ABDOMINAL NORMOTHERMIC REGIONAL PERFUSION IN DONATION AFTER CIRCULATORY DEATH: ORGAN VIABILITY OR ORGAN PRESERVATION?

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Summary

Transplants from donation after circulatory death (DCD) provide a viable means to deal with the ever-growing shortage of donors but are burdened by a higher rate of complications and graft loss. Dismal results have prompted the application of stricter donor and graft selection criteria and the use of machine perfusion technologies, such as normothermic regional perfusion (NRP). In this review, we first describe the diffusion of NRP worldwide. Next, the role of NRP in liver transplantation is discussed, with a particular focus on graft selection during perfusion and posttransplant outcomes. Finally, we review the clinical studies reporting on NRP in kidney transplantation. The emerging use of NRP with complementary ex-situ machine perfusion is also described. NRP improves organ quality and maintenance before cold preservation, turns the DCD procedure into a more unhurried one, and allows the assessment of organ function following the warm ischemic injury. Moreover, it is beneficial for both the liver and the kidneys from the same donor.

Key words: extracorporeal membrane oxygenation, kidney transplant, liver transplant, organ preservation, organ procurement

Abbreviations

ALT: alanine transaminase
cDCD: controlled donation after circulatory death
DBD: donation after brain death
DCD: donation after circulatory death
DGF: delayed graft function
FMN: flavin mononucleotide
HOPE: hypothermic oxygenated perfusion
ITBL: Ischemic-type biliary lesions
KT: kidney transplant
LT: liver transplant
NMP: normothermic machine perfusion
NRP: normothermic regional perfusion
RCT: randomized controlled trial
SCS: static cold storage
SRR: super-rapid recovery
uDCD: uncontrolled donation after circulatory death
UK: United Kingdom
INTRODUCTION

Donation after circulatory death (DCD) provides a viable means to deal with the ever-growing shortage of donors. Nevertheless, transplants from DCD are traditionally burdened by a higher rate of complications and graft loss. Dismal results have prompted the application of stricter donor and graft selection criteria in some settings and the use of machine perfusion technologies in others. DCD inevitably involves compromised hemodynamics in the agonal phase, followed by an obligatory additional circulatory standstill for the declaration of death. In super-rapid recovery (SRR), this is hurriedly followed by incision, aortic cannulation, and organ perfusion with hypothermic preservation solution. Normothermic regional perfusion (NRP) temporarily re-establishes blood flow following declaration of death, through arterial and venous cannulae placed in the femoral vessels or directly in the aorta and vena cava after rapid laparotomy (Fig. 1). Supraceliac aortic balloon occlusion prevents cerebral reperfusion during NRP and restricts perfusion to the abdomen. This way, NRP restores previously depleted energy substrates, clears by-products of anaerobic metabolism, and induces endogenous antioxidants, thus helping to improve organ quality and maintenance before cold preservation. Moreover, in contrast to SRR, NRP also allows the assessment of organ function following the warm ischemic injury.

Although some ethical concerns have been raised, especially with premortem cannulation, heparin administration, and potential brain reperfusion, NRP is currently spreading in many European countries. To maintain the permanence principle for death, Manara et al. have recently suggested inserting a cannula in the ascending aorta to identify inadequate occlusion and divert any collateral flow away from the brain. Moreover, antemortem interventions in the potential donor should follow national legislation and are ethically acceptable if they do not add risk, harm, or discomfort to the patient.

In this review, we first describe the diffusion of NRP worldwide. Next, the role of NRP in liver transplantation (LT) is discussed, with a particular focus on graft selection during perfusion and posttransplant outcomes. Finally,

Figure 1. NRP circuit and advantages. The abdominal NRP circuit relies on extracorporeal membrane oxygenation technology and includes a pump, an oxygenator, and a heater. The blood is pumped through arterial and venous cannulae in the femoral vessels. Supraceliac aortic balloon occlusion prevents cerebral reperfusion. aNRP: abdominal normothermic regional perfusion.
we review the clinical studies reporting on NRP in kidney transplantation (KT). The emerging use of NRP with complementary ex-situ machine perfusion is also described.

