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Extracorporeal interval support for organ retrieval delivery regional experience with sharing equipe, equipment & expertise to increase conventionally defined as controlled donor pool in time of pandemic

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Abstract

Donation after circulatory death (DCD) programs are expanding in Europe, in the attempt to expand donors pool. Even in controlled DCD donors, however, a protracted warm ischemia time occurring in the perimortem period might damage organs, making these unsuitable for transplantation. Implementing a strategy of extracorporeal interval support for organ retrieval (EISOR), a regional reperfusion with normothermic, oxygenated blood provides a physiologic environment allowing extensive assessment of potential grafts, and potentially promotes recovery of native function. Here we report the results of a multi-center retrospective cohort study including 29 Maastricht Category III controlled DCD donors undergoing extracorporeal support in a regional DCD/EISOR Training Center, and in the network of referring In-Training Centers, under the liaison of the regional Transplant Coordination Center during COVID-19 pandemic, between March 2020 and November 2021. The study aims to understand whether a mobile, experienced EISOR team implementing a consistent technique and sharing its equipe, expertise and equipment in a regional network of hospitals, might be effective and efficient in implementing the regional DCD program activity even in a highly stressed healthcare system.

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Keywords
extracorporeal interval support for organ retrieval, normothermic regional perfusion, donation after circulatory death, organ donation, organ donor, transplantation

Introduction

Donation after confirmation of death according to circulatory criteria,[1] namely donation after circulatory death (DCD)[2] has evolved in recent years as an effective strategy to retrieve organs for transplantation, expanding donors pool while achieving results comparable with transplantation after confirmation of death according to neurological criteria.[3]

Donation after circulatory death donors are conventionally defined as controlled (cDCD), if permanent cessation of circulation is expected, or uncontrolled (uDCD), if irreversible circulatory arrest is unexpected, occurring after failure of resuscitation attempts.[4] Specifically, according to the modified Maastricht Classification,[4,5] category III DCD donors experience cardiac arrest (CA) after planned withdrawal of life-sustaining therapy (WLST), as life support is no longer considered as being in the best interests of the patient. Futility is typically related to devastating brain injury, not fulfilling criteria for brain death (BD).[1,4,6,7,8]

In DCD donors, however, a protracted condition of warm ischemia might damage organs, making these unsuitable for transplantation.[7]

In their recent consensus statement,[9] the European Society for Organ Transplantation (ESOT) recommends to use normothermic regional perfusion (NRP) of the abdomen cDCD procedures, rather than in-situ cooling and cold static storage, if ethical, technical and logistical requirements are met, to improve recipients outcome, potentially preventing some post-transplant complications.[9,10]

Normothermic regional perfusion, or extracorporeal interval support for organ retrieval (EISOR), according to the Extracorporeal Life Support Organization (ELSO) nomenclature,[11] is an in-situ strategy of postmortem splanchnic re-perfusion with normothermic blood between declaration of death and organ retrieval. The implementation of EISOR allows to limit warm ischemia time, to evaluate potential grafts function mimic in-vivo settings, and potentially to revert ischemic damage (timeline of events in DCD donors is detailed in Figure 1). Nevertheless, EISOR is a demanding approach requiring specific competencies and equipment in order to overcome technical challenges, fully respecting legal and ethical boundaries.[7,9]

We report a regional experience of EISOR delivery in Italy, aimed to share expertise and, when/as required, human and material resources. This organizational strategy resulted in an effective mean to persist in running and furtherly strengthen a DCD program despite resource constraints in time of pandemic. A positive impact on the availability of organ for the purpose of transplantation is reported.

Methods

We designed a multi-center, observational retrospective cohort study including all potential Maastricht Category III controlled DCD donors undergoing EISOR procedure

