Original article

Negative appendicectomy and perforation rates after laparoscopic appendicectomy

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Background: **Despite widespread use of imaging technologies including ultrasonography and computed tomography, rates of negative appendicectomy and perforated appendicitis remain high. This trend analysis examined whether rates of negative appendicectomy and perforated appendicitis have decreased over time, and sought to evaluate clinical predictors associated with negative appendicectomy and perforated appendicitis.**

Methods: **This analysis was based on the prospective database of the Swiss Association of Laparoscopic and Thoracoscopic Surgery (SALTS). All patients aged 12 years and over undergoing emergency laparoscopic appendicectomy between 1995 and 2006 were included. Unadjusted and risk-adjusted logistic regression analyses were performed.**

Results: **A total of 7964 patients underwent laparoscopic appendicectomy, of whom 7452 (93·6 per cent) had acute appendicitis and 512 (6·4 per cent) had a macroscopically normal appendix. Perforation occurred in 1230 (16·5 per cent) of those with appendicitis. In multivariable analysis, younger age (12–18 years), female sex, absence of local or generalized peritonitis and an early point during the study period were significant predictors of negative appendicectomy. For perforated appendicitis, significant predictors included age over 36 years, presence of localized or generalized peritonitis, and high American Society of Anesthesiologists grade. The rate of negative appendicectomy decreased from 12·7 per cent in 1995 to 2·8 per cent in 2006, there being a significant reduction in both unadjusted and risk-adjusted analyses ($P < 0{\cdot}001$ for trend). In adjusted analyses, the rate of perforated appendicitis did not increase significantly over time.**

Conclusion: **The rate of negative appendicectomy decreased over time, without an accompanying increase in perforated appendicitis. The risk of having a negative appendicectomy was highest in girls aged 12–18 years without local or generalized peritonitis during the early study period, whereas perforation was associated with age over 36 years, presence of localized or generalized peritonitis, and greater co-morbidity.**

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Introduction

Appendicectomy for acute appendicitis is one of the most commonly performed surgical procedures and by some estimates accounts for more than a quarter of a million emergency surgical procedures each year in the USA alone[1]. A substantial proportion of these procedures are performed on appendices that show no sign of infection upon macroscopic examination, a circumstance known as negative appendicectomy. Although appendicectomy is itself considered a relatively routine surgical procedure, rates of negative appendicectomy have been high historically, ranging from 10 to 15 per cent, and even greater in some high-risk populations[2]. Negative appendicectomy is associated with an appreciable degree of morbidity and mortality, including a significant increase in length of hospital stay, complications due to postoperative infection and death[1]. It is also a significant contributor to healthcare costs; Flum and Koepsell[1] estimated that negative appendicectomy accounted for nearly US $750 million in healthcare costs in a single year in the USA alone.

According to reports in the literature, rates of perforated appendicitis range between 12·0 and 35·5 per cent[3–7], with an increased incidence in older patients[7–10]. Perforated appendicitis is related to a twofold increase in length of hospital stay[3] and a significantly higher rate of in-hospital mortality compared with non-perforated appendicitis[8,11].

Although ultrasonography and computed tomography (CT) are used in the diagnosis of acute appendicitis, it remains unclear whether their application has actually resulted in a reduction in rates of negative appendicectomy and perforated appendicitis over time. The published evidence has been equivocal, with some studies showing no significant reduction in negative appendicectomy[2,12–14] and perforated appendicitis[15–19], whereas others reported a correlation between the use of ultrasonography and/or CT and reduced rates of negative appendicectomy[19–22] or perforated appendicitis[23].

More recent studies have suggested that hospital- or practice-level variations in the quality of ultrasonography or CT (or even the uniform use of such imaging techniques) may have important implications for negative appendicectomy rates[21], and magnetic resonance imaging has emerged as a potentially useful imaging tool in some patients with symptoms of acute appendicitis[24]. Nevertheless, the overall problem of negative appendicectomy and perforated appendicitis has remained refractory, and better characterization of their prevalence and clinical predictors is needed.

