

## **Total Joint Arthroplasty In Patients With Liver Cirrhosis: A Systematic Review**

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### **Abstract**

**Background:** Total hip arthroplasties (THAs) and total knee arthroplasties (TKAs) have proven themselves as effective surgical procedures. As a result, the number of such procedures performed is increasing. It is also likely that more cirrhotic patients will undergo THA or TKA.

**Purpose:** We performed a systematic review to assess periprosthetic joint complications, infections, mortality, and the outcome of total joint arthroplasties in patients diagnosed with cirrhosis.

**Material and Methods:** We researched Medline, EMBASE, and Cochrane databases to identify eligible prospective studies. This yielded 346 unique articles. 27 of these articles fit the inclusion criteria, and 7 articles remained eligible after in-depth reading. Demographic characteristics, adverse events, and clinical outcomes were manually extracted from the selected studies.

**Results:** The 7 studies included a total of 2724 TJA of which 1276 were THA and 1448 were THK. 3 studies provided data on the severity of cirrhosis using Child-Turcotte-Pugh. 4.7 % of perioperative complications occurred in class A, 50% in class B, and 100% in class C with a mortality rate of 66.6%. 5 studies provided data on short term (30 days) mortality after TJA. Therefore, these studies showed that mortality in patients with cirrhosis, undergoing TJA, is greater than in noncirrhotic patients (1.13% vs 0.17%). The rate of infection varied from 3.1% to 22% in cirrhotic patients and 0.7% to 1.4% in non-cirrhotic patients.

**Conclusion:** This present systematic review shows that total joint arthroplasty surgery of patients with cirrhosis results in increased postoperative morbidity and mortality compared to similar surgeries for non-cirrhotic patients.

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**Keywords:** Arthroplasty, cirrhosis, complications

## **Introduction**

Liver Cirrhosis is the common end stage of all chronic liver diseases. It is characterized by an irreversible diffuse fibrosis and the formation of nodules after hepatocellular necrosis. Chronic viral infections, especially the hepatitis B virus (HBV) and the hepatitis C virus (HCV), are among the important etiologies of cirrhosis. Excessive alcohol consumption, which is a major cause of osteonecrosis of the femoral head, also plays an important role in the development of cirrhosis. With the increasing prevalence of these conditions and improved survival associated with modern medical care, surgeons are increasingly treating patients with concomitant liver cirrhosis (Pramoosinsup, 2002; Sung, 1997).

Total hip arthroplasties (THAs) and total knee arthroplasties (TKAs) have proven themselves as effective surgical procedures. As a result, the number of these joint arthroplasties performed is increasing. It is also likely that more patients with cirrhosis will undergo THA or TKA. For patient care and economic reasons, there has been an increasing interest in identifying risk factors for complications and poor outcomes, especially in cirrhotic individuals with portal hypertension, hyperdynamic circulation, coagulopathy, and acquired immune deficiencies (Paxton et al., 2010). However, there is little information in literature about the results of joint arthroplasty in patients with liver cirrhosis. In general, these studies performed on small case series agreed that patients with cirrhosis had higher rates of periprosthetic joint infections and increased rate of hospitalization. However, there was limited evaluation of risk factors.

Cirrhotic patients undergoing surgical procedures (especially orthopedic surgery) are at a greater risk of complications and mortality than patients without liver cirrhosis. Based on this fact, we performed a systematic review to assess periprosthetic joint complications, including infections, length of hospitalization, hospital readmission rates, mortality, and the outcome of total joint arthroplasties in groups of patients diagnosed with liver cirrhosis.

## **I.**

### **Material and Methods**

Before commencing a comprehensive literature review for relevant studies, certain eligibility criteria were defined. Papers dealing with patients with liver cirrhosis, regardless of etiology and which were diagnosed before undergoing a total joint arthroplasty intervention, were considered eligible for inclusion in the present study. Experimental or animal studies, case reports, letters to editors, papers containing less than 10 subjects, papers with no specified follow up time or papers dealing with cirrhotic patients

undergoing a surgical intervention other than knee or hip arthroplasty were excluded.

