Langenbecks Arch Surg (2017) 402:987–993
DOI 10.1007/s00423-017-1608-3

ORIGINAL ARTICLE

Risk factors for morbidity after appendectomy

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Received: 22 December 2016 / Accepted: 18 July 2017 / Published online: 27 July 2017

Abstract
Introduction The aim of the present study was to evaluate the risk factors for postoperative complications after an appendectomy with special regard to both the time period from hospital admission to operation and night time surgery.
Patients and methods Patients who underwent an appendectomy due to acute appendicitis and were admitted to the University Hospital Aachen between January 2003 and January 2014 were included in this retrospective analysis. Regarding the occurrence of postoperative complications, patients were divided into the following two groups: the group with complications (group 1) and the group without complications (group 2).
Results Of the 2136 patients who were included in this study, 165 patients (group 1) exhibited complications, and in 1971 patients (group 2), no complications appeared. After a univariate logistic regression analysis, six predictors for postoperative complications were found and are described as follows: (1) complicated appendicitis (odds ratio (OR) 4.8 (3.46–6.66), $p < 0.001$), (2) operation at night (OR 1.62 (1.17–2.24), $p = 0.004$), (3) conversion from laparoscopic to open access (OR 37.08 (12.95–106.17), $p < 0.001$), (4) an age > 70 years (OR 6.00 (3.64–9.89), $p < 0.001$), (5) elevated CRP (OR 1.01 (1.01–1.01), $p < 0.001$) and (6) increased WBC count (OR 1.04 (1.01–1.07), $p = 0.003$). After multivariate logistic regression analysis, a significant association was demonstrated for complicated appendicitis (1.88 (1.06–3.32), $p < 0.031$), conversion to open access (OR 16.33 (4.52–58.98), $p < 0.001$), elevated CRP (OR 1.00 (1.00–1.01), $p = 0.017$) and an age > 70 years (OR 3.91 (2.12–7.21), $p < 0.001$). The time interval between hospital admission and operation was not associated with postoperative complications in the univariate and multivariate logistic regression analyses, respectively. However, the interaction between complicated appendicitis and the time interval to operation was significant (OR 1.024 (1.00–1.05), $p = 0.028$).
Conclusion Based on our findings, surgical delay in the case of appendicitis and operation at night did not increase the risk for postoperative complications. However, the mean waiting time was less than 12 h and patients aged 70 years or older were at a higher risk for postoperative complications. Furthermore, for the subgroup of patients with complicated appendicitis, the time interval to surgery had a significant influence on the occurrence of postoperative complications. Therefore, the contemporary operation depending on the clinical symptoms and patient age remains our recommendation.

Keywords Appendectomy · Delay · Timing of surgery · Appendicitis · Morbidity

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Introduction

The treatment of acute appendicitis is subject to continuous change. It is one of the most common diseases in children and adults requiring emergency operation. Previously, the surgical access for an appendectomy was the object of several studies [1, 2]. Recently, a focus on the appropriate point in time for operation has been the main focus of investigation.

Furthermore, several studies question whether an operation is necessary or if treatment with antibiotics has equivalent results [3–5]. However, until now, no consistent data exists recommending the appropriate point in time for appendectomy.

The main concerns for delaying the appendectomy are increasing risk of perforation, intra-abdominal abscessation and postoperative complications [6]. However, several previous studies have shown that delaying surgery is not a risk factor for perforation or postoperative morbidity [7, 8]. Therefore, conservative management with fluid and antibiotic treatment can be safely performed in the meantime, prior to the operation [8–10]. Other studies have recommended an emergency operation as soon as possible due to an increased risk for perforation and surgical site infections [11, 12].

The timing of appendectomy is, unfortunately, not merely a decision based on medical findings. Hospital size, man power at night and economic values also take part in the decision. During the day, regular operation lists are running, and procedures such as an appendectomy have to wait. During the night, only a limited number of staff members are available, and life-threatening emergencies usually take priority [13, 14].

