Nephrol Dial Transplant (2013) 28: 2637–2644
doi: 10.1093/ndt/gft292
Advance Access publication 30 July 2013

ndt
Nephrology Dialysis Transplantation

Original Articles

Impact of the pre-transplant histological score on 3-year graft outcomes of kidneys from marginal donors: a single-centre study

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Keywords: extended-criteria donor, pre transplant histological score, renal transplantation

ABSTRACT

Background. The reliability of kidney biopsy as the sole means for assessing kidneys from extended-criteria donors (ECDs) to be allocated to single or dual transplantation is still a matter of debate.

Methods. We compared retrospectively 3 years graft survival and renal function in 44 recipients of a single kidney graft from a marginal donor with good renal function and a Karpinski histological score of ≤3 and 56 recipients of a single transplant with a Karpinski score of 4 or 5. The donors' and recipients' characteristics were compared by means of Wilcoxon's rank-sum test and Fisher's exact test, and survival was analysed using the log-rank test and Cox regression survival analysis.

Results. The donors with the worse histological scores were slightly younger (68.0 ± 4.74 versus 71.3 ± 4.6 years, $P < 0.01$) and had a higher glomerular filtration rate (85.8 ± 28.2 versus 76.3 ± 26.53 mL/min, $P = 0.013$), but there was no difference in serum creatinine levels (0.83 ± 0.24 versus 0.85 ± 0.30 mg/dL, $P = 0.381$). Three years after transplantation, there was no difference between the two groups in terms of recipient serum creatinine levels (1.94 ± 0.69 versus 1.74 ± 0.49 mg/dL, $P = 0.134$), estimated glomerular filtration rate (eGFR, 45.6 ± 21.1 versus 51.7 ± 22.0 mL/min, $P = 0.331$) or the rates of graft loss (27.3 versus 35.7%, $P = 0.47$), delayed graft function or acute rejection.

Conclusions. In our experience, provided the donor has a normal renal function, a difference in the pre-transplant histological score of kidneys from marginal cadaveric donors do not have a significant influence on the outcome 3 years after transplantation. Our findings might represent a basis for designing a randomized controlled trial of using a higher histological score threshold for the DKT allocation of grafts from ECDs with a normal renal function.

INTRODUCTION

Renal transplantation is considered the best treatment for end-stage renal disease (ESRD) [1, 2], but the number of transplantations performed every year is not sufficient to reduce the number of patients on the waiting list [3]. Various strategies have been developed in an attempt to address this problem, including the use of extended-criteria donors (ECDs), dual kidney transplantation (DKT) and donation after circulatory death [4, 5].

The criteria used to decide whether kidneys from marginal donors are suitable for single kidney transplantation (SKT) or DKT are not univocal. Useful parameters to consider when making this decision are the history of the donor, his/her renal function, the anatomical appearance of the kidneys at ultrasonography and macroscopic evaluation and the histological findings of the pre-implantation biopsy [6]. Some authors place a great emphasis on donor renal function at the time of retrieval [7, 8], whereas others consider the severity of the renal lesions as classified by particular scoring systems (e.g. Karpinski histological score) [9] as a good predictor of future graft outcome [10–14]. The latter strategy was adopted by many centres in Italy after the publication of two studies by the group of Remuzzi [15, 16], showing that graft outcomes of SKT harvested from standard donors are comparable with those of SKT harvested from ECDs with a Karpinski score of ≤3 or, in the case of DKT, a Karpinski score of >3. In view of these extremely positive results, the number of DKTs performed in Italy each year has increased from 3.98 to 7.33% of all cadaveric kidney grafts over the last decade (data available on the Italian National Transplantation Centre website https://trapianti.sanita.it/statistiche/).

However, although this strategy has allowed the retrieval of kidneys from very old donors that otherwise would have been discarded, doubts still exist concerning the degree of histological damage that is acceptable for SKT. In the graft allocation system of our region, kidneys with a Karpinski score of four or five may be allocated for SKT if the donor's estimated glomerular filtration rate (eGFR) is at least 60 mL/min. In our view, this has the benefit of increasing the number of transplantations without adversely affecting graft outcomes.

