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Predictors for prolonged length of stay after laparoscopic appendectomy for complicated acute appendicitis in adults

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Abstract

Background Appendicitis-related hospitalizations linked with peritonitis or postoperative complications result in longer lengths of stay and higher costs. The aim of the present study was to assess the independent association between potential predictors and prolonged hospitalization after laparoscopic appendectomy (LA) for complicated acute appendicitis (CAA).

Methods A retrospective cohort study was conducted on adult patients diagnosed with CAA in which LA was attempted. The primary outcome was a prolonged length of stay (LOS) after surgery, defined as hospitalizations longer than or equal to the 75th percentile for LOS, including the day of discharge. Hierarchical regression models were run to elucidate the independent predictors for the variable of interest.

Results The present study involved 160 patients with a mean age of 50.71 years. The conversion rate was 1.9%, and the overall postoperative morbidity rate was 23.8%. The median length of stay (LOS) was 5 days (75th percentile: 7 days). Multivariate analyses included nine variables that are statistically and/or clinically relevant to assess its relationship with a prolonged LOS: three preoperative (age, sex, and comorbidity), four intraoperative (appendix gangrene, perforation, degree of peritonitis, and drain placement), and two postoperative (immediate ICU admission and complications). The development of postoperative complications (OR 6.162, 95% CI 2.451–15.493; $p=0.000$) and the placement of an abdominal drain (OR 3.438, 95% CI 1.107–10.683; $p=0.033$) were found to be independent predictors for prolonged LOS. For patients not presenting postoperative complications, drain placement was the only independent predictor for the outcome (OR 7.853, 95% CI 1.520–40.558; $p=0.014$). Sensitivity analyses showed confirmatory results.

Conclusion The intraoperative process of care has a clear impact on LOS after LA for CAA in adults; therefore, the decision of whether to drain in these situations should be made more restrictively yet with judicious caution.

Keywords Acute appendicitis · Laparoscopic surgery · Hospital stay · Postoperative adverse events

Acute appendicitis (AA) includes a large variety of inflammatory conditions of the ileocecal appendix, ranging from mild inflammation to perforation with peritonitis. This is the most prevalent abdominal emergency worldwide, and appendectomy is the most common general surgical procedure performed in the emergency setting [1–3]. A recent observational retrospective population-based cohort study analyzing the national Dutch health-care reimbursement registry showed that the incidence was higher for men and showed a decreasing trend over time with a peak between 10 and 19 years of age [4]. Between 2000 and 2015, the incidence of appendicitis was estimated at 1 per 1000 in Northern America, and 378,614 new cases were expected for 2015 [5]. Appendicitis-related hospitalizations were estimated to

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account for 0.6% of all hospitalizations in U.S. community hospitals, with $3 billion yearly costs within the country [6].

The proportion of complicated acute appendicitis (CAA) varies between the different series, constituting approximately 30% of the total [7]. Patients with CAA are more likely to suffer from postoperative complications than are those with a simple presentation, surgical site infection (SSI) is the most detrimental adverse event [8, 9]. Appendicitis-related hospitalizations linked with appendicecal abscess, peritonitis, and postoperative infectious complications result in longer lengths of stay and higher costs [6]. The use of minimally invasive surgery to treat AA is widespread. Laparoscopic appendectomy (LA) appears to present some benefits when compared with traditional open appendectomy (OA) in reducing pain intensity, wound infections, length of stay, and time until return to normal activity [10, 11]. In contrast to previous systematic reviews and meta-analyses by the Cochrane Collaboration, which reported a higher rate of intraabdominal abscesses for LA in adults, the most recent update showed a trend towards fewer intraabdominal abscesses after LA in a subgroup analysis of randomized controlled trials (RCTs) published since 2007 [11]. Concerning the specific subset of patients presenting with CAA, meta-analyses including both RCTs and clinical case series demonstrated similar favorable postoperative outcomes for LA compared to OA [12–14].

