Systematic Review and/or Meta-Analysis

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Preoperative in-hospital delay increases postoperative morbidity and mortality in patients with acute appendicitis: a meta-analysis

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Background: Complicated appendicitis is associated with high morbidity, mortality, and healthcare costs. However, the relationship of preoperative in-hospital delay > 24 h with complicated appendicitis and postoperative morbidity remains unclear. This meta-analysis investigated the effects of preoperative in-hospital delay on complicated appendicitis and postoperative morbidity in patients with acute appendicitis.

Materials and methods: This study adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 and A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR2) guidelines. The PubMed, Embase, Cochrane Library, and Web of Science databases up to October 14, 2023 (updated on March 16, 2024) were searched for randomized controlled trials and observational studies that evaluated the effect of preoperative in-hospital delays of > 24 h on acute appendicitis. Odds ratios (OR) and 95% confidence intervals (CIs) were also determined.

Results: We yielded 18 130 records, of which 28 studies (512 881 patients) were included in the meta-analysis. The risk of bias was considered serious, moderate, and low for 24, 3, and 1 study, respectively. Although preoperative in-hospital delays of > 24 h were not associated with a higher risk of surgical-site infection (OR: 1.04, 95% CI: 0.97, 1.12, $P = 0.25$), in-hospital delays of > 24 h were a risk factor for complicated appendicitis (OR: 1.60, 95% CI: 1.25, 2.05, $P = 0.0002$), and postoperative complications (OR: 1.51, 95% CI: 1.30, 1.75, $P < 0.00001$). In addition, an in-hospital delay of > 24 h before surgery increased the OR of postoperative mortality (OR: 1.81, 95% CI: 1.33, 2.45, $P = 0.0001$). The sensitivity analyses also confirmed the robustness of our results.

Conclusions: An in-hospital delay of > 24 h is a risk factor for complicated appendicitis, postoperative complications, and mortality. Given the subsequent adverse outcomes of in-hospital delays, appendectomy should not be delayed for > 24 h.

Keywords: acute appendicitis, complicated appendicitis, in-hospital delay, meta-analysis, surgical-site infection

Introduction

Acute appendicitis is one of the most common surgical emergencies worldwide, and it is estimated that approximately 8% of people will suffer from acute appendicitis in their lifetime[1]. Although appendectomy remains the primary treatment for acute appendicitis, the optimal surgical timing remains unclear.

HIGHLIGHTS

- Preoperative in-hospital delay > 24 h was a risk factor for complicated appendicitis and postoperative complications.
- A > 24 h delay was associated with a higher risk of postoperative mortality than a 0–24 h delay.
- Given the subsequent adverse outcomes of in-hospital delay, appendectomy should not be delayed for > 24 h.

Traditionally, surgeons believe that the severity of appendicitis and the risk of perforation increases over time[2]. Previous evidence suggests that an increased time from symptom onset to surgery is associated with an increased risk of complicated appendicitis[3,4]. Complications occur only in 10% of cases with uncomplicated appendicitis, whereas they occur in 25% of cases of complicated appendicitis[5]. Complicated appendicitis not only increases the risk of postoperative infectious complications but also prolongs hospital stay and increases readmission rates[5]. In addition, it can increase the cost of hospitalization[6]. A prospective study by Kong *et al.*[7] found that the average hospitalization cost for perforated appendicitis with localized intra-abdominal sepsis (US $2041) was approximately twice that for simple appendicitis (US $908). However, the effects of in-hospital delay on appendicitis remain controversial.

A retrospective study by Almström *et al.*[8]. showed that in-hospital delays did not increase the risk of appendiceal perforation. In addition, Patel *et al.*[9]. found that delaying

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appendectomy for 24 h after admission did not increase the risk of postoperative complications. However, the 2020 guidelines recommend immediate appendectomy[10] or an in-hospital delay of no more than 24 h[11]. Recently, data from the Arbeitsgemeinschaft für Qualitätssicherung in der Chirurgie (AQC) database indicated that in-hospital delays of >24 h increase the risk of complicated appendicitis[1]. Therefore, it is important to determine the optimal time for appendectomy after admission.

A meta-analysis by van Dijk *et al.*[12] showed that preoperative in-hospital delays of 12–24 h did not increase the risk of complicated appendicitis; however, they were unable to determine whether in-hospital delays >24 h were associated with an increased risk of complicated appendicitis. Given that, a large number of high-quality studies have accumulated in recent years. This study aimed to assess whether adding the latest evidence would change the current recommendations.

Therefore, we hypothesized that in-hospital delays of >24 h would increase postoperative morbidity and mortality. Accordingly, we conducted a systematic review and meta-analysis of the current evidence to determine the impact of preoperative in-hospital delays of >24 h on complicated appendicitis, postoperative morbidity, surgical-site infection (SSI), and mortality in patients with acute appendicitis.

Methods

Search strategy

This meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Supplementary Methods 1, Supplemental Digital Content 1, http://links.lww.com/JS9/D58)[13] and A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR2) (Supplementary Methods 2, Supplemental Digital Content 2, http://links.lww.com/JS9/D59)[14]. The protocol was registered in the International Prospective Register of Systematic Reviews database.

Two authors independently conducted a systematic and comprehensive literature search using the Embase, Web of Science, PubMed, and Cochrane Library databases to identify observational studies and randomized controlled trials (RCTs) published before October 14, 2023 (updated on March 16, 2024) (Supplementary Table S1, Supplemental Digital Content 3, http://links.lww.com/JS9/D60). In addition, we checked the reference lists of the identified articles and related reviews to screen eligible studies further. There were no language restrictions in the search.

