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ORIGINAL SCIENTIFIC REPORT

Preoperative Clinical Factors Associated with Short-Stay Laparoscopic Appendectomy

Aurélie Vuagniaux[1] · Olivier Gié[1] · Fabio Butti[1] · Pedro Manuel Marques-Vidal[2,3] · Nicolas Demartines[1,3] · Styliani Mantziari[1,3]

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Abstract

Background Outpatient appendectomy for acute appendicitis is a feasible, yet not widely performed procedure, as there are no universally accepted criteria for patient selection. The aim of this study was to assess preoperative clinical factors associated with successful short-stay appendectomy (SSA) and establish a predictive score to help with patient selection.

Methods All consecutive laparoscopic appendectomies performed in our institution between January 2013 and June 2015 were retrospectively analyzed. Several preoperative clinical and biological variables were compared between patients with SSA, defined as a postoperative stay <24 h, and those needing inpatient care. Logistic regression analysis was used to identify variables independently associated with SSA, and these variables were then used to create a predictive score.

Results A total of 578 patients were included, 303 (53%) in the SSA group and 275 (48%) in the long-stay appendectomy (LSA) group. In multivariate analysis, male gender (OR 1.61, 95% CI 1.12–2.31, $p = 0.010$), ASA class I–II (OR 9.52, 95% CI 1.65–180.69, $p = 0.037$), absence of generalized guarding (OR 3.55, 95% CI 1.30–11.41, $p = 0.019$), C-reactive protein <100 mg/dl (OR 3.09, 95% CI 1.81–5.42, $p < 0.001$) and leukocyte count <20 g/l (OR 2.06, 95% CI 1.02–4.30, $p = 0.046$) were independently associated with SSA. These five parameters were used to construct a predictive score, whereby ≥ 17 (range 0–21) was defined as the optimal threshold to predict SSA with a high sensitivity (95.6%) and negative predictive value (82.2%).

Conclusions A purely clinical predictive score based on five widely used preoperative parameters can be used to identify eligible patients for short-stay appendectomy.

Introduction

Laparoscopic appendectomy for acute appendicitis is one of the most common surgical procedures. As patients are often young and otherwise healthy, outpatient surgery could offer quicker recovery and return to daily activities. In addition, outpatient surgery may help optimize health

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Aurélie Vuagniaux and Olivier Gié have contributed equally.

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✉ Nicolas Demartines
demartines@chuv.ch

1 Department of Visceral Surgery and Transplantation, Centre Hospitalier Universitaire Vaudois, University Hospital of Lausanne (CHUV), Rue du Bugnon 46, 1011 Lausanne, Switzerland

2 Department of Internal Medicine, University Hospital of Lausanne (CHUV), 1011 Lausanne, Switzerland

3 Faculty of Biology and Medicine, Lausanne University UNIL, Lausanne, Switzerland

care resource management, avoiding unnecessary bed occupancy and limiting the risk of hospital-acquired infections [1, 2]. Ambulatory, day-case or outpatient surgery has yet to be clearly defined in the literature; although the international definition is <12 h after the end of the surgery [3], this is not always practically feasible in all health care structures, especially for emergency procedures, and thus, many authors use 24 h as a threshold [2, 4, 5]. Currently, outpatient surgery is increasingly practiced for elective surgery as laparoscopic cholecystectomy [6], but also for more complex interventions like bariatric [7], antireflux surgery [8], colorectal resections [9] or rectopexy [10]. In all of the above outpatient surgery programs, correct patient selection and efficient perioperative care are the cornerstones of successful ambulatory surgery.

Emergency outpatient procedures may be more challenging, due to unscheduled presentation of patients, variable severity of the clinical context and individual patient background. In recent years, several studies suggested the feasibility of outpatient laparoscopic appendectomy for uncomplicated appendicitis [1, 2, 5, 11–16]; however, selection of optimal candidates remains unclear, which may explain surgeon and patient reluctance for early discharge. Lefrançois et al. [5] suggested a promising scoring system to select patients for outpatient appendectomy, using clinical and radiological parameters. However, as appendicitis is generally a clinical diagnosis and preoperative imaging is not systematically performed in all centers, the generalizability of the score might be limited.

