Impact of Donor Age on Clinical Outcomes of Primary Single Kidney Transplantation From Maastricht Category-III Donors After Circulatory Death

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Background. Standard-criteria donation after circulatory death (DCD) kidney transplants (KTx) have higher primary nonfunction, delayed graft function (DGF), and rejection rates than age-matched donation after brain death (DBD) but similar graft survival. Data on expanded-criteria DCD are conflicting and many centers remain concerned regarding their use. Methods. In this single-center observational study with 5-year follow-up, we analyzed data from 112 primary DCD Maastricht category-III single KTx receiving similar organ preservation and maintenance immunosuppression. Patients were sorted as young DCD (donor <60 years, 72 recipients) or old DCD (donor ≥60 years, 40 recipients). Old DCD outcomes were compared with young DCD and to a DBD control group (old DBD, donor ≥60 years, 40 recipients). Results. After 5 years, old DCD showed lower patient survival (66% vs 85%; P = 0.014), death-censored graft survival (63% vs 83%; P = 0.001), and Modification of Diet in Renal Disease estimated glomerular filtration rate (34, 27.0-42.0 mL/min per 1.73 m² vs 45.0, 33.0-58.0 mL/min per 1.73 m²; P = 0.021) than young DCD with higher DGF (70% vs 47.2%; P = 0.029) and graft thrombosis (12.5% vs 1.4%; P = 0.021). Comparison between old DCD and old DBD showed similar 5-year patient survival (66% vs 67%; P = 0.394) and death-censored graft survival (63% vs 69%; P = 0.518) but higher DGF (70% vs 37.5%; P = 0.007) and lower estimated glomerular filtration rate (34, 27.0-42.0 mL/min per 1.73 m² vs 41, 40.0-42.0 mL/min per 1.73 m²; P = 0.029). Multivariate Cox regression analysis showed that donor 60 years or older (hazard ratio, 3.135; 95% confidence interval, 1.716-5.729; P < 0.001) and induction with anti–IL2-receptor-α monoclonal antibody (hazard ratio, 0.503; 95% confidence interval, 0.269-0.940, P = 0.031 in favor of induction with rabbit antithymocyte globulin) are independent predictors of transplant loss. Conclusions. Overall, single KTx from DCD Maastricht category-III donors 60 years or older have inferior outcomes than KTx from donors younger than 60 years. Comparison with age-matched DBD showed similar patient and graft survivals. However, the discrepancy in graft function between DCD and DBD deserves further investigation.

Kidney transplantation (KTx) is the best therapy for end-stage renal disease.1 Advances in perioperative care and immunosuppression have significantly reduced transplant-related morbidity and mortality.2 Such improvements have allowed to consider the expansion of the donor pool to compensate the increasing amount of patients on

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the waiting list. Progressively, we have moved from the boundaries of donation after brain death (DBD) toward the challenge of donation after circulatory death (DCD). 3

Even though DCD kidneys have higher rates of primary nonfunction (PNF), 4, delayed graft function (DGF), 5, 6 and rejection 7, 8 than DBD, several studies have shown that standard-criteria (SC) DCD can offer excellent results. 6, 7 Nevertheless, because inferior outcomes have been reported for expanded-criteria (EC) DCD, many centers remain concerned regarding their use. 2, 4, 8, 12

Current definition of EC-DCD comes from the experience gained with DBD but it does not consider the intrinsic differences existing between these donor categories. Available data are difficult to interpret because they are often biased by lack of discrimination between Maastricht categories, inclusion of organs preserved on static cold storage (SCS) and hypothermic machine perfusion (HMP), arbitrary single or dual KTx, nonhomogeneous selection of the recipients (ie, different immunological risk and immunosuppression), and use of external databases. Benefit of preimplantation biopsy is also debated. 11, 13

The aim of this study was to assess the outcomes of primary single KTx from Maastricht category-III DCD donors aged 60 years or older in the context of an old for-old allocation policy and to analyze risk factors for transplant failure.

