

# Derivation and Implementation of a Protocol in Israel for Organ Donation after Cardio-Circulatory Death

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**ABSTRACT:** **Background:** Strategies aimed at expanding the organ donor pool have been sought, which has resulted in renewed interest in donation after cardio-circulatory death (DCCD), also known as non-heart beating donors (NHBDs).

**Objectives:** To describe the derivation and implementation of a protocol for DCCD in Israel and report on the results with the first six cases.

**Methods:** After receiving approval from an extraordinary ethics committee at the Ministry of Health, the steering committee of the National Transplant Center defined and reached consensus on the unique challenges presented by a DCCD program. These protocols included clinical aspects (construction of a clinical pathway), social and ethical aspects (presentation of the protocol at a public gathering), legal/ethical aspects (consent for organ preservation procedures being either implied if the donor had signed an organ donor card or received directly from a surrogate decision maker), and logistic aspects (pilot study confined to kidney retrieval and to four medical centers). Data regarding organ donors and recipients were recorded.

**Results:** The protocol was implemented at four medical centers. Consent for organ donation was received from four of the six potential donors meeting criteria for inclusion and in all cases from a surrogate decision maker. Of the eight kidneys retrieved, only four were suitable for transplantation, which was carried out successfully for four recipients. Graft function remained normal in all cases at 6–12 months follow-up.

**Conclusions:** The DCCD program was successfully implemented and initial results are encouraging, suggesting that expansion of the program might further aid in decreasing the gap between needs and availability of organs.

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**KEY WORDS:** organ transplantation, donation after cardio-circulatory death (DCCD), non-heart beating donors (NHBDs)

Organ transplantation remains the optimal therapy for many patients with end-stage organ failure. However, in Israel as in many other countries, despite well-functioning programs of organ retrieval from brain dead and living donors, there remains a significant gap between needs and availability, and many patients die each year while awaiting transplantation.

For this reason, strategies aimed at expanding the donor pool have been sought, which has resulted in renewed interest in donation after cardio-circulatory death (DCCD), also known as non-heart beating donors (NHBDs). In this regard, prior to the introduction of neurological criteria for defining the end of life (i.e., brain death) in the mid to late 1970s, all organ transplants came from cadaveric donors who were declared dead by conventional cardiorespiratory criteria. DCCD is classified according to the modified European Maastricht categories [Table 1], which differentiates DCCD as “uncontrolled” (uDCCD), namely unwitnessed and/or unanticipated sudden death from cardiac arrest, both in- and out-of-hospital, and “controlled” (cDCCD), namely expected cardiac arrest following withdrawal of life-sustaining therapy in the ICU, which is the most widely implemented [1]. Worldwide, increasing use is made of DCCD programs as a source of kidneys, livers, and lungs for transplantation [2].

A protocol for kidney retrieval from uDCCD donors following in-hospital cardiac arrest was recently introduced in Israel. In this article, we described the process leading to its implementation, with special emphasis on the unique challenges presented by such a program, in particular the clinical, social, legal, and logistical aspects. In addition, we report on the initial results with the first six cases.

## PATIENTS AND METHODS

The process to implement a protocol for DCCD in Israel began with the establishment of an extraordinary ethics committee, under the chairmanship of the deputy director general of the Ministry of Health. Following 2 years of deliberation, where

\*The first and second authors contributed equally to this study

**Table 1.** Modified European Maastricht categories of donation after cardio-circulatory death (DCCD)

Category	Sub-category	Description	Type	Possible In Israel
<b>Category I</b> Uncontrolled, unwitnessed CA	IA – in-hospital	Sudden, unexpected, irreversible CA; no attempt of CPR by medical team	Uncontrolled	Yes
	IB – out-of-hospital			
<b>Category II</b> Uncontrolled, witnessed CA	II A – in-hospital	Sudden, unexpected, irreversible CA; unsuccessful resuscitation by medical team	Uncontrolled	Yes
	II B – out-of-hospital			
<b>Category III</b>		Planned, expected CA; withdrawal of life-sustaining treatment	Controlled	No
<b>Category IV</b> Alternative death determination during/after procedure	IV A – uncontrolled and controlled CA while brain dead	Sudden or planned CA during or after BD diagnosis process, but before retrieval	Uncontrolled or controlled	Yes (uncontrolled only)
	IV B – death diagnosis during ECMO-ECLS	Death determination by circulatory or neurological criteria	Partially controlled	

CA = cardiac arrest, CPR = cardiopulmonary resuscitation, BD = brain death, ECMO-ECLS = extracorporeal membrane oxygenator-extracorporeal life support

in particular, questions were raised regarding the ethical and social aspects of the program, the committee recommended that the National Transplant Center proceed with establishing the program. The steering committee was comprised of transplant physicians, legal experts, religious representatives, ethicists, representatives of recipients awaiting transplantation, and social workers. The group defined and deliberated on all the aspects involved with DCCD. Once consensus was reached, a formal document regulating the process was developed and approval was received from the Ministry of Health to proceed with its implementation.

