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Original Article

Uncontrolled donation after circulatory death lung transplantation program: Clinical outcomes and perspectives for implementation

Alessandro Palleschi [1,2], Alberto Zanella [1,3], Marco Sacchi [4], Riccardo Orlandi [1,2,*], Lorenzo Rosso [1,2], Sofia Donada [5], Federico Ambrogi [5], Sara Degiovanni [1], Davide Tosi [2], Paolo Mendogni [2], Ilaria Righi [2], Francesco Damarco [2], Margherita Cattaneo [2], Giulia Grossi [1], Letizia C. Morlacchi [1,6], Valentina Vaira [1,7], Massimo Cardillo [8], Franco Valenza [9], Mario Nosotti [1,2]

[1] *Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy*
[2] *Thoracic Surgery and Lung Transplantation Unit, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Milan, Italy*
[3] *Division of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Milan, Italy*
[4] *Regional Coordination Unit for Organ and Tissue Procurement, Agenzia Regionale Emergenza Urgenza, Lombardy, Italy*
[5] *Laboratory of Medical Statistics and Biometry "Giulio A. Maccacaro," Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy*
[6] *Respiratory Unit and Cystic Fibrosis Adult Centre, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy*
[7] *Division of Pathology, Fondazione IRCCS Ca' Granda-Ospedale Maggiore Policlinico, Milan, Italy*
[8] *Transplantation Immunology, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico of Milan, Milan, Italy*
[9] *Division of Anesthesia and Intensive Care, Fondazione IRCCS Istituto Nazionale Dei Tumori, Milan, Italy*

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ABSTRACT

Lung transplantation (LT) remains limited by the scarcity of suitable donor organs. Uncontrolled donation after circulatory death (uDCD) is a promising yet underutilized source due to logistical barriers. This study presents a prospective, single-center experience with uDCD LT. From 2014 to 2025, all uDCD lung referrals at our center in Milan were prospectively assessed. Lungs were preserved via open-lung ventilation without in situ cooling, followed by ex vivo lung perfusion (EVLP) evaluation. Clinical outcomes were analyzed, and regional donor potential was explored using 2023 cardiac arrest data from Lombardy. Among 72 referred donors, 30 met eligibility criteria, 25 proceeded to

Abbreviations: cDCD, controlled donation after circulatory death; CFS, CLAD-free survival; CI, confidence interval; CLAD, chronic lung allograft dysfunction; CPAP, continuous positive airway pressure; CPR, cardiopulmonary resuscitation; DBD, donation after brain death; DCD, donation after circulatory death; ECMO, extracorporeal membrane oxygenation; eCPR, extracorporeal cardiopulmonary resuscitation; EVLP, ex vivo lung perfusion; ICU, intensive care unit; IQR, interquartile range; LAS, lung allocation score; LT, lung transplantation; OS, overall survival; PGD, primary graft dysfunction; uDCD, uncontrolled donation after circulatory death; WIT, warm ischemia time.

* Corresponding author. Department of Thoracic Surgery, University of Milan, Via Festa del Perdono, 7, 20122 Milan, Italy.
E-mail address: riccardo.orlandi@unimi.it (R. Orlandi).

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recovery, and 18 were transplanted after EVLP (72% post-EVLP utilization rate). The 30-day and 1-year survival rates were 94.4% (95% confidence interval [CI] 83.9%-100.0%) and 83.3% (95% CI 57.5%-99.8%), respectively. Primary graft dysfunction grade 3 within 72 hours occurred in 16.7% (95% CI 6.4%-34.8%), while chronic lung allograft dysfunction developed in 27.8% (95% CI 13.2%-50.3%). Median warm ischemia time was 240 minutes. Regional analysis identified 119 uDCD-eligible cases in 2023, 20 activations, with 5 transplants performed, and major untapped potential. uDCD LT is feasible and effective. Our simplified normothermic strategy is operationally scalable and yields outcomes comparable to those historically reported from conventional LT. Broader implementation, supported by regional coordination, could substantially expand the lung donor pool.

1. Introduction

Lung transplantation (LT) is an established treatment option for patients with end-stage respiratory diseases.[1] Nevertheless, the persistent shortage of suitable donor lungs remains the principal limiting factor to its broader application.[2] To address this issue, donation after circulatory death (DCD) has garnered increasing attention as a complementary source to donation after brain death (DBD).[3]

While controlled DCD (cDCD, eg, Maastricht category III) has become a well-established pathway for lung procurement, uncontrolled DCD (uDCD, Maastricht categories I-II) remains underutilized, primarily due to logistical and organizational challenges.[4]

Pioneering centers in Spain and our own in Italy have demonstrated the feasibility of LT from uDCD donors, highlighting its potential to expand the donor pool.[5-8] More recently, successful experiences have also been reported by North American groups.[9] Despite these advances, the overall utilization rate of uDCD lungs remains low, hindered by concerns regarding prolonged warm ischemia time (WIT) and the complexity of preservation techniques.[10] Aside from that, lungs from uDCD donors may offer functional advantages over those from DBD and cDCD donors, as these individuals are not exposed to the inflammatory cascade triggered by brain death and to the deleterious effects of prolonged hospitalization.[11,12]

Herein, we present our 10-year experience with LT from uDCD donors at a single center in Milan, using a preservation strategy based on in situ normothermic ventilation (without topical cooling), followed by ex situ evaluation with ex vivo lung perfusion (EVLP).[13] The primary objective of this report is to evaluate both the short- and long-term clinical outcomes of our uDCD LT program. In addition, we aim to identify its strengths and limitations, and to assess its potential scalability at the local level, through an in-depth analysis of 2023 cardiac arrest data in the Lombardy region, selected as a sample year.

