TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Kidneys from uncontrolled donors after cardiac death: which kidneys do worse?

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Keywords
donation after cardiac death, kidney transplantation, uncontrolled DCD donors.

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Conflicts of interest
The authors of this manuscript have no other conflicts of interest to disclose as described by *Transplant International*.

Received: 13 November 2012
Revision requested: 23 December 2012
Accepted: 6 January 2013
Published online: 6 February 2013

doi:10.1111/tri.12067

Summary

Kidneys from uncontrolled donors after cardiac death (DCD) expand the donor pool, but are associated with more primary nonfunction (PNF) and delayed graft function (DGF) compared with more conventional donor kidneys. It remains unclear, which factors influence outcome of uncontrolled donation. Therefore, we studied which donor, graft, and recipient characteristics are associated with PNF in a large cohort study. The association between different characteristics and short-term graft function was analyzed for kidneys procured in the Maastricht region from 1 January 1981 to 1 July 2009. Patients were followed until 7 January 2010. A total of 135 uncontrolled donor kidneys were included in this study. The incidence of PNF and DGF was 22% and 61%, respectively. Increasing donor age is an independent risk factor for graft failure in a univariate analysis (OR 1.035, 95% CI 1.004–1.068, $P = 0.028$). Donor age remains strongly associated with PNF in a multivariate analysis (OR 1.064, 95% CI 1.013–1.118, $P = 0.014$). However, the predictive value of donor age alone is poor (AURC 0.640, 95% CI 0.553–0.721). Increasing donor age of uncontrolled DCD donors is a major risk factor for PNF. Other clinically relevant variables were not associated with PNF. Donor age is strongly associated with PNF and remains an important parameter in donor selection.

Introduction

In the past decades, kidney transplantation using organs obtained from donors after cardiac death (DCD) has gained popularity and a wider acceptance in many countries as a valuable tool to decrease the waiting time for kidney transplantation [1–3].

Most DCD kidney donation programs only include kidneys from controlled DCD donors, donors who died after withdrawal of futile medical treatment. Uncontrolled DCD donation has not yet obtained the same wide acceptance, but its use is increasing.

In uncontrolled donors, donors who die after failed resuscitation, the period between circulatory arrest and organ preservation is often not exactly known and the efficacy of cardiopulmonary resuscitation is difficult to assess. Therefore, these kidneys are exposed to unknown ischemic injury during the inevitable period of warm ischemia, which may result in higher incidences of primary nonfunction (PNF) and delayed graft function (DGF). The relatively unknown ischemic injury and the unplanned situation of the procedure have led to a general reluctance to initiate uncontrolled DCD programs and to accept uncontrolled DCD kidneys for transplantation. There are a limited number of uncontrolled DCD kidney transplantation programs in Spain and France with excellent results [4,5]. Furthermore, a recent study shows that the clinical outcome of uncontrolled DCD kidneys is comparable to that of controlled DCD kidneys [6]. This justifies a more widespread use of uncontrolled DCD donors to reduce the still growing waiting list for renal transplantation and may stimulate the implementation of uncontrolled DCD kidney programs.

Most studies which assessed DCD kidney transplantation outcomes analyzed either controlled DCD kidneys or uncontrolled and controlled DCD kidneys together.

Despite the different mechanism of ischemic injury, the risk factors for the outcome of uncontrolled DCD kidney transplantation have not been studied before. Because of the increased popularity, it is essential to know which uncontrolled DCD kidneys can be accepted for transplantation and which kidneys better can be discarded. Our center has a long-time experience with the use of uncontrolled donor kidneys for transplantation since 1981. To describe the opportunities and limits of uncontrolled DCD kidney transplantations, we assessed the results of our uncontrolled DCD program and determined which factors are associated with PNF or inferior graft function after transplantation of uncontrolled donor kidneys.

Materials and methods

Study design

Kidneys from uncontrolled DCD donors, procured in the Maastricht region from 1 January 1981 to 1 July 2009 and transplanted within the Eurotransplant region, were included in the current observational study. Patients were followed until the earliest of death or 1 July 2010. Kidneys were allocated according to the Eurotransplant allocation rules and were matched for HLA and blood group.

