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SCIENTIFIC REVIEW

Mortality Following Appendicectomy in Patients with Liver Cirrhosis: A Systematic Review and Meta-Analysis

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Abstract

Introduction With the global prevalence of liver cirrhosis rising, this systematic review aimed to define the perioperative risk of mortality in these patients following appendicectomy.

Methods Systematic searches of Medline, EMBASE, Cochrane Library databases, ICTRP, and Clinical trials.gov were undertaken to identify studies including patients with cirrhosis undergoing appendicectomy, published since database inception to March 2021. Studies had to report mortality. Two review authors independently identified eligible studies and extracted data. Pooled analysis of in-patient and 30-day mortality was performed.

Results Of the 948 studies identified, four were included and this comprised three nationwide database studies (USA and Denmark) and one multi-centre observational study (Japan). A total of 923 patients had cirrhosis and 167,211 patients did not. In-patient mortality ranged from 0 to 1.7% in patients with cirrhosis and 0.17 to 0.3% in patients without. 30-day mortality was 9% in patients with cirrhosis compared to 0.3% in those without. One study stratified cirrhotic patients into compensated and decompensated groups. In patients with compensated cirrhosis, mortality following laparoscopic appendicectomy (0.5%) was significantly lower than open appendicectomy (3.2%). The meta-analysis highlighted a tenfold increase in perioperative mortality in cirrhotic patients (OR 9.92 (95% CI 4.67 to 21.06, I2 = 28%). All studies reported an increased length of stay in patients with cirrhosis.

Conclusion This review suggests that appendicectomy in the cirrhotic population is associated with increased mortality. LA may be safer in this population. Lack of information on cirrhosis severity and failure to control for age and co-morbidities make the results difficult to interpret. Further large population-based studies are required.

Introduction

Appendicitis is the most common abdominal surgical emergency worldwide, with a lifetime risk of approximately 8.6% for males and 6.7% for females [1]. Since 1990, the global incidence of appendicitis has increased by 11.4%, with 17.7 million cases reported in 2019 [2]. A recent meta-analysis highlighted global variation, with an incidence of 100 per 100,000 person-years in North America, compared to 151 per 100,000 person-years in Western Europe [3].

In the general population, appendicectomy is considered a safe procedure with a 0.08% mortality rate for non-

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perforated appendicitis, increasing to 0.5% for perforated appendicitis [4]. The risk of complications following appendicectomy is approximately 10% [5] with a 4% risk of surgical wound infection, and a 0.4% risk of bleeding requiring transfusion [6–8].

Liver cirrhosis is a major cause of morbidity and mortality, accounting for 2% of deaths annually making it the 11th most common cause of mortality worldwide. In the UK, cirrhosis is increasing at a faster rate than the four most commonly diagnosed cancers [9] and in the US, hospital admissions related to cirrhosis have increased year on year [10]. The reasons underlying the rise in cirrhosis are mainly attributed to increases in alcohol consumption, obesity, and viral hepatitis [11, 12].

With the increasing prevalence of cirrhosis, it is likely that surgeons will encounter this cohort of patients more frequently. In patients with cirrhosis, it is established that emergency surgery is associated with significantly longer post-operative hospital length of stay and higher morbidity, and mortality [13–15]. However, most data regarding appendicitis derives from retrospective cohort studies, with conflicting rates of complications and mortality. For example, a Danish nationwide database study found an eight-fold increase in mortality in patients with cirrhosis [16] whereas a USA nationwide database study found no difference [17]. Consequently, decision-making in daily practice remains unclear. There are no prospective randomized studies to accurately select patients with cirrhosis for open or laparoscopic appendicectomy, or conservative management with antibiotics. This may mean that clinicians and patients are not able to make fully informed decisions regarding treatment.

The aim of this systematic review and meta-analysis is to identify the available evidence, critically appraise it, and synthesize the findings to further understand the risk of post-operative complications, length of stay, and mortality in patients with cirrhosis undergoing appendicectomy.

Methods

This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [18].

Literature search

Systematic searches of Medline, EMBASE, Cochrane Library databases, WHO International Clinical Trials Registry Platform (ICTRP), and Clinical trials.gov were undertaken to identify studies reporting post-operative outcomes in patients with liver cirrhosis, published from database inception to March 2021. Open or laparoscopic appendicectomy was considered. The detailed search strategy is presented in Supplementary Material, Appendix 1. The following keywords, mapped to corresponding Medline subject headings, were used to search for relevant studies: appendix, appendicitis, appendicectomy, appendectomy, and liver cirrhosis. Hand searches of thesis repositories and reference lists of relevant studies were undertaken to ensure comprehensive inclusion.

Inclusion criteria

The titles and abstracts of studies identified from the searches were screened for suitability independently by two authors (AR and AG) and any discordant articles adjudicated by a third author (AA). For a study to meet the eligibility criteria, it had to include adult human subjects, reporting on patients with liver cirrhosis, undergoing appendicectomy. The studies had to report on in-patient or 30-day mortality as an outcome.

Exclusion criteria

Studies reporting liver surgery, liver transplant, or shunt-related surgery were excluded. Studies on liver disease in children were also excluded. Animal studies, case reports and case series (defined as number of study participants <10), meeting abstracts, letters, comments, and editorials were excluded. No language limitation was applied.

