Can we reduce ischemic cholangiopathy rates in donation after cardiac death liver transplantation after 10 years of practice? Canadian single-centre experience

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Background: Outcomes in liver transplantation with organs obtained via donation after cardiocirculatory death (DCD) have been suboptimal compared to donation after brain death, attributed mainly to the high incidence of ischemic cholangiopathy (IC). We evaluated the effect of a 10-year learning curve on IC rates among DCD liver graft recipients at a single centre.

Methods: We analyzed all DCD liver transplantation procedures from July 2006 to July 2016. Patients were grouped into early (July 2006 to June 2011) and late (July 2011 to July 2016) eras. Those with less than 6 months of follow-up were excluded. Primary outcomes were IC incidence and IC-free survival rate.

Results: Among the 73 DCD liver transplantation procedures performed, 70 recipients fulfilled the selection criteria, 32 in the early era and 38 in the late era. Biliary complications were diagnosed in 19 recipients (27%). Ischemic cholangiopathy was observed in 8 patients (25%) in the early era and 1 patient (3%) in the late era (p = 0.005). The IC-free survival rate was higher in the late era than the early era (98% v. 79%, p = 0.01). The warm ischemia time (27 v. 24 min, p = 0.049) and functional warm ischemia time (21 v. 17 min, p = 0.002) were significantly lower in the late era than the early era.

Conclusion: We found a significant reduction in IC rates and improvement in IC-free survival among DCD liver transplantation recipients after a learning curve period that was marked by more judicious donor selection with shorter procurement times.

Contexte : L'issue des greffes de foie suite à un don d'organe après décès cardiocirculatoire (DDC) a été sous-optimale comparativement aux dons suivant la mort cérébrale. Cela serait surtout attribuable à une forte incidence de cholangiopathie ischémique (CI). Nous avons évalué l'effet d'une courbe d'apprentissage échelonnée sur 10 ans sur les taux de CI chez des receveurs de greffe de foie après DDC dans un seul centre.

Méthodes : Nous avons analysé toutes les greffes de foie consécutives à des DDC entre juillet 2006 et juillet 2016. Les patients ont été regroupés en 2 époques, la première, de juillet 2006 à juin 2011, et la seconde, de juillet 2011 à juillet 2016. Ceux pour lesquels on disposait de moins de 6 mois de suivi ont été exclus. Les paramètres principaux étaient l'incidence de CI et le taux de survie sans CI.

Résultats : Parmi les 73 greffes de foie par suite de DDC, 70 receveurs répondaient aux critères de sélection, 32 pour la première époque et 38 pour la seconde époque. Des complications biliaires ont été diagnostiquées chez 19 receveurs (27 %). La cholangiopathie ischémique a été observée chez 8 patients (25 %) de la première époque et 1 patient (3 %) de la seconde (p = 0,005). Le taux de survie sans CI a été plus élevé pendant la seconde époque que pendant la première (98 % c. 79 %, p = 0,01). Le temps d'ischémie chaude (27 minutes c. 24, p = 0,049) et le temps d'ischémie chaude fonctionnelle (21 minutes c. 17, p = 0,002) ont été significativement plus courts durant la seconde époque que durant la première.

Conclusion : Nous avons observé une réduction significative des taux de CI et une amélioration de la survie sans CI chez les receveurs de greffes de foie par DDC après une courbe d'apprentissage qui a été marquée par une sélection plus judicieuse des donneurs et des délais d'obtention plus courts.

Recommended strategies to expand the donor pool in liver transplantation and decrease waiting list mortality include using extended-criteria donors and living donation. Encompassed among extended-criteria donors is donation after cardiocirculatory death (DCD), the process of organ retrieval that follows irreversible cessation of cardiopulmonary function. Donation after cardiocirculatory death has been widely questioned because of its higher rate of biliary complications. Compared to organs from donation after brain death (DBD), organs from DCD are exposed to severe ischemia reperfusion injuries due to prolonged warm ischemia time (WIT), resulting in cytokine storms, circulatory dysfunction and circulatory arrest and, therefore, a higher risk of negative outcomes.[1–4] Among the most feared complications encountered with DCD are ischemic cholangiopathy (IC) and primary nonfunction. Despite the higher rate of complications, the number of centres performing DCD liver transplantation has increased more than 5 times over the last 7 years owing to organ scarcity and high waiting list mortality.[1,4]