MATERIALS AND METHODS

Study Design

In this single-center prospective observational study with 5-year follow-up, we enrolled patients who underwent Maastricht category-III DCD KTx at the Royal London Hospital (London, UK) between January 2007 and February 2013. Inclusion criteria were: recipient age ≥ 18 years, single KTx, and cyclosporine- mycophenolate-steroid immunosuppression. Exclusion criteria were: previous KTx, donor younger than 18 years, organ preservation other than SCS, and induction other than rabbit antithymocyte globulin (rATG) or anti-IL2-receptor-α monoclonal antibody (IL2Mab). Patients were assessed for eligibility immediately before transplant. According to the donor, they were allocated to 2 groups: young DCD (donor <60 years) or old DCD (donor ≥60 years). Donor characteristics, recipient characteristics, and transplant outcomes were prospectively recorded on a central database by dedicated staff and were reviewed by the authors at 1, 3, and 5 years. The follow-up was interrupted in December 2017 or in case of death. The study was conducted according to the WMA Declaration of Helsinki.

Primary Endpoints

The primary endpoint was overall graft survival (GS) of KTx from DCD donors 60 years or older.

Secondary Endpoints

Secondary endpoints were: patient survival (PS), death-censored GS, 1-year estimated glomerular filtration rate (eGFR) less than 30 mL/min per 1.73 m², PNF, DGF, biopsy-proven rejection (BPR), graft function, surgical complications, polyomavirus-associated nephropathy (PVAN), new-onset diabetes after transplantation (NODAT), and posttransplant lymphoproliferative disorder (PTLD). Posttransplant biopsies (PIB) were reviewed to assess microthrombosis, acute tubular necrosis (ATN), glomerular obsolescence (GO), and their relationship with transplant outcomes.

Risk factors for overall graft failure, death-censored graft failure, 1-year eGFR less than 30 mL/min per 1.73 m², death, and DGF were evaluated. The following variables were considered: recipient age, donor age, donor sex, HLA mismatch, cold ischemia time (CIT), induction treatment, and GO.

As a complementary analysis, old DCD were compared to a group of primary single KTx from DBD donors 60 years or older (old DBD) performed during the same period.

Transplant loss was defined as death with function or need for permanent renal replacement therapy. PNF was defined as graft function unable to prevent continuous dialysis when other causes of transplant failure were excluded. Delayed graft function was defined as the need for dialysis during the first postoperative week. Diagnosis of rejection was based on serum creatinine of 30% or higher from baseline and confirmed by histology. Steroid-resistant rejection was defined as a failure of serum creatinine to decrease within 3 days after the third pulse. Biopsies were scored according to Banff 2007 classification. 14

Graft function was measured by Modification of Diet in Renal Disease eGFR. 15 Polyomavirus-associated nephropathy was suspected in case of worsening graft function with polyomavirus plasma quantitative polymerase chain reaction of 1000 copies/mL or greater and confirmed by immunohistochemistry. New-onset diabetes after transplantation was diagnosed according to the criteria of the World Health Organization. 16

Postimplantation biopsies were performed immediately after reperfusion using a 16-gauge needle. Two renal pathologists evaluated: number of glomeruli, percentage of obsolete glomeruli, microthrombosis, and ATN. Only specimens with 5 glomeruli or greater were considered. 17

Histology was deemed positive for ATN if acute tubular injury was mentioned in the report (without regard to severity). 18 Glomerular obsolescence was defined as the presence of 10% or greater of obsolete glomeruli.

Immunosuppression

As induction, patients received intravenous rATG (Thymoglobulin; Genzyme, Cambridge, MA) 4 mg/kg total dose from days 0 to 3 and intravenous methylprednisolone 500 mg on day 0 and 250 mg on days 1 and 2. Recipients with a history of malignancy or hematologic disorder received intravenous basiliximab (Simulect; Novartis, Basel, CH) 20 mg on days 0 and 4 or daclizumab (Zenapax; Roche, Basel, CH) 1 mg/kg on days 0, 14, 28, 42, and 56. As maintenance, patients received oral cyclosporine (Neoral; Novartis) 10 mg/kg per day and mycophenolate mofetil (Myfenax; Teva, Petach Tikva, IL) 2000 mg/d from day 0. Cyclosporine was adjusted to achieve a trough level of 200 ng/mL during the first month and 150 to 100 ng/mL thereafter. From day 3, patients received oral prednisone 20 mg/d, tapered to 5 mg/d by month 1.