Data extraction

Data were extracted by two reviewers independently into predefined templates and adjudicated by a third reviewer, to resolve any discrepancies. Data was collected for type of study, study period, country of origin, and number of patients in the respective studies. For population-based studies, the databases used were also recorded.

The primary outcome was in-patient or 30-day post-operative mortality. Secondary outcomes were hospital length of stay, and post-operative complications including pneumonia, urinary tract infection, surgical site infection, wound bleeding, venous thromboembolism, upper gastro-intestinal bleeding, and C. difficile infection.

Risk of bias

The level of evidence of each paper was established on the basis of the Oxford Centre for Evidence-Based Medicine Level of Evidence scale. Risk of bias from included non-randomized studies was analysed independently by two review authors (AR and AG) using the Newcastle–Ottawa Scale quality assessment.

Statistical analysis

To quantify the risk of mortality following appendicectomy, the total number of in-hospital and 30-day deaths in cirrhotic and non-cirrhotic patients, as reported per study, were pooled. Meta-analysis of the pooled data was performed using Review Manager (RevMan) [computer program], version 5.4. For mortality (dichotomous outcome), the odds ratio (OR) was calculated with 95% confidence intervals (CI). A random-effects model was utilised to account for the anticipated clinical and statistical heterogeneity of the included studies. The amount of statistical heterogeneity of the included studies was evaluated using the I2 statistic. An $I2 < 25\%$ was considered to indicate low heterogeneity and an $I2 > 75\%$ to indicate high statistical heterogeneity [19].

Protocol registration

The protocol was registered with the PROSPERO database (www.crd.york.ac.uk/prospero)—registration number: CRD42021240728.

Results

Selection of studies

A total of 948 studies were identified through database-searching, with a further 14 from hand-searching (Fig. 1). After removing duplicates, 808 titles and abstracts were screened. A total of 796 studies were excluded, and 12 full-text articles were assessed for eligibility. Of these, three were reviews [20–22], three did not specify the severity of liver disease [23–25], one had fewer than 10 patients that underwent appendicectomy [26] and one did not specify the number of patients who underwent appendicectomy [27]. Four studies [16, 17, 28, 29] met the inclusion criteria.

Characteristics of included studies

The studies span an 18-year period from 2001 to 2019. Two studies were undertaken in the USA [17, 29], one in Denmark [16], and one in Japan [28]. Three were nationwide database studies [16, 17, 29], and one, a retrospective observational study undertaken at two centres [28] (Table 1).

Patient characteristics

The total number of patients included was 168,134. There were 923 (0.5%) patients with cirrhosis and 167,211 (99.5%) without cirrhosis. From the data available, 56,654 (51.9%) patients were male and 52,417 (48.1%) were female. The treatment options in each study differed. Garci et al., included open appendicectomy (OA), laparoscopic appendicectomy (LA), and non-operative management (NOM). Tsugawa et al., included OA or LA, and Al-Azzawi et al., included LA only. Poulsen et al., did not specify the method of appendicectomy. In patients with cirrhosis, 630 underwent LA (76.0%), 55 OA (6.6%) and 144 (17.4%) NOM. In patients without cirrhosis, 83,851 underwent LA (77.4%), 12,610 OA (11.7%) and 11,768 (10.9%) NOM.

Mortality outcomes, post-operative complications, and length of stay

Following appendicectomy, three studies reported in-patient mortality [17, 28, 29] which ranged from 0 to 1.7% in patients with cirrhosis and 0.17–0.3% in patients without cirrhosis.

The USA nationwide database study by Garcia et al., reported mortality stratified by intervention (non-operative management, NOM; open appendicectomy, OA; laparoscopic appendicectomy, LA) and severity of cirrhosis (compensated cirrhosis; decompensated cirrhosis). The highest rate of mortality was in patients with decompensated cirrhosis managed with NOM (9.5%, 6/63). In the remaining decompensated cirrhosis cohort, the mortality rates were 4.3%, (2/47) following LA and 4.2% (1/24) following OA. However, the difference between management strategies in patients with decompensated cirrhosis was not statistically significant. In patients with compensated cirrhosis, mortality following LA (0.5%, 1/192) was significantly lower than both OA (3.2%, 1/31) and NOM (3.7%, 3/81) ($p < 0.05$). A similar trend was also found in patients without cirrhosis, with LA (0.1%, 87/83,473) having a lower mortality rate compared to both OA (0.6%, 81/12,610) and NOM (2.5% 290/11,768) ($p < 0.05$).

The Danish nationwide database study by Poulsen et al., reported 30-day mortality. In the group with cirrhosis, mortality was 9% (6/69), compared to 0.3% (413/58,982) in the group without cirrhosis (Table 2).

The three studies reporting hospital length of stay (LOS) [17, 28, 29] demonstrated an increased LOS in patients with cirrhosis following appendicectomy. Al-Azzawi reported LOS in patients with cirrhosis as 1.52 days compared to 1.1 in patients without cirrhosis. Garci et al., reported that LOS for both decompensated cirrhosis (9.5 ± 10.5) and compensated cirrhosis (7.1 ± 15.9) were significantly longer than patients without cirrhosis (3.4 ± 4.7) ($p < 0.05$). When comparing surgical techniques in patients with cirrhosis, Tsugawa et al. reported a significantly longer LOS (14.5 ± 4.3) following OA compared to LA (8.2 ± 2.6) ($p < 0.05$). Garcia et al.

