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Retrospective follow-up of transplantation of kidneys from 'marginal' donors

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The organ shortage has led to extend the procurement to kidneys from 'marginal' donors. As a result, an increasing number of kidneys are discarded, but an extended analysis of the validity of the clinical decision to accept or decline a marginal graft remains to be determined. We have retrospectively analyzed the outcome of 170 kidney transplantations, performed in eight renal transplantation centers between 1992 and 1998. Study group included transplantation from donors accepted after refusal for poor donor or graft quality by at least two centers. Control group included 170 paired recipients from kidneys unanimously accepted by all centers. Main causes of kidney refusal included impaired donor hemodynamics (28%), abnormal pre-harvesting serum creatinine (22%), advanced age in donors (15%), and donor atheroma (14%). The 5-year patient survival (88.2% in the study group and 88.9% in controls) and graft survival (70.4% in the study group and 76.7% in controls, $P = 0.129$) were not significantly different. Delayed graft function occurred significantly more often in the study group patients than in controls patients (63 vs 32%, $P < 0.0001$). Primary non-functioning kidneys were significantly more frequently observed in study patients than in controls (7.7 vs 1.8%, $P = 0.01$). Mean creatinine clearance was significantly lower in the study group patients compared with controls during the post-transplant course. Our results suggest that these initially discarded kidneys provide satisfactory survival rates despite their impaired early functional recovery and poorer long-term renal function, and therefore might be considered acceptable for transplantation in the context of organ shortage.

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Over the last 15 years, the limited supply of cadaver donors for renal transplantation led to consider alternative strategies for making more organs available.[1] One of them is the expansion of the cadaveric kidney donor pool to include those who might have been deemed unsuitable in early times, the use of organs from older donors emerging as the most obvious option.[2] In parallel, global donor characteristics were changing with an increasing number of elderly donors with a history of hypertension and diabetes, deceased because of stroke or other cardiovascular causes.[3] This led in the early 1990s to the concept of 'marginal' donors[4] and, more recently, to the notion of 'expanded criteria donors', defined by the United Network for Organ Sharing as those donors who, because of extremes of age or other clinical characteristics, are expected to produce allografts at risk for diminished post-transplant function.[5,6] However, clinical investigations attempting to clearly delineate the procurement selection and graft acceptance criteria as to assess the donor risk factors for graft and patient outcomes have yielded conflicting results and there is currently neither universal nor unequivocal definition of what constitutes a 'marginal' transplantable kidney.

Thus, it is left to the transplant center to determine on the basis of available information whether to accept or decline these kidneys. As a result of the use of expanded criteria donor organs, an increasing number of kidneys are discarded and never transplanted, contributing to the stagnation of the transplantation activity. United Network for Organ Sharing reported[7] an increase in the number of organs procured but not transplanted from 5.3 to 13% between 1991 and 2000, 70% of them being discarded because of concerns regarding donor or graft quality, based on clinical or histological data.

An accurate analysis of the causes of graft refusal by transplant centers remains to be performed. According to United Network for Organ Sharing criteria's,[5] 32.5% of the kidneys transplanted in the French regional area of Ile de France during 2004 came from expanded criteria donors (unpublished data). This indicates that such criteria's are in fact poorly selective for graft acceptance. It is of concern the validity of the clinical decision to accept or decline a previously discarded renal transplant, because no control study regarding the outcome of such grafts that are subsequently transplanted are yet available.

The present retrospective case-controlled multicenter study was designed to compare the fate of transplants performed with kidneys, defined by their secondary acceptance by centers after primary refusal by two or more other transplant centers, to the outcome of transplantation performed with 'optimal kidneys' directly accepted by centers. The aims were not to propose a new definition of expanded criteria donors but, from an operational point of view, to analyze retrospectively the causes of kidney refusal and to determine whether the local center's concerns about inferior graft function and increased morbidity and mortality in the recipient are justified.

RESULTS

Analysis of kidney refusals

One hundred and seventy patients from the study group received a kidney procured from 111 'marginal' donors. Thus, 52 kidneys were discarded by all transplant centers and never transplanted.

The analyses of the main causes of kidney refusal are listed in Table 1. Thirty-two proposals (28%) were refused because of impaired donor hemodynamics (severe hypotension, prolonged cardiac arrest, or prolonged anuria) during the pre-harvesting period. The second most frequently alleged reason for refusal was abnormal pre-harvesting serum creatinine in 24 donors (22%). Advanced age was recorded in 17 donors (15%). Other causes included donor atheroma in 15 donors (14%), miscellaneous medical history (including donor's history of hypertension or diabetes) in seven donors (6%), anatomic abnormalities in eight donors (7%), abnormal microscopic characteristics in four donors (4%) and prolonged ischemia in four donors (4%). Finally, according to graft refusal criteria, patients could be separated in two groups: group 'acute' ($n=92$, 54%) included patients who received grafts initially refused on the basis of 'acute' criteria occurring just before donation (impaired donor hemodynamics, abnormal initial serum creatinine and prolonged ischemia time); group 'chronic' ($n=78$, 46%) included patients who received grafts initially refused on the basis of 'chronic' criteria (advanced donor age, donor atheroma, anatomic abnormalities, donor history of hypertension and abnormal macroscopic characteristics).

Table 1 | Main causes of graft refusals in the study group

Main cause of refusals	Percentage
Impaired donor hemodynamics	28
Cardiac arrest	16
Anuria	8
Severe hypotension (collapses)	4
Abnormal serum creatinine[a]	21
$120<Cr>200\ \mu mol/l$	5
$200<Cr>400\ \mu mol/l$	13.5
$Cr>400\ \mu mol/l$	2.5
Advanced donor age (years)	15
60–69	9
$\geqslant 70$	6
Donor atheroma	14
Anatomic abnormalities	7
Donor history of hypertension	6
Prolonged ischemia time (>32 h)	5
Abnormal macroscopic characteristics	4

[a]Initial pre-harvesting serum creatinine.