This study was a trend analysis of patients undergoing laparoscopic procedures in community hospitals, academic settings and private practices in Switzerland between 1995 and 2006. The aim was to assess whether rates of negative appendicectomy decreased over time and rates of perforated appendicitis increased. In addition, predictors associated with negative appendicectomy and perforated appendicitis were characterized.

Methods

A trend analysis was conducted on patient data contained in the Swiss Association of Laparoscopic and Thoracoscopic Surgery (SALTS) database. The SALTS database constitutes a complete prospective collection of data from consecutive patients undergoing laparoscopic procedures in community hospitals, academic settings and private practices in Switzerland. Overall, data from patients at 93 hospitals and private practices were available for this investigation.

All patients undergoing an emergency laparoscopic appendicectomy or a laparoscopic appendicectomy that was converted to an open procedure between 1995 and 2006 were included in this study, with the exception of patients who either had an elective appendicectomy and/or were younger than 12 years of age at the time of operation.

All data were collected prospectively and entered into a centralized database (Qualicare™; Qualidoc, Liebefeld-Berne, Switzerland) by a data manager, who was independent of the authors of this study. Any missing data were queried by the data manager who followed up with letters and telephone calls to the site until the missing information had been obtained. The patient information contained in the SALTS database was anonymized; therefore, no ethics board approval was required for this analysis.

The main outcomes of this study were the rates of negative appendicectomy and perforated appendicitis. Negative appendicectomy was defined as a macroscopically normal appendix in a patient who underwent appendicectomy, or diagnostic laparoscopy without removal of a macroscopically normal appendix, based on clinical diagnosis and/or imaging suspicious for acute appendicitis. Because data regarding histopathological evaluation were not collected in the SALTS database, the proportion of patients whose clinical or imaging diagnosis was confirmed by histopathology was unknown.

Statistical analysis

A statistician with extensive expertise in population-based outcomes research performed all statistical computations. Differences in continuous and categorical data between groups were analysed by means of t test and χ^2 test respectively. Rates and mean/median values of outcomes were tested for changes over time using χ^2 test for trend and generalized linear models for continuous outcomes. Trend analyses were first performed with adjustment for age, sex, and co-morbidity assessed by means of the American Society of Anesthesiologists (ASA) grade. For the fully adjusted analyses, rates were modelled using a Poisson regression model that included age, ASA grade, sex, presence of localized peritonitis, presence of generalized peritonitis and year of diagnosis; the latter was included to ascertain whether significant differences persisted over time after adjusting for variables in the model. Characteristics of patients who had a negative appendicectomy or perforated appendicitis were compared with those of people who did not have a negative appendicectomy or perforated appendicitis respectively.

Univariable (unadjusted) and multivariable (adjusted) odds ratios and 95 per cent confidence intervals were estimated using logistic regression. Overall model fit was assessed by estimating the overall likelihood ratio χ^2, the Hosmer–Lemeshow goodness-of-fit test, and the C-statistic to measure the discrimination of the model.

A significance level of $\alpha = 0{\cdot}05$ was used for all tests. All *P* values were two-sided. Statistical calculations were done using SAS® statistical software version 9.1 (SAS Institute, Cary, North Carolina, USA).

Results

From 1995 to 2006, data for 7964 patients undergoing laparoscopic appendicectomy were recorded in the SALTS database. The mean age at the time of the procedure was 34·6 (range 12–100) years and 57·6 per cent of the patients were female. Median ASA grade was I (range I–IV).