Donation after cardiocirculatory death is defined according to the situation of the cardiac arrest: uncontrolled (patient is declared dead on arrival or after resuscitation failure, occurring inside or outside the hospital) or controlled, in which the treating team and family are "awaiting cardiac arrest."[5] The first successful human liver transplantation was performed in 1963 with uncontrolled DCD; however, this practice stopped during the mid-1970s owing to the poor outcomes and establishment of brain death criteria.[5] In 1995, the University of Pittsburgh[6] and the University of Wisconsin[7] published their experiences with the introduction of controlled DCD, and their results encouraged other programs to further pursue this innovative practice. During the following years, DCD was considered an ethical practice by the US Institute of Medicine[8] and gained more popularity, with a steady rise in the number of DCD transplantation procedures for more than 10 years. Nonetheless, the journey was not free of challenges, and this growth levelled out in 2005. Some centres began publishing major complications and inferior survival rates among recipients of DCD organs.[9,10] The wide discrepancy in IC rates between centres (1.4%–50%) prompted the transplantation community to reassess protocols and investigate donor and recipient risk factors.[4,10–12] Foley and colleagues[4] and de Vera and colleagues[13] reported an increased risk of biliary complications in donors older than 40 and 60 years, respectively, but Taner and colleagues[14] and Firl and colleagues[15] did not find age to be a risk factor for IC. Other characteristics associated with higher IC rates are increased donor weight, prolonged cold ischemia time (CIT) and prolonged WIT.[3]

The journey toward the use of DCD organs in Canada started in 2005. After 3 days of extensive examination and more than 100 experts' opinions, the Canadian Council for Donation and Transplantation sanctioned the use of DCD organs.[16] Consequently, the London Health Sciences Centre, London, Ontario, did its first DCD liver retrieval and transplantation in July 2006.[17] Over the next decade, transplantation surgeon expertise, institutional volume and multidisciplinary team experience accumulated, resulting in growth along the DCD learning curve. Expected outcomes of a transplantation centre's learning curve include reduced operative time, reduced number of complications, including IC, fewer unplanned interventions and improved recipient survival. This study aimed to assess the learning curve of the pioneer Canadian DCD liver transplantation program in London, focusing on IC.

Methods

Design and setting

We conducted a cohort study using a prospectively maintained database of all patients who underwent orthotopic liver transplantation at a single transplantation centre in Ontario. We performed a retrospective analysis using data collected from patients who received organs procured via DCD between July 2006 and July 2016. The cohort was divided into early (July 2006 to June 2011) and late (July 2011 to July 2016) eras. We compared donor and recipient characteristics, and transplantation outcomes between eras to assess the effect of the learning curve of our DCD liver transplantation program. Ethics approval was obtained from the Western University Office of Research Ethics.

Population

Patients with end-stage liver disease were evaluated and listed for liver transplantation by a multidisciplinary team. The Model for End-Stage Liver Disease was used for graft allocation. Candidates for DCD grafts were generally similar to candidates for DBD grafts; however, patients with a history of extensive abdominal surgery or portomesenteric vein thrombosis were listed for DBD only. In general, DCD donor age was limited to 60 years, with a preferred WIT of less than 30 minutes; however, cases were considered on an individual basis, and some donor grafts with longer WIT were used. Furthermore, the graft pattern appearance after cold perfusion was assessed subjectively for organ selection.

Only controlled DCD grafts were procured, according to the technique described in the literature.[5] In brief, withdrawal of life support occurred in the intensive care unit or the operating room according to the donor centre's policy. Administration of heparin before death was fully disclosed during the consent discussion based on ethics and institutional policies.[16] In our practice, all donors receive heparin (400 units/kg given intravenously) 5 minutes before withdrawal of life support if allowed by the donor hospital institutional policies. If not allowed, heparin is added to

the preservation fluid. In the current series, all donors received heparin before withdrawal of life support. Death certification was performed by a physician independent from the transplantation team. After a 5-minute standoff period, as is Canada's standard, the donor transferred to the operating room for rapid organ procurement, during which the inferior vena cava was cannulated first to drain the static blood from the liver, followed by aortic and superior mesenteric vein cannulation for flushing of the preservation solution (histidine–tryptophan–ketoglutarate [HTK]). Ice was placed in the abdominal cavity, the bile duct was divided, and bile was drained from the gallbladder and bile duct by flushing with cold saline solution in situ and with HTK preservation solution ex situ.

