set up. IAA was suspected in the presence of fever, leukocytosis, and abdominal pain, and an abdominal imaging investigation confirmed the diagnosis (US and CT scan). Treatment consisted of therapy with broad-spectrum antibiotics for small-sized abscesses and percutaneous drainage for larger abscesses. Abscesses not amenable to percutaneous drainage or associated with peritonitis were best managed by surgical exploration.

Data analysis and statistics

The following parameters were the target of the analysis: gender, age, American Society of Anesthesiologists (ASA) score, intraoperative findings (abscess, gangrenous appendicitis, perforated appendix, pelvic peritonitis), method of management of the mesoappendix, type of technique adopted for the division of the inflamed appendix, and the use of postoperative antibiotics. The Lilliefors test was used to assess the normality of the distributions. A Mann-Whitney test was carried out to analyze quantitative variables. In addition, the Chi-squared test was performed to study categorical variables. Furthermore, stepwise forward multivariate logistic regression was used, and the Hosmer-Lemeshow test was carried out to evaluate the goodness of fit of the multivariate model. The statistical analysis was performed using the IBM SPSS software package, version 17.0.1.

Results

From 2001 to 2017, 2,076 patients underwent laparoscopic appendectomy for acute appendicitis. The mean age was 29.5 years (SD $\pm$ 18.47). There were 1,110 (53.5%) male and 966 (46.5%) female patients. The ASA score was ≥ 2 in 497 patients (23.9%). Table 1 summarizes the patients' demographics and preoperative variables.

At surgical exploration, 269 (12.9%) patients turned out to have an intraoperative abscess, 274 (13.2%) had gangrenous appendicitis, 180 (8.7%) had a perforated appendix, and 374 (18%) had pelvic peritonitis.

In 1,438 cases (69.3%), the mesoappendix was coagulated and dissected by a bipolar current forceps. In the remaining 638 patients (30.7%), the mesoappendix vessel was clipped and divided via scissors.

Endostapling was the preferred method of dealing with the basis of the inflamed appendix in 467 (22.5%) patients, whereas division of the basis of the appendix between endoloop ligatures was the most used method.

Overall, the mean operative time was 59.3 min (SD $\pm$ 29.96), and the mean postoperative hospital stay was 2.6 days (SD $\pm$ 2.13). Postoperative antibiotic treatment was given to 1,083 patients (52.2%).

Thirty-seven patients (1.8%) developed a postoperative intra-abdominal abscess. The average elapsed time from surgery to the diagnosis of IAA was 13.5 days (range 3-163 days). Management included antibiotics only in 19 cases (51%), percutaneous drainage with antibiotics in 13 (35%), and redo surgery (laparoscopic drainage) in the remaining 5 cases (14%).

Using univariate analysis, male gender ($p = 0.04$), ASA score ≥ 2 ($p = 0.04$), intraoperative abscess, gangrenous appendix, signs of appendicular perforation, pelvic peritonitis ($p < 0.0001$), clipping of the mesoappendix ($p < 0.0001$), and the use of the endostapler ($p = 0.02$) were associated with a higher occurrence of postoperative IAA (Table 2).

Prolonged postoperative antibiotic treatment was significantly more frequent in the group with postoperative IAA (73% vs. 52.1%; $p = 0.01$) (Table 2).

Using multivariate analysis, a perforated appendix (OR = 2.3 - 95% CI = 1-5.5; $p = 0.04$), localized peritonitis (OR = 2.9 - 95% CI = 1.4-6.2; $p = 0.004$) and the clipping of the mesoappendix (OR = 6.7 - 95% CI = 3-14.8; $p < 0.0001$) were identified as predictive factors for postoperative IAA (Table 3). The Hosmer-Lemeshow test showed a p -value of 0.47 with an appropriate level of goodness of fit.