2. Materials and methods

2.1. Study design

This is a single-center, prospective cohort study conducted at the IRCCS Foundation Ca' Granda – Ospedale Maggiore Policlinico in Milan, Italy. We analyzed LT outcomes from uDCD donors over a 10-year period (2014-2025).

All referred potential donors were prospectively and systematically documented. Data were collected for each case in which uDCD lungs were evaluated for transplantation. The study was conducted in accordance with institutional and national ethical guidelines, with approval obtained from the local ethics committee and registration on ClinicalTrials.gov (NCT02061462, protocol 749_2016bis).

To evaluate the broader applicability of the uDCD approach, we also conducted a regional analysis by reviewing cardiac arrest cases in Lombardy in 2023, used as a reference period, identifying individuals potentially eligible for lung procurement based on our protocol.

2.2. Donor selection, lung procurement, and recipient allocation

Our donor selection criteria, lung procurement procedures, and preservation strategy have been previously described[13] and are summarized here.

Potential uDCD donors were identified following either in-hospital or out-of-hospital cardiac arrest in cases where full conventional cardiopulmonary resuscitation (CPR) had been administered and ultimately deemed unsuccessful by the medical team. Eligibility criteria for activation included:

- Age $\leq$65 years
- Witnessed cardiac arrest
- No-flow time (time from cardiac arrest to the start of CPR) $\leq$15 minutes
- Low-flow time (time resuscitation maneuvers are maintained) $\leq$60 minutes

- No history of chronic pulmonary disease or active pulmonary infection
- No evidence of massive lung contusion, aspiration, or systemic sepsis
- No history of active or recent malignancy
- No history of active or recent systemic infection (eg, HIV, hepatitis B/C)

Traumatic cardiac arrests were included only when thoracic injuries were minor and did not compromise lung integrity. All donors were classified as Maastricht category II and underwent only-lung procurement without abdominal normothermic regional perfusion. Emergency department or intensive care unit (ICU) coordinators directly notified the recovery team through a regional call system. All donors were preliminarily assessed through chest X-rays and bronchoscopy to evaluate eligibility before procurement, eventually supplemented with chest CT-scan when technically and logistically feasible.

Lung procurement was performed using an open-lung normothermic strategy, with a recruitment maneuver in supine position and continuous positive airway pressure (CPAP) of 10 cmH_2O and 100% FiO_2 via existing endotracheal tube after clinical confirmation of death (5 minutes of "no-touch" period) until declaration of death according to circulatory criteria (20 minutes of flat electrocardiogram, as required by national regulation), followed by low-frequency protective ventilation (PEEP 8-10, I: E 1:1, FiO_2 100%, TV 6 mL/kg respiratory rate 4 breaths/min).[14] Only cases with an endotracheal tube already in place at death declaration were considered. On-site physicians managed the donor throughout the whole procedure, while a specialized team from our transplant center was dispatched to recover the lung block and transport it back to the base center. There, suitability for transplantation was determined based on EVLP evaluation, assessing oxygenation, pulmonary compliance, pulmonary vascular resistance, and airway pressures, in accordance with established criteria.[15]

Recipient allocation followed the usual procedure, based on the lung allocation score (LAS),[16] except for the first case, which occurred before LAS implementation and involved a rapidly deteriorating recipient. All recipients provided specific, additional informed consent for receiving a uDCD lung, both at the time of waitlisting and upon admission for transplantation. Obviously, recipients were required to fulfill the standard eligibility criteria for LT, according to the International Society for Heart and Lung Transplantation.[17] Standard perioperative management protocols were applied, including intraoperative extracorporeal membrane oxygenation (ECMO) when indicated.

2.3. Outcome measures

2.3.1. Primary outcomes

- Thirty-day mortality
- Overall graft survival

2.3.2. Secondary outcomes

- Duration of mechanical ventilation
- ICU length of stay
- Hospital length of stay
- Incidence of primary graft dysfunction (PGD) grade 3 within 72 hours, determined per the International Society for Heart and Lung Transplantation criteria[18] by 2 independent transplant physicians, and adjudicated by a third in case of discrepancies
- Development of chronic lung allograft dysfunction (CLAD)
- Incidence of airway complications
- 1-year and overall survival (OS)

2.4. Ischemia time definitions

- WIT: from cardiac arrest to in situ lung flushing
- Cold ischemia time: from lung flushing initiation to implantation start, excluding EVLP time
- Intraoperative WIT: from the start of graft implantation to reperfusion
- Total ischemia time: from cardiac arrest to reperfusion (EVLP time excluded)
- Total preservation time: from end of CPR to reperfusion (EVLP time included)

2.5. Regional assessment of uDCD potential in Lombardy

To estimate the potential of implementing our protocol, we analyzed out-of-hospital and in-hospital cardiac arrest cases reported across Lombardy in 2023. Regional data were extracted from prospectively collected emergency medical services and hospital administrative databases using ICD-10 and procedural codes, cross-checked with regional registry entries. Cases were screened using the same eligibility criteria applied at our center. Patients with oncologic history were excluded, except in cases of remote or nonmetastatic cancers, which are not absolute contraindications in clinical practice.

We also reviewed ECMO-coded cases from the regional database to estimate the number of patients who, though initially targeted for extracorporeal cardiopulmonary resuscitation (eCPR) according to regional eCPR criteria (Supplementary Methods), might have been eligible as uDCD donors if excluded from eCPR. These cases were filtered using a key operational criterion: hospital arrival time within 60 minutes from arrest (time-to-door).

2.6. Statistical analysis

Descriptive statistics were computed for all analyzed features. Categorical variables were reported using absolute and relative frequencies, whereas numerical variables were reported using median and interquartile range (IQR).

