# liver dysfunction after endoscopic esophageal variceal ligation: A case report and literature review

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**Introduction:**

Since its introduction in 1986[1], endoscopic variceal ligation (EVL) has gained wide acceptance in clinical practice due to its simplicity, short duration, and low complication rates[2, 3]. Clinical guidelines in many countries have been recommended EVL as the first-line treatment for esophageal varices in liver cirrhosis[4-6]. However, there have been reports of potential adverse events associated with EVL. These include esophageal stenosis, ulcer bleeding, esophageal perforation, esophageal hematoma, pneumonia, and spontaneous bacterial peritonitis[7-10]. Although rare, cases of liver dysfunction following EVL have also been reported. In this paper, we present the case of a 50-year-old male patient diagnosed with alcoholic cirrhosis and esophageal variceal rupture and bleeding. He underwent emergency EVL for hemostasis at our hospital. Subsequently, he developed liver dysfunction. The patient's condition improved following active conservative treatment in internal medicine and DPMAS+PE therapy.

**The study was approved by the Ethics Committee of Dazhou Hospital of Integrative Medicine. Written informed consent was obtained from the patient's family.**

**Case report:**

A 55-year-old male patient with a history of more than 30 years of alcohol consumption, averaging about 100-150ml per day, was presented. Six years ago, he was diagnosed with alcoholic liver disease due to liver dysfunction and received symptomatic treatment including abstinence and liver protection at our hospital. Subsequently, he has been regularly followed up at the Digestive and Liver Disease Department. Three years ago, he was admitted to our hospital due to hematemesis. Gastroscopy revealed ruptured and bleeding esophageal varices. After undergoing EVL for hemostasis and receiving comprehensive internal medicine treatment, he showed improvement and was discharged. Post-discharge, he was prescribed oral propranolol (10mg twice a day) to reduce portal vein pressure. On January 26, 2023, the patient experienced recurrent hematemesis after consuming solid food, leading to his emergency admission to our hospital. Routine and biochemical examinations revealed the following: WBC: 4.67X10ˆ9/L, RBC: 3.28X10ˆ12/L, HGB: 88g/L, PLT: 26X10ˆ9/L, AST: 104U/L, ALT: 31U/L, DBIL: 24.2umol/L, TBIL: 43.1umol/L, PT: 16.6sec, ALB: 25.1g/L, APTT: 34.5sec, PTA: 46.6%, INR: 1.46, and FIB: 1.020g/L. Computerized tomography revealed liver cirrhosis, splenomegaly, a small amount of ascites in the abdominal cavity, and esophageal varices. Emergency gastroscopy confirmed the presence of ruptured and bleeding esophageal varices, leading to the clinical diagnosis of alcoholic liver cirrhosis with decompensated esophageal variceal rupture (Child-Pugh B). With consent obtained from the patient and his family members, emergency endoscopic esophageal variceal ligation was performed (refer to Figure I for the specific procedure). Post-surgery, the patient underwent fasting, received somatostatin to reduce portal vein pressure, underwent cefoperazone sodium

treatment for anti-infection, received a 400ml transfusion of suspended red blood cells to correct anemia, and was provided compound amino acids (3AA) with various vitamins for symptomatic nutritional treatment following improvement.