Donor and recipient data

Donor and perfusion characteristics of machine-preserved kidneys were routinely recorded at our institution. Recipient follow-up data were kindly provided by the recipient transplant centers, and was periodically updated in our database. The following graft characteristics were recorded: warm ischemia time (WIT), the period from circulatory arrest or stop of resuscitation until the initial cold flush of the kidneys; cold ischemia time (CIT), the period between the initial flush and the start of first anastomosis of the recipient operation; and the anastomosis period, the time to complete arterial and venous anastomoses.

Short-term graft function after transplantation was classified as (i) PNF: permanent inadequate renal function necessitating continuation of dialysis or retransplantation; (ii) DGF: renal function which was ultimately life sustaining, but required temporary dialysis in the first week after transplantation; and (iii) immediate function (IF): immediate renal function without the need of postoperative dialysis. Graft survival is defined as functional survival off dialysis.

Renal function after transplantation was assessed using the estimated glomerular filtration rate (eGFR), which was calculated with the abbreviated Modification of Diet in Renal Disease equation [7–9]. eGFR rate at 1 year after transplantation and the rate of decline in eGFR thereafter were studied as measures of kidney function.

Collection, storage, and use of patient data were performed in agreement with the code of conduct 'use of data in health research' from the Dutch Federation of Biomedical Scientific Societies (http://www.federa.org/); According to Dutch law, Institutional Review Board (IRB) approval was not required for scientific analysis of anonymous data.

Management of uncontrolled donors after cardiac death

Kidneys were procured from uncontrolled (Maastricht category II) donors according to the Maastricht DCD categories [10,11]. Organs were preserved with the *in situ* preservation (ISP) technique, as described previously [11,12]. In short, after unsuccessful resuscitation and an obligatory no-touch period of 5 min, during which no interventions to the donor were taken, a double-balloon triple-lumen (DBTL) catheter was inserted into the aorta via one of the femoral arteries, followed by ISP of the donor kidneys with histidine-tryptophan-ketoglutarate solution (Custodiol; Dr. Franz Köhler Chemie, Alsbach, Germany) [13,14]. A large Foley catheter is placed in the femoral vein for decompression. This indispensable, minimally invasive technique may provide the opportunity to meet legal and logistical requirements for organ recovery without excessive WITs and, depending on the legal opportunities, can be initiated prior to consent for organ donation. It can be performed in the emergency department and allows fast and effective organ preservation. Insertion of the cannulas can be performed by surgeons with limited experience in donation procedures. After preservation and consent for organ donation, the organs were procured in the operating room. Following recovery of the kidneys in the operating room within 2 h after the start of ISP, most of the kidneys were weighed and prepared for machine preservation and were placed in sterile organ chambers on Gambro PF-3B perfusion machines (Gambro, Lund, Sweden) using Belzer's University of Wisconsin machine perfusion solution since 1985, at a mean temperature of 4 °C. Eurocollins preservation solution was used before 1985 [15]. Since 2006, the Lifeport (Organ Recovery Systems, Des Plaines, IL, USA) has been used as pulsatile perfusion machine. Added to the solution were 40 IU of insulin, 200 000 U of penicillin, and 16 mg of dexamethason. During machine perfusion, pH was adjusted to values >7.10, using sodium bicarbonate.

Statistical analysis

Continuous variables are presented as mean ± standard deviation if normally distributed, and as median and interquartile range (IQR) otherwise. Categorical variables are presented as percentages. Baseline donor, preservation, and

recipient characteristics are compared with the Student's *t*-tests for normally distributed continuous variables, with the Mann–Whitney *U*-test if the distribution was not normal, and with chi-square tests for categorical variables. The effects of all variables on PNF were tested with univariate logistic regression analysis. Multivariate logistic regression analysis was performed to identify potential risk factors for PNF, with correction for those characteristics that are considered to be potential confounders, defined by the 10% change-in-estimate rule [16], or if these criteria were not met, significant variables from the univariate analyses and potential confounders based on clinical relevance were used. The same criteria were used to determine the predictive value for PNF by the area under the ROC-curve (AURC). Sensitivity, specificity, positive predictive value, and negative predictive value were analyzed using MedCalc statistical software.

