Breaking barriers in cardiac donation after circulatory death.

Mario Galván Ruiz[1], María del Val Groba Marco[1], Michelle Tout Castellano[1], Francisco Portela[1], José Luis Romero Luján[1], Miguel Fernández de Sanmamed Girón[1], Eduardo Caballero Dorta[1], and Antonio García Quintana[1]

[1]Hospital Universitario de Gran Canaria Dr Negrin

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Abstract

Background: Heart transplant from controlled donation after circulatory death (cDCD) is an emerging strategy that is rapidly expanding and may help increase the heart donor pool. **Materials and Methods:** The use of thoracoabdominal normothermic regional perfusion (TANRP) with extracorporeal membrane oxygenation device has allowed to perform cardiac transplantation after cDCD. Several experiences have been carried out in recent years, however the maximum cold ischemia time is still unknown. We present a successful case of heart transplantation using a graft from cDCD from another hospital with 201 minutes of cold ischemia time, the longest published in Europe. **Discussion and conclusion:** Heart transplant from cDCD could be a good alternative to brain dead donation. This experience suggests than nonlocal cardiac donation in controlled asystole could tolerate long periods of cold ischemia time and break the main barriers in cardiac donation after circulatory death.

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[a] Service of Cardiology, University Hospital Doctor Negrín, Las Palmas de Gran Canaria.

[b] Transplant Coordination Unit and Service of Intensive Care, University Hospital Doctor Negrín, Las Palmas de Gran Canaria.

[c] Service of Cardiovascular Surgery, University Hospital Doctor Negrín, Las Palmas de Gran Canaria.

[d] Service of Intensive Care, University Hospital Doctor Negrín, Las Palmas de Gran Canaria.

* Correspondence:

Mario Galván Ruiz, Service of Cardiology

University Hospital Doctor Negrín, Las Palmas de Gran Canaria.

Address: Barranco de la Ballena S/N.

Postal code: 35019

Mobile phone: 630786594

FAX: 0034928450086

Email: mariogalvanr@hotmail.com

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INTRODUCTION

The shortage of donors and the long waiting list for heart transplantation (HT), have led to search alternatives to brain-dead donation, reviving interest in controlled donation after circulatory death (cDCD) programs (1). It is developed using thoracoabdominal normothermic regional perfusion (TANRP) with extracorporeal membrane oxygenation (ECMO) devices and preserved in cold storage, allowing to perform cardiac transplantation without ex-situ perfusion. Most of the cases reports with this technique were published of donor and recipient in the same hospital or at a very short distance (2).

Due to the peculiarities of the HT in Canary Islands, Spain, we were obliged to try to expand our radius of action by accepting donors of the entire island territory. We present a cDCD cardiac transplant successfully performed in Gran Canaria, with a donor from La Palma, an island located 70 minutes away by helicopter (250 kilometres). This determined a cold ischemia time of 201 minutes, the longest published in Europe to date with the TA-NRP technique and cold storage.

Case report

A 47-year-old male, with no personal history, admitted to the intensive care unit (ICU) after severe head injury secondary to a fall from height. After 33 days, with irreversible catastrophic brain damage, the responsible medical team in consensus with the family decided to withdraw life – sustaining therapies (WLST). Evaluated by analytical studies, electrocardiogram and echocardiography, he was accepted for cDCD cardiac transplant after obtaining family consent. The usual heart transplant team went to La Palma hospital, equipped with a portable ECMO device and all the necessary material to carry out the extraction.

The cDCD process was carried out according to the protocol of our center approved by the National Transplant Organization, using TANRP with ECMO devices and cold storage preservation.

The functional warm ischemia time (WIT) defined as the time between systolic blood pressure < 60 mmHg and the start TANRP was 11 minutes. The PRN–TA time was 15 minutes (see figure 1).

The recipient was a 56-year-old man with advanced heart failure due to ischemic cardiomyopathy, included 38 days HT waiting list. He was informed of the peculiarities of the HT, signing a specific informed consent for HT with cDCD. An orthotopic HT with bicaval technique was performed. The cold ischemia time was 201 minutes. He was transferred to the ICU, requiring norepinephrine 0.6 mcg/kg/min, isoprenaline 0.2 mcg/kg/min, and milrinone 0.4 mcg/kg/min which were gradually withdrawn. He was extubated 30 hours after HT and was discharged to the ward six days later, where he remained fifteen days more (see table 1). The transthoracic echocardiogram showed good biventricular function (left ventricular ejection fraction 67%), without significant valve disease. After two months of follow-up, the patient is asymptomatic. Two endomyocardial biopsies were performed with a mild cellular rejection (grade 1R of the ISHLT 2004), while the coronary angiography done a month later, showed a slight lesion in the proximal anterior descending artery.

