Outcomes of Liver Transplantations Using Donations After Circulatory Death: A Single-Center Experience

N. Meurisse, S. Vanden Bussche, I. Jochmans, J. Francois, B. Desschans, W. Laleman, S. Van der Merwe, W. Van Steenbergen, D. Cassiman, C. Verslype, R. Aerts, F. Nevens, J. Pirenne, and D. Monbaliu

ABSTRACT

Introduction. Orthotopic liver transplantation (OLT) (LTx) using donation after circulatory death (DCD) donors is increasingly performed, but still considered to risk of poorer outcomes compared with standard donations after brain death (DBD)-OLT. Therefore we reviewed our results of DCD-OLT.

Patients and Methods. Between 2003 and 2010, we performed 30 DCD-OLT (6% of all OLT). We retrospectively reviewed medical records of donors and recipients after DCD versus DBD-OLT to analyze biliary complications, retransplantation rates, and patient/graft survivals.

Results. Median donor age was similar for DCD and DBD-OLT: 51 versus 53 years (P = .244). Median donor warm ischemia time (stop ventilation to cold perfusion in DCD donors) was 24 minutes. Median cold ischemia time was shorter for DCD (6 hours 54 minutes) compared with DBD-OLT (8 hours 36 minutes; $P < .0001$). Median laboratory model of end-stage liver disease score was 15 for DCD, and 16 for DBD-OLT (P = .59). Median post-OLT Aspartate Aminotransferase (AST) peak was higher after DCD: 1178 versus DBD-OLT 651 IU/L (P = .005). The incidence of nonanastomotic strictures was different: 33.3% for DCD versus 12.5% for DBD-OLT (P = .001). The overall retransplantation rate was 3% after both DCD and DBD-OLT. After DCD-LTx actuarial 1, 3- and 5-year patient survivals were 93, 85 and 85%, and corresponding graft survivals, 90%, 82%, and 82% respectively, and not different compared with DBD-OLT: 88%, 78%, and 72% (P = .348) and 85%, 74%, and 68% (P = .524) respectively.

Conclusion. Despite substantial ischemic injury (high peak AST and biliary strictures) short- and long-term survival after DCD-OLT was comparable to DBD-OLT. Rapid donor surgery, careful donor and recipient selection, as well as short warm and cold ischemia times are key factors to optimize outcomes after DCD-OLT. However, strategies to reduce biliary complications remain warranted.

OVER THE LAST DECADE, donation after circulatory death (DCD) has been a rapidly growing source of liver grafts in countries with the necessary legal framework. Contrary to donation after brain death (DBD), the diagnosis of death in DCD is based upon standard circulatory arrest criteria.[1] Organs from DCD donors are invariably exposed to a period of warm ischemia before they are cooled, procured, preserved and transplanted. This additional warm ischemic insult is a significant risk factor for poorer graft survival and ischemic cholangiopathy after DCD-liver transplantation (OLT).[2] DCD donors are classified as uncontrolled and controlled donors. Uncontrolled DCD donors suffer an unexpected cardiac arrest followed

From the Leuven Liver Transplant Team, University Hospitals Leuven, Leuven, Belgium.

Address reprint requests to Nicolas Meurisse, MD, Abdominal Transplant Surgery, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium. E-mail: nicolas.meurisse@med.kuleuven.be

0041-1345/12/$–see front matter
http://dx.doi.org/10.1016/j.transproceed.2012.09.077