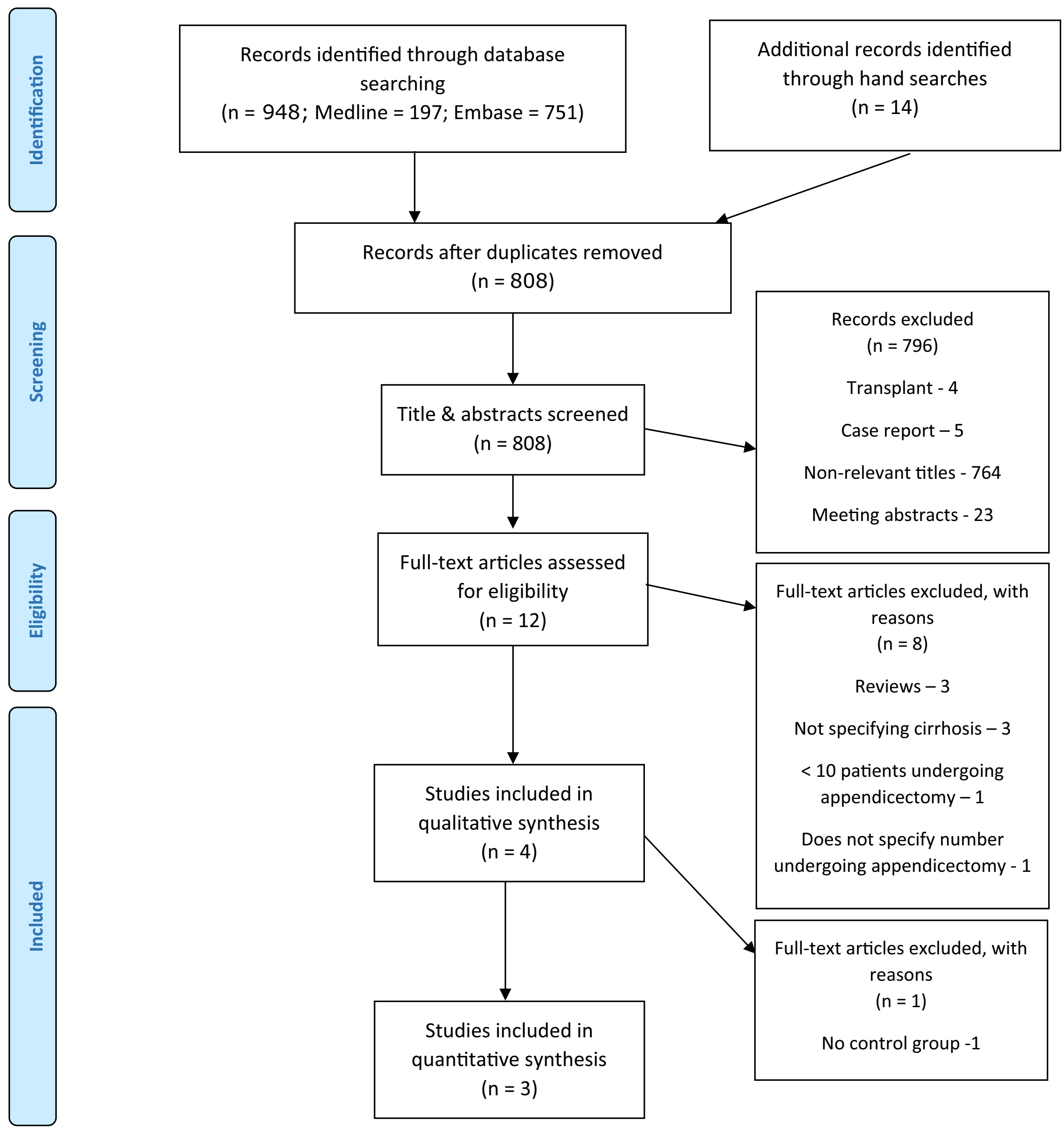


Fig. 1 PRISMA 2009 Flow Diagram

mirrored this trend in the decompensated cirrhosis cohort (OA 14.6 ± 11.7 vs. LA 6 ± 5.9, $p < 0.05$), compensated cirrhosis cohort (OA 11.8 ± 8.6 vs. LA 4.3 ± 4.1, $p < 0.05$), and in patients without cirrhosis (OA 4.8 ± 6.5 vs. LA 2.7 ± 3.1, $p < 0.05$).

Comparing patients with and without cirrhosis, Al-Azzawi et al., reported no significant difference in post-operative rates of pneumonia, urinary tract infections (UTI), surgical site infections (SSI), wound bleeding, pulmonary embolism (PE), C. difficile infections, or upper gastro-intestinal bleeding.

When comparing OA and LA in patients with cirrhosis, Tsugawa et al., showed a higher rate of SSI (OA 20.0%, 5/25 vs. LA 0%, 0/15) and wound bleeding (OA 20.0%, 5/25 vs. LA 0%, 0/15) in patients managed with OA ($p < 0.05$). Garcia et al., also report an increased incidence of SSI following OA in patients with compensated cirrhosis (OA 12.9%, 4/31 vs. LA 2.1%, 4/192), decompensated cirrhosis (OA 20.8%, 5/24 vs. LA 2.1%, 1/47), and patients without cirrhosis (OA 1.8%, 227/12,610 vs. LA 0.7%, 558/83,473) ($p < 0.05$).

