Morbidity and mortality related to non-hepatic surgery in patients with liver cirrhosis: A systematic review

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Best Pract Res Clin Gastroenterol. 2012 Feb; 26(1): 47-59

ABSTRACT

Background: The aim of this study was to systematically review morbidity and mortality after non-hepatic surgery in patients with liver cirrhosis.

Methods: Comprehensive searches were conducted in PubMed, Embase and the Cochrane Library for articles using the words: liver failure, hepatic insufficiency, liver cirrhosis, cirrhosis, cirrhotic, surgical procedures, operative complications, operative mortality, postoperative complications, surgical complication, surgical risk, and hernia.

Results: Forty-six out of 5247 articles were selected after the initial search. The level of evidence provided in these articles varied greatly. Non-hepatic surgery of patients with liver cirrhosis resulted in an increased risk of postoperative morbidity and mortality compared with similar surgery of non-cirrhotic patients. Cholecystectomy, umbilical and inguinal hernia repair were associated with the lowest increased morbidity and mortality, whereas pancreatic, cardiovascular, and trauma surgery were correlated with the highest. The preoperative model for end stage liver disease (MELD) and Child-Turcotte-Pugh (CTP) scores appeared to be predictive of postoperative risks. The presence of portal hypertension and surgery in an emergency setting were associated with even higher mortality and morbidity rates.

Conclusion: This systematic review of the literature showed that, in patients with liver cirrhosis who undergo non-hepatic surgery, postoperative morbidity and mortality rates varied greatly depending on the severity of the cirrhosis and the surgical procedure. The majority of procedures can be safely performed in patients with low MELD scores and CTP grade A liver cirrhosis without portal hypertension.

INTRODUCTION

Hepatic surgery of patients with liver cirrhosis is associated with high morbidity and mortality.[1,2] Considerably more debate, however, concerns the increased postoperative risk in patients with liver cirrhosis undergoing non-hepatic surgery.[3] Literature shows overall mortality rates as high as 45% in patients with liver cirrhosis undergoing non-hepatic surgery.[4] It is, however, not clear which patients with liver cirrhosis are most at risk, and which procedures are most hazardous. This presumed increased risk often results in the advice to avoid surgery in this particular group of patients unless absolutely necessary.[5,6] Refraining from elective surgery in patients with cirrhosis, however, can result in emergency surgery which is associated with probably an even greater risk of morbidity and mortality in this vulnerable group of patients.[7-9] Emergency surgery in patients with liver cirrhosis has been shown to be associated with considerably longer post-operative hospitalization, higher morbidity, and a 7-fold increased risk of mortality compared to elective surgery.[9] In addition, patients with liver cirrhosis have been shown to undergo emergency surgery more often than patients without cirrhosis, and approximately 10% of all cirrhotic patients will require both elective and emergency surgery in the last years of their lives.[2,10] This implies that proper recommendations are required in patients with liver cirrhosis who have to undergo surgery. However, current recommendations for surgery in these patients are mostly derived from retrospective studies.[1,2] Literature on this topic is abundant but varies in quality and is full of individual, non-evidence-based opinions and assumptions. This study aims to review systematically morbidity and mortality accompanying non-hepatic surgery in patients with liver cirrhosis and will provide a risk assessment that enables the counseling of patients with liver cirrhosis undergoing non-hepatic surgery.

METHODS

Literature search strategy

A systematic search of MEDLINE, PubMed, Embase and the Cochrane library was performed for articles relevant to non-hepatic surgery in patients with liver cirrhosis, published between January 1990 and July 2011. To give accurate information and provide the best clinical evidence, literature before 1990 was not included in this systematic review. The following search terms were used to search all databases: liver failure, hepatic insufficiency, liver cirrhosis, cirrhosis, cirrhotic, surgical procedures, surgical complications, operative mortality, postoperative complications, surgical risk, and hernia. The following types of studies were excluded: interviews, case-reports,

letters, comments and editorials, papers on infants or adolescents, and papers written in a language other than English. Manual reference checks of included papers were performed to supplement the electronic searches.