Cox proportional hazards model was used to assess the effect of variables on death censored graft failure of primarily functioning kidneys, correcting for confounders as described for the multivariate analysis. Graft survival censored for recipient death with a functioning graft and patient survival was calculated using the Kaplan-Meier method.

The rate of decline in eGFR is calculated for each patient by simple linear regression from yearly glomerular filtration rate estimates, starting at 1 year after transplantation.

Machine-perfused kidneys were further analyzed to determine machine perfusion characteristics that are associated with outcome after transplantation.

All analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 16.0 for Windows, and a *P*-value <0.05 was considered statistically significant.

Results

Patients

From 1 January 1981 to 1 July 2009, 280 kidneys from uncontrolled DCD donors were procured in the Maastricht region, of which 133 from 85 donors were discarded based on vascular anatomy (e.g. multiple renal arteries, renal artery stenosis, $n = 14$), macroscopic appearance (e.g. poor flush-out, cysts, renal capsula tears, $n = 33$), long WIT ($n = 17$), donor-related problems (e.g. positive virology, diabetic nephropathy, $n = 14$), malplacement of the cannulas ($n = 7$), if there were no suitable recipients ($n = 14$), if the kidneys were considered too marginal to transplant ($n = 24$) or not reported ($n = 10$). Ten kidneys were transplanted outside the Eurotransplant region, data were missing of one transplanted kidney and one recipient died with an unknown graft function. Of the remaining 135 kidneys transplanted in the Eurotransplant region, 110 kidneys were machine perfused and 25 kidneys were stored on melting ice until transplantation (cold-storage).

Donor, graft, and recipient characteristics are summarized in Table 1. Mean donor age was 45 ± 16 years. The mean WITs and CITs were 26 ± 11 min and 27 ± 6 h, respectively. Donors and recipients predominantly comprised of men (73% and 68%, respectively).

Short-term graft function

Of the transplanted kidneys, 30 recipients developed PNF (22%), 83 recipients DGF (62%), and 22 recipients IF (16%). Donor, graft, and recipient characteristics and their association with PNF are shown in Table 1. Only donor age was a significant risk factor for PNF in the univariate analysis (Table 1) and remained an independent risk factor for PNF in the multivariate analysis (Table 2). Further analysis of donor age, using the ROC-curve and its accompanying table (i.e. the point closest to the [1-1]-corner), showed the strongest association with PNF from an age of 54 years and older with an odds ratio of 2.857 (95% CI 1.242–6.571; $P = 0.013$). Kidneys from donors of 54 years and older have a higher percentage of PNF compared with younger donor kidneys (35% vs. 16%, $P = 0.012$, respectively).

The predictive value of donor age on PNF was poor (AURC 0.640, 95% CI 0.553–0.721). Adding the variables as used in the multivariate analysis to the model, the predictive value increased to 'fair' (AURC 0.719, 95% CI 0.618–0.805) (Fig. 1, Table 3).

Long-term outcomes

The median period of follow-up after transplantation was 6.5 (IQR 3.5–12.2) years. Graft survival at 1 and 5 years after transplantation was 75% and 63%, respectively; kidneys with PNF included. Figure 2 shows graft survival, censored for recipient death with a functioning graft, of all transplanted kidneys (Fig. 2a) and functioning kidneys alone (Fig. 2b), with donor age categorized in groups. Graft survival of all transplanted kidneys was significantly lower for donor kidneys of 54 years and older, but graft survival of functioning kidneys was equivalent in both groups. Recipient survival was similar in both groups (Fig. 2c).

Mean eGFR of functioning grafts was 36.2 ml/min/1.73 m^2 at 3 months, 40.7 ml/min/1.73 m^2 at 1 year, and 45.0 ml/min/1.73 m^2 at 5 years after transplantation. Donor age was significantly correlated with a decrease in eGFR (Pearson's $r = -.418$, $P < 0.001$) at 1 year after transplantation and at 5 years after transplantation (Pearson's $r = -.497$, $P < 0.001$).

In the Cox proportional hazards model, donor age was significantly associated with death censored graft failure of

Table 1. Baseline characteristics and their association with primary nonfunction.

