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# Improving the Outcomes of Organs Obtained From Controlled Donation After Circulatory Death Donors Using Abdominal Normothermic Regional Perfusion

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**The use of donation after circulatory death (DCD) has increased significantly during the past decade. However, warm ischemia results in a greater risk for transplantation. Indeed, controlled DCD (cDCD) was associated with inferior outcomes compared with donation after brain death. The use of abdominal normothermic regional perfusion (nRP) to restore blood flow before organ recovery in cDCD has been proposed as better than rapid recovery to reverse the effect of ischemia and improve recipients' outcome. Here, the first Spanish series using abdominal nRP as an *in situ* conditioning method is reported. A specific methodology to avoid restoring circulation to the brain after death determination is described. Twenty-seven cDCD donors underwent abdominal nRP during at least 60 min. Thirty-seven kidneys, 11 livers, six bilateral lungs, and one pancreas were transplanted. The 1-year death-censored kidney survival was 91%, and delayed graft function rate was 27%. The 1-year liver survival rate was 90.1% with no cases of ischemic cholangiopathy. Transplanted lungs and pancreas exhibited primary function. The use of nRP may represent an advance to increase the number and quality of grafts in cDCD. Poor results in cDCD livers could be reversed with nRP. Concerns about restoring brain circulation after death are easily solved.**

**Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; cDCD, controlled donation after circulatory death; CIT, cold ischemic time; DBD, donation after brain death; DCD, donation after circulatory death; ECD, expanded-criteria donor; ECMO, extracorporeal membranous oxygenation; FWIT, functional warm ischemic time; IC, ischemic cholangiopathy; ICU, intensive care unit; IQR, interquartile range; nRP, normothermic regional perfusion; PNF, primary nonfunction; RR, rapid recovery; WLST, withdrawal of life-sustaining therapy**

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## Introduction

The persistent mismatch between supply and demand of organs for transplantation has led the transplant community to reconsider donation after circulatory death (DCD) as a strategy to increase the donor pool (1).

However, the unpredictable consequences of warm ischemia, which characterizes controlled DCD (cDCD), together with poor organ perfusion during the agonic phase, result in a reluctance to use livers and pancreases from these donors, with recovery rates 20–50% lower than those from donation after brain death (DBD) donors (2,3).

In cDCD, the effects of warm ischemia during the hypotensive phase after the withdrawal of life-sustaining therapy (WLST) and, after circulatory arrest, are further exacerbated during the later period of cold ischemia. These phenomena result in a higher incidence of primary nonfunction (PNF) and delayed graft function (DGF) in kidney transplantation (4), as well as in graft loss and biliary complications in liver transplantation (5). Published data have shown inferior patient and graft survival rates among recipients of DCD abdominal organs (6).

In most transplant centers, the recovery of abdominal organs in cDCD is performed with a rapid recovery (RR) technique (7). In recent years, there is a growing interest in using abdominal normothermic regional perfusion (nRP) with extracorporeal membranous oxygenation

(ECMO) devices to restore blood flow after the determination of death and before organ recovery in cDCD (8,9). This *in situ* preservation strategy may restore cellular energy substrates and improve the quality of ischemically damaged organs. Further, the ability to assess organ function before transplantation, what allows a better selection of grafts, may lead to superior outcomes compared with current cDCD transplantation results (10). nRP perfusion also turns an urgent procedure into an elective organ recovery procedure, which could reduce organ damage and organ losses due to surgical events (11). Despite these theoretical benefits, there remains limited evidence that nRP improves the number and the quality of organs in cDCD.

There are several concerns about the use of abdominal nRP and premortem interventions in cDCD, such as the possibility of restoring circulation to the brain once death has been declared should the thoracic aorta not be adequately blocked (12). Surprisingly, no proposal for minimizing such a dangerous possibility has been made.

While RR of organs is the most commonly used approach, some centers have expanded the experience acquired with nRP in uncontrolled DCD (13–15) to the cDCD process. We report the first Spanish series on cDCD using nRP as a method of *in situ* conditioning and procurement of abdominal organs, along with *premortem* cannulation and heparinization. Further, we describe a specific methodology to ensure appropriate blocking of the thoracic aorta. To our knowledge, this is the first time a new proposal is made for minimizing this risk.

