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Controlled donation after circulatory death up to 80 years for liver transplantation: Pushing the limit again

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Our main objective was to compare liver transplant (LT) results between donation after circulatory death (DCD) and donation after brainstem death (DBD) in our hospital and to analyze, within the DCD group, the influence of age on the results obtained with DCD donors aged >70 years and up to 80 years. All DCD-LTs performed were analyzed prospectively. The results of the DCD group were compared with those of a control group who received a DBD-LT immediately after each DCD-LT. Later, the results obtained within the DCD group were analyzed according to the age of the donors, considering 2 subgroups with a cut-off point at 70 years. Survival results for LT with DCD and super rapid recovery were not inferior to those obtained in a similar group of patients transplanted with DBD livers. However, the cost of DCD was a higher rate of biliary complications, including ischemic cholangiopathy. Donor age was not a negative factor.

KEYWORDS

clinical research/practice, donors and donation, donors and donation: deceased, donors and donation: donation after brain death (DBD), donors and donation: donation after circulatory death (DCD), donors and donation: extended criteria, health services and outcomes research, liver transplantation/hepatology, organ procurement and allocation, organ transplantation in general

1 | INTRODUCTION

Liver transplant (LT) currently represents the treatment of choice in the terminal stage of certain liver diseases and is the best treatment option for hepatocellular carcinoma (HCC) associated with liver cirrhosis.[1] Although the demand for LT is growing,[2] the use of livers from donation after brain death (DBD) donors with advanced age and the proliferation of donation after circulatory death (DCD) donors have increased the availability of organs for LT, especially in the case of DCD after the implementation of the changes in legislation made in Spain in 2012.[3-5] DCD donors, who usually have devastating and irreversible cerebral pathology but without reaching brain

Abbreviations: ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; CIT, cold ischemic time; DBD, donation after brainstem death; DCD, donation after circulatory death; fWIT, functional warm ischemic time; GGT, γ-glutamyltransferase; HAT, hepatic artery thrombosis; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; ICU, intensive care unit; LT, liver transplant; MELD, Model for End-stage Liver Disease; NRP, normothermic regional perfusion; OS, overall survival; Re-LT, retransplant; SRR, super rapid recovery; TBI, traumatic brain injury; tWIT, total warm ischemic time; WIT, warm ischemic time.

death criteria, are kept on mechanical ventilation under hemodynamic stability until treatment withdrawal in the operating room and the procurement of organs for transplant. In Spain, the use of DCD represents around one third of the total LTs performed during the past 5 years.

The main problem with DCD is determined by the warm ischemia time (WIT) until organ perfusion is performed. During this time, there is damage to the potential graft, especially to its biliary system, which is highly vulnerable to ischemia. This justifies the appearance of higher rates of primary graft dysfunction and biliary complications, such as ischemic cholangiopathy. These disadvantages were reported at the onset of controlled-DCD programs along with worse graft and patient survival rates.[6,7] Currently, the results can be comparable to those obtained with DBD,[8] but the percentage of potential grafts rejected during the evaluation and extraction process can reach 30% to 40% of the total potential donors evaluated. The most frequent cause of rejection of a DCD graft is the presence of a poor macroscopic aspect at recovery.[9] The best results in LT with DCD have been described from young donors (<50 years), with short total WITs (tWIT, <30 minutes) and limited durations of cold ischemia (CIT, <5 hours). The results were worse in recipients >60 to 65 years of age, with fulminant liver failure, retransplant (re-LT), or dialysis,[10] conditions for which the Spanish National Transplant Organization, in its consensus document, does not recommend the use of DCD.[11,12]

Experience with the use of DCD donors aged > 70 years and up to 80 years is limited. Although in DBD age is no longer a limiting factor when no other risk factors coexist,[13-15] in DCD many groups confine donor selection to those younger than 60 years.[2,16,17] In Spain, an upper donor age limit of 65 years has been proposed for DCD donation, albeit in a flexible manner; this limit is subjected to individual assessment and to the experience accumulated by the different LT groups.

The aim of this work is to compare the LT results between DCD and DBD in our hospital and to analyze, within the DCD group, the influence of age on the results obtained with DCD donors aged > 70 years and up to 80 years.

2 | MATERIALS AND METHODS

All LTs performed with DCD (type III of the Maastricht classification) in the period between November 2014 and December 2018 were analyzed prospectively. In accordance with the recommendations of the Spanish National Transplant Organization,[11] Re-LT, and combined liver-kidney transplants were excluded. The results of the DCD group were compared with those of a control group of patients who received a DBD-LT immediately after each DCD transplant. Later, the results obtained within the DCD group were analyzed according to the age of the donors, considering 2 subgroups with a cut-off point at 70 years.

