Kidney donation after circulatory death in a country with a high number of brain dead donors: 10-year experience in Belgium

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Authorship

IJ, TD, JP designed the study, collected, and interpreted the data and wrote the paper. IJ analyzed the data. DK, DM, EG, MM, HL, LW, PP, CR, JLB, GR, DA, PZ, LDP, AR, JPS provided intellectual content and approved the paper. All authors gave final approval of the version to be published.

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Running title

Kidney transplantation of grafts donated after circulatory death in Belgium

Key words: Belgium, delayed graft function, donation after circulatory death, donation programs, kidney transplantation, risk factors

Abstract

Worldwide shortage of standard brain dead donors (DBD) has revived the use of kidneys donated after circulatory death (DCD). We reviewed the Belgian DCD kidney transplant (KT) experience since its reintroduction in 2000. Risk factors for delayed graft function (DGF) were identified by multivariate analysis. 5-year patient/graft survival was assessed by Kaplan-Meier curves. The evolution of the kidney donor type and the impact of DCDs on the total KT activity in Belgium were compared with the Netherlands. Between 2000 and 2009, 287 DCD KT were performed. Primary non-function occurred in 1% and DGF in 31%. 5-year patient and death-censored graft survival were 93% and 95%, respectively. In multivariate analysis, cold storage (vs. machine perfusion), cold ischemic time and histidine-tryptophan-ketoglutarate solution were independent risk factors for the development of DGF Despite an increased number of DCD donations and transplantations, the total number of deceased KT did not increase significantly. This could suggest a shift from DBDs to DCDs. In order to increase KT activity, Belgium should further expand controlled DCD programs while simultaneously improve the identification of all potential DBDs and avoid their referral for donation as DCDs before brain death occurs. Furthermore, living donation remains underused.

Introduction

Organ shortage has urged transplant physicians to expand the acceptance criteria of deceased donors. The use of expanded criteria donor (ECD) kidneys and kidneys donated after circulatory death (DCD) has increased significantly. About one third of deceased kidney transplant activity in the United States is performed with kidneys from ECDs and DCDs [1]. Although DCD donation was common practice in the early era of transplantation, the introduction of brain death criteria and the superior results achieved with organs donated after brain death (DBD) pushed DCD donation to the background [2]. DCDs were reported to have considerably higher incidences of delayed graft function (DGF) and primary non-function (PNF) as compared with DBD kidneys (28%-88% and 1-18% versus 13%-35% and 1-10%, respectively) [3-4] and inferior graft outcome. However, with the successful course of clinical transplantation activities, the DBD pool rapidly became insufficient to sustain the increasing demand for kidney grafts. Consequently, DCD kidney programs were established since the full potential of the DCD pool was estimated larger than that of the DBD pool and could double or even quadruple the number of deceased donor kidney transplantations [5]. Additionally, some landmark publications at the turn of the century showed that excellent long-term graft survival, equivalent to DBD kidneys, could be achieved with DCD kidneys [6-7]. These early reports were subsequently confirmed in larger series [3,8-9]. The excellent results of DCD kidney transplantation combined with the growing organ shortage has led to a steady increase of DCD kidney transplant activity in countries with the required legal framework and now reaches up to 30-40% of deceased donor kidney transplantations in the United Kingdom (UK) and the Netherlands [8,10].

Despite a legal framework allowing maximal efforts to stimulate organ donation and transplantation (opting-out, legality of DBD, DCD, and living donation [11]) and one of the highest deceased donor rates *per capita* worldwide, Belgium is still confronted with a renal graft shortage. Less than 50% of waitlisted patients are transplanted yearly [10]. Therefore, in an attempt to increase the number of

kidney transplants, DCD kidney transplant programs were reintroduced in Belgium at the turn of the century.

In this report we review the 10-year Belgian DCD kidney transplant experience with particular emphasis on i) results, ii) risk factors for DGF, iii) the evolution of the different types of kidney donation, and iv) the evolution of the overall kidney transplant activity.

Patients and Methods

Study population

Donor and recipient data from all DCD kidney transplants performed in Belgium between January 1, 2000, and December 31, 2009 were retrieved from the registry of the international organ-exchange organization Eurotransplant [10] and the 7 Belgian kidney transplant centers, represented by the Kidney-Pancreas Committee. Recipients younger than 18 years of age at time of transplantation were excluded, as were combined transplantations.

