Delaying surgery to perform CT scans for suspected appendicitis decreases the rate of negative appendectomies without increasing the rate of perforation nor postoperative complications

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Abstract

Purpose Negative appendectomies are costly and are embedded with unnecessary risks for the patients. A careful indication for surgery seems mandatory even more so, since conservative therapy emerges as a potential alternative to surgery. The aims of this population-based study were to analyze whether radiological examinations for suspected appendicitis decreased the rate of negative appendectomies without increasing the rate of perforation or worsening postoperative outcomes.

Method This study is a retrospective analysis of a prospective population-based database. The data collection included preoperative investigations and intraoperative and postoperative outcomes.

Results Based on 2559 patients, the rate of negative appendectomies decreased significantly with the use of CT scan as compared to clinical evaluation only (9.3 vs 5 %, $p=0.019$), whereas ultrasonography alone was not able to decrease this

rate (9.3 vs 6.2 %, $p=0.074$). Delaying surgery for radiological investigation did not increase the rate of perforation (18.1 vs 19.2 %; adjusted odds ratio (OR) 1.01; 0.8–1.3; $p=0.899$). Postoperative complications (surgical reintervention, postoperative wound infection, postoperative hematoma, postoperative intra-abdominal abscess, postoperative ileus) were all comparable.

Conclusion In this population-based study, CT scan was the only radiological modality that significantly reduced the rate of negative appendectomy. The delay induced by such additional imaging did not increase perforation nor complication rates. Abdominal CT scans for suspected appendicitis should therefore be more frequently used if clinical findings are inconclusive.

Keywords Appendicitis · Appendectomy · CT · Ultrasound · Perforated appendicitis · Negative appendectomy

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Introduction

Suspected appendicitis is among the commonest causes of emergency referral and emergency surgeries [1]. The dogma that an inflamed appendix, if left untreated, will lead to perforation is central to the idea that prompt surgery should be the standard of care. This strategy minimized the rate of perforation at the cost of negative exploration rates reaching 15 % or even greater in some high-risk population [2]. As negative appendectomies have a high financial cost and are embedded with unnecessary risks for the patients, a careful selection seems mandatory [3]. This is even more important since conservative therapy emerges as a potential alternative to surgery [4, 5].

The aim of this population-based study was to analyze whether radiological examinations for suspected appendicitis

decreased the rate of negative appendectomies without increasing the rate of perforation or worsening postoperative outcomes.

Methods

We undertook a retrospective analysis of a prospective held multicentric database from six different hospitals covering a population of 492,604 inhabitants. All patients older than 16 years operated for a suspected appendicitis were included from 12 February 2007 to 28 March 2011. All hospitals of the region with the exception of one private hospital only treating patients with a private insurance included patients. All patients were enrolled in a quality assessment project held by the “outcome association” (<http://www.hcri.ch/>). This nonprofit organization was founded by the State of Zurich in 2000 to monitor the health care quality in public hospitals of various surgical interventions. The outcome association did not make any recommendation on any aspect of the medical process. The indication for surgery was made by the attending surgeon based on personal history, clinical status, and laboratory findings. There was no standardized diagnostic algorithm at any of the six hospitals. Indication for radiological investigation was at the discretion of the surgeon. No recommendation concerning the radiological assessment was made by the vereine outcome organization. The surgery was performed either laparoscopically or open (McBurney incision).

The following variables were collected: age, gender, comorbidities (Charlson index), onset of symptoms, histological findings (no appendicitis, appendicitis with or without perforation, and tumor), preoperative radiological modalities (ultrasound, CT) when used, time between admission, surgical incision, and discharge [6]. The data collection included preoperative investigations, intraoperative and postoperative outcomes. Assessment was made through a standardized questionnaire sent to all patients. In case of no response, the patients were contacted twice per telephone. In the end, 1643 patients could be contacted for the 30-day follow-up. The questionnaire and the phone calls assessed information on analgesia at home, time to resume a professional activity, reoperations, and complications after discharge, all nonprimary information for the study. Mortality was recorded. Completeness of data was checked by the outcome association.

To analyze if the risk of perforation was influenced by an increased time to surgery, we defined two groups: surgery within 360 min or after 360 min after admission, reflecting the median waiting time before surgery in our study. A longer cutoff value of 12 h was also included as in previous studies [7].