The aim of this study was to compare graft survival and graft renal function 3 years after SKT in patients receiving a kidney from an ECD with good renal function and a Karpinski score of 4 or 5 and in patients receiving a kidney from an ECD with a similar renal function but a Karpinski score of ≤3.

METHODS

Patients

For this retrospective single-centre study, we selected consecutively from our cohort of transplanted patients those who had received a single renal graft between 2005 and 2010 from a cadaveric donor aged >60 years with an eGFR of >55 mL/min (calculated by means of the Cockroft–Gault formula using the first serum creatinine available during the hospital stay of the donor) [17] that underwent histological evaluation at the time of organ retrieval. The patients were divided into two groups: those who received a transplant from a donor with a Karpinski histological score [9] of ≤3 (Group A) and those who received a transplant from a donor with a Karpinski score of 4 or 5 (Group B). The differences between the two groups were analysed in terms of donor characteristics at the time of transplantation (age, gender, serum creatinine levels, eGFR, kidney longitudinal dimension as measured by means of ultrasonography and cold ischaemia time). The recipients' characteristics were compared in terms of age at transplantation, gender, the incidence of delayed graft function (i.e. the need for dialysis during the first week after transplantation), the number of HLA mismatches and biopsy-proven acute rejections, serum creatinine levels, eGFR and the rate of graft loss after 3 years of transplantation.

Immunosuppressive regimen

All of the patients received induction therapy with basiliximab 20 mg (Simulect, Novartis Pharma, Basel and Switzerland) on post-transplantation days 0 and 4; methylprednisolone i.v. on Days 0–4, followed by oral methylprednisolone in accordance with our institutional protocol; cyclosporine (Sandimmun Neoral, Novartis Pharma); and mycophenolic acid (Myfortic, Novartis Pharma) or everolimus (Certican, Novartis Pharma) (Table 1).

The patients were followed up in our outpatient clinic in accordance with our centre protocol.

Histological analysis and allocation protocol

Pre-implantation specimens were wedge biopsied by the surgeon at the time of organ retrieval. The specimens were stained with haematoxylin eosin, PAS and Masson's Trichrome, and the histological evaluation was made by the Pathology Unit of our institution using Karpinski's histological score [9] (Table 2).

Once the score was obtained, the kidneys were allocated according to the protocol shown in Table 3.

Statistical analysis

The continuous variables are expressed as mean values and standard deviations, or median values and quartiles when they were not normally distributed according to the Shapiro–Wilk test; the comparisons were made using Student's t test for independent samples or Wilcoxon's rank-sum test as appropriate. The non-continuous variables were compared using the χ^2

Table 1. Maintenance immunosuppressive regimen

Maintenance regimen	Group A	Group B
CyA, MPA, Ster	32	33
CyA trough levels: 100–150 ng/mL		
CyA second hour levels: 700–900 ng/mL		
CyA, ERL, Ster	9	19
CyA trough level: 40–70 ng/mL		
CyA second hour level: 350–450 ng/mL		
ERL trough levels: 3–8 ng/mL		
Other regimens	2	4

Cya, cyclosporine; MPA, mycophenolic acid; Ster, corticosteroids; ERL, everolimus.

Table 2. Semi-quantitative scale for the renal biopsy score according to the Karpinski classification [9]

Glomerular score	
0	No globally scleroted glomeruli
1	<20% global glomerulosclerosis
2	20–50% global glomerulosclerosis
3	>50% global glomerulosclerosis
Tubular score	
0	Absent
1	<20% of tubules affected
2	20–50% of tubules affected
3	>50% of tubules affected
Interstitial score	
0	Absent
1	<20% of cortical parenchyma replaced by fibrous connective tissue
2	20–50% of cortical parenchyma replaced by fibrous connective tissue
3	>50% of cortical parenchyma replaced by fibrous connective tissue
Vascular score	
Arteriolar narrowing for hyaline arteriolosclerosis	
0	Absent
1	Increased wall thickness but to a degree that is less than the diameter of the lumen
2	Wall thickness that is equal or slightly greater than the diameter of the lumen
3	Wall thickness that far exceeds the diameter of the lumen with extreme luminal narrowing or occlusion
Arterial sclerosis for intimal fibrous thickening, fibroplasias	
0	Absent
1	Increased wall thickness but to a degree that is less than the diameter of the lumen
2	Wall thickness that is equal or slightly greater than the diameter of the lumen
3	Wall thickness that far exceeds the diameter of the lumen, with extreme luminal narrowing or occlusion