Table 1 Characteristics of patients with acute appendicitis and patients undergoing negative appendicectomy

	Acute appendicitis (*n* = 7452)	Negative appendicectomy (*n* = 512)	*P*
Mean(s.d.) age (years)	34·9(16·6)	30·3(15·1)	< 0·001†
ASA grade*			0·411
I	4553 (61·1)	327 (63·9)	
II	2542 (34·1)	163 (31·8)	
III–IV	355 (4·8)	21 (4·1)	
Localized peritonitis	3323 (44·6)	52 (10·2)	< 0·001
Generalized peritonitis	352 (4·7)	14 (2·7)	< 0·038
Female sex	4197 (56·3)	394 (77·0)	< 0·001

Values in parentheses are percentages unless indicated otherwise. ASA, American Society of Anesthesiologists. χ^2 test, except †*t* test. *Data on ASA status is missing in three patients.

Table 2 Characteristics of patients with and without perforation and acute appendicitis

	Acute perforated (*n* = 1230)	Non-perforated (*n* = 6734)	*P*
Mean(s.d.) age (years)	43·9(19·0)	32·9(15·5)	< 0·001†
ASA grade*			< 0·001
I	609 (49·5)	4271 (63·4)	
II	506 (41·1)	2199 (32·7)	
III–IV	115 (9·3)	261 (3·9)	
Localized peritonitis	711 (57·8)	2664 (39·6)	< 0·001
Generalized peritonitis	303 (24·6)	63 (0·9)	< 0·001
Female sex	680 (55·3)	3911 (58·1)	0·068

Values in parentheses are percentages unless indicated otherwise. ASA, American Society of Anesthesiologists. χ^2 test, except †*t* test. *Data on ASA status is missing in three patients.

Some 7452 (93·6 per cent) of 7964 patients were found to have acute appendicitis. Of 512 patients (6·4 per cent) with no inflammation of the appendix, 440 had an appendicectomy despite having a macroscopically normal appendix, whereas 72 underwent diagnostic laparoscopy alone; all these patients were classified as having a negative appendicectomy. Patient characteristics are listed in *Table 1*. Of all patients, 1230 (15·4 per cent) were found to have perforated appendicitis. Characteristics of patients with and without perforation are listed in *Table 2*.

The rate of negative appendicectomy decreased significantly over time, from 12·7 per cent in 1995 to 2·8 per cent in 2006 ($P < 0{\cdot}001$) (*Fig. 1*). The reduction in the rate of negative appendicectomy was particularly notable in female patients (from 16·5 per cent in 1995 to 3·9

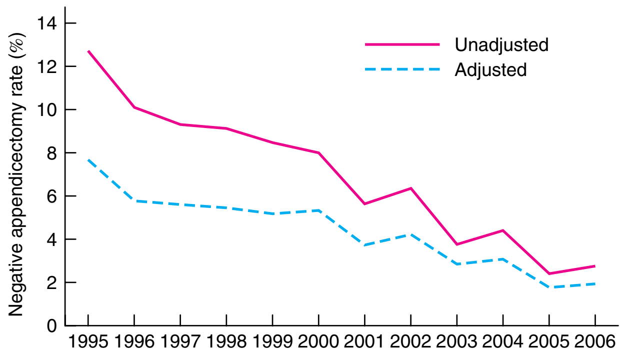

Fig. 1 Rates of negative appendicectomy in the Swiss Association of Laparoscopic and Thoracoscopic Surgery database, 1995–2006. Unadjusted and adjusted $P < 0{\cdot}001$ (χ^2 test for trend)

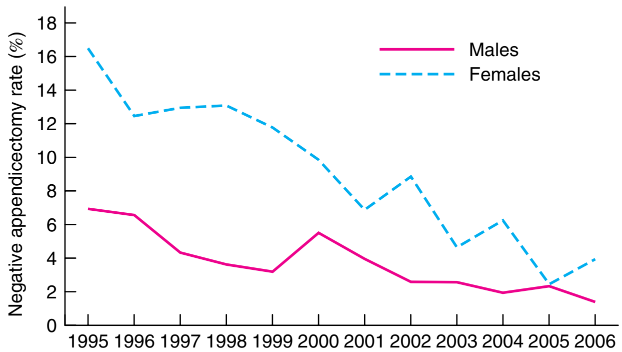

Fig. 2 Negative appendicectomy rates by sex in the Swiss Association of Laparoscopic and Thoracoscopic Surgery database, 1995–2006. Unadjusted and adjusted $P < 0{\cdot}001$ for both sexes (χ^2 test for trend)