Two independent reviewers performed a systematic query of the literature available on Medline, EMBASE, and Cochrane databases to identify articles containing the keywords and Boolean operators: “hip replacement,” “osteoarthritis,” “total joint arthroplasty,” and “cirroshis.” There was no limitation on language or publication status.

The research was performed in March 2016, and all studies published prior to that date were considered and reviewed. In addition to this primary literature research, we performed a secondary research by scrutinizing all references cited in the articles retrieved from the primary research and identified additional studies of interest. Each reviewer was compartmentalized, such that they were not aware of the others' determination.

The initial combined searches with the aforementioned keywords yielded 346 unique articles. Articles whose titles indicated that they were irrelevant to the topic in question were eliminated. The abstracts of the remaining articles were subsequently reviewed independently. Articles that did not meet the inclusion criteria on the basis of the information contained in the title and abstract were eliminated. Therefore, this amounted to 319 articles. The abstracts of the remaining 27 articles were determined to meet the inclusion criteria by at least one reviewer, and the corresponding full text was again reviewed independently. After reviewing the full text, 21 articles were eliminated unanimously by both authors because they failed to meet the inclusion criteria. The remaining 6 articles from the primary search were retained. At each phase of the review, if one author selected an article, it was moved on to the next phase. In the final phase of review (full text), there was no disagreement regarding which article should be ultimately included. Finally, we performed a manual search for the works included in the reference lists of the articles selected for in-depth analysis. Furthermore, there was 1 additional article identified in this secondary research that met the inclusion criteria. Figure 1 shows the flowchart corresponding to the article selection process.