OS and CLAD-free survival (CFS) were analyzed using time-to-event techniques. In these analyses, the time at risk was calculated from the date of transplantation. For OS, the time at risk was calculated up to the date of death or last follow-up, whichever occurred first; for CFS, the time at risk was calculated until the date of death, CLAD, or last follow-up, whichever occurred first.

The Kaplan-Meier estimator was used to estimate survival probabilities for each survival outcome. Median survival times and estimates of survival probabilities at specific time points were reported with 95% confidence intervals (CIs).

The significance level was set at alpha equal to 0.05 for all analyses. Statistical analyses were performed using R statistical software (version 4.3.2).

3. Results

3.1. Study population

From May 2014 to May 2025, a total of 72 uDCD donors were identified and evaluated by our recovery team, resulting in 18 lung transplants performed at our center (Fig. 1). The overall utilization rate was 25%, which increased to 72% when considering only the lungs that were actually procured and evaluated through EVLP. It is noteworthy that, following the first successful transplantation in 2014, the program was suspended until 2017 due to organizational constraints. Excluding the suspension interval, the uDCD program accounted for 8.5% (18/212) of the whole transplantation activity at our center. Organs were excluded for the following reasons: heavy smoking (>40 packs/y, 7 cases), active malignancy (5 cases), SARS-CoV-2 positivity (3 cases), prolonged warm ischemic time (8 cases), logistical impediments (11 cases), family refusal (9 cases), major lung contusions (4 cases), and unsatisfactory performance during EVLP (7 cases).

Within transplanted grafts, the median age of the uDCD donors was 54.5 years, with a predominance of male donors (94.4%). Five donors were active smokers, 2 were former smokers, and the remaining were never-smokers. Donor demographic details are reported in Table 1. All donors were procured in peripheral "spoke" centers within a mean distance of 39 km from our "hub" center, with the furthest being 95 km away.

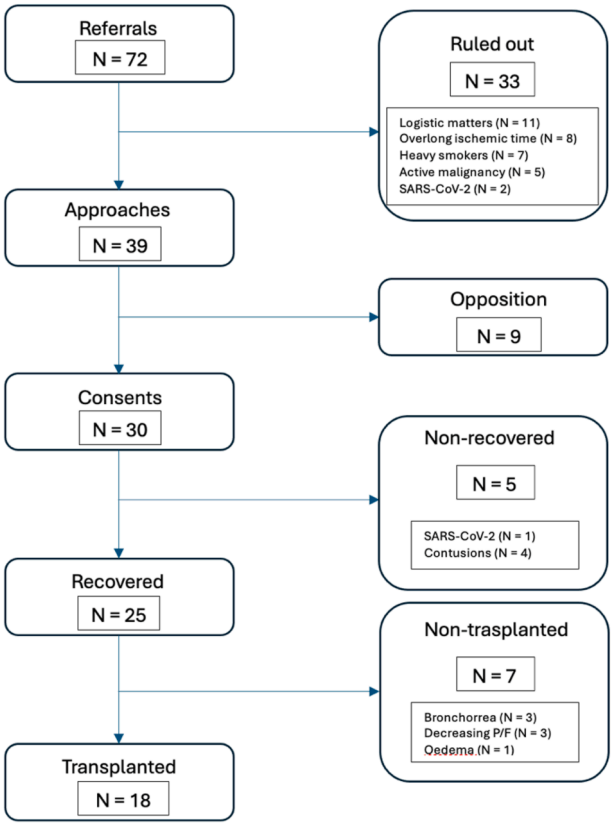

Figure 1. Ten-year cohort flowchart.

Table 1
Characteristics of recovered and transplanted donors' lungs.

Variable		N
Sex (male), n (%)		17 (94.4)
Age, y, median (IQR)		54.5 (11.5)
BMI, kg/m^2, median (IQR)		26.7 (5.9)
Blood group, n (%)		
	0	8 (44.4)
	A	8 (44.4)
	B	2 (11.1)
	AB	0 (0.0)
Comorbidities, n (%)		10 (55.6)
Smoking history, n (%)		
	No	11 (61.1)
	Former	2 (11.1)
	Yes	5 (27.8)
Smoking history (pack-years) of smokers and former smokers, n		
	<20	4
	20-39	2
Chest X-ray, n (%)		
	Clear	15 (83.3)
	Minor	2 (11.1)
	Opacity <1 lobe	1 (5.6)
	Opacity ≥1 lobe	0 (0.0)
Donor secretions, n (%)		
	None	8 (47.1)
	Minor	8 (47.1)
	Moderate	1 (5.9)
	Major	0 (0.0)
Recovered organs, n (%)		
	Lung only	17 (94.4)
	Lung, bones	1 (5.6)
Thrombi at retrograde perfusion, n (%)		2 (11.1)
Sex mismatch (male D to female R), n (%)		4 (22.2)

IQR, interquartile range.

3.2. Ischemic and preservation times

Figure 2 shows the preservation times in cases that proceeded to transplantation. The median WIT was 240 minutes (IQR 56.7); the cold ischemia time was 642 minutes (IQR 235.5) for the first implanted lung and 835 minutes (IQR 166) for the second implanted lung. The intraoperative WIT averaged 69 minutes (IQR 22) for the first lung and 88 minutes (IQR 24) for the second lung. The total ischemia time was 900 minutes (IQR 279) for the first lung and 1095 minutes (IQR 242) for the second lung. The total preservation time was 1154 minutes (IQR 177) for the first lung and 1372 minutes (IQR 216) for the second lung. The median EVLP duration was 240 minutes (IQR 29).

