

## QUESTION 9: Does liver disease (hepatitis C, cirrhosis, etc.) predispose patients to surgical site infection/periprosthetic joint infection (SSI/PJI)? If so, what optimization should be undertaken prior to operating on patients with liver disease?

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RECOMMENDATION: Yes. Patients with liver disease such as hepatitis or cirrhosis have a higher risk of infection. These patients are at increased risk of intraoperative and postoperative bleeding. All efforts should be made to ensure such complications are minimized.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 98%, Disagree: 1%, Abstain: 1% (Unanimous, Strongest Consensus)

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### RATIONALE

Hepatitis C virus (HCV) affects more than 185 million people worldwide, and approximately 80% of infected individuals progress to chronic infection, with 20% developing cirrhosis within 25 years [1–4]. As medical therapy continues to improve the life expectancy of patients with liver disease, there is an increasing demand for orthopaedic procedures in this population [5–8]. Earlier studies evaluating postoperative complications in this patient population were of small sample sizes and were not conclusive [6,9,10]. However, recent studies have predominantly demonstrated that, indeed, SSI and PJI occur at much higher rates among these patients [11].

PJIs can occur at a higher frequency among patients with liver cirrhosis compared with those without liver cirrhosis undergoing elective knee arthroplasty (2.7 vs. 0.8%), elective hip arthroplasty (3.66 vs. 0.69%) and hip fracture patients (6.30 vs. 1.10%), as shown by Jiang et al. by analyzing the data from the Nationwide Inpatient Sample and the State Inpatient Database. The study found that liver cirrhosis was an independent risk factor for PJI (odds ratio (OR): 2.4, confidence interval (CI) 1.87 to 3.12), as was a diagnosis of HCV without cirrhosis (OR: 2.3, CI 1.97 to 2.76) [5]. Another retrospective cohort study of primary total hip arthroplasty (THA) or total knee arthroplasty (TKA) patients within the Danish National Patient Registry also supported a higher rate of PJI within one year of surgery in patients with liver cirrhosis [12]. It is important to note that HCV itself may increase complication rates even in the absence of liver cirrhosis.

Pour et al. observed an increased rate of surgical complications, including PJI, in patients with non-cirrhotic HCV undergoing THA but not TKA [10]. The study by Issa et al. included 6,343 patients with HCV and 19,029 matched controls and demonstrated an increased rate of early postoperative surgical complications following THA or TKA in patients with chronic HCV [6]. The cohort also had a higher rate of 90-day complication and readmission [13]. Best et al. used the National Hospital Discharge Survey to compare 26,444 patients with HCV undergoing THA or TKA with a control cohort of 8,336,882 patients without HCV. They reported higher rates of PJI in patients with HCV undergoing total joint arthroplasty (TJA) (HCV: 0.84%, controls: 0.09%, OR: 9.5, CI 8.3 to 10.8) [14]. Studies by Cancienne et al. using the PearlDiver patient record database showed significant OR of 1.7 to 2.1 for infection in total knee, hip [15] and shoulder [16] arthroplasty at 3, 6 and 12 months after surgery. These 3 groups had respectively 15,383, 8,380 and 1,466 cases with HCV that were compared to, respectively 146,541, 48,440 and 21,502 matched control patients. Kildow et al. have demonstrated that by matching control group with age, gender and Charlson comorbidity index (CCI), patients with HCV had higher rates of complications in a 30-day, 90-day or two-year period after TJA [17].

In addition, hepatitis B virus has been recognized as an independent risk factor for PJI after total knee arthroplasty [18]. The risk of PJI at 90 days and two years after total hip and knee arthroplasty were also significantly increased [17]. As compared to control patients, those with liver cirrhosis have more blood loss, higher complications and higher mortality rates. Among cirrhosis patients, alcohol-related cirrhosis carried the highest rate of perioperative complications [19,20].

There are several different explanations for the higher PJI risk in liver cirrhosis patients. One explanation is that liver disease may impair platelet function and cause thrombocytopenia that increases the risk of intraoperative and postoperative bleeding [21–23]. HCV could suppress the immune system, damage the endothelial cells, and lead to severe medical and surgical complications [6,24,25]. Intraoperative blood loss and the need for concentrated red blood cell transfusions reduce the immunological condition of these patients even further. Moreover, the formation of a hematoma around the surgical wound in the days following the intervention is yet another risk factor for developing a PJI. Also, patients with HCV may have beta-islet cell dysfunction and subsequently may develop diabetes mellitus that may result in an increased prevalence of wound complications and the potential for infection [21]. Also, another possible reason is that patients with liver disease had a decreased ability to activate the reticuloendothelial system, lymphoproliferation, neutrophil mobilization and phagocytic activity, all of which diminish their bactericidal activity and have been suggested as important contributing factors to this predisposition towards bacterial infection [16,26,27].

Orthopaedic surgeons should be increasingly aware of this association which should influence the shared decision-making process of performing TJA in patients with liver disease [12,20]. We believe that it is in these patients that preventative measures should be heightened against infection and that strict postoperative control should be followed to proceed aggressively if the infection is suspected. The hemostatic balance should be corrected before surgery according to established procedures such as vitamin K administration or concentrated plasma transfusions to avoid excessive bleeding or perhaps patients with advanced stage of disease should not subject to elective arthroplasty [28,29]. Also, the immune-compromised status of patients with liver disease should be more stringently monitored before surgery [26].

After correlating the seroprevalence rate and underdiagnosed rate, Cheng et al. have concluded that routine screening for HCV infection is not cost-effective [30]. The other study made the same conclusion by comparing the cost and the transmission rate of HCV through percutaneous contact with blood [31].

Given the presence of overwhelming evidence in the literature, we conclude that liver disease such as hepatitis or cirrhosis predisposes patients to SSI/PJI. The hemostatic balance and immune compromised status should be corrected before surgery in patients with liver disease. There are presently no proposed guidelines to better prepare patients with liver disease for orthopaedic surgery. Future research should address care optimization for these patients. Hepatitis will increase the rate of complication after elective arthroplasty. The advantage of operation and disadvantage of possible complications should be carefully evaluated and discussed with the patient.

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