Supplemental Material

Appendix 1. Detailed methods

Material and methods

Participants, setting and study design

We performed a single centre, observational, retrospective cohort study amongst kidney transplant recipients who participated in the University of Montreal Kidney Transplant Biobank (Centre Hospitalier de l'Université de Montréal site). We screened for inclusion all patients transplanted between June 2008 and 2017. Recipients of non-kidney solid organ transplants were excluded. We included all patients for whom a graft biopsy was available pre-transplantation and 3 to 9 months post-transplantation, whether this post-transplant biopsy was performed for surveillance purposes or to investigate graft dysfunction. We routinely perform wedge biopsies in the operating room immediately prior to implantation, and percutaneous surveillance biopsies are offered to all patients between months 3 and 9 post transplant. For the purpose of this study, if several biopsies were performed between 3 to 9 months post-transplantation, the first one was selected. Recipients of non-kidney solid organ transplants were excluded. Patients were followed for 3 years after transplantation. The study was approved by the local ethics committee (reference number 16.204) and all patients provided informed written consent. The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the 'Declaration of Istanbul on Organ Trafficking and Transplant Tourism'.

Main Outcomes

The change in peritubular capillary density on the pre- *versus* the post-implantation biopsy was the primary outcome. Graft function measured at 1 and 3 years post-transplant were secondary outcomes.

Peritubular capillary density was measured by immunohistochemistry on pre- and post-transplant biopsies with CD34 monoclonal antibodies (ready-to-use, QBEnd/10, Dako, Agilent Technologies, Germany) (Figure 1A).[24,25] CD34 staining was performed on paraffin-embedded sections of 4 µm using the Benchmark XT autostainer (Ventana Medical System, Arizona, USA). Antigen retrieval was obtained using Cell Conditioning 1 (Ventana Medical System, #950-124) for 30 minutes. Pre-diluted antibody (1:2) was manually added to the slides and incubated at 37˚C for 60 minutes. Reactions were performed using the UltraView universal DAB detection kit (Ventana Medical System, #760-500). Counterstaining was achieved with hematoxylin and bluing reagent (Ventana Medical System, #760-2021 and #760-2037). Tissues where dehydrated, cleared and mounted using SubX mounting media (Leica microsystems, Wetzlar, Germany). Slides of whole stained tissues were scanned by a VS-110 scanner microscope (Olympus, Tokyo, Japon) with a 20x/0,75NA objective and a resolution of 0,3225 µm. Immunohistochemistry optimisation for CD31 monoclonal antibodies (ready-to-use, JC70A, Dako, Agilent Technologies, Germany) was also performed. As CD34 antibodies provided a stronger endothelial marking than CD31 and had no non-specific background, we chose to use only CD34 staining. To score peritubular capillary density, CD34-positive staining was quantified using VIS (Visiopharm, Hoersholm, Denmark), an image analysis software (Figure 1B-F). A first application was run on the digital slides to mark out the biopsy area. We manually excluded the medullar area from the analysis. A second application was run in the defined area to determine CD34+ areas using the thresholding method. Using their shape and size, the CD34+ areas could be dichotomized in two labels: glomeruli and peritubular capillaries.

After processing the applications, we corrected misclassified labels and excluded the large vessels from the analysis. The total cortical area, the peritubular capillary area and the glomeruli

area were measured. We defined the efficient cortical area as the total cortical area minus the glomeruli area. The peritubular capillary area was divided by the efficient cortical area and then multiplied by 100, defining the final score for peritubular capillary density. Two readers independently reviewed each slide (AD, FA). There was a strong correlation between the 2 readers (ρ: 0.67 for peritubular capillary density on pre-transplant biopsies ρ: 0.73 for peritubular capillary density on post-transplant biopsies, $p<0.001$ for both coefficients). AD is a trained examiner who was blinded to all clinical information except DGF status. Since AD was not blinded to DGF status, a pathologist (FA), who was blinded to all clinical data including DGF status, independently reviewed all the slides. The 2 readers could have selected different sections of the slide to examine with VIS. Hence, their results could not be averaged, as the raw readings needed to be adjusted for the region of interest examined, which could have differed. Hence, we chose to run the main analysis separately with AD's readings (Table 3) and FA's readings (Supplemental Table 4).

Glomerular filtration rate (eGFR) was estimated with the Modification of Diet in Renal Disease four-variable equation.[26] Patients who lost their graft were imputed with an eGFR of 0 ml/min/1.73m^2.

