Annals of Hepatology

ORIGINAL ARTICLE

October-December, Vol. 10 No.4, 2011: 482-485

Should donation after cardiac death liver grafts be used for retransplantation?

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ABSTRACT

Introduction. Donation after cardiac death (DCD) donors provide an important source of livers that has been used to expand the donor pool. As a consequence of increased numbers of OLT, allograft failure due to early and late complications and disease recurrence are more commonly encountered. The only life saving treatment for patients with liver allograft failure is liver re-transplantation (LR). The use of DCD liver grafts for LR is controversial. **Material and methods.** Between February 1998 and June 2008, 10 patients underwent LR with DCD allografts. Five (50%) patients had no post operative complications. The 30 day, 1 year, and 3 year patient survival are 80, 60, and 60%, respectively. When DCD grafts are used for sick patients with high MELD scores for LR, the patient and graft survivals are prohibitively low. **Conclusion.** We do not recommend utilization of DCD liver grafts for LR if a candidate recipient has moderate to high MELD score.

Key words. Donation after cardiac death. Liver retransplantation.

INTRODUCTION

Orthotopic liver transplantation (OLT) is a life saving procedure for patients with end stage disease. There is a significant disparity between organ availability and the number of patients waiting for OLT. Donation after cardiac death (DCD) donors provide an important source of livers that has been used to expand the donor pool. DCD livers are considered inferior grafts because of higher risk for primary non-function (PNF), hepatic artery thrombosis (HAT), and ischemic cholangiopathy (IC). We previously reported our experience in 108 DCD liver recipients.[1] Our liver transplant program now has performed over 200 OLT using liver grafts from DCD donors between 1998-2010.

In the last two decades, improved patient survival after OLT has been seen as a result of refined surgical technique, improved peri-operative care of the recipient and advances in immunosuppression.[2] As a consequence of increased numbers of OLT, allograft failure due to early and late complications and disease recurrence are more commonly encountered. The only life saving treatment for patients with liver allograft failure is liver re-transplantation (LR). LR requires extensive surgical expertise and experienced decision making process before, during and after the surgical procedure. The use of DCD liver grafts for LR is controversial. To date there has not been any specific report in the literature regarding the short- and long-term outcomes when DCD grafts were used for LR. This report reviews our program's experience, specifically addressing perioperative complications and short- and long-term outcomes of patients who received DCD liver grafts for LR.

MATERIAL AND METHODS

Mayo Clinic Florida database was searched for all patients between February 1998 and June 2010 for patients who had undergone LR with DCD liver grafts. All liver grafts were procured by surgeons from our center and University of Wisconsin solu-

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Manuscript received: June 06, 2011.
Manuscript accepted: June 16, 2011.

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tion was used for preservation solution. Patient demographics including age, sex, date of initial transplantation, date of LR, number of days between initial and LR, primary liver disease, reason for LR, calculated Model for End-Stage Liver Disease (MELD) score on the day of LR, hospital or ICU stay care after LR, and complications. Operative data included recipient warm ischemia time (WIT) defined as time of removal of liver allograft from cold solution until reperfusion, operative time, and number of units red blood cells transfused. Donor surgery characteristics recorded included donor age, race, sex, cause of death, donor warm ischemia time (DWIT) defined as withdrawal of support to initial flush of preservation solution, and cold ischemia time (CIT) defined as initial flush of preservation solution until the removal from cold in the recipient operation. Donor Risk Index (DRI) was calculated retrospectively for each case. The study protocol was reviewed and approved by Mayo Clinic Institutional Review Board.

In DCD donors, withdrawal of support and declaration of death were in strict compliance with donor hospital policies. The transplant team was not involved in the withdrawal process. An independent physician from the donor hospital, separate from the OPO and the transplant center, was assigned to withdraw artificial life support and provide end of life care to the patient. Following the declaration of death by the independent physician a further 2-5 min of mandatory observation was performed as described in the 1997 Institute of Medicine Guidelines.[6] During the 2-5 min waiting period, the patient was transported to the operating room (if not already there) and prepared for organ recovery. Heparin was administered to the patient according to the donor hospital policy. Following the 2-5-min wait period a rapid retrieval technique was performed as described previously. All LR were performed using the piggyback technique without a porto-caval shunt or caval clamping. Standard triple-drug immunosuppression with tacrolimus, mycophenolate mofetil and corticosteroids was used in all cases.

