ORIGINAL ARTICLE

Donation after circulatory death today: an updated overview of the European landscape

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SUMMARY

Donation after circulatory death (DCD) has become an accepted practice in many countries and remains a focus of intense interest in the transplant community. The present study is aimed at providing a description of the current situation of DCD in European countries. Specific questionnaires were developed to compile information on DCD practices, activities and post-transplant outcomes. Thirty-five countries completed the survey. DCD is practiced in 18 countries: eight have both controlled DCD (cDCD) and uncontrolled DCD (uDCD) programs, 4 only cDCD and 6 only uDCD. All these countries have legally binding and/or nonbinding texts to regulate the practice of DCD. The no-touch period ranges from 5 to 30 min. There are variations in *ante* and *post mortem* interventions used for the practice of cDCD. During 2008–2016, the highest DCD activity was described in the United Kingdom, Spain, Russia, the Netherlands, Belgium and France. Data on post-transplant outcomes of patients who receive DCD donor kidneys show better results with grafts obtained from cDCD versus uDCD donors. In conclusion, DCD is becoming increasingly accepted and performed in Europe, importantly contributing to the number of organs available and providing acceptable post-transplantation outcomes.

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Introduction

Shortage of organs is the most important barrier to the expansion of transplant therapies across the world. The majority of transplants are performed with organs derived from donors declared dead using neurological criteria, that is donation after brain death (DBD) donors [1]. However, in recent decades, there has been renewed interest in donation from persons whose death has been determined using circulatory and respiratory criteria, that is donation after circulatory death (DCD). Controlled DCD (cDCD) refers to donation from persons whose death has occurred following the decision to withdraw life-sustaining therapies (WLST) which are no longer considered in the best interests of the patients [2]. Uncontrolled DCD (uDCD) refers to donation from persons who die as a result of an unexpected and sudden cardiac arrest for which resuscitation has been unsuccessful [2]. DCD has expanded in such a way that it represented 20% of the 34 854 deceased organ donors reported to the Global Observatory on Organ Donation and Transplantation in 2016 [1]. The development of DCD has, however, been variable across countries. DCD is only practiced in a minority of jurisdictions. Activity levels vary, with some countries primarily focusing on uDCD, while cDCD is predominant in others [3]. The regulatory frameworks and the procedures applied are heterogeneous, as are the reported outcomes with the transplantation of DCD donor organs.

In 2011, the European Committee on Organ Transplantation of the Council of Europe (CD-P-TO).[1] published a report on the situation of DCD in Europe [4]. Since then, the scene has changed enormously, with more countries developing DCD programs and with practices evolving as new evidence becomes available [5]. Through the present study, the CD-P-TO aims at providing an updated description of the situation of DCD in member states of the Council of Europe, with a focus on regulatory and organisational features, donation and transplantation activities, effectiveness of the process, and results obtained with DCD donor transplants. This information will help health authorities and professionals to set up new DCD programs and improve current practices.

Materials and methods

Two questionnaires were designed and agreed upon by representatives of countries at the CD-P-TO: one questionnaire to compile information about the legal and ethical framework of relevance for DCD and DCD procedures used, and a second questionnaire to collect information about DCD donation and transplantation activity and post-transplant outcomes.

Each CD-P-TO representative collected the requested information from official sources, either the relevant national health authority(ies) or the designated agency (ies). The information on DCD activities was completed with data obtained from the *Newsletter Transplant*, an official publication of the CD-P-TO [6]. Data on post-transplant outcomes of DCD donor organs were obtained from existing national registries, with the exception of 5 countries (Israel, Latvia, Norway, Portugal and Russia) where aggregated data were obtained from center reports.

The information was returned to the CD-P-TO Secretariat for subsequent data quality control and analysis.

Legal and ethical framework and procedures

Questions (single or multiple choice options) referred to general information about DCD programs and legal-regulatory frameworks relevant to DCD and DCD procedures, with particular emphasis on cDCD.

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[1] The European Committee on Organ Transplantation (CD-P-TO) is the steering committee in charge of organ, tissue and cell donation and transplantation activities at the European Directorate for the Quality of Medicines and HealthCare (EDQM) of the Council of Europe. As of April 2019, the CD-P-TO is composed of 36 members (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Montenegro, the Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Republic of Moldova, Turkey, Ukraine, United Kingdom) and 22 observers (Armenia, Belarus, Canada, Georgia, Holy See, Israel, Russian Federation, United States of America, Council of Europe Committee on Bioethics, DTI Foundation, European Association of Tissue and Cell Banks, European Eye Bank Association, European Society for Human Reproduction and Embryology, European Society for Organ Transplantation, European Commission, Eurotransplant, South Europe Alliance for Transplantation, Scandiatransplant, The Transplantation Society, United Network for Organ Sharing, World Health Organization and World Marrow Donor Association).

Donation and transplantation activity

Information on donation and transplantation activity from DCD and DBD donors was collected for the years 2008–2016.

An actual donor (hereinafter donor) was defined as a deceased person from whom at least one solid organ was recovered for the purpose of transplantation. A utilised donor was defined as a deceased person from whom at least one solid organ was transplanted.

Information was also collected on the number of organs recovered and transplanted from DBD, cDCD, and uDCD donors. Organs recovered for the purpose of tissue or cell transplantation were not counted as organs recovered (e.g., pancreas recovered for islet transplantation, hearts recovered for heart valves implants). Organs for transplantation were counted as individual organs, even if double transplants were performed.

