Letters to Editor

Living donor liver transplantation in a patient with severe portopulmonary hypertension

Sir,

Porto-pulmonary hypertension (PoPH) is an uncommon (reported prevalence 5.3%),[1] but a dreaded complication of chronic liver disease (CLD) in patients undergoing liver transplant (LT). Since its development is not related to the severity of liver dysfunction[2] and the symptoms are non-specific, screening for POPH with transthoracic echocardiography (TTE) is recommended. On TTE, the maximum tricuspid regurgitant flow velocity is used to calculate right ventricular systolic pressure (RVSP).[3]

American Association for the Study of Liver Diseases (AASLD) recommends right heart catheterization (RHC) in patients with CLD having RVSP >45 mmHg. A mean pulmonary artery pressure (mPAP) >25 mmHg is diagnostic of PoPH.[4] Severe PoPH (mPAP >45 mmHg) is considered an absolute contraindication for LT as reported mortality from RVF and graft loss is high.[5,6] Pulmonary vasodilators can reduce mPAP. Once mPAP <35 mmHg (moderate PoPH) and pulmonary vascular resistance (PVR)<400 dyn-s/cm^{-5},[7] patients can undergo LT.[5] Post LT survival depends on good right ventricle (RV) function, compliance of pulmonary vasculature and reversibility of pathology with therapy.

A 23-year-old male with hepatitis B related CLD presented for living donor LT with Child Turcotte Pugh score 6 and Model for End-stage Liver Disease Sodium score 15. On evaluation, the patient was well preserved with jaundice, mild ascites, grade 3 clubbing without tachypnoea or exercise limitation. His room air saturation was 98%. However, routine TTE reported RVSP of 70 mmHg. A short course of diuretics was given to reduce ascites and flow-related pressures. Subsequent RHC confirmed severe PoPH with mPAP 57 mmHg and PVR 798 dyn-s/cm^{-5}. Eight weeks of pulmonary vasodilator therapy with oral tadalafil 20 mg, ambrisentan 5 mg and torsemide 10 mg twice daily reduced RVSP [Figure 1]. Under standard monitoring including pulse oxymetry,

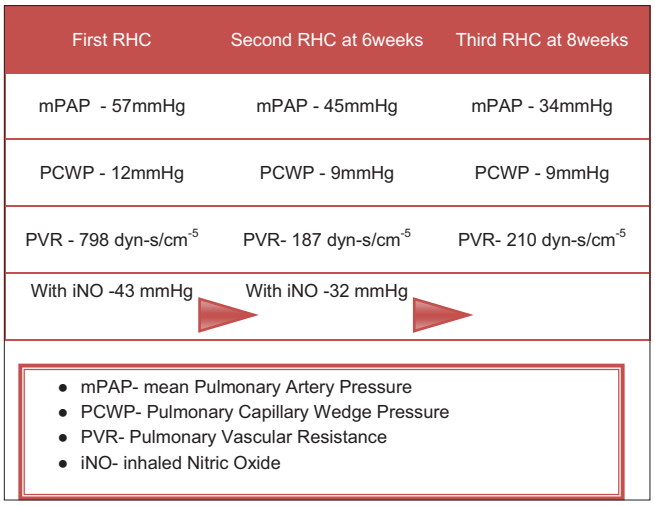

Figure 1: Perioperative right heart catheterization (RHC) pressures

electrocardiography, non invasive blood pressure and capnograpghic monitoring, anaesthesia was induced with fentanyl 250 µg and etomidate 10 mg. Gentle laryngoscopy and smooth tracheal intubation was performed using atracurium. Anaesthesia was maintained with air-O_2 mixture 40:60 in isoflurane, fentanyl and atracurium infusions. End-tidal carbon dioxide was targeted between 30 and 32 mmHg to prevent a rise in mPAP.