The aim of the present study was to identify routinely used preoperative clinical and biological parameters associated with short-stay appendectomy (SSA), defined as a postoperative stay of ≤24 h. Based on these parameters, we aimed to create a predictive clinical score to select appropriate candidates for SSA.

Materials and methods

A retrospective analysis was conducted on all consecutive patients undergoing laparoscopic appendectomy between January 2013 and June 2015 in our tertiary referral center. Patients were identified through the operating room program, using the terms 'appendectomy' and/or 'explorative laparoscopy' and relevant data were obtained from electronic patient files. All patients aged >16 years presenting to the emergency department for suspected acute appendicitis were eligible for analysis. Elective appendectomy after initial percutaneous drainage and appendectomy during laparotomy for another indication were excluded. The study protocol was approved by the Institutional Ethics Committee (Protocol No. 2016-00289), and informed consent was obtained from all patients.

Preoperative workup, surgery and postoperative course

Indication for surgery was routinely established by the board-certified surgeon on duty, upon clinical suspicion of appendicitis with or without preoperative imaging. Preoperative biological workup systematically included inflammatory biomarkers, leukocytes and CRP. In the present analysis, 52.2% of the appendectomies were performed by the resident under direct operative supervision by the surgeon. Laparoscopic appendectomy with a 10-mm umbilical port and two 5-mm ports was the standard surgical technique, the appendix being removed after endoloop placement or 30-mm linear stapling through its basis. In case of contamination of the abdominal cavity, peritoneal washing was performed as needed, and the no-drains policy was the rule with few exceptions such as diffuse fecal contamination of the abdominal cavity needing extensive peritoneal lavage.

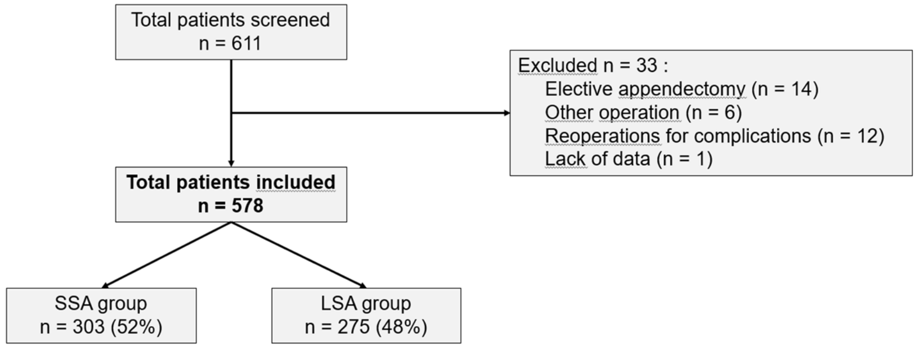
All adverse effects occurring during 30 postoperative days were recorded and graded according to the validated Clavien 5-scale system [17]; when multiple complications occurred, only the most severe was recorded. Based on postoperative length of stay, measured in hours (h) after the end of the intervention, patients were divided into the SSA group, with a ≤24 h postoperative stay, and long-stay appendectomy (LSA) group, including all other patients. For organizational reasons, most appendectomies are performed late in the afternoon or during the night in our hospital. Thus, overnight stay is frequently necessary even in cases where early discharge would have been medically feasible.

Since 2013, a standardized clinical pathway ('*care map*') was applied for laparoscopic appendectomy, adapted to individual patients' course as needed. Discharge criteria after appendectomy included adequate pain control with oral medication, absence of fever or other signs of ongoing sepsis, successful re-instauration of oral nutrition and bladder voiding. Upon discharge, clear instructions are given to patients as well as the emergency phone number of our on-call resident (available 24 h/24 h, 7d/7), in case of any problems at home. After discharge, there was no dedicated nurse day-1 call or planned follow-up visit.