Concomitant Medications

Patients received pneumocystis prophylaxis with oral trimethoprim/sulfamethoxazole 80/400 mg/d 3 times per week for 3 months. Recipients at increased risk of Cytomegalovirus disease (donor positive/recipient negative immunization and/or rATG administration) received oral valganciclovir (dose titrated according to eGFR) for 3 months. As deep vein thrombosis (DVT) prophylaxis, we administered subcutaneous tinzaparin 175 anti-Xa IU/kg per day. Thrombophilic
patients received perioperative intravenous unfractionated heparin (target activated partial thromboplastin time ratio 2.0-2.5).

Statistical Analysis

Categorical and numerical outcomes were described using proportions or medians (1st-3rd interquartile) and were compared using Fisher exact, $\chi^2$ or Mann-Whitney $U$ test as appropriate. Patient survival, overall GS, and death-censored GS were analyzed with the Kaplan-Meier method. Survival curves were compared with log-rank. We assessed the predictive ability of a pool of preoperative variables for the risk of graft loss (overall and death-censored), 1-year eGFR less than 30 mL/min per 1.73 m$^2$, death, and DGF in DCD KTx. We used Cox proportional hazards model for time-dependent events. All the covariates having a $P$ value less than 0.2 were introduced in multivariable models. We chose a backward conditional method to select significant independent covariates. Hazard ratios (HR), odds ratios (OR), and 95% confidence intervals (CI) were reported for significant variables. We ran logistic regressions for dichotomous variables. We reported the crude OR, 95% CI, and $P$ value for each predictor in the univariate analysis whereas we entered only statistically significant variables at univariate analysis into multiple logistic regression analyses to predict the final independent factors. We assessed the model fit by chi-square, degrees of freedom, and $P$ value; we included pseudo-R$^2$ value to provide information about the percentage of variance explained by the model. Significance was defined as $P$ value less than 0.05. We performed analyses with SPSS 23.0 (IBM Corp., Armonk, USA).

RESULTS

Patient Demographics and Characteristics

From January 2007 to February 2013, we performed 635 deceased donor KTx: 264 DBD and 134 category-III DCD. According to our inclusion/exclusion criteria, 112 DCD were enrolled into the study (Figure 1). Reasons for exclusion were: retransplant (n = 9), tacrolimus-based immunosuppression (n = 9), HMP (n = 2), and donor age < 18 years (n = 2). Seventy-two recipients were allocated to young DCD, whereas 40 recipients were allocated to old DCD. No patients were excluded from the analysis. Main characteristics are detailed in Table 1.

Primary Outcome

One- and 5-year overall GS for old DCD and young DCD were 59% versus 84% and 39% versus 75%, respectively (log-rank $P = 0.001$). Overall GS distribution for the 2 arms was significantly different with log-rank $P$ less than 0.001 (Figure 2). Reasons for graft loss were death (n = 6), PNF (n = 4), antibody-mediated rejection (n = 2), PVAN (n = 2), graft thrombosis (n = 1), recurrent renal disease (n = 2), and interstitial fibrosis (IF)/tubular atrophy (TA) (n = 1) in young DCD; death (n = 11), graft thrombosis (n = 5), PNF (n = 2), IF/TA (n = 2), PVAN (n = 1), and pyelonephritis (n = 2) in old DCD. Univariate Cox regression analyses showed that increasing recipient age (HR, 1.032 per year; 95% CI, 1.002-1.063; $P = 0.034$), donor 60 years or older (HR, 3.138; 95% CI, 1.723-5.715; $P < 0.001$), and induction with IL2Mab (HR, 0.499; 95% CI, 0.268-0.929; $P = 0.028$ in favor of rATG) were predictors of overall graft loss. Donor 60 years or older (HR, 3.138; 95% CI, 1.723-5.715; $P < 0.001$) and IL2Mab induction (HR, 0.503; 95% CI, 0.269-0.940; $P = 0.031$ in favor of rATG) remained statistically significant at multivariate analysis (-2ln likelihood: 371.632; model summary: $\chi^2(3) = 20.200$, $P < 0.001$). Characteristics of recipients experiencing premature graft loss versus patients with a functioning graft after 5 years of follow-up are detailed in Table 2.

