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Extended-criteria uncontrolled DCD donor for a fragile recipient: A case report about a challenging yet successful lung transplantation

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ABSTRACT

INTRODUCTION: Lung donation after circulatory death (DCD) has proved to be an effective strategy for expanding the donor pool, but is still considered challenging. We report a successful case of lung procurement from an extended-criteria uncontrolled DCD.
PRESENTATION OF CASE: We evaluated the lungs of an uncontrolled DCD from a hospital without extra-corporeal membrane oxygenation (ECMO) program. The donor was a non-smoker 20-year old male with a history of cardiomyopathy, cardiocirculatory arrests, and Lennox-Gastaut syndrome. Cardiac arrest occurred in a swimming pool, and bronchoscopy showed signs of inhalation. We employed our usual normothermic in-situ open-ventilated lung approach. After retrieval, lungs were stored on ice, then evaluated with ex-vivo lung perfusion (EVLP) and judged suitable for transplantation. The recipient was a 26-year old female with cystic fibrosis on long-term oxygen therapy, on the waitlist for up to 21 months due to her anthropomorphic characteristics. She required central VA-ECMO support during bilateral lung transplantation. Primary graft dysfunction (PGD) within the first 72 h reached grade 3; post-operative peripheral VV-ECMO support was discontinued two days after surgery. The patient was discharged 28 days after surgery; she is alive two years after transplantation with no signs of rejection nor anastomotic complications.
DISCUSSION: Despite the spreading use of lungs from controlled DCD, perplexities remain on uncontrolled DCD, namely: severe PDG, postoperative mortality, airway complications.
CONCLUSION: Our case report suggests that good results can be achieved with uncontrolled DCD despite the presence of relative contraindications: inhalation of water, prolonged ischemic times and recipient in poor conditions.

1. Introduction

Lung transplantation is the gold standard treatment in selected patients affected by end-stage respiratory disease. However, the number of patients waiting for transplantation to date is still high. Organ shortage remains one of the main limiting factors in treating these patients, as lungs achieve a lower retrieval rate when compared to other solid organs. Lung donation after circulatory death (DCD) has proved to be an effective strategy for expanding the donor pool [1]. It is well known that lung tissue can tolerate a prolonged warm ischemia time and that it can dissociate ischemia from hypoxia, using ventilation [2]. Nonetheless, some groups prefer reserving DCD organs for relatively low-risk recipients [3]. In this scenario, the uncontrolled setting is still considered particularly challenging, clinical experiences are limited, and stringent donor suitability criteria, as well as limited preservation times, are employed [4,5]. We report a case of lung procurement from an extended-criteria uncontrolled DCD donor with a long ischemic preservation period, and subsequent successful bilateral lung transplantation in a fragile recipient, carried out in our university hospital in Milan, Italy. Our article is drawn up in line with the SCARE 2018 criteria [6].

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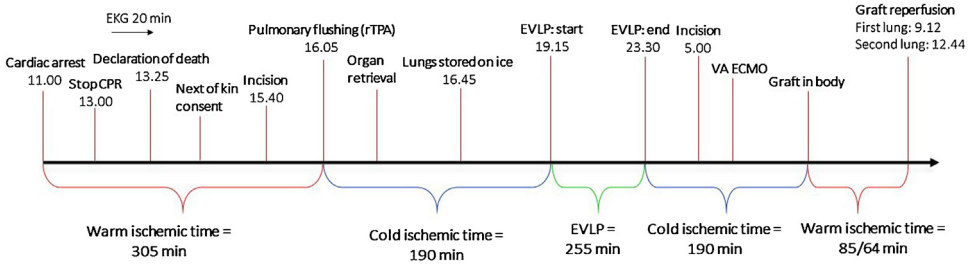

Fig. 1. Timeline.
CPR: cardiopulmonary resuscitation; EKG: electrocardiogram; rTPA = recombinant tissue plasminogen activator; EVLP = Ex-vivo lung perfusion; min = minutes; VA ECMO = veno-arterial extracorporeal membrane oxygenation.