Statistical analysis

All relevant demographic and clinical variables were directly compared between patients in both SSA and LSA groups. Categorical variables were expressed as frequency (%) and compared with the Chi-squared or the Fisher's

Fig. 1 Patient flowchart



exact test as appropriate; continuous variables were expressed as median (range) and compared with the non-parametrical Mann–Whitney U test. Simple and multiple logistic regression analysis was performed to identify preoperative factors associated with SSA. Variables with $p < 0.1$ in simple logistic regression were included in the multivariate model, where the significance threshold was set at $p < 0.05$ and all tests were two-sided. The logistic regression results were expressed as odds ratio (OR) with 95% confidence intervals (CI). The final model was tested for goodness of fit with the Hosmer–Lemeshow test after assessing the absence of multicollinearity between the covariates.

Creation of a clinical score predictive of SSA

Using a previously described validated method, each significant variable on multivariate analysis was allocated a number of points equal to its adjusted OR, and the final score for each patient was the sum of all points [18]. For each of the included variables, 0 point was given to the reference category and X points were given to every other category whereby X = rounded adjusted OR. A higher score was associated with higher probability of SSA. Finally, a ROC curve analysis was conducted to define the threshold with the highest diagnostic accuracy. All analyses were conducted with RStudio (version 3.2.3 'Wooden Christmas-Tree', Boston) and SPSS software (version 23.0, Chicago, IL, USA).

Results

During the study period, 578 consecutive patients had emergency laparoscopic appendectomy and were included in the study (Fig. 1). Among them, the SSA group consisted of 303 patients (52%), whereas 275 patients (48%) stayed >24 h after surgery (LSA). Overall, 56 patients (18.5%) stayed ≤12 h, whereas only 22 patients (7.3%) had surgery without an overnight stay (10 pm–6 am). Patients staying <12 h ('real outpatients') were compared to those staying 12–24 h ('extended outpatients') with no differences found in baseline characteristics, clinical or postoperative outcomes between these two subgroups (Online appendix). Thus, the SSA group reflects correctly both 'real' and 'extended' outpatient groups.

Preoperative demographics and comorbidities

Preoperative demographics and comorbidities are reported in Table 1. In the SSA group, patients were more often male (58.1% vs. 47.6%, $p = 0.012$), younger (median age 28 vs. 32 years, $p < 0.001$) and ASA class I–II (98.7 vs. 91.7%, <0.001) compared to LSA patients. SSA patients were less often residents of nursing homes/care facilities (0.3% vs. 2.5%, $p = 0.031$), whereas insurance type presented no differences. In terms of chronic comorbidity, the only difference was cardiovascular disease, which was significantly less prevalent in the SSA group (5.0 vs. 14.2%, $p < 0.001$).

Preoperative imaging—diagnosis of appendicitis

Preoperative imaging was performed in 446 patients (77%); ultrasound was the exam of choice in 44% of cases in SSA group and 30% in the LSA group, whereas a CT scan was more often performed in the LSA group (45.8% vs. 33% in OA, $p < 0.001$). In 11.2% of the SSA and 24.7% of the LSA patients, preoperative imaging revealed complicated appendicitis ($p < 0.001$). Acute appendicitis was confirmed intraoperatively in 96.4% of SSA and in 92.7% of LSA patients, as well as upon histopathological analysis (97.4% in SSA and 93.1% in LSA groups). Intraoperatively, 8.3% and 27.3% of patients, respectively, ($p < 0.001$) had a necrotic or perforated appendicitis. In cases of misdiagnosis, the underlying pathology was most often gynecological (1.6%) or neoplastic (1.6%), with some rare cases of mesenteric lymphadenitis, diverticulitis and peptic ulcer perforation.