by an unsuccessful cardiopulmonary resuscitation. In very few experienced centers, isolated normothermic extracorporeal membrane oxygenation is then installed to recondition the abdominal organs in situ before procurement.[3] In the controlled DCD setting an 'anticipated' death occurs after planned withdrawal of life-sustaining treatment for patients suffering catastrophic irreversible neurological illness with consent from the family. Cessation of life-sustaining treatment which that usually takes place in the operating room is followed by an "agonal" phase, a period of variable/progressive hypotension and oxygen desaturation, until circulatory arrest. After a no-touch period, a super rapid laparotomy is usually performed and the organs are cooled in situ for procurement. In most centers, DCD livers are then cold stored until transplantation. The incidence of primary nonfunction (PNF) has progressively declined due to a shift toward the use of controlled DCD donors, limited warm and cold ischemic times, and strict donor selection.[4] There is still controversy concerning the definition of donor warm ischemia time (DWIT). The simplest and most reproducible definition is the time between therapy withdrawal and the start of cold perfusion. It is also not clear which recipients benefit the most from a DCD liver grafts, because of the increased risk of biliary complications and the impaired short- and long-term outcomes generally reported after DCD-OLT.[2] The aim of this retrospective study was therefore to evaluate in our center the short- and long-term outcomes after DCD-OLT in terms of patient and graft survivals as well as the incidence of biliary complications.

PATIENTS AND METHODS

We performed a retrospective review of all DBD and DCD-OLT performed in our center between January 2003 and December 2010. Our program of controlled DCD-OLT was initiated in 2003 after approval by our institutional ethical committee and the Belgian National Council of Physicians. Recipients <18 years old, combined transplantations and patients who received a split liver graft were excluded in this study.

For DCD donation, withdrawal of life-sustaining ventilatory support occurred in the operating room except in 2 cases (euthanasia performed outside the operating room). Systemic heparin (300 IU/kg) was administered intravenously to DCD donors before withdrawal of treatment, or to cold flush in DBD donors. Circulatory death diagnosed by 3 independent physicians was followed by a no-touch period of 5 minutes. Then a super rapid sternolaparotomy was performed with caval decompression (by venting the right atrium or the intra-abdominal vena cava) before abdominal aorta cannulation. One liter of pressurized 25°C Hartmann's solution containing streptokinase (1.5×10^6 IU) and epoprostenol (Flolan 200 μg) was first infused through the aorta before cold preservation perfusion. From 2003 to 2009, only histidine-tryptophan-ketoglutarate (HTK) was used as the aortic flush in DCD donors. After 2009, an initial flush is done with pressurized HTK through the aorta followed by a flush using University of Wisconsin (UW) preservation solution.[5] Whenever technically feasible, an additional portal perfusion was performed through the superior mesenteric vein in DCD donors, whereas only a single aortic perfusion was used in DBD donors. Immediately after the start of cold perfusion, abdominal organs were topically cooled with melting ice water. Similar to DBD, both the gallbladder and the common bile duct (whenever possible) were opened in situ and rinsed with cold isotonic sodium chloride. On the back table a second bile duct rinse was performed and the portal vein flushed before packing and transport. To minimize the cold ischemia time (CIT), the recipient operation was started as soon as the DCD liver was found to be transplantable. The standard immunosuppressive protocol consisted of tacrolimus, mycophenolate mofetil, and low-dose prednisone.

We first compared donor characteristics between DBD and DCD-OLT including age, gender, body mass index (BMI), locally procured or imported livers, cause of death, preservation solution, aspartate aminotransferase (AST) level, DWIT (defined as the time interval between withdrawal of therapy until start of cold flush of the liver). Recipient factors evaluated included age, gender, BMI, laboratory Model for End-Stage Liver Disease (MELD) score at the time of OLT, indication for transplantation, urgency, CIT (defined as the time between cold flush of the liver and its leaving from the ice water just before implantation), anastomosis time (defined as the time between the liver leaving the ice water and the reperfusion), and total surgery time.

We then compared, between DBD and DCD recipients, the following parameters: Post-OLT peak of AST and alanine aminotransferase (ALT), defined as the highest value measured during the first 3 days after OLT; intensive care unit (ICU) and hospital stays, PNF incidence, patient survival, graft survival (defined as the time from OLT to either re-transplantation or patient death), retransplantation (reTx) rate, and the incidence of biliary complications. Biliary complications were classified as: clinically suspected; confirmed by endoscopic retrograde cholangiopancreatography (ERCP); requiring percutaneous and/or endoscopic intervention, surgery, and/or retransplantation. They were classified as non-anastomotic strictures (NAS), including ischemic-type biliary strictures in the presence of a patent hepatic artery, anastomotic strictures (AS), or biliary leaks. Biliary strictures secondary to chronic rejection were not included in this classification. Furthermore, we recorded the time from transplantation to the diagnosis of a biliary stricture, and the frequency of subsequent percutaneous and/or endoscopic interventions.