Our policy of using DCD grafts from very old donors (>70 years) is justified by the pressure on our waiting list: from 2013 to 2015, the mortality rate for patients on the waiting list was 18%. As a result, after this period, DCD donors aged >70 years were not systematically rejected. The second reason derives from our experience with donation and LT with DBD donor of an extreme age, the results of which have been previously communicated.[18] Our group prioritizes HCC recipients with donors of this suboptimal type. In these patients, the conventional Model for End-Stage Liver Disease (MELD) allocation system of the waiting list can lead to very long periods with a potential risk of tumor progression that would limit the options for a potentially curative treatment.[19]

All grafts were obtained using the super rapid recovery (SRR) technique[20] by 2 liver surgeons with >15 years of experience in donor surgery. After the treatment withdrawal and subsequent cardiac arrest, the team waited for 5 minutes without performing any maneuver. After this non-touch period, the surgery began with a wide laparotomy, cannulation, and perfusion with the preservation solution (Celsior™) both through the common aorta or iliac artery and through the portal vein. According to Spanish standards,[11] fWIT starts from a mean arterial pressure of 60 mm Hg (Figure S1).

In all cases, a sample was taken for intraoperative biopsy after the onset of perfusion, and those grafts with a steatosis >30% and/or with fibrosis >1 were considered invalid. The grade of graft fibrosis was analyzed with aniline blue/chromotrope 2R staining and macrovesicular steatosis was analyzed with Sudan III-IV staining.

Ischemic cholangiopathy was defined as symptomatic intrahepatic or nonanastomotic and extrahepatic biliary strictures associated with dilatation of the intrahepatic or hilar bile duct in the absence of hepatic artery thrombosis or stenosis. Ischemic cholangiopathy was suspected in patients with symptoms of jaundice, fever, or abdominal pain and/or an abnormal liver function test, such as elevated serum GGT and alkaline phosphatase (ALP). In these cases, diagnosis was confirmed by magnetic resonance cholangiopancreatography or endoscopic retrograde cholangiopancreatography. In asymptomatic patients, ultrasound and blood liver function tests were carried out every 3 months for the first 12 months and every 6 months after the first year post-LT.

2.1 | Statistical analysis

In the data analysis, the following donor variables were taken into consideration: age, sex, cause of death, length of stay in the intensive care unit (ICU), use for vasoactive drugs before and during organ procurement, and analytical values for aspartate transaminase (AST), alanine transaminase (ALT), total bilirubin, γ-glutamyl transferase (GGT), prothrombin activity, and plasma sodium levels. Surgical outcomes in the recipient included CIT, WIT, type and amount of blood derivatives transfused, duration of surgical procedure, age, sex, body mass index, LT indication, Child-Turcotte-Pugh (CTP) and MELD scores, waiting list time, and the postoperative analytical outcomes (at 24 hours and at discharge) for ALT, AST, alkaline phosphatase (ALP), GGT, total bilirubin, and prothrombin activity. The appearance of adverse events such as graft dysfunction and the need for prostaglandins during their stay in the ICU, the appearance of arterial and biliary complications,

the appearance of rejection, and the need for immediate re-LT were also recorded. The parameters of graft and recipient survival at 1, 2, and 3 years were calculated. In the DCD group, the tWIT and fWIT were taken into account (Figure S2).

The qualitative variables were analyzed by the chi-squared test and the quantitative ones by Student's *t* test and/or Kruskal-Wallis test. Differences were considered statistically significant at $P < .05$. Graft and patient survival were analyzed by Kaplan-Meier curves with log-rank and Breslow analysis. The calculations were performed using a statistical package program (IBM SPSS Statistics v24).

3 | RESULTS

3.1 | DBD versus DCD

Between November 2014 and December 2018, a total of 77 LTs were performed with grafts from DCD. The characteristics of donors and recipients of both groups are shown in Tables 1 and 2. No statistically significant differences in age, BMI, sex, or the presence of comorbidities between donors were observed. The mean BMI was 25.6 (range 16.5 to 33) kg/m^2 in the DCD group and 25.4 (range 18.3 to 33) kg/m^2 in the DBD group. The main indication for LT was HCC, which was more frequent in the DCD group, although the difference did not reach statistical significance but was reflected in the value of the MELD scores, which were significantly lower in the DCD group. CITs were significantly lower in the DCD group (5.4 vs 6.7 hours, $P = .002$). After LT, the AST/ALT peak values were higher in the DCD determination group at 24 hours post-LT, although the difference was not statistically significant.