**DIFFUSION OF NRP**

Currently, NRP is mandatorily applied in DCD organ recovery in 3 European countries (Italy, France, and Norway) and is permitted in 5 (Spain, United Kingdom, Belgium, the Netherlands, and Switzerland) 1,3,7,8. Moreover, a progressive increase in NRP use has been registered over time even in those countries where NRP is not mandatory. In Spain, NRP is currently far more frequent than SRR for liver recovery 9. Nevertheless, this practice is still less embraced in the United States, although good results have been reported recently in a series of 13 DCD donors maintained on NRP 2. A few cases have also been reported from Russia and Korea 7,10.

**NRP IN LIVER TRANSPLANTS**

Clinical studies on LTs with NRP are reported in Table I.

**Results of LT with NRP**

NRP has originally allowed recovery and utilization of uncontrolled DCD liver grafts (uDCD; Maastricht category II and IV) in Spain, France, and Italy. Then its use has been shifted to controlled DCD grafts (cDCD; Maastricht category III). NRP turns the cDCD procedure into a more unhurried one compared to SRR, thus enabling graft evaluation and even warm dissection. Ischemic-type biliary lesions (ITBL) are the leading cause of patient morbidity and early graft loss in LTs from DCD. Many retrospective studies have shown that NRP treatment is effective in preventing the occurrence of ITBL compared to SRR, but randomized trials comparing these two techniques have not been reported yet 9,11. Nevertheless, given the ever-increasing use of NRP instead of SRR, such clinical trials are unlikely to be carried out in the future.

**Selection of livers during NRP**

Different criteria are used for graft selection during NRP, and progressive evolution of both parameters and thresholds has been noticed over time (Tab. II). A combination of macroscopic and microscopic assessment, alanine transaminase (ALT) levels, and lactate in perfusate are used to assess the suitability of the liver for transplantation in most protocols. All of these parameters inform about both liver viability and quality of the perfusion and have contributed to the selection of LT series with excellent results. Nevertheless, no strong correlation has been found between each parameter and the transplantation outcome 12,13. According to a recent review, the most used acceptation criterion