For the vascular lesions, both arterioles and arteries are evaluated separately. However, for the final vascular score, the most severe lesion of either arterioles or arteries determines the final grade.

Table 3. Protocol for allocation of kidneys from donors older than 60 years in our institution

Karpinski histological score	Allocation SKT or DKT
≤3	SKT
4–5	SKT if donor eGFR ≥60 mL/min
	DKT if donor eGFR < 60 mL/min
6	DKT
>6	Discarded

SKT, single kidney transplant; DKT, double kidney transplant. Kidneys with a score of 3 in any of the vascular, glomerular, interstitial and tubular sections of the karpinski score were not allocated as SKT. Diabetic donors with a score of Karpinski of 4 or 5 are not allocated as SKT.

test or Fisher's exact test as appropriate. Death-uncensored graft survival and patient survival are expressed using Kaplan–Meier curves; the differences between the survival curves were assessed by means of the log-rank test. Cox regression survival analysis was used to assess the influence of the baseline covariates on 3 years graft survival. All of the tests were made using SPSS software.

RESULTS

We used our database of renal transplant patients to select 100 patients who received a kidney from an ECD: 44 received a kidney with a Karpinski score of ≤3 (Group A) and 56 received a kidney with a Karpinski score of 4 or 5 (Group B).

Donor characteristics

The characteristics of the donors in the two groups were similar in terms of serum creatinine levels (0.87 ± 0.27 versus 0.83 ± 0.24 mg/dL, P = 0.381), gender, the ultrasonographic longitudinal measurement of the transplanted kidney (107 ± 9.4 versus 108 ± 8.0 mm, P = 0.893) and cold ischaemia time (18.0 ± 7.2 versus 19.6 ± 6.5 h, P = 0.17). The donors in Group B had a higher eGFR (76.3 ± 26.53 versus 85.8 ± 28.2 mL/min; P = 0.013), and were slightly younger than those in Group A (71.3 ± 4.6 versus 68.0 ± 4.74 years; P < 0.01). The cause of death of the donors was mainly cardiovascular (86.4% in Group A and 71.4% in Group B). Thirty-one percent of the donors in Group A were hypertensive, as against 50% in Group B (not significant). There was no diabetic donor (Table 4).

Baseline characteristics and result of the recipients

The baseline characteristics of the recipients are shown in Table 5. There was no between-group difference in terms of age, gender or the number of mismatches. All of the recipients were Caucasians, except for two Asian patients. Two recipients in each group were undergoing second transplants.

Table 4. Donors' characteristics

	Group A	Group B	P
Males	(43.2%)	(48.2%)	0.61
Age (years) Median age	71.72 ± 4.59 71.5	68.03 ± 4.73 68	<0.01
Creatinine levels (mg/dL) Median level	0.85 ± 0.30 0.82	0.83 ± 0.24 0.8	0.381
eGFR (mL/min) Median	76.39 ± 26.53 70.83	85.8 ± 28.2 83.35	0.013
Kidney longitudinal dimension by ultrasound (mm) Median	107.54 ± 9.4 Median	108 ± 8.0 110	0.893
Hypertension	31.8%	50%	0.10
Donor cause of death			
Cardiovascular	38 (86.4%)	40 (71.4%)	0.74
Non-cardiovascular	6 (13.6%)	16 (28.6%)	
	Group A	Group B	
Karpinski's histological score	Score 1: 2 (4.5%)	Score 4: 32 (57.1%)	
	Score 2: 13 (29.5%)	Score 5: 24 (42.9%)	
	Score 3: 29 (65.9%)		
Vascular score	Score 0: 4 (9.1%)	Score 1: 34 (60.7%)	
	Score 1: 38 (86.4%)	Score 2: 22 (39.3%)	
	Score 2: 2 (8.3%)		

Continuous variables expressed as mean values + standard deviation and median. P-values refer to Wilcoxon's rank-sum test for continuous variables, and Fisher's exact test for non-continuous variables.