Static cold storage is the most commonly used preservation technique. It is not only the low temperatures that help preservation; preservation fluids also provide homeostasis and delay cell metabolism and cell damage. University of Wisconsin solution, HTK solution, Celsior solution (Waters Medical Systems) and IGL-1 solution are commonly used. In a 2013 meta-analysis, Lema Zuluaga and colleagues[18] found no difference between type of solution in early allograft dysfunction, 1-year patient survival or biliary complications, whereas 2 trials showed inferior outcomes with HTK.[19,20] As a method of preservation, static cold storage has been shown to cause injury to bile duct epithelium in 88% of cases.[19,20]

In our centre, HTK preservation solution is used as the standard in our DCD protocol owing to its low viscosity, which allows a better flow rate and distribution (3 times faster than University of Wisconsin solution) into the liver bed, resulting in quicker organ cooling. Moreover, in contrast to University of Wisconsin solution, the low K^+ concentration (9 mmol/L) of HTK solution means that it can be released safely into the circulation, minimizing the risk of hyperkalemic cardiac arrest.[16]

Data collection

We calculated 4 procurement times: WIT, skin cut to flush time, skin cut to liver out and CIT. We defined WIT as the time elapsed from withdrawal of life support until aortic cold perfusion flush, and CIT as the time from cold perfusion in the donor to reperfusion at implantation in the recipient. We compared donor characteristics, recipient characteristics and outcomes between eras to assess the effect of the learning curve for our DCD liver transplantation program. The primary outcomes were IC incidence and IC-free survival time. Secondary outcomes were graft survival and need for any intervention.

Ischemic cholangiopathy is defined as a complex pathological entity characterized by multiple intrahepatic strictures in the absence of hepatic artery thrombosis or stenosis.[2,21] Biliary tree assessment with imaging modalities was performed only in patients who had biochemical or clinical evidence of biliary obstruction. The diagnosis of IC was made based on cholangiography studies (endoscopic retrograde cholangiopancreatography [ERCP], percutaneous transhepatic cholangiography or magnetic resonance cholangiopancreatography). Ischemic cholangiopathy was considered present if imaging showed 2 or more nonanastomotic intrahepatic biliary strictures in the context of a patent hepatic artery. Internal or external biliary drainage treatment was applied with ERCP or percutaneous transhepatic cholangiography in symptomatic patients (hyperbilirubinemia or cholangitis).

Initially, posttransplantation follow-up was performed twice a week, assessing clinical and biochemical parameters (liver enzyme, bilirubin, alkaline phosphatase and immunosuppression levels). Subsequently, follow-up was done 1 month, 3 months and 6 months after transplantation, based on the patient's clinical progression. The minimal length of follow-up was 6 months and the maximal length, 9 years (median 3 yr). In most cases, IC manifests by 6 months after transplantation.[5] We defined primary nonfunction as early (within the first 72 h) graft failure in the absence of detectable technical, immunological or infectious problems, with alterations in and progressive elevation of transaminase levels, coagulopathy, changes in mental status and metabolic acidosis.[5,22–24]

Statistical analysis

We tested the distribution of continuous variables for normality using the Shapiro–Wilk test. Continuous variables with normal distributions were expressed as mean and standard deviation and were compared by means of the independent sample *t* test. Variables with nonnormal distributions were expressed as median and interquartile range (IQR) and were compared by means of the Mann–Whitney test. We computed categorical variables using the Fisher exact test. We computed survival curves using the Kaplan–Meier method and compared them using log-rank tests. All statistical analysis was performed with IBM SPSS Statistics 23 (IBM Corp.).

Results

From July 2006 to July 2016, 73 consecutive DCD liver grafts were transplanted at University Hospital, of which 70 (96%) met our study criteria. Of the 70 procedures, 32 were performed in the early era and 38 in the late era.