The utilization rate of organ donors was calculated as the percentage of donors who were converted into utilised donors. The number of organs recovered *per* donor resulted from referring the number of organs recovered for the purpose of solid organ transplantation from donors within the country to the number of donors. The number of organs transplanted *per* donor was calculated by dividing the number of organs transplanted as solid organs from donors within the country by the number of donors.

Short-term outcomes of solid organ transplants

Information on the short-term outcomes of recipients of DCD donor organs was requested for those transplants performed between January 1, 2008, and December 31, 2015, to ensure 1-year follow-up data were available for all recipients included in the study.

For survival figures, each country provided cumulative data stratified according to the type of organ transplanted and the type of DCD (cDCD versus uDCD) as specified below:
• A: Number of patients who received a transplant from a DCD donor during the period of study.
• B: Number of patients with no evidence of graft loss and/or patient death, but lost to follow-up before the first year (± 1 month).
• C: Number of patients who lost their graft during the first year and who subsequently or simultaneously died.
• D: Number of patients who lost their graft during the first year and who remained alive for 1 year

(± 1 month). Patients with no follow-up information after graft loss were considered to be alive.
• E: Number of patients who died during the first year with a functioning graft.
• F: Number of patients alive and with a functioning graft at 1 year (± 1 month).

Survival figures *per* type of organ transplanted and *per* type of DCD donor were calculated as follows:

• 1-year censored for death graft survival: $[(E + F)/(A - B)] \times 100$.
• 1-year graft survival (noncensored for death): $[F/(A - B)] \times 100$.
• 1-year patient survival: $[(D + F)/(A - B)] \times 100$.

For kidney recipients, information was also collected on the number of patients developing delayed graft function (DGF), defined as the need for dialysis in the first week after transplantation, and the number of patients with primary nonfunction (PNF), defined as grafts which failed to ever function.

Data are represented as absolute numbers and percentages, when applicable. The incidence of DGF and PNF of recipients of kidneys from cDCD versus uDCD donors was compared by the Chi-Square test. One-year graft and patient survival between these two groups were also compared by the Chi-Square test and the Fisher's exact test, when applicable. When a statistically significant difference was found ($P < 0.05$), the odds ratio (OR) was calculated with its 95% confidence interval. EpiDat v3.1© was used to perform the analysis.

Results

The first questionnaire was returned by 35 of the 47 member states of the Council of Europe (Fig. 1). Of the countries participating in the survey, 17 declared they had no DCD activity, owing to legislative obstacles (Croatia, Estonia, Germany, Greece, Hungary), absence of a specific regulatory framework (Belarus, Cyprus, Denmark, Finland, Moldova, Romania, Slovak Republic, Slovenia, Turkey), lack of technical expertise (Belarus, Bulgaria, Georgia, Greece, Moldova, Slovak Republic, Slovenia, Romania, Turkey), and/or insufficient organisational capacity (Armenia, Belarus, Denmark, Georgia, Slovenia).