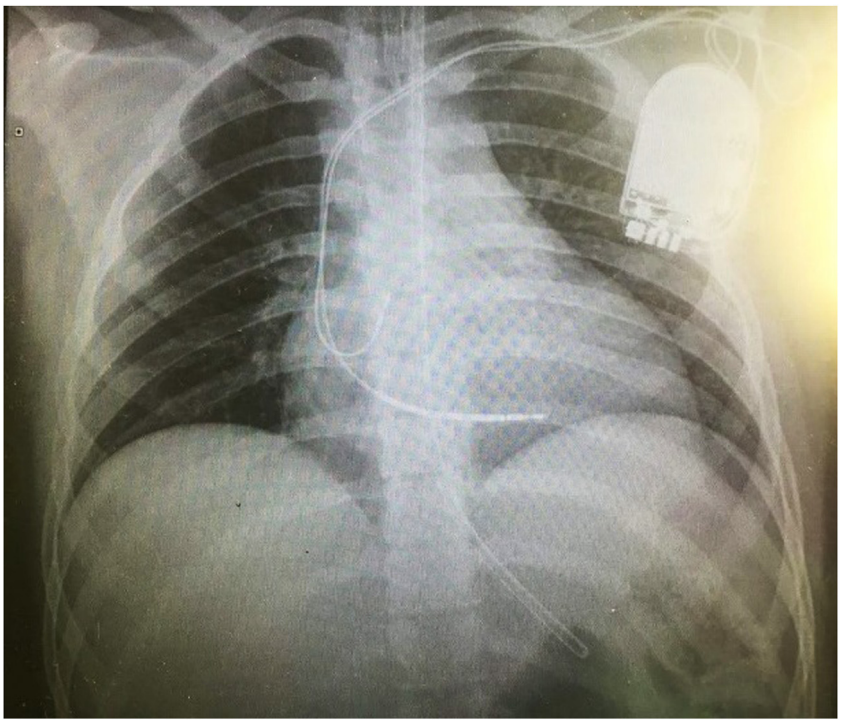

Fig. 2. Donor chest X-ray.

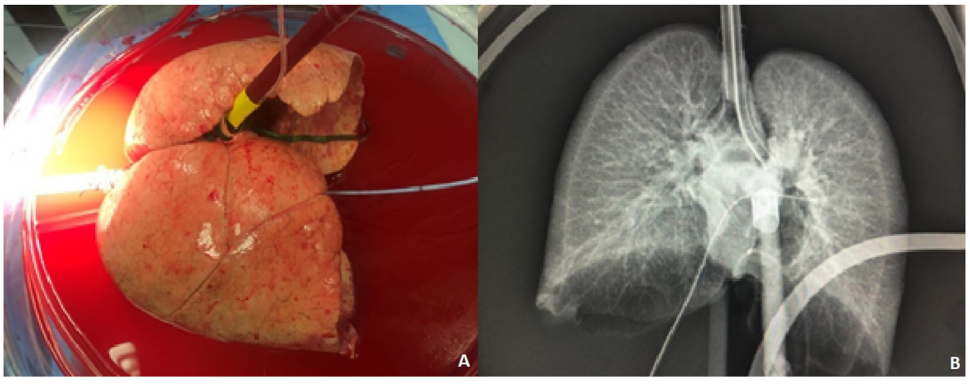

Fig. 3. A: Lungs appearance during EVLP; B: Lungs X-ray after EVLP.

2. Presentation of case

In July 2018, our transplantation centre was offered a potential lung donation from a Maastricht II DCD donor; therefore, we promptly sent our procurement team to assess the suitability of the organs. A 20-year old boy had a witnessed cardiac arrest in a swimming pool and suffered water inhalation. Cardiopulmonary resuscitation (CPR) was started 5 min after the collapse (see the process timeline in Fig. 1); the donor had been brought to a peripheral hospital, located 118 km away from our centre and with no extracorporeal life support program. He had a past medical history of arrhythmia, biventricular hypertrophic cardiomyopathy,

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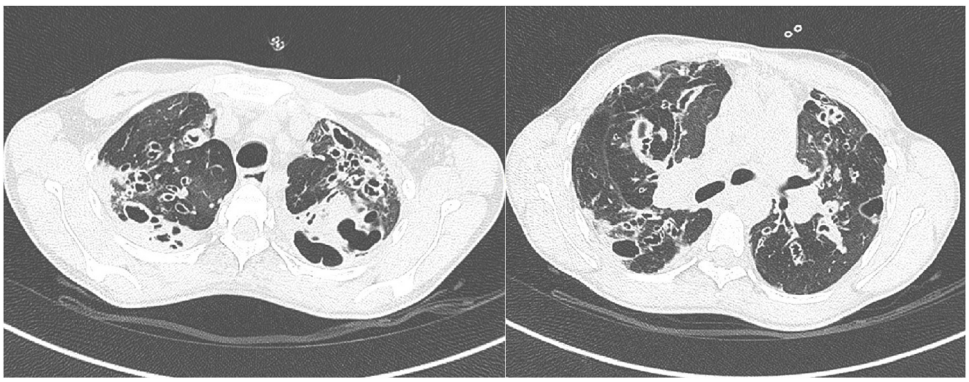

