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Perioperative Assessment of Diabetic Patient with Liver Cirrhosis Undergoing Surgery: A Case Report and Literature Review

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Abstract: ***Liver cirrhosis has been shown to be a major preoperative risk factor in surgery with a strong correlation between the preoperative severity of liver disease and postoperative patient's outcome. In the report, we present a case of perioperative assessment for a 57-year-old female patient with chronic liver disease and diabetic foot undergoing surgery, along with a review of the literature. The patient was diagnosed with liver cirrhosis CTP C and infected diabetic foot wagner IV with unstable blood glucose and thrombocytopenia. Elective surgery was a contraindication and had high risk of morbidity and mortality.***

Keywords: Liver cirrhosis, perioperative assessment, diabetic foot, elective surgery

1. Introduction

Liver cirrhosis is one of the main causes of health burden in the world. According to the 2010 Global Burden Disease study, cirrhosis causes 31 million disability by year of life or Disability Adjusted Life Years (DALYs), or 1.2% of the world's DALYs and 2% of all deaths worldwide in 2010. [1] Liver cirrhosis is included in the 20 the leading cause of death in the world, accounting for 1.3% of all deaths in the world and the top 5 causes of death in Indonesia. It has been estimated that about 10% of patients with cirrhosis will undergo surgery in the last 2 years of their life. Early studies showed mortality for the cirrhotic patient is 11–25%, compared with those without cirrhosis of 1.1%. This wide range of mortality rates is related to severity of liver disease, type of surgery, demographics of patient population, expertise of the surgical, anesthesia and intensive care unit(ICU) team and finally, reporting bias.[2, 3]

Liver cirrhosis has been shown to be a major preoperative risk factor in surgery with a strong correlation between the preoperative severity of liver disease and postoperative patient's outcome. Patients with liver disease have an inappropriate response to surgical stress secondary to the loss of hepatic reserve and because of other systemic derangements that are the result of liver dysfunction (such as hemodynamic impairments). These individuals are accordingly at an increased risk of bleeding, infection, postoperative hepatic decompensation, including hepatic coma or death.[4]

Stratification of risk factors and management of preoperative, intraoperative and postoperative complications are essential to reduce morbidity and mortality. Careful selection of patients with liver cirrhosis requiring surgery depends on many factors, including severity of liver disease, type of surgery, timing of surgery (emergent or elective), and associated comorbid clinical conditions. [1]

In this article, we present a case of perioperative of diabetic patient with chronic liver disease undergoing amputation and debridement on right foot.

2. Case Presentation

A 57-year-old female patient was admitted to our hospital with wound on the right foot. Her symptoms was known 2 weeks ago with swollen, redness skin, and pus on the wound. Six months history of chronic liver disease and ten years history of type 2 Diabetes Mellitus (T2DM) were reported. Other symptoms described included enlarged abdomen without pain, constipation, sleep disturbance and anxiety over night occasionally. Her family history were not known. On her physical examination, patient seemed pale skin, conjunctival pallor, and slight jaundice. Necrotic lesion with bone exposure on fourth finger and widely deep ulcer on right plantar foot were found. Clinical features can be seen in Figure 1. On abdominal examination, as cites grade III and caput medusae was visible. Complete blood count (CBC) revealed the following results. Hemoglobin was 8%, Leukocyte 24.790/uL, and Platelet 100.000/uL. Table 1 showed CBC results during hospitalization.In liver function tests, Albumin was 2.1 g/dL, INR 1.34, total bilirubin 2.1 mg/dl, direct bilirubin 1.6 mg/dl, and other tests were normal range.Random plasma glucose was 387 g/dL, Fasting Plasma Glucose 248 g/dL and HbA1c9.6%. Electrolyte imbalance was exhibited with hyponatremia (128 mmol/L) and hyperkalemia (6.3 mmol/L). Creatinin serum was 1.7mg/dl and Ureum was 77 mg/dl. On a chest x-ray, There was aortae elongation. Right foot radiography with anteroposterior view showed osteomyelitis on the medial and distal phalanges of the fourth toe and gangrenous gas (Figure 2). The patient was diagnosed as Type 2 Diabetes Mellitus with diabetic foot wagner IV on the right foot and chronic liver disease (CTP class C). She was consulted to surgery department for diabetic foot treatment. Daily wound care was performed. The patient therapy included furosemide injection 20mg three times daily, Ceftriaxon injection 1g twice daily, Metronidazole drips 0.5 g three times daily, and Lactulose syrup (15cc three times daily). Blood glucose was regulated with Novorapid injection 8 IU three times daily and Lantus injection 6 IU once daily at night. Intravenous calcium gluconate, Insulin 20 IU administered with Intravenous Dextrose 40%, and salbutamol nebulizer were given together to treat hyperkalemia during admission. During her follow-up, the

patient was planned to undergo a below knee amputation. Patient was hospitalized for 1 month and discharged with conservative treatment.