Table 1 Patient characteristics and comorbidities for short-stay appendectomy (SSA) and long-stay appendectomy (LSA) patients

	All patients $N = 578$ (%)	SSA $N = 303$ (%)	LSA $N = 275$ (%)	p value
Male gender	307 (53.1)	176 (58.1)	131 (47.6)	0.012
Median age (range)	30 (16, 93)	28 (16, 77)	32 (17, 93)	0.007
ASA class				<0.001
I–II	551 (95.4)	299 (98.7)	252 (91.7)	0.492
III	18 (3.1)	1 (0.3)	17 (6.2)	
Median BMI [kg/m^2 (range)]	24 (16, 61)	24 (16, 61)	23 (16, 37)	
Active smoking	166 (28.7)	93 (30.7)	73 (26.5)	0.340
Alcohol abuse	17 (2.9)	7 (2.3)	10 (3.6)	0.328
Social status				
Living alone	73 (12.6)	34 (11.2)	39 (14.2)	0.837
Living in care facility	8 (1.4)	1 (0.3)	7 (2.5)	0.031*
Insurance type				0.109
General	532 (92.0)	284 (93.7)	248 (90.2)	
Private	45 (7.8)	19 (6.2)	9 (9.5)	
Immunosuppression	13 (2.2)	5 (1.7)	8 (2.9)	0.308
Diabetes mellitus	13 (2.2)	4 (1.3)	9 (3.3)	0.109
Chronic renal failure	12 (2.1)	3 (1.0)	9 (3.3)	0.099
Cardiovascular comorbidity	54 (9.3)	15 (5.0)	39 (14.2)	<0.001
Anticoagulation	9 (1.6)	0 (0)	9 (3.3)	0.001*
Antiplatelet agents	15 (2.6)	4 (1.3)	11 (4.0)	0.075
Cognitive troubles	12 (2.1)	8 (2.6)	4 (1.5)	0.479

SSA short-stay appendectomy, *LSA* long-stay appendectomy, *ASA* American Society of Anesthesiologists, *BMI* body mass index, *HIV* human immunodeficiency virus

*Fisher's exact test

Preoperative clinical status and inflammatory biomarkers

Table 2 illustrates preoperative clinical variables and biomarkers for all patients. There were no differences in preoperative pain patterns between the two groups, with most patients presenting localized weak to moderate pain. Nausea and vomiting were also comparable; however, LSA patients presented more frequently intestinal transit disorders. LSA patients also presented higher temperature upon diagnosis, with 3.9% versus 0% patients having >39 °C ($p = 0.006$), whereas they had also more often general guarding (8% vs. 0%, $p < 0.001$) than the SSA group. SSA patients had a significantly lower acute inflammatory reaction, in terms of leukocyte count (4.6% SSA vs. 10.0% LSA had >20 g/l, $p < 0.001$), CRP (7.6% SSA vs. 25.5% LSA had CRP >100 mg/l), as well as acute renal failure (3.0% SSA vs. 8.0% in LSA, $p = 0.007$).

Multivariate analysis—predictive score for SSA

As illustrated in Table 3, five variables remained independently associated with SSA: male gender (OR 1.61, 95% CI 1.12–2.31, $p = 0.010$), ASA class I–II (OR 9.52, 95% CI 1.65–180.69, $p = 0.037$), absence of generalized guarding (OR 3.55, 95% CI 1.30–11.41, $p = 0.019$), CRP <100 mg/dl (OR 3.09, 95% CI 1.81–5.42, $p < 0.001$) and leukocytes <20 g/l (OR 2.06, 95% CI 1.02–4.30, $p = 0.046$). The multivariable model presented a good fit to the data, AIC = 709.13, Hosmer–Lemeshow test p value =0.304.

These five variables were used for the construction of a predictive score, whose possible values ranged between 0 and 21 points (Table 4), higher scores being associated with a higher probability of SSA. ROC curve analysis identified as the cutoff with the optimal predictive value a score ≥17 (AUC = 0.654, 95% CI 0.609–0.699, $p < 0.0001$) (Fig. 2). For this threshold, high values of sensitivity (95.6%) and negative predictive value (82.2%) were observed.