## Methods

This is a single-center retrospective review of all cDCD procedures from the start of the program in September 2014 to September 2016.

### *Donor selection*

cDCD was considered in patients with a devastating brain injury or a terminal heart, lung, or neurodegenerative disorder in whom the treating team had made the decision to WLST. Neurocritical patients were considered as potential cDCD donors only if their Glasgow Coma Scale score was <5 points, and cDCD was considered only in patients aged ≤70 years.

An expanded-criteria donor (ECD) was considered to be any donor older than 60 or a donor older than 50 with two of the following: a history of high blood pressure, a creatinine level of ≥1.5 mg/dL, or death resulting from a stroke (16).

Functional warm ischemic time (FWIT) for abdominal grafts was defined as the time from systolic blood pressure <60 mm Hg to nRP started (5 min of nontouch period is included). For lungs, FWIT was defined as the time from systolic blood pressure <60 mm Hg to the administration of Perfadex® (Vitrolife, Kungsbacka, Sweden) solution through the pulmonary artery.

For FWIT, an upper limit time of 30 min for liver and pancreas and 60 min for kidneys and lungs was considered.

### *Normothermic regional perfusion*

The extracorporeal membranous oxygenation circuit used was a Maquet Rotaflow (Maquet, Rastatt, Germany).

According to the Spanish regulatory framework, specific informed consent from the legal representatives of the potential donor was obtained for premortem interventions. These consisted of the administration of heparin (600 units/kg) and cannulation of femoral vessels before the WLST. The femoral artery and femoral vein were cannulated surgically or percutaneously by using the Seldinger technique at bedside in the intensive care unit (ICU). An aortic occlusion balloon was placed at the contralateral groin to prevent brain and coronary perfusion during nRP.

To ensure that the thoracic aorta was totally blocked with the aortic occlusion balloon, a radiograph was obtained before the WLST to confirm the balloon's position. Two arterial lines, one from the femoral arterial cannula and a second one from the left radial artery, were monitored in the potential cDCD donor to avoid brain and/or coronary perfusion after death declaration.

Before the WLST, the aortic occlusion balloon was filled in, for just 3 s, to confirm that the arterial pressure from the femoral arterial cannula disappeared while the pressure of the left artery line was maintained. This meant that was an adequate blocking of the thoracic aorta. Immediately afterward, the balloon was emptied again. Once nRP had started, the arterial pressure from the left radial artery disappeared with adequate blocking of the thoracic aorta while the pressure from the femoral arterial cannula was maintained, but it was a continuous, nonpulsatile pressure because it was provided by the ECMO device.

When lung donation was considered, the same procedure was performed, but just after nRP was initiated, the thoracic surgeon performed a sternotomy and clamped the thoracic aorta just over the aortic occlusion balloon. At the same time, the donor was reintubated and ventilated 5 min after nRP started with 100% oxygen and a positive end-expiratory pressure value of 5 cm $H_2O$. The pulmonary artery was cannulated for cold flush perfusion with Perfadex®. Only 1 L of cold serum saline was delivered in both hemithoraces for topical cooling. Finally, the superior vena cava was ligated to separate the thoracic and the abdominal compartments. To avoid low blood flow in the pump because of the absence of venous return from the thorax and head, 1–1.5 L of serum saline was administered to the cDCD donor just before the vena cava ligation.

In all cases, the WLTS was performed in the ICU, but if lungs were recovered, the WLTS was performed in theatre. Relatives were allowed to be with their beloved one during the entire process. Following the determination of death, nRP was initiated, and the donor was transferred to the operating room.

### *Normothermic regional perfusion monitoring*

The aim of performing abdominal nRP was to maintain a pump flow of 2–2.4 L/min. A continuous pressure of 60–65 mm Hg in the femoral arterial cannula was maintained, and a temperature of 37°C was maintained; bicarbonate was always administered just after nRP had started, to maintain pH 7.35–7.45, and a hematocrit >25% was targeted.

Blood samples from the ECMO device were obtained just after starting nRP and at least every 30 min for biochemistry analysis, serum lactate levels, and hematocrit values. If alanine transaminase (ALT) or aspartate transaminase (AST) levels at 30 or 60 min after nRP were >4 times the normal values, the liver was discarded even if it had a normal macroscopic appearance.