Table 1 Characteristics of included studies

Author (year)	Country	Database used and years included	Total number of participants	Sex Male n (%) Female n (%)	Number of participants with cirrhosis	Severity of cirrhosis n (%)	Number of participants without cirrhosis (n)	Method of surgery (n)	Definition of mortality	Secondary outcomes reported	Number of centres	Risk of bias (Newcastle–Ottawa Scale)
Nationwide database studies												
Al-Azzawi et al. (2018)	USA	NIS (2010)	754	334 (44) 420 (56)	376	Not recorded	378	LA (754)	In-patient	LOS, Pneumonia, SSI, UTI, wound bleeding, PE, C. diff, UGIB	Nationwide	****** Medium risk
Garcia et al. (2019)	USA	NIS (2012–2014)	108,289	56,293 (52) 51,984 (48)	438	CC 304, (69) DC 134 (31)	107,851	OA (12,665) LA (83,712) NOM (11,912)	In-patient	LOS, SSI, VTE, UTI	Nationwide	******* Low risk
Poulsen et al. (2000)	Denmark	DNRP (1977–1993)	59,051	Not available	69	Not recorded	58,982	Not recorded	30-day	N/a	Nationwide	***** Medium risk
Observational study												
Tsugawa et al. (2001)	Japan	40	27 (68) 13 (32)	40	CTP A 35 (87.5) B 5 (12.5) C 0	0	OA (25) LA (15)	Not recorded In-patient	LOS, SSI, wound bleeding, ileus, intra-abdominal abscess, UTI	Two centres	**** Medium risk	

NIS—Nationwide Inpatient Sample (United States of America). DNRP—Danish National Registry of Patients. CTP, Child-Turcotte-Pugh Classification. CC, Compensated Cirrhosis; DC, Decompensated Cirrhosis; OA, Open Appendicectomy; LA, Laparoscopic Appendicectomy; NOM, Non-Operative Management; SSI, Surgical Site Infection; UTI, Urinary Tract Infection; PE, Pulmonary Embolism; C. diff, Clostridium difficile infection; UGIB, Upper Gastro-intestinal Bleed; VTE, Venous Thromboembolism

Table 2 Outcomes of included studies

Author (year)	Mean Age ± SD (Cirrhosis)	Mean Age (without Cirrhosis)	Mortality, n (%) Cirrhosis vs without Cirrhosis	LOS ± SD (days) Cirrhosis vs without Cirrhosis	Complications, n (%)	p value	OR (95% CI)
Al-Azzawi et al. (2018)	46.68	43.75 (p = 0.54)	**In-patient** 2 (0.5) vs 1 (0.3) (p = .56, OR = 2, 95% CI: 0.18–22.3)	1.52 vs 1.1 (no SD)	**Cirrhosis versus No Cirrhosis**		
					Pneumonia 8 (2.1) vs 3 (0.8)	.142	2.72 (0.71–10.32)
					SSI 3 (0.8) vs 2 (0.5)	.652	1.52 (0.25–9.10)
					UTI 18 (4.8) vs 12 (3.2)	.26	1.53 (0.72–3.22)
					Wound bleeding 3 (0.8) vs 2 (0.5)	.65	1.51 (0.25–9.1)
					PE 1 (0.3) vs 0	.94	0 (0.03–0.8)
					C. diff 1 (0.3) vs 0	.99	0 (0.0–0.0)
					UGIB 3 (0.8) vs 1 (0.3)	.332	3.02 (0.3–29)
Garcia et al. (2019)	CC 56 ± 13 DC 55 ± 13 (Not significant)	NC 44 ± 18 (p < 0.05 NC vs CC and NC vs DC)	**In-patient** CC 5 (1.6) vs DC 9 (6.7) vs 458 (0.4) (p < 0.05 All pairs)	**Overall** CC 7.1 ± 15.9 vs DC 9.5 ± 10.5 vs 3.4 ± 4.7 (p < 0.05 NC vs CC and NC vs DC)	**NOM vs OA vs LA**		
					No Cirrhosis		
					SSI N/a vs 227 (1.8) vs 558 (0.7)	< 0.05	
					VTE 168 (1.4) vs 70 (0.6) vs 149 (0.2)	< 0.05 All pairs	
					UTI 752 (6.4) vs 475 (3.8) vs 2270 (2.7%)	< 0.05 All pairs	
					Compensated Cirrhosis		
					SSI N/a vs 4 (12.9) vs 4 (2.1)	< 0.05	
					VTE 1 (1.2) vs 0 (0) vs 1 (0.5%)	Not significant	
					UTI 12 (14.8) vs 5 (16.1) vs 10 (5.2)	< 0.05 NOM vs LA	
					Decompensated Cirrhosis		
					SSI N/a vs 5 (20.8) vs 1 (2.1)	< 0.05	
					VTE 1 (1.6) vs 1 (4.2) vs 1 (2.1)	Not significant	
					UTI 1 (1.6) vs 4 (16.7) vs 6 (12.8)	Not significant	

