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Case Study

Purpose of the measurement of intraoperative hepatic hemodynamics in liver transplant surgery

Abstract

Liver graft function depends on different biological factors that are related to the donor, the recipient and the potential damage arising from the organ preservation technique. However, adequate hepatic artery flow and portal vein flow rates ensure a sufficient flow of oxygen and nutrients in order to ensure a suitable cellular graft function after the extreme metabolic decrease condition induced by hypothermia and the preservation solution. Liver inflow is a highly complex system due to its double irrigation system. These two systems are connected by the well-known "hepatic arterial buffer response" concept. This mechanism explains changes in hepatic arterial flow (HAF) as a compensation for changes in the portal vein flow (PVF), so that the hepatic artery adjusts total flow in relation to alterations in the portal blood flow. At the moment, the minimum HAF and PVF required for an adequate regeneration and functional recovery of the liver graft have not been yet established. The hyperdynamic circulation state observed in cirrhosis could influence liver hemodynamics during liver transplantation; with this situation can be modified intraoperative surgical maneuvers if necessary. A decrease in the HAF could lead to hepatic artery thrombosis. The changes in microcirculation also play an important role in the damage caused by the ischemia reperfusion injury; for instance, sinusoidal diameter narrowing and vascular flow are the first changes to occur after damage by ischemia reperfusion. The damage produced in the sinusoidal endothelium manifests itself as alterations in the early stages of intraoperative hemodynamics. Therefore, and in conclusion, early intraoperative detection of alterations in liver hemodynamics during liver transplantation could be used to prevent worse outcomes in the postoperative time.

Abbreviation

EAD: Early Allograft Dysfunction; HAF: Hepatic Artery Flow; LDLT: Living Donor Liver Transplantation; PH: Portal hypertension; PVF: Portal Vein Flow; PVP: Portal Venous Pressure; TACE: Transarterial Embolization; THF: Total Hepatic Flow

Case Study

The intraoperative measurement of coronary flow began to be clinically relevant [1,2], when it demonstrated its short and long term predictive value in the functional evaluation of the revascularizations in patients undergoing revascularization surgery , especially with the advent of minimally invasive revascularization surgery over the heart, in which the quality control of the anastomosis is paramount [3].

In the field of liver transplantation, experimental studies have shown the importance of adequate perfusion of the liver graft to ensure its correct function. However, the relevance of the hepatic artery and portal vein flows in that function are still unknown.

Measurement of intraoperative vascular flows

The measurement of the intraoperative flows is made with a VeriQ™ flowmeter (Medistin, Norway), VeriQ™ offers both proven transit time flow measurement (TTFM) and Doppler velocity measurements that are specifically designed for intraoperative blood flow and graft patency verification. The Doppler effect uses the transmission of a continuous wave and the MFTT employs the transmission of pulses. By applying the Doppler concept on the components of the blood, we can measure the vessel blood flow velocity. If the sound is directed in the direction of flow, the received signal will be different depending on whether the blood components are near or far from the transducer. The sensor used by the MFTT contains two transducers and a reflector. The two transducers are located on one side of the vessel and the reflector on the opposite side, this arrangement causes a double ultrasound passage through the vessel.

The crystal located in the direction of flow generates a pulse of ultrasound that is captured by the glass of the opposite

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direction. The difference in transit time will depend on the volume of blood flow.

Measurement probes of a 5-7mm caliber are used for the hepatic artery and of 8-12 mm for the portal vein. Once the vascular anastomoses have been performed, a brief period of about 5 minutes is allowed in order for the intrahepatic flows to settle, then the arterial and the portal flows are measured sequentially at one centimeter distal to the suture, on the side of the graft.

In cases where the arterial intraoperative flow measured is absent or very poor, the revision of the arterial anastomosis is indicated, once the absence of compensatory effect of the portal flow ("hepatic arterial buffer effect") has been proven.

Hepatic hemodynamics in native liver

The liver volume constitutes 25% of the total body weight. It receives a total hepatic flow (THF) of 100-130 mL / min per 100 grams and approximately 25% of the cardiac output.

