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How to Optimize the Patient with HRS/HPS/PPH

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Pulmonary and kidney concerns in liver transplant (LT) candidates may have implications on perioperative outcomes. Particularly, in the era of evolving Model for End-stage Liver Disease (MELD) exception, it is important to assess transplant priority and optimize for problems such as hepatopulmonary syndrome (HPS), hepatopulmonary syndrome (HRS), and portopulmonary hypertension (PPHTN) for the safe management perioperatively. Herein, the lecture will discuss about LT recipients with HRS, HPS, and PPTHN. Acute kidney injury (AKI) is frequently confronted in patients with cirrhosis, and it is related with adverse results. In patients with cirrhosis, HRS-AKI is the most important etiology. HRS-non-AKI as functional kidney injury in cirrhosis, evaluated by estimated glomerular filtration rate (eGFR), which does not meet criteria for HRS-AKI. HRS-non-AKI is divided by two subgroups based on the duration of damage: HRS- acute kidney disease (AKD) diagnosed if eGFR less than 60 mL/min/1.73 m^2 for <3 months, HRS-chronic kidney disease (CKD) if eGFR <60 mL/min/m^2 for more than 3 months. The treatment of HRS-AKI focused mainly on vasoconstriction, and on the basis of clinical trial evidence, norepinephrine and terlipressin are the most useful drugs to deal with HRS-AKI. Discontinue diuretics, volume expand with albumin in prerenal azotemia. If intra-abdominal hypertension (IAH) or abdominal compartment syndrome is present, therapeutic large-volume paracentesis should perform. HPS, documented in 4–32% of patients evaluated for LT, has no proven medical therapy to cure the arterial hypoxemia. A triad defines HPS: (1) Portal hypertension with or without cirrhosis, (2) Arterial hypoxemia, and (3) Intrapulmonary vascular dilatations (detected by contrast echocardiography or 99mTc macroaggregated albumin lung–brain perfusion scanning). LT can enhance the five-year survival of HPS from 23 to 63%. The poor prognostic factors contain a pre-transplant PaO_2 < 50 mmHg, poor functional status despite domiciliary oxygen therapy, macroaggregated albumin shunt fraction >20%, and have a mortality rate as high as 67% in the post-transplant. Thus, the notion of a 'transplant window' has been suggested in HPS in patients with PaO_2 ≥60mmHg is prioritized for transplant while those with more severe hypoxemia are excluded from listing. Resolution of gas exchange abnormalities will take place within 6 to 12 months of LT, although persistence after 12 months has been reported. PPHTN is pulmonary arterial hypertension (PAH) associated with portal hypertension of cirrhotic or noncirrhotic etiology with end stage

liver disease. Main characteristic of PPHTN is that it has high cardiac output (CO) and increased pulmonary vascular resistance (PVR), which hyperdynamic circulatory state in cirrhosis leads to high pulmonary blood flow exposing the pulmonary vasculature to increased shear stress and initiating the cascade of endothelial cell injury and vascular remodelling. Consequently, changes in pulmonary vascular bed result in increased pulmonary pressures, elevated PVR, and finally permanent right heart failure. The diagnostic is the following: mPAP ≥ 20 mmHg, PVR ≥ 240 dyne/s/cm^{-5}, or 3 WU, and pulmonary capillary wedge pressure (PCWP) of ≤ 15 mmHg. Current guidelines from the American Association for the Study of Liver Diseases (AASLD) are all liver transplant candidates with PASP ≥ 45 mmHg should be examined for right heart catheterization (RHC) to confirm the diagnosis of PPHTN. Severity of PPHTN, classifying it as mild (≤35 mmHg), moderate (35–45 mmHg), and severe (≥45 mmHg). Medical treatment with PAH-specific agents could be used as a bridge therapy to transplant, the only available curative treatment. Despite the improvement seen in patients with PPHTN after LT, moderate-to-severe disease has been associated with increased perioperative mortality risk, and its prompt identification in prospective LT candidates is important for surgical planning and optimization of patient care. Severity classification of PPHTN is essential, as mPAP ≥35 mmHg and PVR ≥ 3 WU has an increased risk of peri- and postoperative mortality in liver transplant candidates. Notably, PPHTN with severe hemodynamic impairment (mPAP ≥45 or 50 mmHg or PVR ≥3 WU) is associated with 100% mortality and is considered an absolute contraindication. Similarly, patients with mPAP of 35mmHg to less than 50mmHg and PVR ≥240 dyne/s/cm^{-5} appear at high risk for cardiopulmonary-related mortality after LT. The most crucial phase of LT is the one after allograft reperfusion, due to an increased risk of acute right heart failure. MELD exception program allows LT waitlist candidates with PPHTN to gain waitlist priority based on the following criteria: diagnosis of PPHTN established by RHC, initiation of PAH-specific treatment with confirmed hemodynamic improvement (mPAP <35 mmHg, PVR <5 WU), and MELD exception assessment every 3 months. Some limitations regarding the implication of the MELD exception system: Significant proportion of patients with PPHTN and MELD exception points lack pre- and post-transplant hemodynamic parameters (e.g., CO, cardiac index) to help predict the risk of cardiopulmonary complications; and evidence of favorable post-transplant outcomes originates from small case series susceptible to publication bias that may falsely lead to consider PPHTN as an absolute indication of transplantation. Therefore, PPHTN MELD exception score warrants more investigation and consideration of additional variables (e.g., baseline PVR and MELD score) for accurate estimation of pre- and postoperative risk transplant candidates with PPHTN. Figure 1. Portopulmonary hypertension Model for End-Stage Liver Disease exception criteria