3.3. Recipient outcomes

Recipient demographics and perioperative characteristics are summarized in Tables 2 and 3, respectively. Overall, 27.8% were female, the median age was 56 years; main indications for transplant were cystic fibrosis (27.8%) and chronic obstructive pulmonary disease (27.8%). The median LAS was 41.9. All the recipients underwent bilateral LT, 77.8% through Clamshell approach, the remaining through bilateral anterior thoracotomy; intraoperative ECMO was applied in 61.2% of cases. The median follow-up was 18.6 months (557 days). Only 1 patient died within 30 days posttransplant due to unexpected acute rejection.[19]

PGD grade 3 occurred in 16.7% (95% CI 6.4%-34.8%) of recipients within the first 72 hours.

The median ICU length of stay was 3 days, and the median hospital stay was 29 days. Airway complications occurred in 2 recipients (11.1%), one requiring endoscopic dilatation (5.5%), and the other one a stenting (5.5%).

CLAD developed in 5 patients (27.8%; 95% CI 13.2%-50.3%), with a median onset of 986 days posttransplant. The Kaplan-Meier estimated CFS rates at 1, 3, and 5 years were 64% (95% CI 44.5%-92%), 53% (95% CI 32%-88.7%), and 42.6% (95% CI 21.8%-83.5%), respectively (Table 4). The median CFS time was 41 months (Supplementary Fig. S1).

Survival rates (Table 5) were 94.4% (95% CI 83.9%-100.0%) at 30 days, 88.9% (95% CI 74.4%-100.0%) at 90 days, and 83.3% (57.5%-99.8%) at 1 year, with 3 deaths recorded in the first year. The 3-year survival rate was 72.2% (95% CI 48.5%-96.2%), while the median OS had not yet been reached at the time of analysis (Supplementary Fig. S2). Because none of the recipients underwent retransplantation during the study period, OS was assumed to overlap with overall graft survival. A total of 5 deaths were observed during the follow-up period, as detailed in Table 6.

3.4. Regional potential assessment

As of 2023, 9 centers in Lombardy actively reported potential uDCD donors, within a total of 14 active centers. That year, a total of 12 154 cardiac arrests were recorded in the region. Among these, 119 cases met eligibility criteria for lung procurement (Fig. 3). Twenty were activated, leading to 5 successful lung transplants, corresponding to a utilization rate of 25% (Fig. 4).

The primary reasons for nonactivation were that in 62% of cases, patients were transported to hospitals not participating in uDCD programs; in 21% of cases, they were admitted to active centers but outside the operational time windows.

An additional 30 cases initially labeled for ECLS arrived >60 minutes after the call and were excluded from the primary analysis, though they may represent an additional potential donor pool.

Among the 119 eligible cases, the mean age was 55.7 years; 80.7% were male (n = 96), and 19.3% were female (n = 23). The mean time to first emergency medical services arrival was 12 minutes, and the mean time to hospital arrival was 59 minutes and 27 seconds. Further exclusions occurred following emergency department reassessment, although detailed clinical information was unavailable.

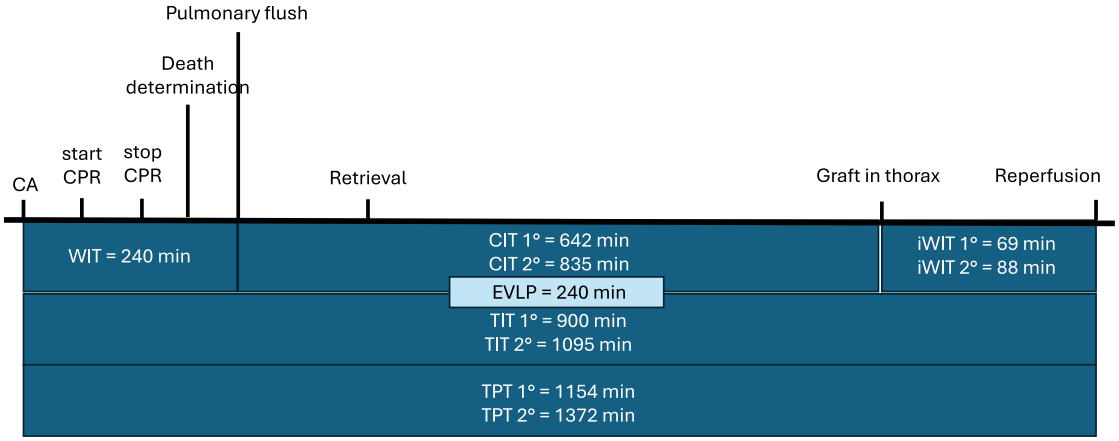

Figure 2. Uncontrolled donation after circulatory death (uDCD) preservation times. CA, cardiac arrest; CIT, cold ischemia time; CPR, cardiopulmonary resuscitation; EVLP, ex vivo lung perfusion; iWIT, intraoperative warm ischemia time; TIT, total ischemia time; TPT, total preservation time; WIT, warm ischemia time.

Table 2
Characteristics of recipients.

Variable		N
Sex (male), n (%)		13 (72.2)
Age, y, median (IQR)		56.0 (23.5)
BMI, kg/m^2, median (IQR)		21.2 (4.7)
Blood group, n (%)		
	0	5 (29.4)
	A	9 (52.9)
	B	2 (11.8)
	AB	1 (5.9)
Disease, n (%)		
	Cystic fibrosis	5 (27.8)
	COPD	5 (27.8)
	Bronchiectasis	2 (11.1)
	IIP	1 (5.6)
	IPF	3 (16.7)
	Sarcoidosis	1 (5.6)
	HPc	1 (5.6)
LAS, median (IQR)		41.9 (9.4)
Urgent transplantation, n (%)		1 (5.6)
Comorbidities, n (%)		17 (94.4)
Diabetes, insulin-dependent, n		4
Colonization, n (%)		9 (52.9)
Bacteria, n		
	Pseudomonas aeruginosa	7
	MSSA	1
	MRSA	1
	Mycobacterium kansasii	1
	Klebsiella pneumoniae	1
PAPm, median (IQR)		23.0 (7.2)
$PaCO_2$, median (IQR)		46.5 (8.0)
DLCO, median (IQR)	CF	52 (4.0)
	COPD	23 (7.5)
	IPF	28 (8.0)
	Others	22 (5.5)
FEV1%, median (IQR)	CF	23.5 (3.5)
	COPD	18 (4.0)
	IPF	40 (7.5)
	Others	30 (6.5)
6MWD, median (IQR)		355.0 (117.7)
Supplemental O_2 at rest, median (IQR)		2.0 (1.2)
Assisted ventilation, n (%)		
	No	1 (5.6)
	Continuous noninvasive ventilation	17 (94.4)
ECMO bridge to transplantation, n (%)		1 (5.6)