In terms of post-LT complications (Table 3), there were no differences in the rates of primary graft dysfunction (1.3% DCD vs 2.6% DBD, $P = .560$), hepatic artery thrombosis (HAT), or early re-LT (first 7 post-LT days) between the 2 groups (7.8% DCD vs 9.1% DBD, $P = .772$). Regarding global biliary complications, despite higher percentages in the DCD group, there were no statistically significant differences between the 2 groups. Requirement for early re-LT was always because of HAT, and late re-LT requirement was due to 1 of the following: ischemic cholangiopathy (2 in the DCD group and 1 in the DBD group), portal vein thrombosis (1 in the DCD group), hepatic veins thrombosis (1 in the DCD group), and fulminant hepatic failure due to hepatitis B virus (HBV) in 1 patient of the DCD group.

Of the 5 patients with ischemic cholangiopathy in the DCD group, 2 were treated with re-LT (at 4 and 6 months after the first LT), 2 are currently awaiting re-LT, and the fifth patient died of biliary sepsis. The incidence of ischemic cholangiopathy was lower, although not statistically significantly, in the group of DBD patients, where only 1 case of ischemic cholangiopathy was identified ($P = .209$). In none of these 5 patients with ischemic cholangiopathy was concomitant arterial thrombosis found.

No patients were lost to follow-up. After a median follow-up of 15 months, graft and patient overall survival (OS) at 1 year were similar between DCD and DBD (graft: 72.7% vs 78.5%, $P = .226$; patient: 78.6% vs 85%, $P = .244$, respectively) (Figure 1).

3.2 | DCD ≥ 70 years versus DCD < 70 years

In this analysis, 45 DCD donors aged <70 years, and the remaining 32 donors were aged ≥70 years. The characteristics of donors and recipients in both groups are shown in Tables 4 and 5. When specifically analyzing DCD with a cut-off point of 70 years, no significant differences were found in the profiles of donors and recipients (except for age), post-LT blood test, ICU stays, and post-LT hospital stays. This group of 32 DCD donors >70 years was compared with the group formed by DCD donors <70 years old of the same study period (n = 45). The mean CIT, fWIT, and tWIT values were similar in both groups, as well as the use of vasoactive drugs and the mean length of ICU stay.

In terms of post-LT complications (Table 6), there were no statistically significant differences between DCD donors >70 years

TABLE 1 Donor characteristics: DBD versus DCD

Variable	DCD, n = 77	DBD, n = 77	*P*
Age (y)	65.3 (22-79)	68.4 (29-92)	.778
Sex (male/female) (%)	61/39	55.8/44.2	.513
BMI (kg/m^2)	25.6 (16.5-33)	25.4 (18.3-33)	.542
Cause of death, n (%)			
Stroke	37 (48)	55 (71)	**.000**
TBI	5 (6.5)	12 (16)	
Others	35 (44)	10 (13)	
Stay in the ICU (h)[a]	169.3 ± 143.4	57 ± 68.5	**.000**
Use of vasoactive drugs (%)	33	86	**.000**
Blood test parameters[a]			
Plasmatic sodium (mmol/L)	141.7 ± 5.9	143.3 ± 8.9	**.000**
AST (U/L)	66.7 ± 193.6	40.3 ± 37.1	.535
ALT (U/L)	63.1 ± 137.8	26.8 ± 28.6	.401
QUICK (%)	79.8 ± 15.6	77.1 ± 8.9	.609
Donor biopsy			
Steatosis (%)	—	—	.053
No	61.6	52.6	
<5%	23.3	13.2	
5% to 30%	15.1	34.2	
Fibrosis F1 (%)	10.7	2.6	.135
Functional warm ischemia time (min)	12.6 ± 5.2	—	N/A
Total warm ischemia time (min)	18.9 ± 7.4	—	N/A
Cold ischemia time (h)	5.4 ± 1.8	6.7 ± 3.1	**.002**

Statistically significant variables ($P < .05$) are bold.
ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; DBD, donation after brainstem death; DCD, donation after circulatory death; ICU, intensive care unit; Quick, prothrombin activity; TBI, traumatic brain injury.
[a]Mean ± SE.

