Outcomes Using Grafts from Donors after Cardiac Death

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BACKGROUND: Previous reports suggest that donation after cardiac death (DCD) liver grafts have increased primary nonfunction (PNF) and cholangiopathy thought to be due to the graft warm ischemia before cold flushing.

STUDY DESIGN: In this single-center, retrospective study, 866 adult liver transplantations were performed at our institution from January 2005 to August 2014. Forty-nine (5.7%) patients received DCD donor grafts. The 49 DCD graft recipients were compared with all recipients of donation after brain death donor (DBD) grafts and to a donor and recipient age- and size-matched cohort.

RESULTS: The DCD donors were younger (age 28, range 8 to 60 years) than non-DCD (age 44.3, range 9 to 80 years) ($p < 0.0001$), with similar recipient age. The mean laboratory Model for End-Stage Liver Disease (MELD) was lower in DCD recipients (18.7 vs 22.2, $p = 0.03$). Mean cold and warm ischemia times were similar. Median ICU and hospital stay were 2 days and 7.5 days in both groups ($p = 0.37$). Median follow-ups were 4.0 and 3.4 years, respectively. Long-term outcomes were similar between groups, with similar 1-, 3- and 5-year patient and graft survivals ($p = 0.59$). Four (8.5%) recipients developed ischemic cholangiopathy (IC) at 2, 3, 6, and 8 months. Primary nonfunction and hepatic artery thrombosis did not occur in any patient in the DCD group. Acute kidney injury was more common with DCD grafts (16.3% of DCD recipients required dialysis vs 4.1% of DBD recipients, $p = 0.01$). An increased donor age (>40 years) was shown to increase the risk of IC ($p = 0.006$).

CONCLUSIONS: Careful selection of DCD donors can provide suitable donors, with results of liver transplantation comparable to those with standard brain dead donors. (J Am Coll Surg 2015;221:142−152. © 2015 by the American College of Surgeons)

Orthotopic liver transplantation (OLT) has become an extremely successful method of treating patients with end-stage liver disease. Each year, more patients are added to the waiting list, though the number of available donors remains relatively static, leaving a well-publicized donor shortage.[1] Maximizing organ use with extended criteria donor grafts, living donors, and split cadaveric grafts have all been used as techniques to attempt to reduce the gap between those who are waitlisted and suitable grafts available for transplantation. Another source of marginal donors is grafts from nonheart-beating donors, also termed donation after cardiac death donors (DCD). Because support is withdrawn before organ procurement, DCD donation results in a period of organ warm ischemia before perfusion with cold preservation solution—a factor that is not encountered in donation after brain death (DBD) donors.

In the past 10 years in the US, 2,710 liver donors have been DCD organ donors, with the largest numbers used in the last 2 years.[2] Since the concept of brain death became widely accepted in 1968, use of organs after cardiac death fell out of favor.[3,4] But with improved preservation and procurement techniques, there has been a renewed interest in this technique. Early reports using DCD grafts were

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Abbreviations and Acronyms

DBD = donation after brain death
DCD = donation after cardiac death
HCC = hepatocellular carcinoma
HCV = hepatitis C virus
HTK = histidine-tryptophan-ketoglutarate solution
IC = ischemic cholangiopathy
MELD = Model for End-Stage Liver Disease
OLT = orthotopic liver transplantation
PNF = primary nonfunction
TPA = tissue plasminogen activator
WIT = warm ischemia time

favorable,[5] demonstrating graft and patient survivals similar to those with DBD donors.[6] However, in subsequent reports, biliary complications appeared to be significantly more prevalent in recipients of DCD grafts, with reduced graft and patient survival.[7-9]

Determination of exclusion criteria for suitable donors is difficult, and as with any innovation in transplantation, there is a learning curve involved in the use of these organs. There have been suggestions that donor age less than 45 to 50 years, warm ischemic time less than 30 minutes, and cold ischemic time less than 10 hours are associated with better patient and graft survival outcomes.[8-10] Recipient factors are another area of uncertainty. Recipients older than age 60, recipients requiring retransplantation, patients on dialysis, and patients in the ICU have all been suggested to have a worse outcome with DCD donation.[8] In this report, we investigated our results with DCD donation for liver transplantation over the last 10 years.

METHODS

This study was completed as part of our institutional review board (IRB)-approved protocol that used our prospectively maintained transplant database to retrospectively review recipients who received grafts from DCD donors from January 2005 to August 2014. These patients were compared with recipients of whole organ grafts from DBD donors during the same time period. All cases were studied for recipient and donor demographics, cause of end-stage liver disease, Model for End-Stage Liver Disease (MELD) score, operative details, immediate and later postoperative complications, and short-term as well as long-term overall and graft survivals. For more accurate analysis, a 2:1 propensity score matched comparison group was identified using recipient age, sex, BMI, hepatitis C virus liver disease (HCV), hepatocellular carcinoma (HCC), calculated MELD score, and donor age as the predictor variables.

For DCD donation, strict protocols from the local organ procurement organization were followed. Ventilatory support was withdrawn in the operating room in most cases, except for in 3 donors, in whom withdrawal occurred in the ICU. Five minutes after pronouncement, organs were rapidly procured. A midline laparotomy incision and cannulation of the distal aorta were carried out rapidly, and perfusion with HTK (histidine-tryptophan-ketoglutarate solution, Chemie GmbH) was performed. Ice was placed surrounding the organs and the supraceliac aorta was cross-clamped. The portal system was separately cannulated and flushed in situ in 3 patients, and the remaining grafts received a portal flush on the back table. This period of warm ischemia before flush is unique to DCD donors. We refer to this in this article as donor warm ischemia time (WIT). This is to be differentiated from the standard WIT during implantation of the liver in the recipient before reperfusion. Donor WIT was recorded in several ways because there are no standardized recommendations to date: extubation to flush and cross-clamp, oxygen saturations less than 70% to flush and cross-clamp, and systolic blood pressure less than 50 mmHg to flush and cross-clamp. The WIT also includes the mandatory 5-minute period of waiting, after asystole, before donor incision. This acirculatory phase (asystole to aortic flush) is also recorded. Cold ischemia time is measured from flush of preservative solution to the liver being taken out of ice before implantation in the recipient. Standard WIT is defined as the time from liver "out of ice" to reperfusion in the recipient. All recipients consented to receive a graft from a DCD donor. The possibility of an increased risk of ischemic cholangiopathy (IC) was explained to the recipient before surgery. In the earlier part of the series (before 2009), DCD donors were considered at any age and we used a donor WIT (extubation to flush) cut-off of 30 minutes. Because 3 cases of IC had developed in this time, we changed our policy to donor age less than 45 years and donor WIT to 20 minutes or less.

As a standard practice, most transplantations were performed in a piggyback technique, and choledochocholedochostomy was done for biliary reconstruction. We used standard 3-drug immunosuppression regimen including tacrolimus, steroids (stopped by 3 to 6 months), and antimetabolites. Antibody induction therapy was not used. All liver transplants undergo a protocol reperfusion biopsy at the time of liver transplantation. All other postoperative biopsies are performed on the basis of clinical indication.

All postreperfusion liver biopsies of DCD and propensity score matched DBD recipients were re-examined for this study by the 2 study pathologists in a blinded fashion. Histologic features, including portal inflammation, bile duct injury, ductular reaction, with and without pericholangitis, steatosis, endotheliitis, endophlebitis, hepatocyte drop-out,