TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Residual urinary volume is a risk factor for primary nonfunction in kidney transplantation

Josep M. Cruzado,[1] Anna Manonelles,[1] Helena Vila,[2] Edoardo Melilli,[1] Neus Sala,[1] Oriol Bestard,[1] Joan Torras,[1] Cristian Tebé,[3] Lluís Riera[2] and Josep M. Grinyó[1]

1 Nephrology Department, Hospital Universitari de Bellvitge, University of Barcelona, IDIBELL, L'Hospitalet de Llobregat, Spain
2 Urology Department, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Spain
3 Statistical Advisory Service, Bellvitge Biomedical Institute-IDIBELL, Faculty of Medicine and Health Sciences, University Rovira i Virgili, L'Hospitalet de Llobregat, Spain

Keywords
early graft failure, renal transplantation, residual renal function.

Correspondence
Josep M Cruzado, MD, Nephrology Department, Hospital Universitari de Bellvitge, IDIBELL, Feixa Llarga s/n. L'Hospitalet de Llobregat, Barcelona, Spain.
Tel.: +34 93 2607604;
fax: +34 93 2607607;
e-mail: jmcruzado@bellvitgehospital.cat

Conflicts of interest
The authors declare no conflict of interest to be disclosed

Received: 21 January 2015
Revision requested: 26 February 2015
Accepted: 15 June 2015
Published online: 6 Jul 2015

doi:10.1111/tri.12625

Summary

Primary nonfunction is a severe complication after kidney transplantation. Residual renal function could be a risk factor for this complication in the current era of kidney transplantation from extended criteria donors (ECD). This is a single-center case–control study. Between 2000 and 2012, 1112 patients received a kidney transplant from a deceased donor. We identified 56 cases of early graft loss (kidney that never recover renal function and/or graft thrombosis <48 h after kidney transplantation). As controls we used patients receiving the contralateral kidney. Donor age was 55 ± 17 years with 57% fulfilling ECD criteria. Among the 56 cases, 14 were due to vascular rejection and 42 to primary nonfunction. Risk factors for early graft loss due to vascular rejection were previous transplant, time on dialysis, and HLA sensitization. Risk factors for primary nonfunction were first transplant, short period on dialysis, mainly peritoneal dialysis, and a residual urinary volume ≥500 ml/24 h. Conditional logistic regression analysis showed that residual urinary volume (OR = 20.01) rather than the dialysis modality was a major risk factor for primary nonfunction. In conclusion, residual urinary volume seems to be a risk factor for primary nonfunction in the current era of kidney transplantation.

Introduction

Kidney transplantation is the best option for renal replacement therapy [1]. So far, the main limitation for implementing such strategy is organ shortage [2]. Indeed, there are many patients waiting for years to be transplanted. To overcome the scarcity of kidneys for transplantation, clinicians develop some innovative policies, such as ABO incompatible [3] and paired kidney exchange programs [4] in the case of living-donor kidney transplantation and extended criteria [5] and cardiac death donor programs [6] in the case of deceased-donor kidney transplantation.

In the particular case of deceased donors, these programs lead transplant teams to explore the limits of organ viability. The assessment of kidney vascular resistance [7] and/or kidney histology [8] before kidney transplantation may be useful to minimize primary nonfunction. These kidneys are especially sensitive to the ischemic damage mostly related to organ preservation after recovering and cold ischemia time [9,10]. It is accepted that transplantation of kidneys from extended criteria donors (ECD) is associated with higher risk of primary nonfunction [11]. In addition, there are other well-known causes of early graft loss such as HLA sensitization that can be associated with endothelial damage and acute vascular rejection causing graft thrombosis [12,13]. Thus, immunological and nonimmunological factors can cause early graft loss, either primary nonfunction (related to nonimmunological risk factors) or acute vascular rejection (related to immunological risk factors).

There is evidence suggesting that preemptive kidney transplantation in the case of living as well as deceased donors is associated with better outcome [14,15]. In fact, preemptive living-donor kidney transplantation is the best therapeutic option for end-stage chronic kidney disease [16]. However, in kidney transplantation there are experimental studies suggesting that residual renal function aggravates allograft ischemic damage [17]. In the current era of kidney transplantation from ECD, in which the risk of delayed graft function is high [11] perhaps residual renal function could aggravate the ischemic damage putting the transplant at risk for primary nonfunction.