Postoperative complications—readmissions

Surgical technique was exactly similar in the two groups, with no conversion from laparoscopy to open surgery. Median length of stay was 16 h in the SSA group and 42 h in the LSA group. Overall, 30-day morbidity was significantly lower for SSA patients (3.3% vs. 12.4%, $p < 0.001$). There were no differences in minor complications between SSA and LSA patients, with 0.7% grade I in both groups and 2.0% versus 4.0% grade II events ($p = 0.150$). However, the LSA group presented significantly more grade IIIa (2.2% vs. 0.3%, $p = 0.042$), grade IIIb (3.3% vs. 0.3%, $p = 0.015$) and grade IV complications (0 vs. 2.2%, $p = 0.011$). No postoperative deaths occurred in the series. Readmission rate was similar with 2.0% rate for SSA and 4.7% for LSA patients ($p = 0.100$).

Discussion

In this single-center high-volume series, 52% of all appendectomies were performed with a postoperative stay <24 h. The identified parameters: male gender, ASA class I–II, absence of generalized guarding, leukocyte count <20 g/l and CRP <100 mg/dl were significantly associated with SSA.

Laparoscopic appendectomy, though a frequent intervention with relatively few adverse effects, has not yet found its place among the standard outpatient procedures in Europe and in our institution [19]. Its emergency character, with diagnosis and surgery performed late in the afternoon or during the night, are one major drawback in our hospital; the absence of validated selection criteria for patients that could benefit from outpatient surgery is another issue. Identifying good outpatient candidates early during the

Table 2 Preoperative clinical variables and biomarkers for short-stay appendectomy (SSA) and long-stay appendectomy (LSA) groups

	All patients *N* = 578	SSA *N* = 303 (%)	LSA *N* = 275 (%)	*p*-value
Pain at home				0.849
No pain	10 (1.7)	5 (1.7)	5 (1.8)	
Localized	397 (68.7)	212 (70.0)	185 (67.3)	
Diffuse	169 (29.2)	86 (28.4)	83 (30.2)	
Pain, 10-point VAS scale				0.368
<5	145 (42.3)	134 (44.9)	109 (39.6)	
6–8	246 (42.6)	128 (42.2)	118 (42.9)	
9–10	74 (12.8)	33 (10.9)	41 (14.9)	
Nausea	299 (51.7)	163 (53.8)	136 (49.5)	0.285
Vomiting	210 (36.3)	110 (36.3)	100 (36.4)	0.796
Transit disorders	81 (14.0)	33 (10.9)	48 (17.5)	0.016
Temperature				0.006*
<37.5 °C	460 (79.6)	252 (83.2)	208 (75.6)	
37.6–39 °C	102 (17.6)	47 (15.5)	55 (20.0)	
>39 °C	8 (1.4)	0 (0)	8 (2.9)	
Clinical status				0.001
No guarding	158 (27.3)	85 (28.1)	73 (26.5)	
Localized guarding	386 (66.8)	210 (69.3)	176 (64.0)	
General guarding	27 (4.7)	5 (1.7)	22 (8.0)	
CRP				<0.0001
<50 mg/l	363 (62.8)	219 (72.3)	144 (52.4)	
50–100 mg/l	111 (19.2)	57 (18.8)	54 (19.6)	
>100 mg/l	93 (16.1)	23 (7.6)	70 (25.5)	
Leukocyte count				0.037
<10 g/l	137 (23.7)	80 (26.4)	57 (20.7)	
10–20 g/l	386 (66.8)	205 (67.7)	181 (65.8)	
>20 g/l	42 (7.3)	14 (4.6)	28 (10.2)	
Acute renal failure	31 (5.4)	9 (3.0)	22 (8.0)	0.007

SSA short-stay appendectomy, *LSA* long-stay appendectomy, *VAS* visual analog scale, *CRP* C-reactive protein

*Fisher's exact test

Table 3 Simple and multiple logistic regression analysis of preoperative factors associated with short-stay appendectomy (SSA)