***Outcome data***

Information was collected for organs recovered and transplanted from actual cDCD donors and compared with information for organs from DBD donors at the center during the study period. Reasons for organ discard were also analyzed.

Recipient outcome data for all patients and grafts from cDCD donors were obtained from the center transplant database or from those centers at which some grafts were finally transplanted. These outcome data were compared with patient and graft survival data for organs obtained from DBD donors at the center and that were also transplanted in our center.

Cold ischemic time (CIT) for recipients was defined as the time from the end of abdominal nRP to organ reperfusion in the recipient. For lung recipients, CIT was defined as the time from Perfadex® administration to organ perfusion in recipients.

All transplant recipients had a minimum 3-month follow-up. The outcome for the recipients was recorded at 1 week and 3, 6, and 12 months after the transplant procedures. Kidney DGF was defined as the need for dialysis during the first week posttransplantation. The incidence of biliary complications was also recorded. In liver recipients with a Kehr tube, a cholangiogram was performed within the first 3 months. In liver recipients without a Kehr tube, magnetic resonance cholangiopancreatography was performed. In successive controls, ischemic cholangiopathy (IC) was evaluated through the use of clinical signs, laboratory studies, and Doppler echography. If there was any sign of IC, magnetic resonance cholangiopancreatography was performed to confirm the diagnosis.

***Statistical analysis***

A descriptive analysis of the sample was performed. Results are presented here as absolute numbers and percentages for categorical variables and as measures of central tendency and dispersion for continuous variables.

Comparisons between cDCD and DBD donors and recipients are performed with the Student t-test or the Mann–Whitney U test for continuous variables according to the sample distribution and the Kolmogorov–Smirnov/Shapiro–Wilk normality testing. For comparisons of categorical variables, the $\chi^2$ test is used with the Fisher correction where applicable. Patient and graft survival data are studied according to the Kaplan–Meier method and compared with use of the log-rank test.

## Results

A total of 27 cDCD donors underwent abdominal nRP. As controls, 51 DBD donors were evaluated. Demographic characteristics are shown in Table 1.

The median time under nRP was 109 min (interquartile range [IQR]: 93–138 min). The number of grafts recovered and transplanted *per* donor was significant lower in cDCD compared with DBD. The median number of organs recovered was two (IQR: two to three) versus four (IQR: three to four; p = 0.001), and the median number of organs transplanted was two (IQR: two to three) versus three (IQR: two to five; p = 0.017), respectively.

A total of 37 kidneys, 11 livers, six bilateral lungs, and one pancreas obtained from cDCD donors were finally transplanted. The median follow-up of recipients was 17 months (IQR: 7–22 months).

**Table 1:** Donor characteristics

| | DCD (n = 27) | DBD (n = 51) | p |
|---|---|---|---|
| Donor age (years) | 58 (50–67) | 63 (51.5–71) | 0.235 |
| Gender (male) | 20 (74.1%) | 28 (54.9%) | 0.098 |
| Hypertension | 3 (14.3%) | 28 (54.9%) | 0.001 |
| Diabetes | 2 (9.5%) | 6 (11.8%) | 1.000 |
| Cause of death | | | |
| CVA | 11 (40.7%) | 34 (66.7%) | 0.001 |
| Anoxia | 9 (33.3%) | 8 (15.7%) | |
| TBI | 1 (3.7%) | 9 (17.9%) | |
| Others | 6 (22.2%) | 0 | |
| ICU stay (days) | 7 (5–10) | 2 (1–4) | 0.001 |
| ECD (%) | 15 (55.6%) | 38 (74.5%) | 0.08 |

Results are presented as absolute number (percentage) or median (IQR). DCD, donation after circulatory death; DBD, donation after brain death; CVA, cerebrovascular accident; TBI, traumatic brain injury; ICU, intensive care unit; ECD, expanded-criteria donor.

***Kidney transplantation***

A total of 48 renal grafts were recovered, and 37 were eventually transplanted (77.1%). The reasons to discard the remaining 11 kidneys were as follows: seven had unacceptable anatomy, two had positive serology, and two had nRP technical reasons.

