Study Title

Hepatic Vein Flow During Orthotopic Liver Transplantation as Predictive Factor for Postoperative Graft Function

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Study Protocol

Patient Cohort

Inclusion criteria are adult patients undergoing the orthotopic liver transplantation (OLT) piggyback technique with transesophageal echocardiography (TEE)-measured hepatic vein (HV) flow. Exclusion criteria are patient refusal to participate in the study, absolute TEE contraindication, inability to acquire appropriate images for HV flow measurement, or unavailability of a cardiac trained anesthesiologist.

All patients receive general anesthesia with endotracheal intubation, standard American Society of Anesthesiologists monitoring, arterial blood pressure monitoring, central venous pressure monitoring, pulmonary artery pressure monitoring, and comprehensive TEE examination with designated protocol. Intraoperative anesthetics, mechanical ventilation, vasopressor, inotropic, and fluid/transfusion management are performed based on department protocol such as to maintain mean arterial pressure > 65 mmHg, tidal volume 6-8 ml/ideal body weight (kg), positive end-expiratory pressure at 5-7 cmH2O.

Data Collection

TEE images are intraoperatively collected by National Board of Echocardiography-certified advanced perioperative echocardiographers using an iE33 echocardiographic machine with an X7 TEE probe (Philips Medical Systems, Andover, MA), and stored in Syngo Workflow (Siemens Medical Solution, Malvern, PA, USA). Timing for acquiring TEE modified transgastric HV view is in neohepatic phase before fascia closure. To obtain HV flow, the Pulse Wave Doppler (PWD) sample volume is set in the graft HV just distal to IVC-graft anastomosis where an acceptable flow envelope is obtained.

Echocardiography Parameters

Three investigators (A, B, and C), who was also National Board of Echocardiography (NBE)-certified advanced perioperative echocardiographers, measures hepatic vein flow (HVF) in systole and diastole independently using TEE images which are acquired by a single cardiac anesthesiologist (advanced TEE boarded). We calculate HVF as follows: HVF (L/min) = HV area (cm2) x HV max velocity (cm/s) in systole and diastole x 60/1000, where HV area (cm2) = square of HV radius (cm) x 3.14, and HV max velocity (cm/s) is measured by TEE PWD with sample volume selected in the HV, where diameter of HV is measured as well. Efforts are made to align PWD and HV. We define HV flow index (HVFi) as HVF/donor liver weight (kg). We adjust HVF with graft weight because it is more common to assess graft flow with graft size recently. To minimize selection bias, all the investigators are blinded to the hypothesis of the study.

Outcomes

Primary outcome is early allograft dysfunction (EAD), which is defined by the presence of one or more of the following: total bilirubin (t-bil) ≥ 10 mg/dL (171 μmol/L) or, INR ≥ 1.6 on day 7, and ALT/AST > 2,000 IU/L within the first 7 days. Secondary outcome is acute rejection within 6 to 8 weeks post-transplant), prolonged (> 7 days) time to normalize total bilirubin (TIME t-bil), prolonged (>7 days) time to normalize INR (TIME inr), and prolonged (>7 days) time to normalize platelet count (TIME plt).

Statistical Analysis

For continuous variables, the normality test is performed using the Kolmogorov-Smirnov test. Continuous variables with normal distribution are displayed as mean ± standard deviation, while those with non-normal distribution are displayed as median and interquartile range. Categorical variables are presented as proportions and absolute numbers. The differences between the two groups are investigated using unpaired and paired Student t tests or the Mann-Whitney U test. Chi-square test or Fisher's exact test is used for categorical variables. HVFi (systolic and diastolic) are compared in groups of EAD vs. no EAD, acute rejection vs. no acute rejection, no prolonged INR, t-bil, low plt vs. no prolonged INR, t-bil, low plt.

Intra-rater and inter-rater reliability analyses of HVFi are performed using intraclass correlation coefficient (ICC). We randomly pick up 30 images and obtain consistency ICC for inter-observer variability using all three investigators (A, B, and C), and absolute-agreement ICC for intra-observer variability using investigator C, who measure all images twice with an interval between 6 and 8 weeks. For inter-observer variability, 3 investigators post-hoc determine HV diameter, the peak systolic and peak diastolic flow based on the pulse-wave Doppler signal. All statistical analyses are performed using R (The R Foundation for Statistical Computing, Vienna, Austria. ver 4.0.2). P values of less than 0.05 are considered statistically significant.