Given the increasing pressure to limit disbursements for health-care systems in many countries, a better understanding of the economic burden of AA together with its determinants is needed. Despite its high incidence, to date, only a few large-scale evaluations of the expenditures derived from AA management have been reported [4, 6, 15]. The length of stay (LOS) is correlated with direct costs and is considered an important marker for resource consumption [16]. This outcome would be useful as a surrogate to evaluate the impact of preexisting patient conditions (i.e., age and comorbidities) and intraoperative process of care on the outcomes and costs derived from a procedure with relatively low expected morbidity, even for its complicated forms [7, 17]. Recognizing those factors could be helpful for clinicians upgrading the delivery of patient care and for healthcare providers in mitigating the financial burden. Therefore, the aim of the present study was to assess the association between potential independent predictors of prolonged LOS after LA for CAA.

Methods

Study design

The study was designed as an ancillary analysis of the *COMplicated INtraabdOminal infections (COMINO) Project.* The complete database included 571 adults (≥ 18 years old) admitted at the Doctor Peset University Hospital (Valencia, Spain) from January 2014 to December 2017 presenting with suspected complicated intraabdominal infections. The original study was performed in accordance with the last version of the Declaration of Helsinki. The protocol was reviewed and approved by the local ethics committee (CEIm7419). Written informed consent was waived according to the present legislation. Data from patients diagnosed intraoperatively with CAA were retrospectively extracted for the purposes of the current analysis. Complicated appendicitis was defined as the presence of a walled-off abscess, local peritonitis (purulent material in the periappendicular area or in the pelvis), or diffuse peritonitis [3]. Patients operated on by a conventional open surgical procedure or receiving nonoperative management due to the presence of a palpable mass owing to abscess or phlegmon were not included in the analyses.

The initial diagnosis of AA was based on physical examination, laboratory tests, and abdominal ultrasound, whereas a CT scan was only requested for selected patients. LA was performed with 3 trocars: 11-mm umbilical (optic), 5-mm suprapubic, and 11-mm in the left lower quadrant. The mesoappendix was dissected using monopolar electrocoagulation, and the appendicular artery and appendix stump were usually divided after clipping and ligation, respectively. Laparoscopic abdominal irrigation was not routinely used and was limited to the minimum for assuring the complete removal of all abdominal purulent fluid. The specimen was removed using a retrieval bag through the left lower quadrant port. The indication of drain placement was made at the discretion of the senior surgeon participating in the procedure based on the presence of necrotic or infected tissue, extensive peritonitis, doubtful hemostasis or stump's closure. The drain was usually open and placed on the right lower quadrant and the pelvis, externalized by a new incision in the right iliac fossa. All patients received prophylactic antibiotics, which were continued for at least 3–5 days [18, 19]. Oral antibiotics were prescribed if the patients were discharged earlier. The decision to continue, de-escalate, or stop antibiotic treatment was made on patient symptoms, laboratory data and the results of microbiological testing. Criteria for hospital discharge included resolution of fever, controlled pain by oral analgesics, normalization of the peripheral white-cell count, resume of regular diet, and bowel function recovery. All patients were evaluated at least 3 months after surgery to capture postdischarge morbidity and outcomes.

The collected data included demographic, diagnostic, and perioperative features. The primary outcome was the LOS after surgery, and a prolonged hospitalization was defined as hospital admissions longer than or equal to the 75th percentile for LOS, including the day of discharge [16,

20, 21]. Postoperative complications were defined as any adverse event that occurred during hospitalization or within 90 days after surgery and were categorized according to the Clavien-Dindo classification system for surgical complications [22]. Other potential predictors for the main outcome were investigated, including baseline characteristics [23], symptoms and signs upon admission, including sepsis status defined according to the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) consensus conference [24], surgical findings including disease features such as the degree of peritonitis [25], or surgical decisions regarding drainage placement or conversion to open surgery. Postoperative ileus was defined as an interval from surgery until passage of flatus/stool and tolerance of an oral diet ≥ 4 days [26].