The main characteristics of kidney recipients are presented in Table 2. In the cDCD group, there were two (5%) cases of PNF due to arterial thrombosis. Overall, 10 (27%) recipients developed DGF, of whom six required only one or two dialysis sessions. Serum creatinine levels after kidney transplantation from cDCD donors were 2.7 (IQR: 1.2–3.7), 1.3 (IQR: 1.1–1.8), 1.5 (IQR: 1.2–1.6), and 1.3 (IQR: 1.0–1.8) mg/dL at 1 week, 1 month, 6 months, and 1 year, respectively.

There was no difference in kidney graft survival from cDCD donors (91.8% at 6, 12, and 18 months) compared with DBD donors (97.2% at 6, 12, and 18 months; p = 0.315) (Figure 1).

***Liver transplantation***

A total of 12 liver grafts were procured, and 11 (91.6%) were eventually transplanted. One liver was discarded because of severe steatosis in the intraoperative biopsy sample. There were three donors whose livers were not recovered for prolonged FWIT.

The median values of ALT in liver cDCD donors were 46 (IQR: 19–63) IU/L before WLST and 33 (IQR: 24–44) IU/L after 60 min of abdominal nRP. For AST, values were 33 (IQR: 23–42) and 34 (IQR: 28–61) IU/L, respectively.

The main characteristics of liver recipients are presented in Table 3. There was one case of PNF in the cDCD

**Table 2:** Kidney recipients' characteristics and outcomes

| | DCD (n = 37) | DBD (n = 36) | p |
|---|---|---|---|
| Age (years) | 57 (47–63) | 55.5 (49–61) | 0.838 |
| Gender (male) | 26 (70.6%) | 23 (60.8%) | 0.562 |
| HLA incompatibility >3 | 19 (73.1%) | 31 (88.6%) | 0.179 |
| FWIT in donors (min) | 12 (10–19) | – | |
| Cold ischemic time (min) | 960 (475–1290) | 1140 (900–1290) | 0.350 |
| History of previous transplantations | 5 (13.5%) | 8 (22.8%) | 0.331 |
| DGF | 10 (27%) | 12 (33.3%) | 0.557 |
| No. of dialysis sessions | 2 (2–3) | 2.5 (2–3) | 0.674 |
| Patients with <3 dialysis sessions[1] | 6 (60%) | 6 (50%) | 0.691 |

Results are presented as absolute number (percentage) or median (IQR). DCD, donation after circulatory death; DBD, donation after brain death; FWIT, functional warm ischemic time; DGF, delayed graft function.
[1]Those who had DGF.

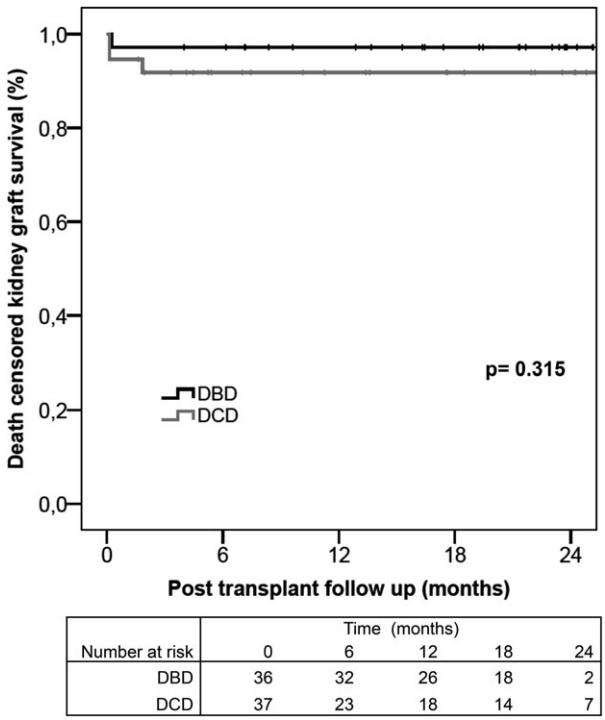


**Figure 1: Adjusted death-censored graft survival for cDCD and DBD donor kidneys.** cDCD, controlled donation after circulatory death; DBD, donation after brain death.

group, resulting in the recipient's death. The other 10 liver recipients had neither radiological nor clinical evidence of biliary lesions.