Renal function 3 years after transplantation was not different between the two groups in terms of serum creatinine levels (1.94 ± 0.69 versus 1.74 ± 0.49 mg/dL, P = 0.134) or eGFR (45.6 ± 21.1 versus 51.7 ± 22.0 mL/min, P = 0.331). The rates of graft loss uncensored for death were similar (27.3 versus 32.1%, P = 0.47). Death with a functional graft occurred in eight cases in Group A and 10 in Group B (P = 0.967): the cause of death was related to infectious complications in all cases, except for three cases in Group A (two cardiovascular and one neoplastic) and two in Group B (one cardiovascular and one secondary to a surgical complication). Graft loss and dialysis resumption occurred in four patients in Group A and eight in Group B (P = 0.52); in each group, these were two cases due to acute rejection and two cases related to surgical complications plus four graft losses due to chronic rejection occurred in Group B.

Survival analysis

In Figures 1 and 2 are shown, respectively, the Kaplan–Meier curves of death-censored graft survival and patient survival. The log-rank analyses of both curves did not reveal any statistically significant difference in 3-years graft survival (P = 0.45) or patient survival (P = 0.9) between the two groups.

In the multivariate analysis, recipient age at transplantation and the occurrence of DGF had a significant influence on 3 years graft survival (Table 6).

Other parameters

The other parameters that we evaluated that might have had an influence on graft survival or renal function resulted similar between the two groups. In particular, we observed seven acute cellular rejections (one case 2a, three cases 1a and one case 1b according to the Banff classification [18]. Two patients were treated with corticosteroids but did not undergo a kidney biopsy) and one humoral-mediated rejection in Group A and eight cellular rejections in Group B (one case 2a, three cases 1a, the others not biopsy proven). The rate of delayed graft function was comparable in the two groups (56 versus 39%; P = 0.06).

DISCUSSION

We found no differences in 3 years graft survival or renal function between patients undergoing SKT with a kidney from an ECD with good renal function and a Karpinski score of ≤3

Table 5. Recipients' characteristics and results 3 years after transplantation

	Group A	Group B	P-value
Cold ischaemia time (hours) Median	18.0 ± 7.2 19	19.6 ± 6.5 22	0.17
HLA mismatches, median (quartiles)	4 (3–4)	4 (3–4.75)	0.263
Creatinine levels (mg/dL) Median	1.94 ± 0.69 1.81	1.74 ± 0.49 1.59	0.134
eGFR (mL/min) Median	45.67 ± 21.1 44.5	51.73 ± 22.0 46.25	0.331
Proteinuria (mg/24hh)	311 ± 233.1 277	393.24 ± 341.39 300	0.41
Age (years) Median	60.18 ± 6.09 59	60.33 ± 6.07 59	1.0
Males	32 (72.7%)	40 (73.2%)	1.0
DGF	25 (58.1%)	22 (39.3%)	0.063
Cause of renal failure			
ADPKD	8 (18.2%)	13 (23.2%)	
Chronic GN	9 (20.5%)	8 (14.3%)	
Nephrosclerosis	10 (22.7%)	7 (12.5%)	
Unknown	6 (13.6%)	8 (14.3%)	
IgAN	2 (4.5%)	5 (8.9%)	
Diabetes	0	3 (5.2%)	
Others	9 (20.5%)	12 (21.4%)	
Biopsy-proven acute rejection	8 (18.2%)	8 (14.3%)	0.598
Death-uncensored graft loss	12 (27.3%)	18 (32.1%)	0.47
Death	8 (18.2%)	10 (17.9%)	0.967
Cause of death			
Infections:	5 (62.5%)	8 (80%)	
Cardiovascular:	2 (25%)	1 (10%)	
Neoplastic	1 (12.5%)		
Other		1 (10%)	
Return to dialysis	4 (9.1%)	8 (14.3%)	0.542