Discussion

The severity of the appendix inflammation is believed to be the main risk factor associated with IAA. The IAA rate after laparoscopic appendectomy reported in non-perforated appendicitis is 1-4%, but the incidence of postoperative IAA increases by up to 26% in patients with gangrenous perforated appendicitis [10-13]. We found perforated appendicitis in 45.9% of patients that developed a postoperative IAA but in only 8% of the patients who did not suffer this complication (Table 2). According to Schlottmann *et al.* the higher the grade of intraperitoneal bacterial contamination, the higher the risk of postoperative IAA [14], and few doubts exist about the fact that perforation increases the grade of contamination of the peritoneum surrounding the appendix. Indeed, this study strongly supports the hypothesis that a perforated appendix should be regarded as a predictive factor for postoperative IAA (Table 3). Also, pelvic peritonitis was significantly more frequent in patients who developed postoperative IAAs (43.2% vs. 17.5%; $p < 0.0001$) (Table 2) and was recognized as a predictive factor for postoperative IAA via multivariate analysis (OR 2.9; $p = 0.004$) (Table 3).

According to the WISS study, acute appendicitis is still the most frequent cause of intra-abdominal sepsis [15]. A delayed diagnosis, mostly occurring in patients who are unreliable or have an atypical clinical onset, may lead to severe, life-threatening complications such as gangrene, perforation, appendiceal mass, and peritonitis [16]. Overall, 17.5% of the patients enrolled in the study had a peritonitis localized to the pelvis or the paracolic gutter: this result is in line with rate reported in the literature (17.3%) [13].

The clipping of the mesoappendix is associated with a higher incidence of postoperative IAAs. In this study, the use of clips was left to the operating surgeon's discretion, but such use was always limited to the management of the mesoappendix. Compared to bipolar coagulation, we recorded a significantly higher occurrence of IAA when the mesoappendix was secured with polymeric clips (62.1% vs. 29.7%; $p < 0.0001$). Polymeric clips have been increasingly used for the closure of the appendiceal stump [17-18], but the correlation between the use of polymeric clips and the increased rate of IAA, if it exists, remains unexplained. Some studies have indeed investigated the possible correlation between the method of mesoappendix dissection and the onset of IAA, with no significant conclusion. Wright *et al.*, in a review of 565 patients undergoing laparoscopic appendectomy for uncomplicated appendicitis, analyzed 149 patients (26%) who had a transection of the mesoappendix and appendix with a single staple line, 259 (46%) who had multiple staple lines, and 157 (28%) who had their mesoappendix dissected with the aid

of ultrasonic shears and their appendix divided by a single staple line. They found that the incidence of complications was low, with hematoma/abscess, transfusion, and reoperation occurring in only 1.4%, 0.4%, and 0.9% of cases, respectively. There were no significant differences between groups [19]. In a retrospective study of about 1178 patients who received laparoscopic appendectomy, Lee *et al.* compared 460 (39%) patients who had their mesoappendix managed with endoclips, 346 (29%) who had their mesoappendix managed by an ultrasonic device, and 346 (32%) who had their mesoappendix managed by monopolar electrocautery. They found no significant differences in terms of postoperative complications, including wound infection, abscess, paralytic ileus, and hemorrhage [20].

It emerges from this study that a prolonged administration of postoperative antibiotics had no significant effect on the occurrence of postoperative IAA. From this point of view, we confirm the data reported by Kimbrell *et al.* on a cohort of 52 young patients undergoing appendectomies for complicated appendicitis. They found that the occurrence of an abdominal abscess was not significantly lower if the postoperative antibiotics regimen was prolonged for more than 24 hours compared to when antibiotics were withdrawn within 24 hours after surgery. Thus, they concluded that postoperative antibiotics might not provide an appreciable clinical benefit in terms of preventing intra-abdominal abscesses [21]. The postoperative use of antibiotics for complicated appendicitis has proven to be beneficial [22], but the optimal duration of treatment has not yet been established. In a recent retrospective study on 6,412 patients with complicated acute appendicitis, Anderson *et al.* suggested that not all patients with complicated appendicitis should be discharged with antibiotics after surgery. Accordingly, only patients exhibiting SSI before discharge or those whose clinical progress requires a more extended in-hospital stay might benefit from extra-time antibiotic treatment. [23].