There was no difference in liver graft survival from DCD donors (90.9% at 6, 12, and 18 months) compared with DBD donors (100%, 91.6%, and 91.6%, respectively; p = 0.571) (Figure 2).

### *Lung and pancreas transplantation*

A total of six double lungs were recovered and successfully transplanted. Median follow-up was 11 months (IQR: 5–13 months). Simultaneous kidney–pancreas transplantation was performed with appropriate graft function after 6-month follow-up.

## Discussion

The number of DCD donors has expanded in a number of countries in recent years (17,18). In Spain, there has been a 10-fold increase in the number of cDCD donors from 2012 to 2015 (17,19).

cDCD has been associated with limited organ use and lower postransplantation outcomes compared with DBD, especially in liver transplantation (20), where increased incidences of PNF, IC, and relisting for liver transplantation have been observed (21,22). However, in nearly all reported procedures, organ recovery has been performed with the RR method.

To our knowledge, only two studies have been published on the use of abdominal nRP in cDCD (23,24). There are important differences between the present study and these two other studies. Donors in our series were much older (median age 58 years) than those in the series of Rojas-Peñas et al (23) (37 years) and Oniscu et al (24) (46 years). Despite the age differences, the incidence of DGF in kidney recipients was lower and early kidney and liver graft survival rates were better. However, in the UK study (24), premortem heparinization and femoral cannulation were not allowed.

Donor age in our series also contrasts with other experiences in cDCD. A recent analysis of the UK Transplant Registry reported a median cDCD donor age of 49 years (25). Also, most of the liver transplantations performed with cDCD donors describe a donor age of 40 years or younger (26–28). Despite an older donor age in our study, outcomes for the recipients of all kinds of grafts were excellent, including those receiving a liver. Moreover, four of the 11 liver transplantations in our series were performed with grafts obtained from donors aged 65 years or older.

**Table 3:** Liver recipients' characteristics and outcomes

| | DCD (n = 11) | DBD (n = 19) | p |
|---|---|---|---|
| Gender (male) | 9 (81.8%) | 15 (78.9%) | 1.000 |
| Age (years) | 55.2 (13) | 55.8 (9.9) | 0.985 |
| Retransplantation | 0 | 3 (15.8%) | 0.279 |
| FWIT in donors (min) | 12 (11–16) | – | |
| Cold ischemic time (min) | 266.5 (82.7) | 299.4 (65.6) | 0.335 |
| ALT at ICU admission (U/L) | 422 (242–502) | 285 (241–701) | 0.975 |
| AST at ICU admission (U/L) | 249 (186–336) | 275 (162.5–532.5) | 0.828 |
| ALT at day 7 (U/L) | 77 (57–81) | 71 (42.5–137) | 0.780 |
| AST at day 7 (U/L) | 164 (139–189) | 244 (145–361) | 0.475 |
| ICU stay (days) | 6.5 (4–9) | 7 (3–16) | 0.871 |
| Graft loss | 1 (9.1%) | 1 (5.3%) | 1.000 |

Results are presented as absolute number (percentage), mean (standard deviation), or median (IQR). DCD, donation after circulatory death; DBD, donation after brain death; FWIT, functional warm ischemic time; ICU, intensive care unit; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

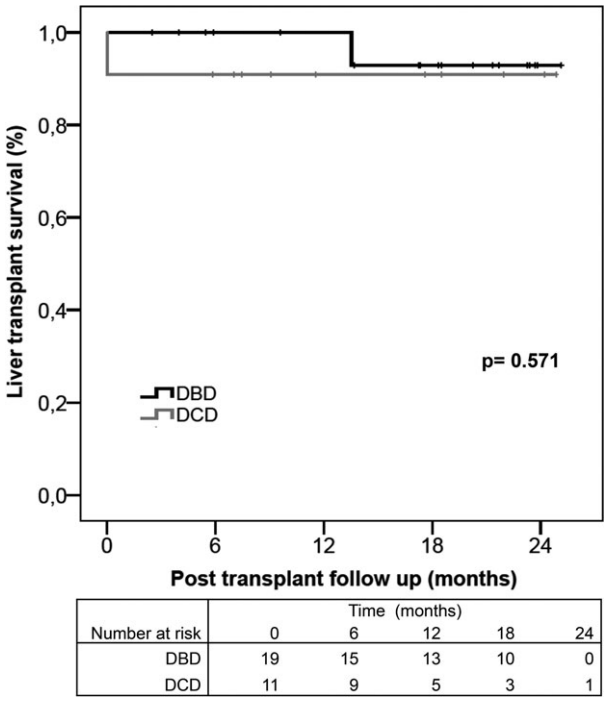


**Figure 2: Patient survival for cDCD and DBD donor livers.** cDCD, controlled donation after circulatory death; DBD, donation after brain death.