Table 2 continued

Author (year)	Mean Age ± SD (Cirrhosis)	Mean Age (without Cirrhosis)	Mortality, n (%) Cirrhosis vs without Cirrhosis	LOS ± SD (days) Cirrhosis vs without Cirrhosis	Complications, n (%)	*p* value	OR (95% CI)
Poulsen et al. (2000)	Not reported	Not reported	**30-day** 6 (9) vs 413 (0.7) Adjusted OR (age, sex, co-morbidity) = 8 (95% CI 3–20)	Not reported	Not reported		
Tsugawa et al. (2001)	OA 59.5 ± 11.5 LA 61.5 ± 8.5 (Not significant)	N/a	OA 0 vs LA 0	Cirrhotic OA 14.5 ± 4.3 vs Cirrhotic LA 8.2 ± 2.6) (p < 0.05)	**Cirrhotic OA vs Cirrhotic LA**		
					SSI 5 (20) vs 0	< 0.05	
					Wound bleeding 5 (20) vs 0	< 0.05	
					UTI 1 (4) vs 1 (6.7)	Not significant	

CC Compensated cirrhosis; *DC* Decompensated cirrhosis; *NC* No cirrhosis; *OA* Open appendicectomy; *LA* Laparoscopic appendicectomy; *NOM* Non-Operative management; *SSI* Surgical site infection; *UTI* Urinary tract infection; *PE* Pulmonary embolus; *VTE* Venous thromboembolism; C. diff, Clostridium difficile infection; *UGIB* Upper gastro-intestinal bleed; *OR* Odds ratio; *CI* Confidence interval

Meta-analysis

Mortality

All studies considered mortality as an outcome. The duration of follow-up in these studies ranged from in-hospital admission to 30 days post-operation. For the purpose of the meta-analysis, in-patient and 30-day mortality data were combined to calculate a pooled estimate. Patients undergoing NOM were excluded from the analysis. Due to the absence of a control group, results from Tsugawa et al. were excluded from the meta-analysis. Post-operative mortality for patients with cirrhosis was 1.76% (13/739) whereas for patients without cirrhosis it was 0.37% (582/155443). Compared with the control group, patients with cirrhosis had a significantly increased risk of mortality following appendicectomy (OR 9.92 (95% CI 4.67 to 21.06)), with a moderately-low heterogeneity between studies (I^2 28%) (Fig. 2).

There was insufficient data to undertake a meta-analysis of LOS or complications.

Risk of bias

Three of the included studies were nationwide population-based reports and one was a multi-centre observational study. The level of evidence of these studies was level II/III. Reasons for high risk of bias included a lack of using secure records (e.g. medical records) to ascertain a diagnosis of liver cirrhosis, failure to control for confounding

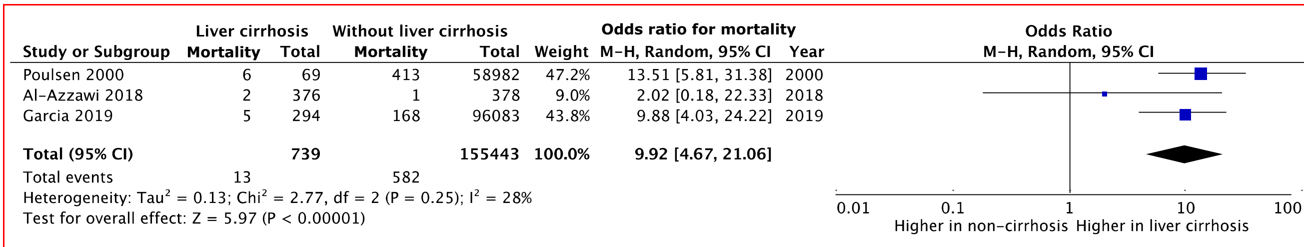


Fig. 2 Meta-analysis of the mortality following appendicectomy in patients with and without liver cirrhosis

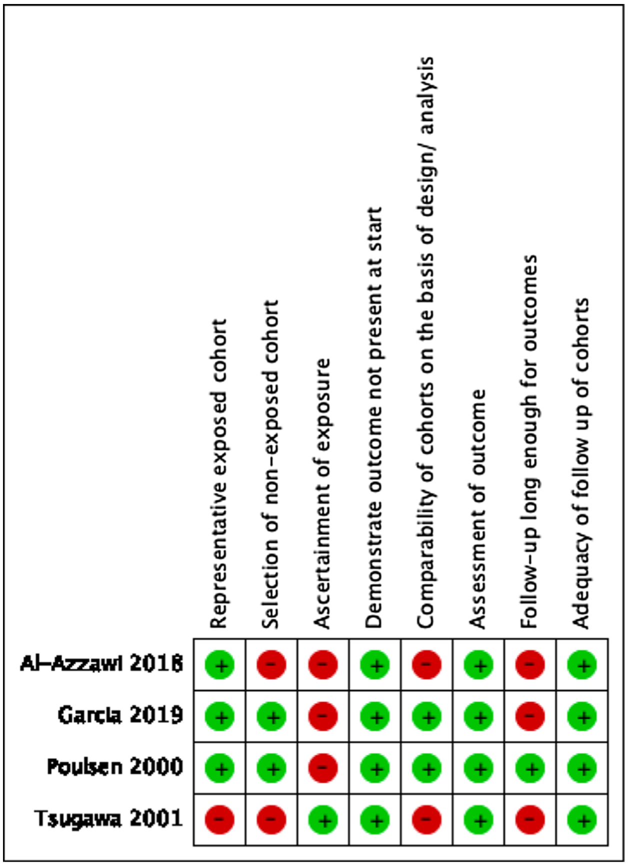


Fig. 3 Risk of bias summary: review authors' judgements about each risk of bias item for each included study

factors between the cirrhotic and non-cirrhotic group (e.g. age, ethnicity, co-morbidities), and short-follow-up time (Fig. 3).