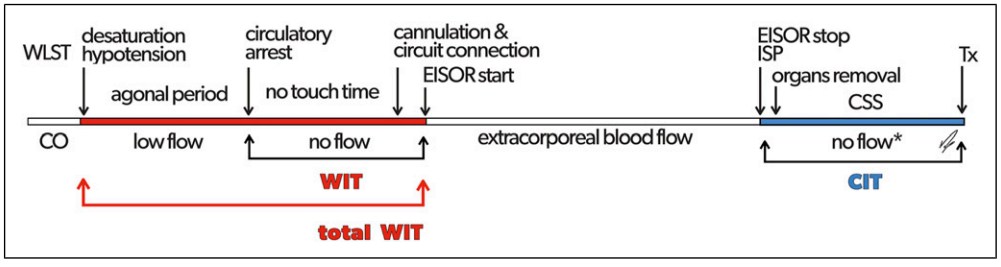

Figure 1. Timeline of events in Maastricht category 3 controlled DCD donors: a variable agonal period occurs after WLST preceding cardiac arrest, with hypotension and desaturation potentially contributing to the ischemic damage (functional warm ischemia). We consider warm ischemia time starting with agonal period, as mean arterial pressure drops below 50 mmHg or peripheral saturation drop below 50% (whichever occurring first). If EISOR is implemented, warm ischemia ends after decannulation and circuit connection, as oxygenated normothermic reperfusion starts. EISOR lasts till clamping of hepatic artery, when cold preservation solution is rapidly infused and topical cooling performed. Cold ischemia time (blue line) begins, persisting during cold static storage, which ends as grafts are reperfused in the recipient after transplantation; *cold ischemia time may be shortened or prevented if ex-vivo organ perfusion is performed. WLST: withdrawal of life-sustaining treatment; CO: cardiac output; WIT: warm ischemia time; EISOR: extracorporeal interval support for organ retrieval; ISP: in situ perfusion; CSS: cold static storage; CIT: cold ischemia time. (Note: Times not to scale).

managed or supervised by the extracorporeal membrane oxygenation (ECMO) team of the Bufalini Hospital - AUSL Romagna, Italy, during COVID-19 pandemic, between March 2020 and November 2021. The Research Ethics Committee board of the sub-region (Comitato Etico della Romagna - C.E.ROM) thoroughly evaluated the study protocol and approved data analysis and reporting.

The study aims to describe an organizational strategy based on mobile EISOR team implementing a consistent technique and sharing its expertise and equipment in a regional network of hospitals in order to implement the cDCD activity, effectively retrieving organs for transplantation, even in a highly stressed healthcare system during pandemic (Figure 2). A detailed description of the technique is provided.

Potential donors enrolment

Agreement on futility of persisting with life support achieved, eligibility for deceased organ donation according to circulatory procedure is fulfilled, strictly evaluating disease process, eventual comorbidities, recent and past history.[3]

A national registry is queried to assess if any statement about willingness to donate organs has been stated during patient's lifetime; otherwise, family members are asked about eventually known viewpoint of their beloved one and for consent. Family members are informed about treatment-limitation decisions[6,12] and both WLST and EISOR procedure, and their rationale, are explained in details. Moreover, in the attempt to facilitate an uncomplicated grief,[12] family presence at the bedside before WLST is encouraged.

To avoid any potential perceived or substantial conflict of interest, the organ procurement team is not involved in approaching the family about WLST,[3,6] in bedside care of the patient prior to declaration of death, in suspension of life support, nor in any phase of EISOR procedure. On the contrary, physicians involved in WLST and EISOR are not involved in checking if an