On the third day following the surgery (January 30, 2023), the patient exhibited yellowing of the skin and sclera. The results of blood tests, liver function, and coagulation function showed deterioration. The findings were as follows: WBC: 5.73X10ˆ9/L; RBC: 2.79X10ˆ12/L; HGB: 76g/L; PLT: 36X10ˆ9/L; AST: 222U/L; ALT: 69U/L; DBIL: 219umol/L; TBIL: 309umol/L; PT: 23.5sec; APTT: 49.9sec; PTA: 29.3%; INR: 2.10; FIB: 1.52g/L. The clinical diagnosis was acute-on-chronic liver failure (type B). The patient was advised to observe bed rest and received magnesium isoglycyrrhizinate injections for liver protection, Transmetil (Ademetionine 1,4-Butanedisulfonaate) injections to manage jaundice, a 300ml infusion of fresh frozen plasma, and a 400ml intravenous drip of suspended red blood cells to improve coagulation function and address anemia. Two days later (February 2, 2023), a re-examination of blood routine and biochemical indicators revealed the following values: WBC: 6.53x10ˆ9/L; RBC: 3.0x10ˆ12/L; HGB: 81g/L; PLT: 49x10ˆ12/L; AST: 48U/L; ALT: 131U/L; DBL: 278.4umol/L; TBL:435u/L; PT: 21sec; APTT: 50.4sec; PTA: 34%; FIB: 2.11g/L. However, bilirubin levels continued to rise, and the patient showed poor response to the comprehensive internal medicine treatment. With the patient's and family's consent, DPMAS+PE treatment was administered on February 3, 2022. One day later (February 4, 2023), a blood re-examination showed the following results: WBC: 6.17x10ˆ9/L; RBC: 2.63x10ˆ12/L;HGB:72g/L; PLT:48x10ˆ12/L; AST:79U/L; ALT: 37U/L; DBL:196.3umol/L; TBL :316.0u/L; PT:17.4sec; APTT:41.6sec; PTA:43.7%; FIB:2.040g/L. DPMAS+PE treatment was administered once again on February 6th, 2023. The subsequent blood routine and biochemical indicators, reviewed on February 7th, 2023, showed the following values: WBC: 5.53x10ˆ9/L; RBC: 2.91x10ˆ12/L; HGB: 77g/L; PLT: 53x10ˆ12/L; AST: 88U/L; ALT: 43U/L; DBL: 183.9umol/L; TBL: 279.3u/L; PT: 18.7sec; APTT: 40.6sec; PTA: 39.7%; FIB: 1.870g/L. The patient's symptoms of poor appetite and fatigue had significantly improved. On February 9th, 2023, a blood test showed the following results: WBC: 5.99x10ˆ9/L, RBC: 2.93x10ˆ12/L, HGB: 77g/L, PLT: 55x10ˆ12/L, AST: 99U/L, ALT: 58U/L, DBL: 193.5umol/L, TBL: 284.2u/L, PT: 19.3sec, APTT: 42.2sec, PTA: 38.1%, FIB: 1.620g/L. The patient continued to receive basic treatment such as liver protection and jaundice relief. Additionally, due to the presence of anemia, another transfusion of suspended red blood cells (400ml) was administered to address the anemia. On February 12th, 2023, a blood test showed the following results: WBC: 8.36x10ˆ9/L, RBC: 3.23x10ˆ12/L, HGB: 83g/L, PLT: 47x10ˆ12/L, AST: 95U/L, ALT: 81U/L, DBL: 185.2umol/L, TBL: 267.6u/L, PT: 20.1sec, APTT: 45.1sec, PTA: 36.1%, FIB:1.270g/L. Considering the patient's persisting symptoms of fatigue and poor appetite, as well as the prolonged elevation of bilirubin levels, DPMAS+PE treatment was administered again on February 13th, 2023. Two days later (February 15th), a review of blood routine and biochemical indicators revealed the following values: WBC: 9.05x10ˆ9/L; RBC: 3.22x10ˆ12/L; HGB: 82g/L; PLT: 46x10ˆ12/L; AST: 58U/L; ALT: 55U/L; DBL: 142.3umol/L; TBL: 197.5u/L; PT: 17.2sec; APTT: 38.4sec; PTA: 44.4%; FIB: 1.680g/L. Two days later (February 17th), the blood routine and biochemical indicators were reviewed again, showing the following values: WBC: 5.66x10ˆ9/L; RBC: 3.14x10ˆ12/L; HGB: 80g/L; PLT: 34x10ˆ12/L; AST: 58U/L; ALT: 66U/L; DBL: 112.8umol/L; TBL: 148.1u/L; PT: 18.4sec; APTT: 42.7sec; PTA: 40.6%; FIB: 1.210g /L. The patient's condition remained relatively stable, and maintenance treatment, including liver protection and jaundice relief, was continued during this period. Another transfusion of suspended red blood cells (400ml) was administered to address the anemia.

Two days later, on February 20th, a follow-up blood routine and biochemical analysis was conducted, revealing the following results: WBC: 5.95x10ˆ9/L; RBC: 3.87x10ˆ12/L; HGB: 96g/L; PLT: 34x10ˆ12/L; AST: 88U/L; ALT: 96U/L; DBL: 114.6umol/L; TBL: 159.2u/L; PT: 17.1sec; APTT: 36.7sec; PTA: 44.7%; FIB: 1.640g/L. With the patient's condition being stable, the patient and their family requested discharge due to the high medical expenses. They were informed that the patient should have a follow-up outpatient visit at the hospital where the author is located after discharge. Subsequent telephone follow-ups conducted after March indicated that the patient's general condition was good, and they were able to engage in light physical activity.