	Unadjusted OR	95% CI	*p* value	Adjusted OR	95% CI	*p* value
Gender						
Male	1.52	1.09–2.12	0.012	1.61	1.12–2.31	0.010
Female	1					
ASA class						
I–II	19.89	4.05–359.77	0.004	9.52	1.65–180.69	0.037
III	1					
General guarding						
No	5.19	2.09–15.68	0.001	3.55	1.30–11.41	0.019
Yes	1					
CRP						
≤100 mg/l	4.16	2.55–7.01	<0.001	3.09	1.81–5.42	<0.001
>100 mg/l	1					
Leukocyte count						
≤20 g/l	2.39	1.25–4.78	0.009	2.06	1.02–4.30	0.046
>20 g/l	1					

OR odds ratio, *95% CI* 95% confidence intervals, *ASA* American Society of Anesthesiologists, *CRP* C-reactive protein

diagnostic process might avoid admission and unnecessary bed occupancy in the surgical ward. Performing interventions during the day in a dedicated structure and even allowing discharge directly from post-anesthesia care unit could be more suitable for these patients, as proposed by Frazee et al. [15].

In the present study, we confirmed the predictive value of preoperative leukocyte count and CRP for outpatient surgery, also suggested by previous authors, though with much lower thresholds [4, 5]. General guarding, associated with a severe intra-abdominal inflammation, was used in this series to indicate clinical diagnosis of a complicated appendicitis. Indeed, all of the above elements, although much less specific than radiological imaging, can already indicate the presence of severe inflammation, contraindicating outpatient management. Other clinical factors such as BMI have been associated with SSA in two recent French studies [1, 5], but this was not confirmed in this series. Previously, patients with comorbidities or those >65 years were automatically excluded from outpatient management [1, 4, 5] which was not the case in the present study. To identify more precisely the health conditions

Table 4 Preoperative clinical score for short-stay appendectomy

Variables	Adjusted OR in multivariate analysis	Points
ASA class III	9.52	10
General guarding	3.55	4
Preoperative CRP >100 mg/dl	3.09	3
Male gender	1.61	2
Preoperative leukocytes >20 g/l	2.06	2
Total points (range)		(0–21)

OR odds ratio, *ASA* American Society of Anesthesiologists, *CRP* C-reactive protein

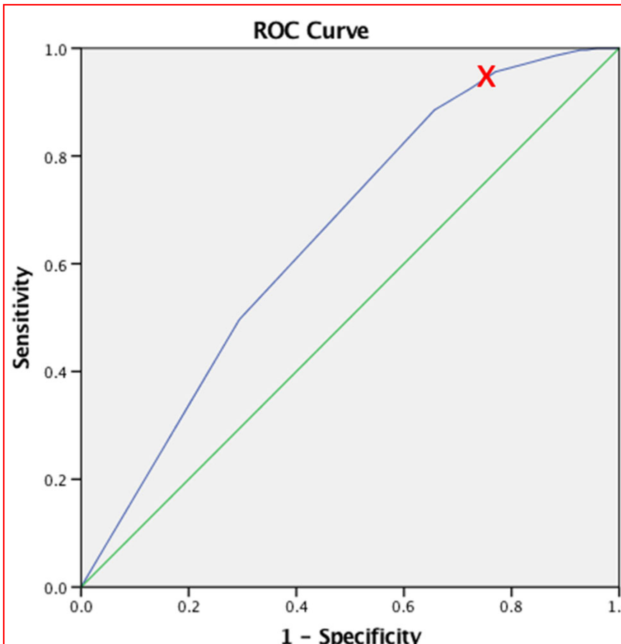


Fig. 2 ROC curve analysis to define cutoff for short-stay appendectomy (SSA). The optimal cutoff value to predict SSA was defined a score ≥17 (AUC =0.654, 95% CI 0.609–0.699, $p < 0.0001$). For this threshold, sensitivity and specificity are, respectively, 95.6% and 23.0%, positive predictive value 58.3% and negative predictive value 82.2%. *ROC* receiver operator characteristics, *SSA* short-stay appendectomy, *AUC* area under the curve

