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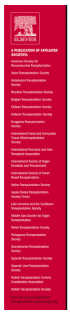

TRANSPLANTATION PROCEEDINGS

Liver Transplant from Controlled Cardiac Death Donors using Normothermic Regional Perfusion. a Comparison with Liver Transplants From Brain Death Donors

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TITLE PAGE

LIVER TRANSPLANT FROM CONTROLLED CARDIAC DEATH DONORS USING NORMOTHERMIC REGIONAL PERFUSION. A COMPARISON WITH LIVER TRANSPLANTS FROM BRAIN DEATH DONORS.

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LIVER TRANSPLANT FROM CONTROLLED CARDIAC DEATH DONORS USING NORMOTHERMIC REGIONAL PERFUSION. A COMPARISON WITH LIVER TRANSPLANTS FROM BRAIN DEATH DONORS.

INTRODUCTION

The growing need for organ transplantation, including liver, together with the shortage of cadaveric donors has led to the search for new sources of organs. One of them is donation after cardiac death (DCD), either uncontrolled (Maastricht II) or controlled (Maastricht III) [1].

In the case of liver transplants, however, the warm ischemia together with cold ischemia times - usually longer with the resultant tissue hypoxia- make some postoperative complications more probable, such as ischemic cholangiopathy (IC) or graft primary nonfunction (PNF) [2,3]. When compared with liver transplants from donors after brain death (DBD), significantly more IC, PNF and retransplantation happened in DCD patients [4].

IC is due to the special sensitivity of the biliary tree to the hypoxia, with frequencies ranging from 3% [2] to 16% [3]. In order to diminish the hypoxia, normothermic regional perfusion (NRP) using extracorporeal membrane oxygenation (ECMO), between the cardiac arrest and the beginning of organ procurement, has been proposed. Clinical and experimental data support its use in uncontrolled donors to better maintain liver function, showing additional benefits over traditional cold storage [5]. The results in controlled donors are also promising, with low rates of both IC and PNF [6]. In Spain, the first liver transplantation using NRP in controlled DCD was reported in 2014 [7].

The aim of this work is to report our initial experience with liver transplants with controlled DCD using NRP with ECMO with a comparison with the outcomes of liver transplants from DBD performed in the same period.

MATERIALS AND METHODS

From September 2014 to March 2017 a liver transplant was performed from DCD in 11 patients (group 1) and in 51 from DBD (group 2) at the University Hospital "Marqués de Valdecilla" (Santander, Spain). Seven patients were included in a previous general overview of DCD from the same center [8]. Our inclusion criteria for liver transplant in the case of DCD are the same as those of DBD and, in addition, they had to fulfill the following conditions: donor age under 70 years, functional warm ischemia under 30 min, warm ischemia under 90 min, donor AST/ALT serum levels less than three times the normal values and absence of liver disease based on a normal ultrasound and AST/ALT serum levels.

Warm ischemia was defined as the time between life support withdrawal, including extubation, and the beginning of the preservation procedure –start of NRP-. Functional warm ischemia, or agonal time, was defined as the time from the systolic pressure drop under 60 mm Hg and the beginning of the preservation procedure, 5 minutes after the cardiac arrest. Cold ischemia was defined as the time between the start of cold infusion of the graft to the clamping relief of the recipient portal vein.

The protocol was as follows: Upon family information and acceptance of the life support limitation, informed consent for donation and premortem cannulation and heparin administration was obtained. The procedure is performed in the intensive care unit, with the presence of relatives if desired. In addition to cannulation through the femoral artery, a deflated aortic balloon is inserted to isolate the abdominal and thoracic circulation. After the cardiac arrest happened, there was a waiting time of 5 minutes to avoid autoresuscitation, according to the Spanish law. Then, the aortic balloon is inflated and the NRP starts at 37ºC with a flow of 2.2-2.4 liters per minute. The donor is taken to the operating room for the procurement procedure, performed with a standard technique [9]. University of Wisconsin solution is used. The graft is also implanted with a standard technique of cava preservation [10]. The biliary anastomosis is done between the donor

hepatic duct and the recipient choledochus. In one patient having sclerosing cholangitis, Roux-en-Y hepatico-jejunostomy was done for biliary reconstruction.

DCD were 5 women and 6 men with an average age of 49.9 (14-65) years. Mean body mass index (BMI) was 24.9 (sd: 2.5). The cause of death and other clinical data are shown in Table 1. All the procurement procedure were local but one.