Despite this, four countries (Croatia, Denmark, Hungary, Turkey) declared they were interested in developing cDCD programs. Five countries (Bulgaria, Moldova, Romania, Slovak Republic, Slovenia) stated interest in both cDCD and uDCD. Finally, 8 member
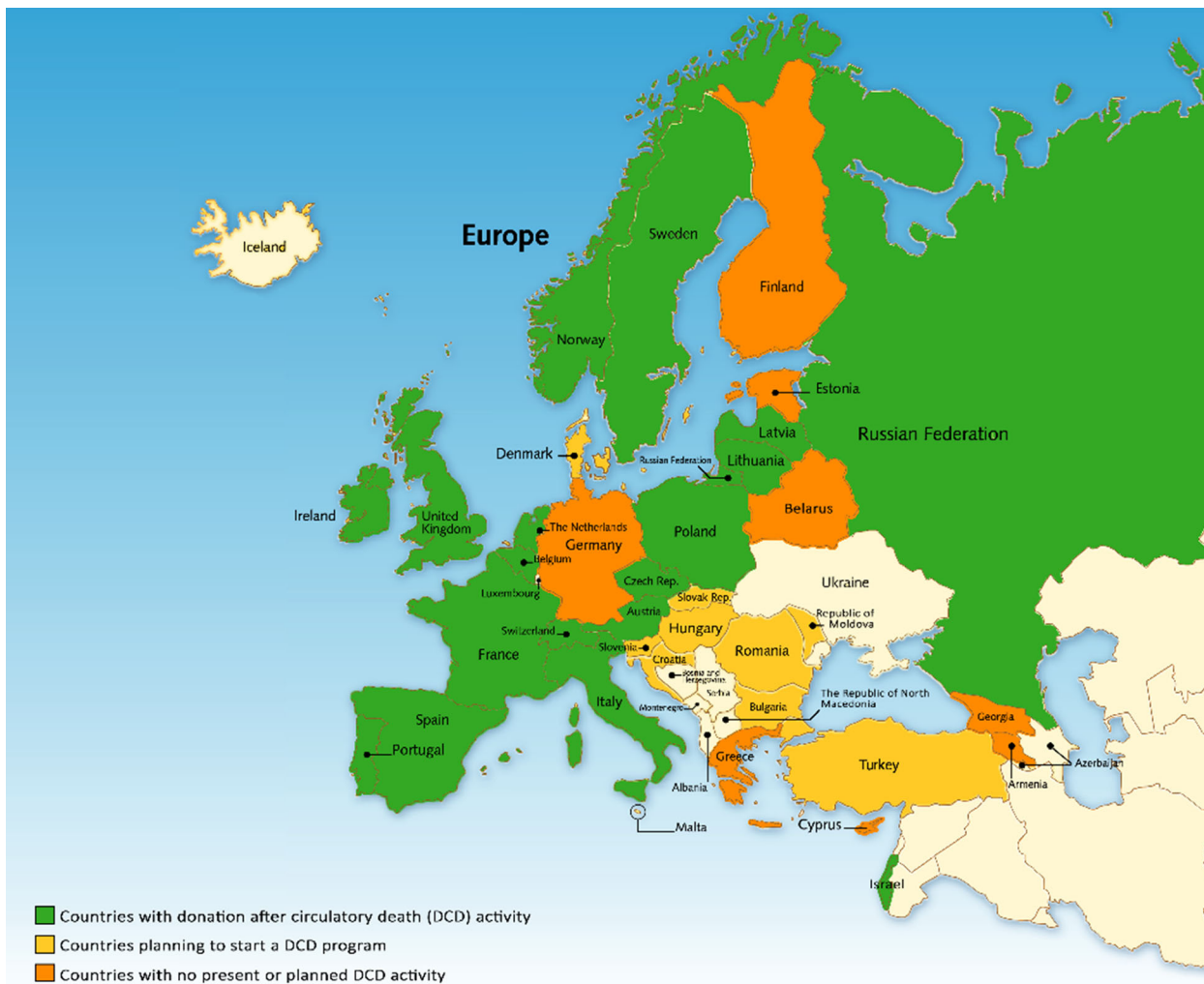
Figure 1 Member states of the Council of Europe participating in the survey (coloured). Countries with donation after circulatory death activity in green: Austria, Belgium, Czech Republic, France, Ireland, Israel, Italy, Latvia, Lithuania, the Netherlands, Norway, Poland, Portugal, Russia, Spain, Sweden, Switzerland, and United Kingdom. Countries planning to start a donation after circulatory death program (yellow): Bulgaria, Croatia, Denmark, Hungary, Moldova, Romania, Slovak Republic, Slovenia, and Turkey. Countries with no present or planned donation after circulatory death activity (orange): Armenia, Belarus, Cyprus, Estonia, Finland, Georgia, Germany, and Greece. DCD, donation after circulatory death.

states (Armenia, Belarus, Cyprus, Estonia, Finland, Georgia, Germany, Greece) declared they were not planning to develop DCD programs because it was considered they were not needed (Belarus, Estonia, Finland), due to lack of professional confidence in such programs (Cyprus, Georgia, Greece), logistical difficulties (Georgia, Greece), legal obstacles (Germany), and potential costs (Greece).

Eighteen countries confirmed having DCD programs in place and registered at least one DCD donor during 2008–2018. Eight countries had both cDCD and uDCD, 4 only cDCD and 6 only uDCD programs (Fig. 2).

Regulatory framework and procedures applied to donation after circulatory death

General characteristics of DCD programs are shown in Table 1. Twelve countries have legal provisions related to the practice of DCD and 16 rely on nonlegally binding texts that provide recommendations for the development of DCD. The six countries where legislation does not make reference to DCD have national guidelines. Of note, the no-touch period, defined as the time between the cessation of circulation and respiration and the determination of death, ranges from 5 min in 13

Figure 2 Member states with donation after circulatory death (DCD) programs (coloured). Both controlled and uncontrolled DCD programs (dark green): Austria, Belgium, Czech Republic, France, Italy, the Netherlands, Spain, and Switzerland. Only controlled DCD (medium green): Ireland, Norway, Sweden, and United Kingdom. Only uncontrolled DCD (light green): Israel, Latvia, Lithuania, Poland, Portugal, and Russia.

countries to 10 min in three countries, 20 min in Italy, and 30 min in Russia. In member states where cDCD and uDCD programs coexist, the duration of the no-touch period and the criteria to assess the cessation of circulation to determine death are the same in both the cDCD and the uDCD programs.

Regulatory framework and procedures applied to controlled donation after circulatory death

Specific features of the regulatory framework and the procedures applied in cDCD in the 12 European countries with such a program were further explored. A summary of some selected aspects is depicted in Table 2.

Regarding the categories of patients who can be considered as potential cDCD donors following the decision to WLST, all countries referred to patients with a devastating brain injury. Currently, patients with terminal neurodegenerative disorders are not considered as potential cDCD donors in four countries (France, Italy, Norway, Sweden), patients with terminal respiratory diseases in 5 (Belgium, France, Italy, Norway, Sweden), and patients with terminal heart failure, including those under therapeutic ECMO, in 2 (Belgium, Sweden). It should be noted that in Belgium and the Netherlands, donation is also considered following euthanasia.

When cDCD is considered in patients with a devastating brain injury in whom the decision has been made to WLST, only six countries (France, Italy, Norway, Spain, Sweden, Switzerland) recommend that professionals consider delaying the WLST when brain death (BD) is a likely outcome, to enable death to be determined by neurological criteria and DBD to be activated.

Table 1. Selected features of the regulatory framework and the procedures applied to donation after circulatory death in member states of the Council of Europe.