Independent variables

DGF was the main independent variable of interest, and was defined as the need for dialysis in the first week post-transplant, failure of serum creatinine to decreased by more than 10% on 3 consecutive days post-transplant, or serum creatinine >250 µmol/L on day 5 post-transplant in the presence of scintigraphic evidence of acute tubular necrosis on the graft scintigraphy performed on the first post-operative day.[27-29] We have previously used this definition of DGF,[28] and found that patients who experienced DGF as per this definition had significantly decreased eGFR 1 year post transplant versus those who did not, suggesting that this definition is clinically significant.

To identify other variables associated with peritubular capillary loss, we also collected data on recipient age, sex, height, weight, cause of chronic kidney disease, number of previous transplantation, pre-transplant panel reactive antibodies, medication before and after transplantation, comorbidities, smoking habits, cold and warm ischemic time, induction and maintenance immunosuppressive protocols, on allograft acute rejection occurring before or on the post-transplant biopsy defined as per the Banff 2015 classification[30], and on donor type, sex, age, height, weight, hypertension, diabetes, and cardiovascular disease. Donor comorbidities such as hypertension and diabetes were defined as the clinical diagnoses provided by the organ donation organization transplant coordinators to the transplant team. All donors after cardiocirculatory arrest (DCD) were performed under controlled conditions (Maastricht category 3), awaiting death in the operating room. We had no access to information on the length of the agonal phase.

Statistical analyses

Continuous variables are reported as means and standard deviations when normally distributed or as medians and interquartile ranges otherwise. Categorical variables are summarized as proportions. We used chi-square tests (or Fisher's exact test when expected number of events was less than 5 in a cell) to compare categorical variables and Student T tests (or Wilcoxon rank-sum test when not normally distributed) to compare continuous variables in patients with and without DGF. We used Pearson correlation coefficient (ρ) to assess correlations between continuous variables.

We fit a multivariable linear regression model to determine whether DGF was associated with the extent of change in peritubular capillary density between the pre-implantation and the post-transplant biopsies. We subtracted the pre-implantation from the post-transplant peritubular capillary density and hence, a negative difference in change signifies that an independent variable

is associated with peritubular capillary loss compared with the reference category (or loss per unit change for a continuous independent variable). In this model were included all variables associated with i) DGF (Table 1) and ii) change in peritubular capillary density adjusted for pre-transplant peritubular capillary density (Supplemental Table 3) with a p-value <0.15 to control for potential confounders. Pre-transplant peritubular capillary density was strongly associated with peritubular capillary density change and confounded the association between multiple independent variables and peritubular capillary change. Hence we decided to assess the univariable associations between independent variables and the outcome while keeping the pre-transplant peritubular capillary density constant when selecting the variables to include in the multivariable model. All pre-implantation biopsies were wedge biopsies and all post-transplant samples originated from core biopsies. Biopsy size was adjusted for in the multivariate model when we observed an association with pre- or post-transplant peritubular capillary density with a p-value <0.15. The normality assumption was verified by plotting the model residuals. In 9 instances, the same donor was used for 2 different recipients. The potential impact of correlated data was assessed by running a mixed model with a random effect on donor identity and found to be negligible. The analysis was repeated separately for peritubular capillary density readings obtained separately by the 2 readers as mentioned above.

To understand whether peritubular capillary loss was associated with subsequent graft dysfunction at 1 and 3 years post transplant, we fit multivariable linear regression models with eGFR 1 and 3 years post-transplantation as the dependent variables. We included in the initial multivariable model all independent variables that were associated with 1 or 3-year eGFR (Supplemental Tables 5 and 6) with a p-value <0.15 on univariable analyses. We present models

with and without the inclusion of DGF as peritubular capillary density loss could mediate part of the association between DGF and subsequent eGFR.

Last, we performed a sub-group analysis in patients with DGF to understand whether specific factors were associated with peritubular capillary loss in this patient population. We fit a multivariable linear regression model with peritubular capillary density change as the dependent variable of interest and included all the variables associated with the dependent variable (adjusted for pre-transplant peritubular capillary density) with a p-value <0.15 in the multivariable model. As the number of observations was small (n=61), we then simplified the initial multivariable model by removing variables that had p-values >0.15 to avoid overfitting. Analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC).

Supplemental Table 1. Characteristics of patients with and without post-transplant biopsies.