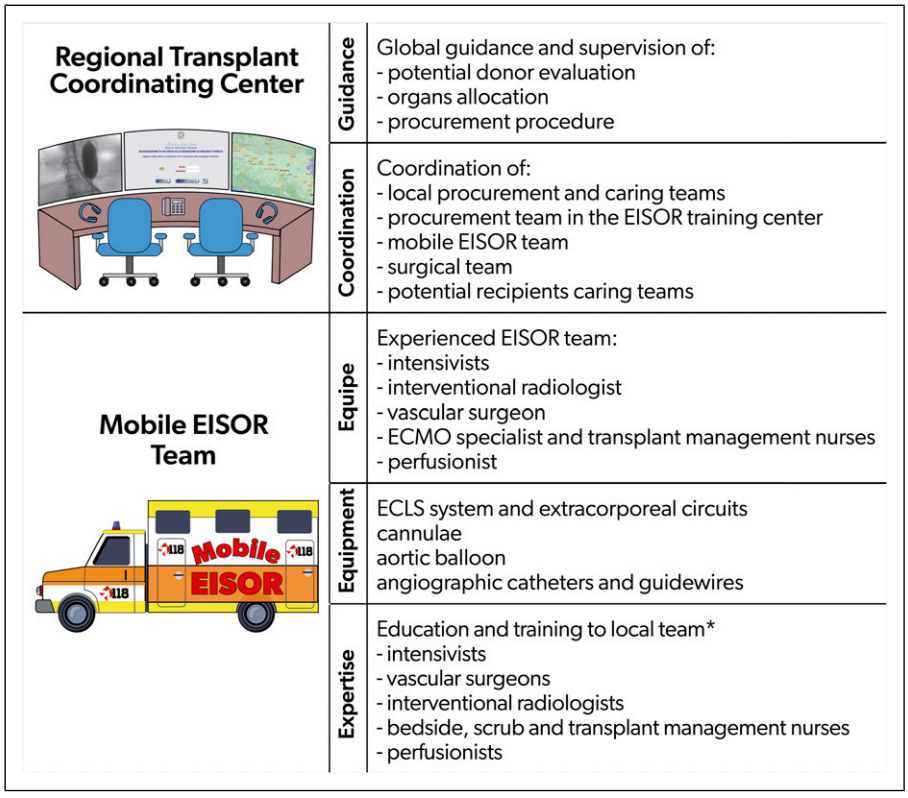

Figure 2. The Mobile Team, working under the supervision and according to the coordination of the Regional Transplant Reference Centre through the interposition of the Procurement Team of the EISOR Training Center, directly provided the 3 pillars of the EISOR delivery strategy: an experienced equipe, mobile when and as needed; the equipment required for safely performing the procedure, on a case-by-case assessment; EISOR education and training provided to the local in fieri team, in order to furtherly implement the program. *Education and trining were provided during procedures both in the mobile team center, to visiting equipes, and in referring centers. Dedicated workshops were also organized. EISOR: extracorporeal interval support for organ retrieval; ECMO: extracorporeal membrane oxygenation; ECLS: extracorporeal life support.

active donor decision has been registered, nor in asking for the family consent; moreover, physicians involved in EISOR are not involved in WLST.

Organizational strategy

Under the coordination of the Regional Transplant Reference Centre an experienced EISOR team including:

- intensivists skilled in ECMO cannulation and management, and in resuscitative endovascular balloon occlusion of the aorta (REBOA) catheter positioning;
- interventional radiologist;
- vascular surgeon;
- ECMO specialist nurses experienced in supporting cannulation procedure, even in the role of scrub