Finally, the following donor and recipient variables were tested for their association with the development of biliary strictures after DCD-OLT: CIT > 8 hours, donor and recipient age >60 years, lab MELD score >20, donor BMI > 25, cause of death (trauma vs nontrauma), DWIT > 30 minutes; and peak AST > 2000 IU/L. These variables were selected because they are generally considered to be significant risk factors for a suboptimal outcome.

Statistical Analysis

Data are expressed as median values and interquartile ranges (IQR). Continuous variables were analyzed using the Mann-Whitney U test. Categorical variables were analyzed using Pearson's chi-square or Fisher's exact test when appropriate. Patient and graft survival analysis was performed using the Kaplan-Meier method and survival between groups was compared using the log-rank test. Potential risk factors for biliary complications were entered into univariate analysis. Statistical significance was assumed for $P < .05$.

RESULTS

During the study period, we performed 30 (6%) and 385 (94%) OLT from DCD and DBD donors, respectively

(total 415). The follow-up which varyed from 12 to 96 months was complete for all patients.

There was no statistical difference with respect to donor factors of age, gender, BMI, or AST between the 2 groups (Table 1). Most DCD livers were procured locally by our own team (80%), which was different for DBD livers: 39% locally procured compared with 61% imported ($P < .001$). In the DCD group, there was a greater incidence of suicides and euthanasia compared with DBD donors (23% vs 4% [$P < .01$] and 7% vs 0% [$P < .01$] respectively). HTK was more often used as the flush solution for DCD compared with DBD livers: 77% vs 23% respectively ($P < .001$). The median DWIT in the DCD group was 24 minutes (range, 18–30), exceeding 30 minutes in 5 cases (34, 36, 49, 55, and 56, respectively).

There was no significant difference with respect to recipient factors of age, gender, BMI, laboratory MELD score, anastomosis time, total surgery duration as well as ICU and hospital stays (Table 2). Indications were not different: Most OLT were performed as first transplantations; there was no difference in high urgency OLT. CIT was shorter in DCD versus DBD-OLT; 6 hours 54 minutes versus 8 hours 36 minutes ($P < .01$). Peak AST and ALT were higher after DCD-OLT compared with DBD-OLT; 1178 IU/L (560–1997) versus 651 IU/L (333–1243; $P < .01$); and 948 IU/I (610–1457) versus 622 IU/I (319–1128; $P < .03$), respectively. No PNF was observed in either group.

There was no difference in the 5-year actuarial patient (Fig 1) and graft (Fig 2) survival rates between DCD and DBD recipients: 85.5% versus 72.6% ($P = .348$) and 82.1% versus 68.7% ($P = .374$), respectively.

The overall biliary complication rate was higher among the DCD group: 50% versus 28.3% ($P = .012$; Table 3). The overall rate of biliary strictures (AS and NAS) was higher in the DCD group: 46.7% versus 26.5%; ($P = .018$). The incidence of NAS alone was significantly higher in the DCD group: 33.3% versus 12.5%; ($P = .001$). The rates of AS and biliary leak were not different. There was no difference with respect to the median time to diagnose biliary strictures after DCD versus DBD: 95 versus 76 days respectively ($P = .916$). The number of patients treated by percutaneous/endoscopic interventions or in whom a retransplant was required was not different after DCD versus DBD-LTx: 9 versus 72 ($P = .630$) and 0 versus 11 ($P = .175$).