	Patients with available post-transplant biopsies n=220	Patients with no post-transplant biopsies n=251
Recipient characteristics		
Age in years, mean (SD)	49 (13)	50 (13)
Sex, female, n (%)	75 (34)	96 (38)
Smoker or ex-smoker, n (%)	110 (50)	143 (57)
Weight in kg, mean (SD)	73 (16)	74 (16)
Height in m, mean (SD)	1.69 (0.10)	1.68 (0.10)
Race, n (%)		
Caucasian	165 (75)	208 (83)
Black	18 (8)	14 (6)
Other	36 (16)	30 (12)
Cause of chronic kidney disease, n (%)		
Glomerular diseases	85 (39)	80 (32)
Diabetes	20 (9)	44 (18)
Hypertension/vascular	10 (5)	13(5)
Polycystic kidney disease	43 (20)	42 (17)
Auto-immune disease	11 (5)	12 (5)
Urological	26 (12)	21 (8)
Unknown	25 (11)	39 (16)
First transplantation, n (%)	193 (88)	223 (89)
Pre-transplant PRA >0%	32 (15)	44 (18)
Donor characteristics		
Donor type, n (%)		
Living donor	66 (30)	67 (27)
Neurologic determination of death	134 (61)	166 (66)
Donation after cardiac death	20 (9)	18 (7)
Age in years, mean (SD)	47 (14)	48 (14)
Sex, female, n (%)	115 (52)	117 (47)
Hypertension, n (%)	37 (17)	46 (18)
Diabetes, n (%)	10 (5)	12 (5)
Smoker or ex-smoker, n (%)	86 (39)	112 (45)
Median number of HLA mismatches with recipient (IQR)	4 (3-5)	4 (2-5)
Peri-transplantation events		
Cold ischemic time in hours, mean (SD)	8.5 (5.1)	8.5 (4.8)
Warm ischemic time in minutes, mean (SD)	39 (10)	40 (11)
Induction, n (%)		
Thymoglobulin	64 (29)	64 (25)
Anti-CD25	155 (70)	188 (75)
Post-transplant estimated glomerular filtration rate (eGFR) in ml/min/1.73m^2		
Mean eGFR 1 year post transplant (SD)	58 (17)	58 (17)
Mean eGFR 3 years post transplant (SD)	56 (19)	57 (20)

Supplemental Table 2. Pre-transplant peritubular capillary density and clinical outcome 1 and 3 years post-transplant according to the various definitions of delayed graft function.

	Dialysis in the first post-transplant week n=22	Failure of serum creatinine to decrease by more than 10% on 3 consecutive days post-transplant, n=19	Serum creatinine >250 µmol/L on day 5 post-transplant in the presence of scintigraphic evidence of acute tubular necrosis, n=34	p-value
Mean peritubular capillary density on the pre-transplant biopsy in %, (standard deviation (SD))	15.06 (3.83)	15.62 (4.38)	15.42 (3.95)	0.92
Mean eGFR 1 year post transplant in ml/min/1.73m^2, (SD)	46.65 (19.61)	51.83 (10.71)	49.75 (13.80)	0.28
eGFR 3 years post transplant in ml/min/1.73m^2, (SD)	45.36 (14.95)	50.56 (17.36)	49.95 (17.89)	0.74

Supplemental Table 3. Associations between recipient, donor and procedure characteristics on peritubular capillary density change in univariable analyses.

Recipient/ Donor/ Procedure characteristics	Difference in change * (95 % CI) in %	p-value
Recipient age at transplant (per 10 year higher)	0.1 (-0.5, 0.6)	0.86
Recipient female sex (versus male)	0.9 (0.1, 1.7)	0.03
Recipient African American race (versus Caucasian)	-1.0 (-2.4, 0.4)	0.15
Cause of CKD		
Other or unknown (reference)	0	
Glomerular diseases	-0.1 (-0.9, 0.7)	0.85
Diabetes	-0.2 (-1.4, 1.1)	0.78
Hypertension/vascular	-0.7 (-2.3, 1.0)	0.43
Time on dialysis pre-transplant (per 1-month higher)	-0.0 (-0.0, 0.0)	0.21
Pre-emptive transplantation	1.1 (-0.0, 1.2)	0.05
Previous transplantations	-0.3 (-1.5, 0.8)	0.60
Recipient diabetes	-0.5 (-1.5, 0.5)	0.32
Recipient body mass index (per 1 unit higher)	-0.01 (-0.1, 0.1)	0.89
Recipient active smoking at transplantation	-0.6 (-1.7, 0.5)	0.27
Recipient statin use at transplantation	0.6 (-0.2, 1.3)	0.15
Recipient ACE inhibitor use at transplantation	-0.2 (-1.0, 0.6)	0.60
Pre-transplant PRA > 0% (versus 0%)	-0.0 (-0.0, 0.0)	0.95
Peak historical PRA > 0% (versus 0%)	0.0 (-0.0, 0.0)	0.89
HLA mismatches (reference 0-2)	0.3 (-0.6, 1.3)	0.50
3-6		
Thymoglobulin induction	-0.4 (-1.3, 0.4)	0.33
Cold ischemic time (per 1-hour higher)	-0.0 (-0.1, 0.1)	0.39
Use of hypothermic perfusion machine	0.9 (0.1, 1.6)	0.02
Donor type (reference neurologically deceased)		
Living donor	0.7 (-0.2, 1.6)	0.13
Donor after cardiac arrest	-0.6 (-1.8, 0.7)	0.39
Histological findings on the pre-implantation biopsy		
Peritubular capillary density (per 1% higher)	-0.8 (-0.9, -0.9)	<0.001
Percent global glomerulosclerosis (per 1% higher)	-0.0 (-0.1, 0.1)	0.70
ci score > 0 (versus 0)	-0.5 (-1.3, 0.3)	0.19
cv score > 0 (versus 0)	0.7 (-0.1, 1.4)	0.09
Donor age (per 10-year higher)	-0.0 (-0.1, 0.0)	0.11
Female donor sex (versus male)	-1.1 (-1.8, -0.3)	0.005