<p>| Table I. Main series of LT from controlled and uncontrolled DCD donors maintained on NRP. |
|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|</p>
<table>
<thead>
<tr>
<th>Author, year</th>
<th>Country</th>
<th>DCD type, n</th>
<th>Utilization rate (from NRP to LT)</th>
<th>EAD</th>
<th>PNF</th>
<th>AKI</th>
<th>ITBL</th>
<th>Graft survival (follow-up)</th>
<th>Patient survival (follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>uDCD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fondevila, 2012</td>
<td>Spain</td>
<td>uDCD: 34</td>
<td>34/290 (12%)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>8%</td>
<td>70% (1y)</td>
<td>82% (1y)</td>
</tr>
<tr>
<td>Savier, 2015</td>
<td>France</td>
<td>uDCD: 13</td>
<td>13/183 (7%)</td>
<td>31%</td>
<td>23%</td>
<td>N/A</td>
<td>8%</td>
<td>69% (1y)</td>
<td>85% (1y)</td>
</tr>
<tr>
<td>Justo, 2020</td>
<td>Spain</td>
<td>uDCD: 75</td>
<td>N/A</td>
<td>N/A</td>
<td>8%</td>
<td>20%</td>
<td>4%</td>
<td>78.3% (1y) excluding PNF</td>
<td>82% (1y) excluding PNF</td>
</tr>
<tr>
<td>cDCD (multicentre/national)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Watson, 2019</td>
<td>UK</td>
<td>cDCD: 43</td>
<td>61%</td>
<td>12%</td>
<td>18%</td>
<td>N/A</td>
<td>2%</td>
<td>88% (2y)</td>
<td>90% (2y)</td>
</tr>
<tr>
<td>Savier, 2020</td>
<td>France</td>
<td>cDCD: 50</td>
<td>20%</td>
<td>18%</td>
<td>N/A</td>
<td>26%</td>
<td>2%</td>
<td>97.7% (90d) excluding PNF</td>
<td>100% (90d)</td>
</tr>
<tr>
<td>De Carlis, 2021</td>
<td>Italy</td>
<td>cDCD: 44</td>
<td>85%</td>
<td>N/A</td>
<td>5%</td>
<td>36%</td>
<td>2%</td>
<td>91% (2y)</td>
<td>98% (2y)</td>
</tr>
<tr>
<td>Hessheimer, 2021</td>
<td>Spain</td>
<td>cDCD: 545</td>
<td>70%</td>
<td>15%</td>
<td>3%</td>
<td>N/A</td>
<td>1%</td>
<td>90% (1y)</td>
<td>92% (1y)</td>
</tr>
<tr>
<td>Sellers, 2022</td>
<td>US</td>
<td>cDCD: 13</td>
<td>23%</td>
<td>N/A</td>
<td>0%</td>
<td>N/A</td>
<td>0%</td>
<td>92% (439d) excluding PNF</td>
<td>92% (439d)</td>
</tr>
<tr>
<td>Mixed series (uDCD and cDCD)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>De Carlis, 2018</td>
<td>Italy</td>
<td>cDCD: 6 uDCD: 14</td>
<td>20/25 (80%)</td>
<td>24%</td>
<td>10%</td>
<td>30%</td>
<td>10%</td>
<td>85% (1y)</td>
<td>95% (1y)</td>
</tr>
<tr>
<td>Ghinolfi, 2020</td>
<td>Italy</td>
<td>cDCD: 7 uDCD: 11</td>
<td>18/31 (58%)</td>
<td>28%</td>
<td>0%</td>
<td>28%</td>
<td>6%</td>
<td>94% (15mo.)</td>
<td>94% (15mo.)</td>
</tr>
</tbody>
</table>

AKI: acute kidney injury; cDCD: controlled donation after circulatory death; EAD: early allograft dysfunction; ITBL: ischemic-type biliary lesions; LT: liver transplant; NRP: normothermic regional perfusion; PNF: primary nonfunction; SRR: super-rapid recovery; uDCD: uncontrolled donation after circulatory death; UK: United Kingdom; US: United States
Table II. Main selection criteria of the liver during NRP.

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Type</th>
<th>Pump flow</th>
<th>Lactate</th>
<th>Transaminase</th>
<th>Macroscopical aspect</th>
<th>Liver biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fondevila, 2007&lt;sup&gt;39&lt;/sup&gt;</td>
<td>uDCD</td>
<td>&gt;1.7 L/min (&gt;4h)</td>
<td>-</td>
<td>Initial &lt; 3 ULN Final &gt; 4 ULN</td>
<td>Before/after cold flush</td>
<td>-</td>
</tr>
<tr>
<td>Oniscu, 2014&lt;sup&gt;13&lt;/sup&gt;</td>
<td>cDCD</td>
<td>1.7-4 L/min/m² (60-120 min)</td>
<td>-</td>
<td>Initial ALT &lt; 3 ULN Final ALT &lt; 4 ULN</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Savier, 2015&lt;sup&gt;15&lt;/sup&gt;</td>
<td>uDCD</td>
<td>efficient flow for &gt; 240 min</td>
<td>-</td>
<td>ALT at 2h &lt; 200 IU/L</td>
<td>-</td>
<td>MaS &lt; 20%</td>
</tr>
<tr>
<td>De Carlis, 2017&lt;sup&gt;60&lt;/sup&gt;</td>
<td>uDCD</td>
<td>-</td>
<td>Stable or downward</td>
<td>ALT &lt; 1000 IU/L</td>
<td>Color, surface, margins, consistency</td>
<td>MaS &lt; 30% Ishak 0-1</td>
</tr>
<tr>
<td>Watson, 2019&lt;sup&gt;91&lt;/sup&gt;</td>
<td>cDCD</td>
<td>2.5-3 L/min</td>
<td>Fall is encouraging</td>
<td>ALT &lt; 200 IU/L ALT &lt; 500 IU/L</td>
<td>Steatosis</td>
<td>-</td>
</tr>
<tr>
<td>Savier, 2020&lt;sup&gt;77&lt;/sup&gt;</td>
<td>cDCD</td>
<td>&gt; 60 min</td>
<td>-</td>
<td>AST-ALT &lt; 200 IU/L</td>
<td>-</td>
<td>MaS &lt; 20%</td>
</tr>
<tr>
<td>Hesseimer, 2021&lt;sup&gt;9&lt;/sup&gt;</td>
<td>cDCD</td>
<td>2.2-2.4 L/min/m² (60-120 min)</td>
<td>Ideally downward</td>
<td>Ideally stable and &lt; 200 IU/L</td>
<td>Liver, gallbladder, bile duct and bowel</td>
<td>-</td>
</tr>
<tr>
<td>De Carlis, 2021&lt;sup&gt;12&lt;/sup&gt;</td>
<td>cDCD</td>
<td>1.7-3 L/min/m² (ideally 120 min, no upper limit if stable)</td>
<td>Ideally stable or downward</td>
<td>Ideally final ALT &lt; 1000 IU/L</td>
<td>Perfusion, congestion</td>
<td>Ideally MaS &lt; 30% Ishak 0-2</td>
</tr>
</tbody>
</table>