DBD were 26 women and 25 men with an average age of 64.4 (14-85) years. Donor age was significantly lower in group 1 than in group 2 (p=0.01). Mean BMI was 25.9, not significantly different to the group 1 (p=0.4). Thirty-three procurement procedures were local and 18 were from other regional centers. The cause of death was a stroke in 42 (82.4%), head trauma in 6 (11.8%), anoxia after cardiac arrest in 2 (3.9%) and hipoglycemic coma in 1 (2%).

The DCD recipients (group 1) were 5 men and 6 women with a mean age of 55.3 (28-68) years (sd: 12.3), with a mean BMI of 26 (sd: 2.8) and a mean MELD score of 14.7 (sd: 8). The DBD recipients were 43 men and 8 women with a mean age of 55.6 (14-69) years (sd: 10.1), a mean BMI of 26 (sd: 4.8) and a mean MELD score of 14 (sd: 5.8). No significant difference was found in BMI, MELD score or recipient age between both groups, although the proportion of men in the group 2 was significantly higher. Recipient mean MELD score was not significantly different: 14.7 (6-31) in group 1 and 14 (2-29) in group 2.

The outcome measures were postoperative complications such as (I) vascular complications: arterial or venous thrombosis –found on postoperative ultrasound-, arterial disruption, pseudoaneurisms (II) PNF - when according to the Olthoff 's criteria [11]- one or more of the following variables were present: (a) bilirubin >10 mg/dL on postoperative day 7; (b) INR >1.6 on postoperative day 7; (c) aminotransferase level (alanine aminotransferase [ALT] or aspartate aminotransferase [AST]) >2000 IU/mL within the first 7 postoperative days –, (III) IC defined as a

diffuse stenosis of the intrahepatic biliary tree –suspected by jaundice, cholangitis, abnormal biochemical liver test, or abnormal findings on ultrasound or T-tube cholangiography- provided there is no hepatic artery thrombosis [2], (IV) acute renal failure defined as peak serum creatinine ⩾2 times the baseline level.

For the statistical analysis, Chi-square test was used for comparison of discrete variables, means and analysis of variance for continuous variables and Kaplan-Meier and Log-rank for survival.

RESULTS

In the group 1, the mean time of warm ischemia was 31.4 (16-78) min and time of functional warm ischemia was 15.8 (7-40) min (Table 2). The mean time on NRP was 94.1 (20-150) min. One of the cases was only 20 min on NRP in the setting of a combined procurement of liver and lungs, with a dramatic drop in the ECMO flow after vena cava clamping with the resulting need of shortening the procedure. Since the liver perfusion had been satisfactory the graft was considered suitable for transplantation. The mean time on NRP excluding this case was 101.5 (47-150) min. The ischemic damage of the liver was minimal, according to the slight increase in mean ALT and AST values in the donor blood after one hour or NRP: 54 U/L (13-115) and 53 U/L (21-115), respectively.

The mean value of cold ischemia time in the group 1 was 243.6 (147-375) min and 334.3 (145-665) in the group 2 (p=0.009).

Recipient serum ALT and AST values exhibited an initial increase and then, gradually decreased. Twenty-four hours after transplantation the AST and ALT peaks were 520 U/L and 339 U/L in the group 1 and 717 U/L and 653 U/L in the group 2, respectively (NS), indicating similar ischemia/reperfusion damage.

The overall retransplantation rate was 8.1%, none in group 1 and 9.8% in group 2 (NS). The overall in-hospital death rate was 4.8%, 9.1% in group 1 and 3.9% in group 2 (NS).

Short-term morbidity (Table 3):

In the group 1, the serum bilirubin values were under 10 mg/dl and the INR was less than 1.6 in all cases but one, so according to the Olthoff's criteria [11], only one case developed PNF. This case rapidly evolved into universal bleeding resulting in death. Among survivors, one case of early hepatic artery thrombosis and no case of portal vein thrombosis happened, as shown by the ultrasounds routinely performed in the postoperative period. There were three cases of abdominal hemorrhage leading to reoperation, originated: one in a branch of the common hepatic artery of the graft, at the anastomosis cava-cava in the second one and at the Roux-en-Y jejuno-jejunostomy suture line in the third case. There was no case of renal failure. There were 3 biliary leaks (27.3%). The minimum follow-up was 3 months in every case.