Univariate analysis was employed to evaluate the impact of several donor and recipient characteristics on the risk to develop a biliary strictures among the DCD population. Only CIT > 8 hours reached significance ($P = .03$). The other variables including donor age >60 years ($P = .22$), recipient age >60 ($P = .46$), donor BMI > 25 kg/m^2 ($P = .79$), nontraumatic cause of death ($P = .15$), MELD score > 20 ($P = .46$), and peak AST > 2000 IU/L ($P = .81$) were not significant.

DISCUSSION

Our DCD-OLT program which was started in 2003, has since then represented 6% of total activity. Our results have not demonstrated a significant difference in 5-yr actuarial patient and graft survivals between the DCD and DBD recipients. These findings are consistent with those of other single center experiences that have reported favourable outcome after DCD-OLT[6–9] which contrasts with inferior outcomes reported by registries and other early series.[4,10–13] To avoid PNF and severe graft dysfunction, we have limited the DWIT to 30 minutes in most cases. This restriction is based upon our preclinical studies on the maximal tolerance of livers to warm ischemia. It has also been recommended by other workers and included in international clinical guidelines.[14,15] No PNF was observed. The 5 cases in which we accepted a DWIT > 30 minutes occurred in the early part of the series. DCD liver grafts tolerate cold ischemia poorly. Therefore, we always seek to keep the CIT as short as possible. Reducing the CIT has been made possible by a center-driven allocation system foreseen by Eurotransplant for DCD livers. Once a DCD

Table 1. Donor Characteristics

Donor Characteristics	DBD ($n = 385$)	DCD ($n = 30$)	P
Age (yrs), median, IQR	53 (42–64)	51 (37–59)	.244
Gender ratio (%): M/F	54/46	67/33	.657
BMI (kg/m^2)	24.22 (22.40–26.12)	23.94 (22.49–25.82)	.657
Locally procured vs. imported (%)	39/61	80/20	<.001
Cause of death (%)			
Cerebrovascular accident	56	40	.13
Trauma	29	27	.84
Suicide	4	23	<.01
Euthanasia		7	<.01
Other	11	3	.23
Aminotransferase level (IU)	39 (23–64)	40 (21–60)	.657
Preservation solution: UW/HTK (%)	77/23	23/77	<.01
DWIT (min): median, IQR	—	24 (18–30)	—

Data are given as median [interquartile range (IQR)].
Abbreviations: BMI, body mass index; UW, University of Wisconsin; HTK, histidine-tryptophan-ketoglutarate; DWIT, donor warm ischemia time.

Table 2. Recipient Characteristics

Recipient Characteristics	DBD (n = 385)	DCD (n = 30)	P
Age (yrs): median, IQR	58 (49–64)	60 (52–65)	.255
Gender ratio (%): M/F	60/40	73/27	.18
BMI (kg/m^2): median, IQR	26 (18–34)	26 (13–47)	.89
Lab MELD: median, IQR	16 (11–23)	15 (11–17)	.595
Indications			
Acute liver failure	33 (8.5%)	1 (3.3%)	.495
Metabolic disease	44 (11.4%)	4 (13.3%)	.766
Tumor	140 (36.7%)	10 (33.3%)	.845
Chronic liver disease	262 (68.1%)	24 (80%)	.220
HCV	49 (12.7%)	4 (13.3%)	.545
Others	4 (1%)	0 (0%)	.925
Retransplantation	33 (8.5%)	2 (6.6%)	.943
High urgency transplantations	36 (9.3%)	1 (3.3%)	.367
CIT (hrs): median, IQR	8h 36=(7h 13=-10h 06=)	6h 54=(5h 25=-7h 51=)	<.001
Recipient warm ischemic time (min): median, IQR	48=(27–112)	51=(35=-94=)	.26
Total surgery time (hrs): median, IQR	5h 05=(4h 19=-6h 15=)	5h 13=(4h 24=-6h 22=)	.596
Peak AST (IU): median, IQR	651 (333–1243)	1178 (560–1997)	.01
Peak ALT (IU): median, IQR	622 (319–1128)	948 (610–1457)	<.03
ICU stay (ds): median, IQR	4 (2–9)	4.5 (2–8.75)	.969
Hospital stay (ds): median, IQR	20 (15–32)	20.5 (15.75–39.25)	.749