Continuous noninvasive ventilation refers to nocturnal or continuous bilevel support prior to transplantation. "Urgent transplantation" indicates listing under emergency priority due to rapid respiratory decline.
CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; HPc, chronic hypersensitivity pneumonitis; IIP, idiopathic interstitial pneumonia; IPF, idiopathic pulmonary fibrosis; IQR, interquartile range; LAS, lung allocation score; DLCO, diffusing capacity of the lungs for carbon monoxid; PAPm, medium pulmonary artery pressure; 6MWD, 6-minutes walking test; MRSA, meticilline-resistant Staphylococcus areus; $PaCO_2$, partial pressure of arterial carbon dioxide; FEV1, forced expiratory volume in 1 second.

4. Discussion

This study presents our 10-year experience with LT from uDCD donors. Over this period, 18 lung transplants were successfully performed out of 72 uDCD donor referrals, demonstrating the feasibility and effectiveness of this strategy in our center. The crude utilization rate was 25%, which increased up to 72% when considering only lungs that were actually procured. In our cohort, the use of a standardized preservation protocol, combining in situ normothermic ventilation and EVLP, proved its reliability for viability assessment and its potential contribution to favorable posttransplant outcomes.

A similar protocol was pioneered in the United States,[20] but this program was constrained by regulatory and logistical barriers, including the requirement for prior donor authorization and limited availability of surgical staff.

Since the first successful uDCD LT by Steen et al in 2001,[21] the field has evolved considerably. Nonetheless, its clinical adoption remains limited, primarily due to persistent legal, ethical, technical, and logistical challenges.[22] Furthermore, broader adoption of uDCD programs outside universal health care systems is further hindered by legal and ethical mistrust, particularly in opt-in frameworks.[23]

Our findings contribute to the growing body of evidence indicating that, with appropriate selection and preservation strategies, uDCD lungs can yield outcomes comparable, or even superior, to those from cDCD or DBD donors.[7]

An often-overlooked advantage of uDCD lungs is the absence of injuries associated with prolonged ICU stays and brain

Table 3
Intraoperative and postoperative characteristics of recipients.

Intraoperative	Variable		N
	Incision, n (%)		
		Clamshell	14 (77.8)
		Bilateral anterior thoracotomy	4 (22.2)
	Resection, n (%)		2 (11.1)
	EC, median (IQR)		4.0 (6.0)
	FFP, median (IQR)		2.0 (3.0)
	PLT, median (IQR)		1.0 (2.0)
	Intraoperative extracorporeal support, n (%)		
		No	7 (38.9)
		Veno-arterial ECMO	10 (55.6)
		Veno-venous ECMO	1 (5.6)
	WIT (min), median (IQR)		240.0 (56.7)
	CIT, first lung (min), median (IQR)		642.0 (235.5)
	CIT, second lung (min), median (IQR)		835.0 (166.0)
	TIT, first lung (min), median (IQR)		900.5 (278.5)
	TIT, second lung (min), median (IQR)		1095.0 (242.0)
	TPT, first lung (min), median (IQR)		1154.5 (176.7)
	TPT, second lung (min), median (IQR)		1372.5 (216.0)
	WIT, first lung (min), median (IQR)		68.5 (22.2)
	WIT, second lung (min), median (IQR)		88.0 (24.0)
	EVLP/OCS (min), median (IQR)		240.0 (28.7)
Postoperative			
	PGD 24-72 h grade 3, n (%)		3 (16.7)
	Postoperative mechanical ventilation (d), median (IQR)		2.0 (1.0)
	Postoperative extracorporeal support, veno-venous ECMO, n (%)		3 (17.6)
	Tracheo, n (%)		2 (11.1)
	ICU stay (d), median (IQR)		3.0 (5.7)
	ICU readmission, n (%)		3 (17.6)
	Hospital stay (d), median (IQR)		29.0 (28.2)
	Airway complications, n (%)		2 (11.1)
	Airway complications, side, n	Left	0
		Right	2
	Airway complications, treatment, n	Dilatation only	1
		Dilatation + stent	1
	Best FEV1%, median (IQR)		80 (38.7)
	ALAD, n (%)		5 (27.8)
	CLAD, n (%)		5 (27.8)

(*continued on next page*)

Table 3 (*continued*)

Intraoperative	Variable		N
	CLAD type, n		
		BOS	3
		BOS + RAS	2

CIT, cold ischemia time; CLAD, chronic lung allograft dysfunction; ECMO, extracorporeal membrane oxygenation; EVLP, ex vivo lung perfusion; ICU, intensive care unit; IQR, interquartile range; PGD, primary graft dysfunction; TIT, total ischemia time; TPT, total preservation time; WIT, warm ischemia time; FFP, fresh frozen plasma; PLT, platelets; ALAD, acute lung allograft dysfunction; BOS, bronchiolitis obliterans syndrome; RAS, restrictive allograft syndrome; FEV1, forced expiratory volume in 1 second; OCS, organ care system.