ALT: alanine aminotransferase; cDCD: controlled donation after circulatory death; MaS: macrosteatosis; uDCD: uncontrolled donation after circulatory death; ULN: upper limits of normal

in cDCD is the macroscopic aspect, while in uDCD ALT level is considered the most reliable<sup>4</sup>. This attitude has been partially reflected in a recent Italian survey, where macroscopic assessment was highly considered in the opinion of the participants, along with the stability of NRP perfusion conditions<sup>14</sup>. Although transaminase release is a widely accepted marker of liver injury, its cut-off has, however, been modified from initially 3-4 times the normal values to upper thresholds reported in the most recent series<sup>11,12</sup>. Lactate clearance has been proposed as a parameter to assess liver function, as in normothermic machine perfusion, with a downward lactate trend indicating a well-functioning liver<sup>4</sup>. However, Watson et al. noted that lactate leaking back from non-perfused areas in the donor decreases the reliability of this parameter as an indicator of liver function<sup>15</sup>. Wang et al. have recently analysed flavin mononucleotide (FMN) in the perfusate during NRP and found that FMN levels were significantly higher in those livers that were declined for transplantation<sup>16</sup>. Unfortunately, no correlation was made with the LT outcomes in the livers that were accepted. Further insight on this topic will probably be given by a nonrandomized trial on viability assessment during NRP, which is currently ongoing in France (NCT05361044).

**NRP vs machine perfusion**

Various dynamic ex-situ preservation strategies have been explored to ameliorate the outcomes of DCD livers, including hypothermic oxygenated perfusion (HOPE) and normothermic machine perfusion (NMP). Preference for in-situ NRP or ex-situ techniques varies among centres and countries. NRP is most frequently undertaken in tertiary hospitals with extracorporeal membrane oxygenation devices and cardiothoracic intensive care units, although good results have also been reported with mobile NRP teams<sup>17,18</sup>. A few studies have compared NRP with HOPE or NMP, but no randomized trials have been published. In a large-scale international multicentric study, the utilization rate was significantly lower in the NRP group, despite shorter warm ischemic times and lower donor age compared to the HOPE group. However, after propensity-score adjustment of donor-recipient combinations, both strategies achieved similar posttransplant outcomes<sup>19</sup>. In a single-centre retrospective analysis from the United Kingdom (UK), the NRP group had a lower incidence of cholangiopathy than static cold storage, but the same benefit was not achieved with NMP (NMP vs NRP: hazard ratio 3.5, p = 0.02)<sup>17</sup>. Conversely, a multicentric study comparing NRP cases from France with NMP cases from the UK, Germany, Spain, and Belgium, failed to show any significant difference in the incidence of non-anastomotic biliary strictures (1.5 vs 2.9%; p > 0.99) and 30-day graft loss (4.4 vs 8.8%; p = 0.40) between the two groups<sup>20</sup>.