		Univariate analysis	
		OR (95% CI)	*P*
Donor related			
Donor age (years)	45 ± 16	1.035 (1.004–1.068)	0.028
Donor sex (male)	99 (73%)	0.658 (0.273–1.585)	0.351
Cause of death (cardiovascular/other)	71/29%	2.934 (0.843–6.798)	0.101
Donor hypertension (n = 107) (yes)	11%	1.479 (0.409–5.354)	0.551
Donor creatinine (μmol/l)	122 ± 37	1.002 (0.991–1.013)	0.671
Total CPR time (min)*	48 ± 25	1.001 (0.984–1.018)	0.911
Graft related			
Warm ischemia time (min)	26 ± 13	1.021 (0.988–1.054)	0.221
Machine perfusion/cold storage†	81.5/18.5%	1.625 (0.511–5.164)	0.410
Cold ischemia time (h)	27 ± 6	0.999 (0.935–1.067)	0.972
Of which machine perfusion time (h)	22 ± 6	1.026 (0.951–1.108)	0.505
Anastomosis time (min)	39 ± 14	0.998 (0.968–1.028)	0.878
GST T_4 (U/l/100 g)	71 (52–111)‡	1.005 (0.999–1.010)	0.089
LDH T_4 (U/l/100 g)	565 (405–756)‡	1.001 (1.000–1.001)	0.104
Renovascular resistance T_0	1.03 ± 0.63	1.542 (0.768–3.093)	0.223
Recipient related			
Recipient age	51 ± 13	1.012 (0.980–1.044)	0.472
Recipient sex (male)	92 (68%)	2.118 (0.794–5.651)	0.134
Re-transplantation (yes)	15 (11%)	1.301 (0.382–4.424)	0.674
Total HLA mismatches	2.5 ± 1.1	1.066 (0.722–1.572)	0.746
Transplant center (regional/export)	64/36%	1.182 (0.502–2.782)	0.702
Kidney disease (renovascular/other) (n = 116)	18/82%	0.964 (0.317–2.931)	0.949
Dialysis time (years)	3.2 ± 2.6	1.020 (0.874–1.190)	0.799
Dialysis type (hemodialysis)	88 (65%)	0.773 (0.310–1.931)	0.582
Calcineurin inhibitor (yes)	118 (87%)	0.645 (0.208–2.003)	0.448
Anti-metabolite (yes)	55 (41%)	0.449 (0.183–1.099)	0.080
Sirolimus (yes)	29 (21%)	1.148 (0.436–3.022)	0.780
Induction therapy (yes)	12 (9%)	1.185 (0.300–4.686)	0.809

*Resuscitation time + CPR after declaration of death.
†Odds ratio relates to machine perfusion.
‡Expressed as median (interquartile range).

primarily functioning kidneys (HR 1.038, 95% CI 1.015–1.060, $P < 0.001$) (Table 2).

Discussion

The use of kidneys from controlled Maastricht category III DCD donors for transplantation is generally accepted in most countries where it is legal to withdraw futile medical treatment [17,18]. The pool of controlled DCD donors, however, is limited. Only a small proportion of intensive care patients, in whom further treatment is considered to be futile and who are not brain-dead, meets donation criteria. The number of patients who die after failed resuscitation is much higher [6]. Therefore, these patients can be a valuable addition to the DCD donor pool as uncontrolled Maastricht category I and II DCD donors. However, uncontrolled DCD donor kidneys are rarely used. There is a general reluctance to use uncontrolled DCD kidneys, with only a few uncontrolled DCD programs, mainly in Spain and in France [19].

In this study, Maastricht categories I and II are analyzed together as 'uncontrolled donors'. It is difficult to distinguish category I from category II DCD donors, estimate resuscitation time, and ischemic damage. In the Netherlands, patients are not taken to the hospital after declaration of death on the street as category I donors in Spain. It is forbidden to transport dead people to a hospital, but allowed for resuscitation only. So, potential donors are resuscitated and if the patient dies, only in the hospital death is declared. This results in longer resuscitation periods of our category II donors than the category I donors in Spain.

The use of uncontrolled kidney donors has led to an increase in the number of available donor kidneys for transplantation at our center. A recent study from our group showed no difference in transplant outcomes of uncontrolled compared with controlled donor kidneys [6].