Donor characteristics

The donor characteristics are summarized in Table 1. The median Donor Risk Index score was significantly lower in the late era than in the early era (2.1 v. 2.5) (p = 0.02). Late-era donors were younger than early-era donors, although not significantly so, and were more likely to be

Table 1. Study population characteristics

Characteristic	No. (%) of patients* Early era *n* = 32	Late era *n* = 38	*p* value
Donors			
Demographic			
Age, yr, median (IQR)	44 (18–62)	38 (12–59)	0.1
Male sex	16 (50)	28 (74)	0.04
Height, cm, median (IQR)	169 (150–193)	175 (152–188)	0.1
Weight, kg, mean ± SD	76 ± 5.6	75 ± 14.6	0.49
Body mass index, median (IQR)	25 (17–46)	24 (17–35)	0.2
Donor Risk Index score, median (IQR)	2.46 (1.7–3.2)	2.1 (1.6–3.4)	0.02
Location			0.04
Local	15 (47)	27 (71)	
Regional	17 (53)	11 (29)	
Cause of death			0.049
Trauma	13 (41)	15 (39)	
Anoxia	6 (19)	16 (42)	
Cerebrovascular accident	13 (41)	7 (18)	
Procurement times			
Warm ischemia time, min, median (IQR)	27 (18–121)	24 (16–48)	0.049
Cut–cannulation–flush, min, median (IQR)	6 (2–12)	4 (2–8)	0.02
Skin cut to liver out, min, median (IQR)	56 (21–97)	52 (28–121)	0.2
Cold ischemia time, h, median (IQR)	5.56 (4.45–6.45)	5.10 (4.46–6.37)	0.4
Recipients			
Demographic			
Age, yr ,median (IQR)	54 (26–69)	57 (36–66)	0.3
Male sex	26 (81)	26 (68)	0.2
MELD score, median (IQR)	15 (8–40)	17 (3–35)	0.7
Diagnosis			0.003
Hepatitis C	12 (38)	4 (10)	
Hepatocellular carcinoma	8 (25)	15 (39)	
Alcoholic liver disease	5 (16)	2 (5)	
Autoimmune	3 (9)	0 (0)	
Nonalcoholic steatohepatitis	0 (0)	5 (13)	
Primary biliary cirrhosis	0 (0)	3 (8)	
Primary sclerosing cholangitis	0 (0)	3 (8)	
Other	4 (12)	6 (16)	

IQR = interquartile range; MELD = Model for End-Stage Liver Disease; SD = standard deviation.
*Except where noted otherwise.

male (28 [74%] v. 16 [50%]) (p = 0.04). Anoxia was more common as the cause of death in the late-era group than in the early-era group (16 [42%] v. 6 [19%]) (p = 0.049), and local donor allocation was significantly higher in the late era than in the early era (27 [71%] v. 15 [47%]) (p = 0.04).

Procurement times

The median time from cut to cannulation and flush in the early era was 6 minutes (IQR 2–12 min) versus 4 minutes (IQR 2–8 minutes) in the late era (p = 0.02) (Table 1). The WIT was 27 minutes (IQR 18–121 min) versus 24 minutes (IQR 16–48 min), respectively (p = 0.049), and the CIT was 5.56 hours (IQR 4.45–6.45 h) versus 5.10 hours (IQR 4.46–6.37 h), respectively (p = 0.4).

Recipient characteristics

Recipient characteristics including age and sex in the 2 eras were comparable. The Model for End-Stage Liver Disease score was similar between the 2 groups (p = 0.7); however, recipients had a significantly higher incidence of hepatocellular carcinoma in the late era than in the early era (15 [39%] v. 8 [25%]) (p = 0.003) (Table 1).

Transplantation outcomes

Biliary complications

The overall incidence of biliary complications during the follow-up period was 27% (19/70). There was a trend toward a higher proportion of biliary complications in the early era than in the late era (12 [38%] v. 7 [18%]) (p = 0.07) (Table 2).

Overall, IC (9 [13%]) and anastomotic stricture (7 [10%]) represented the most common type of biliary complication. The incidence of IC was significantly higher in the early era (8 [25%]) than in the late era (1 [3%]) (p = 0.005), whereas the incidence of anastomotic stricture was similar between the 2 eras (p = 0.9). The IC-free survival rate at 1 and 2 years was 79% in the early era and 98% in the late era (p = 0.01).