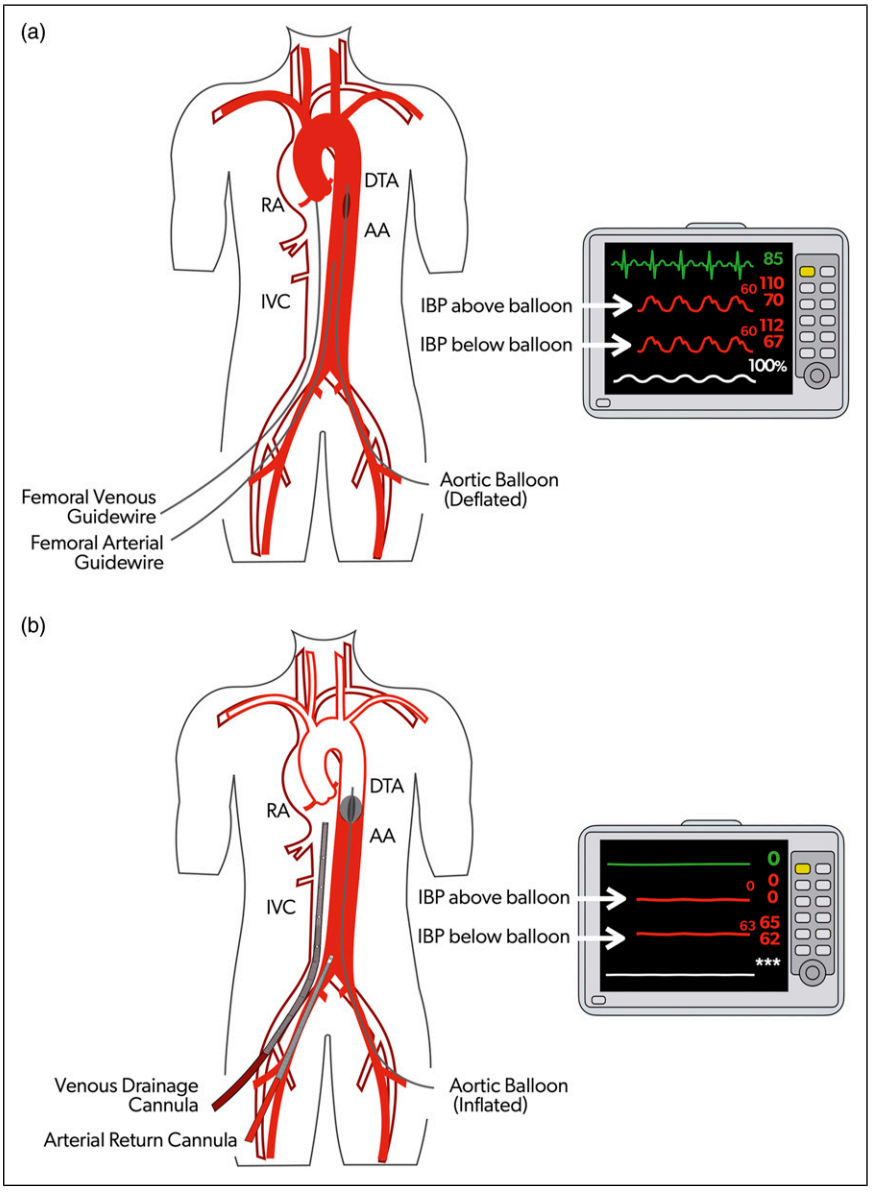

Figure 3. (a) Before withdrawal of life sustaining treatments (WLST) aortic balloon is inserted through the femoral artery, and kept deflated; contralateral femoral artery and vein are located trough guidewire insertion. Above and below-balloon invasive blood pressure (IBP) signals and waveforms are comparable; parameters are optimized to ensure end-organ delivery before WLST. (b) After cannulae positioning and circuit connection, aortic balloon is fully inflated and reperfusion is implemented. Mean arterial pressure is assessed through a catheter inserted in a vessel below the balloon, avoiding vessels below the arterial cannula, potentially hypoperfused; invasive blood pressure (IBP) waveform is flat due to continuous extracorporeal blood flow provided by the centrifugal pump. Above-balloon IBP and electrocardiographic monitoring is implemented throughout the procedure to early detect signs of eventual thoracic reperfusion (see text for details). bRA: right atrium; IVC: inferior vena cava; DTA: descending thoracic aorta; AA: abdominal aorta; IBP: invasive blood pressure.

nurses, and in managing patients on extracorporeal support;
- transplant management nurses interfacing with CRT for screening of the potential donor, definition of risk for recipient and organ allocation;
- perfusionist expert in emergent, resuscitative and procedural extracorporeal life support (ECLS) is alerted about potential donors fulfilling criteria to be enrolled in the EISOR pathway in the referral Center or in several Centers in the region not EISOR experienced. On a short notice, a mobile team is able to leave to performe the procedure in any of the referring Centers, and is prepared to provide all the eventually required equipment, including machine and devices (Figure 2). The CRT also alerts a mobile surgical equipe for retrieving organs.

In the referral center, or upon arrival in the referring center, a short briefing before procedure is run in order to share details on the case, discuss eventual expected challenges, define roles and timing. The mobile EISOR team-members are prepared to cover for any role, to train other health care professionals (HCPs) for playing roles or merely to supervise local HCPs who directly play the role, on a case-by-case base.

Aortic balloon catheter positioning and vessels location

Antemortem, as permitted by national law, an aortic balloon catheter, ER-REBOA (Prytime Medical Devices, Inc, Boerne, TX, USA), with integrated distal pressure monitoring is inserted through a 7F introducer sheath; as alternative, a sizing balloon, PTS-X (NuMED, Inc., Hopkinton, NY, USA) is inserted through a 8F introducer. The balloon was advanced to the lowest portion of the thoracic aorta, and kept deflated till EISOR initiation. The aim of the balloon is to prevent cerebral and cardiac reperfusion, completely occluding the vessel above celiac trunk during reperfusion (Figure 3).

Contralateral common femoral artery and femoral vein are located through guidewire insertion under ultrasonographic guidance. Proper balloon and guidewires positioning was confirmed and fluoroscopy or chest X-ray, depending on availability.

Withdrawal of life sustaining treatments

Withdrawal of Life Sustaining Treatments is performed discontinuing mechanical ventilation and estubating the patient, and terminating eventual inotropes, vasopressors or mechanical circulatory support. All the efforts are made to prevent and approach any eventual sign of pain and discomfort in the potential through the administration of analgesic and sedative medications. We consider warm ischemia time starting with agonal period, as mean arterial pressure (MAP) drops below 50 mmHg or peripheral saturation drops below 50% (whichever occurring first).

According to Italian law, death is declared after 20 min of touch time, with lack of cardiac electrical activity continuously recorded during this period.[13–16]

Cannulation and EISOR initiation

Following declaration of death, percutaneous cannulation of femoral vessels is performed over previously introduced guidewires: drainage cannula, VFEM Femoral Venous Cannula (Edwards Lifescience, Irvine, CA, USA), size 22 to 24 is inserted in the femoral vein and advanced to the inferior vena cava/right atrium junction, while return cannula, Optisite arterial cannula (Edwards Lifescience, Irvine, CA, USA), size 18 to 22, is inserted in the femoral artery and advanced to the common iliac artery or to aortic bifurcation. Extracorporeal circuit is then connected, and following full aortic balloon inflation, EISOR initiated (Figure 3).

Proper cannulae positioning is confirmed by ultrasonography or fluoroscopy or chest X-ray, depending on availability.

Extracorporeal system and re-perfusion settings

Depending on systems and circuit availability, abdominal reperfusion is implemented using alternatively a CardioHelp console, equipped with an Organ Donor Perfusion set integrating a QUADROX-i adult microporous polypropylene hollow fiber membrane lung (Maquet, Getinge, Rastatt, Germany), or a Xenios console equipped with an Emergency support set integrating a Hilite 7000 microporous polypropylene hollow fiber membrane lung (Xenios AG, Heilbronn, Germany). Both membrane lungs are connected to the HU 35 Heater Unit (Maquet, Getinge, Rastatt, Germany) water supply device.

