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RISK AND OUTCOME

Preoperative Assessment of Risk in Liver Transplantation: A Multivariate Analysis in 2376 Cases of the UW Era

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WITH THE number of organ donors consistently falling behind the estimated need,[1,2] we must continuously strive to improve organ utilization. It has been shown that optimal organ utilization does not consist of simply choosing the healthiest prospective recipient,[3,4] and that even hepatic retransplantation is an appropriate treatment under carefully selected conditions.[5]

The purpose of this study was to identify, from information readily available at the time of surgery, the risk factors associated with an unfavorable outcome following orthotopic liver transplantation (OLTx). This knowledge can help us stratify prospective donor-recipient combinations according to their predicted risk of failure, providing insight as to the probable outcome of individual patients, and the factors that determine it. Moreover, it can also be used to describe study populations—stratified according to their risk—and allow uniform comparison of outcomes. The results of our preliminary work in this area have previously been published.[6–10]

MATERIALS AND METHODS

From November 1, 1987 to December 31, 1993, a total of 2019 adults underwent 2376 liver transplantations at the University of Pittsburgh Medical Center and the Veterans Administration Medical Center, Pittsburgh, Pennsylvania. Cases were excluded if the liver was received as part of a multivisceral transplant that included intestine. Minimum follow-up time was at least one year (censoring date: January 18, 1995). All grafts were flushed with UW solution during cold preservation.[11] The information was obtained from the clinical database maintained by the Transplantation Institute, and a review of all the donor charts that are kept on file at the Center for Organ Recovery and Education (Western Pennsylvania Organ Procurement Organization), Pittsburgh, Pennsylvania.

For the purpose of this study we defined graft failure as either patient death or retransplantation within one year following OLTx. Donor variables studied were: age, gender, ABO type, cause of death, length of stay in the intensive care unit, body mass index, use of pressors (dopamine infusion > 10 μg/kg/min, or continuous infusion of epinephrine or norepinephrine), use of pitressin, need for cardiopulmonary resuscitation, terminal transaminases (alanine aminotransferase and aspartate aminotransferase), serum sodium at the time of procurement, and total ischemia time. The latter was defined as the time elapsed from aortic cross-clamping in the donor to portal or arterial reperfusion in the recipient.[7] Recipient variables studied were: age, gender, ABO type, indication for OLTx, history of prior OLTx, history of prior upper abdominal surgery, need for preoperative mechanical ventilation, type of primary immunosuppression, preoperative creatinine, preoperative bilirubin, preoperative prothrombin time, and UNOS urgency status. UNOS status is a measure of severity of disease, according to UNOS candidate classification: UNOS 1: patient stable at home; UNOS 2: waiting at home, but requiring medical support; UNOS 3: unstable, in need of continuous hospitalization; UNOS 4: requirement of life-support systems. We should note that this classification was changed on April 1, 1995, but we will use the classification that was in effect during the study period throughout this paper.

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Table 1. Variables Independently Associated With Graft Failure

	Odds Ratio	95% CI
Donor Age	1.7*	1.4 to 2.1*
Female Donor Sex	1.4	1.1 to 1.7
Ischemia Time	1.3†	1.1 to 1.5†
Recipient Age	1.2*	1.1 to 1.4*
Prior Liver Transplant	2.0	1.5 to 2.7
Preoperative Mechanical Ventilation	2.2	1.7 to 2.9
Preoperative Bilirubin	1.3‡	1.1 to 1.5‡
Preoperative Creatinine	1.12§	1.03 to 1.21§
Indication		
Other	Reference	
Hepatitic	1.4	1.1 to 1.8
HCC-CholangioCa	2.2	1.4 to 3.1
Immunosuppression		
Tacrolimus‖	Reference	
CyA	2.7	2.1 to 3.4

*For each 10-year increase after age 45.
†For each 6-hour increase after 8 hours.
‡For each 10-mg increase after 15 mg/dL.
§For each 1-mg increase.
‖Includes Tacrolimus-rescue cases.

A screening univariate analysis was conducted, using either a two-tailed *t*-test (for continuous variables) or Pearson's chi square (for categorical variables). Variables with a $P \leq .3$ were then entered into a stepwise logistic regression analysis, to identify those variables independently associated with outcome. After a preliminary model was fit, the functional form of the continuous variables was explored by fitting generalized additive models, where the continuous covariates were entered as smooth terms, using a local regression procedure. A final logistic regression model was then fit, incorporating suitable linearizations of the continuous covariates.

RESULTS

There were 1635 successful transplants, while 741 failed. The variables found to be independently associated with outcome were (see Table 1): donor age (odds ratio 1.7 for each 10-year increase after the age of 45; 95% CI 1.4 to 2.1), female donor sex (odds ratio 1.4; 95% CI 1.1 to 1.7), total ischemia time (odds ratio 1.3 for each 6-hour increase in ischemia time after the first 8 hours; 95% CI 1.1 to 1.5), recipient age (odds ratio 1.2 for each 10-year increase after the age of 45; 95% CI 1.1 to 1.4), prior OLTx (odds ratio 2.0; 95% CI 1.5 to 2.7), need of preoperative mechanical ventilation (odds ratio 2.2; 95% CI 1.7 to 2.9), preoperative bilirubin (odds ratio 1.3 for each 10 mg increase after 15 mg/dL; 95% CI 1.1 to 1.5), preoperative creatinine (odds ratio 1.12 for each 1 mg increase; 95% CI 1.03 to 1.21), indication for OLTx (odds ratio for hepatitic vs other nontumor etiologies 1.4; 95% CI 1.1 to 1.8; odds ratio for tumors vs other [excluding hepatitis] 2.2; 95% CI 1.4 to 3.1), and primary immunosuppression used (odds ratio for cyclosporine vs tacrolimus 2.7; 95% CI 2.1 to 3.4).

DISCUSSION

The outcome of liver transplantation is a complex phenomenon, being the result of the interaction of two different biological systems—the donor and the recipient. Therefore, when assessing risk prior to liver transplantation we cannot limit ourselves to take into account either only the donor or the recipient. In our study, we analyzed only information that is obtained as part of a routine pretransplant recipient and donor work-up, and that is always available at the time of organ allocation. Our goal was to select simple parameters that are widely available and easily reproducible. Variables such as degree of encephalopathy, nutritional status, and degree of ascites can be biased by subjective judgment, while others like helper to suppressor T cell ratio or the number of documented episodes of spontaneous bacterial peritonitis might not be routinely available.

Three donor variables (donor age, female donor sex, and total ischemia time) and 7 recipient variables (recipient age, indication for OLTx, history of prior OLTx, need for preoperative mechanical ventilation, preoperative bilirubin and creatinine, type of primary immunosuppressant) were found to be independently associated with graft failure (Table 1). Our study shows that candidates for liver transplantation can be stratified into differential risk categories at the time of the actual surgery. This stratification can be useful when comparing results across different groups, or helping to choose among different prospective donor-recipient combinations.

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