**NRP and subsequent HOPE or NMP**

Prolonged cold ischemia and indication for retransplantation were found to be independent risk factors for graft loss among 545 DCD livers treated with NRP in Spain<sup>9</sup>.
These data support a potential role for complimentary 
*ex situ* perfusion preservation for those cases with prolonged 
cold ischemia and/or technically complex recipients. The 
combined use of NRP with subsequent HOPE was first 
proposed in 2016 by our group to face the detrimental ef-
teffects of the 20-min stand-off period in Italy, thus providing 
safe prolonged preservation and further reconditioning to 
the DCD livers 21. Although a direct comparison between 
NRP with subsequent HOPE and NRP only is still lack-
ing in the Italian population, some indirect evidence ex-
ists to support this approach 14. In a recent multicentric 
analysis, the combined protocol has yielded good results 
compared to a static-preserved comparator group from 
the UK, despite the higher risk profile in Italy 12. Moreover, 
the same Italian cohort had shown similar results to the 
benchmark outcomes in LT from DCD 22. The combined 
use of NRP and NMP was first reported by Pavel et al. 23. 
More recently, Ghinolfi et al. have proposed a flow-chart, 
where machine perfusion is used following the initial DCD 
liver evaluation during NRP. While HOPE is suggested 
for cases partially fulfilling the criteria, the authors rec-
commend NMP when the criteria are not fulfilled 24. This 
proposal sounds promising but is still mainly based on 
a small number of uDCD cases, and only a few centres 
currently use both HOPE and NMP in Italy 14. The results 
of a currently ongoing randomized trial in Italy between 
sequential HOPE and NMP after NRP (NCT04744389) will 
hopefully provide further insight into this matter.

### NRP IN KIDNEY TRANSPLANTS

A few clinical series on KT after NRP have been published, 
mainly from cDCD donors (Tab. III).

#### Results of KTs with NRP

Foss et al. compared the outcome of 14 DCD kidneys 
recovered with NRP with 163 transplants from donation 
after brain death (DBD) and observed no differences in 
delayed graft function (DFG) and 1-year graft survival be-
tween the groups 25. Similarly, Miñambres et al. reported 
nonsignificant differences in DGF and short-term graft 
survival comparing DCD kidneys treated with NRP with 
DBD controls 26. However, these studies did not compare 
the use of NRP with the widespread SRR. Ramirez et al. 
found that DCD kidneys treated with NRP had a lower rate 
of DGF than those with SRR 27. In a recent Spanish nation-
wide propensity score analysis, Padilla et al. have found 
that NRP was associated with improved rates of DGF and 
1-year graft loss compared to SRR 28.

#### Selection of kidneys during NRP

For the acceptance of the kidneys during NRP, published 
reports mention macroscopic aspect, microscopic find-
ings, and urine production. However, the absence of urine 
output is frequent during NRP and should not per se lead 
to organ discard 3. Rodríguez-Villar et al. investigated the 
evolution of biochemical parameters during NRP between