Statistic analysis

Primary endpoint (histologically no appendicitis) between groups was compared using univariate and multivariate logistic regression model with “no appendicitis” as the dependent, and group allocation as the independent variables. We also applied univariate and multivariate logistic regression models for further binary outcomes (perforation, morbidity, and mortality). Based on this, the multivariate model was adjusted for possible confounders such as age, sex, duration of pain, Charlson index, and different hospitals. For all results, we reported point estimates, 95 % confidence intervals (CI) and *p* values ($p \leq 0.05$ considered significant). All statistical analyses were performed using STATA software (version 12, Stata Corp., College Station, TX).

Results

Patient demographics

Two thousand five hundred fifty-nine appendectomies were performed over a 4-year period. One thousand three hundred sixty-one (53.2 %) patients were male, and 1191 (46.5 %) were female (missing data for 7 patients; 0.3 %). The median age was 34 years (interquartile range (IQR) 24–49 years), and 44 (1.7 %) patients had a Charlson index ≥ 3 . Laparoscopy was performed in 1989 (77.7 %) patients with a conversion rate of 2 % ($n = 50$) whereas 520 patients (20.3 %) were operated with a McBurney incision. Two hospitals were responsible for 78 % of all open appendectomies. No open appendectomies were performed in the academic centers.

The histological examination of the surgical specimen confirmed the diagnosis of appendicitis in 2400 (93.8 %) cases. In our cohort, the rate of perforation reached 19 % ($n = 486$). A normal appendix was found in 114 (4.5 %) patients and an incidental tumor in 43 (1.7 %). For two (0.08 %) patients, histology was missing.

Preoperative imaging increased the time to surgery

One hundred ninety-three patients (7.5 %) were operated without preoperative radiological assessment among which 175 (91 %) had a histologically proven appendicitis. This percentage dropped to 83 % when considering female patients only. The rate of perforation was 11 % for both genders. In three patients (all female), an incidental tumor was found.

Preoperative CT scan, ultrasonography, or both were performed in 2210 patients (86.4 %) (Table 1), and there are missing data in 156 patients (6.1 %). The distribution of radiological assessments seemed to be hospital dependent and not patient dependent. There were hospitals where the majority of patients

Table 1 Preoperative imaging modalities (population of 492,604)

	Patients, <i>n</i> = 2559
None	193 (7.5 %)
Ultrasonography	1792 (81 %)
Computed tomography	649 (29 %)
Both	231 (10 %)
Missing information	156 (6.1 %)

were assessed with CT scan and other were US was the initial examination of choice (Table 5, Supplementary data).

A multivariate logistic regression analysis showed that the rate of negative appendectomies decreased significantly when CT scan was performed as compared to clinical evaluation only ($p=0.019$). Ultrasonography alone was not able to decrease the rate of negative appendectomies significantly ($p=0.074$) (Table 2).

We investigate the influence of radiological assessment on the time to surgery (door to incision time). The median time from admission to surgery in our cohort was 360 min (IQR 251–558 min). This time was increased to 366 min (IQR 255–565 min) after ultrasonography and to 420 min (IQR 285–626 min) after CT scan. It was 260 min (IQR 180–411 min) when the indication for surgery was based solely on clinical evaluation. A multivariate logistic regression analysis showed that any radiological examination would at least double the time until surgery (no radiology vs sonography: adjusted time difference (95 % CI, p value): 135 min, IQR 85–216 min, $p<0.001$). A CT scan increased this time by at least 1 h as compared to sonography (adjusted differences (95 % CI, p value): 60 min (IQR 31–74 min), $p=0.009$).

Does the duration of pain have an impact on perforated appendicitis?

To analyze if the duration of symptom is linked with an increased rate of perforation, patients having a perforated

appendix were divided in three groups according to the onset of pain: less than 12 h, between 12 and 24 h, and more than 24 h. A total of 486 perforations were recorded. For 449 cases, the information about onset of pain was recorded (missing data $n=37$, 8 %). A regression analysis adjusted for cofounders found a significant difference between each group (Table 3).

Does delay to surgery for radiological investigation increase the risk for perforation?

To investigate if a prolonged in-hospital waiting time could have influenced the rate of perforation, we calculated the risk of perforation as a function of time. We used the time spent from arrival to the hospital to the skin incision (door to incision time). We choose a cutoff value of 360 min which represented the median waiting time in our cohort: 241 patients (19.1 %) operated within the first 360 min and 245 (18.9 %) operated beyond 360 min presented a perforation of the appendix. A regression analysis adjusted for cofounders did not reach statistic significance (adjusted odds ratio (OR) 1.01, 95 % CI 0.9–1.2, $p=0.899$) (Table 4). For a longer cutoff value of 720 min, the histology found that 409 patients (19.1 %) operated within 720 min and 77 (18.5 %) patients operated after 720 min had a perforated appendix. Again, a regression analysis could not find any statistic difference between these two groups ($p=0.72$) (data not shown).