The hepatic flow is an important variable in the early graft function. Liver inflow is a highly complex system due to its double irrigation system. The hepatic artery contributes 25% of the THF (30 mL / min per 100 grams) and provides 30-50% of the oxygen requirement of the liver. On the other hand, the portal vein provides 75% of the hepatic flow (90 mL / min per 100 grams of liver mass) and offers 50-70% of the oxygen requirements of the liver with partially deoxygenated blood arriving from the splanchnic circulation. These two systems are connected by the well-known "hepatic arterial buffer response" concept. This mechanism explains changes in hepatic arterial flow (HAF) as a compensation for changes in the portal vein flow (PVF), so that the hepatic artery adjusts total flow in relation to alterations in the portal blood flow. The "hepatic arterial buffer response" is a one-way compensatory mechanism because the portal vein cannot control its blood flow, so it is unable to compensate for changes in the arterial flow. Cantre et al. showed that the hepatic arterial buffer system was present after a liver transplant was performed [4-6].

Multiple mediators regulate liver inflow; these act on the hepatic sinusoid, focusing on the non-parenchymal cells (endothelial cells, stellate cells and Kupffer cells). These vasoactive substances act through autocrine and paracrine signaling. Endothelial cells play a fundamental role in vasomotor control. They act as sensors between the blood and the vessel wall, regulating these mediators' production that control vascular tone, activation of platelets and leukocytes, coagulation, growth and cell death. The final effect on vascular tone will depend on the final balance between the different mediators.

In normal conditions, these physiological hemodynamic changes that occur in the liver aim to maintain a balance between the liver's metabolic function and its supply of oxygen and nutrients. However, this homeostasis is altered in liver diseases, in liver resection surgery and in liver transplantation.

Liver hemodynamics in cirrhotic liver

Portal hypertension (PH) is defined as an increase in the intraluminal pressure of the portal vein and its collaterals with an average pressure greater than 12 mmHg; this may manifest as variceal bleeding or other clinical consequences.

At a cellular level, PH induces hepatocyte damage and necrosis, an inflammatory response is triggered thus stellate cells transform into contractile cells; fibrogenic myofibroblasts produce large amounts of extracellular matrix and inflammatory cytokines, which in the end lead to cirrhosis. The increase of sinusoidal resistance results in a decrease in PVF and a reactive increase in portal venous pressure (PVP). In contrast, the splanchnic circulation undergoes a progressive vasodilation due to vasodilators molecules such as nitric oxide, which is also related to increased vascular stress and intestinal absorption of lipopolysaccharides. Vasodilators induce the progressive vasodilatation of the splanchnic circulation and a related increase in the PVF contributing to the development of a hyperdynamic circulation with reactive splenomegaly and portosystemic collateralization at multiple locations. However, the development of collaterals and splenomegaly varies individually.

Cirrhotic patients suffer of different kinds of liver and splanchnic circulations at the moment of being transplanted. These circulations can be divided into two types; those patients with venous and splanchnic congestion without collateral formation and those patients who, in the absence of congestion, have extensive portosystemic collateralization.

Hepatic hemodynamics in the liver graft after transplantation

A proper THF is fundamental for the graft survival and its good function. It is assumed that PVF should be at least 1000 ml / min in order to maintain an appropriate perfusion [7-9], Prastcke et al. demonstrated that a decrease of PVF under 1300 ml / min was associated with a worse graft survival in the univariate analysis; nevertheless this was not demonstrated in the multivariate analysis. In contrast, a low hepatic artery flow (HAF) was related to a higher incidence of early allograft dysfunction (EAD) and worse survival, with cutoffs between 100-270 ml / min [10].

At the moment, the minimum HAF required for an adequate regeneration and functional recovery of the liver graft has not been yet established. However, Prastcke et al. found that HAF of less than 100 ml / min was an independent predictor of severe complications [10].

Patients with venous and splanchnic congestion are less likely to present low or a lack of PVF. Nevertheless, a high PVF that causes a critical decrease in HAF to less than 100 ml / min could have adverse effects on the postoperative liver function. Feng et al recommended intraoperative maneuvers such as splenic artery ligation or splenectomy when, once the adequacy of the hepatic arterial buffer system had been checked, a PVF greater than 1300 ml / min accompanied by a HAF of less than 100 ml / min were observed [11].

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It is established that in recipients suffering from many portosystemic collaterals there is a lack of PVF. Castillo-Suescun et al described a series of cases diagnosed with spontaneous splenorrenal shunt where disconnection of the shunt was performed when. PVF was less than 1200 ml / min without observing renal impairment [12].

Causes of alterations in liver intraoperative inflow

Recipient liver hemodynamic conditions: In normal conditions patients who start with advanced cirrhosis develop PH. This situation could cause liver hemodynamic inflow changes in the patient, such as venous dilatation, endothelial damage, formation of collateral circulation and the development of shunts [13]. This hemodynamic state is referred to as a "hyperdynamic state" and it is characterized by an expansion of blood volume, high cardiac output and a decrease in peripheral vascular resistance. These alterations in systemic hemodynamics do not disappear in the follow-up after liver transplantation, so their stabilization is essential for an adequate PVF [14].