Materials and methods

Patient population and study design

This is a case–control study performed in deceased-donor kidney transplant recipients. Between January 2000 and December 2012, a total of 1112 patients received a kidney transplant from a deceased donor at Bellvitge Hospital. We retrospectively identified and reviewed all cases suffering from early graft loss. As controls we used patients receiving the paired/contralateral kidney. This design was used to minimize donor effect on the event and therefore focusing on surgical and recipient factors. This study was approved by Bellvitge Hospital Research Committee.

Definition of clinical variables

Early graft loss was defined as kidney that never recover renal function and/or graft thrombosis diagnosed <48 h after kidney transplantation. In all cases, allograft nephrectomy was performed and histology evaluated. Early graft loss was divided into two categories, acute vascular rejection (immunological cause) and primary nonfunction (nonimmunological cause).

The following variables were evaluated from donors: age, gender, ECD criteria (aged 60 years or older, or over 50 years with at least two of the following conditions: hypertension history, serum creatinine >1.5 mg/dl or cause of death from cerebrovascular accident), preimplantation biopsy Remuzzi's score [8], estimated glomerular filtration rate. The following variables were evaluated from recipients: age, gender, previous transplant, body mass index (BMI), body surface area (BSA), severe vascular calcification in external iliac arteries, preemptive transplantation, dialysis duration, type of dialysis, residual urinary volume, cause of end-stage renal disease (ESRD), anti-HLA antibodies (Panel reactive antibodies >20%), number of HLA mismatches and immunosuppressive treatment. Regarding immunosuppression protocols, basiliximab was used in the case of kidneys from ECD and thymoglobulin in high-immunological-risk recipients. Steroids, calcineurin inhibitor, and mycophenolate mofetil were given to all patients, although calcineurin inhibitor was either commenced before or after transplantation depending on clinical judgment. A pretransplant dialysis session was performed to all patients on hemodialysis. Daily urinary volume was asked to the patient at transplantation and recorded in our database as categorical variable: <500 ml or ≥500 ml. Similarly to oliguria definition, we considered low daily urinary volume when it was <500 ml/24 h and preserved daily urinary volume when it was ≥500 ml/24 h.

In addition, we evaluated the following variables related to surgery: cold ischemia time, vascular anastomosis time, bench repair of complex vascular lesions, left or right kidney, left or right iliac fossa allograft placement, renal vein elongation, and single versus multiple kidney transplant arterial anastomosis.

Statistics

In our study, early graft loss patients were matched with nonearly graft loss patients based on deceased donors. This design removes the effect of measured or unmeasured donor risk factors in the analysis. Data are presented as frequencies for categorical variables or mean and standard deviation for normally distributed continuous variables. Groups were compared using the chi-squared test for categorical variables, *t*-test for normally distributed data and nonparametric Mann–Whitney *U*-test for non-normally distributed variables. This statistic analysis was performed with SPSS version 20.0 (IBM SPSS Statistics for Windows, Version 20.0; Armonk, NY, USA). The statistical significance level was defined as *P*-value <0.05. In addition, McNemar test and conditional logistic regression were used in matched case–control studies for univariate and multivariate association analysis, respectively. Daily urinary volume was tested as associated factor with early graft loss using a conditional logistic regression controlled by type of dialysis and anti-HLA antibodies. Daily urinary volume was also tested on a subgroup of matched patients. A selection criterion was primary nonfunction as early graft loss cause. A conditional logistic regression controlled by type of dialysis and anti-HLA antibodies was also used. The conditional logistic regression model was fitted in R 3.1.3, using the clogit function in R's Survival package.

Results

HLA sensitization and pretransplant preserved daily urinary volume are associated with early graft loss

From 1112 deceased-donor kidney transplants performed in the study period, 56 fulfilled the definition of early graft loss (5%). Donor and surgical characteristics are described in Table 1. Donor age was 55.0 ± 17.7 years (38 male and

Table 1. Donor and surgical characteristics.