The timing of an appendectomy has far-reaching consequences. Therefore, the aim of the present study was to evaluate the risk factors for postoperative complications after an appendectomy with special regard to the time period prior to operation and night time surgery.

Patients and methods

All patients with an appendectomy, due to acute appendicitis, performed at the Department of General, Visceral and Transplant Surgery of the University Hospital of the RWTH Aachen between January 2003 and January 2014 were included in this retrospective analysis. Appendicitis was defined due to the histological findings. Patients with an appendectomy in the context of other operations or without histological verified appendicitis were excluded. The flow chart in Fig. 1 depicted exclusion criteria in detail.

The Ethics Committee of the RWTH Aachen University Hospital approved this retrospective study (EK 305/16).

The patient cohort was divided into two groups according to the occurrence of postoperative complications. Group 1 included all patients who developed postoperative complications. Patients without postoperative complications belonged to group 2.

From 2003 until 2009, all appendectomies were routinely performed via an open access protocol. Since 2010, the standard procedure has been the laparoscopic appendectomy. The intraoperative and postoperative care was followed according to the standard of care. In case of laparoscopic appendectomy, the appendix was removed with a specimen retrieval pouch.

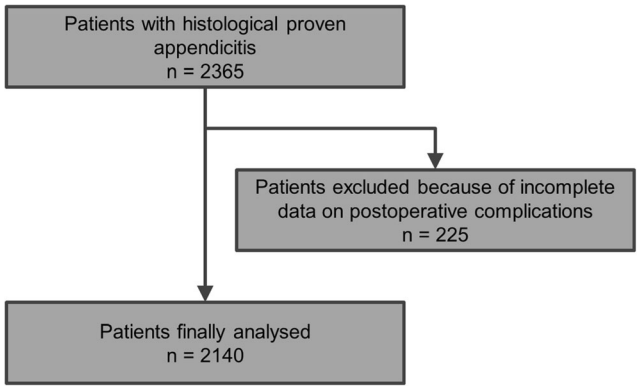

Fig. 1 The flow chart depicted exclusion criteria in detail

Patients were not treated with antibiotics in the waiting time for surgery, but all patients received a single dose of antibiotic prophylaxis (Cefuroxim and Metronidazol) intraoperatively. Postoperative antibiotic treatment was based on the intraoperative diagnosis of perforation or abscessation. Oral intake and mobilisation were conducted following the fast track pathway.

The following patient characteristics were collected: sex, age, time of admission, time from admission to operation, time of surgery (day (6:00 am to 11:59 pm), night (12:00 pm to 5:59 am)), surgical approach (open vs laparoscopic, conversion to open), type of appendix stump closure (ligation, endoloop or stapler), white blood cell count (WBC) on admission (10^9/l), C-reactive protein (CRP) (mg/dl) level on admission, postoperative complications, length of hospital stay and 30-day mortality. All postoperative complications were classified according to the five grades of the *Clavien-Dindo* classification system [15].

Gangrenous or perforated appendicitis and periappendicular abscesses were graded as complicated appendicitis. We defined wound infection as localised signs of inflammation. Intra-abdominal abscess was defined as a fluid collection detected by ultrasound or CT scan. Appendiceal stump insufficiency was an intraoperative diagnosis in case of reoperation.

Statistics

Statistical analyses were performed with SAS (Version 9.4, SAS Institute Inc., Cary, NC, USA). Categorical data are presented as frequencies and percentages. Continuous variables are expressed as the mean values ± standard deviation (SD). At first, a univariate logistic regression was used to analyse each possible risk factor separately. Next, a backward variable selection was conducted to reveal the main important risk factors for complications. Because the variables "time of appendectomy (day/night)" and "time to appendectomy" are the focus of this investigation, they were not excluded from the multivariate model. We choose the model with the lowest Akaike information criterion. Significant interactions were

included in the multivariate model. Because of the exploratory nature of this study, we made no adjustment to the significance level to account for multiple testing. Statistical tests were performed two-tailed, and p values less than 0.05 were considered as significant test results.