3. Discussion

Liver cirrhosis has been shown to be a major preoperative risk factor in surgery with a strong correlation between the preoperative severity of liver disease and postoperative patient's outcome. Careful selection of patients with liver cirrhosis requiring surgery depends on many factors, including severity of liver disease, type of surgery, timing of surgery (emergent or elective), and associated comorbid clinical conditions.[1]

Patients with liver disease have an inappropriate response to surgical stress secondary to the loss of hepatic reserve and because of other systemic derangements that are the result of liver dysfunction (such as hemodynamic impairments). These patients are at an increased risk of perioperative mortality due to the effects of surgery and anesthesia such as an increased risk of bleeding, infection, postoperative hepatic decompensation, including hepatic coma or death. Stratification of risk factors and management of preoperative, intraoperative and postoperative complications are essential to reduce morbidity and mortality.[4, 5]

Table 1: Complete Blood Count (CBC) Results

Date (2018)	WBC (10^3/ul)	RBC (10^6/ul)	Hb (%)	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g/L)	PLT (10^3/ul)
June 27th	24.79	2.6	8	23.3	89.6	30.8	34.3	100
July 5th	17	3.18	9.3	27.2	85.5	29.2	34.2	52
July 7th	16.9	2.83	8.4	23.9	84.5	29.7	35.1	40
July 8th	11.27	3.96	11.7	33.7	85.1	29.5	34.7	33
July 10th	9.84	4	12.1	34	85	30.3	35.6	35
July 13th	7.1	4.42	13.2	37.8	85.5	29.9	34.9	45
July 16 th	5.86	3.98	11.9	34.5	86.7	29.9	34.5	37

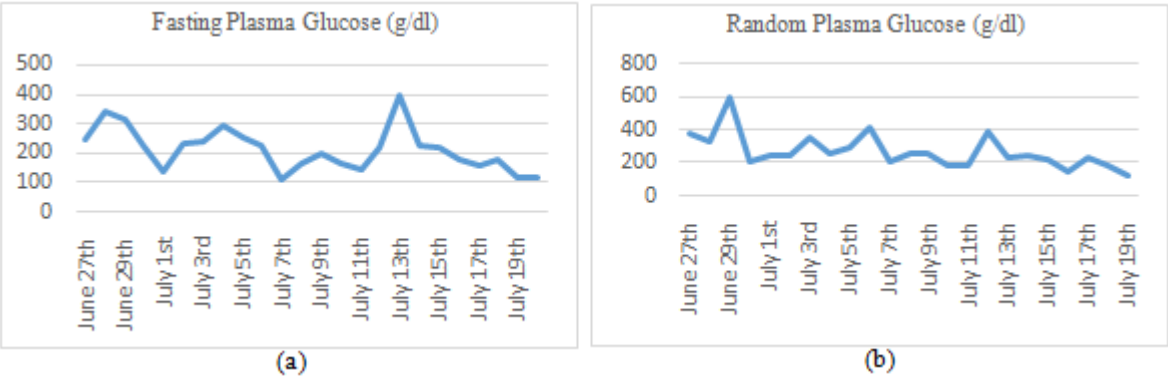

Chart 1: (a) Random plasma glucose at 10.00 pm; and (b) Fasting plasma glucose at 06.00 am.