Data are given as median [interquartile range (IQR)].
Abbreviations: BMI, body mass index; MELD, Model for End-Stage Liver Disease; HCV, hepatitis C virus; CIT, cold ischemia time; ICU, intensive care unit.

liver is regarded to be transplantable at the donor center, the recipient operation is usually started immediately at the recipient transplant center. In addition, we sought to select recipients in whom we anticipated a straightforward hepatectomy by usually avoiding recipients with previous major liver surgery. However, in our clinical practice, allocation of DCD livers was still guided at least in part by the urgency of the OLT which explains the similar MELD scores for DCD versus DBD recipients. In some rare occasions we even used DCD grafts for retransplants or hyperurgent OLT.

DCD livers suffer greater hepatocellular and ischemia reperfusion injuries as reflected by the higher AST and ALT peaks. Despite these circumstances, post OLT recovery was similar as reflected by comparable ICU and hospital stays. Similar to most published series,[12,16] we did observe a greater incidence of biliary complications, in particular NAS. Among the variables considered to be risk factors for developing NAS in a previous large series of DCD,[4] our univariate analysis identified only CIT > 8 hours as a risk factor. Unfortunately, with only 10 cases of NAS, we could not perform a multivariate analysis to determine independent risk factors.

The pronounced effect of CIT on NAS strictures was consistent with recent analyses by Foley et al[16] and by Chan et al.[17] In contrast, donor age > 60, DWIT > 30 minutes, BMI > 25 kg/m^2, MELD > 20, and peak AST > 2000 IU/L did not correlate with a greater risk of NAS. Donor age has often been suggested to be an important factor leading to biliary strictures.[4,14,15] In our series, the median donor age was 51. Interestingly, 3 of the 4 donor livers from individuals older than 60 (65, 69, 62, and 68 years old) developed NAS. Another generally accepted risk factor for ischemic

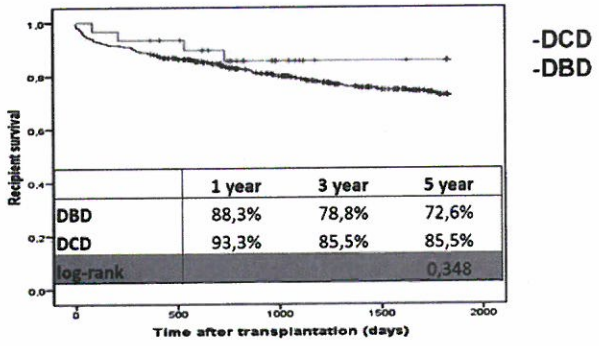

Fig 1. Patient survival after liver transplantation using donation after brain death (DBD) and donation after circulatory death (DCD) grafts.

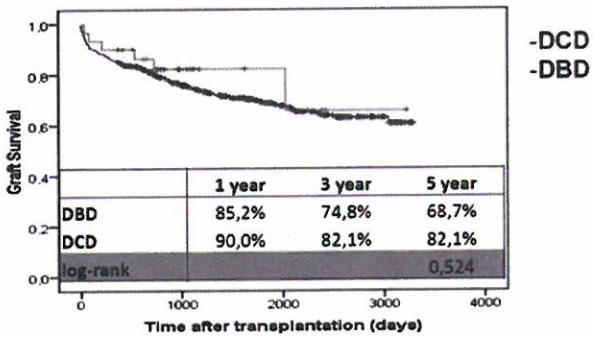

Fig 2. Graft survival after liver transplantation using donation after brain death (DBD) and donation after circulatory death (DCD) grafts.