Table 4
Kaplan-Meier estimated CFS rates.

CFS											
Median survival time (mo)			1-year survival probability			3-year survival probability			5-year survival probability		
Est	95% CI		Est.	95% CI		Est.	95% CI		Est.	95% CI	
41.4	11.9	NA	0.639	0.445	0.920	0.533	0.320	0.887	0.426	0.218	0.835

95% CI = 95% confidence interval, lower and upper limits.
CFS, chronic lung allograft dysfunction–free survival; Est., estimate.

Table 5
Kaplan-Meier estimated OS rates.

OS													
Median survival time (mo)			30-day survival probability			90-day survival probability			1-year survival probability			3-year survival probability		
Est.	95% CI		Est.	95% CI		Est.	95% CI		Est.	95% CI		Est.	95% CI	
NA	16.0	NA	0.944	0.844	1.000	0.885	0.748	1.000	0.833	0.575	0.998	0.722	0.483	0.962

95% CI = 95% confidence interval, lower and upper limits.
Est., estimate; OS, overall survival.

Table 6
Deaths occurring during the follow-up period.

Patient	Sex	Age (y)	Disease	Hospital stay (d)	Survival (d)	Cause of death	Graft related	Transplant related
1	M	30	CF	24	24	Acute dysfunction	Yes	No
2	M	56	COPD	22	488	CLAD	Yes	No
3	F	65	IPF	30	126	SAH	No	No
4	M	61	IPF	77	367	Sepsis	No	No
5	F	63	IPF	53	76	Pneumonia	No	Yes

CF, cystic fibrosis; CLAD, chronic lung allograft dysfunction; COPD, chronic obstructive pulmonary disease; IPF, idiopathic pulmonary fibrosis; SAH, subarachnoid hemorrhage.

death–related systemic inflammation. These donors typically avoid exposure to catecholamine surges, neurogenic edema, and aggressive fluid management, all of which can impair graft quality.[11,12] As a result, despite the inherent ischemic burden, uDCD lungs may exhibit more favorable histologic and functional profiles than those from traditional DBD or cDCD donors.

Another key strength of our protocol lies in its operational simplicity and scalability. Unlike strategies involving in situ cooling[24] or abdominal normothermic regional perfusion,[25] our approach—based on open-lung protective ventilation, CPAP, and recruitment maneuvers—requires no specialized devices and can be implemented even in nontertiary hospitals. This design enhances its reproducibility and transferability across a regional or national network. Similar decentralized models have been successfully validated in Canada, further confirming the effectiveness of this streamlined preservation strategy.[2] In contrast to the Toronto experience, where the median time to initiation of mechanical ventilation was 166 minutes, our protocol maintains ventilation almost continuously—interrupted only by the 5-minute "no-touch" period and the subsequent 20 minutes of CPAP during circulatory death confirmation. This uninterrupted ventilatory strategy, which prevents alveolar collapse,

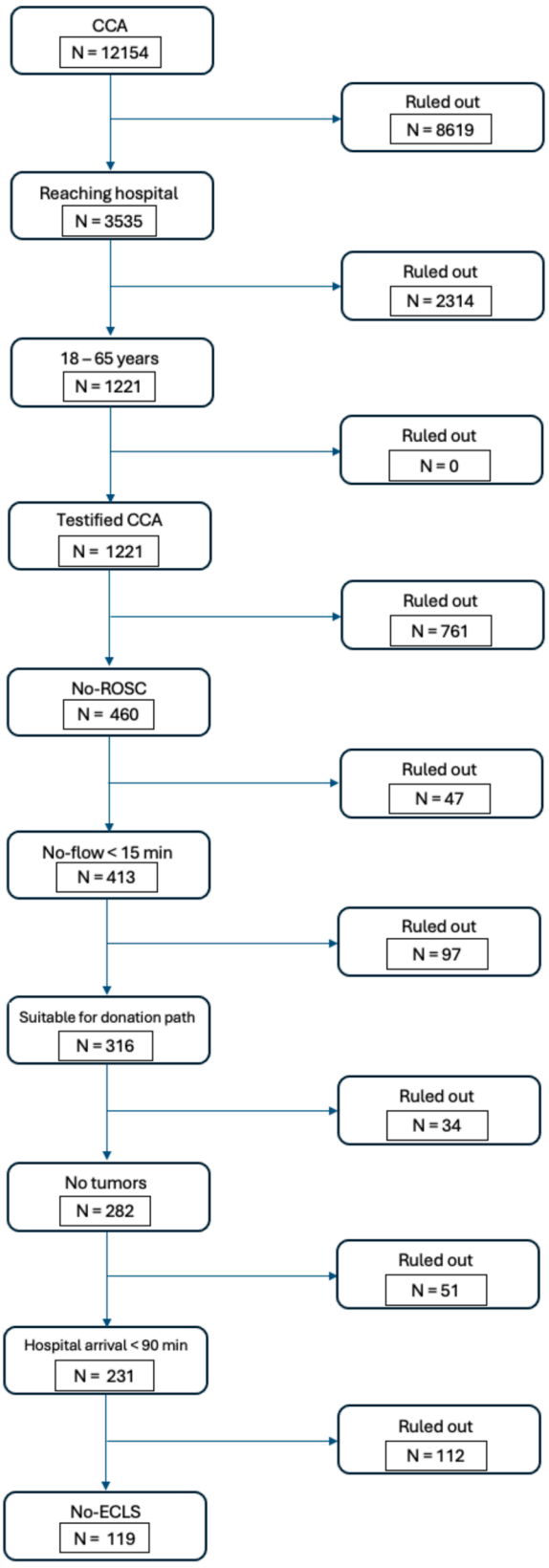

Figure 3. Flowchart of cardiocirculatory arrests in the 2023 cohort, in Lombardy, Italy. CCA: cardiocirculatory arrest; ECLS: extracorporeal life support; ROSC: return of spontaneous circulation.