Figure 1: (a) Dorsal aspect of right foot; and (b) Plantar aspect of right foot

Figure 2: Right foot X-ray in AP and lateral view

Preoperative Evaluation

Preoperative evaluation includes history taking and physical examination aim to identifying risk factors, prophylactic measures to prevent complications and early recognition and treatment of complications. History taking should includes: (1) Symptoms of chronic liver disease such as pruritus, fatigue, bleeding, yellowish skin, oedema, mental alteration, (2) History of prior blood transfusion, jaundice or liver disease, and family history of liver disease, (3) History of metabolic diseases such as diabetes mellitus, hypertension, hyperlipidemia, obesity, (4) History of autoimmune disease such as systemic lupus erithematosus, autoimmune thyroid disease, and (5) Social history, which includes drug abuse, sexual promiscuity, tattoo, excessive alcohol use, use of hepatotoxic medicine and herbal. It is important to elicit any previous or prior history of decompensation such as ascites, edema, or hepatic encephalopathy, variceal bleeding or anesthesia related complications. Physical examination should be performed with focus on the clinical signs of chronic liver disease and features of portal hypertension. A preoperative evaluation should comprise laboratory tests such as comprehensive metabolic profile, complete blood counts and coagulation factors. Early recognition of comorbid condition and optimal treatment of complications may decrease the risk of complications or death following surgery. Preparation should include correction of coagulopathy, treating preexisting encephalopathy, controlling ascites, preventing sepsis, and optimizing renal function.[1, 6]

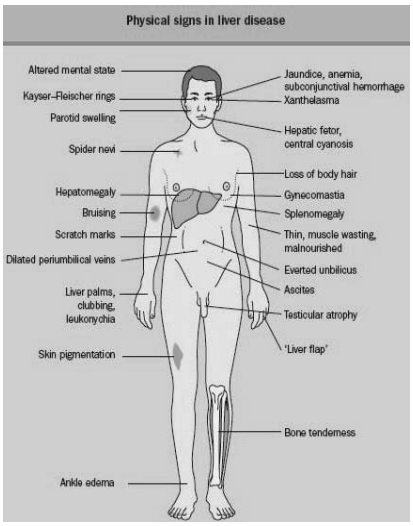

Figure 3: Physical signs in liver disease[7]

Coagulopathy and Thrombocytopenia

Preoperative correction of coagulopathy is essential. Coagulopathy in liver disease could be due to hepatic synthetic dysfunction or vitamin K deficiency usually caused by malabsorption secondary to prolonged cholestasis. [1, 5, 8]Coagulopathy due to hepatic synthetic dysfunction cannot be corrected with vitamin K supplements. Vitamin K administration should still be tried in case malabsorption had contributed to coagulopathy. If there is inadequate response to vitamin K or in emergency situations, fresh frozen plasma can be administered. If patients do not respond to fresh frozen plasma, cryoprecipitate, may be given intravenously preoperatively.

Thrombocytopenia can be found in patient with cirrhosis. It is affected by increasing destruction through hypersplenism and impaired synthesis of thrombopoietin which provoke platelet formation. Several studies suggested to perform platelet transfusion with platelet count < 50.000/mm^3. In 2014, Glance LG et al investigated 316,644 patients undergoing noncardiac surgery without clinical indication for preoperative coagulation testing. In the result, Risk of 30-day mortality increased in patient with thrombocytopenia. Prophylactic platelet transfusions may be considered for severe thrombocytopenia (< 50 000/mL).[1, 9]

The patient had a platelet count of 100.000/mm^{3}when she was hospitalized at beginning. During preoperative preparation, Platelet count was decline until 35.000/mm^3 and decided to perform blood transfusion with 4 bag platelet. However, there was no significant increase.

Hepatic Encephalopathy

Assessment of the mental status should be performed to identify sign of hepatic encephalopathy (HE). Conditions such as constipation, alkalosis, central nervous system depressants, hypoxia, infection, azotemia and gastrointestinal bleeding may precipitate overt HE, and thus conditions should be avoided. [1, 10]

Management of hepatic encephalopathy should include dietary protein intake of 1.0 to 1.5 g/kg daily with sodium restriction to 2 g in those with ascites. Lactulose should be administered with the target of 2 to 3 soft bowel movements each day. Treat infections with administration of non-absorpable antibiotics such as neomicyne&rifaximin, avoid using ofCNS depressants.[1,4, 6]

This patient had a complain ofsleep disturbance and anxiety over night, which was included in grade I of hepatic enchephahopathy. According to West Haven Criteria, patient with trivial lack of awareness, euphoria, anxiety, shortness attention span, or impaired performance of addition was classified in grade I of hepatic encephalopathy. The patient was given dietary protein of 1,0 g/kg/day and lactulose syrup 15cc every 8 hour/ day.