Continuous variables expressed as mean values + standard deviation and median, except for HLA mismatch (expressed as median values and quartiles). P-values for continuous variables refer to Wilcoxon's rank-sum test for continuous variables. Non-continuous variables expressed as the number of cases and percentages. P-value for non-continuous variables refers to the χ^2 test or Fisher's exact test for non-continuous variables when appropriate.
ADPKD, autosomal dominant polycystic kidney disease; GN, glomerulonephritis; IgAN, IgA nephropathy.

and those undergoing SKT with a kidney from an ECD with a similar renal function but a Karpinski score of 4 or 5. On the basis of these findings, it could be concluded that allocating organs such as those of our Group B to SKT might make it possible to reduce the number of patients on the waiting list in comparison with allocating kidneys only on the basis of pre-implantation biopsy score.

It is difficult to find comparable studies in the literature, but there are some published data that seem to be indirectly in line with our conclusions. Cruzado *et al.* [19] demonstrated that DKT recipients who lost one of the two kidneys (mainly because of thrombosis) had 5- and 10-year graft survival rates similar to those receiving a DKT with two functioning kidneys, albeit with a lower eGFR.

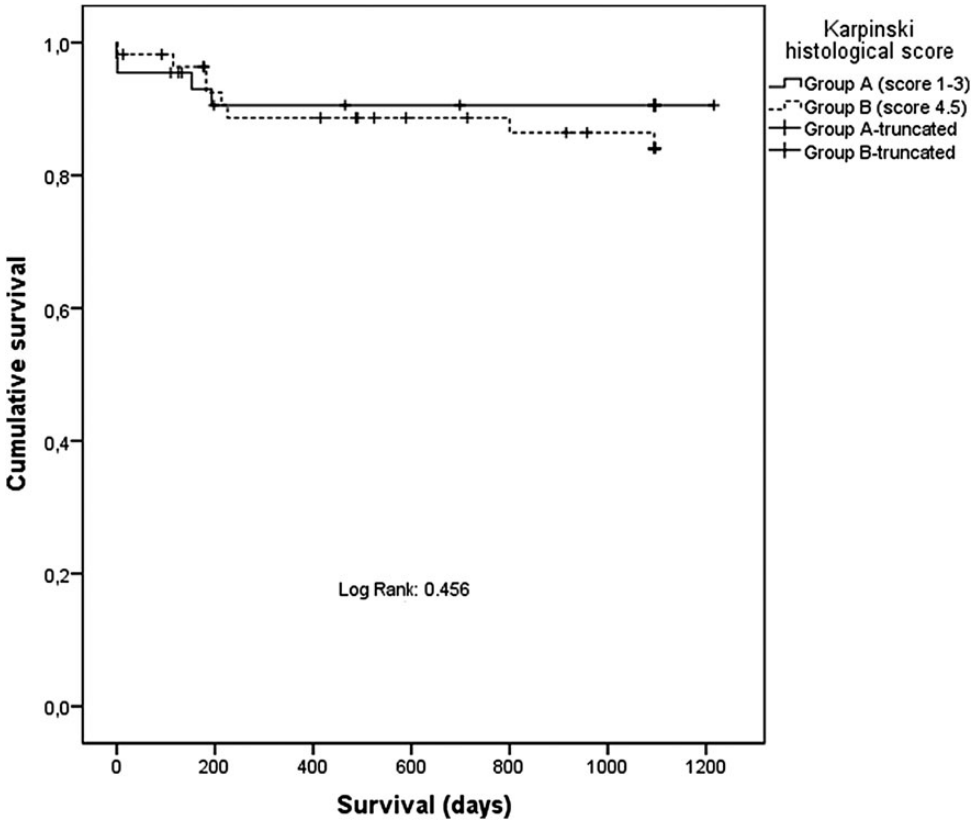

FIGURE 1: Death censored graft survival.