DGF was defined as the need for dialysis in the first week after transplantation, preceding return of graft function. PNF was defined as a graft that never regained function. Warm ischemic time was defined as the time from withdrawal of life support to start of cold perfusion, acirculatory time as the time from cardio-circulatory arrest until start of cold perfusion, cold ischemic time as the time from start cold perfusion to start of the vascular anastomoses, and anastomotic time as the time from start of the vascular anastomoses until reperfusion of the graft. HLA mismatching between donor and recipient was categorized according to differences at the HLA-A, HLA-B, and HLA-DR loci; with 0-1 of 6 possible mismatches categorized as 'level 1', 2-4 mismatches as 'level 2', and 5-6 as 'level 3'. Graft survival was defined as the time from transplantation to return to dialysis, graft nephrectomy or to patient death with a functioning graft, whichever came first. Early acute rejection was defined as the treatment of biopsy-proven rejection within the first 3 months after transplantation.

The evolution of kidney donation and transplantation rates in Belgium and the Netherlands, both Eurotransplant countries, was studied by comparing activity in three chronological eras (1995-1999, 2000-2005, 2006-2010). Kidney donation and kidney-only transplantation rates were obtained from the Eurotransplant registry. Rates were adjusted for the number of inhabitants using Eurostat population data [12].

Statistical analysis

Continuous variables are expressed as median (inter-quartile range), categorical variables as number (and percentage). Comparisons of continuous variables between groups were performed by Mann-Whitney U test or Kruskall-Wallis test. Comparisons of categorical variables were performed by χ^2 test or Fisher exact test. Univariate and multivariate logistic regression models were constructed to find independent risk factors of DGF. The multivariate model was constructed by backward stepwise regression using covariates with a univariate p-value <0.15. Because only 3 cases of PNF occurred, no further analyses on PNF were performed. Kaplan-Meier curves were used to assess patient and graft survival. The effect of DCD type (controlled *versus* uncontrolled DCD) on 5-year patient and graft survival was assessed by log-rank testing. Because of a limited number of deaths and graft losses (n=25 and n=18, respectively), no Cox regressions were performed. P-values <0.05 were considered to indicate statistical significance. All data analyses were performed in SPSS-16.

Results

Study population

287 DCD kidney transplants were performed in Belgium during the 10 year study period (i.e. 7.4% of all deceased donor kidney transplants). In the same period, 175 DCD procedures were performed (i.e. 7.8% of all deceased donor procedures). Donor and recipient characteristics are shown in Table 1. During the study period, pediatric donors were not considered for DCD donation and

generally the upper age limit for DCD donation was considered to be 60 years. DCD kidneys were allocated following standard Eurotransplant allocation rules and were transplanted for all common transplant indications (Table 2). 91% of DCD kidneys were procured in Belgium whereas 9% were imported. 93% of kidneys were recovered from controlled Maastricht Category III donors leading to relatively short warm ischemic and acirculatory times, 7% were recovered from uncontrolled Maastricht Category II donors (Table 1) [13]. Prior to 1998, duration of the 'no-touch' period varied from 2 to 10 minutes, depending on center practice. However, since the US recommendation of the Institute of Medicine, a 5 minutes period became standard in most centers [14].

Histidine-tryptophan-ketoglutarate (HTK) solution was used as flush solution in 83% of donors, and University of Wisconsin solution (UW) in 16%. Kidneys were preserved either by cold storage (47%) or by machine perfusion (53%), depending on the preference of the recipient center. Of machine-perfused kidneys, 82% were placed on the machine directly after procurement in the donor center (immediate perfusion). In 18%, machine perfusion was started after an initial period of cold storage (delayed perfusion). All kidneys preserved on the machine were perfused with Belzer's machine perfusion solution, available as KPS-1 (Organ Recovery Systems, Itasca, IL, USA) [15]. Between 2000 and 2003, the RM3 machine (Waters Medical Systems, Rochester, MN, USA) was used. Thereafter, kidneys were perfused on LifePort Kidney Transporter machines (Organ Recovery Systems). 89% of machine-preserved kidneys were perfused on LifePort machines.