Ascites

The presence of ascites may increased risk of abdominal wound dehiscence, abdominal wall herniation, respiratory compromise, spontaneous bacterial peritonitis (SBP). Ascites could be managed by a combination of low sodium diet and administration of diuretics such as furosemide and spironolactone with careful monitoring of creatinine and electrolyte levels. Large volume paracenthesis could be performed in patient with refractory ascites with replacement 8 g of albumin for each liter of ascites drained to maintain intravascular volume and to reduce the risk of hepatorenal syndrome.It is important to analyze the ascites fluid for differential white cell counts. If absolute ascites neutrophil counts exceed 250 neutrophils/mL, the patient should be treated for SBP with a third generation cephalosporin such as ceftriaxone or a fluoroquinolone such as ciprofloxacin as the common pathogens are usually Escherichia coli and Klebsiella pneumoniae.[11]

In this patient, ascites was visible on the abdominal examination. According to European Association for the Study of The Liver 2010, It was classified in grade III because of abdominal distention and large ascites. The patient was treated with low sodium diet, furosemide injection 80mg/day, and oral spironolactone 100 mg/day. There was no water restriction in the beginning. [12]

Renal and Electrolyte Abnormalities

Renal insufficiency in patient with liver cirrhosis could present from a variety of etiologies including iatrogenic causes such as medications (diuretics, non-steroidal antiinflammatory drugs or other nephrotoxic agents), large volume paracentesis performed without albumin replacement, infections, gastrointestinal bleeding, or hepatorenal syndrome(HRS). Management should include avoiding nephrotoxic drugs, using contrast agents for diagnostic studies, blood volume and fluid support should be in the form of a volume expander such as concentrated albumin and if HRS present, consider combination terlipressin with albumin/midodrine with ocreotide.[1, 4, 6, 8]

Hyponatremia is common in advanced liver disease. Hyponatremia in liver cirrhosis may represents the fluid overload resulting from reduced solute-free water clearance. Severe hyponatremia may lead to seizures and worsening of hepatic encephalopathy. The patient's sodium level was 128 mmol/L. No water restriction was needed in this condition. Hyponatremia is usually corrected by fluid restriction when the serum Na is less than 125 mmol/L and discontinuation of all diuretics.[1, 4, 6, 8]

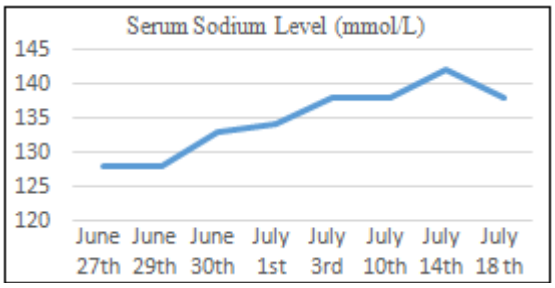

Chart 2: Serum sodium level during hospitalization

Malnutrition among patients with liver cirrhosis is very common, and more than 80% of patients suffer from malnutrition. Reduced food intake due to anorexia and ascites, impaired absorption of nutrients, and increased catabolism can contribute to malnutrition. Hypoalbuminemia can be the manifestation of malnutrition. Hypoalbuminemia leads to reduced oncotic pressure and intravascular hypovolemia, impaired wound healing, sepsis, delay in recovery, impaired mobility, and respiratory muscle dysfunction resulting from muscle wasting.[1, 11] From the study that Gibs et al conducted, hypoalbuminemia is a predictor of mortality in patients with cirrhosis undergoing surgery. In this case, a serum albumin level was 2.1 g/dL. A low serum albumin level of 2.1 g/dL when compared with serum albumin level of 4.6 g/dL was associated with higher mortality of 29% vs 1%, as well as higher morbidity of 65% vs 10%, respectively.[13]

Patients with advanced liver disease should receive nutritional supplementation, both enteral and parenteral in the perioperative period. Nutritional supplementation should be high in carbohydrate/lipid content and low in amino acid content to prevent worsening of preexisting hepatic encephalopathy.[1, 11]

Estimating The Risk Factor

Risk factor stratification in patient with liver disease is influenced by (1) Severity of liver disease; (2) Comorbid condition; and (3) Timing & type of surgery. [6, 8]

Severity of liver disease is calculated using Child Turchotte Pugh (CTP) score and model for end stage liver disease (MELD) score. The CTP and MELD are not mutually exclusive and in practice it is advised that both be used to guide clinical management.[1]

CTP Score

CTP Score was originally designed for predicting the outcome after surgery for portal hypertension (portocaval shunting and trans-section of the esophagus) in patients with cirrhosis. The CTP score has 5 measures, and each measure is given a score from 1 to 3, with 3 reflecting the most severe derangement of the respective clinical or laboratory parameter.