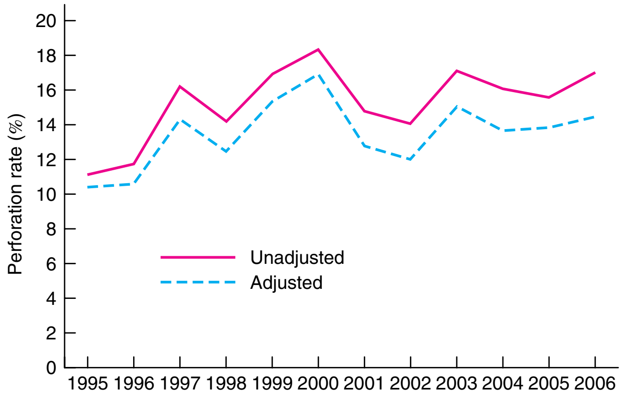

Fig. 3 Rates of perforated appendicitis in the Swiss Association of Laparoscopic and Thoracoscopic Surgery database, 1995–2006. Unadjusted $P = 0{\cdot}015$, adjusted $P = 0{\cdot}074$ (χ^2 test for trend)

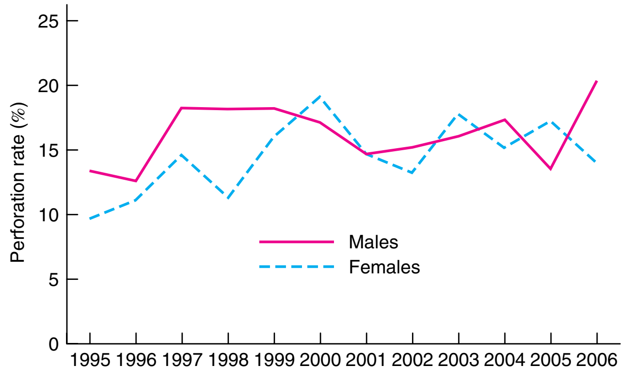

Fig. 4 Rates of perforated appendicitis by sex in the Swiss Association of Laparoscopic and Thoracoscopic Surgery database, 1995–2006. Unadjusted $P = 0{\cdot}401$ for men, $P = 0{\cdot}014$ for women (χ^2 test for trend)

per cent in 2006; $P < 0{\cdot}001$) (*Fig. 2*). The rate of perforated appendicitis increased from 11·2 per cent in 1995 to 17·0 per cent in 2006 (unadjusted $P = 0{\cdot}015$; adjusted $P = 0{\cdot}074$) (*Fig. 3*). Although the perforation rate for male patients remained unchanged over time ($P = 0{\cdot}401$ for trend), there was a significant increase among female patients ($P = 0{\cdot}014$ for trend) in unadjusted analyses (*Fig. 4*).

In adjusted analyses, younger age (12–18 years), female sex, earlier time point in the observation period, and absence of localized or generalized peritonitis were all significant predictors of a negative appendicectomy (*Table 3*). The multivariable (adjusted) models demonstrated good model fit and high discrimination (likelihood ratio $\chi^2 = 462{\cdot}65$: $P < 0{\cdot}001$; C-statistic 0·77). Age over 36 years, presence of localized or generalized peritonitis, and higher ASA grade were significant predictors of perforated appendicitis in adjusted analyses; year of operation, however, was not a significant predictor for perforated appendicitis ($P = 0{\cdot}277$) (*Table 4*). The multivariable models demonstrated good model fit and high discrimination (likelihood ratio $\chi^2 = 1598{\cdot}35$: $P < 0{\cdot}001$; C-statistic 0·81).