associated with prolonged hospital stay, several subtypes of baseline comorbidity were analyzed; only cardiovascular disease and the—often associated—anticoagulant medication were specifically associated with LSA. Interestingly, no study has previously suggested ASA class as a predictive factor, although it is a validated indicator of current health status and severity of the ongoing disease; in our study, however, ASA class I–II was the strongest predictor for SSA (OR = 9.5, $p < 0.001$). Interestingly, male gender was independently associated with SSA. One might speculate that male patients' family caregivers, often female, might be more at ease with having patients home even early after an operation, as personal care of an ill patient, but also household tasks are more frequently assured by women caregivers in our experience.

Previous authors used as selection criteria an uncomplicated appendicitis diagnosed through a mandatory preoperative CT scan, as well as intraoperatively [4, 5, 15]. Although these elements are undoubtedly helpful, they cannot be used preoperatively to preselect patients and thus could be of little help during the decision-making process as mentioned above. Moreover, CT scan is not routinely performed in all cases of suspected appendicitis, especially in Europe, where ultrasound is a widespread diagnostic modality. In the present series, 23% of patients had no preoperative imaging; although abdominal CT was performed in only 45.8% of LSA and 33% of SSA patients, very few cases of misdiagnosis were discovered intraoperatively.

Complicated appendicitis has also been equivocally treated in existing literature so far. Alvarez et al. [20] reported that complicated appendicitis in recent years was treated in an outpatient manner in up to 57% of patients, with minimal risk of conversion. In our center, conversion to open surgery was practically never performed, even for complicated appendicitis; instead, a second look laparoscopy and abdominal washing were performed at 24–48 h if needed. However, in the present series 8.3% of complicated appendicitis patients were successfully treated as SSA, whereas in all previously mentioned studies they were systematically excluded [1, 4, 5].

Except careful patient selection, successful SSA also depends on the quality of instructions and contact information given before discharge [21, 22]. Recent data confirmed a low readmission rate after outpatient appendectomy (0–3%) once a standardized pathway were applied [2, 5]. In our department, clear information is given to patients upon discharge concerning potential adverse effects, accompanied by a discharge sheet with contact details of the on-call resident, which is often used, reassuring patients and families.

From a methodological point of view, taking into account the individual weight (OR) of each covariate to create the score reinforces the robustness of the present predictive score, which was not performed by other authors [5]. The threshold of 17 points in the present study has a very high sensitivity (95.6%) and negative predictive value (82.2%), allowing to correctly identify poor outpatient candidates (negative score <17 indicates patients needing in-hospital management). Thus, despite the low overall accuracy of the test (AUC =0.654), it can successfully predict of poor candidates for outpatient management, which is of utmost importance in order to avoid wrongly discharging patients that would need in-hospital management.

The present study has some limitations to be discussed. The first one is its retrospective character, with the entailing missing data. Broad selection criteria, including complicated appendicitis and pregnant patients, might add heterogeneity in our study population. Although no safe conclusions can be drawn for these subgroups in the present study, our results might provide further insight to a more efficient management even for these high-risk patients. Furthermore, the 24 h threshold set in the present study is longer than the internationally accepted 12-h definition; this is largely due to the internal organization of our hospital as previously explained, whereby very few patients can 'escape' nighttime surgery and admission in the surgical ward, because of logistic reasons. This was the primary goal of this study, to define selection criteria of good outpatient candidates, in order to develop a true outpatient management pathway, with a dedicated operating theater and discharge structure, without compromising patient safety.

In conclusion, the present study provides some easy-to-use clinical criteria with high predictive value for outpatient appendectomy. These criteria may be used in all types of health care structure, irrespective of preoperative imaging policy.

Authors' contributions OG, AV, SM and ND conducted conception of the study, interpreted the results and drafted the manuscript. AV and FB were involved in data collection, and SM and MVPM performed statistical analysis. ND performed critical editing of the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Informed consent Informed general consent was obtained from all participants included in the study.

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