When compared with the group 2, no significant difference was found in early hepatic artery thrombosis, portal thrombosis, pseudoaneurism or disruption of the hepatic artery, or biliary leak. However, significantly more patients had acute renal failure in the group 2 (42.9%) than in the group 1 (0), even after excluding a patient with a double transplant liver-kidney and another one with acute renal failure clearly related with a septic shock.

A subgroup of 23 patients aged 60 years or older from the group 2 was also studied to exclude a possible poorer outcome than in the group 1. Again, no significant difference was found in the short-term morbidity variables.

Long-term results (Table 1):

No group 1 patient showed clinical data (no jaundice), biochemical (normal AST, ALT, alkaline phosphatase, gamma glutamyl transpeptidase) or radiological (normal postoperative ultrasound and T-tube cholangiography) suggesting IC, with the exception of two cases (13.3%) with demonstrated stenosis limited to the bile duct anastomosis, without significant difference with 13 (27.7%) in the group 2.

Only 1 case (10%) in the group 1 and 3 (6.1%) in the group 2 underwent delayed hepatic artery thrombosis, also without any significant difference.

The liver function has been normal in the group 1 patients after hospital discharge, for the studied follow-up. One patient was diagnosed as having diffuse large B-cell lymphoma (germinal center type) 14 months after transplantation, with good response to chemotherapy.

Estimated mean survival was 24.6 months (95% CI: 20.2-29.1) in the group 1 and 32.3 months in the group 2 (95% CI: 30.4-34.2) with no significant difference (p=0.7).

DISCUSSION

We report a comparison between the results of liver transplantation in two different groups according to the type of donor: DCD and DBD. Both groups were comparable in terms of recipient features –age, MELD- although donor age was lower in DCD cases, because age is a selection criterion by itself. Also, cold ischemia time was lower in DCD cases, reflecting that most of the procurement procedures were local by comparison with 18 (35.3%) of the DBD procedures that were performed in other centers.

Our results of liver transplant from DCD using NRP with ECMO are quite good, in terms of nihil incidence of IC and one case of PNF. These results as well as the incidence of thrombosis and other

hepatic artery complications, portal thrombosis, biliary anastomotic complications or in-hospital postoperative death rate were similar to transplants from DBD.

In a recent paper, significantly more complications happened in DCD patients with grafts retrieved with the super-rapid technique when compared with liver transplants from DBD: IC 11% vs 3%, PNF 3% vs 1%- and retransplantation 15% vs 5% [4]. The clinical consequences of IC are very harmful, with bouts of cholangitis and frequent need of biliary invasive procedures as well as retransplantation [3]. A meta-analysis of papers published between 1990 and 2008 comparing outcomes of liver transplants from DBD and controlled DCD reports IC rates of 3% and 16%, respectively [3]. Later studies report IC rates of 8.5% [12], 12% [13] and 9.9% [14]. A recent series with controlled DCD reports, however, a lower IC rate of 2.5%, with less clinical impact, since there was no need for retransplantation and with both patient and graft survival comparable to that of patients receiving a liver from donors after brain death [2].

Another crucial problem with DCD is the development of PNF, having 3.6 times increased hazard by comparison with DBD transplants [3].

NRP can decrease and even revert the ischemic damage produced by the hypotension after the life support withdrawal and the interval period of 5 minutes after cardiac arrest required by the law. Also, both experimental [16] and clinical works [17] have shown that NRP for 30 minutes can restore the systemic mixed venous pH and vSO_2 to near basal values in mixed venous blood. As a result, NRP reduces the hypoxemia duration with a decrease of graft ischemia hazard, especially of the biliary epithelium. Therefore, a decrease in the PNF and IC rates are expected.

Only a few case reports and case series of liver transplant from DCD using NRP have been published, showing a low incidence of IC. Studies with uncontrolled DCD report IC rates of 5% [18] and 13% [5], as well as a 10% rate of PNF [18]. Concerning controlled DCD, Pelletier et al [19] report 11

transplants with only one case -9%- of IC. Rojas-Peña et al [17] report 13 transplants with one case -14.3%- of biliary stenosis and PNF. The most recent paper reports no case of PNF or IC in a short series of 5 liver transplants [15]. Oniscu et al [20] report 11 transplants, using NRP without cannulation or heparinization prior to the life support withdrawal, with the resultant risk of microcirculation thrombosis, with 4 cases of PNF -36.4%- and a death, although no IC case. On the contrary, Butler et al [21] published a short series of 3 cases, also without cannulation or heparinization prior to the life support withdrawal, with no case of IC or PNF. Other case reports have been published, without IC [7,22]. We have had no case of IC, after a minimum follow-up of 3 months of every patient, which is the usual interval to assess its development [2].