Donor positive smoking history (versus negative or unknown)	0.3 (-0.5, 1.1)	0.50
Donor peripheral vascular disease	-1.2 (-3.2, 0.8)	0.24
Donor hypertension	-1.6 (-2.6, -0.5)	0.003
Donor diabetes	-1.0 (-2.8, 0.8)	0.29
Donor terminal serum creatinine (per 10 µmol/L increase)	0.1 (-0.1, 0.2)	0.27
Delayed graft function	-3.4 (-4.4, -2.4)	<0.001
Rejection before the post-transplant biopsy	-0.7 (-1.6, 0.2)	0.12
Surveillance biopsy (ref indication biopsy)	2.3 (1.0, 3.6)	<0.001
Time elapsed between the pre- and post-transplant biopsies (per month higher)	0.3 (0.1, 0.6)	0.01

*All reported differences are adjusted for pre-transplant peritubular capillary density and biopsy size.

Supplemental Table 4. Associations of delayed graft function and other clinical characteristics with change in peritubular capillary density: Independent blinded validation using readings from trained pathologist (FA), n=191.

	Adjusted difference in change* (95% CI), in %	**p-value**
Delayed graft function	-2.8 (-3.8, -1.9)	<0.001
PTC density on pre-implantation biopsy *(per 1% higher)*	-1.0 (-1.0, -1.0)	<0.001
Donor type (*ref neurologically deceased*)		
Living donor	1.0 (-0.0, 2.0)	0.05
Donor after cardiac death	0.2 (-1.0, 1.5)	0.71
Donor age *(per 10-year higher)*	-0.2 (-0.5, 0.1)	0.19
Rejection	-0.1 (-1.0, 0.8)	0.86
Donor hypertension	0.2 (-0.9, 1.3)	0.76
Pre-transplant statin use	-0.4 (-1.1, 0.4)	0.19
Surveillance biopsy *(ref indication biopsy)*	1.4 (0.2, 2.7)	0.02
Pre-emptive transplantation	0.7 (-0.4, 1.7)	0.19
Use of hypothermic perfusion machine	0.5 (-0.2, 1.3)	0.14
cv score on the pre-implantation biopsy	0.6 (-0.2, 1.3)	0.12
Time to biopsy (*per month higher*)	0.0 (-0.2, 0.3)	0.85

*All reported differences were adjusted for pre-transplant and post-transplant biopsy sizes

Supplemental Table 5. Associations between recipient, donor and procedure characteristics on estimated glomerular filtration rate 1 year post-transplant in univariable analyses.

Recipient/ Donor/ Procedure characteristics	Difference (95 % CI) in ml/min/1.73m^2	p-value
Cause of CKD glomerular disease (versus all others)	4.9 (0.4, 9.4)	0.03
Time on dialysis pre-transplant (per 1-month higher)	0.0 (-0.1, 0.1)	0.99
Pre-emptive transplantation	-3.9 (-10.8, 3.0)	0.26
Previous transplantations	-5.1 (-11.7, 1.5)	0.13
Recipient diabetes	-4.1 (-10.1, 1.8)	0.17
Recipient body mass index (per 1 unit higher)	0.1 (-0.4, 0.5)	0.84
Recipient active smoking at transplantation	-2.3 (-8.8, 4.3)	0.50
Recipient statin use at transplantation	1.9 (-2.5, 6.3)	0.39
Recipient ACE inhibitor use at transplantation	2.6 (-1.9, 7.0)	0.26
Pre-transplant PRA > 0% (versus 0%)	2.5 (-3.9, 8.8)	0.44
Peak historical PRA > 0% (versus 0%)	-1.9 (-6.3, 2.6)	0.41
3-6 HLA mismatches (reference 0-2)	-3.3 (-8.8, 2.2)	0.23
Thymoglobulin induction	-2.8 (-7.7, 2.1)	0.26
Cold ischemic time (per 1-hour higher)	-0.2 (-0.6, 0.3)	0.40
Donor type (reference neurologically deceased) Living donor Donor after cardiac arrest	 2.9 (-2.0, 7.7) -1.1 (-8.6, 6.5)	 0.25 0.78
Use of hypothermic machine perfusion	2.7 (-1.7, 7.1)	0.23
Donor age (per 10-year higher)	-2.6 (-4.2, -1.0)	<0.001
Donor creatinine (per 10 µmol/L higher)	0.1 (-0.7, 1.0)	0.75
Female donor sex (versus male)	-7.5 (-11.8, -3.3)	0.001
Donor positive smoking history (versus negative or unknown)	1.0 (-3.5, 5.5)	0.66
Donor peripheral vascular disease	-9.3 (-21.0, -1.6)	0.11
Donor hypertension	-7.6 (-13.6, -1.6)	0.01
Donor diabetes	3.2 (-7.2, 13.6)	0.55
Delayed graft function	-9.2 (-13.7, -4.6)	<0.001
Rejection before the post-transplant biopsy	-2.9 (-8.2, 2.4)	0.28