Study selection

Trials included in this meta-analysis were chosen according to the patient, intervention, comparator, outcome, and study type (PICOS) criteria. There were no language restrictions during the process of literature selection.

Patients: both children and adults with acute appendicitis.

Intervention: delayed appendectomy (in-hospital delays of >24 h).

Comparator: immediate appendectomy (in-hospital delays 0–24 h).

Outcome: the primary outcome was the incidence of complicated appendicitis. Secondary outcomes included total postoperative complications (Clavien–Dindo classification I–V), SSI, and postoperative mortality. SSI was defined as a wound infection and/or intra-abdominal abscess.

Study type: RCTs, cohort studies, case–control studies, and cross-sectional studies.

Exclusion criteria were as follows: studies that included data from patients with pathologies other than acute appendicitis that could not be analyzed separately; studies that did not clearly define the boundaries of time intervals for in-hospital delays; studies that did not report absolute numbers (e.g. 10 out of 124 patients had complicated appendicitis); and studies without available data from publications or corresponding authors. Reviews, case reports, conference abstracts, editorials, letters, animal studies, and studies that did not define the boundaries of time intervals were excluded.

Data extraction

Data from all eligible studies were independently extracted by two reviewers on the basis of a previously established form, and any disagreements were resolved by discussion with a third-party independent reviewer. The main fields to be extracted included the author's name, year of publication, country in which the study was conducted, study design, study population (sample size, age, and sex), delayed appendectomy group and immediate appendectomy group definitions, incidence of complicated appendicitis, total postoperative complications, and postoperative mortality. When data of interest in an article were unavailable, the corresponding author was contacted by mail to obtain the necessary data. Studies without available data from publications or corresponding authors were excluded.

Quality assessment

The risk of bias in the RCTs was assessed independently by two authors using the Cochrane risk-of-bias tool 2[15]: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported results, and overall risk of bias. The quality of the non-RCTs was assessed independently by two authors using the ROBINS-I tool[16]. Any discrepancy was resolved through discussion and intervention by a third reviewer whenever necessary.

Statistical analysis

The meta-analysis was performed using Review 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration 2014; Copenhagen, Denmark) and Stata 15.1 (Stata Corp., College Station, TX, USA) software. Odds ratios (ORs) for individual studies were calculated. The I^2 statistic was used to assess inter-study heterogeneity. When the I^2 value was >50%, the heterogeneity was considered to be high, and the random effects model was adopted; otherwise, the fixed effects model was adopted[17]. Sensitivity analyses (one-study excluding method) were performed to assess the robustness of the results. Subgroup analyses were performed according to age, definitions of complicated appendicitis, preoperative stage included, and study design. Publication bias was assessed using Egger's tests and funnel plots if 10 or more studies were identified. The impact of publication bias was further analyzed using the trim and fill method. Statistical significance was set at P value <0.05.

Results

Literature search

The search strategy yielded 18 130 records, of which 6533 duplicates were excluded. After excluding a further 11 379 studies by reviewing the titles and abstracts, the full text of the remaining 218 studies was evaluated. Finally, 28 eligible studies[1,8,9,18–42] were included in the analysis (Fig. 1). The reasons for exclusion are summarized in Supplementary Table S2 (Supplemental Digital Content 4, http://links.lww.com/JS9/D61).

Study characteristics

The main characteristics of the 28 included studies are shown in Table 1. The studies were published between 1995 and 2023 and included 512 881 participants. Overall, 22 studies[1,8,9,19,20,23,24,26–29,31–38,40–42] were retrospective cohort studies and six studies[18,21,22,25,30,39] were prospective cohort studies. Of these, three studies[8,21,31] analyzed only children, eight studies[9,24,26,27,37–39,42] included only adults, and the remaining 17 studies[1,8,18–20,22,23,25,28–30,32–36,40,41] did not place any age restrictions on participants. Complicated appendicitis was defined as perforated or gangrenous appendicitis in seven studies[19,22,29,30,35,40,42] and perforated appendicitis in 18 studies[1,8,9,18,20,23–28,31,32,36–39,41], while the definition was unclear in three studies[21,33,34]. Twelve studies[8,9,19,22,24,26,29–32,39,40] calculated the in-hospital delay on the basis of the time from the emergency department to the operating room, three studies[33,38,42] calculated it from diagnosis to the operating room, and 13 studies[1,18,20,21,23,25,27,28,34–37,41] calculated it from admission to surgery. The risk of bias was considered serious, moderate, and low for 24[1,8,9,18–22,24–28,30,31,33–40,42], 3[23,29,32], and 1[41] studies, respectively, and the primary reason for a serious risk of bias assessment was an inappropriate adjustment of clinically important confounding factors (as defined by study authors) in the analyses. Details of the quality evaluation are summarized in Supplementary Table S3, Supplemental Digital Content 5, http://links.lww.com/JS9/D62.