Discussion

Following appendicectomy, in-patient mortality ranged from 0 to 1.7% in those with cirrhosis compared to 0.17–0.3% in those without. At 30-days, mortality was 9% in patients with cirrhosis compared to 0.3% in those without. Pooled in-patient and 30-day mortality indicated an almost tenfold increase in mortality in patients with cirrhosis.

All three studies measuring LOS reported increased LOS in patients with cirrhosis. This may be due to numerous factors, including increased risk of acute liver decompensation, fluid and electrolyte imbalance, and sepsis. Compared to patients without cirrhosis, Garcia et al. reported significantly higher rates of SSI in patients with compensated cirrhosis (2.1%) and decompensated cirrhosis (2.1%). This may be attributed to cirrhosis causing impaired immunity [30]. However, these figures are lower than the widely accepted 4% risk of SSI [7]. The two studies comparing LA and OA [28, 29], demonstrated higher rates of surgical site infection (SSI) in patients managed with OA, reflecting previous findings [31].

When accounting for all studies, patients with cirrhosis were more likely to undergo NOM (17.4%) compared to patients without cirrhosis (10.9%). Patients with high-risk characteristics (e.g. perforated appendix, co-morbidities, frailty) may have also been more likely to undergo NOM. This may account for the high mortality rate in patients with cirrhosis undergoing NOM (9.5%). In the light of the COVID-19 pandemic, there has been increasing interest in the potential for antibiotics in the treatment of appendicitis. Large studies have found NOM to be safe and effective in the short term, with fewer complications when compared to appendicectomy [32, 33]. Despite this, the available evidence demonstrates that this may not be the case for patients with cirrhosis.

Limitations

There is a limited evidence base, with four studies identified. Although the total number of patients included in the review was 168,134, only 0.5% of patients had cirrhosis, which further highlights a paucity of data. Despite the meta-analysis indicating increased mortality in patients with cirrhosis, there was a small number of deaths (1.76%) in this group suggesting operative intervention may be safe in comparison to NOM.

Many of the studies did not control for confounders (such as age or co-morbidities) between the cirrhotic and non-cirrhotic groups. No study accounted for the severity of appendicitis (e.g. uncomplicated or perforated) or severity of cirrhosis. Cirrhosis spans a spectrum of severity that can be categorised using prognostic tools such as the Child–Pugh score (CTP) [34]. A study evaluating mortality following abdominal surgery showed mortality rates of 2%, 12%, and 12% in CTP classes A, B, and C, respectively [26]. This highlights that operative mortality rises with increasing severity of liver disease. However, only one study [28] in the currently available literature, described patients using the CTP score. Yet this study did not report mortality based on CTP categories. Although Garcia et al. used two broad categories (compensated and decompensated cirrhosis) and demonstrated higher mortality in patients with decompensated cirrhosis, the study relied on the accuracy of ICD-9 clinical codes, rather than clinical information.

Tsugawa et al., specified that to be eligible for LA, there must be no evidence of adhesions, CTP class A or B, and no high-risk co-morbidities. This may result in selection bias with lower risk patients being selected for LA and in turn, account for the shorter LOS and lower complication rates.

With the longest follow-up period being 30-days, the studies may have underestimated mortality figures. A previous study evaluating mortality after general surgical procedures in patients with cirrhosis demonstrated an increase in mortality between 30 and 90 days, from 20% to almost 30% [35]. Consequently, our findings may underestimate the true risk of post-operative mortality and future studies evaluating surgical outcomes in the context of liver cirrhosis should use 90-day mortality.

The available studies span a period of twenty years, meaning that the data is unlikely to be contemporaneous. During this time, both surgical techniques and technology have advanced, as well as the management of cirrhosis.

Differences in follow-up time, severity of cirrhosis, and year of study are factors which could account for the heterogeneity between studies.

How this study fits with the literature

Emergency surgery in patients with cirrhosis is associated with a higher mortality rate than elective surgery [36, 37]. Despite appendicectomy being a minor procedure, the emergency nature may contribute to the raised mortality demonstrated in this review. Although not statistically significant, Garcia et al. showed the mortality in patients with compensated cirrhosis undergoing LA was only 0.5%, compared to 3.2% undergoing OA. This supports the notion that LA may be feasible for these patients and mirrors similar findings regarding laparoscopic cholecystectomy in patients with cirrhosis [20, 38], with shorter operative time, reduced complication rates, and reduced length of hospital stay.