Recipient immunosuppression varied according to centre specific practice (Table 1): 72.6% of recipients received induction therapy, the introduction of calcineurin inhibitors was delayed in only 12.3% of cases. Maintenance immunosuppression consisted out of calcineurin inhibitors (100%), mycophenolate mofetil (93%), and corticosteroids (100%).

Recipients were followed for a median of 34 months (18–46), during which time PNF developed in 1% and DGF in 31% of cases. Machine-perfused kidneys experienced a numerically 9% lower DGF rate compared to cold stored kidneys (27% and 36%, respectively, p=0.07). The DGF incidence of

kidneys with delayed versus immediate machine perfusion was similar (33% and 26%, respectively, p=0.48). DGF rate in uncontrolled DCDs was higher compared to controlled DCDs (65.0% vs. 28.5% respectively ; p=0.001), however PNF rates were similar (0% vs. 1%, respectively; p=0.63). DCD kidney transplantation resulted in excellent 5-year patient and death-censored graft survival (93% and 95%, respectively) (Table 1, Fig. 1). Patient and death-censored graft survival of uncontrolled DCDs were similar to controlled DCDs (85% vs. 93%; p=0.22 and 94% vs. 95%; p=0.98, respectively).

Risk factors for the development of DGF

Results from univariate and multivariate regression analysis are shown in Table 3. After correction for donor and recipient variables, cold storage (*versus* machine perfusion), cold ischemic time, and flush with HTK were independent risk factors for DGF. The type of DCD donor (uncontrolled or controlled) was not an independent risk factor in multivariate analysis, nor was warm ischemic time or acirculatory time.

Evolution of kidney donation and transplantation rates in Belgium since 1995

Between 1995 and 2010, the majority of effective Belgian kidney donors were deceased donors [20.6 pmp (19.0-22.4)], mainly DBDs [19.4 pmp (18.3-20.9)] with a small portion of DCDs [0.4 pmp (0.2-2.8)]. Living donation [2.2 pmp (1.5-3.8)] increased the total number of effective kidney donors in Belgium to 23.0 pmp (21.1-26.0) (Fig. 2A). Kidney transplantation rates showed a similar distribution: a majority of deceased donors [37.9 pmp (31.9-38.8)], mainly DBDs [33.5 pmp (30.3-37.1)] and a few DCDs [0.7 pmp (0.3-4.8)]. Living donation [2.5 pmp (1.5-4.0)] increased the total number of kidney transplants to 39.2 pmp (34.7-42.8) (Fig. 2B). Although Belgium reintroduced DCD kidney transplantation in 2000, the number of DCD transplants was low until 2003, after which a steady increase occurred with DCDs comprising up to 16% of deceased donor kidneys in 2010. Between 2000 and 2005, only 1.5% (0.75-4.25) of all transplanted deceased donor kidneys originated from

DCD donors. Between 2006 and 2010 this number increased to 16% (12-16.5; p=0.04). Table 4 shows the evolution of kidney donation and transplantation rates. Despite an increase in DCD donation, total deceased kidney donor rates did not increase. Living donors only slightly increased the total kidney donation rates. Increased kidney transplants from DCDs and living donors did not result in a significant increase of total kidney transplant activity.

Evolution of kidney donation and transplantation rates in the Netherlands since 1995

In the Netherlands, effective kidney donation rates reached 25.0 pmp (19.9-34.9) between 1995 and 2010. Kidney donors were equally distributed between living donors [12.2 pmp (7.3-20.8)] and deceased donors [12.5 pmp (12.0-13.6)], with DBDs [8.1 pmp (7.4-10.2)] as well as DCDs [4.1 pmp (2.2-5.5)] (Fig. 2C). Kidneys were mainly transplanted from deceased donors [23.2 pmp (22.1-24.9)], both from DBDs [14.7 pmp (13.7-19.1)] and DCDs [7.6 pmp (3.7-10.0)]. Living donor transplants [12.4 pmp (7.3—20.8)] increased the total number to 35.4 pmp (31.3-44.6) (Fig. 2D). Table 4 shows the evolution of kidney donation and transplantation rates. Living donation resulted in increased kidney donation rates. Deceased donation activity remained stable, but DBD activity decreased significantly while an exponential increase in DCDs was observed (Table 4, Fig. 3). Kidney transplantation rates also increased, mainly because of increased living donations (in 2010, 57% of transplantations were with living donor kidneys). Deceased donor kidney transplant rates remained stable, with increasing use of DCD kidneys and decreasing transplants from DBDs (Table 4, Fig. 3).