Only one of our DCD cases developed PNF. Several predictors of PNF have been identified [14]: hepatitis C virus, liver tumors or body mass index over 30, in the recipient; hepatitis B virus anti-core, mean arterial pressure under 60 mm Hg for more than 20 min after life support withdrawal in the donor or cold ischemia longer than 6 hours. None of these factors was present in our patients. There was only one case of hepatic arterial thrombosis in DCD patients. This complication was reported in relation to the first experiences with DCD [23] although more recent reports do not confirm a higher frequency in comparison with DBD [2,3,4,24].

Also, there was no case of acute renal failure, a reported complication in 16.3-53.4% of controlled DCD cases – but with no use of ECMO-, by comparison with 4.1-31.8% in DBD patients [12,25]. Other authors also report higher rates in DCD by comparison with DBD recipients, although in DBD recipients the acute renal failure rate ranges from 12% to 80%, depending on the definition criteria [26]. In our experience significantly more DBD recipients – as high as 42.9%- developed acute renal failure. The reason is not clear since the functional status of the recipients, according to the MELD score, the postoperative treatment or the immunosuppressive regimes were not significantly different. In the group 2 the cold ischemia time was longer, although this probably

does not explain the difference sufficiently. Another factor which could influence is intraoperative hemodynamic instability, although the piggy-back technique used in all of our cases reduces such instability [26]. Also, the post-reperfusion syndrome is an important factor in the origin of the acute renal failure [26]. But we have not an explanation of the lower rate in DCD patients, although a possible protective effect of the ECMO could exist. Most studies concerning DCD donors were performed with the rapid recovery technique. However, several studies [8,17,20] showed that kidney grafts obtained using NRP with ECMO devices decreased the rates of delayed graft function in kidney recipients. We do believe that as our initial experience, grafts were only accepted if the functional warm ischemic time was short, in most cases less than 30 minutes. This factor combined with the potential protective effect of the ECMO device and the low cold ischemic time could explain the low rate acute renal failure.

One of our cases had a primary sclerosing cholangitis, having no long-term complications. Although previously considered a bad indication for receiving a DCD liver, a recent paper also reports excellent results in terms of graft and patient survival [27].

Since more advanced donor age is associated with poorer results, we also compared a subgroup of transplants from DBD patients older than 60 years with the DCD patients, but the results were not significantly different in terms of PNF, vascular or biliary complications. As a result, we cannot support that DCD transplants are better than DBD transplants with older donors, although probably the age cut-off value is not very high. However, cut-off values higher than 60 provide small numbers to reach any conclusion, so we have to wait for future studies.

One limitation for the widespread acceptance of the NRP in controlled DCD is ethical concerns such as the theoretical possibility of resuscitating the patient after death declaration because of an inadequate use of the aortic occlusion balloon[28]. However, a specific methodology to avoid

restoring circulation to the brain after the determination of death when using NRP and *ante mortem* cannulation has been recently described [8] and validated in a multicenter study [29]. This proposal avoids the aforementioned ethical concern, guaranteeing the absence of cerebral resuscitation.

In conclusion, in our experience, the use of NRP with ECMO in the procurement of liver grafts from controlled DCD was associated with a minimal risk of PNF, IC, thrombotic complications and acute renal failure, not higher than in transplants from DBD. However, the limitation of the short numbers precludes the option of reaching a definitive conclusion, and as well as this, more patients and a more prolonged follow-up are needed. A possible protective effect of ECMO in preventing acute renal failure should be investigated.