Statistical analysis

All categorical data are presented as the number of cases and percentages. Chi-square and Fisher's exact tests, when appropriate, were used to compare proportional data between patients with or without a prolonged LOS. Continuous nonparametric data were expressed as the median with interquartile range (IQR), and parametric data were expressed as the mean with standard deviation (SD). The Mann–Whitney *U* test was used for comparing nonparametric variables, and the t test was used for parametric continuous variables from the abovementioned groups. The variables of interest were divided according to the hierarchical order in which they were expected to occur in the process of patient care for a laparoscopic appendectomy: (1) preoperative patient features, (2) operative factors and decisions, and (3) postoperative adverse events. Converted cases were considered on an intention-to-treat basis. All the tests were 2-sided, and the threshold of significance was set at $p < 0.05$. Multivariate hierarchical logistic regression analyses were planned, including statically significant variables at the univariate level and those judged to be clinically relevant irrespective of statistical significance, to adjust for covariates and to obtain the odds ratio (OR) and parameter estimates. The models were run entering the groups of variables in the previously mentioned order. Each step of introducing a set of variables leads to controlling for the effects of variables retained from the previous steps. At each step, multivariate goodness-of-fit was evaluated using the Hosmer–Lemeshow test, and the model performance was evaluated by the Nagelkerke R^2. Additionally, the improvement in model performance in each step was established by calculating the p values from the change in chi-square resulting from each inclusion. Ad hoc sensitivity analysis was planned via hierarchical multiple regression with hospital stay as the continuous dependent variable. Subgroup analyses were anticipated to determine the robustness of the main findings. Statistical analyses were performed using Statistical Package for Social Sciences software (IBM SPSS Statistics, Version 25 for Macintosh; IBM Corp., Armonk, NY, USA). The results were reported according to the strengthening of the reporting of observational studies in epidemiology (STROBE) statement guidelines [27].

Results

A total of 173 consecutive patients with complicated acute appendicitis were admitted during the study period. Eight patients received nonoperative management due to the presence of abscess or inflammatory phlegmon at clinical or radiologic explorations, four of whom required further percutaneous drainage. Of the remaining 165 patients receiving surgical treatment that confirmed the diagnosis of CAA, five underwent laparotomy for bowel obstruction (2), suspicion of malignancy (2), or unknown reason (1). Therefore, 160 patients in which laparoscopic appendectomy was attempted were included in the present analyses (Supplemental Fig. 1). The mean age was 50.71 years, 53.1% were men, and 16.9% received previous abdominal surgeries by either open (20) or laparoscopic (7) approaches. The preoperative diagnostic work-up included the performance of abdominal ultrasound in 140 (87.5%) and/or computed tomography in 43 (26.9%) cases. Preoperative baseline, disease, and diagnostic features are displayed in Table 1. The most prevalent comorbidity was diabetes (20%), followed by chronic pulmonary (15%) or artery (14%) diseases (Supplementary Fig. 2).

Intraoperatively, gangrene or macroscopic perforation of the appendix was evidenced in 103 (64.4%) and 81 (50.6%) of the procedures, respectively. Three patients (1.9%) required conversion to laparotomy due to adherences (1) or intense inflammation at the periappendicular area (2), one of the latest finally receiving ileocecal resection. An abdominal drain was left in 96 (60%) of the patients. 5 (3.1%) of them were admitted to the ICU immediately after surgery, due to severe sepsis (4) or preexisting cardiopulmonary disease (1). Overall postoperative morbidity was 23.8%. The previously mentioned patient developed an anastomotic leak leading to surgical re-intervention, similar to another presenting with multiple intraabdominal fluid collections. Ileus was the most prevalent complication (9.4%), followed by deep (5.6%) and superficial (5%) SSI. Four patients (2.5%) were readmitted due to intraabdominal collections (2) or ileus (2), all were successfully managed by conservative treatments. The main operative and postoperative features are summarized in Table 2. The median length of stay (LOS) was 5 days, and the 25th and 75th percentiles were 3 and 7 days, respectively. Prolonged LOS was then defined as a hospital stay equal to or greater than 7 days.

