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Original Research

Readmission and reoperation rates following negative diagnostic laparoscopy for clinically suspected appendicitis: The "normal" appendix should not be removed – A retrospective cohort study

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ABSTRACT

Background: In cases with clinically suspected appendicitis, there is controversy regarding the decision to remove a macroscopically normal appearing appendix during laparoscopy when no other intra-abdominal pathology is found. The aim of this study was to examine the rate of appendicitis, along with readmission and reoperation rates following diagnostic laparoscopy of clinically suspected appendicitis in patients where the appendix was not removed.

Methods: We performed a retrospective cohort analysis of patients who underwent a diagnostic laparoscopy due to clinical suspicion of appendicitis where no other pathology was found and the appendix was not removed. The study period was from 2008 to 2013 and involved patients from two university hospitals in the Copenhagen area.

Results: Of the 271 patients included (81.6% women, median age 27), 56 (20.7%) were readmitted with right iliac fossa pain after a median time of 10 months (range 1–84). Twenty-two patients (8.1%) underwent a new laparoscopic procedure. Appendix was removed in 18 patients, of which only one showed histological signs of inflammation. The median follow-up time was 5.6 years (range 1–109 months).

Conclusion: There was a low rate of appendicitis after a previous negative diagnostic laparoscopy. Therefore, based on results from the current study, we do not consider that it is necessary to remove a macroscopic normal appendix during laparoscopy for clinically suspected appendicitis. The high readmission rate warrants the need for further investigation or follow-up.

1. Introduction

The surgical management of appendicitis has shifted towards laparoscopy over the last 10–20 years [1]. In contrast to an open approach, where the classical scar in the right lower quadrant is synonymous with an appendectomy, a laparoscopic approach allows the surgeon to leave a macroscopic normal appendix in situ. However, even with diagnostic laparoscopy (DL), an uninflamed appendix, evaluated by the pathologist, is removed in 10–18% of the cases with over-representation of younger women [2–4]. There is a lack of consensus regarding the management of a macroscopic normal appendix during laparoscopy, where some studies are showing false negative rates of up to 29% (macroscopic normal appendix, but pathological signs of inflammation), while the risk of later developing appendicitis after a negative DL is 1% in studies not removing the macroscopic normal appendix [5–7]. Macroscopic evaluation of the appendix may be difficult [8–10], leaving the surgeon with an intra-operative dilemma especially when no other pathology is found [5]. However, performing an appendectomy regardless of inflammation is not without risk, and complications may include wound infections, hemorrhage, and ileus [11,12].

Current consensus in our country is not to remove a macroscopic

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normal appendix in situ when a laparoscopic approach is taken. However, the readmission and reoperation rate following negative DL is unknown.

The primary aim of this study was to examine the rate of readmission and reoperation rates following negative diagnostic laparoscopy of clinically suspected appendicitis in patients where the appendix was left in situ. The secondary aim was to analyze the rate of appendicitis following a negative diagnostic laparoscopy.

2. Material and methods

The study was a retrospective cohort study based on consecutive patients undergoing DL for clinically suspected appendicitis at two university hospitals for a four-year period between January 2008 and December 2011. Radiological imaging and clinical scoring systems are not routinely used in Denmark. There is no standard protocol for criteria to proceed to the operating room at the two departments in this study. The referral for diagnostic laparoscopy for suspected appendicitis is generally based on clinical evaluation of the patient, with localized tenderness and muscular rigidity in the right iliac fossa with or without rebound tenderness and pain in the right iliac fossa when palpating left iliac fossa (Rovsig's sign), combined with blood test analysis. All appendices with any visual signs of macroscopic inflammation were removed after assessment by the operating surgeon. An appendix was considered inflamed if there was signs of thickened mesentery or appendix, adhesion, injected serosal vessels on the appendix, fibrin, perforation or necrosis of the appendix. After negative laparoscopy patients are discharged without any additional treatment or antibiotics.