The incidence of PNF was relatively high in this group of patients, which enabled us to adequately assess risk factors for nonfunction after transplantation. Reasons for the high incidence of PNF may be influenced by several factors. First, the definition of PNF used in our center is permanent inadequate renal function necessitating continuation of dialysis or retransplantation. This includes kidneys, which failed because of hyperacute rejection, graft thrombosis, and surgical complications. Second, the CIT with a mean period of 27 h is much longer than in other studies. All kidneys are allocated according to the Eurotransplant allocation rules. As many centers are reluctant to accept marginal DCD kidneys and decline an organ offer, it usually takes hours before kidneys are finally offered to our center. Third, because of the shortage of donor organs, we had a liberal acceptance strategy for DCD kidneys. Despite our

Table 2. Multivariate analysis of the risk of primary nonfunction and graft failure*.

	Multivariate logistic regression		Cox regression	
	Odds ratio (95% CI)	*P*	Hazards ratio (95% CI)	*P*
Donor age (years)	1.064 (1.013–1.118)	0.014	1.038 (1.015–1.060)	<0.001
Warm ischemia time (min)	1.045 (0.997–1.096)	0.068	1.015 (0.992–1.039)	0.202
Cold ischemia time (hours)	1.047 (0.946–1.158)	0.376	1.045 (0.996–1.096)	0.074
Renovascular resistance T_0 (mmHg/ml/min/100 g)	1.256 (0.602–2.618)	0.544		

*A logistic regression model was used to determine the odds ratio for PNF, and a Cox proportional hazards model was used to determine the hazards ratio for death censored graft failure of primarily functioning kidneys.

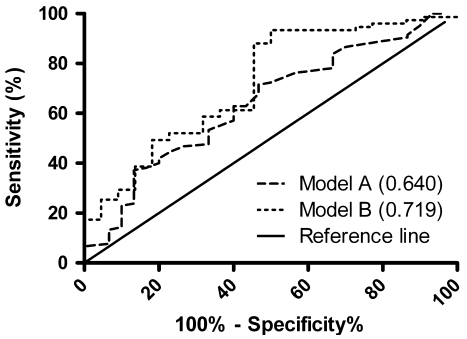


Figure 1 Receiver operating characteristics (ROC) curve for primary nonfunction: Model A: Donor age; Model B: multivariate model with donor age, warm ischemia time, cold ischemia time, and renovascular resistance at T_0. The number in brackets indicates the area under the curve for each line.

Table 3. Predictive values of donor age for PNF.

	AURC (95% CI)	Sensitivity	Specificity	PPV	NPV
Model A	0.640 (0.553–0.721)	0.533	0.714	0.348	0.843
Model B	0.719 (0.618–0.805)	0.500	0.933	0.687	0.864

Model A, donor age alone; model B, donor age, warm ischemia time, cold ischemia time, and renovascular resistance at T_0; PPV, positive predictive value; NPV, negative predictive value.

finding of a higher incidence of PNF and DGF in kidneys from DCD donors, patients who receive a DCD kidney have better survival rates than patients who continue dialysis treatment while waiting for a kidney from a conventional brain-dead donor [3,20,21].

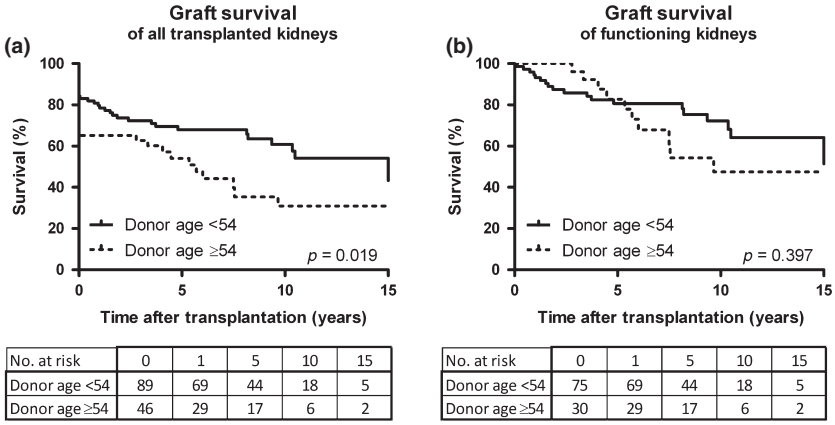
Kidneys from DCD donors that overcome the early posttransplantation period function as long as DBD (donation after brain death) kidneys. Contrary to DBD kidneys, DGF in DCD kidneys hardly affects graft survival [22,23]. As transplantation of nonviable kidneys results in unnecessary risk of surgery and immunosuppression, and sensitizes the recipient for future transplants, it is essential, particularly for DCD kidneys with a relatively high risk of PNF, to adequately assess the risk of nonfunction after transplantation [21].