Table 1 Preoperative baseline characteristics and diagnostic features of the patients with complicated appendicitis treated by laparoscopic appendectomy ($n=160$)

	Whole simple ($n=160$)	Prolonged LOS ($n=44$)	Control group ($n=116$)	p value[test]
Patient characteristics				
Age (years)[a]	50.71 (18.09)	55.34 (19.13)	48.95 (17.45)	0.046[f]
Male gender[c]	85 (53.1)	29 (65.9)	56 (48.3)	0.046[d]
BMI (kg/m^2)[b]	27 (6.8)	26 (6.9)	27 (6)	0.798[g]
Presence of any comorbidity[c]	58 (36.3)	21 (47.7)	37 (31.9)	0.063[d]
Charlson comorbidity index[b]	0 (1)	0 (2)	0 (1)	0.094[g]
Symptoms and signs at admittance				
Duration of symptoms (hours)[b]	24 (63)	24 (83)	20 (44)	0.313[g]
Fever (> 38 ºC)[c]	56 (35)	15 (34.1)	41 (35.3)	0.882[d]
Sepsis status				0.712[d]
No sepsis	51 (31.9)	13 (29.5)	38 (32.8)	
Sepsis	89 (55.6)	24 (54.5)	65 (56)	
Severe sepsis	20 (12.5)	7 (15.9)	13 (11.2)	

BMI Body Mass Index

[a][mean (SD)]

[b][median (IQR)]

[c][n (%)]

[d]$\chi 2$ test

[e]Fisher's exact test

[f]Student's *t*-test

[g]Mann-Whitney *U* test

Univariate analyses identified variables with a potential independent correlation with prolonged LOS. There were two preoperative (i.e., age and sex), four intraoperative (i.e., appendicular gangrene or perforation, degree of peritonitis, and drain placement), and two postoperative (i.e., immediate ICU admission and presence of complications) variables. Hierarchical logistic regression analyses were run, including the presence of comorbidities in the model disregarding the lack of statistical significance at the univariate level. The first model input including baseline characteristics resulted in an R^2 of 0.079 (Hosmer–Lemeshow $p=0.072$). The addition of the intraoperative variables to the prediction of prolonged hospitalizations led to a statistically significant increase in R^2 of 0.176 (X^2 $p=0.000$). Additional improvement in the model performance was observed when the set of postoperative predictors was entered, with R^2 increasing by 0.167 (X^2 $p=0.000$). In the final model, two variables were found to be independent predictors for prolonged LOS after LA for CAA: the development of postoperative complications (OR 6.162, 95% CI 2.451–15.493; $p=0.000$) and the placement of an abdominal drain (OR 3.438, 95% CI 1.107–10.683; $p=0.033$). The final model correctly classified the dependent variable in 80.6% of the cases. The Hosmer–Lemeshow goodness-of-fit test significance was 0.829, and the Nagelkerke R^2 was 0.422 (Table 3).

Ad hoc hierarchical multiple regression analyses showed that the LOS was independently correlated with both postoperative complications ($B=3.149$, 95% CI 2.270–4.029; $p<0.000$) and abdominal drain placement ($B=1.788$, 95% CI 0.939–2.637; $p=0.000$). Sensitivity analyses, by establishing the cutoff for prolonged LOS of equal to or greater the median of hospitalization or excluding the patients needing readmission, also showed confirmatory results. Subgroup analysis including only patients without postoperative complications revealed that drainage positioning was the only independent predictor of prolonged LOS with an OR of 7.853 (95% CI 1.520–40.558; $p=0.014$). Post hoc analyses revealed that the median duration of drain placement was 4 (IQR 2) days. The median duration of hospital stay was 6 (IQR 3) and 3 (IQR 2) days in patients with and without drain, respectively ($p=0.000$).