Fig. 4. Recipient CT-scan before transplantation.

previous cardiocirculatory arrests, and Lennox-Gastaut syndrome. Also, he had had an episode of pulmonary embolism, for which he was treated with anticoagulant drugs, but his clinical record did not mention pulmonary hypertension; he had no history of smoking. After 115 min of ineffective CPR, the local emergency medical team decided to withdraw further treatments. After that, we started with our usual donor preservation approach, consisting of normothermic *in-situ* open-lung, as previously described [7]. After the clinical diagnosis of death (5 min no-touch), recruitment manoeuvres and continuous positive airway pressure were used in order to preserve the lungs. As required by the Italian law, 20 min of flat electrocardiogram were recorded to declare the patient's death. After obtaining next-of-kin consent to organ donation, heparin was administrated. Chest x-ray was clear (Fig. 2), but the bronchoscopic evaluation confirmed the signs of pool water inhalation and copious frothy secretions. After sternotomy, the lungs appeared heavy at inspection due to pulmonary oedema; declivous zones with moderate atelectasis were recruited under direct vision. After usual bi-pulmonary *en-bloc* retrieval, lungs were stored on ice and transferred to our centre. Grafts were evaluated with *ex-vivo* lung perfusion (EVLP) as previously described [8]. After 255 min of normothermic perfusion, grafts were judged suitable for transplantation according to the usual parameters [9] (Fig. 3). Namely, in the final evaluation, PaO_2/FiO_2 was 567 and bronchoscopy was clear. The recipient was a 26-year old female with cystic fibrosis who had chronic colonization from *Pseudomonas aeruginosa* and allergic bronchopulmonary aspergillosis (ABPA) (Fig. 4). Also, she had a low BMI (17.9 kg/m^2). Her lung allocation score was 44.93; she was on permanent intravenous antibiotic therapy and required long-term oxygen therapy. On her last six-minute walking test, performed with supplemental oxygen (FiO2 = 31%), she covered a distance of 330 m. Her anthropometric characteristics had made it difficult to find a compatible donor; therefore, she had been on the waitlist for 21 months. Transplantation began five and a half hours after the end of EVLP, due to logistical issues. At pulmonary artery clamp test, pulmonary hypertension and haemodynamic instability occurred, requiring central veno-arterial extracorporeal membrane oxygenation (ECMO) support. At the end of surgery, post-operative peripheral veno-venous ECMO support was started and then discontinued 2 days later. Primary graft dysfunction (PGD) within the first 72 h reached grade 3. Mechanical ventilation was necessary for 5 days, and the intensive care unit length of stay was 10 days, probably due to her previous physical deconditioning too; she was discharged 28 days after surgery. The patient is alive and well two years after transplantation (FEV1 = 69%, last room air 6-minutes-walking-test = 590 m, bronchoscopy: no signs of acute rejection nor anastomotic complications), she has a good quality of life and is leading an extremely active life (Fig. 5).

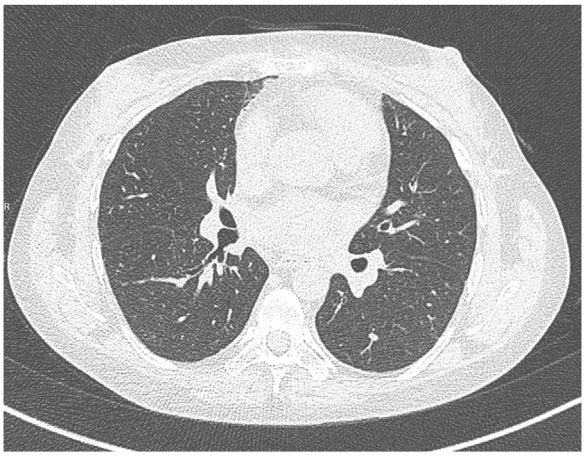

Fig. 5. Recipient CT-scan 2 years after lung transplantation.