**CLINICAL PATHWAY**

The clinical pathway was constructed after consultation with experts from France, where uDCCD has been practiced since 2006 [3]. The protocol included only patients who had a witnessed cardiac arrest in the emergency department (category II A). In category II, cardiopulmonary resuscitation (CPR) is initiated immediately and continued until evidence of irreversible cessation of circulation, as demonstrated by failure to reverse the cardiac arrest despite continuous attempts for at least 30 minutes [4]. This is followed by a 5 minute no-touch period during which all treatment, including mechanical ventilation and cardiac compressions, is stopped. Thereafter, death is declared by the treating physician in the absence of electrical activity on the electrocardiogram, absence of spontaneous breathing, fixed and dilated pupils, absent corneal reflexes and unresponsiveness to nociceptive stimuli [3,5]. At this time, the local hospital transplant coordinator is notified. This person then screens the case for inclusion as a uDCCD donor [age < 55 years, body mass index (BMI) < 35, absence of major intra-abdominal trauma and usual contraindications to organ donation such as active cancer, human immunodeficiency virus (HIV) positive]. If eligible, a dedicated uDCCD team, including an intensive care unit (ICU) physician who oversees the process, a physician with the ability to perform venous and arterial cut-downs at designated hospitals, and an extracorporeal membrane oxygenator (ECMO) team, is mobilized.

After consent is obtained, in situ preservation of intra-abdominal organs is achieved either by perfusion with cold preservation solution (UW) or by connection to normothermic ECMO. Both require the insertion of cannulae into the femoral artery and vein as well as an intra-arterial balloon catheter that is inflated at the level of the diaphragm to isolate the perfusion of abdominal organs. Following kidney retrieval, the preservation protocol consists of hypothermic pulsatile perfusion (Lifeport®, Organ Recovery System, Des Plaines, IL, USA) until the time of transplantation.

**SOCIAL AND ETHICAL ASPECTS**

The extraordinary ethics committee from the Ministry of Health suggested that the procedure be presented to the wider public to gauge public response and promote transparency. In this regard, a “mock trial” was held, where a “plaintiff” sued a hospital for inserting cannulae into the body of a deceased parent after unsuccessful CPR without permission of the family for the purpose of organ preservation. An actual prosecutor and defense lawyer participated in the trial in the presence of 200 members of the general public. Following evidence provided by medical experts, the “judges” (two senior lawyers and a senior physician/ethicist) ruled that the procedure did not result in any unnecessary harm to the deceased and that the process was legally and morally acceptable.

**LEGAL/ETHICAL ASPECTS**

Consent for the insertion of cannulae to facilitate the rapid preservation of intra-abdominal organs is considered obligatory. The steering committee agreed that this would be either implied, if the patient had signed an organ donor card, or obtained directly from a surrogate decision maker (immediate family member). In all cases, consent for organ retrieval and transplantation is required from a family member.

**LOGISTICAL ASPECTS**

The pilot program was limited to four major hospitals in Israel: Rabin Medical Center (Beilinson Campus), Petah Tikvah;

Rambam Medical Center, Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa; Hadassah–Hebrew University Medical Center, Jerusalem; and Soroka Medical Center and Faculty of Health Sciences, Beer Sheva. The program was active between the times of 07:00 and 16:00 from Sunday to Thursday to ensure the immediate presence of appropriate medical staff. Finally, it was decided to limit the pilot program to kidney retrieval. Prior to implementation, relevant medical personnel received training from both local and international experts.

#### DATA COLLECTION

Data was collected for all cases who fulfilled criteria for uDCCD and included age, reason for sudden death, whether registered as an organ donor, family response, and whether organs were retrieved and transplanted.

#### RESULTS

Since its implementation in 2014, six cases fulfilled inclusion criteria [Table 2]. The mean age of the donors was 41.8 years and there were three males and three females. Reasons for death included suicide by hanging in one patient and sudden collapse and cardiac arrest in the remaining five cases. None of the patients was a registered organ donor and consent was obtained for cannula insertion and organ donation in four cases from surrogate decision makers. In two cases, both kidneys were retrieved and transplanted into four recipients. Six months following transplantation all patients were alive with fully functioning grafts. In the remaining two cases the kidneys were rejected at laparotomy as they were found to be markedly ischemic and nonfunctional.

#### DISCUSSION

A protocol for uDCDD in Israel was derived following deliberation of the unique clinical, social, legal/ethical, and logistical aspects involved. Initial results revealed that implementation

was possible and that transplantation of kidneys was practical and would yield excellent results.

DCCD is increasingly accepted as an important source of all organs for donation and from 2000 to 2008 for example, 5004 organs from such donors were transplanted in Europe, including 4261 kidneys, 505 livers, 157 lungs, and 81 pancreases [6]. Worldwide, the majority of organs are retrieved from donors corresponding to Maastricht category III, that is, after withdrawal of therapy. However, this classification requires the discontinuation of all treatment including mechanical ventilation, a procedure that is not allowed under current Israeli legislation [7]. For this reason, the DCCD program in Israel was implemented using category II donors, that is, uncontrolled donors. uDCCD was started in Maastricht, the Netherlands in 1981, and successful programs have since been instituted in a number of countries, including Spain, France, Italy, the United Kingdom, and the United States.