Histological findings on the pre-implantation biopsy		
Peritubular capillary density (per 1% higher)	0.6 (0.1, 1.0)	0.01
Percent global glomerulosclerosis (per 1% higher)	-0.7 (-1.1, -0.3)	0.001
ci score (per 1 point higher)	-3.0 (-7.0, 1.0)	0.14
cv score (per 1 point higher)	-0.9 (-3.3, 1.5)	0.45
Histological findings on the post-transplant biopsy		
Peritubular capillary density (per 1% higher)	1.9 (1.2, 2.6)	<0.001
Percent global glomerulosclerosis (per 1% higher)	-0.3 (-0.6, -0.1)	0.02
g score (per 1 point higher)	-2.2 (-7.6, 3.2)	0.42
i score (per 1 point higher)	-2.3 (-6.3, 1.8)	0.27
ci score (per 1 point higher)	-4.3 (-8.6, 0.0)	0.05
cv score (per 1 point higher)	-1.5 (-3.8, 0.9)	0.21
ptc score (per 1 point higher)	-3.7 (-16.2, 8.8)	0.56
Surveillance biopsy (reference indication biopsy)	15.7 (8.6, 22.8)	<0.001

*The associations between recipient sex, age and race are not included given these are variables included in the calculation of estimated glomerular filtration rate.

Supplemental Table 6. Associations between recipient, donor and procedure characteristics and estimated glomerular filtration rate 3 years post-transplant in univariable analyses.

Recipient/ Donor/ Procedure characteristics	Difference (95 % CI) in ml/min/1.73m^2	p-value
Cause of CKD glomerular disease	2.4 (-3.2, 8.0)	0.40
Time on dialysis pre-transplant (per 1-month higher)	-0.0 (-0.1, 0.1)	0.76
Pre-emptive transplantation	-2.2 (-10.3, 5.9)	0.59
Previous transplantations	-6.0 (-14.2, 2.1)	0.14
Recipient diabetes	-2.8 (-10.2, 4.6)	0.45
Recipient body mass index (per 1 unit higher)	0.1 (-0.5, 0.7)	0.77
Recipient active smoking at transplantation	-1.0 (-9.0, 7.1)	0.81
Recipient statin use at transplantation	1.6 (-3.9, 7.0)	0.58
Recipient ACE inhibitor use at transplantation	0.8 (-4.7, 6.3)	0.78
Pre-transplant PRA > 0% (versus 0%)	3.6 (-4.2, 11.4)	0.36
Peak historical PRA > 0% (versus 0%)	-3.2 (-8.7, 2.3)	0.26
HLA mismatches (reference 0-2) 3-6	-2.8 (-9.6, 3.9)	0.41
Use of hypothermic perfusion machine	3.0 (-2.4, 8.5)	0.28
Thymoglobulin induction	-3.3 (-9.3, 2.8)	0.29
Cold ischemic time (per 1-hour higher)	0.1 (-0.5, 0.6)	0.83
Donor type (reference neurologically deceased) Living donor Donor after cardiac arrest	 3.1 (-2.9, 9.2) -0.9 (-10.3, 8.4)	 0.31 0.85
Donor age (per 10-year higher)	-4.6 (-6.5, -2.7)	<0.001
Female donor sex (versus male)	-5.6 (-11.0, -0.2)	0.04
Donor positive smoking history (versus negative or unknown)	0.8 (-4.8, 6.4)	0.78
Donor peripheral vascular disease	-9.2 (-23.6, 5.3)	0.21
Donor hypertension	-10.5 (-17.9, -3.2)	0.005
Donor diabetes	-7.9 (-20.7, 4.9)	0.22
Donor creatinine (per 10 µmol/L higher)	0.5 (-0.6, 1.6)	0.35
Delayed graft function	-10.0 (-15.7, -4.3)	<0.001
Rejection before the post-transplant biopsy	-0.1 (-6.7, 6.5)	0.98
Surveillance biopsy (reference indication biopsy)	11.0 (0.9, 20.3)	0.03