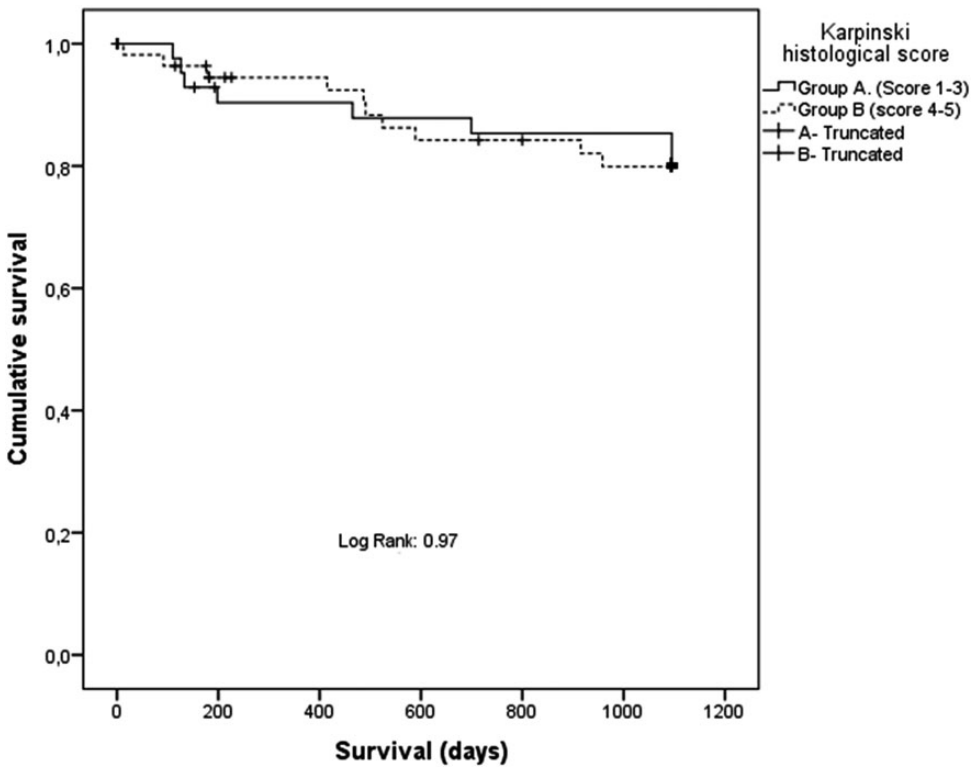

FIGURE 2: Patients' survival.

Table 6. Cox regression analysis of graft survival

Covariate	P Value	Exp(B)	IC 95.0% for exp(B)	
			Inferior	Superior
Donor's cause of death (Vascular/non vascular)	0.629	0.746	0.226	2.456
Karpinski score 1–3 versus 4–5	0.170	0.441	0.137	1.421
Recipient age at transplantation (years)	0.004	1.149	1.045	1.264
Donor age (years)	0.559	1.030	0.933	1.138
Cold ischaemia time (hours)	0.427	1.060	0.918	1.225
Donor sex	0.693	1.241	0.424	3.628
Donor eGFR (mL/min)	0.300	1.011	0.991	1.031
Kidney longitudinal dimension by ultrasound (mm)	0.168	0.958	0.902	1.018
Immunosuppressive therapy (mTOR-i versus non mTOR-i)	0.865	1.114	0.319	3.895
Acute rejection	0.068	0.298	0.081	1.095
Delayed graft function	0.027	0.245	0.070	0.855

Donor age and donor eGFR were slightly but statistically different between our two groups insofar as the donors with the worse histological scores were younger and had better renal function.

This is an important point that merits comment. First of all, it might be said that the two groups were not perfectly comparable because Group B donors had slightly better baseline characteristics, although the differences between the two groups were small (about 3 years of age and 9 mL/min of eGFR), and we do not consider this as a significant bias of this study since the donor eGFR and donor age did not have any impact on graft survival when assessing the covariate influence on survival analysis by Cox regression. Second, this difference in donors' characteristics allows us to emphasize the main message of this study, namely the fact that if we want to allocate safely to SKT kidneys with a score of 4 or 5, we must be particularly careful in selecting only those kidneys with a preserved renal function.