Malnutrition

The general consensus is that elective surgery is well tolerated in patients cirrhosis with CTP class A, permissible with preoperative preparation in patient with CTP class B.

Table 2: CTP score calculation. Abbreviation: CTP, Child-Turcotte-Pugh; INR, international normalized ratio. CTP score is obtainedby adding the scorefor each parameter.CTP class:A = 5 to 6 points, B = 7 to 9 points, and C = 10to15point. [1]

Laboratory or Clinical Parameter	1Point	2 Points	3 Points
Albumin,g/dL	>3.5	2.8–3.5	<2.8
Bilirubin,mg/dL	<2	2–3	>3
Prothrombin time, seconds prolonged or INR	<4 <1.7	4–6 1.7–2.3	>6 >2.3
Hepaticencephalopathy	None	Grades 1–2	Grades3–4
Ascites	None	Mild and moderate	Severe

except those who undergoing extensive liver resection surgery and cardiac surgery. While the elective surgery in cirrhotic patient with CTP class C is contraindicated, and nonoperative selection is recommended. This patient was categorized in CTP class C. The overall 30-day mortality of CTP-A is 10%, CTP-B is 30% and CTP-C is 76–82%, and these figures have not altered significantly despite more modern surgical and anesthetic techniques. [6]

MELD Score

The model for end-stage liver disease (MELD) was originally developed to determine survival after transjugular intrahepatic portocaval shunt (TIPS) procedures. Nowdays MELD is widely used to estimate relative disease severity and likely survival of patients awaiting for liver transplantation. MELD uses the patient's values for serum bilirubin, serum creatinine, and the international normalized ratio for prothrombin time (INR) to predict survival. This objective score has been shown to reflect the 90 day

mortality in patients with cirrhosis. MELD is calculated according to the following formula:

MELD = 3.78 x loge serum bilirubin (mg/dL) + 11.20 x loge INR + 9.57 x loge serum creatinine (mg/dL) + 6.43

Model for End-Stage Liver Disease scores of <10, 10 to 14, and >14 are comparable to CTP classes A, B, and C, respectively. The general guidelines is that elective surgery in patient with an MELD score below 10 is well tolerated, patient with an MELD score of 10-15 should be managed with caution, and patients with an MELD score above 15, elective surgery should be avoided and the patient should be considered for liver transplantation. Northup et al found a 1% increase in mortality for each MELD point until 20 and a 2% increase in mortality with each MELD point after 20. A MELD score of 5 to 15 had mortality of 5% to 11%, as compared with mortality of 26%, 50%, and 67% when the MELD reaches the value of 25, 35, and 45, respectively.The patient was included in MELD score 18, which avoidance of surgery was needed.[1]

The largest study looking at MELD to predict mortality in cirrhotic patients having a surgical procedure was done by Teh et al. These authors developed the Mayo clinic model in 2007, sought to determine the short-term and long-term mortality risks of cirrhotic patients having surgery, with a control group of ambulatory patients with cirrhosis matched for age and MELD score. The results showed an increased mortality to 90 days postoperatively compared with ambulatory patients (P = 0.03), but no difference at 12 months (P = 0.44). The ASA (American Society of Anesthesiologists Physical Status Classification System, Table 4) score was the best predictor of 7-day mortality, and MELD score was the strongest predictor of mortality beyond 7 days and long-term, this is shown in Table 4.[14]

Table 4: Median survival following surgery by model for end-stage liver disease (MELD) category in the study by Tehetal[2]

MELD	0–7	8–11	12–15	16–20	21–25	≥ 26
Median survival	4.8yrs	3.4yrs	1.6yrs	64days	23days	14days

Henje & Patel have proposed an algorithm for the preoperative assessment of patients with liver disease based on severity of liver disease.[5]

Comorbid Condition

Several studied showed that liver disease has correlation with DM. In 2003, EL-Serag et al. concluded that DM was an independent risk factor for chronic liver disease and Hepatocellular carcinoma in their cohort study for 10 years of follow-up. Furthermore, Verona diabetes study reported the prevalence of chronic liver disease in type 2 diabetes approximately 28% and 55% and an increased risk of death based on 7148 type 2 diabetic patients undergoing follow-up for 5 years in 2005. In 2017, Xu Li et al. reported DM increased the risk of developing liver cirrhosis 2-fold [AOR, 2.132; 95% CI, 1.344-3.382].[15, 16, 17]