Search strategy: Medline

(Hepatic Insufficiency[mesh] OR Liver Cirrhosis[mesh] OR Liver Cirr*[tw] OR liver insufficien*[tw] OR hepatic insufficien*[tw] OR Cirrhosis[tw] OR Cirrhotic[tw] OR Cirrosis[tw] OR Cirrotic[tw]) AND (Surgical Procedures, Operative/complications[mesh] OR Surgical Procedures, Operative/mortality[mesh] OR Postoperative Complications[mesh] OR surgical complication*[tw] OR surgical risk*[tw] OR Surgery complication*[tw] OR Surgery risk*[tw] OR operative complications[tw] OR postoperative complication*[tw] OR hernia[mh] OR hernia*[tw]) AND (English[lang]) NOT (editorial[pt] OR letter[pt] OR case reports[pt] OR comment[pt] OR interview[pt]) NOT (Child[mesh] NOT adult[mesh])

Search strategy: Embase

('liver failure'/exp OR 'Liver Cirrhosis'/exp OR ((Liver NEXT/1 Cirr*) OR (liver NEAR/3 insufficien*) OR (hepatic NEAR/3 insufficien*) OR Cirrhosis OR Cirrhotic OR Cirrosis OR Cirrotic):de,ab,ti) AND (((Postoperative OR surgical OR Surgery OR operative) NEAR/3 (Complication* OR risk* OR safety)):de,ab,ti OR hernia/exp OR hernia:de,ab,ti) AND ([English]/lim) NOT ([editorial]/lim OR [letter]/lim OR [note]/lim) NOT ([Child]/lim NOT [adult]/lim)

Literature screening

Studies were evaluated for inclusion by two independent researchers (BG, PJK) according to relevance to the subject. A random check was performed by a third person (GK). Study selection was accomplished through 3 phases of study screening. In phase 1, studies were selected on the basis of title. Keywords were "management", "surgical risk", "cirrhosis", and "surgery". If the following types of studies (interviews, case series, non-human, experimental, case-reports, letters, comments, editorials, papers on infants/adolescents, and papers written in a language other than English) were identified, they were excluded. In phase 2, abstracts were reviewed for relevance, and reviews, randomized controlled trials (RCTs), prospective cohort and large retrospective studies were selected and full-text articles were obtained. If good quality studies were lacking, smaller, retrospective or lesser quality studies were selected. In phase 3, full-text articles were reviewed. Included were studies that described management of patients with liver cirrhosis undergoing elective or non-hepatic emergency surgery. The studies had to describe one or more of the following outcome measures to be eligible for inclusion: severity of liver disease, type of surgical procedure, overall morbidity or mortality. Selected studies were categorized in one of the following groups

of non-hepatic surgery: surgical risk assessment, gastrointestinal surgery, abdominal wall surgery, cardio-thoracic and vascular surgery, trauma and orthopedic surgery, and other types of surgical procedures. Any discrepancies in inclusion were resolved by discussion between the reviewers under the supervision of a third person.

Data extraction and critical appraisal

The level of evidence of each paper was established on the basis of the Oxford Centre for Evidence-Based Medicine Level of Evidence scale.[11] The quality of the randomized controlled trials was assessed using the Jadad-criteria.[12] All aspects of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement were followed.[13]

RESULTS

Initial literature search revealed 5247 papers; 180 were selected on the basis of title because only articles of non-hepatic surgery in patients with liver cirrhosis were selected. After screening abstracts for relevance, 116 studies were excluded. After full text reading and assessment of the quality of the included papers, another 19 papers were excluded. One article was included after searching references. Finally, this systematic review was based on a total of 46 papers. Four reviews, 6 RCTs, 4 prospective studies and 32 retrospective studies were included. Studies were categorized into 6 groups. The PRISMA flow diagram for systematic reviews is presented in Figure 1.[13] Level of evidence of included papers and complication rates of different non-hepatic surgical procedures are presented in Table 1.

Surgical risk assessment

In the category of surgical risk assessment 5 retrospective studies were identified. All studies had level of evidence 2B. Overall postoperative morbidity in cirrhotic patients was 30.1% for different general surgical procedures. Mortality within 30 days of surgery was 11.6% for any type of procedure.[1] Patients with cirrhosis undergoing cholecystectomy, colectomy, coronary artery bypass graft (CABG), or abdominal aortic aneurysm (AAA) repair had a 3.4-fold, 3.7-fold, 8.0-fold and 5.0-fold greater risk of mortality when compared to non-cirrhotic patients. Patients with cirrhosis and portal hypertension who underwent the same procedures had a 12.3-fold, 14.3-fold, 22.7-fold and a 7.8-fold greater risk of mortality when compared to non-cirrhotic patients.[3] Laparoscopic procedures for various surgical indications had an overall morbidity and mortality of 16% and 0.6%, respectively.[14] Length of hospital stay and total hospital costs were higher with increased severity of liver disease for all operations.[3] Model

of End-stage Liver Disease (MELD) score was shown to be predictive and helpful for counseling patients prior to surgery.[10] Patients with a MELD score <8 who underwent elective surgery for various indications had a mortality of 5.7% compared with >50% in patients with a MELD score >20.[15]