All cases of IC occurred within the first 6 months after transplantation (Fig. 1). Retransplantation due to IC was performed in 1 patient in the early-era cohort and no patients in the late-era cohort. The remaining 8 patients with IC were treated successfully with ERCP or percutaneous transhepatic cholangiography. At the time of writing, 6 of the 8 were still alive, and 2 had died due to metastatic hepatocellular carcinoma.

Endoscopic (ERCP) intervention was the most common therapeutic approach for patients with biliary complications (19 [27%]). A greater proportion of patients in the early era than the late era required ERCP (13 [41%] v. 6 [16%]) (p = 0.02). Furthermore, the total number of ERCP procedures was higher in the early era (52, range per patient 1–16) than in the late era (7, range per patient 1–2) (p = 0.008). The total number of stents per patient was significantly higher in the early era (20, range of stent per patient 1–4) than in the late era (6, range of stent per patient 1–2) (p = 0.05).

Graft and patient survival

No significant differences between eras were found in graft or patient survival (Table 2). The median length of follow-up for graft failure was 88 months in the early era and 22 months in the late era. Primary nonfunction developed in 4 grafts (6%) during the study period, with no significant difference between eras (p = 0.9). Of the 4 patients, only 1 underwent retransplantation; the remaining 3 died while waiting for a liver graft. A total of 12 grafts (17%) failed, with a significantly higher proportion of failures in the early era than in the late era (9 [28%] v. 3 [8%])

Table 2. Transplantation outcomes

Variable	No. (%) of recipients*		
	Early era n = 32	Late era n = 38	p value
Biliary complications	12 (38)	7 (18)	0.07
Ischemic cholangiopathy	8 (25)	1 (3)	0.005
Anastomotic stricture	3 (9)	4 (10)	0.9
Bile leak	0 (0)	1 (3)	1.0
Choledocholithiasis	1 (3)	1 (3)	1.0
Management of biliary complications			
ERCP	13 (41)	6 (16)	0.02
Total no. of ERCP procedures (range per patient)	52 (1–16)	7 (1–2)	0.008
No. of patients with stent	9 (28)	4 (10)	0.05
Total no. of stents (range per patient)	20 (1–4)	6 (1–2)	0.05
Length of stay, d, median (IQR)	12 (8–161)	13 (7–115)	0.9
Graft function			
Primary nonfunction	2 (6)	2 (5)	0.9
Graft failure	9 (28)	3 (8)	0.02
Survival			
Graft survival, d, mean ± SD	2778 ± 266	1477 ± 131	0.5
90 d	29 (91)	35 (92)	
1 yr	27 (84)	31 (82)	0.8
3 yr	24 (75)	29 (76)	
Retransplantation	3 (9)	1 (3)	0.2
Patient survival, d, mean ± SD	3016 ± 251	1518 ± 158	0.3
90 d	29 (91)	36 (95)	
1 yr	28 (88)	31 (82)	0.5
3 yr	25 (78)	29 (76)	
Death	8 (25)	9 (24)	1.0

ERCP = endoscopic retrograde cholangiopancreatography; IQR = interquartile range; SD = standard deviation.
*Except where noted otherwise.