The present study suffers several limitations. Primarily, this is a retrospective study. Secondly, this series represents a vastly complex, heterogeneous patient population scattered over a considerable period. Thirdly, the lack of including other risks factor can affect the statistics of the multivariate analysis. Furthermore, the number of patients presenting a postoperative IAA constitutes a small cohort of cases. However, since the study was carried out at a tertiary referral center, the high volume of patients undergoing laparoscopy for acute appendicitis makes the statistical analysis credible and valuable. Lastly, we acknowledge that the patients were not routinely followed once symptoms resolved after the surgical intervention, making it possible that patients could have been lost during follow up.

Conclusions

Patients with localized peritonitis, a perforated appendicitis, and a clipped mesoappendix have a higher chance of developing postoperative IAA. The type of technique adopted for the division of the appendix (endostapler vs. endoloop) does not seem to be a risk factor for the development of postoperative IAA. The lack of postoperative antibiotic treatment was not identified as an independent risk factor for abscess formation.

Abbreviations

Declarations

Ethical approval and consent to participate: ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication: not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. All data generated or analysed during this study are included in this published article.

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Authors' contributions: DT, CG, IC and MC provided substantial contributions to the study conception and design. LMF, AM, LP, LC, RF and AB made data acquisition. DT, MM and MC made substantial contributions to data analysis and interpretation. DT, LMF, AM and LP drafted the manuscript. SDS and MC revised critically the study for important intellectual content. All authors read and approved the manuscript.

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Tables

Table 1. Patients' general and perioperative characteristics

DEMOGRAPHICS AND PREOPERATIVE VARIABLES	
Mean Age ($\pm$ SD)	29.5 ($\pm$ 18.47)
Gender	
- Male (%)	1110 (53.5%)
- Female (%)	966 (46.5%)
ASA score $\geq$ 2 (%)	497 (23.9%)
INTRAOPERATIVE FINDINGS	
Complicated acute appendicitis (%)	449 (21.6%)
• Intraoperative abscess	269 (12.9%)
• Gangrenous appendicitis	274 (13.2%)
• Perforated appendix	180 (8.7%)
• Localized peritonitis	374 (18%)
Endostapler for appendix transection (%)	467 (22.5%)
Coagulation of mesoappendix	1438 (69.3%)
Duration of operative time (min) ($\pm$ SD)	59.3 ($\pm$ 29.96)
POSTOPERATIVE OUTCOMES	
Prolonged antibiotic treatment (%)	1083 (52.2%)
Postoperative hospital stay (days) ($\pm$ SD)	2.6 ($\pm$ 2.13)
Postoperative IAA (%)	37 (1.8%)

Table 2. Univariate Analysis

	NO Post-op IAA N = 2039	Post-op IAA N = 37	<i>p</i>
Age (median $\pm$ SD)	25 $\pm$ 18.3	28 $\pm$ 22.5	0.30
M: F	1084:955	26:11	0.04
ASA score $\geq$ 2	483 (23.7%)	14 (37.8%)	0.04
Intraoperative abscess	256 (12.5%)	13 (35.1%)	< 0.0001
Gangrenous appendicitis	261 (12.8%)	13 (35.1%)	< 0.0001
Perforated appendix	163 (8%)	17 (45.9%)	< 0.0001
Localized peritonitis	358 (17.5%)	16 (43.2%)	< 0.0001
Endostapler for appendicular transection	453 (22.2%)	14 (37.8%)	0.02
Clipping of mesoappendix	606 (29.7%)	23 (62.1%)	< 0.0001
Prolonged antibiotic therapy	1062 (52.1%)	27 (73%)	0.01

Table 3. Multivariate Analysis

MULTIVARIATE ANALYSIS	OR	95% CI	<i>p</i>
Perforated appendix	2.3	1-5.5	0.04
Localized peritonitis	2.9	1.4-6.2	0.004
Clipping of mesoappendix	6.7	3-14.8	< 0.0001