Our results show that only donor age is independently associated with PNF. The predictive value of donor age only was poor, but adding the clinically important variables, WIT, CIT, and renovascular resistance during machine perfusion to the model, the predictive value increased to fair. Kidneys from donors of 54 years and older do worse than younger donor kidneys; however, like in controlled DCD kidneys, an absolute cut-off value cannot be provided. In a relatively large group of controlled and uncontrolled DCD kidneys, the results of pretransplant biopsy increase the predictive value for graft survival in older donor kidneys [24].

Kidneys from DCD donors are inevitably subjected to a period of warm ischemia. Our data, however, show no significant association between WIT and PNF. This may be biased as a total WIT longer than 45 min was a reason to discard kidneys for transplantation. Despite this potential bias, we found a trend toward significance in the multivariate analysis. In controlled DCD kidneys, a WIT longer than 45–60 min is also associated with an increased risk of PNF and DGF [25,26].

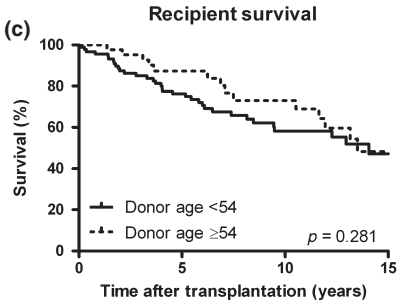
In this study of uncontrolled DCD kidneys only, renovascular resistance was not associated with PNF. In a previous study from our group, we have shown that renovascular resistance of all Maastricht category II and III machine-perfused DCD kidneys at the beginning of machine perfusion is independently associated with PNF; however, its predictive value is low [27].

Perfusate biomarkers of machine-perfused kidneys, including glutathione S-transferase (GST) and lactate dehydrogenase (LDH), have been used to identify risk factors for PNF and DGF in DCD kidneys [28–31]. In some studies, GST has a strong correlation with graft viability, but others have not been able to confirm this association [29–31]. For LDH concentration, no correlations were found with short-term graft function [29,31,32]. This makes it hard to discard DCD kidneys based purely on perfusate biomarker concentrations. In this study, GST and LDH concentrations were not correlated with PNF.



No. at risk	0	1	5	10	15
Donor age <54	89	69	44	18	5
Donor age ≥54	46	29	17	6	2

No. at risk	0	1	5	10	15
Donor age <54	75	69	44	18	5
Donor age ≥54	30	29	17	6	2



No. at risk	0	1	5	10	15
Donor age <54	89	85	58	25	8
Donor age ≥54	46	44	29	18	6

Figure 2 Kaplan-Meier graft survival curves of (a) all transplanted uncontrolled DCD kidneys, (b) functioning kidneys only, all censored for recipient death with a functioning graft, and (c) recipient survival.

Direct cannulation of the aorta is the method of choice to preserve kidneys of DCD donors [33]. In the Netherlands, minor invasive procedures are allowed to preserve the organs of potential donors before consent of the relatives and if a patient is not registered with objection in the national donor registry. Therefore, laparotomy with direct cannulation of the aorta is not feasible in uncontrolled donors. In this study, ISP with cold perfusate has been used to preserve donor kidneys. This technique is associated with longer WITs, a higher discard rate, and inferior graft survival compared with direct aortic cannulation [6]. The use of normothermic extracorporeal membrane oxygenation (ECMO) after cardiac arrest may be a valuable alternative for hypothermic ISP with the DBTL catheter. Advantages of ECMO include recirculation of oxygenated blood until organ procurement, maintaining or restoring adenosine-levels, and it may offer the opportunity of viability testing of normothermic perfused kidneys [34,35]. This technique has the potential to improve organ quality of ischemically damaged uncontrolled DCD kidneys with better graft function and graft survival [36,37]. In addition, preservation with ECMO after cardiac death may provide the opportunity to procure more organs, including the liver, so that they can be used for transplantation [34]. However, more clinical evidence of the benefits of ECMO is necessary [38].