Results

Between January 2003 and January 2014, 2136 patients underwent appendectomy because of acute appendicitis. The patient cohort was divided into two groups according to the occurrence of postoperative complications. Group 1 included 165 patients with postoperative complications and 1971 patients without postoperative complications belonged to group 2.

Patient characteristics

Patients in group 1 were significantly older (37 vs 24 years, $p < 0.001$), and more patients were aged 70 years or older (15 vs 3%, $p < 0.001$). Gender proportion was equal in both groups. The WBC count and CRP at admission were significantly higher in group 1 (WBC count 13.81 vs 12.45 10^9/l, $p = 0.003$; CRP 74 vs 42 mg/dl, $p = <0.001$). The mean waiting time from hospital admission until surgery was 12 h in group 1 and 11 h in group 2. In group 1, more operations were performed at night (41 vs 30%). The type of appendectomy was different in both groups. In group 1, 9% of operations had to be converted from the laparoscopic to the open access, while in group 2, only 1% had to be converted ($p < 0.001$). More patients in group 1 suffered from complicated appendicitis (51 vs 18%, $p < 0.001$). There were no differences between both groups with regard to the type of appendix stump closure. The hospital stay was longer for group 1 (11 vs 5 days, $p = <0.001$).

Postoperative complications

Due to the number of patients in group 1 ($n = 165$), the overall rate of postoperative complications was 7.7%. The rate for patients with grade I or II complications according to the *Clavien-Dindo* classification was 5.4%. Major complications (*Clavien-Dindo* grade III, IV or V) were observed in 1.7% of patients.

Wound infection was the most common postoperative complication, and it occurred in 52 patients (2%). Nine patients needed an operative wound debridement; all other patients were conservatively treated. An intraabdominal abscess occurred in 15 patients (0.6%). Six patients were treated by percutaneous CT-guided drainage, and nine patients needed re-operation. Four patients (0.2%) developed appendiceal stump insufficiency. Bleeding occurred in three patients (0.1%).

Re-operations had to be performed in 28 patients (1.2%) due to either wound infection ($n = 9$), intraabdominal abscess ($n = 9$), appendiceal stump insufficiency ($n = 4$) or postoperative bleeding ($n = 3$). Three patients underwent a second look operation due to severe peritonitis. Table 1 shows the postoperative complications.

Mortality

The overall hospital mortality rate was 0.1%. Both patients died within 24 h after operation because of cardiac shock within the scope of a perforated appendicitis causing severe peritonitis and sepsis. Delay to surgery was <12 h in both cases.

Factors associated with the development of postoperative complications

After a univariate logistic regression, six predictors for postoperative complications were found and included the following: (1) complicated appendicitis (odds ratio (OR) 4.8 (3.46–6.66), $p < 0.001$), (2) operation at night (OR 1.62 (1.17–2.24), $p = 0.004$), (3) conversion from laparoscopic to open access (OR 37.08 (12.95–106.17), $p < 0.001$), (4) an age > 70 years (OR 6.00 (3.64–9.89), $p < 0.001$), (5) elevated CRP (OR 1.01 (1.01–1.01), $p < 0.001$) and (6) increased WBC count (OR 1.04 (1.01–1.07), $p = 0.003$).

In the multivariate logistic regression analysis, operation at night and WBC count were not associated with the development of postoperative complications. A significant association could still be demonstrated for complicated appendicitis (1.88 (1.06–3.32), $p < 0.031$), conversion to open access (OR 16.33 (4.52–58.98), $p < 0.001$), elevated CRP (OR 1.00 (1.00–1.01), $p = 0.017$) and an age > 70 years (OR 3.91 (2.12–7.21), $p < 0.001$).

The time interval between hospital admission and operation was not associated with postoperative complications in the univariate and multivariate logistic regression analyses, respectively (Fig. 2). However, the interaction between complicated appendicitis and time interval to operation was significant. In the subgroup of patients with complicated appendicitis, the time interval to appendectomy had a significant influence on the occurrence of postoperative complications (OR 1.024 (1.00–1.05), $p = 0.0279$) (Fig. 3). For non-complicated appendicitis, the time to appendectomy had no influence on the occurrence of postoperative complications ($p = 0.355$). We could not find any other significant interaction between the time interval to operation and other parameters.