	Year the program started uDCD/cDCD	National legislation (legally binding)	National guidelines (non-legally binding)	No-touch period (min)	Options to assess the absence of circulation for the determination of death
Austria	1990s	No	Yes	10	EC, IBPM
Belgium	2006/2005	Yes	Yes	5	ECG, IBPM
Czech Republic	2002/2015	Yes	Yes	5	ECG, EC
France	2007/2015	Yes	Yes	5	ECG, IBPM
Ireland	–/2011	No	Yes	10	ECG, IBPM
Israel	2014/–	Yes	Yes	5	ECG
Italy	2007/2015	Yes	Yes	20	ECG
Latvia	1973/–	Yes	Yes	5	ECG
Lithuania	2016/–	Yes	No	5	ECG, EC, IBPM
The Netherlands	1980s	No	Yes	5	IBPM
Norway	–/2010	No	Yes	5	IBPM*
Poland	2015/–	Yes	No	5	ECG
Portugal	2016/–	Yes	Yes	10	ECG, IBPM
Russia	1967/–	Yes	Yes	30	ECG
Spain	1980s/2009	Yes	Yes	5	ECG, EC, IBPM
Sweden	–/2018†	No	Yes	5	IBMP
Switzerland	1985‡/1985‡	No	Yes	5§	EC
United Kingdom	2013–2016**/1985	Yes	Yes	5	ECG, IBPM

cDCD, controlled donation after circulatory death; EC, echocardiography; ECG, electrocardiogram; IBPM, invasive blood pressure monitoring; uDCD, uncontrolled donation after circulatory death.

*No national guidance. The responsible physician decides, but IBPM is normally used.

†Pilot program developed between February 2018 and January 2019, with 10 cDCD utilized donors. The program is currently under evaluation to become a national established program.

‡Stopped due to unclear legal situation in 2007 and re-launched in 2011.

§After the no-touch period, the permanent loss of cerebral function must be confirmed by two medical specialists.

**uDCD program ceased in 2016.

In Switzerland, in particular, a minimum of 36 h of observation following catastrophic brain injury is recommended in all cases in which BD may occur.

The *ante mortem* administration of substances (e.g., heparin) for organ preservation is allowed and practiced in seven countries, informing the next of kin about these procedures. Only two countries (Spain, Switzerland) require specific authorization for the *ante mortem* administration of substances from the legal representative of the patient. In Italy, heparin administration is only allowed during the agonal period. In the five countries where the *ante mortem* administration of substances is not allowed, this is mainly due to ethical concerns and lack of professional guidance.

Ante mortem cannulation is not allowed in six countries due to ethical concerns. In France, Italy, Norway, and Sweden, the identification of femoral vessels prior to the WLST is allowed—and practiced—for cannulation to be completed following the determination of death. In Austria, Belgium, and Spain, *ante mortem* cannulation is allowed, but only practiced in Belgium and Spain, with specific authorization by the legal representative of the patient in the latter.

The most frequent location for the WLST when a cDCD procedure is planned is the intensive care unit, with only four countries referring to the operating room. The maximum time between the WLST and circulatory arrest waited by recovery teams varies from 1 h in Belgium to 3 h in the UK, with 2 h being the most common practice.

Modalities of *in situ* preservation/organ recovery procedures used in each country are shown in Table 2, with the rapid recovery of organs being the most frequent practice. *In situ* preservation of organs with normothermic regional perfusion (nRP) based on the use of ECMO devices is applied in eight countries (being a very recent and emerging practice in 2), and is the only procedure in 3. *In situ* cooling of organs with the triple-lumen double-balloon catheter technique is applied in three countries. All countries where nRP is performed

Table 2. Selected features of the regulatory framework and the procedures applied to controlled donation after circulatory death in member states of the Council of Europe.

| | Ante mortem substances allowed | Ante mortem cannulation allowed | Most frequent location for WLST | Time waited by recovery teams (h) | Type of in situ preservation and organ recovery procedure applied | | | |
					Rapid recovery	*In situ* cooling	hRP	nRP
Austria	Yes	Yes*	OR	–	X			
Belgium	Yes	Yes	OR	1	X			X‡
Czech Republic	No	No	ICU	2	X	X		
France	Yes	Yes†	ICU	3				X
Ireland	No	No	OR	1.5	X			
Italy	Yes	Yes†	ICU	–				X
Netherlands	No	No	ICU	2	X			X‡
Norway	Yes	Yes†	ICU	1.5				X
Spain	Yes	Yes	OR	2	X	X	X	X
Sweden	No	No	ICU	3	X			
Switzerland	Yes	No	ICU	2	X	X		X
United Kingdom	No	No	ICU	4	X			X

hRP, hypothermic regional perfusion; ICU, intensive care unit; nRP, normothermic regional perfusion; OR, operating room; WLST, withdrawal of life-sustaining therapies.

*Allowed, but not practiced.

†Identification of femoral vessels to facilitate cannulation after the determination of death.

‡Emerging practice.

resort to the occlusion of the aorta, either by surgical clamping or using an aortic balloon, to avoid restoring circulation to the brain after the determination of death. In Spain and the UK, the steps to achieve the safe isolation of the brain during nRP are specified [7–9].