LOS was greater in patients with cirrhosis, which mirrors other studies [39]. The longest LOS was 14.5 days in cirrhotic patients undergoing OA. This was reported in the Japanese nationwide study by Tsugawa et al. Shorter LOS figures were reported in the USA database studies. Global data shows the average LOS in 2017 was 16.2 days in Japan and 6.1 days in the USA [40]. Therefore, different healthcare practices across the globe may explain the differing LOS. Although Al-Azzawi et al. and Garcia et al. used the same USA nationwide database they reported dramatically different LOS data. This difference cannot be attributed to different healthcare practices but instead may be due to different inclusion criteria, sample sizes, or covariates [41].

Clinical significance

With the prevalence of cirrhosis rising [9], it is likely that surgeons will encounter this cohort of patients more frequently. This systematic review demonstrated increased post-operative mortality in patients with cirrhosis, with the highest rates in those with decompensated cirrhosis. To compound this, the findings also suggest higher rates of mortality are found in decompensated cirrhotic patients managed conservatively. This creates a double-edged sword for patients and healthcare professionals when deciding treatment options. However, taking a closer look at the data leads to the suggestion that laparoscopic appendicectomy may be a safer option in this population.

The studies report short-term outcomes and poorly defined cohorts, meaning the results are difficult to interpret. More contemporaneous data is required to evaluate the long-term impact of treatment options for cirrhotic patients with appendicitis. The increased mortality highlighted in the study should be examined with future datasets, before serving as a recommendation to surgeons.

Appendix1: Search Strategy

Database: Embase < 1974 to 2021 March 4 16 > , Ovid MEDLINE(R) < 1946 to March 4, 2021 >

(Liver cirrhosis or cirrhotic or ((liver or hepatic) and (cirrhosis or fibrosis or insufficiency or failure))).

AND

(appendix or appendicitis or appendicectomy or appendectomy).

Author contributions All authors had access to the data and contributed to the drafting of the paper.

Declarations

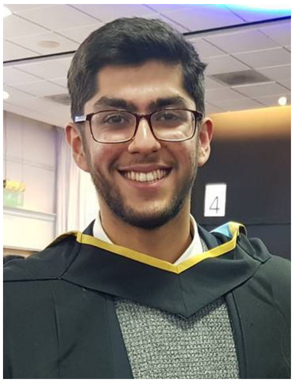
Conflict of interest None of the authors have any conflicts of interest to declare.

Ethical approval All authors complied with ethical requirements.

References

1. Huang T-H, Huang YC, Tu C-W (2013) Acute appendicitis or not: Facts and suggestions to reduce valueless surgery. J Acute Med 3(4):142–147
2. Wickramasinghe DP, Xavier C, Samarasekera DN (2021) The worldwide epidemiology of acute appendicitis: an analysis of the global health data exchange dataset. World J Surg 45(7):1999–2008. https://doi.org/10.1007/s00268-021-06077-5
3. Ferris M, Quan S, Kaplan BS et al (2017) The global incidence of appendicitis. Ann Surg 266(2):237–241
4. Blomqvist PG, Andersson REB, Granath F et al (2001) Mortality after appendectomy in Sweden, 1987–1996. Ann Surg 233(4):455–460