Secondary Outcomes

One- and 5-year PS for old DCD and young DCD were 80% versus 94% and 66% versus 85%, respectively ($P = 0.014$). The PS distributions were significantly different with log-rank $P = 0.014$ (Figure 2). Causes of death in old DCD were: sepsis (n = 8), sudden cardiac death (n = 3), spontaneous rupture of a liver hemangioma (n = 1), and cancer (n = 1). Causes of death in young DCD were: sepsis (n = 4), sudden cardiac death (n = 4), stroke (n = 1), and myocardial

![FIGURE 1. Flow diagram of the study.](image-url)
infarction (n = 1). Univariate analyses showed that recipient age (HR, 1.081 per year; 95% CI, 1.033-1.130; P = 0.001), recipient 60 years or older (HR, 2.805 per year; 95% CI, 1.291-6.092; P = 0.009), and donor 60 years or older (HR, 2.433; 95% CI, 1.178-5.447; P = 0.017) were significant predictors of death. Only recipient age (HR, 1.081 per year; 95% CI, 1.033-1.130; P = 0.001) remained statistically significant at multivariate analysis.

One- and 5-year death-censored GS in old DCD and young DCD were 77% versus 90% and 63% versus 83%.

**TABLE 1.**
Baseline characteristics of primary single kidney transplants from Maastricht category-III DCD donors <60 (young DCD) and ≥60 years (old DCD)

| Variables                                      | Young DCD (n = 72) | Old DCD (n = 40) | P     |
|------------------------------------------------|-------------------|------------------|-------|
| Recipient male sex                             | 43/72 (59.7)      | 28/40 (70.0)     | 0.312 |
| Recipient age, y                               | 49.3 (39.6-55.2)  | 59.4 (55.4-63.9) | <0.001|
| Recipient age ≥ 60 y                           | 7/72 (9.7)        | 19/40 (47.5)     | <0.001|
| White ethnicity
c
|                                                 | 26/70 (37.1)      | 16/38 (42.1)     | 0.681 |
| Afro-Caribbean ethnicity
c
|                                                 | 21/70 (30.0)      | 7/38 (18.4)      | 0.252 |
| Primary kidney disease:                         |                   |                  |       |
| Primary or secondary glomerulonephritis         | 13/72 (18.1)      | 8/40 (20.0)      | 0.805 |
| IgA nephropathy                                | 3/72 (4.2)        | 4/40 (10.0)      | 0.246 |
| Diabetic nephropathy                           | 6/72 (11.1)       | 6/40 (15.0)      | 0.563 |
| Polycystic kidney disease                      | 12/72 (16.7)      | 4/40 (10.0)      | 0.408 |
| Hypertensive nephrosclerosis                    | 2/72 (13.9)       | 0/40 (0.0)       | 0.207 |
| Tubulointerstitial disease                     | 9/72 (13.9)       | 0/40 (0.0)       | 0.296 |
| Genetic kidney disease                         | 4/72 (5.6)        | 0/40 (0.0)       | 0.296 |
| Unknown                                        | 13/72 (18.1)      | 8/40 (20.0)      | 0.805 |
| Preemptive transplant                          | 1/72 (1.4)        | 1/40 (2.5)       | 1.000 |
| Recipient cytomegalovirus IgG positive
c
|                                                 | 52/68 (76.5)      | 29/39 (74.4)     | 0.818 |
| Recipient body mass index, kg/m²                | 26.0 (23.6-29.4)  | 26.3 (24.4-29.4) | 0.657 |
| Recipient body mass index ≥30 kg/m²             | 16/72 (22.2)      | 8/40 (20.0)      | 1.000 |
| Pretransplant diabetes mellitus                 | 9/72 (12.5)       | 10/40 (25.0)     | 0.116 |
| Pretransplant cardiovascular disease            | 4/72 (5.6)        | 6/40 (15.0)      | 0.163 |
| Thrombophilia                                   | 5/72 (6.9)        | 3/40 (7.5)       | 1.000 |
| Donor male sex                                 | 41/72 (56.9)      | 21/40 (52.5)     | 0.695 |
| Donor age, y                                   | 42.5 (29.5-51.8)  | 64.0 (62.0-68.0) | <0.001|
| HLA mismatch (n)                               | 4 (3-4)           | 4 (3-5)          | 0.290 |
cRF (n):                                       | 0 (0-0)           | 0 (0-0)          | 0.869 |
| 0%                                             | 57/72 (79.2)      | 31/40 (77.5)     | 0.815 |
| 1-10%                                          | 8/72 (11.1)       | 5/40 (12.5)      | 1.000 |
| 11-50%                                         | 4/72 (5.6)        | 3/40 (7.5)       | 0.699 |
| 51-80%                                         | 2/72 (2.8)        | 1/40 (2.5)       | 1.000 |
| > 80%                                          | 1/72 (1.4)        | 0/40 (0.0)       | 1.000 |
| CIT, h                                         | 14.0 (12.0-17.0)  | 14.0 (12.6-17.5) | 0.810 |
| Anastomosis time, min                          | 25.0 (23.0-28.5)  | 23.5 (21.0-26.8) | 0.146 |
| Graft with multiple arteries                   | 17/72 (23.6)      | 6/40 (15.0)      | 0.336 |
| Carrel patch sacrifice                         | 8/72 (11.1)       | 6/40 (15.0)      | 0.563 |
| rATG induction                                 | 58/72 (80.6)      | 29/40 (72.5)     | 0.351 |
| Basiliximab induction                          | 5/72 (6.9)        | 5/40 (12.5)      | 0.326 |
| Daclizumab induction                           | 9/72 (12.5)       | 6/40 (15.0)      | 0.775 |
| Cyclosporine-MMF-steroid maintenance           | 72/72 (100)       | 40/40 (100)      | 1.000 |
| Follow-up, mo                                  | 60.9 (35.4-85.5)  | 57.5 (16.1-77.9) | 0.250 |