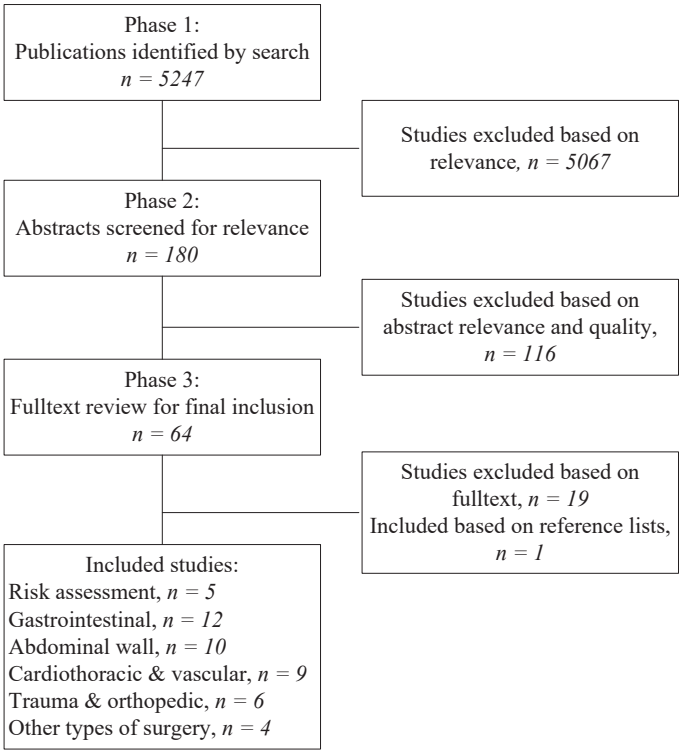

Figure 1. *PRISMA flow chart of the literature search.*

Table 1. Characteristics of included studies.

Author/ Type of surgery	*Level of Evidence*	*Jadad-criteria*	*No. of patients*	*Overall morb.*	*Overall mort.*	*CTP A morb.*	*CTP A mort.*	*CTP B morb.*	*CTP B mort.*	*CTP C morb.*	*CTP C mort.*	*MELD*
General surgical risk assessment												
Csikesz et al.	2B	-	22.569	-	-	-	-	-	-	-	-	-
Ziser et al.	2B	-	733	30.1	11.6	-	-	-	-	-	-	-
Cobb et al.	2B	-	21	16.0	0	-	-	-	-	-	-	yes
Northup et al.	2B	-	131	-	16.4	-	-	-	-	-	-	yes
Teh et al.	2B	-	772	-	5.7 (MELD<8), >50 (MELD >20)	-	-	-	-	-	-	yes
Gastrointestinal surgery												
Cholecystectomy												
Puggioni and Wong.	2A	-	400	20.9	0.6	-	-	-	-	-	-	-
El awadi et al.	2B	2	110									
Open:				35	0	-	0	-	0	-	-	-
Laparoscopic:				13	0	-	0	-	0	-	-	-
El Nakeeb et al.	2B	2										
Harmonic scalpel clipless:			120	8.3	0	-	0	-	0	-	-	-
Conventional:				15.0	0	-	0	-	0	-	-	-
Bessa et al.	2B	2										
Harmonic scalpel clipless:			40	25	0	-	0	-	0	-	-	-
Conventional:				35	0	-	0	-	0	-	-	-
Thulstrup et al.	2B	-	110	-	7.7	-	-	-	-	-	-	-

Table 1. Characteristics of included studies. *(continued)*

Author/ Type of surgery	*Level of Evidence*	*Jadad-criteria*	*No. of patients*	*Overall morb.*	*Overall mort.*	*CTP A morb.*	*CTP A mort.*	*CTP B morb.*	*CTP B mort.*	*CTP C morb.*	*CTP C mort.*	*MELD*
Ji et al.	2B	2	80									
Open:				30.0	-	-	-	-	-	-	-	-
Laparoscopic:				13.2	-	-	-	-	-	-	-	-
Hamad et al.	2B	2	30									
Open:				33	0	-	0	-	0	-	-	-
Laparoscopic:				33	0	-	0	-	0	-	-	-
Colorectal surgery												
Nguyen et al.	2B	-	4042	43	14	-	-	-	-	-	-	-
Gastric surgery												
Jeong et al.	3B	-	18	56	0	53.3	0	66.7	0	-	-	-
Pancreatic surgery												
Warnick et al.	3B	-	32	69	-	3	67	100	100	-	-	yes
Appendectomy												
Tsugawa et al.	3B	-	40	42.5	-	-	-	-	-	-	-	-
Poulson et al.	2B	-	69	-	9	-	-	-	-	-	-	-
Abdominal wall surgery												
Umbilical hernia repair												
Mckay et al.	3A	-	-	-	-	-	-	-	-	-	-	-