Donation after circulatory death activity

The DCD activity for 2008–2016 in the different countries is presented in Table 3. During the study period, 9702 DCD donors were reported, most of whom were cDCD donors (69%). uDCD was only quantitatively prominent in France, Russia, and Spain. The highest DCD activity (absolute numbers) was described in the UK, followed by Spain, Russia, the Netherlands, Belgium, and France. The country with the highest percentage of DCD donors out of the deceased donation activity during the study period was the Netherlands (49%).

In total, 19 325 DCD transplants were carried out, of which almost 15 000 were kidney transplants. Of note, DCD liver and lung transplants were rather frequent, with kidney/liver and kidney/lung ratios of 6:1 and 11:1, respectively. The most prominent DCD pancreas transplant activity was observed in the UK. Up to 2016, the UK was the only country with a cDCD heart transplant program.

The evolution of DCD versus DBD in those European countries with the most active DCD programs is shown in Fig. 3. There has been a progressive increase in the DCD activity in all these countries over the years. In Belgium, France, Spain, and the UK, DCD has increased nearly twofold from 2008 to 2016. In parallel, DBD has remained stable or experienced a slight increase.

The effectiveness of DCD versus DBD programs in Europe for 2016 is depicted in Table 4.

Short-term outcomes of transplants using organs from donation after circulatory death donors

Information was obtained on the short-term outcomes of 13 277 patients (91% of the organs transplanted during 2008–2015) receiving solid organ transplants from DCD donors.

Short-term results were provided for 11 102 recipients of DCD kidneys (7852 controlled and 3250 uncontrolled). Information is summarized in Fig. 4. The incidence of PNF was 7.4% in uDCD vs. 2.8% in cDCD ($P < 0.001$). The incidence of DGF was significantly higher in recipients transplanted with uDCD donor kidneys (52.6% vs. 30.7%; $P < 0.001$). One-year graft survival was significantly higher in recipients of cDCD

Table 3. DCD donation and transplantation activities in member states of the Council of Europe for the years 2008–2016.

	DCD donors (n) 2008–2016		DCD donors	% DCD donors over total deceased donors	Transplants from DCD donors (n) 2008–2016*					
	uDCD	cDCD	(n) 2008–2016	2008–2016 (%)	Kidney	Liver	Lung	Pancreas	Heart	Total
Austria	14	20	34	1.9	63	5	4	0	0	72
Belgium	16	633	649	23.7	870	440	326	37	0	1673
Czech Republic	0	23	23	1.2	40	1	0	0	0	41
France	457	62	519	3.5	716	48	0	0	0	764
Ireland	–	21	21	3.0	42	0	3	0	0	45
Israel	8	–	8	1.2	11	0	0	0	0	11
Italy	29	9	38	0.3	45	14	4	0	0	63
Latvia	115	–	115	37.6	71	0	0	0	0	71
Lithuania	2	–	2	0.5	3	0	0	0	0	3
Netherlands	47	1048	1095	49.1	1785	336	418	29	0	2568
Norway	–	10	10	1.0	18	4	0	0	0	22
Poland	10		10	0.2	18	0	0	0	0	18
Portugal	10	–	10	0.4	12	0	0	0	0	12
Spain	997	757	1754	11.5	2348	339	164	3	0	2854
Switzerland	1	70	71	7.3	96	45	21	3	0	165
Russia	1280	–	1280	32.1	2171	0	0	0	0	2171
United Kingdom	3	4060	4063	39.1	6630	1268	441	401	32	8772
Total	2989	6713	9702	12.7	14 939	2500	1381	473	32	19 325

cDCD, controlled donation after circulatory death; DCD, donation after circulatory death; uDCD, uncontrolled donation after circulatory death.

*Transplants performed with organs obtained from DCD donors within the country.

versus uDCD donor kidneys (90.1% vs. 88.1%; $P = 0.002$). Significant differences favouring cDCD kidneys were also found when comparing 1-year graft survival censored for death (93% vs. 90.5%; $P < 0.001$).

Short-term results of liver transplants were collected for 1563 recipients (1497 cDCD and 66 uDCD). No statistically significant differences were found between the two groups in terms of 1-year graft (82% vs. 77%) and patient survival (90% vs. 85%).

Concerning lung transplantation, short-term results were collected for 278 recipients (226 cDCD and 52 uDCD). No statistically significant differences were found between the two groups in terms of 1-year graft (87% vs. 78%) and patient survival (87% vs. 78%).

Results of pancreas transplantation were collected for 334 recipients of cDCD organs. Results showed a 1-year censored for death graft survival of 85% and 1-year patient survival of 98%.

Discussion

Donation after circulatory death can help increase the availability of organs for transplantation and offer more patients the opportunity of donating their organs after their death. The concept that decision-making at the end of life should be based not only on medical aspects, but also on moral, societal, and welfare considerations [10], has set the basis for many professional societies to consider that donation should be offered as an option in end-of-life care [11–14]. However, although a large number of persons die following an unsuccessfully resuscitated cardiac arrest or the decision to WLST, DCD is only developed in a limited number of countries [15].