Discussion

The present study found that the development of postoperative complications and the placement of an abdominal drain were independent predictors for prolonged LOS in patients undergoing LA for CAA after adjusting for patient, disease, and perioperative features. Although preoperative factors were related to a prolonged LOS, the intraoperative features

Table 2 Surgical details and outcomes within 90 days for patients with complicated acute appendicitis treated by laparoscopic appendectomy ($n=160$)

	Whole simple ($n=160$)	Prolonged LOS ($n=44$)	Control group ($n=116$)	p value[test]
Operative findings and procedure details				
Delay admission to surgery (hours)[b]	7 (9)	6 (10)	7 (8)	0.928[g]
Conversion to laparotomy[c]	3 (1.9)	2 (4.5)	1 (0.9)	0.184[d]
Appendix gangrene[c]	103 (64.4)	35 (79.5)	68 (58.6)	0.010[d]
Appendix perforation[c]	81 (50.6)	30 (68.2)	51 (44.0)	0.005[d]
Walled-off abscess[c]	50 (31.3)	10 (22.7)	40 (34.5)	0.106[d]
MPI[b]	15 (11)	19 (10)	15 (10)	0.030[g]
Drain placement[c]	96 (60.0)	39 (88.6)	57 (49.1)	0.000[d]
Operative time (min)[b]	60 (31)	61.50 (39)	60 (26)	0.160[g]
Postoperative outcomes				
Immediate ICU admission after surgery[c]	5 (3.1)	5 (11.4)	0 (0)	0.001[e]
Postoperative complications	38 (23.8)	24 (54.5)	14 (12.1)	0.000[d]
Clavien grade (I/II/IIIa/IVa)	18/15/3/2	10/11/1/2	8/4/2/0	
Superficial SSI	8 (5)	5 (11.4)	3 (2.6)	
Deep SSI	9 (5.6)	5 (11.4)	4 (3.4)	
Ileus	15 (9.4)	14 (31.8)	1 (0.9)	

MPI Manheim Peritonitis Index, *ICU* intensive care unit, *SSI* surgical site infection

[a][mean (SD)]

[b][median (IQR)]

[c][n (%)]

[d]$\chi 2$ test

[e]Fisher's exact test

[f]Student's *t*-test

[g]Mann-Whitney *U* test

Table 3 Results from hierarchical logistic regression analyses on the association between the variables of interest and prolonged length of stay after laparoscopic appendectomy

	Odds ratio	(95% CI)	*P* value	Nagelkerke R^2 (H–L test p value)	R^2 change X^2 (p value)
Preoperative variables				0.079 (0.072)	0.079 9.002 (0.029)
Age	1.006	0.969–1.044	0.766		
Male gender	0.633	0.235–1.705	0.366		
Comorbidity	1.202	0.309–4.675	0.790		
Operative variables				0.255 (0.552)	0.176 22.071 (0.000)
Gangrene	1.417	0.482–4.168	0.526		
Perforation	1.695	0.649–4.424	0.281		
MPI	1.023	0.950–1.102	0.543		
Drain placement	3.438	1.107–10.683	0.033		
Postoperative variables				0.422 (0.829)	0.167 24.012 (0.000)
Immediate ICU admission	1.468	0–n.a	0.999		
Postoperative complications	6.162	2.451–15.493	0.000		

H–L Hosmer–Lemeshow test, *MPI* Manheim peritonitis index, *ICU* intensive care unit