The extracorporeal circuit is primed with a balanced isotonic crystalloid solution; no heparin, blood products, nor other additives are incorporated.

Priming is pre-warmed to 37° connecting the membrane lung to an heater unit to early restore a normothermic environment since EISOR initiation, and the whole procedure is run targeting normothermia, except for the time required to move the potential donor to the operating room (OR), in order to promote organ reconditioning process.

At EISOR initiation (time 0) and every 30 min during EISOR, post-membrane lung (POST-ML) blood sampling allows for strict monitoring of returning blood gas analysis.

Fresh gas flow (FGF) at start is set to 1:1 FGF/EBF ratio, and adapted according to blood gas analysis to target normocapnia ($P_{POST\text{-}ML}CO_2$ 35 to 45 mmHg) and progressive normalization of blood pH, or at least of reduction of the acidemia. The fraction of oxygen in the FGF to the device (FdO_2) is set to 50% at initiation, and adapted to target normoxemia ($P_{POST\text{-}ML}O_2$ 80 to 100 mmHg). Hyperoxemia, thus excessive FdO_2 and $P_{POST\text{-}ML}O_2$ and their potential impact on ischemia-reperfusion injury and vascular tone[17,18] are avoided, even if, to date, no diriment data exist.

The extracorporeal blood flow (EBF) is predicted in advance to maintain a cardiac index (CI) of 2.4 L/min/m^2 due to the normothermic condition,[19,20] for an halved body surface area (BSA):

$$(BSA \times 2.4)/2$$

Attempt is made to achieve the target blood flow at initiation. During EISOR pump flow rate is adjusted targeting a MAP above 60–65 mmHg. Moreover, to optimize oxygen delivery (DO_2), hemoglobin level is maintained is maintained above 9–10 g/dL.

At EISOR initiation (time 0) and every 30 min during EISOR, POST-ML blood is also tested to assess evolving kidney and liver function; urinary output is continuously evaluated.

An initial unfractioned heparin dosage of about 250 units pro-kilo, calculated based on ideal body weight (IBW)[21] is administered during the before re-perfusion: $^1/_3$ of the total dose is injected during the agonal period, to prevent peri-mortem vascular thrombosis, potentially impeding reperfusion, while the remaining $^2/_3$ after cannulation, to prevent catheter and intracircuit thrombosis.[22] According to the law, if the patient is at