Discussion

This Belgian survey shows that DCD kidney transplant programs resulted in good immediate function and excellent medium-term outcome. Indeed, a 31% DGF incidence in DCD kidneys is lower than commonly reported and is in fact comparable to DGF rates observed in DBD kidneys (13%-35%) [3-4]. This low DGF rate likely results from short cold ischemic times and the use of machine perfusion. Our

multivariate analysis, although limited by its retrospective nature, showed that cold ischemic time and cold storage are independent risk factors of DGF. This is in line with a recent Eurotransplant randomized controlled trial showing that machine perfusion significantly reduces the risk of DGF in DCD kidneys [16-17]. Of note, 16% of the kidneys in the current analysis were part of the Eurotransplant trial. Following the report of a UK randomized controlled trial that did not show a benefit of machine perfusion [18], it has been suggested that kidneys should be machine perfused immediately following procurement until transplantation [19].In the present analysis no difference was observed in DGF between immediate *versus* delayed perfusion. However, an effect could have remained undetected because only a minority of kidneys underwent delayed machine perfusion.

We observed only 3 PNF cases (1%), contrary to generally higher PNF rates reported in DCD kidneys [3-4]. Although no formal analysis on the risk factors of PNF could be performed, the low PNF rate is likely explained by the majority of controlled Maastricht Category III donors, the relatively short warm ischemic and acirculatory times, anastomotic time and cold ischemia time, and possibly the use of machine perfusion [20]. In addition, donors were young with excellent kidney function and only rarely suffered from hypertension.

Unfortunately, the introduction of DCD kidney transplantation did not lead to a major increase in the Belgian kidney transplant activity. There are several possible contributing factors.

Firstly, despite the high number of DBDs in Belgium there is room for improvement. Only 67% of potential DBDs are identified and of these 10% are never reported [21]. One strategy to improve donor identification and referral is the Spanish model of the 'donor facilitator'; professionals responsible for donor identification and evaluation, supporting intensive care personnel charged with donor maintenance, and interviewing donor families [22]. In Belgium donor facilitators have recently been appointed through a national initiative, the GIFT-project [23]. In addition, training of

health-care professionals involved in donation and transplantation and national campaigns to increase public awareness should be pursued [23].

Secondly, the full potential of controlled DCDs is not used. As many as 26% of all ICUs deaths are potential controlled DCD donors but less than 4% of DCDs are identified, indicating a real possibility to increase the donor pool (survey Ministry of Health, L. De Pauw, personal communication). A possible explanation could be the extreme caution and scepticism by which DCDs were originally approached in Belgium. The initial mixed results of international DCD programs reporting high DGF and PNF rates [6,24-28] held the Belgian DCD programs back for another 2-3 years [29]. At the time it was advocated that *"the development of a non-heart beating program is no longer acceptable if machine perfusion and viability testing are not available"* [30]. The publication by Weber *et al.*, showing equal long-term results for DBD and DCD kidneys, even without machine perfusion [7], increased confidence in DCD donation and lead to a marked increase in DCD kidney transplants after 2003. Meanwhile, it has also been shown that viability testing - based on vascular renal resistances and biomarkers in the perfusate – is not as straightforward as has always been assumed [31-33].