Continuous data were reported as mean with range listed. Categorical data were compared with the Chi-square or the Fisher exact test. Long term sur-

Table 1. Demographic data of the recipients.

Patient	Age	Sex	MELD score	Primary disease	Reason for LR	OLT-LR interval
1	69	M	29	Hepatitis C	Hepatitis C	146
2	57	F	31	Hepatitis C	Hepatitis C	489
3	49	M	10	Alcohol	Biliary necrosis	174
4	61	F	17	PSC	HAT	49
5	50	F	16	PSC	PSC	2,932
6	48	M	40	Hepatitis C	PNF	21
7	55	M	35	Hepatitis C	Graft failure	24
8	48	F	25	Hepatitis C	Hepatitis C	301
9	47	M	37	Cryptogenic	Chronic rejection	199
10	50	M	16	Hepatitis C	Biliary necrosis	13

Table 2. Donor and operative data.

Patient	Donor (age)	DRI	Donor WIT (min)	Donor CIT (min)	Recipient WIT (min)	Operative Time (min)	PRBC (units)
1	19	1.4	20	320	29	254	25
2	57	2.1	18	389	36	271	18
3	41	1.6	63	438	38	344	3
4	31	1.7	20	343	32	282	12
5	54	2.2	18	458	24	332	38
6	48	1.6	17	247	23	131	8
7	20	1.4	13	279	38	317	10
8	23	1.9	29	336	21	198	13
9	37	1.9	25	486	26	404	34
10	36	1.8	30	362	25	218	8

vival was estimated using Kaplan-Meier analysis by Log Rank testing. Significance was defined at a p value of < 0.05.

RESULTS

Between February 1998 and June 2010, 211 patients underwent liver transplantation using DCD liver grafts; of those 10 patients underwent LR with DCD grafts. Demographic data are given in table 1. Mean recipient age was 50.9 years (range 48-69). Mean MELD scores at the time of LR was 25.6 (range 10-40). Three patients received LR for recurrent Hepatitis C, 4 patients received LR within 60 days of their initial transplant secondary to technical and early graft complications. One patient was retransplanted for chronic rejection, 1 for biliary necrosis and 1 for recurrent PSC.

Donor and recipient operative data are given in table 2. Donor age was 36.6 (range 19-54) years. Five donors died from trauma, 2 from stroke, 2 from intracranial hemorrhage, and 1 from myocardial infarction. The DWIT was 25.3 min (range 18-63) and CIT was 365.8 min (range 247-486). Recipient WIT was 29.2 min (range 21- 38), operative time was 275.1 min (range 131-404), and number of packed red blood cell units was 16.9 (range 3-34) transfused. Mean DRI score was 1.73 (range 1.4-2.2).

Post-operative complications and outcomes are listed in table 3. Five (50%) patients had no post-operative complications. One patient died in the operating room from a cardiac arrest. One patient had primary non-function that required a third transplant 12 days later. Three died from complications of sepsis and none of those patients ever left the hospital in the post transplant period. Recipients who had peri-operative death or graft loss (due to PNF) had mean MELD score of 34.4, while the recipients who survived long term had mean MELD score of 16.8 ($p = 0.0004$). Patients who survived long term did not have any complications necessitating return to the OR, other invasive procedures or readmission. Similarly, the mean hospital stay in recipients with long-term survival was significantly shorter (18.0 *vs.* 86.2 days, $p = 0.05$). Mean DRI score were similar between the long-term survivors and deceased recipients (1.80 *vs.* 1.68, $p = 0.9$). The calculated 30 day, 1 year, and 3 year graft survival are 70, 60, and 60%, respectively. The 30 day, 1 year, and 3 year patient survival are 80, 60, and 60%, respectively.