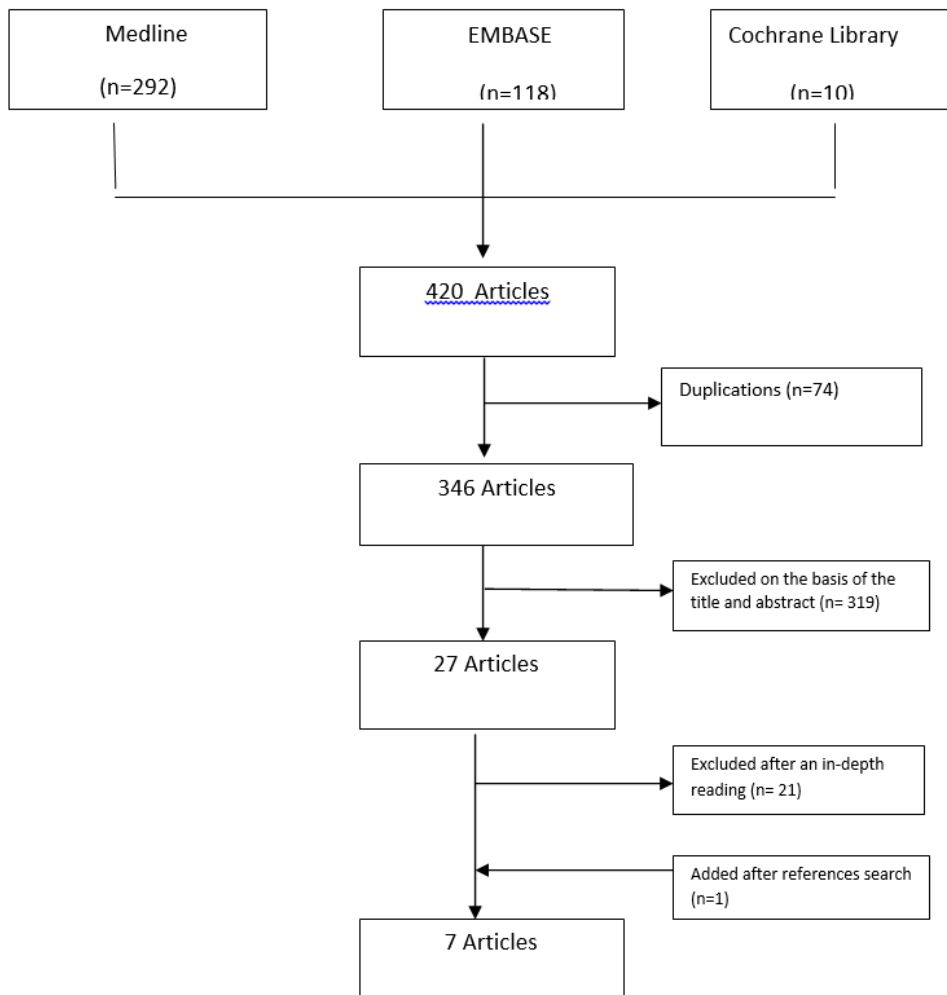


Figure 1. Flow chart of articles included

Study quality was assessed by considering controls for bias, confounding, and chance within each study as suggested by the MOOSE group for meta-analysis of observational studies (Stroup et al., 2000). Although some rudimentary statistical analyses were used, no study used logistic regression to control confounding factors. No blinding was used, and no controls for selection bias were present in controlling the sample population.

The outcomes, design and (in many cases) the study population of each study, were too heterogeneous to compare directly even with random effects models. To remedy this, we used data from individual studies to generate statistics. In cases where the data in some of the studies were similar, we pooled together the results and statistics which were generated. To test the hypotheses within each individual study that the findings were

independent of etiology versus the alternative that they were related, the Chi square test with Yates correction or the Fisher's exact test was used. These statistics were calculated using Java stat two-way contingency table analyses.

## Results

In total, 27 full-text studies were retrieved. Of these, 7 studies were eligible for inclusion in the systematic review (Figure 1). Three studies were designed as case control investigations, and four were cohort studies. Two studies were published in 2003 and 2005, while the remaining 5 were published between 2010 and 2014.

Table 1 summarizes the characteristics of the included studies. The 7 studies included for final analysis included an aggregated total of 2724 total joint arthroplasty (TJA). Out of it, 1276 were the total hip arthroplasty (THA) and 1448 were the total knee arthroplasty (THK). There were 1376 males and 1341 females with a mean age of  $60.57 \pm 7.27$  years. Follow-up ranged from 1 to 52 months.

Table 1. Descriptive Characteristics of Component Studies

Study Country	Publication date	Cases	Type of study	Age	Gender	FU (months)	Type of surgery: number
Deleuran et al., Denmark	2014	363	Case Control	66	196 M/167 F	12	THA: 211 TKA: 152
Hsieh et al., Taiwan	2003	45	Chort	$55.2 \pm 10.3$	29 M/9 F	24	THA: 45
Tibieri et al., USA	2014	115	Case Control	62.9	59 M/65 F	52	THA: 60 TKA: 55
Shirley et al., USA	2014	2109	Case Control	$66.2 \pm 12.6$	1018 M/1091 F	6	THA: 1018 TKA: 1091
Young-Wan et al., South Korea	2007	30	Cohort	60 (15-63)	26 M/4 F	1	THA: 30
Hsieh et al., Taiwan	2010	33	Cohort	47 (29–73)	24 M/9 F	36	THA: 33
Cohen et al., USA	2005	29	Case Control	$66.7 \pm 10.7$	24 M/5 F	1	THA: 19 TKA: 10

Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty; FU, follow-up; M, male; F, female.

Table 2. Postoperative Complications

Study	Types of complications	Follow up (days)	Rate of complication	
			Cirrhotic patience	Noncirrhotic patience
Cohen et al.	Cardiovascular events deep Venous thrombosis renal failure Pulmonary embolus systemic Infection Joint dislocation Deepi nfection Intra-articular bleeding Hematoma	90	20.7% (6)	3.23% (3)
Deleuran et al.	Infection Liver failure Acute renal failure Venous thromboembolism Cardiovascular disease Hip dislocation Mechanical complications	30	19.0% (69)	10% (10915)
Tibieri et al.	Urinary tract infection Acute renal failure Gastrointestinal hemorrhage Surgical complications (infection, dislocation, reoperation, revision)	30	25.0% (29)	4% (5)
Hsieh et al.	Pneumonia Wound infection Acute renal failure Bleeding oesophageal varices Urinary tract infection Peritonitis Septicaemia of unknown cause Deteriorating encephalopathy Congestive heart failure Stroke	30	26.7% (12)	
Young-Wan et al.	Wound infection Operative site bleeding Coagulopathy Encephalopathy Gastrointestinal bleeding Pneumonia	30	26.7% (8)	