This study provides an overview of the current situation of DCD in Europe. In 2011, only 10 countries reported having a DCD program [4]. At present, DCD is developed in 18 of the 35 countries that participated in this initiative. Legislative obstacles and ethical concerns constitute the main barriers for the development of new DCD programs [16]. Overcoming such obstacles requires exchanging views and practices between countries and building consensus on aspects such as the determination of death by circulatory criteria [3]. Indeed, immediately after finalizing the present work, we were informed that the DCD program in Norway had been temporarily halted due to ethical and juridical concerns regarding the practice that required national
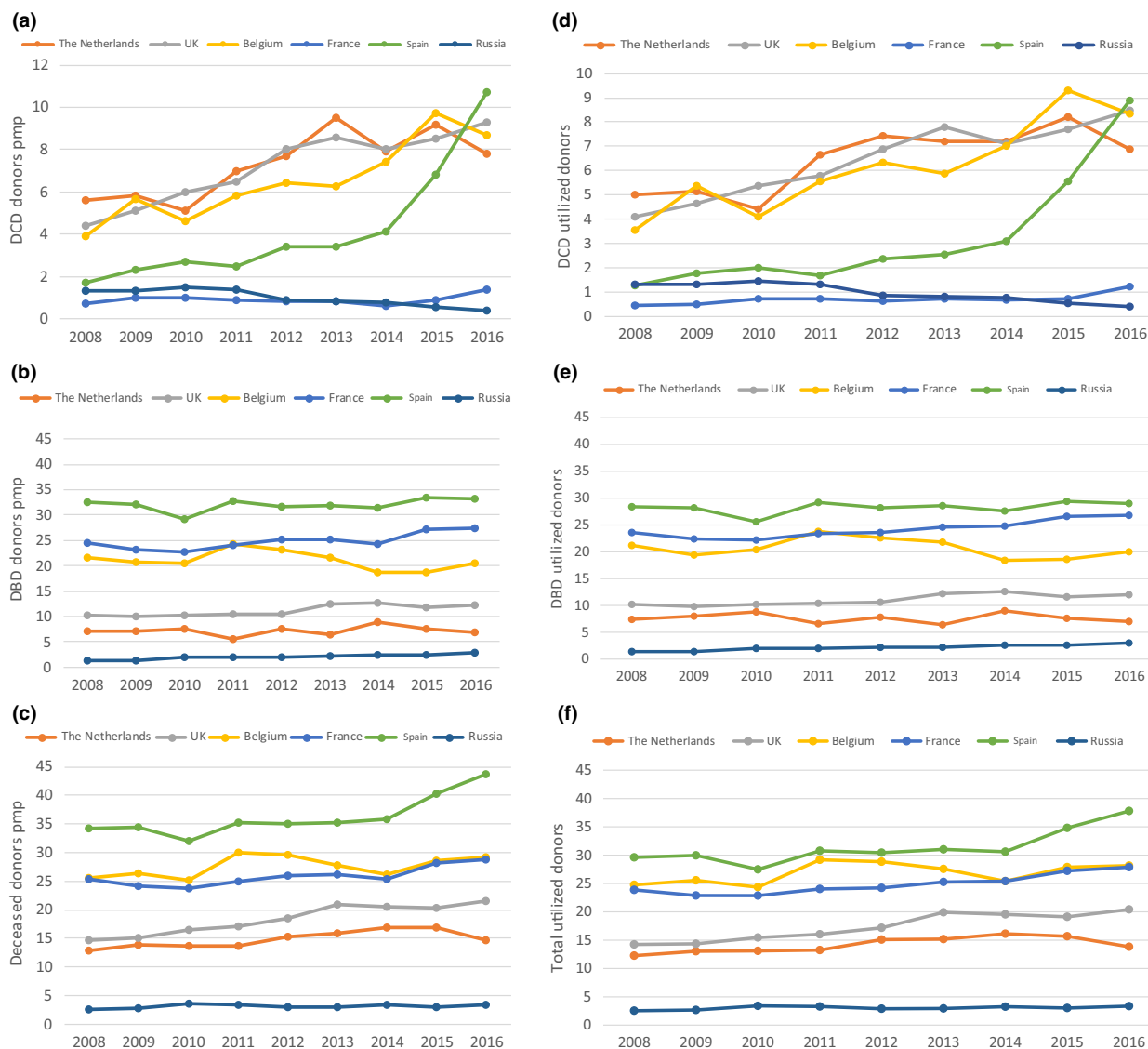
Figure 3 Evolution of actual donation after circulatory death (a), donation after brain death (b) and overall deceased donation rates (c) and of utilized donation after circulatory death (d), donation after brain death (e) and overall deceased donation rates (f) per million population in the five Council of Europe member states with the most active DCD programs. Years 2008–2016. DBD, Donation after brain death; DCD, Donation after circulatory death; pmp, per million population.

scrutiny and agreement. The results from this national DCD program evaluation are expected for the end of 2019.