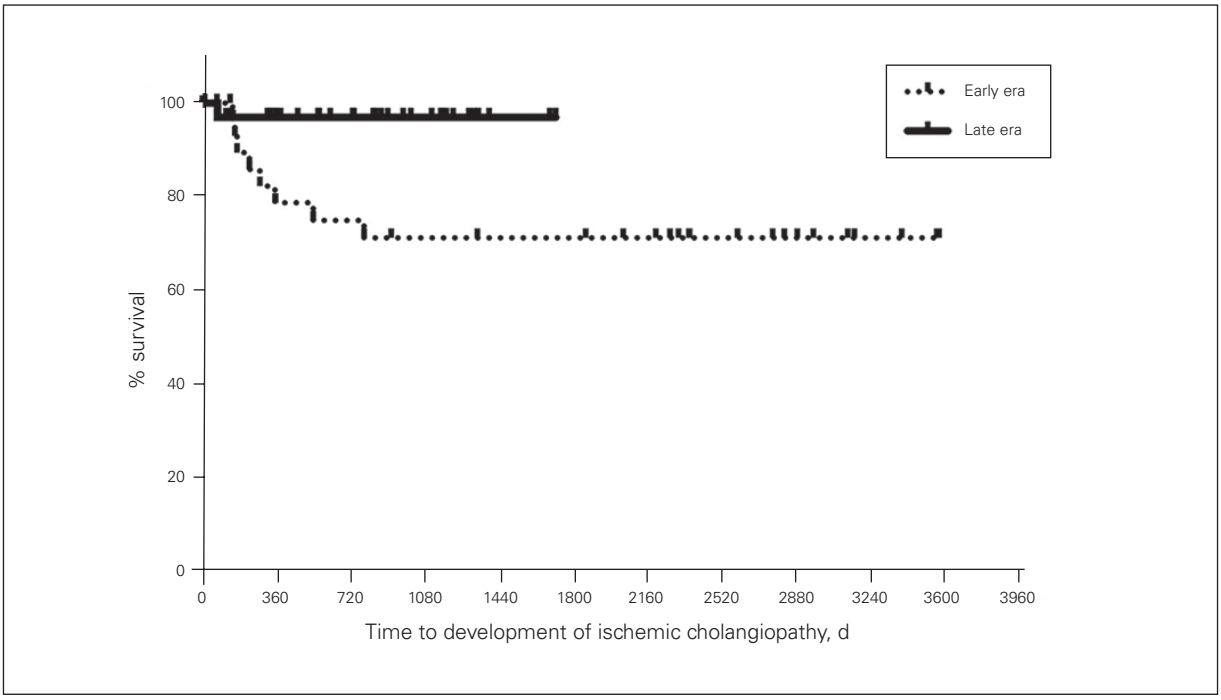

Fig. 1. Rate of survival free of ischemic cholangiopathy (IC) in patients who received liver grafts from donation after cardiocirculatory death donors, July 2006 to July 2016. All cases of IC occurred within the first 6 months after transplantation.

(p = 0.02). Four patients (6%) underwent retransplantation, without a significant difference between eras (p = 0.2): there were 3 cases (9%) (1 case each of primary nonfunction, IC and hepatitis C recurrence) in the early era and 1 case (3%) (hepatitis C recurrence) in the late era (Table 2). Of the 5 remaining patients who did not undergo retransplantation, 2 had sepsis with subsequent multisystem organ failure, and metastatic hepatocellular carcinoma developed in 3.

Discussion

In this study we assessed the learning curve of the pioneer Canadian DCD liver transplantation program in London. Donor and recipient selection characteristics in the late era were significantly more favourable than those in the early era. Consequently, the incidence of IC and overall biliary complications, and the need for ERCP and stenting were significantly reduced in the late era, and the IC-free survival time was significantly improved. These findings suggest that IC rates at centres introducing the DCD technique may be decreased with judicious donor selection and accrual of multidisciplinary transplantation team experience.

DCD liver transplantation has been associated with a higher complication rate than DBD liver transplantation. Reported rates of biliary complications have ranged from 13% to 50%.[2,11,25] According to different reports, the incidence of IC can vary from 4.5% to 16%.[9,11,12,14,26,27] Therefore, multiple strategies have been implemented to improve outcomes and reduce biliary complication rates. These strategies include using thrombolytic therapy based on the hypothesis that thrombolysis will break down the microthrombi forming in the peribiliary vascular capillary plexus during DCD procurement. Although different groups have shown promising results with this practice,[28,29] recent evidence from a group in the Netherlands shows no reduction in nonanastomotic biliary strictures from the use of urokinase before liver transplantation.[30] We believe that the low rates of IC attributed to thrombolytic therapy are actually due to the multifactorial effect of accumulating experience with DCD liver transplantation (i.e., proper donor/recipient selection and shorter ischemic times). In our DCD liver transplantation protocol, we do not use thrombolytic therapy.