	Total (n = 112)	Control (n = 56)	Early graft loss (n = 56)	P-value
Histological Score (0/1/2/3)	17/26/35/34	8/13/18/17	9/13/17/17	0.993
Cold ischemia time (h)	20.2 ± 4.0	19.7 ± 3.7	20.7 ± 4.3	0.535
Vascular anastomosis time (min)	43.1 ± 12.2	41.8 ± 13.3	44.4 ± 11.0	0.100
Arterial anastomosis (single/multiple)	92/20	47/9	45/11	0.806
Donor kidney (right/left)	56/56	26/30	30/26	0.756
Iliac fossa (right/left)	60/52	33/23	27/29	0.344
Vein elongation (yes/no)	38/74	18/38	20/36	0.842

18 female) and more than 57% of kidneys were from ECD (32 of 56). No significant differences were found between early graft loss and controls. Mean donor estimated GFR was 73.9 ± 13.2 ml/min. Both, GFR and preimplantation biopsy suggested some degree of chronic renal damage at baseline. Cold ischemia time was 20 h, longer than optimal. Of note, vascular anastomosis time, type of arterial anastomosis, donor kidney, iliac fossa, and requirement for vein elongation were similar between groups. Bench surgery was performed just in two cases, one in each group. There were no kidney transplants from cardiac death donors, although this type of transplant was seldom performed at our institution during the study period.

Recipient characteristics are showed in Table 2. Causes of chronic kidney disease were as follows: 33 glomerulonephritis (16 early graft loss and 17 control), 4 hypertension (1 early graft loss and 3 control), 7 diabetes (3 early graft loss and 4 control), 14 adult kidney polycystic disease (6 early graft loss and 8 control), 20 chronic interstitial nephropathy (12 early graft loss and 8 control), and 34 unknown (18 early graft loss and 16 control). No differences were observed in renal disease etiology between groups. Early graft loss and control groups were similar regarding the majority of variables, including type of dialysis and immunosuppression. Interestingly, HLA sensitization and preserved daily urinary volume were associated with early graft loss.

HLA sensitization is associated with early graft loss due to acute vascular rejection whereas preserved daily urinary volume is associated with primary graft failure

To investigate causes of early graft loss, we divided this event in acute vascular rejection and primary nonfunction. From 56 cases of early graft loss, 42 were due to primary graft failure and 14 to acute vascular rejection. Donor and surgical characteristics of these groups are showed in Table 3. Among the variables analyzed, we found that cases of acute vascular rejection were younger and consequently received kidneys from donors with higher GFR and with less chronic damage. Donor and surgical variables were not identified as risk factors because of study design (case and mate kidney recipient).

Recipient characteristics are described in Table 4. The acute vascular rejection group showed a trend to be

Table 2. Recipient characteristics.

	Total (n = 112)	Control (n = 56)	Early graft loss (n = 56)	P-value
Recipient age (year)	54.6 ± 14.1	55.5 ± 13.1	53.7 ± 15.1	0.310
Recipient sex (male/female)	63/49	36/20	27/29	0.127
Vascular calcification (yes/no)	18/94	11/45	7/49	0.441
BSA (m^2)	1.72 ± 0.17	1.76 ± 0.16	1.68 ± 0.17	0.533
BMI (kg/m^2)	26.6 ± 3.5	27.3 ± 3.3	25.8 ± 3.6	0.376
Transplant number (1/2/3)	99/9/4	50/5/1	49/4/3	0.571
Dialysis time (months)	37 ± 46	32 ± 42	42 ± 50	0.152
Preemptive transplant (yes/no)	9/103	4/52	5/51	0.728
Peritoneal Dialysis (yes/no)	17/95	5/51	12/44	0.065
Hemodialysis (yes/no)	86/26	47/9	39/17	0.073
Daily urinary volume (≥500/<500 ml)	38/74	10/46	28/28	0.001
Anti-HLA antibodies (yes/no)	25/87	8/48	17/39	0.041
HLA-DR mismatch (0/1/2)	18/73/21	10/34/12	8/39/9	0.609
HLA-Class I mismatch (1/2/3/4)	12/36/48/16	4/15/25/12	8/21/23/4	0.093
Induction therapy (yes/no)	62/50	33/23	29/27	0.447
Without pretransplant CNI (yes/no)	22/90	11/45	11/45	1.000

BSA, body surface area; BMI, body mass index; HLA, human leukocyte antigen; CNI, calcineurin inhibitor.

Table 3. Donor and surgical characteristics.