Inclusion criteria were patients with DL due to clinical suspicion of appendicitis, where no pathology was found during surgery and the appendix was left in situ. Exclusion criteria were findings of other pathology and DL performed on patients with other suspicion than appendicitis. All patients were followed up through chart review from the time of surgery until January 2017 for readmission, reoperations and histological evaluation in case of removal of appendix at subsequent surgery. Furthermore, patients' demographics, details on primary and secondary surgery, date of first readmission, and reoperation were registered.

Data are presented as mean with standard deviation (SD) or median with range. Data were analyzed using the statistical package IBM® SPSS® Statistics version 25.0. This study has been reported in line with the STROCSS criteria [13] and the protocol registered in the German Clinical Trials Register (DRKS00015833). No ethics approval was required as per national standard.

3. Results

A total of 272 patients were included in the study (Fig. 1). The majority of the patients (81.6%) were women with a median age of 27 years (Table 1). The intraoperative complication rate for the initial DL was 1.1% (3/272; two bowel perforations and one uterine laceration). One of the patients with intraoperative bowel perforation, an 89-year-old woman, died on the 15th post-operative day. Regarding post-operative complications, one patient had a surgical wound infection at the site of umbilical port, which was treated with surgical debridement and secondary healing.

Of the 271 patients with negative DL remaining for analysis, 56 patients (20.7%) were readmitted with a renewed suspicion of appendicitis (Table 2). The median time to readmission was 10 months. Women represented the majority of the re-admitted patients (51/56). Twenty-two of the readmitted patients underwent a new DL for suspected appendicitis of which appendix was removed in 18 patients. In 12/18 patients, the appendix was removed due to a preoperative agreement between the patient and the operating surgeon regardless of operative findings. Inflammation was histologically confirmed in only one of the 18 removed appendices. There were no intraoperative

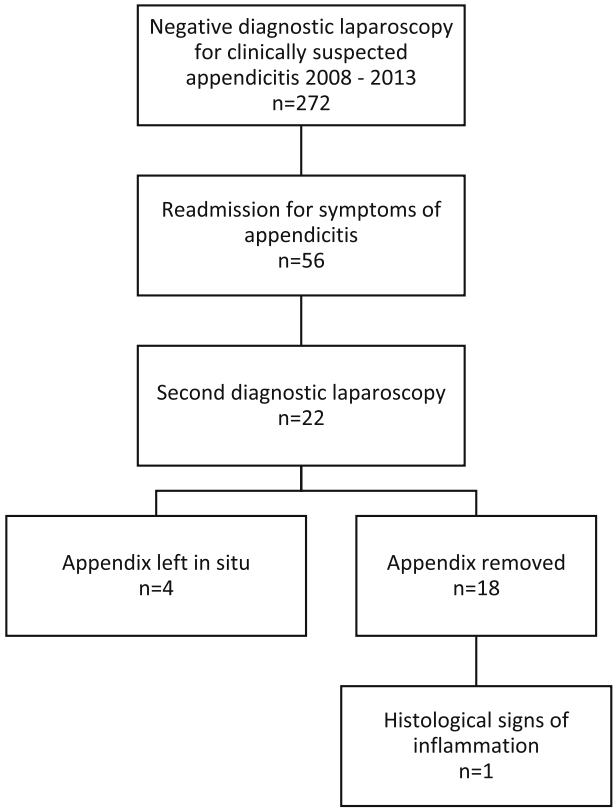

Fig. 1. Flowchart of patients included in the study.

Table 1
Patients demographics and operative details at first diagnostic laparoscopy.

Variables	n
Gender (%)	
Female	222 (81.6)
Male	50 (18.3)
Age **	27 [8−89]
BMI *	24.4 (5.2)
ASA (%)	
1	205 (75.4)
2	63 (23.2)
3	4 (1.5)
Operating time (min)**	37 [13−153]
Intraoperative complications (%)	3 (1.1)
Postoperative complications (%)	1 (0.4)
Mortality (%)	1 (0.4)

Variables are expressed as n = numbers and percentages, * mean ± standard deviation (SD) or ** median [range]. ASA = American Society of Anesthesiologists score. BMI = body mass index (kg/m^2).

Table 2
Operative and pathological details following second diagnostic laparoscopy.