Table 3. Biliary Complications and Treatment Options

	DBD (n = 385)	DCD (n = 30)	P
Overall biliary complications	109 (28.3%)	15 (50%)	.012
Overall rate of biliary strictures (Anastomotic and nonanastomotic)	102 (26.5%)	14 (46.7%)	.018
Nonanastomotic strictures	48 (12.5%)	10 (33.3%)	.001
Anastomotic strictures	72 (18.7%)	8 (26.7%)	.287
Biliary leaks	24 (6.2%)	2 (6.7%)	.925
Time to diagnose biliary stricture (d) (median)	95	76	.916
Treatment for biliary strictures (number of patients)			
Percutaneous and/or endoscopic interventions	72 (18.7%)	9 (30%)	.630
Retransplantation (%)	11 (2.8%)	0	.175

cholangiopathy is a DWIT > 30 minutes.[14–16] Our median WIT was 24 minutes. As stated, in 5 patients the DWIT was >30 minutes and was even >40 minutes in 2 recipients. Of these 5 patients, 3 developed biliary strictures.

Despite the increased incidence of biliary strictures observed in our series, short- and long-term graft and patient survivals were not different significantly between DCD and DBD-OLT. At the present time, no graft loss has been experienced and no retransplant performed in case of biliary stricture after DCD-OLT. However, 1 patient, who received a graft exposed to 56 minutes of DWIT early in our series, developed diffuse biliary strictures and had been listed for retransplantation before succumbing to biliary sepsis on the waiting list. Another DCD-OLT recipient was retransplanted because of ductopenic rejection which was apparently related to subtherapeutic immunosuppression due to well-documented erroneous tacrolimus concentration monitoring.

The majority of DCD-OLT who developed biliary strictures (64.3%) were successfully managed endoscopically in our series. When reviewing the endoscopic retrograde cholangiopancreatography images, the biliary strictures in these patients were mainly located at the main bifurcation of the bile ducts which allowed efficient percutaneous and endoscopic treatment. However we must acknowledge that biliary strictures in DCD livers are an important source of morbidity. Repeated diagnostic and therapeutic endoscopic and percutaneous interventions[18,19] represent a significant burden for these patients and a source of additional costs.

Seeking to ameliorate outcomes of DCD-OLT we have implemented a series of strategies: better penetration of the cold preservation solution by the preliminary injection of vasodilatator (epoprostenol) and fibrinolytics (streptokinase); use of a low viscosity preservation solution (HTK) before UW; biliary tree flush not only in situ but also ex situ in the donor center before cold storage; reduction of the DWIT usually to a maximum of 30 minutes by appropriate donor selection and ultra rapid donor surgery; reduction of the CIT by starting the recipient operation immediately after acceptance of the donor liver; careful selection of the donor seeking an age below 60 years with a normal macroscopic appearance of the graft (no obvious macrovesicular steatosis, complete flush). These measures, albeit achieving equivalent results to DBD in terms of survival, have not allowed us to reduce the incidence of biliary complications. Surgical alternatives like reperfusion of the hepatic artery first, as proposed by the King's college,[20] to rapidly restore oxygenation to the biliary tree, venting first of the vena cava before the cold flush to avoid liver congestion, augmented frequency and nature of the flush for the biliary tree to reduce the toxicity of the bile,[21] infusion of tissue plasminogen activator into the hepatic artery on the back table[22] or after portal reperfusion,[23] biological modulation,[24] and machine liver perfusion need to be validated in prospective trials.