Patient characteristics and the results of the univariate and multivariate regression analyses are presented in Table 2.

Table 1 Postoperative complications

Postoperative complications	*n* (%)
Wound infection	52 (2%)
Intra-abdominal abscess	15 (0.6%)
Appendiceal stump insufficiency	4 (0.2%)
Re-operation	27 (1.2%)
Bleeding	3 (0.1%)
Clavien Dindo Classification	
Grade I	101 (4.3%)
Grade II	25 (1.1%)
Grade III	30 (1.3%)
Grade IV	7 (0.3%)
Grade V	2 (0.1%)

Discussion

The aim of the present study was to analyse risk factors associated with the development of postoperative complications after an appendectomy, particularly with regard to the time interval from hospital admission to the operation and night time surgery.

The main concern about a delayed appendectomy is an increased rate of perforation and postoperative complications [6, 11, 12]. Conversely, several studies revealed that conservative treatment with antibiotics for acute appendicitis is feasible and safe [3, 4]. However, until now, only incongruent data are available and the impact of time interval to surgery remains unclear.

In the clinical routine, the question is raised of whether a patient can be treated with antibiotics only, or needs elective or emergency surgery.

In our patient collective, we did not observe an association between the time interval to appendectomy and the occurrence of postoperative complications in the univariate and multivariate logistic regression analyses, respectively.

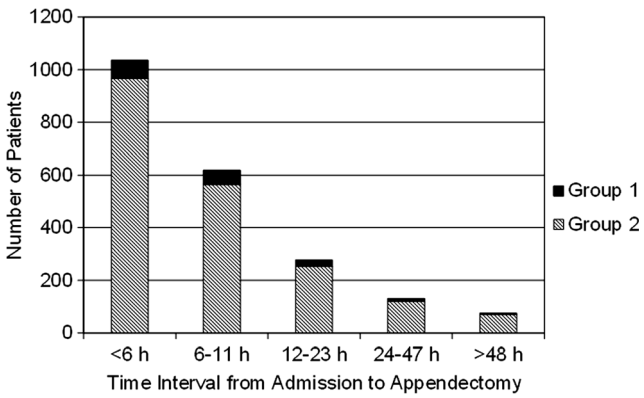

Fig. 2 Time interval between hospital admission and appendectomy

However, it should be noted that nearly 50% of patients had a waiting period prior to surgery of less than 6 h. If acute appendicitis was suspected, the operation was performed as soon as possible.

Of note, we could show that the waiting time to surgery had a significant influence on the occurrence of postoperative complications for the subgroup of patients with complicated appendicitis. Therefore, patients with clinical signs of perforation or abscessation should undergo immediate appendectomy.

In addition to the expected factors such as complicated appendicitis, elevated CRP and the conversion to an open access, an age > 70 years was a predictor for postoperative complications in the multivariate analysis. This finding is consistent with the observations of other studies showing that older patients who present with more advanced forms of appendicitis have a higher risk for perforation and suffer more often from postoperative complications [12, 23, 24]. Therefore, any delay of surgery should be avoided in elderly patients and those with co-morbidities.

The results of *Almström* et al. and *Yardeni* et al. for children with acute appendicitis indicate that the time interval to surgery was not an independent risk factor for postoperative complications [7, 8]. They did not observe a higher rate of perforations due to surgical delay.

Congruent data were provided by *Abou-Nukta* et al. in a series of 380 adult patients. They demonstrated that an appendectomy delay greater than 12 h was not associated with increased length of hospital stay, operative time or complications [16].

The British Multicentre Cohort Study, supplemented by a meta-analysis with a mixed patient collective (children and adults), also showed that a short delay of 12 to 24 h was not associated with an increased rate of complex appendicitis and infectious complications [17].