Table 3 Unadjusted predictors and multivariable logistic regression model predicting negative appendicectomy (model with significant terms only)

	Unadjusted predictors*		Multivariable logistic regression		
	Odds ratio	*P*	Odds ratio	*P*	*P* (level specific)
Age (years)		< 0·001		< 0·001	
12–18	1·00		1·00		
19–25	1·05 (0·82,1·35)		0·99 (0·77, 1·29)		0·952
26–35	0·73 (0·56, 0·95)		0·72 (0·54, 0·95)		0·020
36–48	0·55 (0·42, 0·74)		0·72 (0·53, 0·97)		0·029
≥ 49	0·47 (0·35, 0·64)		0·68 (0·50, 0·94)		0·018
ASA grade		0·412			
I	1·00				
II	0·89 (0·74, 1·08)				
III–IV	0·82 (0·52, 1·30)				
Localized peritonitis	0·14 (0·11, 0·19)	< 0·001	0·15 (0·11, 0·21)	< 0·001	
Generalized peritonitis	0·57 (0·33, 0·98)	0·040	0·39 (0·22, 0·67)	0·012	
Female sex	2·59 (2·10, 3·20)	< 0·001	2·21 (1·78, 2·74)	< 0·001	
Year	0·87 (0·84 to 0·89)	< 0·001	0·88 (0·86 to 0·91)	< 0·001	

Values in parentheses are 95 per cent confidence intervals. *Identified by univariable logistic regression. ASA, American Society of Anesthesiologists. Multivariable logistic regression model fit statistics: likelihood ratio $\chi^2 = 462{\cdot}65$, $P < 0{\cdot}001$; Hosmer–Lemeshow goodness-of-fit test: $\chi^2 = 10{\cdot}16$, $P = 0{\cdot}254$, C-statistic 0·77.

Table 4 Unadjusted predictors* and multivariable logistic regression model predicting perforated appendicitis (model with significant terms only)

	Unadjusted predictors		Multivariable logistic regression model		
	Odds ratio	*P*	Odds ratio	*P*	*P* (level specific)
Age (years)		< 0·001		< 0·001	
12–18	1·00		1·00		
19–25	0·90 (0·71, 1·16)		0·92 (0·70, 1·21)		0·548
26–35	1·11 (0·88, 1·40)		1·16 (0·90, 1·51)		0·255
36–48	2·15 (1·74, 2·66)		1·91 (1·51, 2·43)		< 0·001
≥ 49	4·52 (3·70, 5·52)		3·34 (2·64, 4·21)		< 0·001
ASA grade		< 0·001		0·001	
I	1·00		1·00		
II	1·61 (1·42, 1·84)		1·26 (1·09, 1·47)		0·003
III–IV	3·09 (2·44, 3·91)		1·54 (1·15, 2·05)		0·003
Localized peritonitis	2·09 (1·85, 2·37)	< 0·001	4·45 (3·78, 5·23)	< 0·001	
Generalized peritonitis	34·60 (26·15, 45·77)	< 0·001	78·16 (57·30, 106·63)	< 0·001	
Female sex	0·89 (0·79, 1·01)	0·070			
Year	1·03 (1·01, 1·04)	0·008	1·01 (0·99, 1·03)	0·277	

Values in parentheses are 95 per cent confidence intervals. *Identified by univariable logistic regression. ASA, American Society of Anesthesiologists. Multivariable logistic regression model fit statistics: likelihood ratio $\chi^2 = 1598{\cdot}35$, $P < 0{\cdot}001$; Hosmer–Lemeshow goodness-of-fit test: $\chi^2 = 8{\cdot}54$, $P = 0{\cdot}383$; C-statistic 0·81.

Discussion

This population-based analysis of 7964 patients undergoing laparoscopic appendicectomy for suspected acute appendicitis provides compelling evidence that the rate of negative appendicectomy among patients at Swiss hospitals and surgical practices has decreased significantly over time, particularly among female patients, while the overall rate of perforated appendicitis has remained constant.