When comparing the regulatory frameworks of countries with DCD, notable differences were identified. One of the most outstanding refers to the duration of the no-touch period. The majority of countries have established a 5-min no-touch period, but others have extended this period of observation to 10, 20, or even 30 min. The acceptance that human death is based on the permanent loss of brain function allows the confident determination of death soon after the loss of circulation [17]. Death using circulatory criteria can be based on the permanent cessation of circulation, that is, the point when circulation "will not" be re-established, either spontaneously or artificially. If circulation is not re-established, the cessation of blood flow to the brain will lead to the irreversible loss of neurological functions—and hence to death. Following the decision to WLST, return of spontaneous circulation has not been observed beyond 5 min based on a recent systematic review [18]. However, there was a reduced number of studies and cases included in such review. Further evidence is required to determine if longer periods of observation, such as those described in some European countries, can be subject to review. The need to

Table 4. Effectiveness of the donation after circulatory death and the donation after brain death processes in member states of the Council of Europe providing the relevant information.* for 2016

	cDCD	uDCD	DBD
Actual donors	1284	262	7268
Utilised donors	1165	196	6771
Utilisation rate (%)	**91**	**75**	**93**
Organs recovered per donor	**2.8**	**2.2**	**3.8**
Organs transplanted per donor	**2.6**	**1.6**	**3.5**
Kidneys recovered	2421	472	12 628
Kidneys transplanted	2017	322	11 036
Kidneys transplanted (%)	**83**	**68**	**87**
Livers recovered	647	35	6074
Livers transplanted	492	17	5411
Livers transplanted (%)	**76**	**49**	**89**
Lungs recovered	249	17	2610
Lungs transplanted	218	15	2316
Lungs transplanted (%)	**88**	**88**	**89**

cDCD, controlled donation after circulatory death; DBD, donation after brain death; uDCD, uncontrolled donation after circulatory death.

Numbers highlighted in bold refer to % or rates.

*Data provided by Belgium, Czech Republic, France, Ireland, Israel, Italy, Lithuania, Latvia, Netherlands, Norway, Portugal, Russia, Spain, Switzerland and United Kingdom.

perform an exploration to assess if brain death criteria are met following the nontouch period, as required in some countries, could also be reconsidered, since the prerequisite of hemodynamic stability for brain death testing is obviously not met in the context of a circulatory arrest.

In cDCD, practices also vary with regards to the use of *ante mortem* and *post mortem* interventions. The use of substances and the cannulation of vessels before the WLST or during the agonal period—but before death—are practiced in some countries, while not allowed in others. *Ante mortem* interventions could be justified from an ethical perspective based on their proportionality, that is, the balance between the damage caused to the potential donor and the benefits for the recipients. These benefits can be measured in terms of the number of organs valid for transplantation and of post-transplant outcomes. The use of heparin may be considered appropriate, except in cases of intracranial hemorrhage or active bleeding. However, good post-transplant outcomes have been reported without its administration [19]. Some authors consider the *ante mortem* cannulation of vessels or the placement of guides to facilitate recovery and shorten the duration of warm ischemia a

less proportionate approach, since these measures will improve results only in theory. Of note, not all countries request specific authorization for cannulation from the legal representatives of patients for these *ante mortem* interventions.

The use of ECMO devices to allow the perfusion of organs with oxygenated blood after the determination of death has proven to improve post-transplant outcomes in recipients of cDCD livers. Two recent studies from Spain and the UK have shown that nRP is associated with improved graft survival and a decreased incidence of ischemic-type biliary lesions and other biliary complications [20,21]. In addition, thoraco-abdominal nRP is being used in Belgium and the UK to validate and preserve cDCD donor hearts prior to recovery and transplantation [22,23]. The Papworth team has combined this approach with the *ex situ* preservation of hearts which are then subject to an additional validation [24]. The question of whether thoraco-abdominal nRP can provide enough reassurance for the safe transplantation of these hearts without *ex situ* machine perfusion is currently being explored [22,23]. Given the high costs of *ex situ* preservation strategies, such an approach could make cDCD heart transplantation a reality in other countries soon. These findings make the use of nRP in DCD a potential fertile area for future research. One of the main concerns regarding the use of nRP in cDCD is the risk of restoring circulation to the brain during the procedure [25]. To minimize the occurrence of such events, the aorta is blocked with an intraluminal balloon or is subject to surgical clamping or vessel ligation. In Spain, a procedure is in place for the early identification of failure to properly block the aorta and immediately halt the procedure to avoid cases of auto-resuscitation [6,7].