Kim et al. provided similar results. In a review of 4065 patients who underwent a laparoscopic appendectomy, patients were divided into 4 groups based on the time elapsed from the evaluation at the emergency room to the appendectomy (0–6, 6–12, 12–18, over 18 h). No significant differences in perforation and postoperative complications were observed between the four groups [18].

Fair et al. analysed the data of 69,926 patients of the American College of Surgeons National Surgical Quality Improvement Project dataset who underwent open or laparoscopic appendectomy. These data demonstrate equivalent outcomes between time to appendectomy of less than 24 and 24 to 48 h. After a delay of more than 48 h, they observed a 2-fold increase in complication rate [19].

March et al. investigated patients with a waiting time of more than 48 h, and they did not demonstrate any statistically significant differences due to the incidence of complications and perforation compared with patients having appendectomy

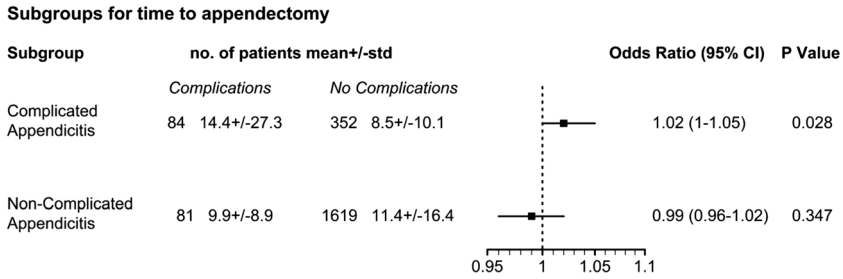

Fig. 3 In case of complicated appendicitis the time interval to appendectomy had a significant influence on the occurrence of postoperative complications

performed without or with less delay [20]. These findings indicate that 50% of patients with a waiting time of more than 48 h had a normal, and not inflamed, appendix removed. These results confirm our experience. An appendectomy after 48 h was only performed if conservative management failed and patients still had unspecific abdominal pain.

Conversely, there are several studies that have revealed contradictory findings.

Table 2 Results of the uni- and multivariate regression analysis

	Group 1 (n = 165)	Group 2 (n = 1971)	Univariate				Multivariate			
			Odds ratio	lower CL	upper CL	p value	Odds ratio	lower CL	upper CL	p value
Age	37 ± 25.47	24 ± 16.92				*<0.001*				
Age > 70						*<0.001*				
no	140 (85%)	1914 (97%)								
yes	25 (15%)	57 (3%)	*6.00*	*3.64*	*9.89*	*<0.001*	*3.91*	*2.12*	*7.21*	*<0.001*
Gender						0.257				
male	88 (53%)	951 (48%)								
female	77 (47%)	1020 (52%)	0.83	0.60	1.12	0.257				
Time of operation						*0.004*				
day time	97 (59%)	1376 (70%)								
night time	68 (41%)	595 (30%)	*1.62*	*1.17*	*2.24*	*0.004*	1.16	0.75	1.78	0.511
Time to appendectomy (h)	12 ± 20	11 ± 15	1.01	1.00	1.01	0.301	1.02	1.00	1.05	0.522
Time to appendectomy						0.594				
<6 h	70 (42%)	966 (49%)								
6–11 h	54 (33%)	564 (29%)								
12–23 h	25 (15%)	252 (13%)								
24–47 h	11 (7%)	119 (6%)								
≥48 h	5 (3%)	70 (4%)								
Admission CRP value (mg/dl)	(n = 119) 74 ± 76	(n = 1228) 42 ± 51	*1.01*	*1.01*	*1.01*	*<0.001*	*1.00*	*1.00*	*1.01*	*0.017*
Admission WBC (10^9/l)	(n = 165) 13.81 ± 5.06	n = 1890) 12.45 ± 5.23	*1.04*	*1.01*	*1.07*	*0.003*	1.00	0.96	1.04	0.851
Type of operation						*<0.001*				
Open	95 (58%)	1359 (69%)								
Laparoscopic	55 (33%)	602 (31%)	1.30	0.92	1.84	0.132	1.18	0.74	1.86	0.490
Conversion	15 (9%)	10 (1%)	*37.08*	*12.95*	*106.17*	*<0.001*	*16.33*	*4.52*	*58.98*	*<0.001*
Appendix stump closure						0.461				
Endoloop	3 (2%)	47 (2%)								
Stapler	54 (32%)	563 (29%)	1.50	0.45	4.99	0.506				
Ligation	106 (65%)	1353 (69)	1.23	0.38	4.01	0.735				
Complicated appendicitis						*<0.001*				
no	81 (49%)	1619 (82%)								
yes	84 (51%)	352 (18%)	*4.80*	*3.46*	*6.66*	*<0.001*	*1.88*	*1.06*	*3.32*	*0.031*
No complicated appendicitis * Time to appendectomy							0.99	0.96	1.02	0.355
Complicated appendicitis * Time to appendectomy							*1.02*	*1.00*	*1.05*	*0.028*
Hospital stay (days)	11 ± 7.77	5 ± 2.49				*<0.001*				