3. Discussion

With organ shortage being one of the most significant limiting factors in lung transplantation, interest in DCD has been resurging in the last few years. However, while the number of transplanted lungs retrieved from controlled DCD donors has been increasing, and studies have shown outcomes comparable to those of brain-dead donors (DBD), uncontrolled DCD donors (Maastricht categories I and II) are still an underused option for organ retrieval [10,11]. In fact, this setting poses a major challenge to physicians, especially in terms of logistics. Moreover, there are still perplexities on the use of uncontrolled cardiac dead donors, mostly regarding severe PGD observed after lung transplantation, post-operative mortality, and healing of bronchial anastomoses [12]. Only a few series of cases have been published around the world, mostly from Spain [4,13] and recently from North America [5]. Our centre started an uncontrolled DCD program in 2014, and to this day we have achieved good results in terms of outcomes [7]. In this study, we report a case of successful lung transplantation carried out despite the many donor- and recipient-related risk factors. For donor selection, we usually apply the same criteria used for DBDs. Various observations on this specific case can be made. First of all, despite being a young non-smoker, our donor had a complicated past medical history which included direct and indirect injuries to the lungs: pulmonary embolism and cardiac diseases, respectively. Furthermore, he collapsed in a swimming pool and the bronchoscopic evaluation confirmed the presence of aspiration, which is considered a contraindication for the usage of lungs from DBD donors too [4,5,14,15]. The suitability of lungs from an uncontrolled DCD donor is established using stringent criteria, especially regarding ischemic

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time; however, the limit of tolerated ischemic time varies among different centres. In our case, the warm ischemia time (WIT) (from cardiac arrest to pulmonary flushing) was quite long (305 min), and total preservation time (from the end of resuscitation until reperfusion of the first lung) was prolonged too, as it was 20 h and 12 min. Most centres tolerate a WIT period of 120–150 min maximum [4,12]. In a recently published work by Healey et al., the highest WIT period reached was 199 min [5]. Generally, in our centre we tolerate a maximum total WIT of 150 min; however, our original open-lung approach allows us to extend the ischemic times, both in the controlled and uncontrolled setting, without detrimental effects on graft [7,16]. In our protocol for DCD donors, the assessment of graft function through EVLP is considered mandatory; after EVLP we consider lungs unsuitable for transplantation in case of worsening in terms of ventilation mechanics, vascular resistance, or PaO_2/FiO_2 < 450mmHg [9]. Using EVLP is strongly advised for marginal donors and questionable organs, as in the case of uncontrolled DCDs [11,17]. Specifically, in this situation, using EVLP enabled us to both evaluate lungs function and gain time. In this particular case, EVLP allowed us to rule out any irreversible injury to the lungs that may have occurred as a consequence of the donor's previous medical conditions or water inhalation. Despite the good pulmonary function observed during evaluations, the lungs had to be categorized as of an extended-criteria uncontrolled DCD donor. In some centres, those grafts tend to be reserved for baseline or low-risk recipients in an attempt to minimize the likelihood of complications [3,18]. Our recipient can be considered a high-risk patient: she was fragile, with a low BMI, and she was deconditioned in terms of muscular strength. The patient required postoperative extracorporeal support, had a prolonged intensive care unit stay, and experienced severe PGD. The grade 3 PGD, in particular, could have been the result of both prolonged ischemia time and pulmonary oedema, which is often found in DCDs. Despite these early events, the mid-term post-operative outcomes are satisfactory, and the patient reports an excellent quality of life. Finding a common ground between the risk of early complications and those of high mortality on the waiting list is of paramount importance in these clinical scenarios.

4. Conclusion

Despite the perplexities on uncontrolled DCD, we strongly believe that, after careful evaluation, these donors could be an invaluable asset in fighting organ shortage. Our protocol offers a very flexible approach, which allows lung retrieval in peripheral hospitals with non-standard donors and long ischemic times either. Namely, evaluating grafts function both *in-situ*, during normothermic ventilation, and *ex-situ*, during normothermic perfusion makes it possible to successfully overcome the challenges of the uncontrolled setting.

Declaration of Competing Interest

None.

Sources of funding

None.

Ethical approval

The study was approved by Ethics committee of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milano. Mortality risk factors in patients waiting and submitted to lung transplant. Ref. n° 181 (24/01/2017).

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Study concept: Palleschi Alessandro.

Data collection: Musso Valeria, Scaravilli Vittorio, Morlacchi Letizia Corinna, Croci Giorgio Alberto.

Data analysis/interpretation: Musso Valeria, Mendogni Paolo, Palleschi Alessandro.

Writing/editing paper: all authors.

Registration of research studies

NA.

Guarantor

Paolo Mendogni, Alessandro Palleschi.

Provenance and peer review

Not commissioned, externally peer-reviewed.

CRediT authorship contribution statement

Valeria Musso: Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization. **Paolo Mendogni:** Conceptualization, Investigation, Writing - original draft, Writing - review & editing, Visualization, Supervision. **Vittorio Scaravilli:** Investigation, Resources, Data curation, Writing - review & editing. **Letizia Corinna Morlacchi:** Resources, Data curation, Writing - review & editing. **Giorgio Alberto Croci:** Investigation, Resources, Writing - review & editing. **Alessandro Palleschi:** Conceptualization, Investigation, Writing - original draft, Writing - review & editing, Visualization, Supervision, Project administration.

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