Table 1. Characteristics of included studies. *(continued)*

Author/ Type of surgery	*Level of Evidence*	*Jadad-criteria*	*No. of patients*	*Overall morb.*	*Overall mort.*	*CTP A morb.*	*CTP A mort.*	*CTP B morb.*	*CTP B mort.*	*CTP C morb.*	*CTP C mort.*	*MELD*
Ammar et al.	2B	2	80									
Mesh repair:				11	0	-	-	-	-	-	-	-
Primary closure:				14	0	-	-	-	-	-	-	-
Gray et al.	2B	-	120	9.5	-	-	-	-	-	-	-	-
Eker et al.	2B	-	30	7	0	-	-	-	-	-	-	yes
Belghiti et al.	3B	-	40	20	0	-	-	-	-	-	-	-
Carbonell et al.	2B	-	1197	16.5	2.5							
Hansen et al.	2B	-										
Inguinal repair:			201	-	2.7	-	-	-	-	-	-	-
Umbilical repair:			256	-	5.5	-	-	-	-	-	-	-
Marsman et al.	3B	-	34									
Umbilical repair:				18	0	-	-	-	-	-	-	-
Conservative treatment:				77	15	-	-	-	-	-	-	-
Inguinal hernia repair												
Patti et al.	2B	-	32	6.3	0	-	-	-	-	-	-	-
Oh et al.	2B	-	129	10.9	0.8	11.1	-	9.1	-	16.7	-	-
Cardiothoracic and vascular surgery												
Elective cardiac surgery												
Bizouarn et al.	2B	-	12	58.3	16.7	-	-	-	-	-	-	-
Shaheen et al.	2B	-	711	43.3	17	-	-	-	-	-	-	-

Table 1. Characteristics of included studies. *(continued)*

Author/ Type of surgery	*Level of Evidence*	*Jadad-criteria*	*No. of patients*	*Overall morb.*	*Overall mort.*	*CTP A morb.*	*CTP A mort.*	*CTP B morb.*	*CTP B mort.*	*CTP C morb.*	*CTP C mort.*	*MELD*
Marui et al.	2B	-	332	40.8	1.8	-	-	-	-	-	-	-
Hayashida et al.	5	-	-	-	-	-	-	-	-	-	-	-
Modi et al.	3A	-	-	-	-	-	-	-	-	-	-	-
Elective infrarenal aortic aneurysm repair.												
Marrocco et al.	3B	-	24	20.8	0	-	-	-	-	-	-	yes
Lung cancer surgery (NSCLC)												
Iwasaki et al.	4	-	17	29.5	5.9	0	0	30.8	7.6	-	-	-
Iwata et al.	4	-	37	13.5	2.7	-	-	-	-	-	-	-
Iwata et al.	4	-	33	18.2	6.5	-	-	-	-	-	-	-
Trauma and orthopaedic surgery												
Trauma surgery												
Georgiou et al.	2B	-	468	10.2	11.5	-	-	-	-	-	-	-
Demetriades et al.	2B	-	40	45.0	45.0	-	-	-	-	-	-	-
Lin et al.	2B	-	30	41.2	43.3	-	-	-	-	-	-	-
Hip & Knee surgery												
Hsieh et al.	3B	-	38	26.7	0	-	-	-	-	-	-	-

Table 1. Characteristics of included studies. *(continued)*

Author/ Type of surgery	*Level of Evidence*	*Jadad-criteria*	*No. of patients*	*Overall morb.*	*Overall mort.*	*CTP A morb.*	*CTP A mort.*	*CTP B morb.*	*CTP B mort.*	*CTP C morb.*	*CTP C mort.*	*MELD*
Cohen et al.	3B	-	29			14.3	4.8	28.6	14.3	100	100	-
Hip:				35.7	0	-	-	-	-	-	-	
Knee:				10	0	-	-	-	-	-	-	
Emergency hip:				80	60	-	-	-	-	-	-	
Shih et al.	3B	-	51									
Knee:				25.5	0	-	-	-	-	-	-	-
Other surgery												
Splenectomy												
Wang et al.	3B	-	96	17.7	0	-	-	-	-	-	-	-
Tomikawa et al.	3B	-	31	-	0	-	0	-	0	-	-	
Imura et al.	2B	-	18	33	-	-	-	-	-	-	66.7	-
Transurethral resection of the prostate (TURP)												
Nielsen et al.	2B	-	30	-	6.7	-	-	-	-	-	-	-

Gastrointestinal surgery in patients with liver cirrhosis

In the group of gastrointestinal surgery 1 review, 1 meta-analysis, 5 randomized controlled trials, and 6 retrospective studies were identified with levels of evidence ranging between 2A and 3B.