Endoscopic interventions are the most common therapeutic strategy for biliary complications, and the need for repeated interventions in patients with severe complications, such as IC, are associated with increased cost, prolonged hospital stays, and hospital readmission for diagnostic and therapeutic measures.[11,25,31,32]

We have previously hypothesized that judicious donor selection and cumulative transplantation team experience would have a positive impact on IC rates.[17] Limited investigation has not shown a correlation between experience and improved outcomes for DCD liver transplantation.[11] However, we believed that improvements in procurement and implantation times would mitigate ischemic injury and prevent development of complications such as IC. To assess the learning curve of our DCD liver transplantation

program, we used donor and recipient selection and procurement times as proxy measures for evidence of learning, which is supported by other studies.[4,11,14,25,26,32,33]

Assessment of graft survival and biliary complications in DCD liver transplantation has shown that donor age, donor WIT greater than 30 minutes and CIT greater than 10 hours are highly predictive of poor graft outcomes compared to DBD liver transplantation.[4,14,25,30] In our present series, compared to patients in the early era, those in the late era had a significantly shorter time to cannulation and flush, lower WIT and a trend toward decreased CIT. These improvements likely explain the significant reductions in biliary complication rates achieved in the late era.

Devising preventive strategies is crucial to encourage greater use of DCD grafts. The American Society of Transplant Surgeons published its support toward procurement and transplantation of DCD organs, recommending different strategies and protocols to improve the use of these grafts.[34] In our experience, adequate resources, improved knowledge, understanding of the DCD surgical technique and proper multidisciplinary team organization were fundamental for our achievements.

A learning curve can be defined as an improvement in performance over time or with increasing experience or training.[35] Outcome measures used to depict learning curves are mostly proxy measures and include time to completion of a task, increasing experience by volume of procedures, decreasing rate of complications and proportion of satisfactory results.[35] The proportion of biliary complications decreased after we reached 30 DCD liver transplantation procedures. This might represent the beginning of the expertise point of the learning curve in DCD liver transplantation owing to improvement in the donor procurement technique (faster cannulation) but also to better donor and recipient selection criteria for DCD organs.

The lower rate of IC observed in the late era of our study was associated with significantly decreased use of ERCP and therapeutic stents. Reducing the number of preventable interventions and hospital readmissions, and minimizing the risk of intervention-related patient complications shows how improvements in specific outcomes following DCD liver transplantation may have an impact on hospital resources and cost.

Although our graft and patient survival rates were not as high as with DBD grafts, our results were acceptable. Moreover, waiting list mortality decreased, proving the use of DCD grafts as an option for liver transplantation.

Important recommendations arise from this study. During the development of a DCD liver transplantation program, a learning curve can account for early inferior results. However, as experience accumulates, shorter procurement ischemia times, improved organ procurement technique, and meticulous donor and recipient selection may enable superior transplantation outcomes and wider acceptance of DCD liver transplantation. Thus, recruitment of staff with prior experience in DCD organ procurement may benefit new DCD programs with the goal of minimizing initially poorer transplantation outcomes. In the current series, fewer cases of IC and biliary complications occurred in the late era, in which significantly more local donors were procured. Therefore, avoiding external factors that can prolong WIT and CIT is important. In addition, through meticulous donor and recipient selection, refinements in the DCD procurement technique may yield better transplantation outcomes. In our practice, contrary to the traditional DCD liver transplantation procurement technique, we ensure drainage of the inferior vena cava to remove static blood from the liver and then flush the aorta, divide the bile duct and irrigate the gallbladder in the initial stage of procurement. This is aimed at rapidly flushing out toxins to reduce toxic hepatic effects. Thus, making improvements in factors that can be controlled by the transplantation team, including donor and recipient selection, surgical technique and minimization of ischemia times, may result in better DCD outcomes and an overall reduction in adverse outcomes.

Advancements of the near future will likely involve developing and improving present technology and pharmacological innovations that can reduce, restore or revert the consequences of ischemic reperfusion. Ongoing research is focused on the development and use of perfusion machines, not only in restoring hepatobiliary function and mitochondrial oxygenation but also in reducing or repairing a preexisting hepatobiliary injury sustained during procurement. Moreover, the information provided by machine perfusion provides the opportunity of identifying and testing DCD livers at risk for failure or future complications.

Limitations

Some limitations arise as a result of the study design. The retrospective nature and the sample size limited the analysis. Furthermore, although the observed results are attributed to the transplantation team's progression along a learning curve, other, unmeasured factors may have played a role.

Conclusion

Experience with DCD liver transplantation over a 10-year period at our institution has resulted in lower rates of IC, associated with better donor selection and improvement in procurement ischemia times in the late era. This suggests that a learning curve exists for DCD liver transplantation.

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