Post induction, ultrasound-guided radial artery and right internal jugular vein cannulations were performed. A pulmonary artery catheter was floated for measurement of mPAP and Cardiac output (CO). PVR (dyn-s/cm^{-5}) was calculated using the formula [(mPAP–PCWP)*80]/CO. Transoesophageal echocardiography (TOE) probe was placed in mid oesophageal position for continuous assessment of RV function. During surgery, large fluid shifts and acid-base changes were minimised. Close communication was maintained with surgeon for management of coagulopathy and reduction of anhepatic and cold ischaemia times. After quick explant of cirrhotic liver, a porto-caval shunt was made to decongest the bowel reducing reperfusion injury and RV strain. Implantation of donor's liver was done via piggyback technique avoiding complete caval clamping.

Inhaled NO (iNO) was titrated to manage PAPs. Before reperfusion of implanted graft, iNO was increased to 40 ppm (mPAP 29 mmHg), then gradually tapered and stopped with abdominal closure (mPAP 32 mmHg). Tadalafil 20 mg and ambrisentan 5 mg were administered via nasogastric tube 6 hours

into the surgery. On TOE, RV contractility was well maintained throughout.

Electrolytes, blood gases and glucose were monitored and maintained in normal range. Intraoperative transfusions guided by Rotational Thromboelastometry included 6 Units cryoprecipitate during dissection and 1 Unit Single donor platelet post-reperfusion.

After reperfusion metabolic acidosis, lactate levels, urine output and coagulation steadily improved. Intraoperative dopplers confirmed good hepatic blood flow. After elective overnight ventilation and confirming satisfactory liver function, ventilatory supports were weaned off and trachea extubated. Oral tadalafil 20 mg OD and ambrisentan 5 mg BD were continued. Injection furosemide was started to mobilise fluid maintaining mPAP between 32 and 38 mmHg. On third postoperative day (POD3), PA catheter was removed, patient was ambulated and liquid diet started. On POD4 diuretics were discontinued and immunosuppression with tacrolimus withheld following a drop in urine output and a rise in serum creatinine. Steroids and mycophenolate mofetil were continued till acute kidney injury improved by POD10. The patient was shifted from ICU on POD16 and discharged from hospital on regular immunosuppression and pulmonary vasodilator therapy on POD30 after documenting RVSP of 44 on TTE.

Prostacyclins have a vasodilatory and remodelling effect on the pulmonary vasculature and are the mainstay of therapy. Oral preparations of PDE_5 inhibitors and endothelin receptor antagonists are used on outpatient basis. Intraoperatively intravenous preparations are preferred if available. We used iNO, a rapidly acting smooth muscle relaxant with selective effect on pulmonary vasculature. It activates guanyl cyclase which causes vascular smooth muscle relaxation by increasing cyclic GMP levels. Diuretics helped mobilise fluid, reduce circulatory volume and PAPs. β blockers and calcium channel blockers were avoided [Table 1].

Table 1: Drugs available for treatment of POPH

Group	Drugs available
Prostacyclins	Epoprostenol
	Trepostil
	Iloprost (inhaled)
PDE 5 Inhibitors	Tadalafil
	Sildenafil
Endothelin receptor blockers	Bosentan
	Ambrisentan
Beta-blockers	Worsen exercise capacity
Calcium channel blockers	Worsen portal hypertension

Intraoperatively, PAPs were measured using a pulmonary artery catheter. Use of mild hyperventilation, hyperoxia, pulmonary vasodilators and iNO helped lower PAPs. Release of inflammatory mediators and reperfusion of allograft causes a sudden increase in CO which could increase PAPs precipitating RVF. TOE helped monitor RV function and guide volume status. Reduction of cold ischaemia time, anastomosis using piggyback technique, avoiding complete caval clamping were surgical measures which helped reduce RV strain.

The patient remains on regular follow-up for 18 months with normal liver function tests and pressures on TTE. Though uncommon, POPH has very high perioperative mortality. Hence, RVSP must be recorded in all patients evaluated for LT with TTE. Through our case, we highlight that preoperative detection and optimisation of PoPH along with judicious intraoperative management enables a good outcome post LT.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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