It cannot be excluded that there are more risk factors for poor uncontrolled DCD kidney function than old age. Despite the relatively high percentage of PNF, which increases the power to identify risk factors and, compared with others, the large group of DCD transplantations, the number of analyzed donor kidneys remains relatively small to identify all possible risk factors for PNF.

This study shows that donor age is associated with graft function of uncontrolled DCD kidneys, so that this may influence the decision to accept or discard an uncontrolled DCD kidney.

Authorship

All authors had full access to all of the data in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. PH, TvS, and EvH were involved in the design of the study. MC collected the data in the recipients' registry. PH extracted the data and did the statistical analysis. PH drafted the article, whereas all

other authors took part in its revision. PH had final responsibility for the decision to submit for publication and is the guarantor for the study.

Funding

No funding sources were used for the preparation of this manuscript.

References

1. Barlow AD, Metcalfe MS, Johari Y, Elwell R, Veitch PS, Nicholson ML. Case-matched comparison of long-term results of non-heart beating and heart-beating donor renal transplants. *Br J Surg* 2009; **96**: 685.
2. Ledinh H, Bonvoisin C, Weekers L, *et al.* Results of kidney transplantation from donors after cardiac death. *Transplant Proc* 2010; **42**: 2407.
3. Snoeijs MG, Schaubel DE, Hene R, *et al.* Kidneys from donors after cardiac death provide survival benefit. *J Am Soc Nephrol* 2010; **21**: 1015.
4. Sanchez-Fructuoso AI. Kidney transplantation from non-heart-beating donors. *Transplant Proc* 2007; **39**: 2065.
5. Fieux F, Losser MR, Bourgeois E, *et al.* Kidney retrieval after sudden out of hospital refractory cardiac arrest: a cohort of uncontrolled non heart beating donors. *Crit Care (London, England)* 2009; **13**: R141.
6. Hoogland ER, Snoeijs MG, Winkens B, Christaans MH, van Heurn LW. Kidney transplantation from donors after cardiac death: uncontrolled versus controlled donation. *Am J Transplant* 2011; **11**: 1427.
7. Gera M, Slezak JM, Rule AD, Larson TS, Stegall MD, Cosio FG. Assessment of changes in kidney allograft function using creatinine-based estimates of glomerular filtration rate. *Am J Transplant* 2007; **7**: 880.
8. Poge U, Gerhardt T, Palmedo H, Klehr HU, Sauerbruch T, Woitas RP. MDRD equations for estimation of GFR in renal transplant recipients. *Am J Transplant* 2005 Jun; **5**: 1306.
9. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function–measured and estimated glomerular filtration rate. *N Engl J Med* 2006; **354**: 2473.
10. Kootstra G, Daemen JH, Oomen AP. Categories of non-heart-beating donors. *Transplant Proc* 1995; **27**: 2893.
11. Snoeijs MG, Dekkers AJ, Buurman WA, *et al.* In situ preservation of kidneys from donors after cardiac death: results and complications. *Ann Surg* 2007; **246**: 844.
12. Hoogland ER, Snoeijs MG, van Heurn LW. DCD kidney transplantation: results and measures to improve outcome. *Curr Opin Organ Transplant* 2010; **15**: 177.
13. Heineman E, Daemen JH, Kootstra G. Non-heart-beating donors: methods and techniques. *Transplant Proc* 1995; **27**: 2895.
14. Kootstra G, Kievit JK, Heineman E. The non heart-beating donor. *Br Med Bull* 1997; **53**: 844.
15. Moers C, Smits JM, Maathuis MH, *et al.* Machine perfusion or cold storage in deceased-donor kidney transplantation. *N Engl J Med* 2009; **360**: 7.
16. Maldonado G, Greenland S. Simulation study of confounder-selection strategies. *Am J Epidemiol* 1993; **138**: 923.
17. Snoeijs MGJ, Heurn LWEv, Mook NKAv, Christiaans MH, Hooff JPv. Controlled donation after cardiac death: a European perspective. *Transplant Rev* 2007; **21**: 219.
18. Brook NR, Waller JR, Nicholson ML. Nonheart-beating kidney donation: current practice and future developments. *Kidney Int* 2003; **63**: 1516.
19. Dominguez-Gil B, Haase-Kromwijk B, Van Leiden H, *et al.* Current situation of donation after circulatory death in European countries. *Transpl Int* 2011; **24**: 676.
20. Cho YW, Terasaki PI, Cecka JM, Gjertson DW. Transplantation of kidneys from donors whose hearts have stopped beating. *N Engl J Med* 1998; **338**: 221.
21. Snoeijs MG, Winkens B, Heemskerk MB, *et al.* Kidney transplantation from donors after cardiac death: a 25-year experience. *Transplantation* 2010; **90**: 1106.
22. Renkens JJ, Rouflart MM, Christiaans MH, van den Berg-Loonen EM, van Hooff JP, van Heurn LW. Outcome of nonheart-beating donor kidneys with prolonged delayed graft function after transplantation. *Am J Transplant* 2005; **5**: 2704.
23. Gok MA, Shenton BK, Buckley PE, *et al.* Long-term renal function after transplantation from non-heart-beating donor kidneys. *Transplant Proc* 2002; **34**: 2598.
24. Snoeijs MG, Buurman WA, Christiaans MH, *et al.* Histological assessment of preimplantation biopsies may improve selection of kidneys from old donors after cardiac death. *Am J Transplant* 2008; **8**: 1844.
25. Reich DJ, Mulligan DC, Abt PL, *et al.* ASTS recommended practice guidelines for controlled donation after cardiac death organ procurement and transplantation. *Am J Transplant* 2009; **9**: 2004.
26. Manara AR, Murphy PG, O'Callaghan G. Donation after circulatory death. *Br J Anaesth* 2012; **108**(Suppl. 1): i108.
27. de Vries EE, Hoogland ER, Winkens B, Snoeijs MG, van Heurn LW. Renovascular resistance of machine-perfused DCD kidneys is associated with primary nonfunction. *Am J Transplant* 2011; **11**: 2685.
28. Daemen JH, Heineman E, Kootstra G. Viability assessment of non-heart-beating donor kidneys during machine preservation. *Transplant Proc* 1995; **27**: 2906.
29. Daemen JW, Oomen AP, Janssen MA, *et al.* Glutathione S-transferase as predictor of functional outcome in transplantation of machine-preserved non-heart-beating donor kidneys. *Transplantation* 1997; **63**: 89.
30. Gok MA, Pelzers M, Glatz JF, *et al.* Do tissue damage biomarkers used to assess machine-perfused NHBD kidneys predict long-term renal function post-transplant? *Clinica chimica acta; Int J Clin Chem* 2003; **338**: 33.