* Four (3.6%) of 112 missing cases.

* Five (4.5%) of 112 missing cases.

* The follow-up was interrupted on December 2017 and/or in case of recipient death.

cRF, calculated reaction frequency; IQR, interquartile range; MMF, mycophenolate mofetil.

FIGURE 2. Actuarial Kaplan-Meier PS (A), overall GS (B), and death-censored GS (C) curves for primary single kidney transplants from Maastricht category-III DCD donors <60 years (young DCD, dashed line) and ≥ 60 years (old DCD, continuous line).
respectively (log-rank \( P = 0.033 \)). Death-censored GS distribution for the 2 arms was significantly different with log-rank \( P < 0.001 \) (Figure 2). Univariate Cox regression analyses for death-censored graft loss identified only donor 60 years or older (HR, 2.363; 95% CI, 1.039-5.373; \( P = 0.040 \)) as a significant predictor. As a consequence, no multivariate analysis could be performed.

The proportion of recipients with 1-year eGFR less than 30 mL/min per 1.73 m\(^2\) was 23.5% in young DCD and 41.0% in old DCD (\( P = 0.057 \)). At univariate analysis, increasing donor age (OR, 1.042 per year; 95% CI, 1.010-1.074; \( P = 0.033 \)).
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TABLE 4.
Main results after 5 years of follow-up for primary single kidney transplants from Maastricht category-III DCD donors <60 (young DCD) and ≥60 years (old DCD)

| Variables | Young DCD (n = 72) | Old DCD (n = 40) | P |
|-----------|-------------------|-----------------|---|
| 1-year eGFR <30 mL/min per 1.73 m² | 16/68 (23.5) | 16/39 (41.0) | 0.057 |
| 1-year eGFR ≥30 mL/min per 1.73 m² | 56/68 (82.4) | 23/39 (59.0) | 0.001 |
| PNF | 4/72 (5.6) | 6/40 (15.0) | 0.613 |
| DGF | 34/72 (47.2) | 28/40 (70.0) | 0.029 |
| 5-y BPR | 17/72 (23.6) | 6/40 (15.0) | 0.138 |
| 5-y BPR (n) | 19 | 6 | — |
| Cell-mediated (n) | 11 | 4 | — |
| Antibody-mediated (n) | 2 | 1 | — |
| Borderline (n) | 2 | 1 | — |
| Steroid-resistant (n) | 2 | 0 | — |
| 1-year eGFR <30 mL/min per 1.73 m² | 49.0 (37.0-62.0) | 36.0 (28.5-47.0) | 0.001 |
| 5-year eGFR, mL/min per 1.73 m² | 43.0 (30.0-58.0) | 34.0 (29.0-48.0) | 0.028 |

DISCUSSION

In the United Kingdom, the immense efforts produced by the Organ Donation and Transplantation services have led to a remarkable increase of organs donated and transplanted. In 2016 to 2017, we achieved the highest number of transplants performed in the Country: 3710 from 1413 deceased donors. This impressive result would not have been possible without the efforts and innovations that have taken place in the past years. The Organ Donation and Transplantation services have led to a remarkable increase of organs donated and transplanted.