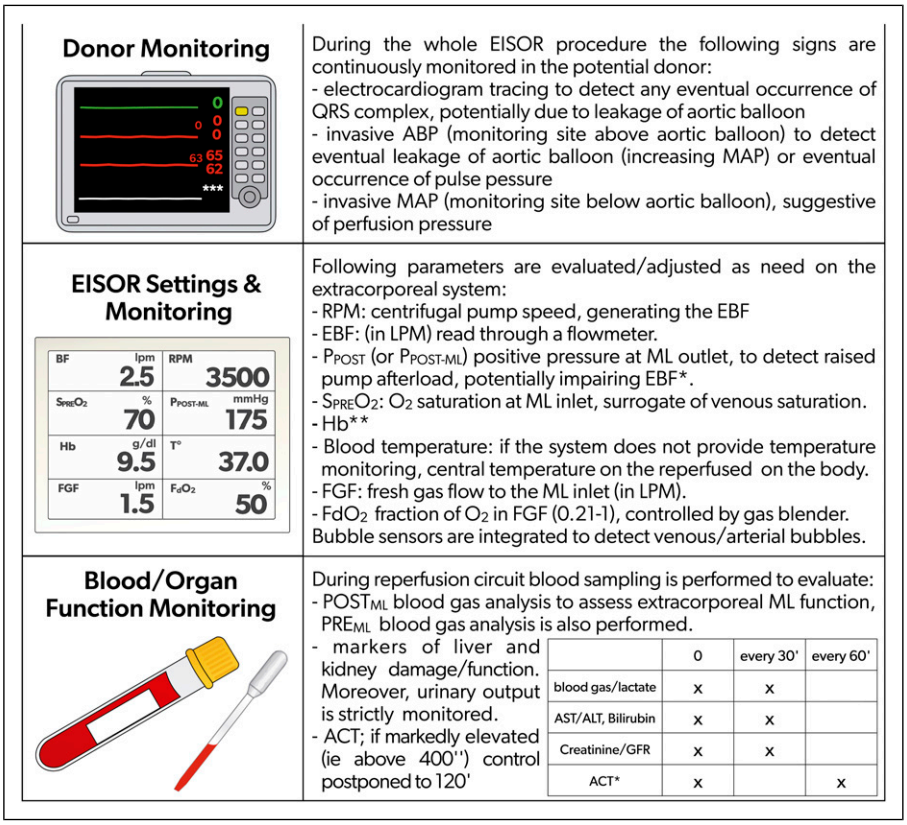

Figure 4. In this visual summary, main monitorings to be fulfilled on potential donor, on extracorporeal system, and on blood during EISOR, and reperfusion settings. EISOR: extracorporeal interval support for organ retrieval; ABP: arterial blood pressure; MAP: mean arterial pressure; RPM: revolutions per minute; EBF: extracorporeal blood flow; LPM: liters per minute; PPOST: post membrane lung pressure; ML: membrane lung; Hb: hemoglobin; FGF: fresh gas flow; ACT: activated clotting time; AST: aspartate aminotransferase; ALT: alanine transaminase; GFR: glomerular filtration rate. *The low-cost circuits used for EISOR do not usually include advanced integrated pressure monitorings, so a conventional pressure transducer is connected post-ML. **If the system does not provide Hb monitoring, this is assessed through blood sampling.

high bleeding risk, heparin administration does not occur before the declaration of death.[15,16]

During EISOR, bedside assessment of activated clotting time (ACT) is performed at time 0 and every 60–120" targeting a level above 300".

If any medication, including additional heparin, or if packed red blood cells transfusion is required, a femoral venous catheter is used for administration, if available; otherwise medications are administered on the extracorporeal circuit through a pre-membrane lung luer-lock connector. To avoid any dosage loss loss related to non-physiologic circulation, central venous catheters are only used to eventually infuse fluids.

Extracorporeal interval support for organ retrieval settings and monitorings are summarized in Figure 4.

Statistical analysis

Data are reported as mean ± standard deviation (SD) or median and interquartile range (IQR), as appropriate.

Results

Between March 2020 and November 2021 EISOR procedures have been implemented in 29 Maastricht Category III controlled DCD potential donors in a network including the referral center and 6 referring centers; 48.3% of the potential donors (n = 14) were female; age varied from a minimum of 32 years to a maximum of 84 years, with a mean age of 67.4 years (13 SD, 14 QR).

Total warm ischemia time, ranged from a minimum of 37 min to a maximum of 109 min, with a mean WIT of 51.5 min (13.8 SD, IQR 10). Median WIT is 49 min.

Among the 29 livers and 58 kidneys reperfused post-mortem with in-situ with normothermic oxygenated blood, 27 livers were retrieved, and 25 grafts transplanted (whole liver transplantation); 44 kidneys were retrieved, 34 grafts transplanted (16 single kidney transplantations - 9 double kidney transplantations). Most kidneys were not considered for retrieval if past

Table 1. Potential donor characteristics, WIT and EISOR variables, and outcome. Analysis of discrete variables are reported as the number (percent), with total number n = 29; continuous variables are reported as mean (standard deviation - SD/interquartile range IQR).

	n/mean (% - SD, IQR)
Female sex, *n* (%)	14 (48.3)
Potential donor age, mean (SD, IQR)°	67.4 (13, 14)
Total WIT*, minutes mean (SD, IQR)	51.5 (13.8, 10)
EISOR, minutes mean (SD, IQR)°	194 (56.1)
Lactate trend, mean (SD, IQR), mmol/L	−4 (3.09, 3.63)
pH trend, mean (SD, IQR)▪	0.28 (0.17, 0.22)
Liver retrieval *n* (%)▪	27 (93.1)
Liver transplantation *n* (%)	25 (86.2)
Liver discarded *n* (%)	4 (13.8)
Total WIT* for transplanted livers, minutes mean (SD, IQR)	51.2 (14.7, 9)
EISOR for transplanted livers, minutes mean (SD, IQR)°	201.5 (56.8, 57.5)
Liver recipients 6 and 12 months survival *n* (%)●	14 over 17 (82.4)
Kidneys retrieval *n* (%)	44 (75.9)
Kidney transplantation *n* (%)	34 (58.6)
Single kidney transplantation *n* (%)§	16 (47)
Double kidney transplantation *n* (%)§	9 (26.5)
Kidney discarded *n* (%)	24 (41.4)
Total WIT* for transplanted kidneys, minutes mean (SD, IQR)	48.7 (16.5, IQR 2.3)
EISOR for transplanted kidneys, minutes mean (SD, IQR)°	177.5 (42.6, 56.5)
Kidney recipients 6 months survival *n* (%)●	17 over 18 (94.4)

*total warm ischemia time defined as time elapsing from agonal period to reperfusion initiation, including the 20" of no touch time.
°Data referred to EISOR duration are missing for 3 runs (globally and for transplanted livers), and for 2 runs (for transplanted kidneys).
▪The trend for pH and lactate referred to timeframe elapsing from first blood sample at time 0, reperfusion initiation, to last blood sample, immediately before normothermic reperfusion interruption at time of cold in situ perfusion before retrieval (details in Figure 4).
●To date, 6 months and 1 year outcomes are available for 18 donors. Among recipients of these grafts, 14 over 17 liver recipients were alive at 6 and 12 months. In 2 of the 3 deceased, liver function was not compromized (causes of death sepsis and pulmonary mycotic infection). In one of the liver recipients death occurred due to severe pulmonary failure related to delayed graft function. 17 over 18 kidney recipients were alive at 6 months; of these one patient required renal replacement therapy; 12 months evaluation was not feasible for kidney recipients due to the lack of most follow up data.
§Percentages are over the total of kidney transplantation; double kidney transplantation percentage to be doubled to get 100%.

history of renal failure and/or if any sign of ongoing acute kidney injury (according to creatinine or urinary output criteria). Kidneys discarded after retrieval were excluded according to the results of intra-operative biopsy, performed on all organs.