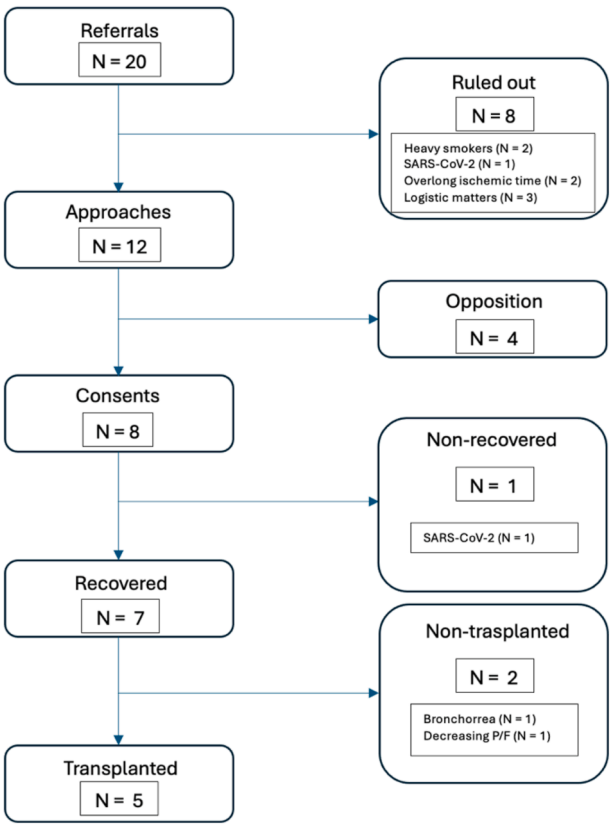

Figure 4. Flowchart of the 2023 cohort.

may help preserve lung architecture and gas exchange capacity, thereby contributing to the favorable outcomes observed in our cohort. Recently, an interesting experimental study in a swine model from a Japanese group[26] demonstrated that the combination of topical cooling and CPAP at 20 cmH_2O might improve graft function in animal uDCD settings. In contrast, our protocol, employing protective mechanical ventilation rather than static CPAP without topical cooling, appears simpler to implement and has yielded favorable clinical results.

In the literature, a WIT of 180 minutes is generally considered the upper limit for accepting lungs for transplantation in the absence of topical cooling, which, when applied, can extend the viable window up to approximately 6 hours. For instance, the Toronto experience—using postmortem ventilation with 50% FiO_2—included only donors with WITs below 3 hours, except for 1 case reaching 199 minutes. In contrast, the median WIT in our cohort was 240 minutes, exceeding the values reported by Spanish centers employing in situ cooling.[7,27] This discrepancy likely reflects variations in logistics and preservation strategies. Nevertheless, our outcomes remained comparable to those in the literature, possibly owing to the use of 100% FiO_2 during postmortem ventilation, which may have contributed to enhanced oxygenation and graft preservation despite the longer ischemic interval. Notably, the use of EVLP allowed for safe extension of preservation windows and facilitated the management of marginal grafts.[28]

In our cohort, all the EVLPs were performed centrally at our transplanting center. Indeed, although EVLP demands resources, centralized hubs have shown that cost-effective implementation is feasible.[29] The 72% post-EVLP utilization rate achieved in our cohort exceeds those reported by Canadian (35.7%), American (11.1%), and Spanish (50%; only 2 lungs evaluated by EVLP, of which 1 was deemed suitable) experiences.[7,9,10] This difference may reflect the highly selective criteria applied at our center for determining donor lung eligibility for EVLP, a practice also influenced by the considerable cost associated with this procedure. It is noteworthy to understand that EVLP is an expensive procedure, and some United States experiences were probably discontinued also due to funding challenges, emphasizing the importance of sustained organizational support.[23]

The postoperative outcomes were encouraging and comparable to or even better than those reported in literature from centers applying topical cooling,[24] despite the longer ischemic times observed in our cohort. The median ICU and hospital stays were 3 and 28 days, respectively. The incidence of PGD grade 3 (16.7%) was in line with international benchmarks,[30] suggesting that ischemic injury was not significantly exacerbated despite prolonged WIT. Similarly, the observed CLAD incidence (27.8%) during follow-up was comparable to that reported for DBD and cDCD cohorts.[31] Interestingly, the OS overlapped with that reported in the literature.[32] Furthermore, the acute rejection rate of 27.8% was again comparable to international reported rates.[33] These findings align with our previous data comparing DCD and DBD lung transplants at our institution[14] and are supported by updated analysis from the same cohorts of patients (Supplementary Tables S1-S3).

We conducted an exploratory analysis to identify potential factors influencing OS and CFS (Supplementary Table S4). However, the limited sample size precluded achieving statistical significance, thereby preventing definitive conclusions.

Emerging strategies in graft preservation deserve attention, particularly in the uDCD setting, where delays are often unavoidable. Traditional static cold storage (~4 °C) impairs ion pump function, promoting edema, mitochondrial damage, and oxidative stress.[34] In contrast, intermediate-temperature storage at 10 °C has been shown in preclinical studies to reduce mitochondrial dysfunction, inflammation, and apoptosis.[35] Early human data support its feasibility, and a multicenter trial is now underway to compare 10 °C preservation with standard cold storage.[36] For uDCD programs, implementing this strategy may offer dual benefits: first, by mitigating ischemic injury when immediate EVLP is not feasible; and second, by creating a valuable time window that facilitates coordination of recipient logistics, completion of critical laboratory and histocompatibility test results, and resolution of the operational challenges commonly associated with uncontrolled settings. This temporal buffer can be particularly advantageous in optimizing both donor organ management and recipient setup, ultimately improving the viability and utilization of available grafts.

