ELSEVIER

Liver Transplantation From an Uncontrolled Non–Heart-Beating Donor Maintained on Extracorporeal Membrane Oxygenation

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ABSTRACT

Liver transplantation, a definitive treatment for end-stage liver disease, has achieved excellent results. However, potential recipients on the waiting list outnumber donors. To expand the donor pool, marginal grafts from older donors, steatotic livers, and non–heart-beating liver donors (NHBD) have been used for transplantation. Reducing the warm ischemia time of NHBD is the critical factor in organs preservation. Liver transplantation using grafts from NHBD have been reported to display a high incidence of primary graft nonfunction and biliary complications. The authors report a liver graft donor who was maintained on extracorporeal membrane oxygenation (ECMO) after successful cardiopulmonary resuscitation. Core body temperature was 5°C. Procurement of the liver using a rapid flush technique was performed 4 hours after instituting ECMO. Graft function recovered fully after transplantation. In conclusion, ECMO may be used to reduce warm ischemia time in liver grafts obtained from uncontrolled NHBD, thereby increasing graft salvage rates.

TAIWAN law stipulates that organs procurement in trauma and accidents must await a district attorney signing the legal documents that certify death. Oftentimes, the donor develops hemodynamic instability and cardiopulmonary arrest while awaiting these documents. There is only a short period to prepare for organ procurement after the initial agreement with the donor's family, and aggressive attempts to save the organs must be considered. In these situations, however, the suitability of a donor's organs for transplantation declines rapidly. Transplant surgeons are reluctant to use organs rescued from arrested donors due to threat of primary graft nonfunction due to prolonged warm ischemia time. Koyama et al[1] reported using cardiopulmonary bypass for total body cooling, thereby ameliorating warm ischemic damage by supplying oxygenated blood to the organs. It has been estimated that an increase of 20%–25% in the number of organ donors may be realized through use of organs from non–heart-beating donors (NHBD).[2]

This case is the first liver transplant recipient to receive a graft from an uncontrolled NHBD maintained on extracorporeal membrane oxygenation (ECMO) under hypothermia for 4 hours prior to procurement. The preoperative, intraoperative, including technique of graft harvest, and postoperative care leading to full recipient recovery are described herein.

CASE REPORT

A 22-year-old woman, weighing 55 kg, was transferred from a local hospital after sustaining irreversible brain injury secondary to a motor vehicle crash. On arrival at the hospital, she developed a cardiac arrest. Aggressive cardiopulmonary resuscitation (CPR) successfully revived the patient. She became a potential organ donor. Awaiting brain-death testing, she developed another cardiac arrest and was revived for the second time after 40 minutes of CPR. Circulatory support was maintained using ECMO (Cat. No. CB2505, Medtronic, Anaheim, Calif, United States) until death certification was issued by a district attorney.

ECMO was performed via veno-arterial circuit with whole body cooling. Core body temperature was maintained at 5°C. Flow rate was maintained at 3–3.5 L/ min. The time from initiation of ECMO to organ retrieval was 4 hours and 10 minutes. Preharvest donor aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were 59 U/L and 60 U/L, respectively. Aorta and portal vein were cannulated via a midline laparotomy incision and the abdom-

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inal organs were perfused with University of Wisconsin (UW) organ preservation solution. The liver was retrieved in standard fashion. The portal vein was flushed with UW solution on the back table. Overall cold ischemia time under ECMO support was 3 hours, 30 minutes. The donor liver was soft and appeared well perfused.

The recipient suffered hepatitis B virus (HBV) related end-stage liver disease (ESLD) with ascites, frequent episodes of hepatic encephalopathy, and coagulopathy as the indications for transplantation. Total recipient hepatectomy was followed by side-to-side cavo-caval anatomosis of whole liver graft using a piggy-back technique. The graft was reperfused after portal vein and hepatic artery reconstruction. Biliary reconstruction was performed via an end-to-end choledocho-choledochostomy with cholecystectomy. Operative time was 12 hours. A total of 14 U packed red blood cell and 12 U plasma were given intraoperatively. Overall cold ischemia time from institution of ECMO to completion of the operation was 15 hours, 5 minutes.