TABLE 2 Recipient characteristics: DBD versus DCD

Variable	DCD, n = 77	DBD, n = 77	*P*
Age (y)	58 (36-73)	58.1 (25-74)	.126
Sex (M/F) (%)	86/14	71/29	**.031**
BMI (kg/m^2)	27.5 (19.7-35.3)	28.6 (19-33)	.539
Indication for LT, n (%)			.394
HCC	36 (47)	27 (35)	—
HCV positive	18 (23)	11 (14)	—
Alcohol	20 (26)	20 (26)	—
HCV positive without HCC	3 (4)	8 (10)	—
Emergencies	5 (6)	5 (6)	—
Others	13 (17)	17 (22)	—
Child-Pugh (%)			
A	32.2	25	.692
B	57.1	61.5	
C	10.7	13.5	
Laboratory MELD (mean)	11.7	13	.027
Hemoderivatives			
Red blood cells (units)	4.5 ± 5.2	4.6 ± 2.2	.686
Fresh frozen plasma (units)	1.9 ± 3.1	1.2 ± 1.8	.151
Platelets (units)	1.2 ± 1.5	1.2 ± 1	.376
Post-LT blood test (24 h)[a]			
AST (U/L)	975.6 ± 869.9	559.8 ± 478.6	.314
ALT (U/L)	675.8 ± 487.6	445.8 ± 314.2	.277
Quick (%)	57.2 ± 13	59.9 ± 18.5	.564
Post-LT blood test (1 wk)[a]			
AST (U/L)	60.1 ± 42.7	101.1 ± 337.8	.777
ALT (U/L)	176.7 ± 107.7	166.9 ± 252.3	.777
Quick (%)	74.8 ± 11.1	80.3 ± 11.5	.112
ICU length of stay (d)[a]	3.7 ± 2.5	3.6 ± 2	.537
Length of hospital stay (d)[a]	29.4 ± 35.8	28 ± 19.7	.576
Post-LT blood test (6 mo)[a]			
AST (U/L)	21 ± 2.8	37.5 ± 30.4	.525
ALT (U/L)	29.5 ± 17.7	31 ± 21.2	.946
GGT (U/L)	38 ± 9.9	32 ± 25.4	.785
ALP (U/L)	75.5 ± 13.4	243 ± 302.6	.516
Total bilirubin (mg/dL)	0.28 ± 0.1	0.61 ± 0.36	.337
Post-LT blood test (12 mo)[a]			
AST (U/L)	21.5 ± 6.5	35 ± 22.6	.492
ALT (U/L)	23.5 ± 12	50 ± 49.5	.538
GGT (U/L)	56 ± 42.4	34.5 ± 31.8	.624
ALP (U/L)	107.5 ± 37.5	89 ± 73.5	.781
Total bilirubin (mg/dL)	0.38 ± 0.1	0.43 ± 0.1	.706

Statistically significant variables ($P < .05$) are bold.
ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; DCD, donation after circulatory death; DBD, donation after brainstem death; GGT, χ-glutamyl transferase; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; MELD, Model for End-Stage Liver Disease; ICU, intensive care unit; LT, liver transplant; Quick, prothrombin activity.
[a]Mean ± SE.

and DBD donors >70 years in terms of primary graft dysfunction, HAT, ischemic cholangiopathy, biliary complications, and the rate of re-LT. Graft and patient OSs were similar between the 2 groups (Figure 2).

4 | DISCUSSION

DCD-LT outcomes were similar to DBD-LT at our hospital. This has made it possible to increase the availability of donors for LT in recent years and, in our experience specifically, has meant an increase of

TABLE 3 Complications in the immediate postoperative period and during follow-up in patients in this study: DBD versus DCD

Variable	DCD, n = 77	DBD, n = 77	*P*
Immediate post-LT complications, n (%)			
Primary graft dysfunction	1 (1)	2 (3)	.560
Acute rejection	6 (8)	7 (9)	.772
Early retransplant (hepatic artery thrombosis)	3 (4)	4 (5)	.699
Biliary complications	7 (9)	3 (4)	.421
Biliary leakage	2 (3)	1 (1)	
Biliary peritonitis (retrieval of T-tube)	5 (6)	2 (3)	
Late-onset post-LT complications, n (%)			.316
Ischemic cholangiopathy	5 (6)	1 (1)	.209
Biliary stricture	17 (22)	12 (16)	.205
HCV recurrence	1 (1)	1 (1)	1
Retransplant (causes)	5 (6)	1 (1)	.209
Ischemic cholangiopathy	2 (3)	1 (1)	
Portal vein thrombosis	1 (1)	0	
Hepatic vein thrombosis	1 (1)	0	
ALF by HBV	1 (1)	0	
Chronic rejection	1 (1)	0	.316

ALF, acute liver failure; DBD, donation after brainstem death; DCD, donation after circulatory death; HBV, hepatitis B virus; LT, liver transplant.