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Group/ patient	Donor gender	Donor age (ys)	Donor BMI	Cause of death	Recipient gender	Recipient age (ys)	Recipient BMI	MELD	Indication
1.1	M	51	28,2	Lung fibrosis	F	28	22,2	24	Autoimmune cirrhosis
1.2	M	65	28,3	Complicated lung transplantation	F	58	31,2	6	CHV+HCC
1.3	F	61	24	Stroke	M	53	26	14	Alcohol
1.4	M	58	27,2	Complicated lung transplantation	M	62	28,73	9	Alcohol
1.5	F	54	24,1	Stroke and myocardial infarction	F	36	22,2	6	Sclerosing cholangitis
1.6	F	58	24	Stroke	M	64	28,1	31	Alcohol+hemochromatosis
1.7	F	65	24,2	Strpke	M	68	25,5	13	Alcohol+HCC
1.8	M	36	24,1	Stroke	F	60	24,2	20	Alcohol+HCC
1.9	F	51	22,5	Anoxic encefalopathy	M	62	25,3	16	Alcohol
1.10	M	36	27,5	Brain trauma	F	62	27	6	Alcohol+HCC
1.11	M	14	20,8	Stroke	F	55	26	17	Alcohol
2.1	F	76	22,1	Stroke	M	54	26,8	10	CHV+HCC
2.2	M	77	23	Stroke	M	42	22,9	2	Caroli's disease
2.3	F	14	23	Brain trauma	F	14	17,5	29	Acute failure unknown origin
2.4	M	63	27	Brain trauma	M	38	19,3	16	Autoimmune cirrhosis
2.5	F	84	27	Stroke	M	53	34,5	19	Alcohol
2.6	M	48	24,6	Anoxic encefalopathy	M	48	31,2	22	CHV+alcohol
2.7	F	78	37,1	Stroke	M	60	31,4	14	Alcohol
2.8	F	77	24,8	Stroke	M	58	16,7	15	Hemochromatosis
2.9	M	23	25,5	Anoxic encefalopathy	M	65	27,8	21	Alcohol
2.10	F	30	18,5	Hypoglycemia	M	58	23,5	20	CHV+HCC
2.11	M	64	27,2	Stroke	M	58	21,9	22	Alcohol
2.12	M	67	27,1	Stroke	M	61	24,2	13	Post-transplant cirrhosis
2.13	M	53	25,5	Stroke	F	49	22,9	12	CHV+alcohol

2.14	F	82	29	Stroke	M	63	22,6	10	Alcohol
2.15	M	67	24,8	Stroke	M	46	27,4	23	Alcohol
2.16	F	56	25,6	Stroke	M	65	29,7	19	Alcohol
2.17	F	76	22,7	Stroke	M	63	26	9	Alcohol+HCC
2.18	F	71	25,4	Stroke	M	64	22	7	CHV+HCC
2.19	F	81	29,1	Stroke	M	63	33,8	9	Alcohol+HCC
2.20	F	77	23,9	Stroke	M	63	22,9	11	Postransplant biliary tract necrosis
2.21	M	79	25,4	Stroke	M	51	28,4	6	CHV+HCC
2.22	F	65	30,9	Stroke	M	60	23,9	6	CHV+HCC
2.23	F	71	25,4	Stroke	M	57	20	10	CHV+HCC
2.24	F	64	29,1	Stroke	M	52	22,6	15	Postransplant biliary tract necrosis
2.25	F	59	29,8	Stroke	M	61	26,7	14	Alcohol
2.26	F	75	24,2	Stroke	M	63	21,5	8	CHV+HCC
2.27	M	48	24,3	Brain trauma	F	55	37,8	19	Primary biliary cirrhosis
2.28	F	85	25,1	Stroke	M	66	24,3	9	Alcohol+HCC
2.29	F	75	30,8	Stroke	M	56	26,4	8	Alcohol
2.30	F	84	24,2	Stroke	M	62	26,4	20	CHV+HCC
2.31	M	67	24,2	Stroke	F	33	25,7	14	Autoinmune cirrhosis
2.32	M	81	25	Stroke	M	63	20,3	10	Alcohol
2.33	M	67	24,1	Stroke	M	50	27,2	9	Neuroendocrine metastases
2.34	F	59	29	Stroke	M	62	29,7	23	HCC
2.35	M	45	25,1	Stroke	M	45	29	8	Sclerosing cholangitis
2.36	M	67	24	Brain trauma	M	67	23,9	14	Alcohol
2.37	F	70	29,8	Stroke	M	65	34,9	9	Alcohol+HCC
2.38	M	64	24	Stroke	M	67	32,9	7	HCC
2.39	F	58	23,1	Stroke	M	47	20,2	12	Sclerosing cholangitis