A total of 3 (Hsieh et al., 2003; Moon et al., 2007; Cohen, Te HS & Levitsky, 2005) studies provided data on the severity of cirrhosis using the Child-Turcotte-Pugh (CTP) scoring system with a total of 104 cases. Liver cirrhosis severity was assessed using the CTP scoring system. 68 (70.7%) was the score for A, 30 (31%) was the score for B, and 6 (6.3%) was the score for C. Consequently, 26 (27.0%) of the 104 patients had one or more perioperative complications. Perioperative complications occurred in 7 (4.7%) of 68 [class A cirrhotics], 13 (50%) of 26 [class B], and 6 (100%) out

of 6 [class C]. Thus, among class C cirrhotic patients, the perioperative complications over 30 days was 100% and mortality rate was 66.6% (4 out of 6). Using Chi square statistical test, we searched for a possible association between the severity of cirrhosis and the appearance of perioperative complications. However, we found that decompensated cirrhosis (Child-Turcotte-Pugh B or C) is statistically associated with perioperative complications (P value <0.0001).

We identified 5 (Deleuran et al., 2015; Tiberi et al., 2014; Jiang, Schairer & Bozic, 2014; Moon et al., 2007; Cohen, Te HS & Levitsky, 2005) studies that reported the incidence of deep prosthetic infection after TJA surgery. These studies showed large variations in their study methodology. In particular, the follow-up period varied greatly among them. One study investigated the incidence of deep prosthetic infection in the first 90 days postoperatively, reporting incidence estimates of 4% (Tiberi et al., 2014). Another study (Deleuran et al., 2015) reported, for the first year, an estimate of 3.1% vs. 1.4% in noncirrhotic patients. Furthermore, one study (Jiang, Schairer & Bozic, 2014) showed that the rate of periprosthetic joint infections within 6 months of TJA was greater among patients with liver cirrhosis. 3.7% vs 0.7% HR 5.4 was for patients without hip fracture who underwent THA. Also, 2.7 vs. 0.8 HR 3.3 was for patients who underwent TKA. However, the difference was most pronounced for patients undergoing THAs to treat hip fractures 6.3% vs 1.1% HR 5.8. Only 2 studies, which had a lower number of subjects, provided estimates for time periods of up to and beyond 1 year of 22.2% (Hsieh et al., 2010) and 1.18% (Cohen, Te HS & Levitsky, 2005).

**Table 3.** Intraoperative Blood loss and Operation Frequency: Variables compared in Patients with and without Liver Cirrhosis

	Blood loss (P value)	Operative time (P value)
Cohen et al. USA	0.024*	0.014*
Young-Wan et al. South Korea	0.71	0.27
Hsieh et al. Taiwan	0.041*	0.08

\*significant statistical association

According to the type of anesthesia, 3 studies (Deleuran et al., 2015; Hsieh et al., 2003; Cohen, Te HS & Levitsky, 2005) with a combined number of cases of 437 provided data regarding this data. 34% (149) of the interventions were performed in spinal anesthesia and 66% (288) in general.

Regarding mortality, 5 studies (Deleuran et al., 2015; Hsieh et al., 2003; Tiberi et al., 2014; Jiang, Schairer & Bozic, 2014; Cohen, Te HS & Levitsky, 2005) provided data on short term (30 days) mortality after TJA.

Meta-analysis showed that mortality in patients with cirrhosis, undergoing TJA, is greater than in noncirrhotic patients (1.13% vs 0.17%). The most frequent causes of death reported were liver failure and hepatic encephalopathy, pulmonary edema, pulmonary embolism, renal failure and cardiac arrest. We analyzed these data using Chi square test, and we found a significant association between mortality and the presence of liver cirrhosis: P value <0.001, with an OR: 6.76 at a 95% IC (4.679 to 9.793).