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Study type</th>
<th>n</th>
<th>Donor fWIT (min)</th>
<th>MP</th>
<th>PNF</th>
<th>DGF</th>
<th>Graft survival (follow-up)</th>
<th>Patient survival (follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foss, 2018 25</td>
<td>Single-centre, retrospective, observational</td>
<td>NRP: 14 DBD: 163</td>
<td>NRP: 26.5 (20-49)</td>
<td>No</td>
<td>NRP: 0% DBD: 0%</td>
<td>NRP: 7.1% DBD: 4.9%</td>
<td>NRP: 93% DBD: 95% (1y)</td>
<td>N/A</td>
</tr>
<tr>
<td>Miñambres, 2017 26</td>
<td>Single-centre, retrospective, observational</td>
<td>NRP: 37 DBD: 36</td>
<td>NRP: 12 (10-19)</td>
<td>No</td>
<td>NRP: 5% DBD: 0%</td>
<td>NRP: 27% DBD: 33.3%</td>
<td>NRP: 91.8% DBD: 97.2% (18mo.)</td>
<td>N/A</td>
</tr>
<tr>
<td>Ravaioli, 2018 30</td>
<td>Single-centre, retrospective, observational</td>
<td>NRP: 5</td>
<td>NRP: 151.2 (40-325)</td>
<td>HOPE</td>
<td>NRP: 0%</td>
<td>NRP: 30%</td>
<td>NRP: 100% (6mo)</td>
<td>NRP: 100% (6mo)</td>
</tr>
<tr>
<td>Padilla, 2020 28</td>
<td>Nation-wide, retrospective, observational</td>
<td>NRP: 865 SRR: 1437</td>
<td>NRP: 13 (10-17) SRR: 18 (13-3)</td>
<td>NRP: 15.9% SRR: 7.3%</td>
<td>NRP: 4.8% SRR: 4.4%</td>
<td>NRP: 30.3% SRR: 48.4%</td>
<td>NRP: 93.1% SRR: 91.5% (1y)</td>
<td>NRP: 97.6% SRR: 95.6% (1y)</td>
</tr>
<tr>
<td>Ramirez, 2021 27</td>
<td>Single-centre, retrospective, observational</td>
<td>NRP: 22 SRR: 62 DBD: 98</td>
<td>NRP: 10 (10-35) SRR: 15 (11-28)</td>
<td>No</td>
<td>NRP: 4.55% SRR: 6.45% DBD: 10.20%</td>
<td>NRP: 36.36% SRR: 46.77% DBD: 20.41%</td>
<td>NRP: 91% SRR: 87% DBD: 84.4% (15mo.)</td>
<td>NRP: 77.27% SRR: 88.71% DBD: 85.71% (1y)</td>
</tr>
</tbody>
</table>

DBD: donation after brain death; DGF: delayed graft function; MP: machine perfusion; NRP: normothermic regional perfusion; PNF: primary nonfunction; SRR: super-rapid recovery
accepted and discarded kidneys in 38 uDCD donors. Neither creatinine nor lactate sequential values was a useful tool to predict kidney allocation. Nevertheless, the authors did not correlate any posttransplant outcome with these variables. Ravaoli et al. reported the preliminary experience with sequential NRP and HOPE in 10 KTs from cDCD in Italy. They reported a 30% incidence of DGF and did not find any correlation with creatinine or lactate values during NRP. However, they found that lactate levels in the HOPE perfusate were significantly higher in those cases developing DGF. Marginal kidneys are usually assessed histologically with the Karpinski score, which however does not take into account the ischemic insult. In this context, Zagni et al. have recently reported that ischemic alterations of the proximal tubule are correlated with functional recovery in DCD kidneys. Centres using ex-situ hypothermic perfusion report using renal resistance for further selection, though studies outside the NRP field have shown kidneys should not be discarded based upon renal resistance only.

**CONCLUSIONS**

NRP is beneficial for both the liver and the kidneys from the same donor. Therefore, NRP improves organ quality and maintenance before cold preservation, turns the DCD procedure into a more unhurried one, and allows the assessment of organ function following the warm ischemic injury. Different parameters inform about both graft viability and quality of the perfusion, but no strong correlation has been found between each parameter and the transplantation outcome. Nevertheless, a combination of macro-microscopic assessment, biochemical, and perfusion parameters has contributed to the selection of liver and kidney transplant series with excellent results.

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**Conflict of interest statement**

The Authors declare no conflict of interest.

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**Authors’ contributions**

RDC performed data collection, interpreted data, and wrote the paper; LC, MM, LP, RC, and IV performed data collection and reviewed the paper; AL and LDC critically reviewed the paper.

**Ethical consideration**

The present study did not imply any direct investigation on humans or animals. Formal consent was not required.

**References**


33 de Vries EE, Hoogland ER, Winkens B, et al. Renovascular resistance of machine-perfused DCD kidneys is associated with