Cholecystectomy was the most frequently performed surgical procedure in patients with liver cirrhosis.[3] Open cholecystectomy in patients with cirrhosis resulted in morbidity rates ranging between 30% and 35% compared with morbidity rates after laparoscopic cholecystectomy ranging between 13% and 33%. No mortality was described after laparoscopic cholecystectomy; mortality rates after open cholecystectomy varied between 0% and 7.7%.[16-18] Morbidity rates after laparoscopic cholecystectomy in patients with cirrhosis without the use of clips was between 8.3% and 25.0% compared to rates between 15% and 35% for laparoscopic cholecystectomy with the use clips.[19,20] Compared with open cholecystectomy, laparoscopic cholecystectomy in cirrhotic patients was associated with fewer bleeding complications, shorter operating time, and shorter hospital stay.[21] However, laparoscopic cholecystectomy in cirrhotic patients had higher conversion rates during the procedure, longer surgical time, and more frequent bleeding complications compared to non-cirrhotic patients.[21] One study showed that open cholecystectomy in alcoholic cirrhotic patients had a 11-fold increased risk of 30-day mortality compared to open cholecystectomy of non-alcoholic cirrhotic patients.[22]

The estimated hazard ratio (HR) for mortality after colectomy was found to be 3.7 in cirrhotic patients, and 14.3 in patients with portal hypertension.[3] Overall morbidity after colorectal surgery in cirrhotic patients was shown to be 43%. In-hospital mortality after elective colorectal surgery was found to be 14% in cirrhotic and 29% in patients with cirrhosis and portal hypertension compared to 5% in non-cirrhotic patients (odds ratio (OR) 3.91 and 11.3, respectively). Emergency colorectal surgery led to an even higher mortality rate of 20.9% in cirrhotic patients, and 35.8% in patients with portal hypertension. Cirrhotic patients undergoing emergency surgery had a higher mortality rate compared to elective surgery (OR 2.40). Patients with portal hypertension and cirrhosis undergoing emergency surgery had an even higher mortality rate (OR 5.88).[3,23]

Overall morbidity after radical gastric surgery was shown to be 56% with a morbidity of 53.3% in patients with Child-Turcotte-Pugh (CTP) grade A liver cirrhosis and 67.7% in patients with CTP B liver cirrhosis.[24]

Open appendectomy in cirrhotic patients resulted in a 30-day mortality of 9% compared to 0.7% in non-cirrhotic patients.[25] Laparoscopic approach for an acute appendicitis in cirrhotic patients was shown to be superior with regard to postoperative pain (VAS scores, 35/100 vs. 60/100) and postoperative complications (wound infection: 0% vs. 5% and hemorrhage: 0% vs. 5%).[26]

Overall morbidity after pancreatic surgery was shown to be 69% in cirrhotic patients versus 44% in non-cirrhotic patients. Major morbidity varied greatly (47% vs. 22%) as did the number of reoperations (34% vs. 12%). This resulted in a longer ICU stay and a prolonged hospital stay in cirrhotic patients. Morbidity rates in patients with CTP grade A and CTP grade B liver cirrhosis were 67% and 100%, respectively. Mortality rates in patients with CTP grade A and grade B liver cirrhosis ranged between 3% and 100%, respectively.[5]

Abdominal wall surgery in patients with liver cirrhosis

In the group of abdominal wall surgery 1 review combined with a survey, 1 randomized controlled trial, 3 prospective studies and 5 retrospective studies were identified with levels of evidence ranging between 2B and 3B. It was shown that 20% of patients with liver cirrhosis will develop an umbilical hernia.[8,27] Overall morbidity after elective umbilical hernia repair varied between 7% and 20%. Overall mortality varied between 0% and 5.5%.[7-9,27] Conservative management of umbilical hernia in patients with cirrhosis and ascites resulted in higher mortality compared to elective repair.[8,27] Elective umbilical hernia repair in cirrhotic patients was shown to be safe and was not associated with higher complication rates than in non-cirrhotic patients. Emergency umbilical hernia repair, however, was associated with higher complication rates compared to elective repair in cirrhotic patients.[7-9,27] High CTP score, presence of ascites, symptomatic hernia, and emergency surgery were associated with a worse outcome.[7,28] Uncontrolled ascites was shown to result in a relative risk of 8.51 for umbilical hernia recurrence.[28] Recurrence of umbilical hernia was found to be lower after mesh repair (2.7%) compared to suture repair (14.2%). In this study, mesh repairs were more likely to become infected (16.2% vs. 8.5%) but the difference was not statistically significant.[29] In the same study, no significant differences were noted in the rate of other early postoperative complications such as transient ascitic fluid leakage. Umbilical hernia repair was shown to be safe under local anesthesia in patients with cirrhosis.[29]