31. Moers C, Varnav OC, van Heurn E, *et al.* The value of machine perfusion perfusate biomarkers for predicting kidney transplant outcome. *Transplantation* 2010; **90**: 966.
32. Jochmans I, Pirenne J. Graft quality assessment in kidney transplantation: not an exact science yet!. *Curr Opin Organ Transplant* 2011; **16**: 174.
33. Wind J, Snoeijs MG, van der Vliet JA, *et al.* Preservation of kidneys from controlled donors after cardiac death. *Br J Surg* 2011; **98**: 1260.
34. Fondevila C. Is extracorporeal support becoming the new standard for the preservation of DCD grafts? *Am J Transplant* 2010; **10**: 1341.
35. Net M, Valero R, Almenara R, *et al.* The effect of normothermic recirculation is mediated by ischemic preconditioning in NHBD liver transplantation. *Am J Transplant* 2005; **5**: 2385.
36. Lee JH, Hong SY, Oh CK, Hong YS, Yim H. Kidney transplantation from a donor following cardiac death supported with extracorporeal membrane oxygenation. *J Korean Med Sci* 2012; **27**: 115.
37. Magliocca JF, Magee JC, Rowe SA, *et al.* Extracorporeal support for organ donation after cardiac death effectively expands the donor pool. *J Trauma* 2005; **58**: 1095.
38. Moers C, van Rijt G, Ploeg RJ, Leuvenink HG. The effect of normothermic recirculation before cold preservation on post-transplant injury of ischemically damaged donor kidneys. *Transpl Int* 2012; **25**: 210.