	Control (n = 56)	Primary non-function (n = 42)	Acute vascular rejection (n = 14)	P-value
Donor age (year)	55.0 ± 17.7	58.5 ± 16.2^{ns}	46.4 ± 21.7^{ns}	0.078
Donor sex (male/female)	38/18	27/15^{ns}	10/6^{ns}	0.578
ECD (yes/no)	32/24	28/14^{ns}	4/10^{ns}	0.179
Histological Score (0/1/2/3)	8/13/18/17	2/11/14/15^{ns}	7/2/3/2$^{0.035}$	0.009
Donor GFR (ml/min)	74.0 ± 13.2	71.4 ± 12.0^{ns}	81.3 ± 14.4^{ns}	0.051
Cold ischemia time (h)	19.7 ± 3.7	20.3 ± 4.0^{ns}	22.1 ± 4.8^{ns}	0.121
Vascular anastomosis time (min)	41.8 ± 13.3	45.0 ± 11.6^{ns}	42.4 ± 9.2^{ns}	0.438
Arterial anastomosis (single/multiple)	47/9	33/9^{ns}	12/2 ^{ns}	0.738
Donor kidney (right/left)	26/30	24/18^{ns}	6/8 ^{ns}	0.158
Iliac fossa (right/left)	33/23	18/24^{ns}	9/5 ^{ns}	0.199
Vein elongation (yes/no)	18/38	17/25^{ns}	3/11 ^{ns}	0.395

ECD, extended criteria donors; GFR, glomerular filtration rate.
P-values represent comparisons between primary nonfunction and acute vascular rejection groups.

Table 4. Recipient characteristics.

	Control (n = 56)	Primary non-function (n = 42)	Acute vascular rejection (n = 14)	P-value
Recipient age (year)	55.5 ± 13.1	55.5 ± 15.3 ^{ns}	48.2 ± 13.7 ^{ns}	0.198
Recipient sex (male/female)	36/20	22/20^{ns}	5/9$^{0.052}$	0.127
Vascular calcification (yes/no)	11/45	5/37^{ns}	2/12^{ns}	0.576
BSA (m^2)	1.76 ± 0.16	1.71 ± 0.18^{ns}	1.58 ± 0.12 ^{ns}	0.002
BMI (kg/m^2)	27.3 ± 3.3	26.2 ± 3.2^{ns}	24.4 ± 4.4 ^{ns}	0.013
Transplant number (1/2/3)	50/5/1	39/2/1^{ns}	10/2/2$^{0.09}$	0.135
Dialysis time (months)	32 ± 42	29 ± 33^{ns}	80 ± 71$^{0.007}$	0.001
Preemptive transplant (yes/no)	4/52	5/37^{ns}	0/14^{ns}	0.344
Peritoneal Dialysis (yes/no)	5/51	12/30$^{0.011}$	0/14^{ns}	0.007
Hemodialysis (yes/no)	47/9	25/17$^{0.007}$	14/0^{ns}	0.002
Daily urinary volume (≥500/<500 ml)	10/46	26/16$^{0.000}$	2/12^{ns}	0.000
Anti-HLA antibodies (yes/no)	8/48	6/36^{ns}	11/3$^{0.000}$	0.000
HLA-DR mismatch (0/1/2)	10/34/12	6/30/6^{ns}	2/9/3^{ns}	0.851
HLA-Class I mismatch (1/2/3/4)	4/15/25/12	3/19/18/2^{ns}	5/2/5/2$^{0.04}$	0.005
Induction therapy (yes/no)	33/23	23/19^{ns}	6/8^{ns}	0.554
Without pretransplant CNI (yes/no)	11/45	9/33^{ns}	2/12^{ns}	0.844

BSA, body surface area; BMI, body mass index; HLA, human leukocyte antigen; CNI, calcineurin inhibitor.
P-values represent comparisons between primary nonfunction and acute vascular rejection groups.

younger, to include more females, lower BSA and BMI and more cases of previous transplants than controls. The profile for early graft loss due to acute vascular rejection was a woman patient with a previous transplant with HLA sensitization and with several years on hemodialysis. The recipient profile for early graft loss due to primary nonfunction was completely different; first transplant, short period on dialysis, generally in peritoneal dialysis, and having preserved daily urinary volume. Interestingly, 20 of 56 controls (35.7%) and 14 of 42 primary nonfunction (33.3%) cases were on dialysis for less than 12 months.

Finally, we performed conditional logistic regression analysis. Preserved daily urinary volume was positively associated with early graft loss (OR 4.0 95% CI 1.59–11.96 McNemar test P-value = 0.0014). In a multivariate conditional logistic regression model controlled by relevant recipient risk factors, both the presence of anti-HLA antibodies and preserved daily urinary volume were associated with early graft loss (Table 5). We further analyze recipient risk factors for primary nonfunction. Again, preserved daily urinary volume was positively associated with primary nonfunction (OR 11.5 95% CI 2.84–100.63 McNemar test P-value <0.001). In a multivariate conditional logistic regression model controlled by type of dialysis and anti-HLA antibodies, preserved daily urinary volume remained positively associated with primary nonfunction (Table 6).