Meta-analysis

Complicated appendicitis

Nineteen studies[1,8,18–20,22,24–32,38–41] reported data on in-hospital delays of >24 h. The combined results of the 19 studies showed that the ORs of complicated appendicitis with a >24 h delay were significantly higher than those with a 0–24 h delay [OR: 1.60, 95% confidence interval (CI): 1.25, 2.05, $P=0.0002$], with significant heterogeneity among the studies ($I^2=85\%$, $P<0.00001$) (Fig. 2). Table 2 summarizes the results of the meta-analysis. In addition, the results of the subgroup analysis showed that a >24 h delay was associated with high ORs of perforated appendicitis (OR: 1.65, 95% CI: 1.21, 2.23), with high heterogeneity among the studies ($I^2=85\%$, $P<0.00001$). When subgroup analysis was performed on the basis of the preoperative stage included, the ORs of complicated appendicitis with a hospital delay >24 h was higher than that of a hospital delay between 0 and 24 h in the subgroup with a preoperative diagnosis of uncomplicated appendicitis (OR: 5.09, 95% CI: 1.95, 13.30),

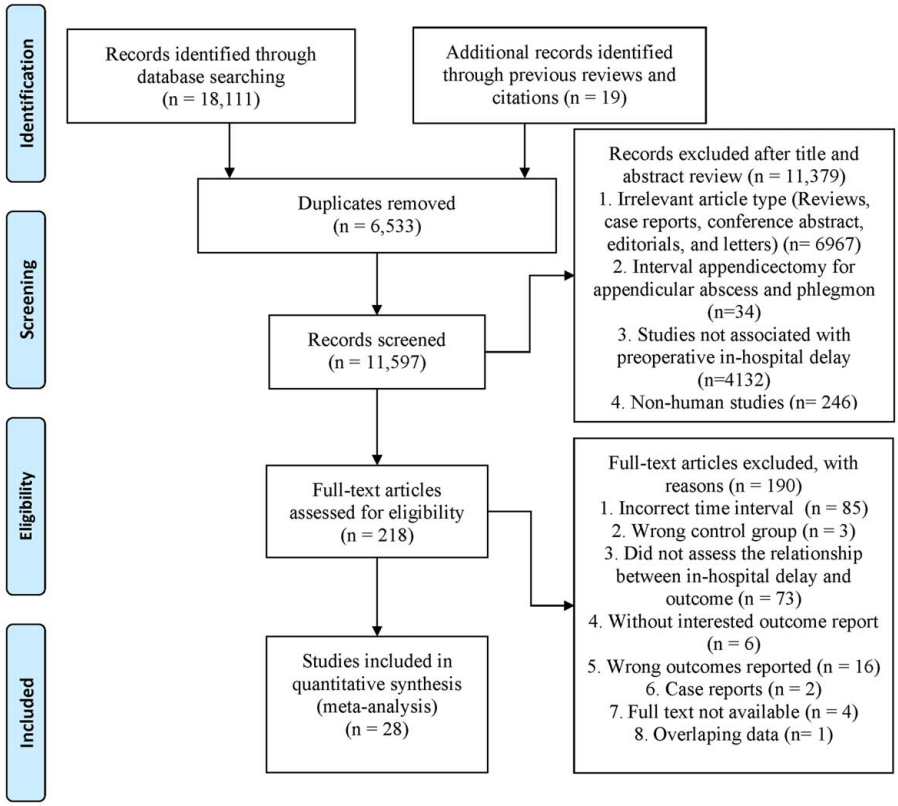

Figure 1. Screening flow chart.

Table 1

Study characteristics of the 28 included studies.

First author, year	Design	Setting	Male	Age	Sample size	In-hospital delay	Complicated appendicitis	Preoperative stage included	Outcome
Walker 1995	Prospective	UK	118 (65.2%)	6–81	181	Admission to surgery	Perforated	No restriction	Complicated appendicitis, mortality
Eldar 1997	Retrospective	Israel	197 (54.1%)	5–85	364	ED to surgery	Perforated or gangrenous	No restriction	Complicated appendicitis
Hale 1997	Retrospective	Worldwide	3184 (75.1%)	0.5–82	4297	Admission to surgery	Perforated	No restriction	Complicated appendicitis
Bachoo 2001	Prospective	UK	225 (50%)	Children	450	Admission to surgery	Unclear	No restriction	Surgical-site infection, all complications
Maroju 2004	Prospective	India	86 (77.5%)	13–56	111	ED to decision to operate	Perforated or gangrenous	No restriction	Complicated appendicitis
Omundsen 2006	Retrospective	New Zealand	216 (62.6%)	7–80	345	Admission to surgery	Perforated	No restriction	Surgical-site infection, all complications, mortality
Sheu 2007	Retrospective	China	288 (47.9%)	60–97	601	ED to surgery	Perforated	No restriction	Complicated appendicitis
Hansson 2008	Prospective	Sweden	141 (55.7%)	>1	253	Admission to surgery	Perforated	No restriction	Complicated appendicitis
Kearney 2008	Retrospective	Ireland	78 (67.8%)	>16	115	ED to surgery	Perforated	No restriction	Complicated appendicitis
Busch 2011	Retrospective	Switzerland	984 (58.7%)	>16	1675	Admission to surgery	Perforated	No restriction	Complicated appendicitis, surgical-site infection
Teixeira 2012	Retrospective	USA	2745 (70.4%)	No restriction	3898	Admission to surgery	Perforated	No restriction	Complicated appendicitis, surgical-site infection, mortality
Giraudo 2013	Retrospective	Italy	343 (47.4%)	3–90	723	ED to surgery	Gangrenous	No restriction	Complicated appendicitis, all complications, mortality
Bhangu 2014	Prospective	Worldwide	1428 (56.9%)	No restriction	2510	ED to skin incision	Perforated or gangrenous	No restriction	Complicated appendicitis
Bonadio 2015	Retrospective	USA	149 (60.1%)	<18	248	ED to surgery	Perforated	Uncomplicated	Complicated appendicitis, mortality
Chen 2015	Retrospective	China	133 (56.4%)	No restriction	236	ED to surgery	Perforated	No restriction	Complicated appendicitis, all complications, mortality
Fair 2015	Retrospective	USA	34083 (48.7%)	No restriction	69926	Diagnosis to surgery	Unclear	No restriction	All complications, mortality
Al-Qurayshi 2016	Retrospective	USA	149742 (56.3%)	No restriction	265972	Admission to surgery	Unclear	No restriction	All complications
Almström 2017	Retrospective	Sweden	1641 (59.5%)	≤ 15	2756	ED to skin incision	Perforated	No restriction	Complicated appendicitis, surgical-site infection
Andert 2017	Retrospective	Germany	1039 (48.6%)	No restriction	2136	Admission to surgery	Perforated or gangrenous	No restriction	All complications, mortality
Alore 2018	Retrospective	USA	58364 (52.1%)	No restriction	112122	Admission to surgery	Perforated	No restriction	All complications, surgical-site infection, mortality
Patel 2018	Retrospective	Canada	12507 (49%)	>18	25517	ED to surgery	Perforated	No restriction	All complications
Meschino 2019	Retrospective	Canada	NA	Adult	336	Admission to surgery	Perforated	No restriction	All complications, mortality
Canal 2020	Retrospective	Switzerland	4999 (54.2%)	No restriction	9224	Admission to surgery	Perforated or rupture	No restriction	Complicated appendicitis, all complications
Lastunen 2021	Retrospective	Finland	402 (48%)	≥ 18	837	CT to surgery	Perforated	Uncomplicated	Complicated appendicitis
Yeh 2021	Prospective	USA	1668 (53.7%)	≥ 18	3108	ED to surgery	Perforated	No restriction	Complicated appendicitis
Ashkenazi 2022	Retrospective	Israel	1741 (63.3%)	0.5–92	2749	ED to surgery	Perforated or gangrenous	No restriction	Complicated appendicitis
Kabir 2022	Retrospective	Singapore	328 (52.8%)	No restriction	621	Admission to skin incision	Perforated	No restriction	Complicated appendicitis, all complications
Laverde 2023	Retrospective	Germany	747 (47.6%)	≥ 18	1570	First clinical examination to the first incision	Perforated or gangrenous	No restriction	All complications, mortality