Although it might be too early to distinguish the effect of DCD programs on the overall transplant activity, there is an increasing concern that DBDs are being recovered as DCDs, i.e. potential donors with major, irreversible neurological injury are prematurely referred as DCDs, before brain death occurs. Especially in the UK [34] and the Netherlands (Fig. 2, 3, Table 4) the increase in DCDs has been accompanied by an alarming decrease in DBDs. The shortage of ICU resources and perhaps the erroneous perception that DCDs and DBDs have equivalent results may encourage physicians to refer potential donors earlier as DCDs, even if they may progress to brain death at a later stage. In addition, the possibility to offer withdrawal of life support earlier could avoid unnecessary prolonged suffering for patients and families in case of unrecoverable neurological damage [35]. Furthermore,

improved and more aggressive neurosurgical decompressive treatments delay or even prevent development of brain death after neurological disasters [35]. Although an alleged substitution of DBDs for DCDs is very difficult to prove, the possibility of it occurring is extremely worrisome because, as a result, total deceased donor transplant activity is not increasing. Furthermore, DCD liver transplantation results in higher rates of biliary complications and decreased graft survival, DCDs critically diminish the donor population for heart transplantation, and there are fewer organs retrieved from DCDs with a lower utilization rate. The observation that DBD activity has continued to increase – albeit slightly – in most European countries, except those with established DCD programs like the Netherlands and UK, supports a substitution phenomenon. A survey of the Belgian Ministry of Health has shown that the potential of DBD has decreased from 8% to 6 % of ICU deaths between 2007 and 2010 (L. De Pauw, personal communication).

In order to effectively increase the deceased donor pool without compromising the excellent results of transplantation, DCD donation should ideally only concern donors that would otherwise not progress to brain death. In this regard, uncontrolled DCDs (Maastricht Category I and II) represent a scarcely explored source of kidney grafts that does not compete with DBDs. Uncontrolled DCD donation is predominant utilized only in Spain and France where controlled DCD is not allowed [36]. Although graft survival of uncontrolled DCD kidneys seems to be similar to controlled DCDs in experienced centers, data on long-term results in large patient cohorts are scarce [20,36-38]. Our limited experience with uncontrolled donation has resulted in a higher DGF rate but equally good 5-year outcome compared with controlled DCDs. Unfortunately, procurement and organ utilization rates in these uncontrolled DCDs are lower than in controlled DCD with considerably increased use of resources and potentially demotivating for donor hospitals and procurement teams [36].

Another potential source of DCD organs are organs donated after euthanasia. Since 2002 euthanasia is legal in Belgium under strict conditions [39]. At the explicit wish of the patient requesting

euthanasia and after Ethical Committee approval, organ donation can be considered. A limited number of cases have been performed with excellent results [40-41]. The potential of donation after euthanasia is substantial; 335 cases of euthanasia with a non-cancerous diagnosis were performed in Belgium between 2002-2007, with increasing numbers every year [42].

Because of the high rate of deceased donation in Belgium it has long been thought that the need for living donation was less urgent than in countries with low deceased donation. However, this review shows that overall deceased donor activity has not increased significantly over the last 15 years whereas waiting times for a deceased kidney have increased (median of 787 days in 2000 and 864 days in 2010). Extensive worldwide experience with living kidney donation, the safety of unilateral nephrectomy in selected healthy living donors [43-45], the development of minimally invasive surgery, and the superior results of living *versus* deceased donor kidney transplantation [46], support the further development of living donation in Belgium. Matching the living donor activity to that in the Netherlands or in the United States would double the total transplant activity in Belgium.

In conclusion, DCD kidney transplantation in Belgium results in good immediate function and excellent medium-term outcome. However, until now DCD programs have not resulted in an increase of total deceased donor kidney transplant activity, possibly related to a substitution of DCD to DBD donors. To increase its kidney transplant activity, Belgium should i) improve the identification and reporting of all DBD donors with support of appointed donor facilitators ; ii) pursue the development of controlled DCD donation while avoiding premature referral of potential donors who may progress to brain death; iii) explore uncontrolled DCD donation; and iv) increase living donation.

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Tables

Table 1. Characteristics of donors and recipients of kidneys donated after cardiac death in Belgium between 2000 and 2009.