The success of a uDCCD program depends on a critical element, namely the early institution of organ preservation after death declaration both to reduce the time of warm ischemia and to allow time for the family to make an informed decision regarding organ donation. However, the procedure requires the cannulation of large vessels, the infusion of organoplegic solutions and heparin, or the use of ECMO. This reality raised the question of authorization for preservation without consent. Some countries with existing uDCDD programs, such as Spain and France, have passed legislation allowing presumed consent so that organ preservation procedures can be initiated without consent unless the patient has specifically opted out [8]. In other countries, for example in the state of New York in the United States, prior first-person consent is required [9]. The overriding consideration for approving the protocol in Israel was the continued severe shortage of organs for transplantation, which overrode the fear of possible non-acceptance of cannula insertion for preservation purposes without consent. In addition, in this regard, it has been stated that preserving the family's opportunity to choose donation under these circumstances may be ethically preferable to failing to do so [10]. This situation resulted in the recommendation that the preservation process could be initiated where the deceased was known to have signed an organ donor card, thus taking into account the wishes of the deceased, or in their absence, where consent is obtained from surrogate decision makers, thus allowing the family the opportunity to donate their loved one's organs if they choose to do so. It was realized that these circumstances would impose a significant limitation on the program since only 14% of the Israeli population has signed a donor card and family members are frequently not present at the time of the cardiac arrest. In our limited experience, none of the six potential uDCCD donors to date had signed an organ donor card, yet consent for donation was obtained from family members in four of the cases. While the numbers are still very small, this initial experience suggests

**Table 2.** Characteristics of the uDCCD donors

Age of donor	Reason for death	Signed donor card	Family response	Organs retrieved and transplanted
42	Suicide by hanging	No	Refused	
36	Sudden cardiac arrest	No	Consent	Kidneys retrieved; rejected due to presence of necrosis
45	Sudden cardiac arrest	No	Consent	Kidneys retrieved; rejected due to presence of necrosis
27	Sudden cardiac arrest	No	Consent	Kidneys retrieved; successfully transplanted
55	Sudden cardiac arrest	No	Refused	
46	Sudden cardiac arrest	No	Consent	Kidneys retrieved; successfully transplanted

uDCCD = uncontrolled donation after cardio-circulatory death

that the program might be acceptable to the Israeli public.

A unique aspect of the process was the holding of a mock trial. It was decided to use this format as a way of exposing the public to the possible ethical and legal aspects involved with the procedure under the scrutiny of directed questioning by expert lawyers. It was a particular concern of the ethics committee that the new practice might increase public suspicion toward the medical teams who might favor facilitating organ donation over providing maximum efforts at resuscitating a patient. Transparency was therefore an important factor in this case, since organ transplantation is based on the public's participation and reciprocity. The response of the "presiding judges" and of the public encouraged the steering committee to proceed with implementation.

The pilot program was limited to kidney donation, for which there is the widest experience and best outcomes. Indeed, while the rate of delayed graft function is high (between 60 and 80%), long term outcomes are generally excellent and approach those following donation from heart-beating, brain-dead donors. Thus at 1 year, patient and graft survival of 98 and 91.4%, respectively, was achieved in a recent study from France [10] and 1 year graft survival of 89% was reported from the Netherlands [11]. We were able to utilize the kidneys retrieved from two of the four cases consenting to donation and all four recipients are alive with normal functioning grafts at 1 year of follow-up. In the remaining two cases, poor function at the time of retrieval was the reason for non-acceptance. This was probably due to technical problems related to inadequate anticoagulation and prolonged time to cannulation. Experience from other centers suggests that, in fact, only 25% of potential donors proceed to actual donation [3]. In this regard an essential aspect of the program was the use of machine preservation following kidney retrieval. This procedure may aid in the resuscitation of already compromised, warm ischemic organs, thereby improving their quality and early outcomes [12]. More importantly, kidney viability may be tested allowing the selection of transplantable kidneys versus non-viable ones for discard, which may occur in up to one-third to one-half of kidneys tested [13]. This statistic is important since it prevents the transplantation of non-viable kidneys and the unnecessary risks of surgery and immunosuppression as well as recipient sensitization to future transplants.

**CONCLUSIONS**

In conclusion, we have described the derivation and implementation of a protocol for DCCD donation in Israel, which resulted

in the successful transplantation of kidneys with good results. While the process of DCCD is particularly demanding in terms of logistics and resources, the ongoing disparity between grafts required and their supply demands that no potential sources of transplantable organs be needlessly overlooked.

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**"Without deviation, progress is not possible"**

Frank Zappa, (1940–1993), an American musician, composer, songwriter, producer, guitarist, actor, and filmmaker whose work was characterized by nonconformity, free-form improvisation, sound experiments, musical virtuosity, and satire of American culture

**"Those who write clearly have readers, those who write obscurely have commentators"**

Albert Camus, (1913–1916), French philosopher, author, and journalist. His views contributed to the rise of the philosophy known as absurdism