CT, computed tomography; ED, emergency department.

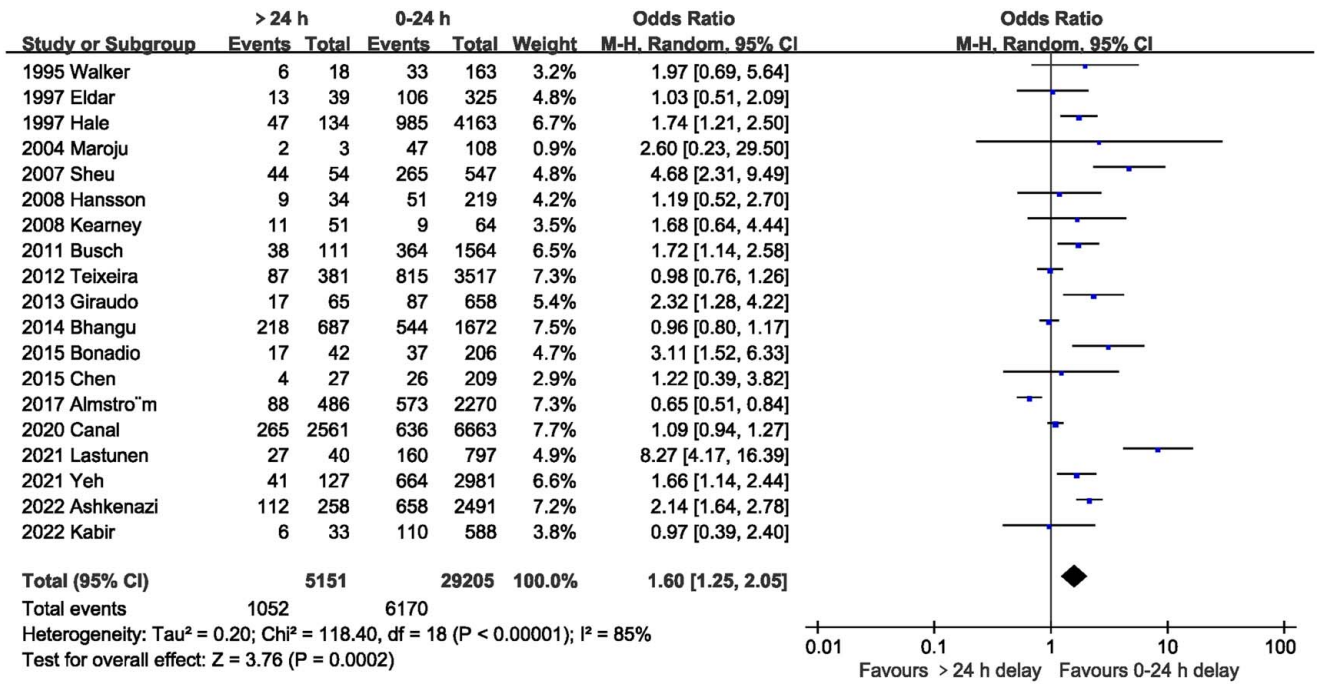

Figure 2. Effect of preoperative in-hospital delay > 24 h on complicated appendicitis.

with high heterogeneity among the studies ($I^2 = 74\%$; $P = 0.05$) (Supplementary Table S4, Supplemental Digital Content 6, http://links.lww.com/JS9/D63).