Table 5. Conditional logistic multivariate model for early graft loss (56 matched pairs).

Covariates		OR	95% CI	*P*-value
Hemodialysis	No vs. yes (ref)	2.88	0.44–18.92	0.270
Peritoneal dialysis	Yes vs. no (ref)	2.32	0.34–15.81	0.389
Anti-HLA antibodies	Yes vs. no (ref)	5.67	2.50–19.28	0.005
Daily urinary volume	≥500 ml vs. <500 ml (ref)	11.54	1.67–53.18	0.002

Table 6. Conditional logistic multivariate model for primary nonfunction (44 matched pairs).

Covariates		OR	95% CI	*P*-value
Hemodialysis	No vs. yes (ref)	1.56	0.16–15.08	0.701
Peritoneal dialysis	Yes vs. no (ref)	1.74	0.16–19.23	0.653
Anti-HLA antibodies	Yes vs. no (ref)	3.29	0.58–18.63	0.179
Daily urinary volume	≥500 ml vs. <500 ml (ref)	20.01	2.51–159.29	0.004

Discussion

The main finding in our study was that candidates to deceased-donor kidney transplantation with preserved daily urinary volume had a significant risk for primary nonfunction. This observation is clinically relevant to improve transplant allocation and to further evaluate whether strategies addressed to minimize the ischemic damage, such as reducing cold ischemia time [18] or pulsatile perfusion devices [19], could be effective to avoid this event after kidney transplantation.

Early graft loss is a dramatic complication in kidney transplantation. Causes can be related to the quality of donor organ, the surgical procedure itself and recipient characteristics [20]. We found that immunological causes (acute vascular rejection) accounted for 25% of early graft loss. As expected, risk factors were related to class I HLA mismatch, pretransplant HLA sensitization as well as factors associated with HLA sensitization such as previous transplantation and gender (women can be sensitized to HLA antigens in the course of pregnancy). As no pretransplant donor-specific antibodies (DSA) screening by solid phase assays were performed before 2010, it is feasible that some causes of acute vascular rejection causing graft loss were due to the presence of DSA. Obviously, current strategies for organ allocation are effective to reduce immunological early graft loss. Of course, kidney allocation-based virtual cross-match [21] can help to minimize this complication among HLA-sensitized kidney allograft recipients.

As far as primary nonfunction is concerned, we found this complication accounts for 75% of cases of early graft loss. Risk factors are usually related to the donor and surgery. Regarding the kidney, ECD are particularly prone to primary graft failure [11]. In fact, the outcome of ECD kidneys is greatly influenced by cold ischemia time and the severity of ischemia–reperfusion injury [22,23]. In fact, kidneys from older donors show poor transplant outcome if delayed graft function appears [9].

The effect of residual renal mass on postischemic acute renal failure was analyzed in some experimental studies. Finn *et al.* [24] found that the presence of a contralateral normally functioning kidney aggravated the acute kidney injury induced by warm ischemia. Similar findings were described in a syngenic rat kidney transplant model when one or two functioning native kidneys were retained in place [17]. These authors suggest that the detrimental effect induced by a residual kidney could be mediated either by potentiating the severity of ischemic injury or, alternatively, by impairing the recovery from ischemia and reperfusion injury. Finn [25] reported that contralateral nephrectomy performed 2 weeks after ischemic injury resulted in increased renal plasma flow and accelerated the renal function recovery of the postischemic kidney. Furthermore, some clinical studies showed that bilateral native nephrectomy was associated with a significant increase in graft survival in first time recipients of deceased-donor renal transplants [26,27]. This increase was most marked in patients who experienced delayed graft function, as suggested by experimental studies.