Postoperative complications and long-term recurrence after inguinal hernia repair in cirrhotic patients did not differ compared to non-cirrhotic patients. Overall complication rates after inguinal hernia repair ranged between 6.3% and 10.9% in cirrhotic patients compared to 6.8% in non-cirrhotic patients. Overall mortality ranged between

0% and 0.8%. Elective repair of symptomatic inguinal hernia in patients with cirrhosis was recommended.[30] Even in patients with advanced and decompensated cirrhosis.[31] However, one study reported an overall mortality of 2.7% after inguinal hernia repair compared to 0.7% in non-cirrhotic patients (OR of 4.4).[32] Complication rates after inguinal hernia repair were shown to be independent of the CTP score.[30-32] Inguinal hernia repair outcomes were relatively unaffected in the presence of ascites.[9,33] Inguinal hernia repair in cirrhotic patients was shown to be a safe procedure under local or general anesthesia with the use of a polypropylene mesh whereas repair of a symptomatic inguinal hernia improved quality of life, particularly in patients with grade CTP C cirrhosis, and patients with refractory ascites.[31]

Cardio-thoracic and vascular surgery in patients with liver cirrhosis

In the group of cardiac-thoracic and vascular surgery 2 reviews, 1 prospective study and 6 retrospective studies were identified with levels of evidence ranging between 2B and 5.

Postoperative morbidity rates in patients with CTP A, B, and grade C liver cirrhosis undergoing elective cardio-vascular surgery have been shown to be 25% to 50% 100%, and 100%, respectively. The consensus among these clinical studies is that patients with CTP A cirrhosis tolerate cardiac operations. No mortality was observed among patients with CTP A cirrhosis undergoing elective cardiac surgery irrespective of the use of a cardiopulmonary bypass (CPB). Patients with more advanced cirrhosis (CTP B or C cirrhosis), however, had a significantly higher mortality rate (50-100%) after placement of a cardiopulmonary bypass.[34-36]

Patients with cirrhosis undergoing CABG had an increased risk of mortality (17 vs. 3%; OR 6.67), complications (43 vs. 28%; OR 1.99), and longer hospitalization and costs compared in non-cirrhotic patients. Predictors of mortality included age >60 years (OR 2.21), female gender (OR 1.92), ascites (OR 3.80), and congestive heart failure (OR 1.75). Mortality rate was 7.7% in patients with fewer than two complications compared in 59% for those with two or more complications (OR 17.48). Hospital volume and off-pump CABG did not affect mortality.[37] No difference in adjusted in-hospital mortality was found between patients with cirrhosis undergoing percutaneous coronary intervention (PCI), conventional CABG or off-pump CABG compared to non-cirrhotic patients.[38]

No intraoperative or 30-day mortality was recorded after elective open infrarenal AAA repair. No significant differences in terms of major perioperative complications were observed between cirrhotic patients and controls. Operating time and the need for in-

traoperative blood transfusion were significantly higher in cirrhotic patients. Length of hospitalization was nearly doubled in cirrhotic patients. CTP grade B was associated with higher need for intraoperative blood transfusions. The estimated survival at 2 years was 77.4% in cirrhotic and 97.8% in non-cirrhotic patients. Both patients with CTP B cirrhosis (100%) died within 6 months. CTP B cirrhosis and a MELD score >10 were associated with reduced midterm survival rates. MELD score ≥10 was associated with reduced midterm survival rates with an estimated survival at 2 years of 0% in patients with CTP B cirrhosis compared to 84.4% in CTP A cirrhosis. Patients with MELD <10 compared to MELD ≥10 had an estimated survival of 90% versus 47.6%.[6]

Lung surgery in cirrhotic patients with Non-Small Cell Lung Cancer (NSCLC) had an overall morbidity and mortality between 13.5 - 29.5% and 2.7% - 6.5%, respectively. Overall 1-, 3- and 5-year survival ranged between 77.3% to 87.8%, 57.0% to 59.9%, and 37.6% to 45.6%, respectively.[39-41]

Trauma and orthopedic surgery in patients with liver cirrhosis

In the group of trauma and orthopedic surgery, 6 retrospective studies were identified with levels of evidence ranging between 2B and 3B. Overall mortality of general cirrhotic trauma patients was 12% and 6% for the non-cirrhotic group (OR 5.65). ARDS, trauma-associated coagulopathy, and septic complications were significantly more common among patients with liver cirrhosis. Overall severe complication rate for the two groups was 10 and 4%, respectively (OR 2.05). For the subgroup of patients who underwent a laparotomy for trauma, the mortality rate increased to 40% compared to 15% in non-cirrhotic patients (OR 4.35).[42]