Immunosuppression was initiated with Basiliximab (Simulect) induction followed by Tacrolimus (FK 506) and prednisolone. Human immunoglobulin was given in a protocol to prevent HBV infection recurrence. The recipient was discharged well with a good liver graft function on the 28th postoperative day. He is alive to the present date, 24 months posttransplantation, without an episode of graft rejection.

DISCUSSION

Liver transplantation, a definite treatment for ESLD, has achieved excellent results.[3,4] To expand the donor pool, NHBD have been used for liver transplantation. NHBD organ procurement may be controlled or uncontrolled. In controlled NHBD, patients with irreversible brain injury have not met the criteria for brain death. The decision to donate follows withdrawal of treatment within the hospital. In uncontrolled NHBD, organs are removed after the patient experiences a sudden cardiopulmonary arrest and death is declared after resuscitation fails to restore cardiac function.[4]

Johnson et al[5] reported successful use of a liver allograft from a donor maintained on ECMO for 29 days. AST and ALT levels were 3825 U/L and 2376 U/L, respectively, after transplantation. Four days following transplantation, the AST and ALT levels had decreased to 246 U/L and 748 U/L, respectively. Prothrombin time reached a peak of 17 seconds at 24 hours postoperative and decreased to 14 seconds on the 2nd postoperative day. Bilirubin was normal by the 3rd postoperative week. The patient was discharged on the 22nd postoperative day.

Liver transplantations from NHBD have been reported to show a higher incidence of primary graft nonfunction and biliary complications.[6] The authors believed that, because the biliary epithelium is sensitive to ischemia-reperfusion injury, warm ischemia with subsequent cold ischemia-reperfusion resulted damage to sensitive cell populations in the liver, particularly the bile canaliculi. This theory is corroborated by the findings of Abt et al among 15 patients receiving hepatic allografts from controlled NHBD who showed 66.6% with biliary complications of intrahepatic strictures versus 19.2% among heart-beating patients.[7,8]

A high incidence of early graft failures due to primary nonfunction and hepatic artery thrombosis in liver transplantation in an uncontrolled setting has been reported. Graft survival in these cases was $<50\%$.[9] Other researchers observed no differences in hepatic artery, portal vein, or biliary complications between heart-beating donors and NHBD; but the rate of primary nonfunction was higher among recipients of livers from NHBD (10.5% vs 1.3%; $P = .36$) as was allograft survival lower. No difference in patient survival was seen between recipients of grafts from heart-beating donors or NHBD.[2] Significant factors that seemed to contribute to graft nonfunction were the length of warm ischemia and the preservation technique.

The UCLA (University of California at Los Angeles) experience comparing controlled versus uncontrolled NHBD, namely 13 versus 16 cases of liver transplantations, the 1-year patient and graft survival rates were 85% and 77% for the former versus 88% and 75% for the latter group, respectively. Authors of this report also claimed that warm ischemia time of <30 minutes did not affect either patient or graft survival.[10]

Fortunately, the complications described by other authors did not happen in this patient. ECMO and hypothermia may have reduced liver warm ischemia time in this case of uncontrolled NHBD contributing to graft preservation.

In conclusion, a high incidence of HBV carriers and negative socio-cultural beliefs contribute to the shortage of liver donors in Taiwan. In addition, failure to provide physiologic support to prevent early cardiac death is a frequent cause of remediable procurement failure. Liver allografts from uncontrolled NHBD maintained on ECMO and hypothermia may alleviate the organ shortage. However, until a large series with long-term follow-up is available, no recommendation regarding the use of NHBD can be effectively drawn for liver transplantation. The described case does suggest that early consideration be put to use of circulatory-arrested patients on ECMO with hypothermia. The treatment should be instituted to increase the number of donors through use of organs from uncontrolled NHBD.

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