The follow-up was interrupted on December 2017 and/or in case of patient loss. Because comorbidities may reduce the chances of receiving a kidney or jeopardize posttransplant outcomes, 21 the availability of large numbers of organs from elderly DCD (42% of all DCD donors recorded in 2016-2017) deserves some special considerations on how to guarantee the best utilization. 13 Age discrepancy between donor and recipient is a limiting factor for using kidneys from elderly donors. However, the development of old for old allocation strategies along with a wise use of preimplantation histology have allowed optimization of EC-DBD kidneys. 22-25 Initial experience with DCD showed poor GS with high rates of PNF and DGF. 3-5 Further studies in following years demonstrated encouraging improvements but general concern regarding the use of EC-DCC kidney, because comorbidities may reduce the chances of receiving a kidney or jeopardize posttransplant outcomes. 21 The availability of large numbers of organs from elderly DCD (42% of all DCD donors recorded in 2016-2017) deserves some special considerations on how to guarantee the best utilization. 13 Age discrepancy between donor and recipient is a limiting factor for using kidneys from elderly donors. However, the development of old for old allocation strategies along with a wise use of preimplantation histology have allowed optimization of EC-DBD kidneys. 22-25 Initial experience with DCD showed poor GS with high rates of PNF and DGF. 3-5 Further studies in following years demonstrated encouraging improvements but general concern regarding the use of EC-DCC kidney.

TABLE 5.
Baseline characteristics of primary single kidney transplants from Maastricht category-III DCD (old DCD) and DBD (old DBD) donors ≥60 years

| Variables | Old DCD (n = 40) | Old DCD (n = 40) | P |
|-----------|----------------|----------------|---|
| Recipient male sex | 20/40 (50.0) | 28/40 (70.0) | 0.110 |
| Recipient age, y | 56.5 (50.3-65.5) | 59.0 (55.0-63.0) | 0.534 |
| Recipient age ≥60 y | 15/40 (37.5) | 19/40 (47.5) | 0.498 |
| White ethnicityb | 12/37 (32.4) | 16/38 (42.1) | 0.476 |
| Afro-Caribbean ethnicityb | 7/37 (18.9) | 7/38 (18.4) | 1.000 |

Primary kidney disease:  
- Primary or secondary glomerulonephritis  
- IgA nephropathy  
- Diabetic nephropathy  
- Polycystic kidney disease  
- Hypertensive nephrosclerosis  
- Tubulointerstitial disease  
- Genetic kidney disease  
- Unknown  
- Preemptive transplant  
- Recipient cytomegalovirus IgG positive  
- Recipient body mass index, kg/m²  
- Pretransplant diabetes mellitus  
- Pretransplant cardiovascular disease  
- Donor age, y  
- HLA mismatch  
- GIT, h  
- GIT >12 h  
- Anastomosis time, min  
- Graft with multiple arteries  
- Carrel patch sacrifice  
- rATG induction  
- Basiliximab induction  
- Daclizumab induction  
- Cyclosporine-MMF-steroid maintenance  
- Follow-upc, mo  

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susceptibility to ischemia-reperfusion injury. With such limitations, it is difficult to provide adequate informed consent to our patients, as the impact of several variables remains unclear. We focused on category-III DCD and investigated the relationship between donor age and transplant outcomes in the setting of an old for-old allocation policy. To reduce bias, only organs preserved on SCS and transplanted in de novo recipients on the same immunosuppressive scheme were considered. We chose 60 years as a cut-off to discriminate between younger and older donors because such a parameter is widely accepted per se to define both EC-DBD and EC-DCD kidneys.

In line with another UK study and with more recent data from the Eurotransplant Senior Program, our experience shows that KTx from DCD 60 years or older have inferior PS, GS, and function than DCD younger than 60 years. As described in old for-old DBD KTx, we found that the risk of graft loss is highest during the first year with death representing the leading cause of failure. Nevertheless, 5-year death-censored GS of the present series is reasonable enough to promote KTx from elderly DCD in age-matched recipients. Comparison between DCD and DBD ≥ 60 years supports this point of view as it demonstrated similar PS and GS. How the difference in eGFR observed between KTx from elderly DCD and DBD may affect long-term outcomes remains unclear. Theoretically, the inferior life expectancy of elderly recipients should overcome the risk of premature transplant loss due to chronic deterioration of function but longer follow-up is needed to confirm this hypothesis.