Variables	n
Readmission (%)	56 (20.7)
Time to readmission. months **	10 [0−84]
Reoperations (%)	22 (8.1)
Appendix removed	18
Histological signs of inflammation	1
Intraoperative complications (%)	0
Postoperative complications (%)	2 (11.1)

Variables are expressed as n = numbers and percentages, * mean ± standard deviation (SD) or ** median [range].

complications among the patients who had a second laparoscopy. Postoperative complications occurred in two patients (one patient had surgical wound infection at the umbilical port site and one patient developed acute respiratory distress syndrome (ARDS) following pneumonia). The mean follow-up time for the entire study population was 5.6 years (SD ± 1.5 years).

4. Discussion

In the present study, we found a low rate of histologically inflamed appendix following a previous negative DL for clinically suspected appendicitis (1/271, 0.4%). However, the readmission rate was high (20.7%) and a second DL was performed in 8.1% of the patients.

Current recommendations by World Society of Emergency Surgery (WSES) and European Association of Endoscopic Surgery (EAES) are to perform an appendectomy in case of a macroscopic normal appearing appendix during surgery for suspected appendicitis [5,14]. The "normal" appendix is not, however, routinely removed during DL for suspected appendicitis in our country. The recommendations from WSES and EAES are based on a few studies showing high rate of up to 29% false negative results (macroscopic normal appendix, but pathological signs of inflammation) [1,15–17]. However, several of the studies referred to had a low number of patients, with a study population with a macroscopic normal appendix of less than 50 patients in three of the studies [15–17]. In a larger study, Strong et al. performed a multicenter audit, in which 375 patients underwent laparoscopic appendectomy with removal of a macroscopic normal appendix. Histological examination revealed inflammation in 26.6% [8].

Most studies report on histological findings after removal of the macroscopic normal appendix, and studies reporting outcomes after leaving the appendix in situ are lacking. The results from the current study differentiate significantly from the studies reporting histological findings following removal of a normal appendix. Of the 272 patients, eighteen had the appendix removed at a second DL, mostly due to preoperative agreement with the patient, but only one showed histological inflammation. The long-term mean follow-up time of five years and median time to readmission of 10 months in this study indicate that readmissions were not likely to be caused by missed acute appendicitis on the initial admission. Likewise, van den Broek et al. demonstrated in a study with 109 patients a low rate of 1% for developing appendicitis following negative DL for suspected appendicitis, and therefore concluded that a normal appendix should be left in place, as the risk of developing appendicitis was no higher than that in a normal population [18].

Considering the low risk of subsequent appendicitis, the risk for complications following laparoscopic appendectomy should be taken into consideration in decision making of removing a normal looking appendix. There is no difference in complication rates between laparoscopic removal of an inflamed or macroscopic normal appendix [11] and the prevalence of long-term surgical complications after appendectomy is low [11,19]. However, significantly higher complication rates are seen when removing the appendix than performing a DL without removal of the appendix [20]. Furthermore, removal of the appendix has been linked to higher risks of developing several gastrointestinal and inflammatory diseases [19,21].

Despite a low rate of appendicitis following a negative DL, we found a high readmission rate of 20.7% and reoperation rate of 8.1%. Other studies have reported readmission in 8–38% of the cases, though the number of patients in follow-up was low [18,22]. The majority of the patients with both initial negative laparoscopy, and patients with readmission were young women in the child-bearing age. This finding has also been reported in other studies [1,6]. Singal et al. found that in a large number of female patients in whom macroscopically normal appendices had been removed, other histological findings were noted making another abdominal pathology as cause of pain a possibility [23]. In addition, there are multiple gynecological differential diagnoses in women and it could as a result be argued that all women of childbearing age with clinical signs of appendicitis should in addition to a human chorionic gonadotropin (hCG) test and standard gynecological examination also receive gynecological consultation prior to decision for surgery. This is, however, not routinely performed in our departments. Besides, pelvic ultrasonography has shown limited value in diagnostics in women with right iliac fossa pain [24]. Unfortunately, we do not have data on how many of the female patients in our study that received gynecological consult.