Postoperative morbidity

The association between in-hospital delays of > 24 h and total postoperative complications was reported in 13 studies[1,9,21,23,29,32–37,41,42], and the combined results showed an in-hospital delay of > 24 h significantly increased the ORs of total postoperative complications compared with an in-hospital delay of 0–24 h (OR: 1.51, 95% CI: 1.30, 1.75, $P < 0.00001$), with significant heterogeneity among the studies ($I^2 = 90\%$, $P < 0.00001$) (Fig. 3). Five studies[8,21,23,28,36] provided data on postoperative SSI with a > 24 h of delay, and there was no significant difference in the ORs between delays of between 0–24 and > 24 h (OR: 1.04, 95% CI: 0.97, 1.12), with no significant heterogeneity observed among studies ($I^2 = 0\%$, $P = 0.61$) (Fig. 4).

Mortality

Mortality was reported in 10 studies[18,23,28,29,31–33,35–37], and no deaths were observed in five studies. However, a delay of > 24 h was associated with increased postoperative mortality (OR: 1.81, 95% CI: 1.33, 2.45, $P = 0.0001$). Furthermore, the heterogeneity was low ($I^2 = 29\%$, $P = 0.23$) (Fig. 5).

Publication bias and sensitivity analysis

According to the funnel plots and Egger's tests (Fig. 6), no evidence of publication bias was found for total postoperative complications. Egger's tests indicated publication bias for complicated appendicitis. After the trim and fill procedure, the results for complicated appendicitis did not change significantly. The results of the sensitivity analysis are summarized in Supplementary Table S5 (Supplemental Digital Content 7, http://links.lww.com/JS9/D64). Briefly, the analysis showed that no single study affected the heterogeneity and overall effect size of complicated appendicitis, total postoperative complications, SSI, and mortality.

Table 2

Summary of results from all outcomes.

							Heterogeneity	
Indicators (> 24 h vs. 0–24 h)	**Number of studies**	**Events for delay**	**Events for control**	**Effect size**	**95% CI**	***P***	I^2	***P***
Complicated appendicitis	19	1052/5151	6170/29205	1.60	1.25, 2.05	0.0002	85%	< 0.00001
Total postoperative complications	13	6965/89685	28582/399853	1.51	1.30, 1.75	< 0.00001	90%	< 0.00001
Surgical-site infection	5	991/26150	3403/93421	1.04	0.97, 1.12	0.25	0%	0.61
Postoperative morbidity	10	61/40443	125/150068	1.81	1.33, 2.45	0.0001	29%	0.23

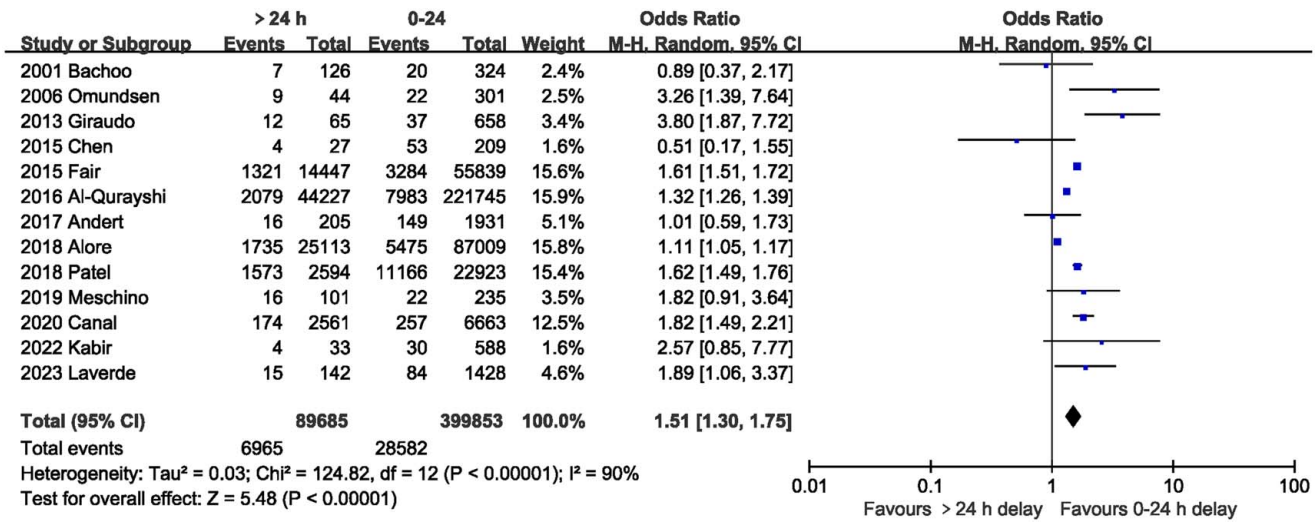

Figure 3. Effect of preoperative in-hospital delay > 24 h on total postoperative complications.

Discussion

Despite numerous previous studies on the effects of delayed surgery after hospital admission for acute appendicitis, there is still no consensus on the timing of surgery for acute appendicitis. Our meta-analysis suggests that in-hospital delays of > 24 h are associated with an increased risk of complicated appendicitis, total postoperative complications, and mortality. In addition, the results of the subgroup analysis indicated that a delay in admission > 24 h was a risk factor for appendicitis perforation.