For transplanted livers, total WIT ranged from a minimum of 37 min to a maximum of 109 min, with a mean WIT of 51.2 min (14.7 SD, 9 IQR), and median WIT 49 min. For transplanted kidneys, total WIT ranged from a minimum of 37 min to a maximum of 109 min, with a mean WIT of 48.7 min (16.5 SD, 6 IQR).

Normothermic reperfusion lasted from a minimum of 124 min to a maximum of 341 min, mean duration 194 min (56.1 SD, 61 IQR); median time 180 min.

For transplanted livers, reperfusion lasted from a minimum of 129 min to a maximum of 341 min, with a mean EISOR of 201.5 min (56.8 SD, IQR 57.5); median EISOR 192.5 min.

For transplanted kidneys, reperfusion lasted from a minimum of 124 min to a maximum of 263 min, with a mean EISOR of 177.5 min (42.6 SD, IQR 56.5); median EISOR 171 min.

Potential donors characteristics, procedure timings, lactate and pH trends, and outcomes are reported in Table 1.

In one potential donor, successful procedure was implemented, but the detection of a previously unrecognized lung lesion lead to retrieval discontinuation due to unacceptable risk for the recipient. In another case, organs were deemed as not suitable for transplantation due to macroscopic and microscopic appearance, despite a short warm ischemia time of 58 min.

Cannulation and aortic balloon positioning were successful in all the potential DCD donors; no mechanical complications involving the circuit or the cannulae were reported during EISOR. Drainage insufficiency was common both at reperfusion initiation and during the run with a mean of 2 episodes for procedure, managed with packed red blood cells or fluids, depending from hemoglobin level. For drainage failure occurring at initiation, careful drainage cannula manipulation under sonographic or fluoroscopy guidance was attempted before volume replacement.

No episodes of EISOR denial due to equipe or equipment unavailability occurred during the observation period.

Discussion

Donation after circulatory death programs are expanding in Europe, with most countries reporting an active program, including only controlled or uncontrolled, or both controlled and uncontrolled donors, to overcome shortage of donation after brain death (DBD) donors.[22] Additional countries report being planning to implement a DCD program in the next future.[22]

However, according to variable regulations and laws, variable practices are described. The most variable of these are the duration of the no-touch time (ranging from 5 to 30"), and the permitted antemortem interventions, including both cannulation and medication administration.[3,6,9,22] Moreover potential for ethical concerns is still perceived,[3,23–25] and an accurate and timely appropriate neuroprognostication is mandatory before WLST.[7,8]

In Italy, the National Transplant System is arranged in regional networks, involving a Regional Transplant Reference Centre (CRT) reporting to a National Transplant Center (CNT). In the Emilia-Romagna region first transplants from DCD donors occurred in 2016.[26] To enhance this activity, the CRT, located in Bologna, designated Bufalini Hospital ECMO Center as

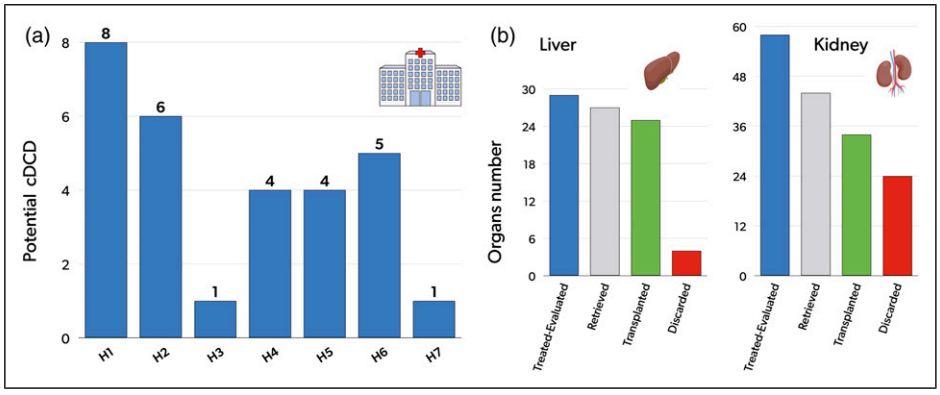

Figure 5. (a) Involved centers H1 to H7, and number of potential donors enrolled in each institution. (b). Potential grafts and their outcome. cDCD: controlled donation according to circulatory determination of death.