Variable	
Donor characteristics (n=179)	
Age (y)[a]	44 (31-55)
Gender - n (%)	
Male	116 (65%)
Female	63 (35%)
Terminal serum creatinine value (mg/dL)[a,]	0.70 (0.56-0.91)
History of arterial hypertension, n (%)[b]	27 (17%)
Donor type – n (%)[c]	
Uncontrolled DCD (Category I + II)	11 (6%)
Controlled DCD (Category III + IV)	168 (94%)
Warm ischemic time (min)[a]	20 (15-29)
Acirculatory time (min)[a]	10 (8-14)
Flush solution, n (%)	
Histidine-tryptophan-ketoglutarate	149 (83%)
University of Wisconsin solution	28 (16%)
Other	2 (1%)
Process (n=287)	
Preservation method – n (%)	
Machine perfusion	152 (53%)
Cold storage	135 (47%)
Cold ischemic time (h)[a]	16 (12-19)
Anastomotic time (min)[a]	31 (11-71)
Recipient characteristics (n=287)	
Age (y)[a]	54 (45-61)
Gender - n (%)	
Male	173 (60%)
Female	114 (40%)
Duration dialysis therapy (mo)[a]	29 (17-48))
Previous transplants - n (%)	
First transplant	261 (91%)
Retransplant	26 (9%)
Panel reactive antibodies - %	

n= 0-5 %	257 (89.5 %)
n= 6-84 %	29 (10.1%)
n≥ 85 %	1 (0.3%)
HLA mismatches – n (%)	
Level 1	32 (11%)
Level 2	252 (88%)
Level 3	3 (1%)
Donor type – n (%)	
Uncontrolled DCD (Category I + II)	20 (7%)
Controlled DCD (Category III + IV)	267 (93%)
Immunosuppression, n (%) [b]	
Induction therapy	207 (72.6%)
Anti-thymocyte globulin	67 (32.4%)
Interleukin 2 receptor antagonist	139 (67.1%)
Other	1 (0.5%)
Calcineurin inhibitor	285 (100%)
delayed	35 (12.3%)
Mycophenolate mofetil	265 (93%)
Corticosteroids	285 (100%)
Outcome data – n (%) (n=287)	
Primary non-function	3 (1%)
Delayed graft function	89 (31%)
Immediate function	195 (68%)
Acute rejection[b]	50 (17.5%)
Graft loss 5 years after transplantation	
all causes	34 (12%)
censored for patient death	14 (5%)
Recipient death 5 years after transplantation	21 (7%)

[a] median (inter quartile range)

[b] data are missing from some recipients who were excluded from percentage calculations

[c] donor type is stratified according to the Maastricht Categories [13]

Table 2. Indication for transplantation in 287 recipients of kidneys donated after circulatory death in Belgium between 2000 and 2009.

Indication for transplantation[a]	**n (%)**
Glomerular diseases	77 (27%)
Polycystic kidneys	58 (20%)
Uncertain etiology	35 (12%)
Tubular and interstitial diseases	30 (11%)
Retransplant / Graft failure	26 (9%)
Diabetes	22 (8%)
Hypertensive nephroangiosclerosis	15 (5%)
Congenital, rare familial, metabolic disorders	11 (4%)
Renovascular and other renal vascular diseases	9 (3%)
Neoplasms	3 (1%)
Other (familial nephropathy)	1 (< 1%)

[a] Indications for transplantation

DCD: donation after circulatory death

Table 3. Uni - and multivariate logistic regression for the development of delayed graft function.[a]

	Univariate (n=287)[b]		Multivariate (n=203)[c]	
Variable	**Odds Ratio (95% CI)**	**p-value**	**Odds Ratio (95% CI)**	**p-value**
Donor and surgical characteristics				
Age (y)	1.00 (0.97-1.02)	0.73		
Gender – female vs male	0.78 (0.46-1.34)	0.37		
Terminal serum creatinine (mg/dL)	1.93 (0.90-4.12)	0.09		
History of arterial hypertension	0.91 (0.44-1.90)	0.80		
Uncontrolled vs controlled DCD	4.59 (1.77-11.96)	0.002	3.13 (0.99-9.91)	0.05
Preservation solution - UW vs HTK	0.14 (0.04-0.47)	0.001	0.19 (0.57-0.67)	0.01
Machine perfusion vs cold storage	0.66 (0.40-1.09)	0.11	0.35 (0.16-0.74)	0.01
Delayed vs immediate machine perfusion	1.44 (0.59-3.52)	0.43		
Warm ischemia time (min)	1.01 (1.0-1.03)	0.10		
Acirculatory time (min)	1.05 (1.01-1.10)	0.03		
Cold ischemic time (h)	1.06 (1.01-1.12)	0.03	1.11 (1.32-1.19)	0.01
Anastomotic time (min)	1.00 (0.97-1.02)	0.73		
Recipient characteristics				
Age (y)	1.02 (1.00-1.04)	0.07		
Gender - female vs male	0.65 (0.39-1.10)	0.11	0.52 (0.26-1.04)	0.06
Duration pre-transplant dialysis (mo)	1.01 (1.00-1.02)	0.09	1.02 (1.00-1.03)	0.06
Retransplant vs first transplant	1.18 (0.50-2.76)	0.71		
Panel reactive antibodies (%)	1.01 (0.99-1.02)	0.58		
HLA mismatches		0.73		
Level 2 vs Level 1	0.73 (0.34-1.57)			