The traditional disease model assumes that acute appendicitis progresses from a simple to a complicated condition. Therefore, the risk of appendiceal perforation may increase with delays in surgery[5]. According to the guidelines updated in Jerusalem in 2020, hospital delays of > 24 h are associated with poor outcomes, and therefore, these delays should not exceed 24 h[11]. However, Bhangu[30] included 14 observational studies in a meta-analysis in 2014, using 12 h as a time interval to compare the risk of complicated appendicitis with delays of between 0–12 and 12–24 h, and the results showed that a delay of 12–24 h did not increase the risk of complicated appendicitis. A subsequent 2018 update by Li *et al.*[4] showed that an in-hospital delay of 6–12 h did not increase the risk of complicated appendicitis but that a delay of 6–12 h was associated with an increased risk of postoperative SSI (OR: 1.40, 95% CI: 1.11–1.77, $P = 0.004$). However, neither study assessed whether in-hospital delays of > 24 h were associated with the risk of complicated appendicitis. Similarly, van Dijk *et al.*[12] included evidence from studies conducted between 1990 and 2016, suggesting that delayed appendectomy performed within 24 h of hospital admission was not a risk factor for complicated appendicitis, SSI, and morbidity. The meta-analysis noted, however, that because of the large uncertainty of results in the literature, it is unclear whether in-hospital delays of > 24 h affect surgical outcomes. Our results, based on currently published data, suggest that in-hospital delays of > 24 h should be avoided because they are associated with an increased risk of complicated appendicitis and increased postoperative morbidity. These inconsistencies may be related to differences in the length of the delay, as the traditional theory is that acute appendicitis progresses from a simple to a complex form over time[5]. Therefore, a short delay may not increase postoperative morbidity and mortality, whereas a longer delay may be associated with a poorer prognosis. This is consistent with a large number of previous studies. Kovler *et al.*[5] found that the incidences of complicated appendicitis with delays of 0–3, 4–7, 8–11, and 12–15 h in hospital were 27.1, 26.1, 25.9, and 26.7%, respectively. When the delay reached 16–24 h, the incidence of complicated appendicitis increased to 30.3%. A post-hoc analysis

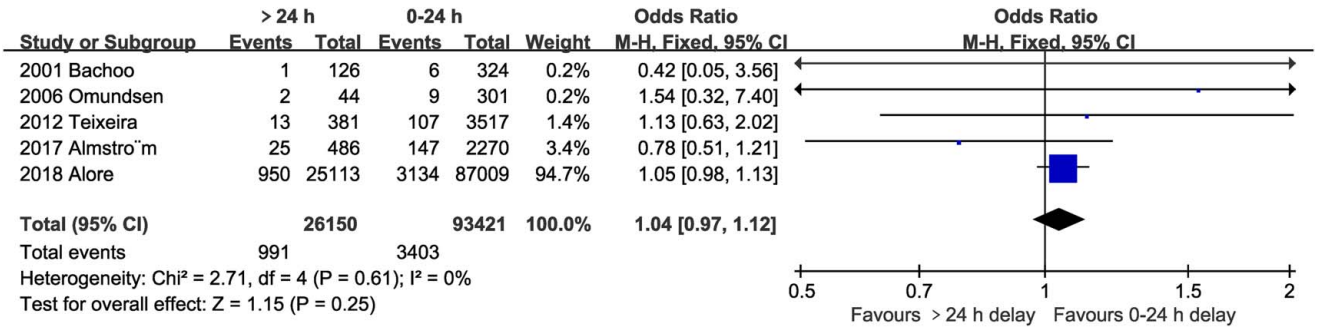

Figure 4. Effect of preoperative in-hospital delay > 24 h on surgical-site infection.

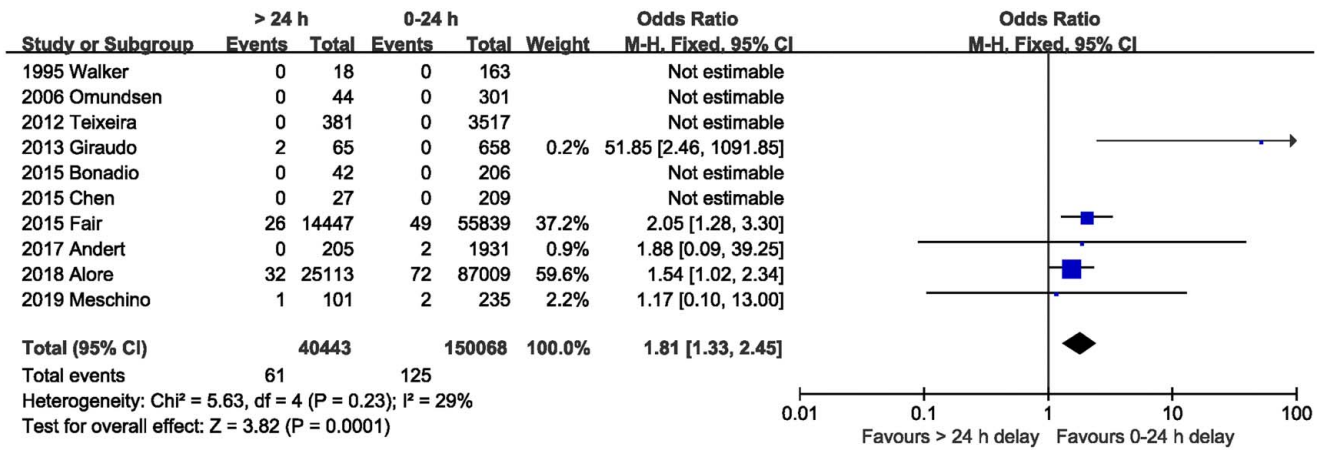

Figure 5. Effect of preoperative in-hospital delay > 24 h on mortality.