Furthermore, there are concerns about the use of the preimplantation biopsy. A donor's histological score does not correlate perfectly with renal function, and there are some doubts about the reliability of histological scores because a renal biopsy is by definition focal and usually performed on the sub-capsular region. In addition, it has been argued that the Karpinski score is an operator-dependent, poorly reproducible procedure whose value should be reduced or at least not overestimated for clinical or scientific purpose. In a small study, Murve *et al.* [20] took kidneys that had been refused by United Network for Organ Sharing centres on the basis of biopsy findings and compared the results of a detailed histological examination with those of the wedge biopsy at the time of retrieval, finding that the latter may overestimate the percentage of glomerulosclerosis. On the other hand, Mazzucco *et al.* [21] instead found that wedge and fine needle biopsy findings provide reliable data concerning the actual kidney status, especially if the size of the biopsy is sufficient and there are more than 10 glomeruli.

The 3-year graft and patient survival in our study was, respectively, around 70 and 80% in both groups. These outcomes are in line with data of grafts from ECD derived from larger clinical trials and registers. ([22] and reviewed in [5]).

Our study has the limitations of being retrospective, single-centre and with a small patient population. Furthermore, biopsies were not re-evaluated retrospectively by a single pathologist in order to reduce the interoperator variability. Nevertheless, all of the transplantations were performed within a period of 5 years, and a 3-year follow-up may be a sufficient time to reveal the effect of a reduced number of functioning nephrons in the group with the worse histological score and to anticipate long-term graft survival.

This hypothesis is also supported by the better results of the study of Lucarelli *et al.* [23], which even found that 5-year graft survival was better for DKT than SKT of ECD kidneys allocated on the basis of their Karpinski score. The immunosuppressive therapy deserves a further comment. Given that a slightly higher percentage of patients in the group with the worst score were treated with everolimus, one might argue that the difference in GFR in favour of this group may be due to a reduced exposure to the calcineurin inhibitor. In our opinion, this observation is unfounded, because the difference in the proportion of patients treated with mTOR-inhibitors (mTOR-i) in the two groups is very small (20% in the first and 33% in the second) and occurred by chance because we do not adopt a policy of treating patients transplanted with organs from ECD with everolimus or sirolimus. Finally, from the data of the literature [24–26] the mean difference of eGFR between patients treated with standard doses of cyclosporine plus mycophenolic acid versus everolimus plus low dose of cyclosporine is ~10 mL/min, which is more or less the difference of GFR that we found between our two groups. Given that only 13% more

of the patients in Group B was treated with mTOR-i, the difference in GFR cannot be attributed only to the lower exposure to cyclosporine.