2.40	F	67	23,2	Stroke	F	60	21,9	14	Alcohol
2.41	M	79	27	Stroke	F	55	25,3	24	Alcohol
2.42	M	68	26	Stroke	M	61	24,2	11	CHV+HCC
2.43	M	58	26,5	Stroke	M	48	36,1	13	CHV+HCC
2.44	M	79	27,5	Stroke	M	44	22,6	21	BVH + DVH
2.45	F	52	26,7	Stroke	F	60	27,9	15	CVH
2.46	M	70	30,2	Stroke	M	63	34,3	9	Alcohol+HCC
2.47	F	53	20,8	Stroke	M	66	24,1	24	Alcohol
2.48	M	22	25,8	Brain trauma	M	58	21	12	BVH+HCC
2.49	M	77	24,5	Brain trauma	M	56	28,4	17	Alcohol
2.50	M	81	31	Stroke	M	48	28	13	HCC
2.51	M	30	20,4	Brain trauma	F	54	27,1	18	Alcohol

Group/patient	**Primary failure**	**Artery thrombosis**	**Ischemic Colangiopathy**	**Acute renal failure**	**Postop death**	**Retransplant**
1.1	N	N	N	N	N	N
1.2	N	N	N	N	N	N
1.3	N	N	N	N	N	N
1.4	N	N	N	N	N	N
1.5	N	N	N	N	N	N
1.6	N	N	N	N	N	N
1.7	N	Y	N	N	N	N
1.8	Y	-	-	-	Y	-
1.9	N	N	N	N	N	N
1.10	N	N	N	N	N	N
1.11	N	N	N	N	N	N
2.1	N	N	N	Y	N	N

2.2	N	N	N	N	N	N
2.3	Y	N	N	N	N	N
2.4	N	N	N	N	N	N
2.5	N	N	N	N	N	N
2.6	N	N	N	Simultaneous liver-renal transplant	N	N
2.7	N	Y	N	Y	N	N
2.8	N	N	N	N	N	N
2.9	N	N	N	N	N	N
2.10	N	N	N	Y	N	N
2.11	N	N	N	N	N	N
2.12	N	N	-	Y (septic shock)	Y	-
2.13	N	N	N	N	N	N
2.14	N	Y	N	N	N	N
2.15	N	N	N	N	N	N
2.16	N	N	N	Y	N	N
2.17	N	N	N	Y	N	N
2.18	N	N	N	N	N	N
2.19	N	N	N	Y	N	N
2.20	N	Y	N	N	N	N
2.21	N	N	N	N	N	N
2.22	N	Y	N	N	N	N
2.23	N	N	N	N	N	N
2.24	N	N	N	Y	N	N
2.25	N	Y	N	Y	N	N
2.26	N	N	N	N	N	N

2.27	N	N	N	N	N	N
2.28	N	N	N	Y	N	N
2.29	N	N	N	N	N	N
2.30	N	N	N	Y	N	N
2.31	N	N	N	N	N	N
2.32	N	N	N	Y	N	N
2.33	N	N	N	Y	N	N
2.34	N	N	N	Y	N	N
2.35	N	Y	-	Y	Y	-
2.36	N	N	N	Y	N	N
2.37	N	N	N	Y	N	N
2.38	N	N	N	N	N	N
2.39	N	N	N	N	N	N
2.40	N	N	N	Y	N	N
2.41	N	N	N	Y	N	N
2.42	N	N	N	N	N	N
2.43	N	Y	N	N	N	Y
2.44	N	N	N	Y	N	N
2.45	N	N	N	Y	N	N
2.46	N	N	N	N	N	N
2.47	N	N	N	N	N	N
2.48	N	Y	N	Y	N	N
2.49	N	N	N	N	N	N
2.50	N	N	N	N	N	N
2.51	N	N	N	N	N	N

Table 1: Individual donor and recipient clinical data. Postoperative results. M: male; F: female; Y: yes; N: no