of a recent RCT by Jalava *et al.*[43] found that perforation risk may increase with delays close to or beyond 24 h. A national cohort study of 683 590 patients showed a perforation rate of 28.8% during appendectomy on the day of admission; this increased to 33.3% on day 2 and 78.8% on day 8[44]. Similarly, a meta-analysis of 21 studies by Li *et al.*[4] showed that patients with a delay of 24 48 h were 1.99 and 1.84 times more likely to develop complicated appendicitis than patients with a prehospital delay and a total delay of <24 h, respectively. Interestingly, the results of the subgroup analysis suggest that a delay in admission of > 24 h is also a risk factor for appendicitis perforation. In addition, two of the included studies excluded patients with a preoperative diagnosis of complicated appendicitis. We separately performed a subgroup analysis of studies that included only preoperative assessments of uncomplicated appendicitis, and the results still showed that a delay in hospitalization > 24 h increased the risk of complicated appendicitis. Therefore, our study has important clinical implications, and we provide the first evidence to support the recommendation of the guidelines – that in-hospital delays should not exceed 24 h.

In addition to a higher incidence of complicated appendicitis, our study observed a higher risk of postoperative complications in the group with in-hospital delays > 24 h than in the group with a 0–24 h in-hospital delay. A multicenter prospective study by Yeh *et al.*[39] showed that adverse clinical outcomes, including higher postoperative morbidity, re-intervention, and incision infection rates, were more common in complicated appendicitis than in uncomplicated appendicitis. Therefore, the increased risk of postoperative complications may be associated with a higher incidence of complicated appendicitis in the > 24 h delay group. In addition, delaying surgery may increase exposure to colon bacteria, which increases the risk of deep-space infections[45]. The increase in the incidence of complicated appendicitis and postoperative morbidity may further translate into increased hospital costs and longer hospital stays. It is estimated that the cost of hospitalization for perforated appendicitis with an abscess is almost twice that for simple appendicitis[45,46]. Serres *et al.*[47] found that in-hospital delay is an independent factor affecting hospitalization costs. Therefore, in-hospital delays may increase the financial burden. In addition, although the meta-analysis showed that in-hospital delays > 24 h did not increase the risk of

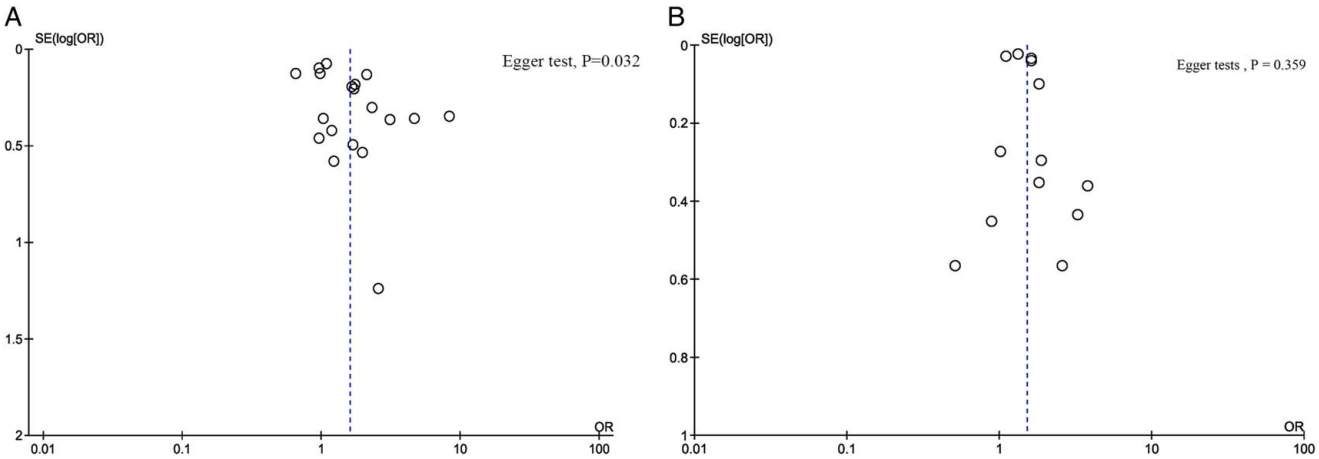

Figure 6. Funnel plots of the effect of an in-hospital > 24 h on (A) complicated appendicitis and (B) total postoperative complications.

postoperative SSI, this was based on evidence from five studies; thus, more studies are needed to further evaluate the effect of in-hospital delays > 24 h on SSI. Notably, although mortality after appendectomy is low, our results suggest that in-hospital delays of > 24 h are still associated with an increased risk of death (OR: 1.81). Therefore, to reduce the risk of death after appendectomy, clinicians should try to avoid > 24 h delays in clinical practice.

Sleep deprivation and fatigue can lead to reduced cognitive ability and surgical performance[48]. Some studies have suggested that night surgery may negatively affect noncardiac surgery outcomes[49,50]. Those who support delayed surgery in hospitals argue that delaying appendectomy from night to day minimizes sleep deprivation and fatigue on the night surgical team[41,51]. However, performing the procedure at night did not seem to affect the outcome of appendectomy. A prospective study conducted by Schuster *et al.*[52]. at five different hospitals found similar outcomes for surgeries performed by sleep-deprived emergency surgeons and fully rested surgeons. A nationwide cohort study by Canal *et al.*[1]. showed that appendectomies performed at night did not have any significant effect on complications or mortality compared with those performed during the day. In addition, several retrospective studies[51,53–55] have confirmed that the surgical outcomes of night and day appendectomies are comparable, and delaying appendectomy is not recommended. Therefore, delayed appendectomy after admission was unnecessary.