Does delay to surgery for radiological investigation increase postoperative morbidity?

Next, we analyzed if a prolonged waiting time could influence postoperative morbidity and mortality. Five different complications were looked at: surgical reintervention, postoperative wound infection, postoperative hematoma, postoperative intra-abdominal abscess, and postoperative ileus. We used again the cutoff value of 360 min to evaluate if a prolonged surgery could influence the postoperative complications (Table 4). The regression analysis performed for each

Table 2 Logistic regression analysis: can a computed tomography decrease significantly the rate of negative appendicitis compared to no exams or sonography alone?

	Radiological investigation	Radiological investigation	Unadjusted OR (95 % CI, p value)	Adjusted ^a (95 % CI, p value)
No appendicitis	US, <i>n</i> = 1560	CT, <i>n</i> = 418		
	97 (6.2 %)	21 (5 %)	0.8 (0.5–1.3, $p=0.361$)	0.6 (0.3–1.1, $p=0.120$)
No appendicitis	None, <i>n</i> = 193	CT only, <i>n</i> = 418		
	18 (9.3 %)	21 (5 %)	0.5 (0.3–0.9, $p=0.046$)	0.3 (0.1–0.8, $p=0.019$)
No appendicitis	None, <i>n</i> = 193	US only, <i>n</i> = 1560		
	18 (9.3 %)	97 (6.2 %)	0.6 (0.4–1.1, $p=0.102$)	0.6 (0.3–1.1, $p=0.074$)

OR odds ratio, CI confidence interval, US ultrasonography, CT computer tomography

^a Results were adjusted for cofounders such as age, sex, duration of pain, Charlson index, and different hospitals

Table 3 Logistic regression analysis: does the duration of pain have an impact on perforated appendicitis?

	<12 h, <i>n</i> = 487, group 1	12 to 24 h, <i>n</i> = 830, group 2	>24 h, <i>n</i> = 1041, group 3	Adjusted ^a OR (95 % CI, <i>p</i> value), group 2 vs 1	Adjusted ^a OR (95 % CI, <i>p</i> value), group 3 vs 1	Adjusted ^a OR (95 % CI, <i>p</i> value), group 3 vs 2
Perforation (%)	31 (6.4 %)	99 (11.9 %)	319 (30.6 %)	2.0 (1.3–3.0, <i>p</i> = 0.001)	5.4 (3.6–8.1, <i>p</i> < 0.001)	1.9 (1.3–2.8, <i>p</i> = 0.002)

All results are presented in median (interquartile range)

^a Results were adjusted for confounders such as age, sex, duration of pain, Charlson index, and different hospitals

complication between these two groups did not show any statistic difference. No death was recorded during the study.

Discussion

To our knowledge, this is one of the largest population-based study with histologically proven appendicitis showing that delaying surgery to optimize the preoperative diagnosis did not increase the rate of perforation nor the rate of postoperative complications, but decreased the rate of negative appendectomies.

The overall rate of histologically confirmed negative appendectomies in this cohort of 2559 patients was 6.2 % and increased to 17 % in females operated without radiological imaging. In the literature, the overall rate of negative appendectomies varies between 3 and 29 % with significant variations among studies and subgroups of patients [8]. Patients with suspected appendicitis are a real challenge for clinicians: the benign nature of appendicitis coupled with the fear of perforation, if left untreated, represents a dilemma—either to urge for the operation to minimize the risk of perforation at a cost of negative findings or to wait for preoperative diagnostic procedures with the increased risk of perforation. Decreasing the threshold for surgery is an acceptable option only if the risk/benefit ratio is favorable to the patients. However, negative appendectomy does not seem to be so harmless as previously thought not only due to the potential surgical complications but also due to the diagnostic failure. In a study of 119, 060 patients, Andersson et al. showed that negative