These results were supported by another study that focussed only on laparotomies in cirrhotic trauma patients. The overall mortality for patients with cirrhosis undergoing laparotomy for trauma was significantly higher compared to non-cirrhotic patients (45% vs. 24%, HR 7.60). Mortality for patients with an Injury Severity Score ≤15 was 29% for cirrhotic patients and 5% in non-cirrhotic patients; in patients with an Injury Severity Score of 16–25 mortality was 56% and 11%, respectively. Overall complication rate was 45% in cirrhotic patients and 23% in the non-cirrhotic group, but this result was not statistically significant. Longer ICU stay and higher hospital costs were reported in patients with cirrhosis undergoing trauma surgery compared to non-cirrhotic patients.[4] Analysis by ROC curve identified cirrhotic patients undergoing laparotomy for blunt abdominal trauma with a MELD score ≥17 as the best cut-off value for predicting postoperative death. Postoperative mortality of patients with MELD <17 was 6.2% compared with 85.7% in patients with a MELD score ≥17.[43]

In patients undergoing elective total hip arthroplasty (THA) or elective total knee arthroplasty (TKA), significant adverse outcomes (including major complications such as hepatic decompensation, and mortality) occurred in 20.7% of cirrhotic compared to 3.2% in non-cirrhotic patients. No significant differences were found between elective THA and TKA. However, 80% of cirrhotic patients undergoing emergency THA secondary to a fracture had major complications with a mortality rate of 60%.[44] These results were supported by another study that reported a 30-day complication rate of 26.7% in cirrhotic patients undergoing elective THA.[45] Overall complication rate after TKA was also significantly higher among patients with cirrhosis than in control patients, but no perioperative mortality was reported.[46] Advanced liver cirrhosis was associated with a higher risk of complications.[44,45] Major complications occurred in 14.3%, 28.6%, and 100% of cirrhotic patients with CTP A, B and C cirrhosis, respectively. Death occurred in 4.76%, 14.3%, and 100% of cirrhotic patients with CTP A, B, and C cirrhosis, respectively, but these results were statistically insignificant.[44]

First-time prosthetic hip infection (PHI) was described in 9.5% of patients with liver cirrhosis. Debridement with retention of the prosthesis (DWROP) was the initial treatment and cured the infection in 29% of the patients. Excision arthroplasty (EA) was required in 79% and eradicated PHI in 92% of cases. Recurrent PHI occurred in 30% of cirrhotic patients who had a re-implantation. Patients who developed hepatic decompensation after re-implantation had a significantly higher risk of recurrent PHI (RR 7.5).[47]

Other types of surgical procedures in patients with liver cirrhosis

In the group of splenectomy and transurethral resection of the prostate (TURP) 4 retrospective studies were identified with levels of evidence ranging between 2B and 3B.

Overall morbidity among cirrhotic patients after splenectomy was shown to range between 17.7% and 33%. No mortality was reported in patients with grade CTP A and grade B liver cirrhosis.[48,49] Mortality rate in patients with CTP grade C liver cirrhosis was shown to be 66.7%.[48-50] Overall survival rate after splenectomy of patients with cirrhosis was 83.3% at 1 year, and 62.7% at 2 years of follow-up. The survival rate of patients with CTP C cirrhosis was 80.0% at 1 year, and 60.0% at 2 years of follow-up. Postoperatively, portal pressure decreased after splenectomy in most patients by a mean of 4.7 mmHg.[48]

TURP in patients with cirrhosis was accompanied with a 30-day mortality of 6.7% compared to 2% in non-cirrhotic patients (OR 3.0).[51]

DISCUSSION

Our review of the literature showed that patients with liver cirrhosis who undergo non-hepatic surgery, exhibit postoperative morbidity and mortality rates that vary greatly depending on the severity of liver cirrhosis and the nature of the surgical procedure. Both CTP and MELD scores were shown to be predictive of postoperative morbidity and mortality in these patients. Portal hypertension and emergency surgery in patients with liver cirrhosis were associated with even higher morbidity and mortality rates irrespective of the surgical procedure compared to elective surgery. Patients with portal hypertension and cirrhosis undergoing emergency surgery had the highest mortality rates. A laparoscopic approach was often preferred over an open procedure.