Level 3 vs Level 1	0.83 (0.07-10.2)	

[a] Multivariate model was constructed by backward stepwise regression of covariates with a univariate p<0.15.

[b] Data are missing for some recipients; these were excluded case wise from multivariate analysis

[c] Hosmer-Lemeshow test of final model: χ^2 5.8 on 8 degrees of freedom, p=0.67

CI: confidence interval

DCD: donation after cardiac death

UW: University of Wisconsin preservation solution

HTK: histidine-tryptophan-ketoglutarate solution

Table 4. Evolution of kidney donors and transplants in Belgium and the Netherlands between 1995 and 2010.

	1995-1999	2000-2005	2006-2010	p-value
Belgium				
Kidney donors (pmp)				
Total	22 (21-24)	21 (21-24)	26 (25-27)	0.01
Living donor	2 (2-3)	1 (1-2)	4 (4-5)	<0.01
Deceased donor	20 (19-22)	20 (19-23)	22 (21-24)	0.30
DBD	20 (19-22)	19 (18-22)	19 (17-21)	0.62
DCD	0 (0-0)	0 (0-1)	3 (3-4)	0.01
Kidney transplants (pmp)				
Total	40 (34-41)	35 (33-40)	43 (40-43)	0.10
Living donor	2 (2-3)	1 (0-3)	4 (4-5)	0.01
Deceased donor	38 (31-38)	33 (31-39)	39 (36-39)	0.21
DBD	37 (31-38)	32 (30-38)	33 (30-34)	0.57
DCD	0 (0-1)	1 (0-2)	5 (5-6)	0.01
the Netherlands				
Kidney donors (pmp)				
Total	19 (19-20)	25 (23-29)	37 (33-39)	<0.01
Living donor	6 (6-8)	12 (11-16)	25 (20-27)	<0.01
Deceased donor	14 (11-15)	13 (12-13)	12 (12-14)	0.59
DBD	13 (9-13)	8 (8-9)	7 (7-9)	0.01
DCD	1 (1-2)	5 (3-6)	5 (5-6)	0.01
Kidney transplants (pmp)				
Total	31 (30-32)	35 (33-40)	49 (42-50)	<0.01
Living donor	6 (6-8)	12 (11-16)	25 (20-27)	<0.01
Deceased donor	25 (22-26)	24 (22-25)	23 (21-25)	0.57
DBD	23 (18-24)	14 (14-16)	14 (12-16)	0.01
DCD	2 (2-4)	9 (6-11)	10 (8-10)	0.01

Values are presented as median (interquartile range)

DBD: donation after brain death

DCD: donation after cardiac death

pmp: per million population

Legends to figures

Fig. 1: Patient and graft Kaplan-Meier survival curves until 5 years posttransplant of all kidneys donated after cardiac death in Belgium between 2000 and 2009.

Fig. 2: Total number of effective kidney donors and transplantations per milion population in Belgium (panel A-B) and the Netherlands (panel C-D) between 1995 and 2010.

Data adapted from Eurotransplant [10,12].

LD: living donor

DBD: donation after brain death

DCD: donation after circulatory death

Fig. 3: Evolution of effective deceased kidney donors per milion population in Belgium and the Netherlands between 1995 and 2010.

Data adapted from Eurotransplant [10].

DBD: donation after brain death

DCD: donation after circulatory death