appendectomies were strongly associated with mortality (OR 5.11; confidence interval (CI) 2.09–12.48; *p* < 0.001 and OR 2.38; CI 1.24–4.57; *p* = 0.009, respectively) in contrast to perforated appendicitis (OR 1.60; CI 0.95–2.70; *p* = 0.078) after adjustment for age, sex, and comorbidity [9]. An update from the study of the same authors confirmed this increased mortality (30-day standardized mortality ratio 8.95, CI 6.68–12.61) [10]. In the literature, few studies analyzed the financial costs associated with negative appendectomies. Flums et al. estimated direct costs to reach US\$741.5 million per year in the USA [3]. A recent study showed that the use of preoperative imaging not only decreased the rate of negative appendectomies but also led to a reduction of the cost-per-patient by 594 euros, confirming older results published by Rao et al. showing that CT scan can prevent 13 % of unnecessary appendectomies inducing an overall cost savings from up to US\$44,731 [11, 12]. These controversial data should raise caution, and the risk/benefit ratio should be carefully evaluated before taking these patients to the operating room as a lack of preoperative diagnostic procedures can have deleterious consequences for them [13]. Moreover, a recent study suggested an association between appendectomy and colorectal cancer [14].

In our study, 86.4 % of patients were preoperatively assessed by either CT scan (26.5 %), ultrasonography (73.4 %), or both 9 %. These numbers are high and raise the question whether not all patients with suspected appendicitis should undergo radiological investigations [15]. Interestingly, the initial choice of the radiological assessment was hospital dependent in our study (Table 5, Supplementary data). The

Table 4 Logistic regression analysis: does the time until surgery have an impact on perforated appendicitis and/or postoperative?

	<360 min, <i>n</i> = 1263	≥360 min, <i>n</i> = 1296	Unadjusted OR (95 % CI, <i>p</i> value)	Adjusted ^a OR (95 % CI, <i>p</i> value)
Perforation (%)	241 (19.1 %)	245 (18.9 %)	0.99 (0.8–1.2, <i>p</i> = 0.909)	1.01 (0.8–1.3, <i>p</i> = 0.899)
Reoperation (%)	45 (3.6 %)	43 (3.3 %)	0.93 (0.6–1.4, <i>p</i> = 0.731)	0.85 (0.5–1.3, <i>p</i> = 0.464)
Wound infection (%)	8 (0.6 %)	15 (1.2 %)	1.8 (0.8–4.3, <i>p</i> = 0.167)	1.2 (0.5–2.9, <i>p</i> = 0.690)
Hematoma (%)	5 (0.4 %)	4 (0.3 %)	–	–
Intra-abdominal abscess (%)	20 (1.6 %)	15 (1.2 %)	0.7 (0.4–1.4, <i>p</i> = 0.354)	0.8 (0.4–1.6, <i>p</i> = 0.535)
Ileus (%)	8 (0.6 %)	5 (0.4 %)	–	–

– no statistical analysis due to less than ten events, *min* minutes, *OR* odds ratio, *CI* confidence interval

^a Results were adjusted for confounders such as age, sex, duration of pain, Charlson index, and different hospitals

UK National Surgical Research Collaborative reported in 2013 that 2236 out of 3326 (67.2 %) patients did not have a preoperative imaging. The rate of negative appendectomy was as high as 20.6 % [16]. In our study, a logistic regression analysis showed that the rate of negative appendectomies decreased significantly with the use of CT scan as compared to clinical evaluation only ($p=0.019$), whereas ultrasonography alone was not able to decrease this rate significantly ($p=0.074$). In western countries, the use of CT scans in the emergency room steadily increased during the last 10 years, paralleling the performance of the multislice CT [17]. The newest models can reach a sensitivity to detect a pathological appendix that oscillates between 98.3 and 100 % [18]. In one study, the percentage of patients undergoing a CT scan for suspected appendicitis increased from 18.5 % in 1998 to 94.2 % in 2007 [8]. Concomitantly, the rate of negative appendectomy showed a decrease from 42.9 to 7.1 %. In the Netherlands, the rate of negative appendectomies was dropped from 22.9 to 6.2 % when preoperative imaging was used [19]. This 6.2 % match with our result and confirm the benefit of preoperative imaging in a different population. However, sonography is still preferred in many countries even if it is less accurate [18, 20]. It has the advantage to be easily available and to avoid unnecessary irradiations particularly for women [8]. However, a recent randomized trial showed that low-dose CTs are noninferior to standard-dose CT scan in terms of negative appendectomies with a reduction of the irradiation to a fifth of the normal dose [21]. If these data are reproducible, low-dose CT scan will emerge as the imaging of choice to reduce negative appendectomies.