DISCUSSION

HT from cDCD is estimated to increase exponentially in the following years, accounting more than 10% HT per year (2). Published data with cardiac donors in cDCD showed similar short-term results compared with brain-dead donors, however more studies to assess the long-term impact are required (3).

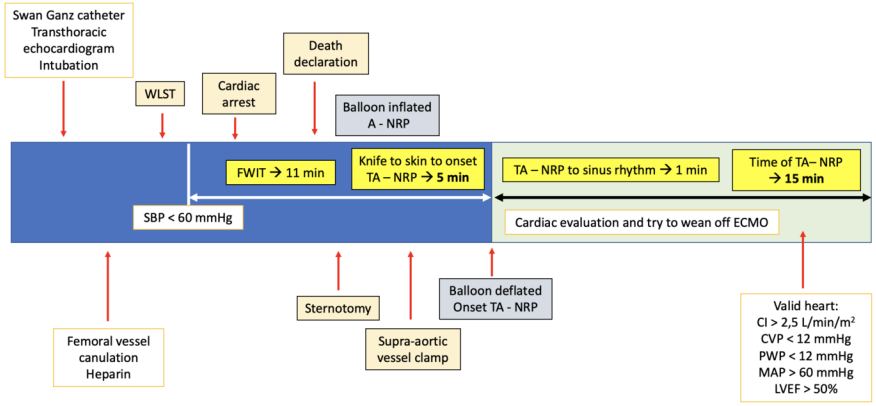
After the reinitiation of HT activity from donors in controlled asystole, different extraction protocols have been used with different donor acceptance criteria. Most of the Spanish protocols for HT in cDCD include donors under 55 years old, although the first cases were restrictive in the inclusion criteria (< 45 years) (4) (5). An exhaustive cardiac evaluation (including electrocardiogram, echocardiogram, biomarkers and sometimes coronary angiography) and the re-evaluation after cessation of circulatory function and the beginning of TANPR with ECMO device, could allow, as in our case, to expand the inclusion of donors older than 45 years and probably in the future, also order than 55 years.

Because it is a recent technique in most of the protocols, it is recommended that extraction and transplant are performed in the same hospital, since the maximum cold ischemia time that these hearts can tolerate is unknown, without increasing the risk graft dysfunction or morbimortality transplant associated. Although preclinical studies demonstrated adequate tolerance to ischemia times of less than two hours (6) (7), the *Tennessee group* (8) confirms the safety of 225 minutes. However, in this cohort, recipients were younger and, in some cases, used different cDCD heart transplant protocols (shorter "no touch" time), compared to our case.

CONCLUSION

In Spain, the longest cold ischemia time published cDCD heart transplant in adult was 80 minutes. Our case was a cDCD performed in a hospital located on another island of the Canary Island, which determined the longest cold ischemia time. This experience suggests that nonlocal cardiac donation in controlled asystole in adults with PRNTA could tolerate long periods of cold ischemia, without compromising the prognosis, at least in the short term.

Figure 1. The protocol for controlled donation after circulatory death and the times of heart transplant of the clinical case.



Abbreviations: WLST = withdrawal of life sustaining therapies; SBP = systolic blood pressure; A-NRP = abdominal normothermic regional perfusion TA–NRP = toracoabdominal normothermic regional perfusion; ECMO = extracorporeal membrane oxygenation; CI = cardiac index; CVP = central venous pressure; PWP = pulmonary wedge pressure; MAP = mean arterial pressure; LVEF = left ventricular ejection fraction.

TABLE 1. Donor characteristics and key features of cDCD heart transplant.

DONOR	DONOR	RECIPIENT	R
Age	47	Age	56

DONOR	DONOR	RECIPIENT	R
Sex	Hombre	Sex	H
Cause of death	Fatal head trauma	Cold ischemia time	20
Time in the ICU	33 days	Dobutamin	-
FWIT	11 min	Norepinephrine	0,(
Knife to skin to onset of TA-NPR	5 min	First day LVEF	70
Time to restoration of spontaneous sinus rhythm after TA-NRP	1 min	Post surgery device	N(
Time of TA-NRP	15 min	Invasive mechanical ventilation	30
LVEF% at 60 min	68%	Time in the ICU	6 (
Cardiac index at validation	4,1 l/m^2	Time in cardiology ward	15

Abbreviations: ICU = Intensive care unit; FWIT = functional warm ischemic time; TA - NRP = Thoracoabdominal normothermic regional perfusion; LVEF = left ventricular ejection fraction.

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