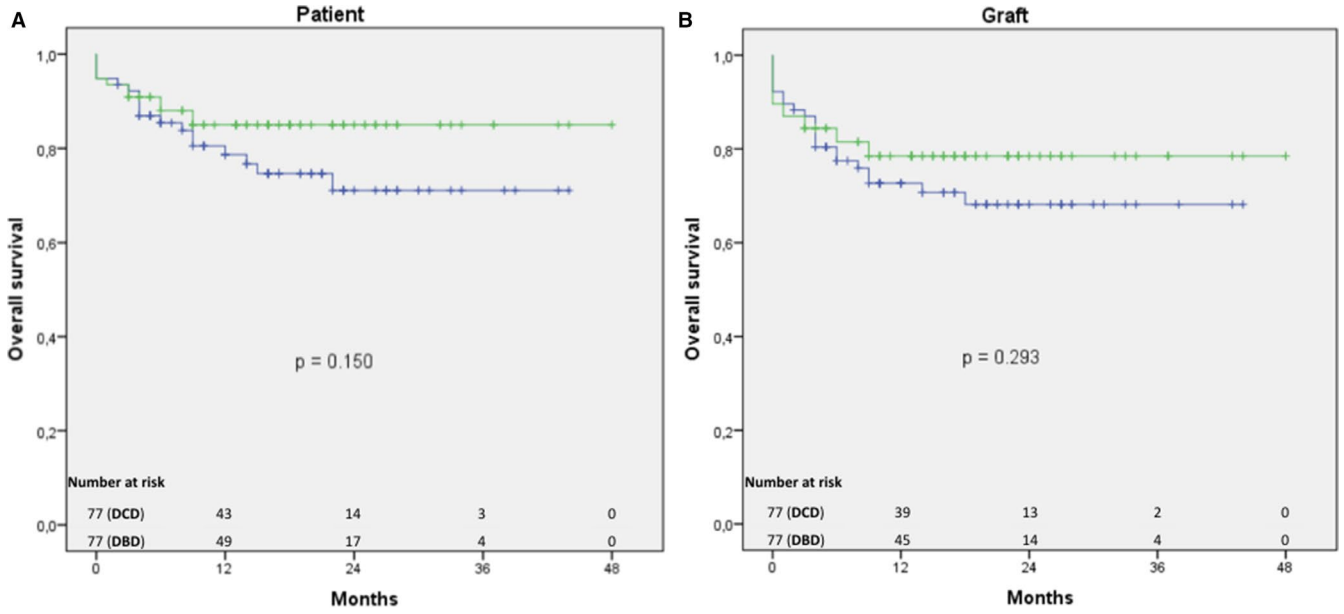

FIGURE 1 Patient (A) and graft (B) survival after liver transplant. DBD (green) versus DCD (blue). DBD, donation after brainstem death; DCD, donation after circulatory death [Color figure can be viewed at wileyonlinelibrary.com]

30% in the total number of annual transplants performed since the beginning of the program, which allowed us to reduce our waiting list mortality from 18% in 2013-2015 to 9% in 2018.[3-5,21] A recent meta-analysis confirmed the main limitation of this type of donors: the development of a higher rate of biliary complications in relation to preservation failures, a consequence of biliary damage during the period of warm ischemia. Because of preservation problems, a higher prevalence of primary graft dysfunction has also been described. Although this complication was not present in our study, we found worse ALT/AST values at 24 hours and 7 days after LT in the DCD group, a manifestation of the damage produced during the period of warm ischemia.

The mechanisms of production of this ischemic cholangiopathy are not well established. It seems that direct injury of the biliary epithelium derived from warm and cold ischemia is not as important as injury of the peribiliary structures, especially small arterioles, which, along with the release of reactive oxygen species and low levels of endogenous antioxidants after reperfusion, would lead to the damage that appears a few months after transplant. A characteristic situation of clinical and analytical cholestasis occurs in the absence of biliary stricture of the anastomosis and/or HAT. Typically, in magnetic resonance cholangiopancreatography, irregular and sometimes multisegmental stenosis of the proximal biliary tree can be observed, with typical involvement of the bifurcation of the right and left bile ducts.[22-24]