Despite these almost vintage evidences, recipient characteristics were not further investigated as a cause of primary nonfunction probably because of implementation of some effective policies to minimize ischemia and reperfusion injury in the context of good quality kidneys from deceased donors. However, deceased-donor characteristics have changed dramatically in the last decade. Nowadays donors are older, the cause of death is usually stroke and suffer from hypertension and/or diabetes [28]. Kidneys from these donors are obviously more vulnerable to ischemic damage and have an impaired ability to mount a tissue repair process [22]. Consequently, the concept of residual renal function as risk factor for increasing kidney damage after transplantation can be revisited. Our study design was aimed to neutralize donor characteristics as cases shared donor with controls. Accordingly, we did not find significant differences in classical risk factors of primary nonfunction as donor age, proportion of ECD, preimplantation histological score, donor GFR, and cold ischemia time. Moreover, surgical-related risk factors, such as vascular anastomosis time, bench repair of complex vascular lesions, left or right kidney, left or right iliac fossa allograft placement, renal vein elongation, and single versus multiple kidney transplant arterial anastomosis [29], were similar between groups. Regarding recipient risk factors neither

anthropometric parameters, time in dialysis, preemptive transplantation nor type of immunosuppression were related to primary nonfunction. Interestingly, as suggested by experimental studies, we found that preserved daily urinary volume rather than type of dialysis itself was a risk factor for primary nonfunction. In fact, a recent single-center study suggests that the pretransplant dialysis modality does not influence long-term graft loss risk [30]. However, large observational studies indicate that peritoneal dialysis patients may experience increased rates of graft thrombosis and early graft failure [31]. Our results suggest that peritoneal dialysis deleterious effect on initial graft outcome can be related to the better preservation of residual renal function in comparison with hemodialysis. We did not find differences regarding preemptive kidney transplantation, although in our study only 9 patients were transplanted before dialysis initiation. Nevertheless, one-third of patients were transplanted within the first year on dialysis.

Studies based on Registry data show that preemptive kidney transplantation is the best therapeutic option in ESRD and this is true either for living as well as deceased kidney transplantation [14,15]. Therefore, living-donor preemptive kidney transplantation is an increasing therapeutic modality. On the other hand, preemptive deceased-donor kidney transplantation is ethically controversial as the majority of patients waiting for a kidney are on dialysis for years. Although more studies are needed, our results suggest additional caution when there is significant amount residual renal function, particularly in the setting of transplantation of kidneys with increased susceptibility to ischemia–reperfusion injury.

Our study has some limitations. First, the relatively low number of cases included. Early graft loss is (fortunately) and uncommon complication affecting <5% of transplants. Second, daily urinary volume is a patient reported variable, so it could be inaccurate. However, its uncertainty was improved as we recorded and managed it as a categorical variable. Third, isolated pretransplant urine output may not differentiate between patients with or without preserved capacity to concentrate the urine. Finally, odd ratio and confidence interval were rather wide probably as a result of the low proportion of discordant matched pairs.

In conclusion, our study contributes to revisit the old concept of residual renal function as risk factor for early kidney allograft loss in the current era of kidney transplantation based on the use of kidneys from ECD. More studies are needed to corroborate these findings.

Authorship

JMC: study design, analyzed data, and wrote the paper. AM and EV: data collection, study design, and results discussion. EM, NS, OB, JT, LR, and JMG: contributed to study design and discussion of the results. CT: performed statistical assessment.

Funding

This research was supported by The Red de Investigación Renal (REDinREN, ISCIII RD12/0021/0003) and by Spanish Government ISCII grants PI12/01427 and INT13/00126.