Airway complications remain a recognized challenge in LT following DCD. In our series, 11.1% of recipients required intervention for bronchial complications: 1 pneumatic dilation and 1 stenting. Notably, no cases of anastomotic dehiscence were observed. Instead, the 2 cases of bronchial stenosis were identified during routine follow-up bronchoscopy and were managed accordingly, despite lacking a clear clinical correlation. While this rate is consistent with DCD series in the literature or even slightly better,[37] the absence of anastomotic dehiscence, along with the prompt management of still asymptomatic bronchial stenoses, highlights the adequacy of our recovery strategy and postoperative monitoring.

Furthermore, we performed a detailed analysis of the causes of death to assess their potential relationship with the graft or transplant. Among the 5 recorded deaths, only 1 was directly transplant-related (pneumonia during dialysis within 3 months posttransplant), and 2 were graft-related (1 due to unspecified acute dysfunction and 1 due to CLAD). The remaining 2 deaths were unrelated: 1 from subarachnoid hemorrhage and 1 from Klebsiella pneumoniae carbapenemase (KPC) sepsis occurring more than 1 year after transplantation. Ultimately, the observed mortality rate aligns with those commonly reported in LT cohorts. A further objective was to ascertain whether any mortality could be specifically linked to donor type or transplant protocol. Upon comprehensive review, according to our assessment, no evidence was found to support a direct correlation between mortality and these variables: indeed, such events could have occurred even in the context of traditional donor use.

Our 2023 regional data analysis highlights the significant untapped potential of uDCD donors in Lombardy. Among 12 154 cardiac arrests, 119 individuals met eligibility criteria, yet only 20 were activated, resulting in 5 transplants (25% utilization rate). The main barriers were hospital inaccessibility and limited coverage outside operational hours. Notably, an additional 30 ECMO-coded cases arrived beyond the time-to-door limit and may represent a further expansion opportunity. Furthermore, the regional analysis offers insights into missed opportunities during the study period, illustrating how many potential donors were lost over those years. Extrapolated to the national level, these findings suggest that uDCD programs could substantially reduce the current mismatch between donor availability and transplant demand in Italy.

This study has several limitations. Its single-center design and small sample size may limit generalizability. The transatlantic generalizability of these results is limited by the Italian universal health care and opt-out donation framework, which contrasts with systems in many other countries. Besides, due to the limited sample size, model fit statistics were not assessed. Additionally, evolving logistics and donor selection practices over a decade may have introduced heterogeneity. Nonetheless, the consistency of our preservation and assessment protocols reinforces the validity of the observed outcomes. Furthermore, regional data analysis, though rigorous and cross-validated, was exploratory in nature and based on administrative data; although not intended for causal inference, it provides an estimate of potential donor availability and highlights systemic inefficiencies warranting future optimization.

Finally, it is noteworthy to acknowledge that early outcomes of the first uDCD transplants included in this manuscript were previously compared with matched DBD recipients in another study by the same authors.[14] The present study extends follow-up and includes additional uDCD cases with updated long-term results, providing a comprehensive evaluation of uDCD cases performed over the full 10-year period.

In our setting, and in centers aiming to implement this approach, ensuring the sustainability and further regional expansion of uDCD programs requires the consolidation and strengthening of key structural components already in place. These include a robust organizational infrastructure to support communication, logistics, and clinical operations; the continued involvement of dedicated organ procurement coordinators to manage donor identification and interhospital coordination; the progressive integration of additional active centers to achieve comprehensive territorial coverage; and the implementation of structured training programs—potentially including simulation—to maintain staff readiness for the specific challenges of uDCD protocols.

5. Conclusions

Our 10-year experience confirms that uDCD is a valuable yet underutilized source of donor lungs. With appropriate protocols and coordinated network efforts, this approach can be safely scaled and widely adopted to help address the persistent shortage of transplantable lungs.

The protocol we applied—based on normothermic ventilation without complex equipment or abdominal interventions—proved not only feasible but also highly adaptable, making it suitable even for nontertiary hospitals. Its simplicity enhances reproducibility and potential for broader implementation.

Despite concerns about prolonged ischemia, uDCD lungs may offer intrinsic advantages over DBD and cDCD grafts, being less affected by the systemic inflammatory response, prolonged ICU stays, or abdominal organ competition—factors that can compromise graft quality.

By combining stringent donor selection, optimized in situ preservation, and systematic EVLP evaluation, we achieved outcomes in line with international standards. Moving forward, further research and multicenter collaboration will be essential to refine protocols, improve long-term results, and unlock the full potential of uDCD transplantation within regional and national programs.

Author contributions

All authors contributed to drafting and revising the manuscript for important intellectual content. All authors approved the manuscript for submission.

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Declaration of competing interest

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

Data availability

The data sets generated and analyzed during the current study are not publicly available due to patient privacy and institutional restrictions. Deidentified data may be made available from the corresponding author upon reasonable request and with approval from the local ethics committee.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajt.2026.01.017.

ORCiD

Alessandro Palleschi https://orcid.org/0000-0003-4510-5167
Alberto Zanella https://orcid.org/0000-0002-2967-2527
Riccardo Orlandi https://orcid.org/0000-0002-4113-1598
Lorenzo Rosso https://orcid.org/0000-0002-9809-7140
Valentina Vaira https://orcid.org/0000-0003-4416-6216
Franco Valenza https://orcid.org/0000-0003-0634-2282
Mario Nosotti https://orcid.org/0000-0002-8571-121X

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