Data on elderly patients receiving EC-DBD have shown a survival advantage over dialysis but there are no data demonstrating a survival benefit for primary EC-DCD KTx recipients over patients remaining on dialysis or waiting for a SC-DCD, a SC-DBD or an EC-DBD. As long as PS and GS remain similar for KTx from elderly DCD and DBD donors, we can assume that a comparable survival benefit may be expected. However, this may not be enough to reassure the

FIGURE 4. Actuarial Kaplan-Meier PS (A), overall GS (B), and death-censored GS (C) curves for primary single kidney transplants from Maastricht category-III DCD (old DCD, continuous line) and DBD (old DBD, dashed line) donor ≥60 years.

| Variables | Old DBD (n = 40) | Old DCD (n = 40) | P |
|-----------|-----------------|-----------------|---|
| 1-y eGFR < 30 mL/min per 1.73 m² | 8/39 (20.5) | 16/39 (41.0) | 0.049 |
| PNF | 1/40 (2.5) | 2/40 (5.0) | 1.000 |
| DGF | 15/40 (37.5) | 28/40 (70.0) | 0.007 |
| 5-y BPR | 7/40 (17.5) | 6/40 (15.0) | 1.000 |
| 1-y eGFR, mL/min per 1.73 m² | 41.0 (38.3-45.8) | 35.0 (28.0-46.0) | 0.023 |
| 5-year eGFR, mL/min per 1.73 m² | 41.0 (40.0-42.0) | 34.0 (27.0-42.0) | 0.029 |
| Graft thrombosis | 2/40 (5.0) | 5/40 (12.5) | 0.432 |
| NODAT | 2/40 (5.0) | 2/40 (5.0) | 1.000 |
| Polyomavirus-associated nephropathy | 4/40 (10.0) | 2/40 (5.0) | 0.675 |
| PTLD | 0/40 (0.0) | 1/40 (2.5) | 1.000 |

<sup>a</sup> Thirty-nine (97.5%) of 40 valid cases.
<sup>b</sup> Thirty-nine (97.5%) of 40 valid cases.
<sup>c</sup> Twenty-eight (70.0%) of 40 valid cases.
<sup>d</sup> Twenty-three (57.5%) of 40 valid cases.
<sup>e</sup> Fifteen (37.5%) of 40 valid cases.
<sup>f</sup> Thirteen (32.5%) of 40 valid cases.
<sup>g</sup> Comprises only patients with no diabetes at baseline (66/80, 82.5%).
public on the beneficial use of such organs often addressed as “marginal.” To support those transplant centers that are willing to consider a full utilization of the DCD donor pool currently available, regulatory bodies might consider extracting data of EC-DCD KTx and comparing outcomes, with specific reference to survival benefit versus other renal replacement therapies.

Delayed graft function in KTx from elderly DCD was significantly higher than younger DCD and age-matched DBD.\textsuperscript{3,5} We could not demonstrate any direct effects of DGF on GS or function but impact of DGF on DCD KTx remains controversial.\textsuperscript{12,31} Especially for elderly patients, DGF may represent a severe complication because it is often associated with prolonged dialysis, drug-related side effects, rejection, and cardiovascular events.\textsuperscript{32} Detrimental effects of CIT on DGF can be substantially mitigated having local and national policies restricting EC-DCD KTx only when a CIT less than 12 hours may be expected. Routine use of HMP for DCD kidneys is still debated but it may help assess organ viability and reduce DGF.\textsuperscript{33} Organ procurement using normothermic perfusion has shown promising results but ethical issues, logistical difficulties, and high costs restrict application of the technique to highly specialized centers.\textsuperscript{34} WIT is another risk factor for DGF.\textsuperscript{35} Optimal donor management and sound surgical technique during organ procurement and transplant are key factors for reducing total WIT.\textsuperscript{36}