Table 2

Case	Functional Warm Ischemia (min)	Time on ECMO (min)	Cold Ischemia (min)	AST / ALT 24 hours (U/L)	AST / ALT day 5th (U/L)	Follow-up
1	12	129	240	137 / 160	61/ 133	27 months. Alive. Functioning graft
2	22	125	275	1763/ 731	217/ 886	26 months. Alive. Functioning graft
3	10	140	260	579/ 642	24/ 14	18 months. Alive. Functioning graft
4	12	102	235	163/ 120	86/ 242	26 months. Alive. Functioning graft
5	17	20	217	649/ 399	44/ 172	30 months. Alive. Functioning graft
6	10	47	375	472/ 274	32/ 78	18 months. Alive. Functioning graft
7	40	97	225	54/ 38	76/ 222	19 months. Alive. Functioning liver and kidney grafts
8	12	40	285	-	-	Primary failure. Dead postoperative day 1.
9	17	150	147	168/ 128	98/ 177	11 months. Alive. Functioning graft
10	9	128	270	806/ 529	17/ 109	7 months. Alive. Functioning graft
11	7	57	150	156/ 185	103/ 376	7 months. Alive. Functioning graft

Clinical data of the group 1 recipients.

Table 3

	Group 1	Group 2	Significance
Primary liver failure	1 (9.1)	1 (2)	0.3
Early arterial thrombosis	1 (9.1)	8 (15.7)	0.5
Delayed arterial thrombosis*	1 (10)	3 (6.1)	0.5
Anastomotic arterial disruption	0	1 (2)	0.8
Anastomotic artery pseudoaneurism rupture	0	2 (3.9)	0.7
Portal thrombosis	0	4 (7.8)	0.5
Cava anastomotic leak	1 (9.1)	1 (2)	0.3
Biliary leak	3 (27.3)	10 (19.6)	0.4
Early biliary stricture	0	3 (5.9)	0.6
Delayed biliary stricture*	2 (13.3)	13 (27.7)	0.5
Septic fluid collection	0	2 (3.9)	0.7
Retransplantation	0	5 (9.8)	0.5
Postoperative hospital death	1 (9.1)	2 (3.9)	0.5
Acute renal failure	0	21 (42.9)	0.008

Comparison of surgical outcomes between group 1 and group 2. Values in parenthesis are percentages. (*) Percentage among discharged patients.

In this comparison of liver transplants either from donors after cardiac death (DCD) using ECMO or donors after brain death (DBD) similar ischemia/reperfusion damage, according to non-significant different AST and ALT peaks 48 hours after transplantation. No DCD patients developed ischemic cholangiopathy and only one (9.1%) died. No case of acute renal failure happened in DCD by contrast with 42.9% in DBD patients, perhaps reflecting the protective effect of ECMO. Since there was no significant difference in short and long-term complications when compared with DBD patients, we conclude that liver transplant with DCD is as good as with DBD.

LIVER TRANSPLANT FROM CONTROLLED CARDIAC DEATH DONORS USING NORMOTHERMIC REGIONAL PERFUSION. A COMPARISON WITH LIVER TRANSPLANTS FROM BRAIN DEATH DONORS.

BACKGROUND: Liver transplant from donors after either controlled or uncontrolled cardiac death (DCD) is associated with considerable rates of primary nonfunction (PNF) and ischemic cholangiopathy (IC). Normothermic regional perfusion (NRP) could significantly reduce such rates.

METHODS: Retrospective study to analyze short-term (mortality, PNF, vascular complications) and long-term (IC, survival) complications in 11 liver transplants from controlled DCD using NRP with extracorporeal membrane oxygenation (ECMO) (group 1). They were compared with 51 patients transplanted with grafts from donors after brain death (DBD) (group 2). Mean recipient age, gender and MELD score were not significantly different.

RESULTS: In group 1 mean functional warm ischemia was 15.8 (7-40) min and 94.1 (20-150) min on NRP. The ischemic damage experienced was minimal as shown by the slight ALT and AST rises in the donor serum after 1 hour on NRP and similar rises 24 h after transplantation in both groups. No patient had IC or acute renal failure. No significant difference was found between groups in vascular or biliary complications. One group 1 patient experienced PNF (9.1%), resulting in death. Overall retransplantation and in-hospital death rates were 8.1% and 4.8%, with no significant difference between groups. Estimated mean survival was 24.6 months (95% CI: 20.2-29.1) in group 1 and 32.3 months in group 2 (95% CI: 30.4-34.2) (NS).

CONCLUSIONS: in our experience, liver transplants from controlled DCD using NRP with ECMO is associated with a low risk of PNF and IC, with short and long-term results comparable to those of transplants with DBD.

KEYWORDS: Liver transplantation; donor after cardiac death; normothermic regional perfusion; ECMO