Title: INTRAOPERATIVE INDICATORS OF ACUTE LIVER FAILURE FOLLOWING HEPATIC TRANSPLANTATION

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INTRODUCTION. A damaged donor liver, poor preservation techniques, or technical complications during transplantation may result in hepatic failure in the immediate perioperative period. When hepatic failure is eminent, retransplantation may be required immediately and early recognition is essential to patient survival. The purpose of this study was to identify reliable and accurate intraoperative indicators of liver failure, based upon liver function, thereby permitting an immediate search for another donor and allowing the best possible chance for patient survival.

METHODS. A retrospective review of 89 consecutive patients who underwent orthotopic hepatic transplantation resulted in 3 distinct groupings with reference to their outcomes; group 1 (n=71) patients had no obvious difficulties related to graft function within 30 days of transplantation, group 2 (n=13) patients had acute graft failure (within 30 days) necessitating a second transplant, group 3 (n=5) patients died of causes unrelated to primary graft failure and was not included in this study.

The anesthetic technique for all patients was similar. Intraoperative monitoring included: ECG (leads II and V5); radial or brachial artery pressure; pulmonary artery catheter for pressures, temperature, thermal dilution cardiac output, and mixed venous oxygen saturation; mass spectrometer for whole body oxygen consumption and CO_2 production. Blood gases, electrolytes (Na^+, K^+, Ca^{++}), glucose, serum and urine osmolality, and SGOT and SGPT were measured periodically throughout the procedure. Thrombelastography and hemostasis profiles (Prothrombin Time (PT), activated Partial Thromboplastin Time (aPTT), Fibrinogen, Platelet count) were used to monitor coagulation. Electromagnetic flowmetry was used to measure the hepatic artery (HAF) and portal vein blood flows from the donor liver at least 1 hour after reperfusion. Portal and hepatic vein pressures and blood gases were obtained at the time of of the blood flow measurements.

Multiple variables were derived from those measured above. Portal, hepatic artery (HAPP), and mesenteric perfusion pressures (MPP) were calculated from the portal vein, hepatic vein and mean systemic pressures. Resistances were computed for the systemic, pulmonary, portal and hepatic arterial (HAR) vasculature. Hepatic O_2 consumption and glucose and K^+ uptakes were computed from flow, blood gas and electrolyte measurements.

A total of 75 variables were used in the analysis. The data were analyzed first by comparing the nonfailure and failure groups with Students t test taking into account whether the variances of each group were equal or not. Next, a discriminant analysis was performed using all variables in order to identify those combinations of variables that would best predict the outcome of the transplanted liver.

RESULTS. The table illustrates the variables that were statistically different between the two groups. Notably, there were several variables related to the hepatic arterial vasculature, but none related to the total hepatic blood flow or portal vein flow. There were no differences in the total liver blood flow (hepatic artery + portal vein) or the total liver blood flow percentage of the cardiac output between the groups. The sodium bicarbonate value corresponds to the number of 44.6 mEq/L aliquots of sodium bicarbonate administered to continually buffer an ongoing metabolic acidosis following revascularization.

The variables selected by discriminant analysis were PT, Hepatic Artery Flow and NaHCO3. Of the 84 patients in this study, 53 had complete data sets for these 3 variables.

DISCUSSION. The variables that are identified as being statistically different between the failure and nonfailure groups are not necessarily adequate predictors to classify a single patient into the appropriate group. In this study the PT was the best single classification variable. PT correctly identified 12/13 (92.3%) acute graft failures, but incorrectly classified 17/65 (26.1%) patients without problems into the acute failure group.

It is highly unlikely in hepatic transplant recipients that any single variable could correctly classify all patients, as demonstrated by these data. For this reason discriminant analysis was applied to all variables, measured and derived, in an attempt to improve sensitivity and specificity. The combination of variables that demonstrated the best ability to correctly classify the most patients were PT, hepatic artery flow per 100 grams of wet liver weight, and the amount of sodium bicarbonate that was administered to the patient after reperfusion. Using these 3 variables, 40 of 44 patients (90.9%) in the nonfailure group were classified correctly, 4 were incorrectly classified as acute failures. In the acute graft failure group 8 of 9 patients (88.9%) were classified correctly. This combination was capable of correctly categorizing 48 of 53 (90.6%) patients. Utilizing this classification scheme the probability of incorrectly classifying a nonfailing liver as a failing graft is about equal to not detecting a true failing liver, which is approximately 1 in 10.

In conclusion, a discriminant function was constructed from all available data. The analysis identified 3 intraoperatively measured variables directly related to liver function (PT, hepatic artery flow, and the amount of NaHCO3 administered) that correctly classified 91% of the available cases. The discriminant function, based upon these 3 variables, is capable of predicting the outcome of the transplanted liver with reasonable accuracy beyond the ability of any single variable.

Table: Significant variables related to graft failure (mean ± std. dev.)

	NON FAIL	FAIL	SIGNIFICANCE
HAF	33.3 ± 2.0	21.2 ± 3.2	P< 0.013
(ml min^{-1} $100g^{-1}$)	(N=67)	(N=13)	
HAPP	67.5 ± 1.6	54.8 ± 2.2	P< 0.001
(mmHg)	(N=46)	(N=9)	
HAR	589.4 ± 36.8	1080.5 ± 231.0	P< 0.06
(dyne sec cm^{-5} $100g^{-1}$)	(N=45)	(N=9)	
MPP	60.42 ± 1.7	46.3 ± 3.1	P< 0.001
(mmHg)	(N=45)	(N=9)	
HAPTF	22.7 ± 1.6	14.9 ± 2.5	P< 0.04
(percent)	(N=71)	(N=13)	
PT	15.9 ± 0.2	17.6 ± 0.3	P< 0.001
(seconds)	(N=65)	(N=13)	
Temp. Change	0.39 ± 0.02	0.27 ± 0.05	P< 0.037
(^oC)	(N=64)	(N=13)	
NaHCO3	0.66 ± 0.14	1.8 ± 0.5	P< 0.036
(alliquots)	(N=67)	(N=13)	
K^+ Change	0.12 ± 0.05	0.3 ± 0.16	P< 0.003
(mEq l^{-1})	(N=50)	(N=10)	