Ditilo et al. demonstrated in a retrospective study with 1287 patients that the severity of pathology and the complication rate in adult patients with acute appendicitis are time dependent and therefore suggested that an appendectomy should be performed as expeditiously as possible [11]. *Teixeira* et al. observed an increased incidence of wound infection and intra-abdominal abscess after a delay of more than 6 h for performing appendectomy. Particularly, patients with a non-perforated appendicitis had an increase of surgical site infections after a delay of more than 6 h [21]. *Giraudo* et al. reported a significantly increased complication rate between delayed (>24 h) and early (<24 h) appendectomy groups [22]. In our study, patients who were operated at night developed statistically significant more postoperative complications. This result may be due to a selection bias generated when patients with signs of complicated appendicitis underwent direct operation, whereas patients with mild symptoms and uncertain diagnoses were initially managed conservatively. When an operation was necessary after initial management, it was performed during normal working hours. However, and interestingly, the multivariate analysis did not identify an operation at night as a predictor for postoperative complications.

Busch et al. analysed the outcomes of 1827 adult patients with suspected appendicitis and identified an admission at night as an independent predictor for in-hospital delay as well as for perforation [12].

Several limitations exist concerning the evaluation of our data. First, this analysis was performed retrospectively. Secondly, no data on symptom duration before admission to hospital was documented. Furthermore, we had a selection bias generated when patients with signs of a complicated appendicitis on admission had a shorter time interval to operation compared to patients with mild symptoms.

Conclusions

Based on our findings, surgical delay in the case of appendicitis and operation at night did not increase the risk for postoperative complications. However, the mean waiting time was less than 12 h and patients aged 70 years or older were at a higher risk for postoperative complications. Furthermore, for the subgroup of patients with complicated appendicitis, the time interval to surgery had a significant influence on the occurrence of postoperative complications. Therefore, the contemporary operation depending on the clinical symptoms and patient age remains our recommendation.

Authors' contribution Dr. med. Anne Andert study conception and design, acquisition of data, analysis and interpretation of data, writing manuscript; Dr. med. Patrick Hamid Alizai acquisition of data, critical revision of manuscript; Priv.–Doz. Dr. med. Christian Daniel Klink acquisition of data, critical revision of manuscript; Niklas Neitzke acquisition of data; Dipl. Stat. Christina Fitzner performed statistical analysis; Priv.–Doz. Dr. med. Christoph Heidenhain critical revision of manuscript; Dr. med. Andreas Kroh acquisition of data, critical revision of manuscript; Univ.–Prof. Dr. med. Ulf Neumann study conception and design, critical revision of manuscript; Priv.–Doz. Dr. med. Marcel Binnebösel study conception and design, drafting of manuscript, critical revision of manuscript.

Compliance with ethical standards

Funding No funding necessary.

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

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The Ethics Committee of the RWTH Aachen University Hospital approved this retrospective study (EK 305/16).

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

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