REFERENCES

1. Bernat JL, D'Alessandro AM, Port FK, et al: Report of a National Conference on Donation after cardiac death. Am J Transplant 6:281, 2006
2. Monbaliu D, Pirenne J, Talbot J: Liver transplantation using donation after cardiac death donors. J Hepatol 56:474, 2012
3. Fondevila C, Hessheimer AJ, Flores E, et al: Applicability and results of Maastricht type 2 donation after cardiac death liver transplantation. Am J Transplant 12:162, 2012
4. Mateo R, Cho Y, Singh G, et al: Risk factors for graft survival after liver transplantation from donation after cardiac death donors: an analysis of OPTN/UNOS data. Am J Transplant 6:791, 2006
5. Stewart ZA, Cameron AM, Singer AL, et al: Histidine-Tryptophan-Ketoglutarate (HTK) is associated with reduced graft survival in deceased donor livers, especially those donated after cardiac death. Am J Transplant 9:286, 2009
6. Grewal HP, Willingham DL, Nguyen J, et al: Liver transplantation using controlled donation after cardiac death donors: an analysis of a large single-center experience. Liver Transpl 15:1028, 2009
7. Detry O, Seydel B, Delbouille MH, et al: Liver transplant donation after cardiac death: experience at the University of Liege. Transplant Proc 41:582, 2009
8. Muiesan P, Girlanda R, Jassem W, et al: Single-center experience with liver transplantation from controlled non-heart beating donors: a viable source of grafts. Ann Surg 242:732, 2005
9. Manzarbeitia CY, Ortiz JA, Jeon H, et al: Long-term outcome of controlled non-heart-beating donor liver transplantation. Transplantation 78:211, 2004
10. Abt P, Desai N, Crawford M, et al: Survival following liver transplantation from non-heart-beating donors. Ann Surg 239:87, 2004
11. Merion RM, Pelletier SJ, Goodrich N, et al: Donation after cardiac death as a strategy to increase deceased donor liver availability. Ann Surg 244:555, 2006
12. Foley DP, Fernandez LA, Leverson G, et al: Donation after cardiac death: the University of Wisconsin experience with liver transplantation. Ann Surg 242:724, 2005
13. de Vera ME, Lopez-Solis R, Dvorchik I, et al: Liver transplantation using donation after cardiac death donors: long-term follow-up from a single center. Am J Transplant 9:773, 2009
14. Monbaliu D, Crabbé T, Roskams T, et al: Livers from non-heart-beating donors tolerate short periods of warm ischemia. Transplantation 79:1226, 2005
15. Mathur AK, Heimbach J, Steffick DE, et al: Donation after cardiac death liver transplantation: predictors of outcome. Am J Transplant 10:2512, 2010

16. Foley DP, Fernandez LA, Leverson G, et al: Biliary complications after liver transplantation from donation after cardiac death donors: an analysis of risk factors and long-term outcomes from a single center. Ann Surg 253:817, 2011

17. Chan E, Olson L, Kisthard J, et al: Ischemic cholangiopathy following liver transplantation from donation after cardiac death donors. Liver Transpl 14:604, 2008

18. Jay CL, Lyuksemburg V, Ladner DP, et al: Ischemic cholangiopathy after controlled donation after cardiac death liver transplantation: a meta-analysis. Ann Surg 253:259, 2011

19. Maheshwari A, Maley W, Li Z, et al: Biliary complications and outcomes of liver transplantation from donors after cardiac death. Liver Transpl 13:1645, 2007

20. DeOliveira M, Jassem W, Valente R, et al: Biliary complications after liver transplantation using grafts from donors after cardiac death: results from a matched control study in a single large volume center. Ann Surg 254:716, 2011

21. Buis CI, Geuken E, Visser DS, et al: Altered bile composition after liver transplantation is associated with the development of nonanastomotic biliary strictures. J Hepatol 50:69, 2009

22. Hashimoto K, Eghtesad B, Gunasekaran G, et al: Use of tissue plasminogen activator in liver transplantation from donation after cardiac death donors. Am J Transpl 10:2665, 2010

23. Fung JJ, Eghtesad B, Patel-Tom K: Using livers from donation after cardiac death donor: a proposal to protect the true Achilles heel. Liver Transpl 13:1633, 2007

24. Monbaliu D, Vekemans K, Hoekstra H, et al: Multifactorial biological modulation of warm ischemia reperfusion injury in liver transplantation from non-heart-beating donors eliminates primary nonfunction and reduces bile salt toxicity. Ann Surg 250:808, 2009