As every additional preoperative examination will induce a delay to surgery, it should not compromise the safety of patients by increasing the number of perforation. The median time from admission to surgery in this study was 360 min (251–558 min). This delay increased by only 6 min for ultrasound, but by 1 h if a CT scan was performed. These delays are much shorter than those reported by a recent study showing a mean time of 559 min between admission and disposition of CT and a mean time of 448 min when sonography was chosen [18]. In this study, patients without any imaging were operated within 260 min (180–418 min). We did not detect an increase of perforated appendicitis if the waiting time was greater than our median time of 6 h. To further evaluate if a longer delay before surgery could induce more perforations, we analyzed a longer cutoff value of 720 min. Our results show that 409 patients (19.1 %) operated within 720 min and 77 (18.5 %) patients operated after 720 min had a perforated appendix. Again, a regression analysis could not find any statistic difference between these two groups ($p=0.72$).

This suggests that delaying surgery to perform preoperative imaging refining the diagnosis does not seem to induce a burden of perforated appendicitis. These findings are in contradiction to others concluding that a delay in the care of

patients with suspected appendicitis increases the rate of perforation [7, 22]. The timing of symptoms seems to be an important factor linked to perforation. In our cohort, an onset of pain of more than 24 h is associated with a significant risk of perforation (Table 3). One explanation to reconcile this observation with our results showing that an in-hospital delay does not increase the rate of perforation lies probably within the pathophysiology of appendicitis: an inflamed appendix will not inexorably perforate if left untreated. It will either perforate from the beginning probably due risk factors such as appendicolith or tend to resolve spontaneously. The real challenge for the future will be to recognize both entities as distinct and to adapt our therapies accordingly [23].

We analyzed if a prolonged waiting time before surgery could influence the morbidity of the procedure. Surgical reintervention, postoperative wound infection, hematoma, intra-abdominal abscess, and ileus were not increased.

The treatment of acute appendicitis is evolving and is not anymore the black or white picture it used to be due to the lack of therapeutic options. Recent data supported that conservative therapy could be a reasonable option to treat uncomplicated appendicitis in selected cases [4, 5, 24]. For years, submariners were treated conservatively with antibiotics while at sea showing the feasibility of a conservative therapy [25]. A major criticism against conservative therapy is its high rate of recurrence. In a recent article, Salminen showed that 27 % of patients recurred within 1 year and needed surgery. However, the surgical complication rate was much lower (7 %) in this group than the group of patients operated during the first episode (20.5 %) [26]. Conservative therapy is at its premise, and certainly, more studies are needed to optimize it, such as the outcome of a second line of antibiotherapy to treat recurrences. The therapy of complicated appendicitis is also changing as percutaneous drainage is emerging as an alternative choice to treat appendiceal abscess [27, 28]. Thus, surgery should not be seen as the only acceptable therapy, except for perforated appendicitis with peritoneal signs that remain a surgical emergency. Therefore, the need for an accurate diagnosis is a prerequisite to choose the optimal therapy for our patients.

This study has several limitations. The fact that the rate of perforated appendicitis remains stable in our study favors the idea that a certain number of appendicitis can heal spontaneously [23]. Secondly, we do not know the exact time the CT or ultrasound were performed and therefore cannot exclude a delay by organizational hazards to plan emergent surgery. However, the time differences were similar in all six hospitals.

Finally, information related to radiological examination is missing for 156 patients (6.1 %) which could theoretically influence our results due to the limited CT cohort. As not all the missing data are due to missing CT scans, we can therefore only extrapolate that 45 CT scans were missed during follow-up as 29 % of our patients

were investigated by CT scan (Table 1). Considering that the rate of false-positive CT scan is about 4 % according to the literature, two patients would have been missed, which should not impact our conclusions [29]. Although data was collected in all public hospitals covering an area of nearly half a million inhabitants, it remains unclear how many patients from outside this region were included. This might limit the generalizability of the data.

Conclusion

In this population-based study, CT scan was the only radiological modality that significantly reduced the rate of negative appendectomy. The delay induced by such additional imaging was neither imbedded with an increased rate of perforation nor an increased rate of postoperative complications. Abdominal CT scans for suspected appendicitis should therefore be more frequently used.

Authors' contributions M.-O. Sauvain: Study conception and design, analysis and interpretation of data, drafting of manuscript
K. Slankamenac: Analysis and interpretation of data
M. K. Muller: Critical revision of manuscript, drafting of manuscript
S. Wildi: Critical revision of manuscript
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D. Hahnloser: Study conception and design, analysis and interpretation of data, drafting of manuscript

Compliance with ethical standard

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

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