It could be argued that a high readmission rate is a valid argument for performing appendectomy despite normal macroscopic appearance. Nevertheless, although not confirmed in larger studies, it is suggested that removal of a macroscopic normal appendix does not prevent recurrence of pain in the right iliac fossa and thereby readmissions [18,22]. Still, further attention to potential differential diagnoses in young female patients is needed. A high readmission rate is a problem that needs to be addressed, as it leads to both pain and inconvenience for the patient, but also diagnostic difficulties for the physician and higher health care costs. Considering reports on higher complications rates when removing the appendix versus leaving it in situ, generally low prevalence of surgical complication after appendectomy and results from the current study with high re-admission rates, further studies with cost analysis between the two methods are warranted.

Based on our data, due to the low risk of appendicitis following a negative DL, the threshold for a new DL for the same symptoms should be higher than for the initial procedure, unless the symptoms present immediately after the first procedure giving rise to concern of overseen appendicitis, and patients should be further investigated for other causes of pain in right iliac fossa.

The conclusions of this study are limited by its non-randomized and retrospective nature. We have furthermore no information on the patients' referral to primary care, and may therefore have underestimated simpler post-operative complications such as wound infections, and right iliac fossa pain not requiring hospitalization.

Also, radiological imaging and clinical scoring systems were not used in the diagnosis of appendicitis and referral to surgery in this study which may have contributed to higher number of performed laparoscopies. Although it has been showed that the rate of negative appendectomies may be reduced with diagnostic imaging and clinical scoring systems [14,25,26], peroperative findings of a macroscopic normal appendix will still occur. In a recent worldwide prospective observational study on acute appendicitis, where the 70% of the patients underwent diagnostic imaging and approximately 90% had their Alvarado and Anderson score recorded, it was found that the Alvarado Score was ≥5 in 89.8% cases, while Andersson's Score was ≥5 in 2736 (83.4%) cases of appendicitis confirmed by histopathology [27]. Therefore, the rate of diagnostic imaging and clinical scoring systems may reduce the rate of perioperative findings of a normal appendix, but a complete elimination of such findings is unlikely, and the dilemma of management of the normal appendix would persist.

Despite the abovementioned limitations, this is the largest study on patients with negative DL due to clinically suspected appendicitis, without removal of the appendix, with a long follow-up time of over five years, which strengthens the conclusion of the safety of leaving a macroscopic normal appendix in situ.

In conclusion, the rate of appendicitis after a negative diagnostic laparoscopy is low and based on the results from the present study we do not consider that it is necessary to remove a macroscopic normal appendix during laparoscopy for clinically suspected appendicitis. The high readmission rate, however, warrants the need for further investigation or follow-up, especially in young female patients.

CRediT authorship contribution statement

Amira Khattar Sørensen: Funding acquisition. **Anders Bang-Nielsen:** Funding acquisition, Formal analysis, Writing - original draft. **Katarina Levic-Souzani:** Conceptualization, Formal analysis, Writing - original draft. **Hans Christian Pommergaard:** Funding acquisition, Formal analysis. **Anders Beck Jørgensen:** Funding acquisition, Formal analysis. **Mai-Britt Tolstrup:** Conceptualization. **Bo Rud:** Funding acquisition. **Bojan Kovacevic:** Funding acquisition, Formal analysis. **Orhan Bulut:** Conceptualization.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.02.001.

Ethical approval

No ethics approval was required for this retrospective study.

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No funding was obtained for this research.

Author contribution

AKS: Conceptualization, Formal analysis, methodology, writing - original draft.

ABN: Conceptualization, Formal analysis, methodology, writing - original draft.

KLS: Conceptualization, Formal analysis, methodology, writing - original draft.

ABJ: Data curation, writing - review and edits.

BK: Data curation, writing - review and edits.

BR: Data curation, writing - review and edits.

HCP: Writing - review and edits.

MBT: Writing - review and edits.

OB: Writing - review and edits.

Conflicts of interest

No conflicts of interest to declare.

Research registration number

DRKS00015833 from German Clinical Trials Register.

Guarantor

Amira Khattar Sørensen, Katarina Levic-Souzani and Orhan Bulut

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Data statement

The authors do not have permission to share data.

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