Influence of Cold Ischemia Time and Graft Transport Distance on Postoperative Outcome in Human Liver Transplantation

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Abstract

Purpose. The association between hepatic allograft cold ischemia time (CIT) and graft transport distance (GTD) in human liver transplantation was examined by investigating whether extended graft transportation prolongs the CIT and adversely affects graft survival.

Methods. We retrospectively analyzed 186 consecutive orthotopic liver transplants (OLTs) done between May 1997 and July 1998. The number of miles from the donor hospital to the University of Pittsburgh Medical Center in a straight line was measured in each case, and defined as the GTD. The OLTs were divided into two groups according to whether the GTD was ≤200 miles or >200 miles. The latter group was then subdivided into groups of GTD 200–400 miles, GTD 400–600 miles, and GTD >600 miles. The CIT and graft outcome within 90 days after OLT were assessed.

Results. Extended GTD prolonged the CIT (P < 0.001). The rate of hepatic allograft loss in the long GTD group was significantly higher than that in the short GTD group (P = 0.018). When the OLTs were subdivided according to GTD, the CIT increased and graft survival decreased as the GTD extended. Hepatic allograft transportation for a long distance prolonged the CIT and decreased the graft survival rate.

Conclusion. Since prolonged CIT is a major risk factor, avoiding long-distance graft transportation is recommended when the donor risk factors are high.

Key words Liver transplantation · Cold ischemia time · Graft transportation

Introduction

Since the condition of vital organs and systems in the brain-dead patient, determined by blood electrolytes and hemodynamics, is often unstable because of impaired homeostasis, hypoxia, and severe multiple injuries, postoperative hepatic allograft function should be associated with the condition of the cadaveric organ donor. We previously demonstrated the relationship between early postoperative hepatic allograft outcome and donor condition, including age, cardiopulmonary arrest, the need for vasopressors, and the serum sodium concentration. In addition to these variables, prolonged cold ischemia time (CIT) during organ preservation is an important risk factor. Graft outcome is affected by the duplication of a number of risk factors in human liver transplantation. Therefore, to increase the hepatic allograft survival rate, the risk factors should be minimal.

In contrast to individual factors related to the donor, such as age, hemodynamics, and laboratory data, which are static, CIT is possibly subject to manipulation by the organ-sharing system. Many factors affect CIT during hepatic allograft transportation, such as the transport system (namely, by car, propeller plane, or jet), waiting time at the airport, weather, and communications between the donor and recipient surgical teams. Consequently, long-distance transportation of the graft liver could prolong the CIT. Although previous studies investigating the relationship between graft outcome and risk factors did not address the influence of hepatic allograft transport distance on CIT, graft short-haul transportation is likely to reduce the CIT and improve graft outcome.

In this study, we investigated the influence of CIT on hepatic allograft outcome, and set out to prove our hypothesis that extended graft transportation prolongs CIT, which adversely affects graft survival in human liver transplantation.
Patients and Methods

Patients

Between May 1997 and July 1998, 208 consecutive adult orthotopic liver transplantations (OLTs) were performed at the University of Pittsburgh Medical Center (UPMC), Pittsburgh, PA, USA. A total of 22 cases were excluded from this analysis because the graft was from a donor without a heartbeat in 8 cases; there was distinct technical failure in 6 cases; early death from sepsis after retransplantation occurred in 5 cases; and 3 cases involved combined liver and small bowel transplantation. These cases were excluded because other factors, such as ischemic injury before organ procurement, technical failure during OLT, or severe recipient infection prior to re-OLT can have more influence on outcome than the quality of the donor organ. The remaining 186 cases were entered in this study. The indications for OLT were posthepatitis cirrhosis in 73 patients (39.2%), alcoholic liver cirrhosis in 29 patients (15.6%), cholestatic disease in 28 patients (15.0%), cryptogenic liver cirrhosis in 21 patients (11.3%), retransplantation in 20 patients (10.8%), acute hepatic failure in 4 patients (2.2%), and other reasons in 11 patients (5.9%).

Donor Organ Procurement and Recipient Treatments

All hepatic allograft were perfused and preserved with University of Wisconsin (UW) solution utilizing previously described techniques for multiple organ harvest. Liver biopsy was taken from a small minority of the macroscopically marginal organs, and livers with more than 30% steatosis were discarded. In the recipients, OLT was performed using standard techniques or “piggyback” methods. All patients received similar perioperative intensive care and immunosuppressant therapy. The postoperative immunosuppression regimen consisted of intravenous tacrolimus (Prograf, formerly FK506, Fujisawa USA, Deerfield, IL, USA) with daily adjustments according to the blood level of the drug, and intravenous methylprednisolone with a tapering schedule from 200 to 20 mg in the initial postoperative days.

Donor and Recipient Variables

The following donor data were prospectively recorded: the address of the donor hospital, the donor’s age, sex, cause of death, length of stay in the intensive care unit (ICU), need for dopamine, serum concentrations of aspartate aminotransferase (AST) and total bilirubin (T-Bil), prothrombin time (PT), and sodium. The hepatic allograft ischemia time, which was a composite of cold and warm ischemia time, was also recorded. The CIT was defined as the period from donor aortic cross-clamping in organ procurement until placement of the hepatic allograft in the recipient surgical field. This was followed by the warm ischemia time (WIT). The allograft rewarming time in the recipient surgical field until portal revascularization was regarded as WIT. Donor information was obtained from a review of the donor charts that are kept on file at the Center for Organ Recovery and Education (Western Pennsylvania Organ Procurement Organization), Pittsburgh, PA, USA.

The preoperative recipient variables included age, gender, previous OLT, AST, T-Bil, PT, and the United Network for Organ Sharing (UNOS) status; namely UNOS 1, dependent on life support systems; UNOS 2, unstable in need of continuous hospitalization; UNOS 3, waiting at home, but requiring medical support; UNOS 4, stable at home; in accordance with the old definitions of medical urgency, established prior to February 1998. The recipient information was recorded from the clinical database maintained by the Thomas E. Starzl Transplantation Institute, University of Pittsburgh.

Early Post-OLT Graft Outcome

Patient death or the need for retransplantation within 90 days of transplantation was considered early postoperative graft loss. The causes of graft failure were as follows. (1) Primary nonfunction. A graft with poor initial function due to lactic acidosis, prolonged PT, or multiple organ failure, resulting in retransplantation or death within 1 week. No technical or immunologic causes of failure could be identified. (2) Preservation injury. Damage to the hepatic allograft occurred before or after revascularization without obvious immunologic etiology. Hyperbilirubinemia was sustained without lactic acidosis, prolonged PT, or multiple organ failure. (3) Hepatic arterial thrombosis. Hepatic allograft failure occurred due to severe damage or abscess formation in the allograft from hepatic arterial thrombosis without distinct technical failure. (4) Multiple organ failure due to sepsis, or a preexisting bacterial, viral, or fungal infection.

If a patient died of a documented infection in the early postoperative period, the decision to assign it to “sepsis”, “primary nonfunction,” or “preservation injury” was based on whether there was poor function from the beginning. For example, a death from sepsis involving a graft that never functioned well was coded as “primary nonfunction” or “preservation injury.”

In addition to the graft outcome, arterial and biliary complications after OLT were recorded.