Histological findings on the pre-implantation biopsy		
Peritubular capillary density (per 1% higher)	0.4 (-0.1, 1.0)	0.13
Percent global glomerulosclerosis (per 1% higher)	-0.6 (-1.1, -0.1)	0.02
ci score (per 1 point higher)	-5.1 (-10.0, -0.1)	0.04
cv score (per 1 point higher)	-2.9 (-5.9, 0.1)	0.05
Histological findings on the post-transplant biopsy		
Peritubular capillary density (per 1% higher)	1.7 (0.7, 2.7)	0.001
Percent global glomerulosclerosis (per 1% higher)	-0.5 (-0.8, -0.2)	0.009
g score (per 1 point higher)	-3.2 (-10.0, 3.4)	0.34
i score (per 1 point higher)	-0.6 (-5.5, 4.3)	0.81
ci score (per 1 point higher)	-5.2 (-10.5, 0.1)	0.05
cv score (per 1 point higher)	-2.3 (-5.1, 0.6)	0.12
ptc score (per 1 point higher)	-8.5 (-23.7, 6.7)	0.27

*The associations between recipient sex, age and race are not included given these are variables included in the calculation of estimated glomerular filtration rate

Supplemental Table 7. Factors associated with estimated glomerular filtration rate (eGFR) 3 years post-transplant.

Clinical characteristics	Mean change in ml/min/1.73m^2 (standard deviation)	Unadjusted difference in ml/min/1.73m^2 95% CI	p-value	Adjusted difference in ml/min/1.73m^2 95% CI without delayed graft function*	p-value	Adjusted difference in ml/min/1.73m^2 95% CI with delayed graft function	p-value
Pre-transplant peritubular capillary density (per 1% higher)		0.6 (0.0, 1.2)	0.05	1.7 (0.7, 2.6)	<0.001	1.1 (-0.0, 2.3)	0.05
Peritubular capillary change (per 1% higher)		0.1 (-0.4, 0.7)	0.68	1.4 (0.4, 2.3)	0.01	1.0 (-0.1, 2.1)	0.08
Post-operative graft function							
Immediate graft function	61.0 (18.6)	0				0	
Delayed graft function	51.0 (18.4)	-10.0 (-15.7, -4.3)	<0.001	-		-5.0 (-11.9, 1.7)	0.14
Biopsy type							
For cause	48.1 (22.0)	0		0		0	
Surveillance	58.6 (18.5)	11.0 (0.9, 20.3)	0.03	5.1 (-4.2, 14.5)	0.22	5.5 (-3.9, 14.8)	0.25
Donor sex							
Male donor	60.6 (18.4)	0		0		0	
Female donor	55.1 (19.2)	-5.6 (-11.0, -0.2)	0.04	-2.5 (-7.7, 2.7)	0.34	-2.5 (-7.7, 2.6)	0.34
Donor blood pressure							
Normal blood pressure	59.4 (19.1)	0		0		0	
Donor hypertension	48.9 (16.1)	-10.5 (-17.9, -3.2)	0.005	-4.4 (-11.7, 3.0)	0.24	-4.6 (-11.9, 2.6)	0.21
Donor age (per 10 year higher)		-4.6 (-6.5, -2.7)	<0.001	-3.5 (-5.7, -1.3)	0.002	-3.5 (-5.8, -1.4)	0.002
cv score on the pre-transplant biopsy (per 1 point higher)		-2.9 (-5.9, 0.1)	0.05	-1.7 (-4.6, 1.2)	0.25	-2.2 (-5.3, 0.8)	0.15
Glomerulosclerosis on the pre-transplant biopsy (per 1% higher)		-0.6 (-1.1, -0.1)	0.02	0.0 (-0.6, 0.7)	0.92	0.0 (-0.6, 0.7)	0.90
ci score on the pre-transplant biopsy (per 1 point higher)		-5.1 (-10.0, -0.1)	0.04	0.6 (-5.2, 6.4)	0.84	1.0 (-4.8, 6.8)	0.73
Number of previous transplants							
First transplants	58.5 (19.5)			0		0	
Repeated transplants	52.5 (14.3)	-6.0 (-14.2, 2.1)	0.14	-5.6 (-13.3, 2.2)	0.16	-5.1 (-12.9, 2.1)	0.20

All the variables included in the model are included in the table.