## **Discussion**

Previously published studies have reported a high perioperative risk in patients with liver cirrhosis undergoing general surgery, such as elective abdominal surgery (Aranha, Sontag & Greenlee, 1982; Garrison et al., 1984; Lehnert & Herfarth, 1993; Mansour et al., 1997), thoracotomy (Ueda et al., 1994), and trauma operations (Demetriades et al., 2004; Tinkoff et al., 1990). However, little information is available on clinical outcomes following orthopedic surgery in this group of patients. Ziser et al, in their retrospective review of 733 cirrhotic patients undergoing any type of surgical procedure, reported a perioperative total complication rate of 30.1%. Also, they noted that patients undergoing major orthopedic procedures including hip surgery, spine fusions and operations for long bone fractures had a substantially higher perioperative complication rate than patients undergoing non-orthopedic surgery (Ziser et al., 1999).

The results of this systematic review show that total joint arthroplasty surgery of patients with cirrhosis resulted in increased postoperative morbidity and mortality compared to similar surgeries for non-cirrhotic patients.

CTP score was shown to be predictive of postoperative morbidity and mortality in these patients. Patients with CTP A or B cirrhosis were shown to undergo TJA surgery with slightly increased morbidity and mortality compared to non-cirrhotic patients. However, those who had CTP grade C cirrhosis had a very high risk of postoperative death. Literature on orthopaedic surgery in cirrhotic patients is scarce. Quality assessment of the studies showed that studies with the highest level of evidence often did not provide data on the severity of cirrhosis expressed in CTP scores. Therefore, only morbidity and mortality rates for patients with cirrhosis compared to non-cirrhotic patients could be extracted from the literature. Studies that provided clinical data on CTP were 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 cirrhosis. Future studies should focus on risk assessment for TJA surgical procedures related to MELD or CTP scores of patients to improve decision-making and patient counseling.



Two of the reviewed articles assessed the role of elective/emergent interventions as a risk factor for possible complications in patients with liver cirrhosis. Therefore, Cohen et al investigated the operative risk of hip and knee arthroplasties in cirrhotic population. However, they found that the poor prognosis of cirrhotic patients was mainly attributable to those patients receiving emergency surgery. They concluded that the mortality occurred only in the emergency group. Also, comparing the elective and emergency groups for hip arthroplasties, authors demonstrated significantly more blood transfusions and estimated operative blood loss, longer operative time and length of hospital stay, more complications, and liver decompensation in the emergency group. In addition to this study, Shirley and co found out that hip fractures, solved by emergency intervention, were more common in patients with liver cirrhosis. In addition, they found a higher risk of periprosthetic joint infections in cirrhotic patients with fractures and therefore a higher readmission rate in this study group.

We acknowledge several limitations of this study. First, the insufficient literature data on this subject. It is known that in cirrhotic patients, portal hypertension, hyperdynamic circulation, and acquired immune deficiency are associated with an increased risk of complications after abdominal surgery (Hsieh et al., 2010). Notwithstanding, little data exists on orthopaedic surgery. Second, any study that investigated the outcomes of an orthopaedic procedure that was not an arthroplasty was excluded. As a result, published knowledge concerning certain subset of orthopedic procedures was not included in the final review. Third, due to the substantial heterogeneity of the included studies in terms of reported outcome measures, patient population, stratification of patient factors, follow-up intervals, and study design, it was not possible to perform rigorous quantitative analyses such as a meta-analysis. Fourth, different orthopedic procedures were not equally represented in literature, with 3 included studies performed only on patients undergoing TKA and 4 studies evaluating the outcomes of either TKA or THA.

It is known that orthopedic surgeons are reluctant to perform arthroplasties in patients with cirrhosis, who have a high risk of postoperative complications (Deleurean et al., 2016). However, we believe that this study will provide a novel and important insight into the current state of available literature concerning the rate of perioperative complication after THAs and TKAs in patients with cirrhosis of the liver.

## **Conclusion**

In conclusion, the results of this systematic review and meta-analysis show that total joint arthroplasty surgery for patients with cirrhosis resulted in

increased postoperative morbidity and mortality compared to similar surgery for non-cirrhotic patients.

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