training center for the regional DCD program in 2018. The appointment aimed to supervise and support non-EISOR experienced centers in the region in joining the DCD program, implementing a cDCD program in their own ICUs. Since 2016, 45 EISOR procedures have been performed by our team or with the support of our team; of these, 16 took place in the pre-COVID-19 period (15 in-house, 1 in a referring center). After February 2020, so during pandemic, 29 procedures have been performed in a network of 7 hospital (Figure 5) retrieving a total of 27 livers, with 25 transplanted grafts, and 44 kidneys, 34 of these transplanted.

Since the beginning of coronavirus 2019 (COVID-19) pandemic in early 2020 the Emilia-Romagna region, in the north-west of Italy, has been severely hit by a surge of hospital and intensive care unit (ICU) admissions, sustained throughout subsequents waves, often overstrectching one of the most performing healthcare system in the whole country. Despite this challenging scenario, all the efforts have been made not to compromize the organ procurement program, for both DBD and DCD.

According to the Extracorporeal Life Support Organization (ELSO) guidelines for implementing ECMO during pandemic,[27] as feasible Centers within a region should consider pooling existing resources, including devices, disposables and team members, in order to optimize ECMO capacity. During pandemic, successful experiences of expanded ECMO capacity sharing experienced personnel, technologies and specific material resources,[28] or offering supervision and training by experienced ECMO providers to newly established centers have been reported worldwide.[29]

These recommendations and experiences could be interpreted in a broad sense and translated to any form of extracorporeal support, including EISOR. We demonstrated the feasibility of mobile EISOR team implementing normothermic reperfusion in cDCD donors according to a consistent strategy. To date, there is no consensus on reperfusion settings at EISOR initiation and during the run, and uneven blood flow/target MAP, and gas flow rates, as FdO_2 are used[9]: we implemented a technique based on physiological considerations derived form cardiopulmonary bypass guidelines and adapted to the post-circulatory arrest settings, according to experiences with extracorporeal cardiopulmonary resuscitation. During EISOR, a favourable trend for pH, normalizing, and lactate, dropping or consistently decreasing (Table 1) was observed, potentially suggesting effectiveness for these perfusion settings. However additional evidence is required, particularly to define an optimal length for reperfusion, in order to furtherly improve outcome without increasing the risk of potential EISOR related complications.

The team composition and approach was flexible during the experience, providing an "on demand" support tailored on referral centers needs/capability and resources, ranging from full team performing the full procedure to a 3 members team (1 intensivist, 1 nurse, 1 perfusionist) only providing supervision. The team, also providing a periprocedural theoretical and hands-on EISOR training, again tailored in specific needs, promoted a progressive autonomization of referring equipes, as required and if intended. Moreover, the supply of required devices and equipment, adapted on a case by case basis, allowed the optimization of resources utilization, leveraging economies of scope.

Thanks to the coordination of the Regional Transplant Center and of the local Procurement Team no potential donor was refused due to EISOR or surgical mobile team unavailability. In addition, thanks to the feasibility of sharing ECMO machines and circuits among Centers included in the network, no procedure for equipment unavailability has been denied, despite the increased number of ECMO cases in the region required to to support COVID-19 patients.

Limitations

Our findings should be interpreted with caution because of the observational nature of the study; moreover, the described procedure is adapted to the national regulations and laws; its application in a different setting requires a careful evaluation of allowed ante-mortem interventions. This experience is limited to retrieval of abdominal organ; retrieving thoracic organs in cDCD with prolonged no-touch times has also been reported. Considering that donors have only been enrolled in recents months complete follow-up data on recipients are, to date, missing. Moreover, mostly due to the fact that multiple laboratories in different Institutions were involved to perform intraoperative blood analysis, we are not able to consistently provide some of these data.

Conclusions

The implementation of an organizational strategy based on mobile EISOR team from a regional training center, sharing not only its equipe, but its expertise and equipment, according to the demand, in a regional network of hospitals might be feasible and efficient even in a highly stressed healthcare system during COVID-19 pandemic. In our experience, this strategy successfully expanded controlled DCD donors pool, with a positive impact on transplant programs. The willingness to donate organs of an increased number of potential donors has been fulfilled.

Strict supervision of the Regional Transplant Reference Centre, interposition of local Procurement Teams, extensive and respectful multidisciplinary collaboration among equipes and Centers, and a consistent strategy for normothermic regional reperfusion pivotal to optimize graft outcome and resources utilitization.

Future studies should address effectiveness of this strategy in analogous extended no-touch time settings, comparing data with a matched cohort of potential deceased donors fulfilling criteria for BD determination.

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