In some patients, there may be a subclinical form of ischemic cholangiopathy in which they will not present such derived complications, and they will live a normal life.[25] Once it has been established, ischemic cholangiopathy is not reversible.[26]

In our findings, the occurrence of ischemic cholangiopathy was significantly higher in the DCD group (6%) than in the DBD group (1%). Globally, the rate of biliary complications in the DCD group was 37%.[27] In a meta-analysis by O'Neill et al,[6] the estimated rates of biliary complications and ischemic cholangiopathy were 26% and 16% in LT with DCD. Our WITs are short compared with those of other groups, which could be one of the reasons for the low incidence of ischemic cholangiopathy in the DCD group. In our work, all types of bile complications were recorded, including those that did not require invasive treatment for their resolution, such as self-limited bile leakage.

An alternative technique in the process of obtaining the graft in DCD donors is the preservation of the hepatic graft by normothermic regional perfusion (NRP). Continuous perfusion allows the organ to be maintained under homeostatic conditions and allows in situ analytical tests such as the determination of transaminases and acid-base balance (lactate) in the perfusion circuit. These determinations make it possible to evaluate the functionality of the graft beyond the macroscopic aspect of the organ. There are no clinical trials demonstrating the superiority of NRP over the SRR technique.

Recently, findings of the British experience comparing NRP versus SRR results have been published.[28] In the nonrandomized retrospective analysis, NRP was performed only when qualified personnel were available. Of a total of 230 DCD-LTs (43 with NRP), they showed the superiority of NRP over SRR in terms of ischemic cholangiopathy (0% vs 27%), early allograft dysfunction (12% vs 32%), and the rate of anastomotic bile duct stricture (7% vs 27%).

The initial findings of the Spanish experience published by Hessheimer et al[9] showed an improvement in NRP results to the detriment of SRR, although these findings may reflect an initial experience that, in SRR, could be corrected with time and accumulated experience. The premortem cannulation of DCD donors,

TABLE 4 Donor characteristics: DCD > 70 y versus DCD < 70 y

Variable	DCD > 70, n = 32	DCD < 70, n = 45	*P*
Age (y)	73.7 (70-79)	56.7 (22-69)	**.000**
Sex (male/female)	56.3/43.8	64.4/35.6	.616
BMI (kg/m^2)	25.6 (16.5-33)	26 (23.3-32.6)	
Cause of death, n (%)			
Stroke	17 (53)	20 (44)	.749
TBI	2 (6)	3 (7)	
Others	13 (41)	22 (49)	
Stay in the ICU (h)[a]	136.5 ± 130.1	187.8 ± 146.1	.124
Use of vasoactive drugs (%)	28	37	.409
Blood test parameters[a]			
Plasmatic sodium (mmol/L)	142.4 ± 6.7	141.5 ± 6	.517
AST (U/L)	44.8 ± 47.6	74.8 ± 214.7	.441
ALT (U/L)	43.1 ± 57.9	69.6 ± 151	.351
Quick (%)	80.6 ± 16.0	79.3 ± 15.3	.718
Donor biopsy			
Steatosis (%)	—	—	882
No	64	59.5	
<5%	23	23.8	
5% to 30%	13	16.7	
Fibrosis F1 (%)	12	9.7	.780
Functional warm ischemia time (min)	12.7 ± 4.7	12.5 ± 5.6	.880
Total warm ischemia time (min)	19.0 ± 5.6	18.9 ± 8.6	.982
Cold ischemia time (min)	5.0 ± 1.8	5.7 ± 1.8	.106

Statistically significant variables ($P < .05$) are bold.
ALT, alanine transaminase; AST, aspartate transaminase; DBD, donation after brainstem death; DCD, donation after circulatory death; ICU, intensive care unit; Quick, prothrombin activity.
[a]Mean ± SE.