With such a combination of poor quality organs, DGF, rejection, and frail recipients, careful selection of immunosuppression is mandatory. Our multivariate regression model showed that rATG induction was associated with better GS than anti–IL2-Mab. Albeit the study was not designed to compare induction treatments, such a result deserves further investigation. To the best of our knowledge, this is the first report on a beneficial effect of rATG in DCD transplants receiving a cyclosporine-based maintenance. The fact that most European centers use tacrolimus rather than cyclosporine may limit the value of this finding. However, there are still thousands of transplant patients around the world receiving cyclosporine as chronic immunosuppression (ie, atypical hemolytic uremic syndrome, tacrolimus-related side effects, diabetes, financial constrains). This subgroup of recipients might actually benefit from an ATG-based induction scheme. rATG induction in DCD KTx offers several advantages as it allows to reduce the risk of rejection, the need for early biopsy, and the exposure to calcineurin inhibitors.\textsuperscript{37} Indeed, we observed low rejection rates in both the DCD groups. Moreover, rejection rate in elderly DCD was similar to DBD. These results are encouraging as elderly recipients of elderly DCD are at increased risk of rejection than elderly recipients of young DCD or DBD.\textsuperscript{28,38} At the same time, we realize that sepsis was an important cause of death among our patients. Elderly recipients are more prone to infections.\textsuperscript{39} Moreover, higher infection rates have been recently reported in DCD KTx.\textsuperscript{40} Our experience supports these findings and suggest to further reduce the net state of immunosuppression. Lower-dose rATG in association with basiliximab may represent a valid alternative to standard-dose rATG.\textsuperscript{41} Calcineurin inhibitor minimization protocols should be also favored as they may damper infection, diabetes, cancer, and IF/TA.\textsuperscript{42}

It is well known that elderly patients are more likely to experience complications after major surgical procedures.\textsuperscript{43} Our results are in line with other studies and show that elderly recipients receiving an elderly DCD kidney have more complications than their younger counterpart.\textsuperscript{39} Overall postoperative surgical complication rates in elderly DCD and DBD recipients were not significantly different. However, we observed a very high incidence of graft thrombosis in transplants from elderly DCD. This finding is difficult to explain. We check the quality of kidney perfusion as soon as the organ arrives at the hospital. Recipients are assessed by Doppler-ultrasound before leaving the theater, every day as long as DGF is suspected, and any times there is a decrease in urinary output.\textsuperscript{44} All patients also receive tailored DVT prophylaxis for 2 to 4 weeks after the operation. Higher rate of graft thrombosis has been reported in DCD pancreas transplants but there are no data suggesting that DCD KTx may have an increased risk of thrombosis nor studies addressing this specific issue in KTx from elderly donors.\textsuperscript{45} We could not find any associations between graft thrombosis and DCD transplant characteristics other than donor age and GO. A possible explanation is that the increased incidence of thrombosis could have been related to DGF, which was also more frequently observed in elderly DCD transplants. Perfusion impairment has been demonstrated in grafts with DGF.\textsuperscript{46} High vascular resistances in the capillary bed and parenchymal edema can generate high intraparenchymal pressures eventually leading to engorgement and thrombosis. Increased susceptibility to ischemia-reperfusion injury may also play a role.

Finally, our analysis of PIB did not reveal any associations between ATN and DCD KTx survival. This finding is interesting because, compared with preimplantation histology,\textsuperscript{18} PIB can assess both the components of ischemia-reperfusion injury and better evaluate the spectrum of ATN. As previously reported, whether severe ATN may be associated to inferior outcomes after DCD KTx remains unclear.\textsuperscript{18} Larger populations are needed to address this issue in transplants with such a high prevalence of ATN. Nonetheless, our data show that GO may predict loss of function within the first posttransplant year. As GO is strictly related to renal senescence, this finding confirms that age is an important and independent risk factor for poor transplant outcomes and should foster constant biopsy sampling of EC-DCD kidneys in future trials.

Main limitations of the present study are the relatively small sample size and the arbitrary allocation of kidneys from elderly donors to age-matched recipients. In particular, the lack of donor randomization did not allow to fully rule out the relative impact of recipient age on transplant outcomes. We believe that old for-old transplantation is the best option for optimizing results of EC kidneys and when planning the study we considered nonethical to propose elderly donors to young recipients. Furthermore, regression analysis demonstrated the independent effect of donor age on PS and GS and confirmed that donor age 60 years or older can be a valuable parameter to identify high-risk category-III DCD donors. Our unit, similarly to other centers in the United Kingdom, has used DCD kidneys without changing any aspects of the service to adapt to the challenges posed by these organs. In this series, we did not use preimplantation histology, we excluded dual KTx and all kidneys that have benefitted from reconditioning. The main purpose was offering a honest and consistent representation of a clinical practice that is currently under evaluation in many transplant programs worldwide.