DISCUSSION

Patients with first graft failure requiring LR are commonly seen at most liver transplant centers. The most appropriate use of scarce livers continues to evolve. As the gap between supply and demand for liver grafts is widening world wide, livers from DCD donors should be considered. DCD grafts have been used more extensively since 1997 when Institute of Medicine determined that these organs are medically effective and ethically acceptable DCDs are considered to be less than optimal for transplantation because of damaging effect of variable warm ischemia time before cold preservation.[4,5]

LR causes controversy in the medical, economical and ethical fields as overall graft and patient survival is less than those undergoing initial OLT. The combination of the limited donor organ pool, increased number of patients dying on the waiting list and financial constraints with a failing graft challenges the current organ allocation system to provide efficient distribution of a limited resource.[6] The discrepancy between the number of available organs and increasing number of potential recipients will worsen until significant future advances are made in providing alternative management for chronic liver disease. Allocation of scarce liver grafts, especially for LR, requires balancing of ethi-

Table 3. Post-operative outcomes.

Patient	Age	MELD	Primary disease	Reason for LR	OLT-LR interval	Complication	ICU stay (days)	Graft survival (days)	Patient survival (days)	Status	Cause of death
1	69	29	Hepatitis C	Hepatitis C	146	Biliary sepsis	20	20	20	Dead	Bile leak, liver abscess
2	57	31	Hepatitis C	Hepatitis C	489	PNF	20	12	3133	Alive	-
3	49	10	Alcohol	Biliary Necrosis	174	None	0	2,460	2460	Dead	Renal failure
4	61	17	PSC	HAT	49	None	0	2,889	2,889	Alive	-
5	50	16	PSC	PSC	2,932	None	0	2,039	2,039	Alive	-
6	48	40	Hepatitis C	PNF	21	Intra-operative death	0	0	0	Dead	Intra-operative cardiac arrest
7	55	35	Hepatitis C	Graft Failure	24	Bleeding, sepsis	161	161	161	Dead	Necrotizing pancreatitis
8	48	25	Hepatitis C	Hepatitis C	301	None	0	1,118	1,118	Alive	-
9	47	37	Cryptogenic	Chronic rejection	199	Peritonitis, sepsis	45	45	45	Dead	Intra-abdominal sepsis
10	50	16	Hepatitis C	Biliary Necrosis	13	None	0	2,373	2,373	Dead	Recurrent HCC

cal principles: beneficence, fairness and utility. LR can be regarded as unfair because some patients get multiple liver grafts, whereas other patients die awaiting their first OLT. LR is commonly denied on the basis of historical poorer outcomes compared to first OLT.[7] With increasing life span after OLT, and thus with increase chance of recurrent primary disease in allograft, the transplant community will likely face increased number of OLT recipients with graft failure. LR candidates represent a complicated group and have a more rapid rate of decompensation with a higher rate of postoperative morbidity and mortality than primary OLT candidates.

To date there has not been any specific report regarding the use of DCD liver grafts in the LR setting. The main finding of this retrospective study is that when DCD grafts were used for sick patients with high MELD scores for LR, the patient and graft survivals were prohibitively low. In our experience the only patients who survived long term were the ones with MELD scores ≤ 25 at the time of LR.

This is a single center descriptive analysis of LR recipients managed with uniform surgical technique and medical protocols throughout the study period with complete long-term follow-up. As such, it is a unique contribution to the literature. This study was limited by the relatively small sample size of LR patients who received DCD liver grafts. Small sample size does not permit a multivariable analysis to determine overlapping factors. Another limitation is its retrospective design which spun over a decade. It is possible that other variables, such as significant advances in peri-operative critical care in the last decade could have influenced outcome differences.

CONCLUSION

Utilization of DCD liver grafts for LR resulted in poor patient outcomes in recipients with moderate to high MELD score. There is further need for reports from other large liver transplant programs and comparative analyses of LR using liver grafts from DCD and brain dead donors.

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