Our results highlight the potential harm to patients caused by delayed in-hospital surgery. These findings have important implications in terms of decision-making by surgeons and operating room staffing and workflow. In clinical practice, surgeons need to avoid unnecessary surgical delays as much as possible. In addition, several variables, such as prehospital delay, antibiotics, age (e.g. the elderly), and comorbidities, may play an important role in the pathological progression of acute appendicitis. Future research on this topic needs to balance the influence of these factors. In addition, further investigation of the factors associated with delayed in-hospital surgery is necessary in the future, and improving these factors may help improve the prognosis of patients with acute appendicitis. Delayed in-hospital surgery may be related to delayed diagnosis after admission, availability of operating rooms, and lack of medical resources. Busch and colleagues noted that in-hospital delays are more common in large institutions. This may be due to the high number of emergency cases and the complex and lengthy procedures. In addition, appendicitis generally receives a lower priority than neurological conditions, trauma, and vascular emergencies[27]. The acute surgical unit model may provide a solution to this problem. Hannan and El-Masry[56] found that acute surgical unit reduced the time from admission to surgery by 8 h and reduced the incidence of postoperative complications. In addition, Aubry *et al.*[57] reported 194 patients who had appendectomies in the 24-h emergency outpatient surgery unit, demonstrating the safety and feasibility of 24-h emergency outpatient surgery. A separate emergency outpatient unit allows patients with appendicitis not to compete with other emergency patients for limited medical resources and may help reduce surgical delays. The American College of Surgeons Pediatric National Surgical Quality Improvement Program Procedure Targeted Results from the Appendectomy database suggest that women and minority patients are more likely to have delayed surgery[5], probably because younger women require more time for an extensive differential diagnosis[5]. In addition, surgery is often delayed in the elderly because of delayed diagnosis[27]. In recent years, artificial intelligence has become a transformative tool in the medical field, offering great potential for improving the diagnosis and management of disease. The application of artificial intelligence is expected to improve the accuracy and speed of diagnosis of acute appendicitis[58]. The lack of medical resources in some remote areas may be the reason why ethnic minorities delay surgery[5], and future social progress is needed to facilitate access to surgical services for people in poor areas.

This study has several strengths. On the one hand, our meta-analysis includes the most comprehensive analysis of evidence to date on the outcomes of in-hospital delays > 24 h on acute appendicitis, collating all recent publications. On the other hand, the results of sensitivity analyses also confirm the robustness of our results.

This meta-analysis has several limitations. First, clinically ill patients are more likely to have complicated appendicitis and may experience shorter preoperative delays, which can lead to potential bias[12]. However, we still observed that the in-hospital delay group (> 24 h) was more likely to have adverse surgical outcomes. Second, our study did not consider the effect of prehospital delay, and substantial evidence supports prehospital delay and total delay as risk factors for complicated appendicitis[4,59,60]. However, none of the included studies provided data on preoperative delays. Therefore, the effect of prehospital delay on the outcomes could not be further assessed. Furthermore, some of our findings were highly heterogeneous, which may be due to the inclusion of different populations (children, adults, and elders) and different definitions of complicated appendicitis and in-hospital delays (admission to surgery, emergency department to surgery, and diagnosis to surgery). Although we performed subgroup analyses on the basis of age, definitions of complicated appendicitis, and preoperative stage included, we did not find the source of heterogeneity. Moreover, the subgroup analysis showed that a delay of > 24 h did not increase the risk of complicated appendicitis in the subgroup of children. Since this result is based on data from two studies, the effect of in-hospital delay on appendicitis in children is unclear, and more research is needed to further explore this topic. Finally, antibiotics are an important adjuvant treatment strategy for appendicitis and may affect the incidence of complicated appendicitis and postoperative morbidity[4,5,61]. However, as few studies have reported the duration and dosage of antibiotics, a subgroup analysis based on antibiotic use was not possible.

Conclusions

In summary, this meta-analysis suggests that in-hospital delay has a negative impact on the prognosis after appendectomy. A delay of > 24 h is a risk factor for complicated appendicitis, total postoperative complications, and mortality. Therefore, preoperative in-hospital delays of > 24 h should be avoided. Given the methodological limitations of the included studies, high-quality prospective studies are required to confirm these conclusions. Our study may help clinicians rationally time surgeries for appendicitis to reduce the risk of complicated appendicitis, postoperative complications, and mortality.

Ethical approval

Not applicable.

Consent

This meta-analysis was based on former studies, and consent was not required in this meta-analysis.

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Author contribution

G.T., L.Y.Z., R.C., and L.Y.X.: designed the study. G.T. and J.Z.: designed and conducted the search strategy. G.T., L.Y.Z., and J.Z.: screened the studies for eligibility, completed the data extraction, and assessed the risk of bias. G.T., L.Y.Z., R.C., and R.X.Z.: analyzed the data. G.T.: wrote the manuscript in consultation with L.Y.Z. and L.Y.X.. R.C., J.Z., and R.X.Z.: supervised the project. All authors discussed the results and contributed to the final manuscript. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

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Guarantor

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Data availability statement

The raw data were all collected in the included studies. We declare the authenticity of the data.

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