Supplemental Table 8. Associations between recipient, donor and procedure characteristics and peritubular capillary density change in patients with DGF change in univariable analyses (n=61).

Recipient/ Donor/ Procedure characteristics	Difference* (95 % CI) in %	p-value
Recipient age at transplant (per 10 year higher)	-0.0 (-0.1, 0.0)	0.66
Recipient female sex (versus male)	0.5 (-0.6, 1.6)	0.39
Recipient African American race (versus Caucasian)	-1.0 (-2.6, 0.6)	0.23
Cause of CKD Other or unknown (reference) Glomerular diseases Diabetes Hypertension/vascular	 -0.6 (-1.7, 0.5) 0.4 (-1.1, 1.9) -0.1 (-1.9, 1.8)	 0.29 0.59 0.93
Time on dialysis pre-transplant (per 1-month higher)	-0.0 (-0.0, 0.0)	0.78
Pre-emptive transplantation	1.2 (-0.6, 3.0)	0.18
Previous transplantations	-0.7 (-2.1, 0.6)	0.27
Recipient diabetes	0.4 (-0.7, 1.6)	0.47
Recipient body mass index (per 1 unit higher)	0.0 (-0.1, 0.1)	0.39
Recipient active smoking at transplantation	0.8 (-0.6, 2.2)	0.27
Recipient statin use at transplantation	0.95 (-0.1, 1.8)	0.09
Recipient ACE inhibitor use at transplantation	-0.4 (-1.5, 0.7)	0.49
Pre-transplant PRA > 0% (versus 0%)	-0.4 (-1.7, 0.9)	0.56
Peak historical PRA > 0% (versus 0%)	-0.5 (-1.5, 0.5)	0.30
HLA mismatches (reference 0-2) 3-6	0.8 (-0.5, 2.2)	0.23
Thymoglobulin induction	-0.2 (-1.2, 0.8)	0.69
Cold ischemic time (per 1-hour higher)	0.2 (0.1, 0.4)	0.02
Donor type (reference neurologically deceased) Living donor Donor after cardiac arrest	 -0.6 (-2.6, 1.4) 0.9 (-0.3, 2.1)	 0.55 0.12
Donor age (per 10-year higher)	-0.0 (-0.1, 0.0)	0.07
Female donor sex (versus male)	-0.7 (-1.7, 0.3)	0.14
Donor positive smoking history (versus negative or unknown)	-0.1 (-1.1, 0.9)	0.81
Donor peripheral vascular disease	0.4 (-1.6, 2.4)	0.72
Donor hypertension	-1.2 (-2.3, -0.0)	0.05
Donor diabetes	-1.1 (-2.9, 0.7)	0.22
Rejection before the post-transplant biopsy	0.1 (-1.0, 1.1)	0.91
Surveillance biopsy (ref indication biopsy)	2.3 (1.0, 3.6)	<0.001

Donor terminal serum creatinine (per 10 µmol/L higher)	0.1 (-0.1, 0.3)	0.17
Time elapsed between the pre- and post-transplant biopsies (per month higher)	0.3 (0.0, 0.6)	0.03
Histological findings on the pre-implantation biopsy Peritubular capillary density (per 1% higher) Percent global glomerulosclerosis (per 1% higher) *ci* score > 0 (versus 0) *cv* score > 0 (versus 0)	 -0.9 (-1.0, -0.8) -0.0 (-1.0, 0.1) -0.2 (-1.3, 0.8) 0.2 (-0.8, 1.2)	 <0.001 0.72 0.66 0.74
Use of hypothermic perfusion machine	1.3 (0.4, 2.3)	0.01

*All estimates are adjusted for pre-transplant peritubular capillary density and biopsy size to correct for technical variations in measurement.

Supplemental Table 9. Initial multivariable model for factors associated with change in peritubular capillary density among patients with delayed graft function, n=61.