Donor age is by far the most important factor related to recipients' outcome (25,29), but abdominal nRP instead of RR may allow the expansion of donor age with safety because other risk factors can be minimized, such as prolonged CIT, iatrogenic injuries during retrieval, and assessment of graft functional status before transplantation. Prolonged CIT is undesirable for any type of transplant, but grafts from DCD donors are particularly vulnerable to the effect of cold ischemia. Indeed, one of the great advantages of abdominal nRP is the reduction of CIT and the increase in liver utilization criteria, mainly when donors are not local. A CIT of <8 h is preferred to reduce the risk of IC (30). Once the liver has been deemed suitable for transplantation, abdominal nRP can be maintained until the recipient is under anesthesia and prepared for liver explantation, to reduce CIT.

The optimal duration of abdominal nRP in cDCD has yet to be determined. In our protocol, abdominal nRP is usually maintained for 90–120 min. This allows the restoration of cellular energy substrates and careful assessment of suitability of the grafts (10,31), mainly the liver, based on the macroscopic view and ALT and AST levels at 60 min after abdominal nRP.

cDCD donors are associated with fewer grafts being recovered and transplanted compared with DBD donors, as well as with greater difficulties in recovering nonrenal grafts. In the United Kingdom, with a considerable experience with cDCD, the recovery rate is 2.8 organs per donor (2), similar to our figures. However, we have reported the results of all cDCD donors subject to nRP since the start of our program. The number of organs recovered per cDCD donor during the last 12 months of the program increased to 3.2.

Particularly with livers, our team was initially cautious, so liver donation was not considered in the first three donors. Three livers were rejected due to an FWIT of >30 min. Nevertheless, our recovery rate for livers was 44%, while in some experienced countries that use RR as the most frequent recovery method, only 27% of the livers obtained from cDCD donors are transplanted (2). Indeed, four of the livers in our series were transplanted at other centers, >500 km far from our center.

One important advantage of abdominal nRP is that it may reduce the rate of iatrogenic injuries because it allows the performance of graft retrieval without speed,

as it is performed in DBD. In our series, no graft was lost due to an iatrogenic injury during recovery, something that has been frequently observed with the RR technique, due to the haste to minimize the FWIT (11). However, the surgeon's expertise is very important to minimize iatrogenic injuries during DCD procurement.

Our results suggest that recipients' outcomes with grafts from cDCD donors subject to nRP are not inferior to those obtained from DBD donors, not only for kidney but also for liver transplantation.

In a recent Dutch study, with 1441 recipients who received a first cDCD donor kidney, the rate of PNF was 9.6% (vs. 5.4% in our series) and that of DGF was 63.4% (vs. 27% in our series) (32). Another large research study with >2000 kidneys transplanted from cDCD donor showed a PNF rate of 5% and a DGF rate of 50.2% (25).

Our liver recipients' data are better than those reported in the literature with the RR method (26,27,33), and no biliary complications were observed. The one liver recipient who died is a concern. There were no apparent reasons for that failure (pancreas, kidneys, and lungs were recovered and successfully transplanted from the same donor, who was in her 30s). After being admitted in the ICU, the recipient developed massive bleeding through the abdominal drainage and AST and ALT levels increased to >1500 IU/L. Although liver packing was performed, the recipient died 18 h after transplantation.

The two kidneys lost due to arterial thrombosis were obtained from two different donors, and in both cases the contralateral kidney was transplanted and continued to function.

There are several ethical concerns about the use of abdominal nRP and premortem interventions in cDCD (12), such as the possibility of restoring brain circulation after death declaration if the aortic occlusion balloon fails. The presence of cyanosis in the upper torso and head occurs after several minutes without perfusion. However, they are very late clues to diagnose failure in the thoracic aorta blocking.