and process of care, together with postoperative adverse events, resulted in a greater association with this outcome in the complete model. It has been well established that the development of complications is highly correlated with the complexity of the surgery and the hospitalization length [16, 21, 22]. Therefore, our results are confirmatory. In the same vein of a number of both emergent and elective abdominal surgical procedures, the surgeon's subjective decision of whether to leave a drain at the end of an appendectomy has been a matter of debate. A recent Cochrane systematic review including 6 RCTs (521 participants) compared drainage vs. no drainage at emergency open appendectomy and showed a hospital stay 2.17 days longer and a significantly higher postoperative morbidity and mortality in patients receiving drainage. Nevertheless, the authors acknowledged the great uncertainty of these findings due to the small number of studies and patients included [8]. Recent guidelines recognize that drains do not reduce the incidence of intraabdominal abscess after appendectomy for CAA in adult patients. They recommended its placement only for special indications at the surgeon's discretion but with judicious caution [28, 29]. The effect of drainage on the prevention of postoperative adverse events after LA is even more uncertain. There is a notorious lack of prospective data currently available addressing this issue. To the best of our knowledge, no previous study independently assessed the potential impact of these decisions on the hospitalization extent after LA in adults. Postoperative LOS is considered an excellent indicator of surgical efficiency, directly related to the effectiveness of recovery programs and health resource utilization. It is becoming a critical target for cost evaluation and restraint, especially when pay-for-performance and bundled payment models are becoming more prevalent in determinate health-care systems [17, 21, 30]. The findings regarding the subgroup of patients who did not develop complications are perhaps the most explanatory, revealing nearly 8 times higher odds for prolonged LOS if a drain was placed at the end of the procedure. This observation could be justified by its potential effect on how the patient perceives himself or herself and the caregiver's perception of the patient's health status and successfulness of the early postoperative course. An impact on the timing of care delivery and likely on the patient's compliance with the development of this care is therefore expected. Together, these factors may lead to a more sluggish postoperative course flowing into delayed discharges and increased expenditures.

The present findings are limited by the retrospective nature of the study. The well-known bias inherent to this research design cannot be ruled out. However, we analyzed a large consecutive series of patients from a single high-volume surgical unit over a relatively short period of time, yet low variability within the treatments can be expected. The analyses were adjusted for variables reflecting the severity of the illness (i.e., appendix perforation, degree of peritonitis, and presence of gangrene) that are considered potential confounders when increasing the likelihood of the surgeon's decision to drain over not to drain. Additionally, sensitivity analyses were run displaying confirmatory returns. The results also suggested that minimally invasive surgery is feasible as the paramount approach for treating CAA in adults, with low rates for primary OA, or for conversion after an initial laparoscopic attempt on appendix removal. The incidence of postoperative complications (23.8%, 3.1% grade ≥ 3) can be considered acceptable compared with the literature and is in accordance with our previously reported experience [7]. To leave a drain after CAA surgery is sometimes imperative in the case of extensive fecal contamination or when inflamed tissues (e.g., fragments of wall abscess, greater omentum, mesenterium, etc.) are not completely removed during the procedure. Nonetheless, we observed a 60% rate of abdominal drain placement that clearly exceeded our preconceived expectations and highlighted the need for more accurate selection in the future, especially concerning the impact of this election on the most prevalent group of patients who will not develop any postoperative complications.

Different considerations regarding the definition of complex appendicitis have become a silenced controversy. Our study followed an agreed definition for complicated IAI considered when the infection proceeds beyond a singularly affected organ and causes either localized peritonitis (including intraabdominal abscesses) or diffuse peritonitis [3]. However, the literature demonstrates a wide range of alternatives for defining complex appendicitis. The most popular have been the presence of perforation alone [31–34], gangrene [35–38], with or without peritonitis [7, 39–42], or the latest alone [43, 44]. Differences also exist regarding when and how those findings were suspected or confirmed (i.e., radiology, surgery, histology). This leads to high clinical heterogeneity between the criteria used when dichotomizing an AA and therefore the comparability and generalization of our findings, as those provided by the previous research on the subject are critically jeopardized. A consensus is urgently needed to conceptually define which kind of acute appendicitis should be regarded as complex or complicated, strengthening the accuracy and reproducibility of future research.

In conclusion, intraoperative process of care and postoperative adverse events are associated with prolonged hospitalization after laparoscopic appendectomy for complicated appendicitis in adults. Despite sometimes being unavoidable, an abdominal drain should be placed more restrictively but with judicious caution after those procedures considering its independent impact on further postoperative care delivery and compliance.

Compliance with ethical standards

Disclosures Aleix Martínez-Pérez, Carmen Payá-Llorente, Sandra Santarrufina-Martínez, Juan Carlos Sebastián-Tomás, Elías Martínez-López, and Nicola de'Angelis have no conflict of interest or financial ties to disclose.

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