5. Ceresoli M, Zucchi A, Allievi N et al (2016) Acute appendicitis: Epidemiology, treatment and outcomes- analysis of 16544 consecutive cases. World J Gastrointest Surg 8(10):693–699
6. Addiss DG, Shaffer N, Fowler BS et al (1990) The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol 132(5):910–925
7. Magill SS, Edwards JR, Bamberg W et al (2014) Multistate point-prevalence survey of health care-associated infections. N Engl J Med 370(13):1198–1208
8. Vons C, Barry C, Maitre S et al (2011) Amoxicillin plus clavulanic acid versus appendicectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomised controlled trial. Lancet 377(9777):1573–1579
9. Ratib S, West J, Crooks CJ et al (2014) Diagnosis of liver cirrhosis in england, a cohort study, 1998–2009: a comparison with cancer. Am J Gastroenterol 109(2):190–198
10. Zou B, Yeo YH, Jeong D et al (2020) A nationwide study of inpatient admissions, mortality, and costs for patients with cirrhosis from 2005 to 2015 in the USA. Dig Dis Sci 65(5):1520–1528
11. Williams R, Aspinall R, Bellis M et al (2014) Addressing liver disease in the UK: a blueprint for attaining excellence in health care and reducing premature mortality from lifestyle issues of excess consumption of alcohol, obesity, and viral hepatitis. Lancet 384(9958):1953–1997
12. von Wulffen M, Clark PJ, Macdonald GA et al (2016) Liver-related mortality in countries of the developed world: an ecological study approach to explain the variability. Aliment Pharmacol Ther 44(1):68–77
13. de Goede B, Klitsie PJ, Lange JF et al (2012) Morbidity and mortality related to non-hepatic surgery in patients with liver cirrhosis; a systematic review. Best Pract Res Clin Gastroenterol 26(1):47–59
14. Rice HE (1997) Morbid prognostic features in patients with chronic liver failure undergoing nonhepatic surgery. Arch Surg 132(8):880–884
15. Garrison RN, Cryer HM, Polk HC et al (1984) Clarification of risk factors for abdominal operations in patients with hepatic cirrhosis. Ann Surg 199(6):648–655
16. Poulsen LO, Thulstrup AM, Sørensen HT et al (2000) Appendicectomy and perioperative mortality in patients with liver cirrhosis. Br J Surg 87(12):1664–1665
17. Al-Azzawi Y, Al-Abboodi Y, Fasullo M et al (2018) The morbidity and mortality of laparoscopic appendectomy in patients with cirrhosis. Clin Med Insights Gastroenterol 11:1179552217746645
18 Liberati A, Altman DG, Tetzlaff J et al (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 339:b2700
19. Melsen WG, Bootsma MCJ, Rovers MM et al (2014) The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. Clin Microbiol Infect 20(2):123–129
20. Adiamah A, Ban L, Hammond J et al (2020) Mortality after extrahepatic gastrointestinal and abdominal wall surgery in patients with alcoholic liver disease: A systematic review and meta-Analysis. Alcohol Alcohol 55(5):497–511
21. Bhangui P, Laurent A, Amathieu R et al (2012) Assessment of risk for non-hepatic surgery in cirrhotic patients. J Hepatol 57(4):874–884
22. Carpenter D, Liou P, Mathur A (2020) Management of patients with cirrhosis and portal hypertension requiring surgery. DDI 04(02):168–179
23. Taylor GA, Fagenson AM, Kuo LE et al (2021) Predicting operative outcomes in patients with liver disease: albumin-bilirubin score vs model for end-stage liver disease-sodium score. J Am Coll Surg 232(4):470–480
24. Ho VP, Schiltz NK, Reimer AP et al (2019) High-risk comorbidity combinations in older patients undergoing emergency general surgery. J Am Geriatr So 67(3):503–510
25. Kim MJ, Fleming FJ, Gunzler DD et al (2011) Laparoscopic appendectomy is safe and efficacious for the elderly: an analysis using the national surgical quality improvement project database. Surg Endosc 25(6):1802–1807
26. Telem DA, Schiano T, Goldstone R et al (2010) Factors that predict outcome of abdominal operations in patients with advanced cirrhosis. Clin Gastroenterol Hepatol 8(5):451–457
27 Hemida K (2016) Prediction of post-operative mortality in patients with HCV-related cirrhosis undergoing non-hepatic surgeries. J Clin Diagn Res 10(10):OC18–OC21
28. Tsugawa K, Koyanagi N, Hashizume M et al (2001) A comparison of an open and laparoscopic appendectomy for patients with liver cirrhosis. Surg Laparosc Endosc Percutan Tech 11(3):189–194
29. Garcia M, Gerber A, Zakhary B et al (2019) Management and outcomes of acute appendicitis in the presence of cirrhosis: a nationwide analysis. Am Surg 85(10):1129–1133
30. Jalan R, Fernandez J, Wiest R et al (2014) Bacterial infections in cirrhosis: a position statement based on the EASL Special Conference 2013. J Hepatol 60(6):1310–1324
31. Jaschinski T, Mosch CG, Eikermann M et al (2018) Laparoscopic versus open surgery for suspected appendicitis. Cochrane Database Syst Rev 11(11):001546
32. Javanmard-Emamghissi H, Boyd-Carson H, Hollyman M et al (2021) The management of adult appendicitis during the COVID-19 pandemic: an interim analysis of a UK cohort study. Tech Coloproctol 25(4):401–411
33 Rollins KE, Varadhan KK, Neal KR et al (2016) Antibiotics versus appendicectomy for the treatment of uncomplicated acute appendicitis: an updated meta-analysis of randomised controlled trials. World J Surg 40(10):2305–18. https://doi.org/10.1007/s00268-016-3561-7
34. Pugh RNH, Murray-Lyon IM, Dawson JL et al (1973) Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 60(8):646–649
35. Neeff HP, Streule GC, Drognitz O et al (2014) Early mortality and long-term survival after abdominal surgery in patients with liver cirrhosis. Surgery 155(4):623–632
36. Mansour A, Watson W, Shayani V et al (1997) Abdominal operations in patients with cirrhosis: Still a major surgical challenge. Surgery 122(4):730–735
37. Teh SH, Nagorney DM, Stevens SR et al (2007) Risk factors for mortality after surgery in patients with cirrhosis. Gastroenterology 132(4):1261–1269
38. Laurence JM, Tran PD, Richardson AJ et al (2012) Laparoscopic or open cholecystectomy in cirrhosis: a systematic review of outcomes and meta-analysis of randomized trials. HPB 14(3):153–161
39. El Nakeeb A, Sultan AM, Salah T et al (2013) Impact of cirrhosis on surgical outcome after pancreaticoduodenectomy. World J Gastroenterol 19(41):7129–7137
40. Lorenzoni L, Marino A (2017) "Understanding variations in hospital length of stay and cost: Results of a pilot project." OECD Health Working Papers, No. 94, OECD Publishing, Paris
41 Childers CP, Maggard-Gibbons M (2021) Same data, opposite results? JAMA Surg 156(3):219–220



Adil Rashid was born in Leicester, U.K. and obtained his medical degree from the University of Nottingham. He went on to complete the Academic Foundation Programme in Nottingham under the supervision of Mr. Humes, Associate Professor in GI surgery. There he developed an interest in the epidemiology of post-operative complication following general surgical procedures, in under-represented groups such as patients with liver cirrhosis. Dr. Rashid has recently started an Academic Clinical Fellowship in Sheffield where he hopes to continue combining his interests in epidemiology and general surgery. Outside of medicine, Dr. Rashid enjoys playing tennis.