

# Lighting talks. Patient blood management in liver disease

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## 1. PERIOPERATIVE PBM STRATEGIES IN PATIENTS WITH LIVER CIRRHOSIS

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Patients diagnosed with **liver cirrhosis (LC)** requiring abdominal surgery present a higher level of morbidity (coagulopathy, malnutrition, immune dysfunction, cardiomyopathy, and renal and pulmonary dysfunction) and mortality. Optimizing the patient before surgery and choosing the less invasive type of surgery (laparoscopy) has led to improved results<sup>1</sup>.

### Regarding the surgical approach:

It is well known that LC patients diagnosed with **acute cholecystitis** requiring laparoscopic cholecystectomy present a higher number of complications than the general population. A meta-analysis by Puggioni et al.<sup>2</sup> concluded that laparoscopic surgery to treat acute **cholecystitis** reduced the number of complications (blood losses, wound infection, time of surgery, hospital stay) and mortality versus a conventional approach with laparotomy. Likewise, the HiSCO<sup>3</sup> study also observed a decrease of postoperative complications in patients undergoing liver resection using laparoscopy rather than open surgery.

### Regarding the optimization of the coagulopathy:

It is very common for LC patients to present severe thrombocytopenia ( $PLQ < 50 \times 10^9/L$ ), and when they require an invasive procedure, to receive **transfusions of platelets** or thrombopoietin-receptor agonists to reduce the risk of bleeding. Therefore, the main endpoint of the observational study by Ronca et al.<sup>4</sup> was to analyze the relationship between thrombocytopenia before the procedure and the perioperative bleeding in LC patients requiring surgery to treat hepatocellular carcinoma. Thus, they concluded that the risk of bleeding was not related to the platelet count, classified as low ( $PLQ \leq 50 \times 10^9/L$ ), intermediate ( $PLQ = 50-100 \times 10^9/L$ ), or high ( $PLQ > 100 \times 10^9/L$ ). In this study, the risk of bleeding was significantly and independently related to age, GOT level, anemia, and the liver resection, with respect to radiofrequency ablation.

Furthermore, given the coagulopathy (by conventional coagulation tests) presented by the LC patient, the **transfusion of frozen fresh plasma (FFP)** during surgeries and invasive procedures is frequent. LC patients present a balanced coagulation, so that an alteration in conventional coagulation tests do not always imply coagulopathy and bleeding risk, as proven by viscoelastic tests. Thus, in the observational study by Bednarsch et al.<sup>5</sup>, they observed that LC patients requiring hepatectomy for hepatocellular carcinoma presented as the only independent predictive factor for postoperative major complications having received transfusions of FFP during the intervention. Bonnet et al.<sup>6</sup> proved that transfusion following thromboelastography-based algorithms to correct coagulopathy in severe hemorrhage of LC patients during liver transplant decreased the overall number of transfused blood products, particularly FFP. Likewise, Vuyyuru et al.<sup>7</sup> proved how TEG-guided transfusion reduced the transfusion of blood products without increasing the bleeding risk in LC patients requiring invasive procedures (liver biopsies).

### Regarding the transfusion of packed red blood cells:

It is at **surgery** when we can better help to prevent transfusion of packed red blood cells. For that purpose, blood salvaging and autotransfusion are available, with no negative impact in the evolution of patients that have undergone cancer-related surgery<sup>8</sup>.

The matter of how much anemia can be tolerated in case of an **upper digestive hemorrhage (UDH)** has always raised controversy, that is to say, what is the starting level of hemoglobin for transfusion. The clinical trial by Villanueva et al.<sup>9</sup> compared the efficacy and safety of a restrictive therapy (transfusion when  $Hb < 7$  g/dL) versus a liberal therapy (transfusion when  $Hb < 9$  g/dL). The results showed a higher overall survival after 6 weeks for patients randomized to the restrictive strategy. If the etiology of UDH was due to a peptic ulcer, the odds of death in the restrictive arm were similar to the liberal one. If the etiology was related to varicose veins in patients with Child-Pugh A or B, the odds of death were significantly reduced in the restrictive group [HR 0.3 (IC 95%: 0,11-0.85)]. If the etiology was due to varicose veins in patients with Child-Pugh C, there were no significant differences in terms of mortality between both arms.

### Regarding the optimization of the anemia:

The incidence of postoperative **anemia** in cirrhosis patients requiring surgery is very high (80-90%). All patients requiring major surgery and suffering from anemia before surgery, or experiencing moderate to severe blood loss in the operation room, should be treated. The persistence of anemia is associated to a higher incidence of ischemic events and short- and long-term mortality.

These patients are often treated with **iron** supplements, which brings about an increase in hemoglobin, but besides that, not much is known on its benefits. In this regard, an observational study by Rashidi-Alavijeh et al.<sup>10</sup> concluded that this increase in hemoglobin was significantly associated to better survival after a liver transplant, and that administering iron together with rifaximin caused a more noticeable increase in hemoglobin. However, in clinical trial **HepciFer**<sup>11</sup>, that randomized patients requiring liver surgery to receive 1 g of carboxymaltose 4 hours after surgery versus placebo, no significant increase in hemoglobin was observed with the administration of ferric carboxymaltose seven days after surgery. This is a relevant study, since it suggests that intravenous supplementation of iron right after surgery would be the appropriate administration method for iron, preventing blocking mediated by high hepcidin levels in the postoperative setting.

### Conclusions. In liver cirrhosis patients:

They should preferably be operated on through laparoscopy

Blood salvaging agents should be used in the operation room

Transfusion of PLQ and FFP should be guided by transfusion algorithm based on viscoelastic tests

Patients with UDH and Child Pugh A or B should be transfused with  $Hb < 7$  g/dL

The administration of iron to treat anemia should be intravenous

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