In their landmark study that analysed data from the Washington State Database and identified more than 60 000 patients who underwent appendicectomy, Flum *et al.*[2] reported an overall negative appendicectomy rate of 15·5 per cent. The present investigation complements this important study in a number of ways. First, the time period is different. Flum and colleagues investigated data from patients undergoing appendicectomy from 1987 to 1998, whereas the study reported here included patients from 1995 to 2006. Second, the majority of patients examined in the North American study had an open appendicectomy, but the present study contains data drawn exclusively from laparoscopic appendicectomy. Finally, Flum and colleagues did not find a significant decrease in the frequency of negative appendicectomy in Washington State over their study interval whereas the present study showed a considerable decrease in the rate of negative appendicectomy in Switzerland between 1995 and 2006.

Although it may be hypothesized that improved quality and more frequent use of imaging led to the reduction in negative appendicectomy in the present investigation, the overall rate of perforated appendicitis did not change significantly over time. Similarly, greater diagnostic accuracy was not associated with a decrease in the rate of perforated appendicitis in previous studies[4,15]. Interestingly, there was a slight increase in the rate of perforated appendicitis among female patients, although this was not significant after risk adjustment. Age, ASA grade, and presence of generalized or localized peritonitis (but neither year of operation nor sex) were identified as significant predictors of perforated appendicitis in risk-adjusted analyses. Age has also been associated with higher perforation rates in previous series[7–10].

A positive association between duration of symptoms of acute appendicitis and perforation rate is well established[7,9,25–27]. Patients who experience acute appendicitis frequently delay medical care, and such delay may contribute to perforation[7,10,26–28]. Thus, a lower threshold for diagnostic laparoscopy may not be helpful in relevantly reducing the rate of perforated appendicitis. Conversely, it is critical to educate patients to seek medical care immediately on experiencing pain in the right lower abdominal quadrant.

Given the established burden of risk to patients imposed by negative appendicectomy, as well as the appreciable costs associated with this relatively common clinical occurrence[1], any significant reduction in negative appendicectomy and perforated appendicitis is likely to be paralleled by corresponding reductions in morbidity and mortality, as well as a decrease in associated healthcare costs. The present findings suggest that attention should be focused on the reasons for reduced negative appendicectomy rates, and why such decreases are seen in some settings[19–22] but not others[2,12–15,29]. Many of the above-mentioned findings were derived from relatively small retrospective studies applied to outcomes data from individual hospitals or health systems. In contrast, rates of negative appendicectomy and perforated appendicitis in a large, nationwide sample have been determined in the present study. The reduction in rate of negative appendicectomy was particularly pronounced among female patients. Whether this is attributable to the increased use of ultrasonography in women with suspected acute appendicitis cannot be ascertained from the present data.

A major limitation of this study is the lack of detailed information regarding the use of preoperative imaging. It was therefore not possible to characterize patterns of use of either ultrasonography or CT in relation to the rate of negative appendicectomy or perforated appendicitis. Although it seems reasonable to assume that the reduction in rate of negative appendicectomy could be related to increased use of imaging, this remains speculative.

A further limitation is the definition of negative appendicectomy based on a macroscopically normal appendix and not histopathological findings. The proportion of patients whose clinical diagnosis was confirmed by histopathology is unknown. Macroscopic evaluations that are not confirmed by histopathology may be of limited predictive value in the setting of acute appendicitis[30,31]. Finally, the study was confined to Swiss patients alone; however, on the basis of similarly high standards of laparoscopic surgery in North America and other European countries, as well as the widespread availability of ultrasonography and CT, it is likely that the findings are applicable to other countries with comparable standards of care.

The strengths of the study include the large sample size, compared with other studies on this topic. Thus, the statistical power to detect clinically relevant differences is high. Second, the data span an interval of 12 years, longer than in most previous investigations. In addition, the data in the SALTS database were gathered prospectively with very few missing values. Finally, because this study is population-based, the authors believe it has good generalizability to other patients undergoing laparoscopic appendicectomy, despite being limited to hospitals in Switzerland.

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