The Netherlands was the first country to raise an alert that the development of cDCD could negatively impact upon DBD. By retrospectively reviewing the clinical charts of cDCD donors in a region in the UK, a panel of experts identified that 27% of these donors could have evolved to BD should the WLST have been delayed for a further 36 h [26]. The authors concluded that, by identifying potential cDCD donors who were likely to transition to BD, the pool of potential DBD donors could be expanded. This strategy has been put in place in some organ procurement organizations in the USA as well as in Spain [27,28]. When potential cDCD donors are referred and BD is likely to occur, the treating team and the legal representatives of the family are approached to propose delaying the WLST to enable death to be determined by neurological criteria.
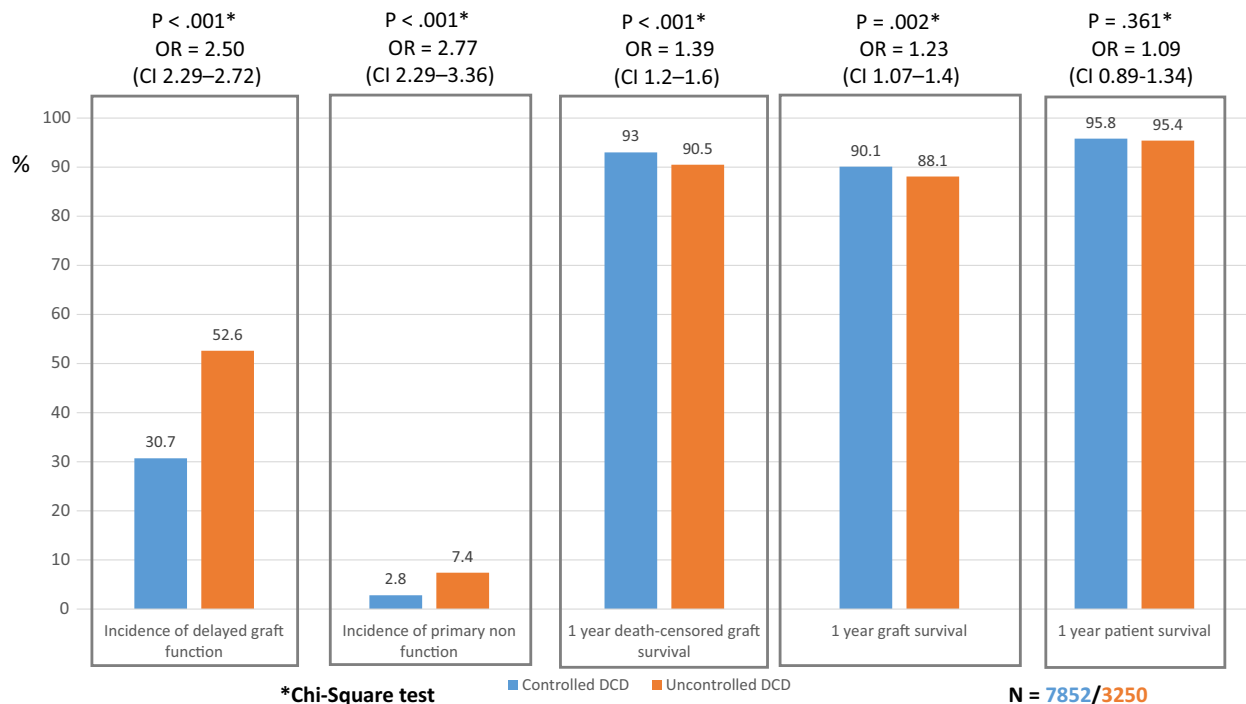
Figure 4 Short-term results of kidney transplantation from controlled versus uncontrolled donation after circulatory death donors in member states of the Council of Europe. *Chi-square test. Reference: controlled DCD. DCD, donation after circulatory death.

Notably, in our study, only a few countries have provided recommendations to professionals to favor DBD versus cDCD—recommendations that are sustained on the lower effectiveness of cDCD compared with DBD (see below) and the better outcomes reported with DBD liver transplantation. Despite this finding, when evaluating the evolution of DCD and DBD in the most active countries during the study period, we could not observe a decline in the DBD rates and DCD seemed to behave as an added-on activity.

The transplantation activities derived from DCD in Europe are impressive. In most countries, DCD has become a multiorgan recovery procedure, with not only kidneys but other organs being actively transplanted. Of note, pancreas and heart transplantation are still rare, with the UK being the most active country. Nevertheless, and as expected, the effectiveness of DCD is substantially lower compared with DBD in terms of organs recovered and transplanted *per* donor. uDCD is also less effective than cDCD. Although a complex process, uDCD can still substantially contribute to increase the availability of organs for transplantation. Effectiveness of the DCD programs was also substantially different between countries when relating the number of specific organ transplants to the number of DCD donors. This is likely due to differences in the predominant DCD program in place (cDCD versus uDCD), but may also depend on variations in donor and organ selection criteria.

Uncontrolled DCD kidney transplants perform worse than cDCD in terms of DGF, PNF, and graft survival, but still with reasonable outcomes, although amenable to improvement. Recent literature on the topic reveals that nRP can substantially reduce the incidence of PNF among uDCD kidney transplants, compared with the *in situ* cooling of kidneys [29]. The function of uDCD kidneys subject to nRP is also better [30]. In fact, large series of uDCD kidneys show extraordinary outcomes with this approach [31,32]. As for the rest of the organs, likely as a result of very strict selection criteria, no differences were found in terms of patient and graft survival when comparing the outcomes of recipients of uDCD versus cDCD donor organs. Overall, results obtained with DCD donor organs can be considered appropriate. Although post-transplant outcomes of DCD organs may be inferior to those reported for organs from standard criteria DBD donors, the benefits of using these grafts must be referred to the alternative of remaining on the waiting list, and its negative impact on survival and quality of life.

Our study has several limitations in the assessment of post-transplant outcomes. No information was gathered

on the outcomes of recipients of DBD organs during the study period to establish a comparison with recipients of DCD organs. Given that post-transplant outcomes were assessed through aggregated, not individual data, we could not study the impact of specific practices and procedures on post-transplant outcomes. This should be a subject of future research to better help professionals and authorities design procedures that are related to improved results. We did not compile information on *ex situ* preservation strategies used, an area of interest given the potential of machine perfusion in improving outcomes of DCD donor organs.

In conclusion, the practice of DCD is expanding, with more countries having embarked on this type of donation and with increasing activity. Procedures are extremely heterogeneous. Although DCD is less effective than DBD, the process has yielded an impressive number of transplanted organs in the European setting over the last few years. Results of organs from DCD donors are appropriate, although improvement is foreseen as knowledge is gained, experience increased, and evidence built on the value of *in situ* and *ex situ* preservation strategies. DCD should be considered as an option in all countries, not only to increase the availability of organs to cover the transplant needs of our population, but also to give more patients the opportunity of donating their organs after their death.

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