In the postoperative period, liver transplant recipients with cirrhosis showed a tendency towards higher PVF when compared to recipients without established cirrhosis. In addition, an adequate balance between cardiac output and blood volume ensures an adequate PVF after transplantation. In this way, these systemic hemodynamic alterations have a greater influence over the PVF than the HAF.

In summary, this hyperdynamic state could influence liver hemodynamics during liver transplantation; this situation can be modified intraoperatively with surgical maneuvers if necessary.

Acute vascular complications

Acute vascular complications are still an important cause of morbidity and mortality after liver transplantation [15]. The hepatic artery plays an important role due to its contribution to the parenchyma and biliary tree blood supply. In those cases in which hepatic artery complications modify the HAF, the graft could survive at the expense of the PVF supply, but only if previous arterial collateral patents were present, which normally do not exist due to total hepatectomy technique performed during liver transplantation. The etiologies of these complications include: thrombosis of the hepatic artery, anastomotic stenosis, formation of pseudoaneurysms and rupture of the hepatic artery. These complications can be classified into two categories: Early (<1 month) or late (> 1 month). Special interest is taken into the identification of early complications, since they lead to worse short-term outcomes [16].

Nowadays, there is an increasing interest in studying the causes of early hepatic artery thrombosis. More than 20% of thrombosis are probably due to technical anastomosis problems, such as technical imperfections, stenosis, small vessels, discordance in size, dissection of the endovascular wall, stenosis of the celiac trunk or compression by the arcuate ligament, presence of multiple arteries, anatomical variants or complex reconstructions in the organ procurement table, poor quality of the donors, or high resistance of the graft microvascularization due to damage by ischemia reperfusion injury. Other factors unrelated to the surgical technique can be, advanced donor age, prolonged cold ischemia time, smoking, hypercoagulable state, retransplantation, or transplants due to primary sclerosing cholangitis or previous TACE (transarterial embolization). (83) Marin Gomez et al. showed that an intraoperative HAF of less than 100ml / min was associated with a higher risk of hepatic artery thrombosis [17].

Sinusoidal damage due to marginal grafting

Microcirculation changes play an important role in the damage caused by ischemia reperfusion injury. Sinusoidal diameter narrowing and reduced vascular flow are the first changes that occur during ischemia reperfusion injury. This is the result of direct damage of sinusoidal endothelial cells, vasoconstriction and expression of adhesion molecules with accumulation of platelets and neutrophils.

Changes associated with age can decrease the graft's regenerative capacity; this leads to an increased susceptibility to ischemia reperfusion injury. Therefore, grafts from donors with expanded criteria are known to be more susceptible to ischemia reperfusion injury. This situation could lead to an increased intrahepatic vascular resistance measured by worse intraoperative hepatic artery flow [18].

In summary, the damage produced in the sinusoidal endothelium could be reflected in alterations in intraoperative liver hemodynamics [19,20].

Graft volume and liver vascular inflow

In all of these previously mentioned studies, the graft weight and volume were not taken into consideration. Kim et al. suggested that a higher rate of biliary complications, both early and late, were associated to HAF rates adjusted to recipient weight of less than 5 ml / min / kg [21]. Asencio et al. demonstrated that the development of the Small for Size syndrome ("small for size") was not only determined by the graft size, but also by the hemodynamic changes that occur in the hepatic circulation regarding high portal flow that could be critical to liver functioning [22,23]. Therefore, when a cirrhotic recipient with liver congestion and splenomegaly undergoes a complete transplant, insufficient liver mass could be submitted to a high portal vein flow and lead to early allograft dysfunction. However, the literature currently published nowadays regarding whole liver transplantation does not show strong evidence to affirm that there is a relationship between high THF after reperfusion and the risk of developing EAD, or of it worsening long-term outcomes.

In relation to grafts with expanded criteria, in which damage by preservation solution has a greater impact, the sinusoid of the hepatocyte may be damaged, which could cause increased resistance to flow. In both cases, both high flow (due to recipient cirrhotic condition) and low flow (due to intrahepatic resistance) could be predictive factors of EAD.

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Conclusion

The early detection of alterations in liver inflow hemodynamics using the intraoperative measurement of liver inflow during the liver transplant procedure could be used to prevent worsened outcomes caused by early allograft dysfunction, acute hepatic artery thrombosis and long-term survival in liver transplantation.

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