However, despite these limitations, we feel that our findings justify our policy of allocating organs: between 2005 and 2010, we increased the number of ECD transplantations by 23%, and the total number of transplants at our centre by 9%, without any adverse effect on transplant outcomes. Our findings might represent a basis for designing a randomized controlled trial of using a higher histological threshold for the DKT allocation of grafts from ECDs with a normal renal function.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Wolfe RA, Ashby VB, Milford EL *et al.* Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med. 1999; 341: 1725–1730
2. Hunsicker LG. A survival advantage for renal transplantation. N Engl J Med. 1999; 341: 1762–1763
3. U S Renal Data System. USRDS 2011 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD 2011
4. Gridelli B, Remuzzi G. Strategies for making more organs available for transplantation. N Engl J Med 2000; 343: 404–410
5. Pascual J, Zamora J, Pirsch JD. A systematic review of kidney transplantation from expanded criteria donors. Am J Kidney Dis. 2008; 52: 553–586
6. Faenza A, Sestigliani E, Zambianchi L *et al.* Utilization of suboptimal kidney donors. Transplant Proc 2004; 36: 485–487
7. Randhawa P. Role of donor kidney biopsies in renal transplantation. Transplantation 2001; 71: 1361–1365
8. Snanoudj R, Rabant M, Timsit MO *et al.* Donor-estimated GFR as an appropriate criterion for allocation of ECD kidneys into single or dual Kidney transplantation. Am J Transplant 2009; 9: 2542–2551
9. Karpinski J, Lajoie G, Cattran D *et al.* Outcome of kidney transplantation from high risk donors is determined by both structure and function. Transplantation 1999; 67: 1162–1167
10. Randhawa PS, Minervini MI, Lombardero M *et al.* Biopsy of marginal donor kidneys: correlation of histological findings with graft disfunction. Transplantation 2000; 69: 1352–1357
11. El-Husseini A, Sabry A, Zahran A *et al.* Can donor implantation renal biopsy predict long-term renal allograft outcome? Am J Nephrol 2007; 27: 144–151. Epub 2007 Feb 16
12. Andres A, Morales JM, Herrero JC *et al.* Double versus single renal allografts from aged donors. Transplantation 2000; 69: 2060–2066
13. Dietl KH, Wolters H, Marschall B *et al.* Cadaveric 'two-in-one' kidney transplantation from marginal donors: Experience of 26 cases after 3 years. Transplantation 2000; 70: 790–794
14. Sung RS, Christensen LL, Leichtman AB *et al.* Determinants of discard of expanded criteria donor kidneys: Impact of biopsy and Mmachine perfusion. Am J Transplant 2008; 8: 783–792. Epub 2008 Feb 19
15. Remuzzi G, Grinyò J, Ruggenenti P *et al.* Early experience with dual kidney transplantation in adults using expanded donor criteria. Double Kidney Transplant Group (DKG). J Am Soc Nephrol 1999; 10: 2591–2598
16. Remuzzi G, Cravedi P, Perna A *et al.*, Dual Kidney Transplant Group. Long-term outcome of renal transplantation from older donors. N Engl J Med 2006; 354: 343–352
17. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976; 16: 31–41
18. Solez K, Colvin RB, Racusen LC *et al.* Banff 07 classification of renal allograft pathology: updates and future directions. Am J Transplant 2008; 8: 753–760
19. Cruzado JM, Fernandez L, Riera L *et al.* Revisiting double kidney transplantation: two kidneys provide better graft survival than one. Transplant Proc. 2011; 43: 2165–2167
20. Muruve NA, Steinbecker KM, Luger AM. Are wedge biopsies of cadaveric kidneys obtained at procurement reliable? Transplantation 2000; 69: 2384–2388
21. Mazzucco G, Magnani C, Fortunato M *et al.* The reliability of pre-transplant donor renal biopsies (PTDB) in predicting the kidney state. A comparative single-centre study on 154 untransplanted kidneys. Nephrol Dial Transplant 2010; 25: 3401–3408. Epub 2010 Mar 31
22. Sung RS, Guidinger MK, Leichtman AB *et al.* Impact of the expanded criteria donor allocation system on candidates for and recipients of expanded criteria donor kidneys. Transplantation 2007; 84: 1138–1144
23. Lucarelli G, Bettocchi C, Battaglia M *et al.* Extended criteria donor kidney transplantation: comparative outcome analysis between single versus double kidney transplantation at 5 years. Transplant Proc 2010; 42: 1104–1107
24. Salvadori M, Scolari MP, Bertoni E *et al.* Everolimus with very low-exposure cyclosporine a in de novo kidney transplantation: a multicenter, randomized, controlled trial. Transplantation 2009; 88: 1194–1202
25. Tedesco Silva H, Jr, Cibrik D, Johnston T, Lackova E, Mange K, Panis C *et al.* Everolimus plus reduced-exposure CsA versus mycophenolic acid plus standard-exposure CsA in renal-transplant recipients. Am J Transplant 2010; 10: 1401–1413. Epub 2010 Apr 28
26. Vítko S, Margreiter R, Weimar W *et al.* Everolimus (Certican) 12-month safety and efficacy versus mycophenolate mofetil in de novo renal transplant recipients. Transplantation 2004; 78: 1532–1540

Received for publication: 17.1.2013; Accepted in revised form: 24.5.2013