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.
2. Spital A. The shortage of organs for transplantation. Where do we go from here? *N Engl J Med* 1991; **325**: 1243.
3. Takahashi K, Saito K. ABO-incompatible kidney transplantation. *Transplant Rev* 2013; **27**: 1.
4. Gentry SE, Montgomery RA, Segev DL. Kidney paired donation: fundamentals, limitations, and expansions. *Am J Kidney Dis* 2011; **57**: 144.
5. Fernández-Lorente L, Riera L, Bestard O, *et al.* Long-term results of biopsy-guided selection and allocation of kidneys from older donors in older recipients. *Am J Transplant* 2012; **12**: 2781.
6. Morrissey PE, Monaco AP. Donation after circulatory death: current practices, ongoing challenges, and potential improvements. *Transplantation* 2014; **97**: 258.
7. Jochmans I, Moers C, Smits JM, *et al.* The prognostic value of renal resistance during hypothermic machine perfusion of deceased donor kidneys. *Am J Transplant* 2011; **11**: 2214.
8. Remuzzi G, Cravedi P, Perna A, *et al.* Long-term outcome of renal transplantation from older donors. *N Engl J Med* 2006; **354**: 343.
9. Moreso F, Serón D, Gil-Vernet S, *et al.* Donor age and delayed graft function as predictors of renal allograft survival in rejection-free patients. *Nephrol Dial Transplant* 1999; **14**: 930.
10. Cavaillé-Coll M, Bala S, Velidedeoglu E, *et al.* Summary of FDA workshop on ischemia reperfusion injury in kidney transplantation. *Am J Transplant* 2013; **13**: 1134.
11. Frei U, Noeldeke J, Machold-Fabrizii V, *et al.* Prospective age-matching in elderly kidney transplant recipients–a 5-year analysis of the Eurotransplant Senior Program. *Am J Transplant* 2008; **8**: 50.
12. Drachenberg CB, Papadimitriou JC. Endothelial injury in renal antibody-mediated allograft rejection: a schematic view based on pathogenesis. *Transplantation* 2013; **95**: 1073.
13. Nankivell BJ, Alexander SI. Rejection of the kidney allograft. *N Engl J Med* 2010; **363**: 1451.
14. Mange KC, Joffe MM, Feldman HI. Effect of the use or nonuse of long-term dialysis on the subsequent survival of renal transplants from living donors. *N Engl J Med* 2001; **344**: 726.

15. Kasiske BL, Snyder JJ, Matas AJ, *et al.* Preemptive kidney transplantation: the advantage and the advantaged. *J Am Soc Nephrol* 2002; **13**: 1358.
16. John AG, Rao M, Jacob CK. Preemptive live-related renal transplantation. *Transplantation* 1998; **66**: 204.
17. Coffman TM, Sanfilippo FP, Brazy PC, *et al.* Bilateral native nephrectomy improves renal isograft function in rats. *Kidney Int* 1986; **30**: 20.
18. van der Vliet JA, Warlé MC. The need to reduce cold ischemia time in kidney transplantation. *Curr Opin Organ Transplant* 2013; **18**: 174.
19. Gallinat A, Moers C, Treckmann J, *et al.* Machine perfusion versus cold storage for the preservation of kidneys from donors ≥ 65 years allocated in the Eurotransplant Senior Programme. *Nephrol Dial Transplant* 2012; **27**: 4458.
20. Ponticelli C, Moia M, Montagnino G. Renal allograft thrombosis. *Nephrol Dial Transplant* 2009; **24**: 1388.
21. Amico P, Hönger G, Steiger J, *et al.* Utility of the virtual crossmatch in solid organ transplantation. *Curr Opin Organ Transplant* 2009; **14**: 656.
22. de Fijter JW. An old virtue to improve senior programs. *Transpl Int* 2009; **22**: 259.
23. Cruzado JM, Torras J, Riera M, *et al.* Influence of nephron mass in development of chronic renal failure after prolonged warm renal ischemia. *Am J Physiol Renal Physiol* 2000; **279**: F259.
24. Finn WF, Fernandez-Repollet E, Goldfarb D, *et al.* Attenuation of injury due to unilateral renal ischemia: delayed effects of contralateral nephrectomy. *J Lab Clin Med* 1984; **103**: 193.
25. Finn WF. Enhanced recovery from postischemic acute renal failure. Micropuncture studies in the rat. *Circ Res* 1980; **46**: 440.
26. Sanfilippo F, Vaughn WK, Spees EK. The association of pretransplant native nephrectomy with decreased renal allograft rejection. *Transplantation* 1984; **37**: 256.
27. Krakauer H, Spees EK, Vaughn WK, *et al.* Assessment of prognostic factors and projection of outcomes in renal transplantation. *Transplantation* 1983; **36**: 372.
28. Audard V, Matignon M, Dahan K, *et al.* Renal transplantation from extended criteria cadaveric donors: problems and perspectives overview. *Transpl Int* 2008; **21**: 11.
29. Benedetti E, Troppmann C, Gillingham K, *et al.* Short- and long-term outcomes of kidney transplants with multiple renal arteries. *Ann Surg* 1995; **221**: 406.
30. López-Oliva MO, Rivas B, Pérez-Fernández E, *et al.* Pretransplant peritoneal dialysis relative to hemodialysis improves long-term survival of kidney transplant patients: a single-center observational study. *Int Urol Nephrol* 2014; **46**: 825.
31. Fuquay R, Teitelbaum I. Transplant outcomes and dialysis modality. *Contrib Nephrol* 2012; **178**: 251.