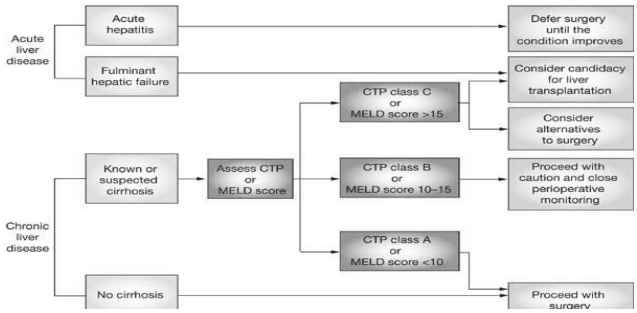

Figure 4: Algorithm for the preoperative assessment of patients with liver disease[5]

Mechanism type 2 diabetes mellitus leading to liver damage has been identified. Insulin resistance and hyperinsulinaemia are considered as the main cause of chronic liver disease through inflammation and necrosis. They initiate peripheral adipocytes to undergo lipolysis and abundance of free fatty acids in the liver. Futhermore, TNF-α and leptin are released by adipocytokine leading to hepatocyte damage and stimulating oxidation stress formation in the mitochondrial. It provokes inflammation process and cellular necrosis causing fibrosis and cirrhosis further. [16, 17]

Diabetic foot is a common complication of type 2 diabetes mellitus. In the United States, About 15- 20% of the estimated 16 million people with diabetes mellitus will be admitted to hospital with diabetic foot during course of their disease. The most of them usually require amputation because of ischemic limb and severe infection. Approximately 85 percent of lower-extremity amputations due to diabetes mellitus are initiated by foot ulceration.[18] According to Indonesian Health Ministery, the percentage of diabetic foot in Cipto Mangunkusumo Hospital Jakarta is about 8.7% in 2011. The rate of mortality following amputation increases about 50-68% in five years. Gangrene, infection, and a non-healing ulcer are the most common reason why amputation is performed. The purpose of minor amputation are to control infection, to depress the expansion of gangrene, to reduce the risk of major amputation and to maximize ambulatory function. Necrotic tissue or gangrene can be a site of infection. Debridement procedure is performed to eliminate it and to help the formation of healthy tissue across the ulcer. [1, 20]

Timing & Type of surgery

Several studies concluded that patients with cirrhosis who undergone emergency surgery have a higher mortality rate than patients with normal liver function and have correlation with increasing CTP score. The mortality rate in cirrhosis patient with CTP class A who underwent emergency surgery was 22 %, 38% in CTP B, and 100% in CTP C. Our patient was classified as Child's class C and was planned to have an elective surgery for an amputation. Some condition that are contraindication for an elective surgery can be seen in Table 6.[6]

Table 6: Contraindications to Elective Surgery in Patients with Liver Disease. [21]

Acute viral hepatitis
Acute alcoholic hepatitis
Fulminant hepatic failure
Severe chronic hepatitis

Child's class C cirrhosis
Severe coagulopathy (prolongation of the prothrombin time of >3 seconds despite vitamin K administration; platelet count <50,000/mm 3)
Severe extrahepatic complications Hypoxemia Cardiomyopathy, heart failure Acute renal failure

Liver cirrhosis is associated with a hyperdynamic circulation and increased cardiac output and decreased systemic vascular resistance. Hepatic arterial and venous perfusion of the cirrhotic liver may be decreased. Portal blood flow is reduced as a result of portal hypertension, and arterial blood flow can be decreased because of impaired autoregulation. Anesthetic agents may reduce hepatic blood flow by 30–50%. Additional factors that may contribute to decreased hepatic blood flow intraoperatively include hypotension, hemorrhage and vasoactive drugs. The decreased hepatic perfusion makes the cirrhotic liver more susceptible to hypoxemia and hypotension.[22]

4. Conclusion

The patient was diagnosed with cirrhosis liver CTP Score C and MELD Score 18 and should undergo amputation due to infected diabetic foot. Based on this patient's risk stratification, elective surgery was a contraindication and had high risk of morbidity and mortality. Finally, This patient was decided for a conservative treatment.

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