Clinical characteristics	Mean change in % and standard deviation	Unadjusted difference in change in % 95% CI	p-value	Difference in change adjusted for pre-transplant peritubular capillary density in % 95% CI	p-value	Fully adjusted difference in change in % 95% CI*	p-value
Peritubular capillary density on the pre-implantation biopsy (per 1% higher)		-0.9 (-1.0, -0.8)	<0.001	-0.9 (-1.0, -0.8)	<0.001	-0.8 (-0.9, -0.7)	<0.001
Donor type							
Neurologically deceased	-3.8 (4.4)	0		0		0	
Living	-6.4 (2.7)	-2.5 (-6.7, 1.8)	0.25	0.6 (-2.6, 1.4)	0.55	1.1 (-1.0, 3.3)	0.28
Cardiocirculatory arrest	-3.4 (3.3)	0.2 (-2.3, 2.7)	0.85	0.9 (-0.3, 2.1)	0.12	2.0 (0.4, 3.6)	0.02
Donor blood pressure							
Normal blood pressure	-3.6 (4.3)	0		0		0	
Donor hypertension	-4.9 (3.6)	-1.7 (-4.1, 0.8)	0.18	-1.2 (-2.3, -0.0)	0.05	-1.0 (-2.1, -0.1)	0.06
Recipient statin use							
No statin use at transplant	-4.3 (3.7)	0		0		0	
Statin at time of transplant	-3.3 (4.7)	0.9 (-1.2, 3.1)	0.38	0.9 (-0.1, 1.8)	0.09	1.0 (0.1, 1.9)	0.03
Biopsy type							
For cause	-7.6 (4.5)	0		0		0	
Surveillance	-3.4 (3.9)	3.6 (0.2, 7.0)	0.04	2.3 (1.0, 3.6)	<0.001	1.4 (-0.1, 2.9)	0.06
Modality of graft transportation							
Cold storage	-4.6 (3.7)	0		0		0	
Hypothermic perfusion	-2.6 (4.6)	1.9 (-0.2, 4.0)	0.08	1.3 (0.4, 2.3)	0.005	0.9 (-0.1, 1.8)	0.06
Cold ischemia time (per 1 hour higher)		0.2 (0.0, 0.4)	0.02	0.2 (0.1, 0.4)	0.02	0.2 (0.0, 0.3)	0.03
Donor sex							
Male donor sex	-2.9 (4.9)	0		0		0	
Female donor sex	-4.6 (3.3)	-2.0 (-4.0, 2.5)	0.06	-0.7 (-1.7, 0.3)	0.14	-0.2 (-1.2, 0.7)	0.62
Time to biopsy (per 1 month higher)		0.6 (0.0, 1.2)	0.04	0.3 (0.0, 0.6)	0.03	0.1 (-0.2, 0.4)	0.45
Donor age (per 10 year higher)		-1.0 (-1.6, -0.3)	0.01	-0.3 (-0.7, 0.0)	0.06	-0.0 (-0.4, 0.3)	0.88

In addition to the variables included in the table, estimates are adjusted for biopsy size to correct for technical variations in measurement.

Supplemental Table 10. Factors associated with change in peritubular capillary density among patients with immediate graft function, n=130.

Clinical characteristics	Mean change in % and standard deviation	Unadjusted difference in change in % 95% CI	p-value	Difference in change adjusted for pre-transplant peritubular capillary density in % 95% CI	p-value	Fully adjusted difference in change in % 95% CI*	p-value
Peritubular capillary density on the pre-implantation biopsy (per 1% higher)		-0.9 (-1.0, -0.8)	<0.001	-0.9 (-1.0, -0.8)	<0.001	-1.0 (-1.1, -0.9)	<0.001
Donor type							
Neurologically deceased	-3.1 (5.2)	0		0		0	
Living	-6.3 (4.6)	-3.0 (-4.8, -1.2)	0.001	0.5 (-0.6 1.5)	0.37	-0.2 (-1.7, 1.4)	0.86
Cardiocirculatory arrest	-6.7 (5.7)	-3.5 (-8.0, 1.1)	0.13	-0.6 (-3.0, 1.8)	0.61	-1.1 (-3.5, 1.3)	0.35
Donor blood pressure							
Normal blood pressure	-4.9 (5.2)	0		0		0	
Donor hypertension	-2.8 (5.2)	2.3 (-0.3, 5.1)	0.09	-1.5 (-2.9, -0.1)	0.03	-1.1 (-2.1, -0.1)	0.04
Recipient statin use							
No statin use at transplant	-4.3 (5.6)	0		0		0	
Statin at time of transplant	-4.9 (4.8)	-0.6 (-2.4, 1.2)	0.52	0.3 (-0.6, 1.2)	0.55	0.3 (-0.6, 1.2)	0.48
Biopsy type							
For cause	-6.2 (2.9)	0		0		0	
Surveillance	-4.5 (5.3)	1.5 (-2.0, 5.0)	0.40	1.9 (0.1, 3.6)	0.03	1.9 (0.2, 3.6)	0.03
Modality of graft transportation							
Cold storage	-5.4 (5.3)	0		0		0	
Hypothermic perfusion	-4.0 (5.0)	1.6 (-0.2, 3.4)	0.08	0.2 (-0.7, 1.1)	0.68	0.5 (-0.4, 1.5)	0.27
Cold ischemia time (per 1 hour higher)		0.3 (0.1, 0.5)	0.003	-0.0 (-0.1, 0.1)	0.40	-0.1 (-0.2, 0.1)	0.52

In addition to the variables included in the table, estimates are adjusted for biopsy size to correct for technical variations in measurement.