Cholecystectomy and abdominal wall surgery in patients with cirrhosis were associated with the lowest morbidity and mortality and with the least increase in morbidity and mortality compared to non-cirrhotic patients. Laparoscopic cholecystectomy had better outcomes compared to an open approach. Elective umbilical hernia repair in cirrhotic patients was associated with low morbidity and mortality rates and had comparable postoperative mortality rates as non-cirrhotic patients. In umbilical hernia repair, emergency repair was associated with higher morbidity and mortality rates. Wait-and-see approach for patients with cirrhosis and umbilical hernia was shown to result in high mortality and morbidity but no RCT was conducted to compare that strategy to elective repair. Uncontrolled ascites was associated with umbilical hernia recurrence. It was also shown that elective umbilical hernia repair with mesh was safe and effective and no difference in surgical site infection or ascitic leakage was noted when compared to suture repair. Local anesthesia was found to have potential for umbilical and inguinal hernia surgery in cirrhotic patients but no RCT has been performed comparing different anesthesia techniques. Gastrointestinal surgery, appendectomy, colorectal surgery, gastric surgery and pancreatic surgery showed increased risks of morbidity and mortality. Patients with CTP grade A cirrhosis were shown to undergo pancreatic surgery with slightly increased morbidity and mortality compared to non-cirrhotic patients, but those who had CTP grade B and C liver cirrhosis were at increased risk of postoperative death. Comparable high risks were reported in patients with CTP grade B and C liver cirrhosis who underwent emergency trauma surgery, particularly laparotomy in trauma or (emergency) vascular surgery. It was recommended that all cirrhotic trauma patients undergoing laparotomy should be admitted to the ICU irrespective of severity of injuries. It was also shown that patients with CTP A cirrhosis were tolerating cardiac operations rather well but for patients with more severe cirrhosis, these operations should be considered most hazardous. No

difference in adjusted in-hospital mortality was found between patients with cirrhosis undergoing other cardiac surgery, such as PCI, conventional CABG or off-pump CABG.

Literature of non-hepatic surgery in cirrhotic patients is abundant and varies with respect to the level of evidence. However, the majority is not of sufficient quality to allow for solid conclusions. Quality assessment of the studies showed that studies with the highest level of evidence often did not provide data on severity of cirrhosis expressed in MELD or CTP scores. Therefore only morbidity and mortality rates in patients with cirrhosis compared to non-cirrhotic patients could be extracted from the literature. Studies that provided clinical data on CTP or MELD were often retrospective, limited in sample size, and prone to patient selection, resulting in lower levels of evidence. All these studies however did show worse outcomes for patients with more severe liver cirrhosis.

Future studies should focus on risk assessment for specific surgical procedures related to MELD or CTP scores in patients to improve decision-making and patient counseling. Secondly, the preventive effect of portal decompression through preoperative transjugular intrahepatic portosystemic shunting (TIPS) to allow non-hepatic surgery in selected patients with liver cirrhosis and portal hypertension should be studied. Several case studies show conflicting effects of this technique.[52,53] Furthermore, RCTs are needed that randomize cirrhotic patients with a surgically treatable diagnosis to a “wait-and-see” approach or the actual operation in an elective setting. In such trials, patients should also be stratified for MELD or CTP scores.

Summary

This review assesses systematically literature on morbidity and mortality after non-hepatic surgery in patients with liver cirrhosis. Level of evidence provided in the articles varied greatly. Non-hepatic surgery in patients with cirrhosis resulted in increased postoperative morbidity and mortality compared to similar surgery in non-cirrhotic patients. Cholecystectomy and umbilical and inguinal hernia correction were associated with the least increased morbidity and mortality, whereas pancreatic, cardiovascular, and trauma surgery were correlated with the highest risks. The preoperative MELD and CTP scores appeared to be predictive of postoperative risks. Portal hypertension and surgery in an emergency setting were associated with extra increased mortality and morbidity rates. The majority of non-hepatic surgical procedures can be safely performed in patients with low MELD scores or CTP grade A liver cirrhosis without portal hypertension. RCTs in this field are, however, often lacking. This implies that many important clinical questions remain unanswered; among them: the value of preventive preoperative measures such as TIPS placement to reduce risks in cirrhotic patients with portal hypertension and elective operation versus wait-and-see approach in cirrhotic patients with for instance abdominal wall hernias.

Practice points

§ MELD and CTP scores of cirrhotic patients predict outcomes in non-hepatic surgery.
§ Majority of non-hepatic surgery in patients with CTP grade A liver cirrhosis without portal hypertension is safe.
§ Avoid emergency surgery in cirrhotic patients.

Research agenda

§ Assess risks for specific surgical procedures related to MELD or CTP scores of patients in all future studies.
§ Assess the preventive effect of portal decompression through preoperative TIPS in patients with liver cirrhosis and portal hypertension who have to undergo non-hepatic surgery.
§ Randomize cirrhotic patients with a surgically treatable diagnosis to a “wait-and-see” approach or the actual operation in an elective setting stratified for MELD or CTP score.

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