**Discussion:**

Since its introduction in 1986, EVL (Endoscopic Variceal Ligation) has been widely recommended as the first-line treatment for esophageal varices in liver cirrhosis by clinical guidelines in numerous countries. When compared to EIS (Endoscopic Injection Sclerotherapy), EVL demonstrates significant superiority in terms of rebleeding rate, variceal eradication rate, and complications[1-6]. Consequently, an increasing number of clinicians consider EVL as the preferred treatment for patients experiencing esophageal variceal rupture and bleeding. Reported complications of EVL mainly encompass esophageal stenosis, ulcer bleeding, esophageal perforation, esophageal hematoma[7-9], pneumonia, and spontaneous bacterial peritonitis[10-12]. However, there have been few reports documenting liver function failure following EVL surgery. Through a comprehensive literature review, we discovered that only one case of elevated bilirubin levels with subsequent liver dysfunction after EVL surgery has been documented thus far. This case involved a 51-year-old female patient with primary biliary cholangitis (PBC) and esophageal variceal rupture and bleeding, who underwent EVL treatment. Following the procedure, the patient experienced an increase in bilirubin levels from 4.0mg/dL to 9.5mg/dL, ultimately necessitating liver transplantation due to the worsening of liver function failure[13].

The mechanism behind liver function failure after EVL surgery remains unclear. In the context of cirrhosis, both hepatic and splanchnic systemic oxygen uptake (VO2) are reduced[14, 15]. Our hypothesis suggests that the cause of liver failure in patients after EVL may be attributed to increased portal pressure, decreased cardiac output, and reduced oxygen delivery following the procedure. Previous studies have reported that 68% of patients undergoing endoscopic variceal ligation experience an elevation in portal vein pressure[16]. It is postulated that the sudden rise in portal vein pressure could exacerbate liver congestion, impair oxygen utilization by liver cells, and subsequently lead to liver cell necrosis. However, a study conducted in 2003 revealed no significant change in the portal vein pressure gradient before and after EVL surgery in patients with liver cirrhosis and esophageal variceal rupture and bleeding[17]. Consequently, further investigation is required to explore whether an increase in portal vein pressure occurs after EVL surgery.

As early as 1996, reports emerged highlighting a related phenomenon wherein EVL surgery may exacerbate liver tissue ischemia and hypoxia. This study observed a decrease in cardiac output and oxygen delivery immediately after EVL surgery, although the underlying causes and implications were not fully understood at the time[18]. This hypoxic condition is particularly pronounced in patients with varicose veins and anemia. Research has shown that patients with liver cirrhosis exhibit a high dynamic circulation, which enhances oxygen delivery but impairs the uptake and utilization of oxygen by tissues, resulting in sustained liver cell hypoxia[19]. Furthermore, all tissues of patients with liver cirrhosis experience a certain degree of hypoxia due to arteriovenous shunting[20]. Therefore, a sudden decrease in cardiac output and oxygen delivery could further intensify liver cell hypoxia, leading to acute massive necrosis of liver cells.Overall, the precise mechanisms underlying liver function failure after EVL surgery necessitate further investigation. The potential impact of increased portal pressure, reduced cardiac output, oxygen delivery, and the exacerbation of liver cell hypoxia requires comprehensive exploration. Future research should focus on elucidating these mechanisms to enhance our understanding and potentially develop strategies for mitigating liver function failure following EVL surgery.

Furthermore, there have been reports suggesting the potential involvement of endogenous nitric oxide in the regulation of systemic hemodynamics in patients with compensated cirrhosis. Serum nitrate and nitrite, which are metabolic byproducts of endogenous nitric oxide, exhibit a sudden decrease in concentration in patients after EVL[21, 22]. Previous studies have demonstrated that nitric oxide can alleviate ischemia-reperfusion injury of the liver and expedite the recovery of liver function[23]. Nitric oxide's protective effects on liver tissue may play a role in the context of EVL surgery, although further research is required to investigate the specific mechanisms and implications of nitric oxide modulation in this setting.

It has been reported in studies that compared to patients with Child-Pugh A/B, patients with Child-Pugh C cirrhosis exhibit higher rates of rebleeding and mortality following EVL[24]. In the case of our patient, their liver function reserve was evaluated as Child-Pugh B upon admission. However, after undergoing emergency EVL, the patient experienced a significant increase in bilirubin levels and developed coagulation dysfunction. We speculate that these effects may be attributed to the blockage of collateral circulation

caused by acute bleeding and the impact of EVL surgery, particularly in the context of poor liver function reserve. This could exacerbate liver congestion symptoms. Additionally, the decrease in cardiac output further intensifies the ischemia and hypoxia experienced by liver cells, ultimately leading to acute necrosis and liver failure. It is important to note that the occurrence of liver failure after EVL surgery is relatively rare, and our understanding of its underlying mechanism is based on plausible pathological and physiological considerations. Further research is required to delve into the intricate mechanisms involved and provide conclusive evidence.

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**Figure I**