TABLE 5 Recipient characteristics: DCD > 70 y versus DCD < 70 y

Variable	DCD > 70 y, n = 32	DCD < 70 y, n = 45	*P*
Age (y)	59.7 (38-72)	57.2 (36-73)	.156
Sex (male/female) (%)	91/9	82/18	.299
BMI (kg/m^2)	27.5 (20.1-34)	28 (19.6-36.4)	.588
Indication for LT, n (%)			.931
HCC	15 (47)	21 (47)	—
HCV positive	8 (25)	10 (22)	—
Alcohol	8 (25)	12 (27)	—
HCV positive without HCC	1 (3)	2 (4)	—
Emergencies	3 (9)	2 (4)	—
Others	5 (16)	8 (18)	—
Child (%)			
A	10 (33)	31.3	.882
B	18 (60)	56.3	
C	4 (8)	12.4	
Laboratory MELD (points)[a]	11.6 ± 3.7	11.6 ± 3.8	.980
Hemoderivatives			
Red blood cells (units)	4.1 ± 3.7	5.2 ± 5.9	.367
Fresh frozen plasma (units)	1.8 ± 2.3	2.3 ± 3.5	.494
Platelets (units)	0.8 ± 1	1.2 ± 1.6	.980
Post-LT blood test (24 h)[a]			
AST (U/L)	934.4 ± 871.4	1674 ± 2942.8	.180
ALT (U/L)	641.3 ± 485.3	1141.7 ± 1882.3	.154
Quick (%)	54.0 ± 12.1	56.5 ± 14.6	.436
Post-LT blood test (1 wk)[a]			
AST (U/L)	107.7 ± 262.0	57.4 ± 39.6	.240
ALT (U/L)	200.3 ± 205.7	179.3 ± 102.6	.580
Quick (%)	73.4 ± 13.6	77.4 ± 13.4	.216
ICU length of stay (d)[a]	4.0 ± 2.0	3.9 ± 2.8	.874
Length of hospital stay (d)[a]	25.9 ± 16.8	31.4 ± 41.1	.499

ALT, alanine transaminase; ALP, alkaline phosphatase; AST, aspartate transaminase; BMI, body mass index; DBD, donation after brainstem death; DCD, donation after circulatory death; GGT, γ-glutamyl transferase; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; ICU, intensive care unit; LT, liver transplant; Quick, prothrombin activity; MELD, Model for End-Stage Liver Disease.
[a]Mean ± SE.

allowed by law in our country, can be a way of enhancing the results, as it would shorten the time of warm ischemia from the beginning of surgical procedures to cannulation and perfusion. Although this method is currently being implemented in our center, it will not be able to answer the question of whether SRR or NRP is the best option for DCD.

The use of older DCD for LT is another question at issue in DCD.[29,30] In DBD, age is no longer a criterion for rejecting grafts for LT, especially when other poor prognostic factors do not coexist. Schlegel et al[31] proposed modifying the age cut-off for these DCD donors, reporting comparable results in donors older than 60 years (and up to a limit of 71 years). Other authors[17,32] have also reported good results with DCD older than 70 years. The fact that, in our hospital, mortality rates among patients awaiting LT were around 18% in 2013-2015 led us to consider these elderly DCD, giving preference to patients with HCC. The prioritization of HCC patients with suboptimal grafts makes it possible to shorten waiting times and avoid the feared tumor progression that would contraindicate the only possibility of long-term survival of these patients, who, on the other

TABLE 6 Complications in the immediate postoperative period and during follow-up in patients in this study: DCD > 70 y versus DCD < 70 y

Variable	DCD > 70 y, n = 32	DCD < 70 y, n = 45	*P*
Immediate post-LT complications, n (%)			
Primary graft dysfunction	0	1 (1)	.313
Acute rejection	1 (3)	5 (11)	.554
Early retransplant (hepatic artery thrombosis)	2 (6)	1 (2)	.554
Biliary complications	2 (6)	5 (11)	.554
Biliary leakage	0	2 (4)	
Biliary peritonitis (retrieval of T-tube)	2 (6)	3 (7)	
Late onset post-LT complications, n (%)			
Ischemic cholangiopathy	1 (3)	4 (9)	.395
Biliary stricture	8 (25)	9 (20)	.781
HCV recurrence	1 (3)	0	.416
Retransplant (causes)	1 (3)	4 (9)	.395
Ischemic cholangiopathy	0	2 (4)	
Portal vein thrombosis	0	1 (2)	
Hepatic veins thrombosis	1 (3)	0	
ALF by HBV	0	1 (2)	
Chronic rejection	1 (3)	0	.416

ALF, acute liver failure; DBD, donation after brainstem death; DCD, donation after circulatory death; HCV, hepatitis C virus; LT, liver transplant.

hand, with a lower MELD score and an adequate functional status, can better tolerate a suboptimal graft.[19]

The reduction of other unfavorable factors such as CIT should also be an objective to reduce the deterioration of the graft. Our group has been especially sensitive in the case of DCD, as shown in the results, with significantly lower CIT compared with DBD. Currently, our group does not consider age as a contraindication of DCD. In fact, up to 42% of DCD donors are older than 70 years, and the results in terms of biliary complications and graft and patient survival were not different based on this setting. In the present series, the results are similar to those described in the literature,[6,33] with rates of re-LT and mortality not significantly worse than DBD LT recipients, so these results could be considered acceptable and thus optimize waiting list times.[31] The cost of using older DCD was not high. The graft and patient survival rates did not differ, and no higher price was paid in terms of biliary complications. In fact, only one of the 5 ischemic cholangiopathies detected in the DCD group occurred in the older subgroup. For all these reasons, at present in our center, we have set the age limit for DCD donation at 80 years.