In addition to obtaining a radiograph to assess the position of the balloon before the WLST, our proposal of using two arterial lines (see Methods) to ensure appropriate blocking of the thoracic aorta is easy and safe and can help to immediately diagnose a failure, in order to prevent donor resuscitation. To our knowledge, this is the first time a proposal is made for minimizing the risk of inappropriate aorta blocking under nRP with *premortem* cannulation.

Another ethical concern relates to the possibility that once premortem interventions have been performed and WLST is undertaken, the patient does not die within the time frame consistent with organ recovery and FWIT would be so prolonged that donation would be rejected. There are no available tools widely accepted for predicting time to death after the WTLS. Some authors have proposed the ICU physicians' opinion as the best independent predictor of death in <60 min after the WLTS (34). Potential cDCD donors in our series were carefully evaluated and selected to predict an FWIT of <60 min. Although we had to reject three livers because of FWIT of >30 min, in no case did actual donation have to be stopped for prolonged FWIT. If the risk of inadequate aortic occlusion and resumption of brain circulation is minimized and only potential donors with a high likelihood of dying in <2 h after WLST are selected, we believe that the ethical concerns regarding nRP with *premortem* interventions would disappear.

Today, it remains unclear what professional background is needed for donor management where there so many pitfalls and potential for errors (35). It has been shown that the involvement of an experienced intensivist in the management of potential DBD donors increased the number of transplantable organs (36). This may also be applicable to the cDCD setting.

An extended withdrawal period is detrimental to the viability of grafts and prolonged WIT is a strong indicator of poor graft survival (4,5,37). Therefore, there is no clear consensus on the magnitude of the effect of WIT on graft viability. However, in current practice, FWIT of >30 min is applied as a contraindication for liver and pancreas and >60 min for kidneys and lungs in most centers (38), but the strict upper limit of FWIT remains controversial (39). The use of premortem interventions before nRP decreases the FWIT and may increase the number and quality of grafts recovered in cDCD. Some authors have proposed increasing donor time from WTLS to death up to 4 h with no negative impact in kidney recipients (40,41). We believe it might also be increased for livers if macroscopic views and biochemical marker analyses during abdominal nRP are not altered.

Lungs are recovered from only 10–20% of organ donors (42). New options such as lungs from DCD (43), better donor management (44,45), and normothermic *ex vivo* lung strategies (46) have been proposed to expand the lung donor pool. It is clear that RR is the ideal method for lungs (43), and abdominal nRP in cDCD donors combined with RR of lungs was first proposed by Oniscu et al (47). Although our method has several differences compared with theirs, it is quite clear that abdominal nRP combined with RR of the lungs is safe for both abdominal and thoracic grafts.

Our main difference with the UK proposal is that FWIT for abdominal grafts is reduced by a total of 10–15 min (abdominal laparotomy, clamp of the thoracic aorta, and cannulation of femoral artery and vein). Thus, in our

view, there is no need for strict topical cooling of both lungs because the FWIT for lungs is also shortened. Therefore, the risk of potential transdiaphragmatic cooling of the liver is minimized.

One limitation for the widespread acceptance of the nRP in cDCD is the existing legal framework across countries. According to Spanish regulations, specific informed consent from the legal representatives of the potential donor must be obtained for any premortem interventions immediately after consent for organ donation has been obtained (one consent for organ donation and another specific informed consent for premortem interventions).

Another logistic limitation to the expansion of nRP is the use of an ECMO device. However, there are portable ECMO devices that could be used for recovering organs in smaller centers that have no device available. The ECMO device should be used by experienced personnel. In our case, the system is managed by perfusionist nurses who are trained to manage ECMO devices, under the supervision of the donor coordinator.

In summary, the use of abdominal nRP with *premortem* interventions may represent a significant advance to increase the number and quality of grafts recovered in cDCD. Abdominal nRP combined with RR of the lungs is safe for both abdominal and thoracic grafts. The poor outcome in cDCD liver transplantation can be reversed by using abdominal nRP. Donor age for cDCD liver donors may be increased safely. Concerns about restoring brain circulation after death can be easily solved. Further studies are needed to confirm our findings and to explore the impact of abdominal nRP on donor age, upper limit for FWIT, ischemic injury modulation, or duration of regional perfusion.

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## Disclosure

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

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