Our work has a number of limitations. The most important is its retrospective nature and the inclusion of a non-randomized control group. This problem is difficult to solve because the availability of organs for transplant makes this type of study difficult; therefore, in the design, we decided to consider every DCD-LT chronologically and the DBD-LT performed immediately after. Another important limitation of our work is the short follow-up duration, especially that of DCD donors older than 70 years. However, the database was closed for analysis 9 months after the last patient was included, enough time to detect functional problems of the graft and ischemic biliary complications.

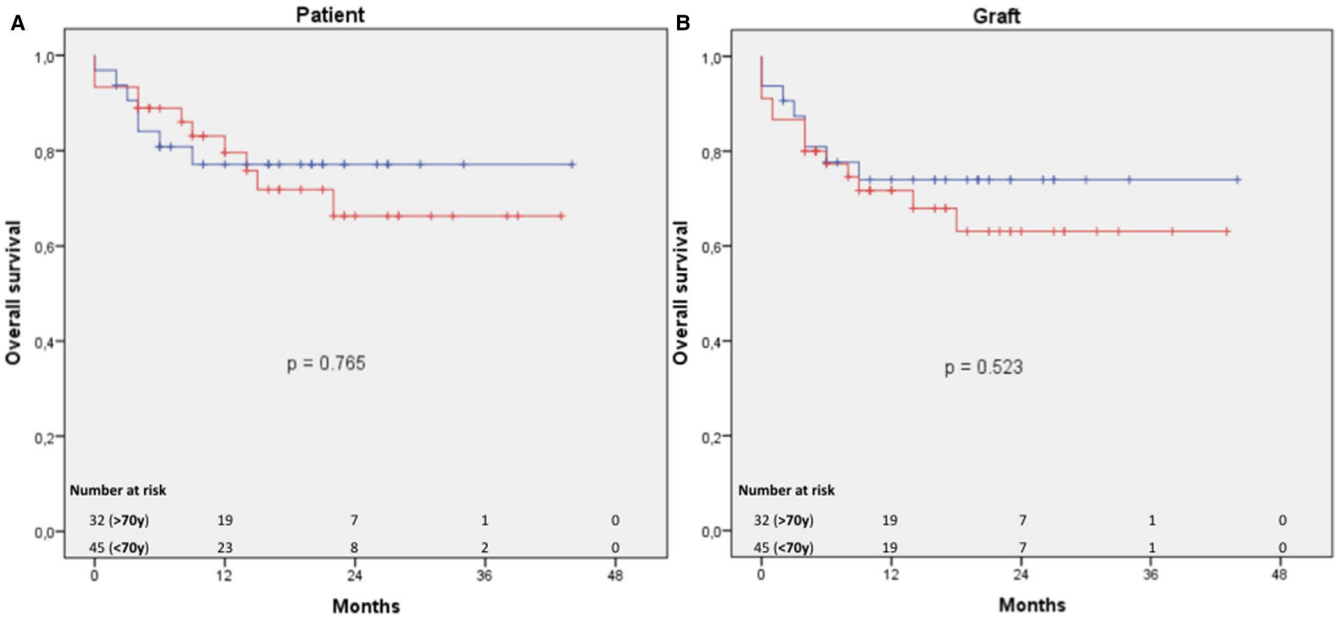

FIGURE 2 Patient (A) and graft (B) survival after liver transplant. DCD > 70 y (blue) versus DCD < 70 y (red). DBD, donation after brainstem death; DCD, donation after circulatory death [Color figure can be viewed at wileyonlinelibrary.com]

5 | CONCLUSION

Survival results for LT with DCD grafts obtained with SRR were not inferior to those obtained in a similar group of patients transplanted with DBD grafts. However, the price of DCD was a higher rate of biliary complications, including ischemic cholangiopathy, as widely described in this type of donor.[34] Age was not a negative factor and, as with the DBD, it is not likely to be an exclusion criterion as we gain more experience. The question of whether the results are better with NRP or SRR awaits further investigation.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author, Dr Alconchel.

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