Characteristics of the donors and the transplant recipients

Characteristics of the kidney recipients and their donors in both groups are presented in Table 2. Donors in the study group were significantly older than in the control group. The analysis of causes of donors death in the study group showed a significantly lower incidence of deaths from traumatic and toxic causes, and an increased though nonsignificant incidence of deaths from cerebrovascular causes. Cardiac resuscitation and oligoanuria episodes were more frequently observed in the study group. Finally, donor serum creatinine was significantly higher in the patients of the study group.

Importantly, no statistical difference was found between patients of both groups according to the recipient risk factors such as pre-transplant immunization rate and human leukocyte antigen matching. Mean cold ischemia times (CIT) were not statistically different between both groups.

Analysis of early post-transplant kidney function and complications (first 6 months)

We found an increased incidence of post-transplant complications in relation with impaired early renal function. A significant number of early failures was recorded in patients receiving a marginal kidney compared to controls receiving an optimal kidney: 13 kidneys (7.7%) in the study group had never functioned vs 3 (1.8%) ($P=0.01$) in the controls. Post-transplant anuria was recorded in 41 patients (24.1%) of the study group and only in 22 in controls (12.9%), this difference being statistically significant ($P=0.013$). Consequently, the incidence of delayed graft function was higher in patients from the study group compared to controls: 63 vs 32%, $P<0.0001$. Finally, the mean length of post-transplant initial hospitalization time was significantly longer in the study group compared to control subjects: 34.9 vs 29.7 days ($P=0.0039$).

Patients of both groups received comparable immunosuppressive regimens. Induction with polyclonal antibodies was given in half of patients (84/170 of study patients and 86/170 controls). Calcineurin inhibitors were given in 145 study patients (85%, including 140 receiving cyclosporine and five tacrolimus) and 154 controls (91%, including 149 receiving cyclosporine and five tacrolimus). The percentage of patients receiving delayed postoperative anticalcineurin therapy was not statistically significant in both groups: 59% in the study group patients and 49% in controls.

The incidence of presumed acute rejection episodes was not significantly different between the two groups and occurs in 61 patients (35.9%) from the study group and in 52 patients from the controls (30.6%).

Table 2 | Characteristics of donors and recipients in both study and control (optimal kidneys) groups; study group included graft refused on the basis of acute (A) or chronic (C) criteria

Characteristic	Study group *N*=170 (A: 92, C: 78)	Control group *N*=170	*P*-value
Mean donor age ± s.d. (years)	50.2 ± 13.5 (A: 46.2 ± 7.5) (C: 54 ± 16.3)	39.5 ± 12.6	<0.0001
Donor cause of death			
CVA/stroke	42.3% (A: 36.9%, C: 46.2%)	32.3%	0.006
Trauma	14.7% (A: 15.4%, C: 14.1%)	25.9%	NS
Suicide	13% (A: 15.6%, C: 11.3%)	9%	NS
Respiratory failure	11% (A: 11.3%, C: 10.9%)	7%	NS
Infection (meningitis)	8% (A: 11.4%, C: 5.2%)	5%	NS
Cardiac arrest	5% (A: 6%, C: 4.2%)	4%	NS
Neurological tumor	3% (A: 3.8%, C: 2.2%)	4%	NS
Toxic	2.9% (A: 3.1%, C: 2.7%)	12.9%	0.0007
Mean donor pre-harvesting serum creatinine ± s.d. (μmol/l)	163 ± 86 (A: 193 ± 97) (C: 127 ± 36)	98 ± 40	<0.0001
Donor episode of prolonged anuria			
Yes	24.1% (A: 30%, C: 18%)	12.9%	0.0136
No	75.9% (A: 70%, C: 82%)	87.1%	
Donor episode of cardiac resuscitation			
Yes	38% (A: 45%, C: 32%)	18.2%	<0.0001
No	62% (A: 55%, C: 68%)	81.8%	
Donor episode of prolonged hypotension			
Yes	21.2% (A: 25.2%, C: 18%)	26.5%	NS
No	78.8% (A: 74.8%, C: 82%)	73.5%	
Mean cold ischemia time ± s.d. (h)	28.3 ± 8 (A: 29.5 ± 10) (C: 27.2 ± 7)	28.5 ± 10	NS
Mean recipient age at transplant ± s.d. (years)	45.8 ± 12.4	42.5 ± 12.3	NS
	(A: 44.9 ± 10)		NS
	(C: 47.1 ± 13)		NS
Mean number of HLA mismatches (A-B-DR) ± s.d.	2.9 ± 1.1	2.8 ± 1.1	NS
	(A: 2.9 ± 1)		NS
	(C: 2.9 ± 1.5)		NS
Peak PRA level (%)			
0–4	77% (A: 80%, C: 74.8%)	69.4%	NS
5–80	21.8% (A: 23.5, C: 20.2%)	25.3%	NS
>80	1.2% (A: 1.1%, C: 1.3%)	5.3%	NS

Kaplan–Meier analysis of kidney and patient survival and causes of graft failures

All patients were followed for at least 5 years. Figure 1 shows graft and patient survivals up to 5 years post-transplant. Patient survival was similar in both groups (88.2 and 88.9% at 5 years in the study and the control group, respectively) (Figure 1a). The 5-year graft survival was, respectively, 70.4 and 76.7 (Figure 1b) in the study and the control groups, but the difference did not reach statistical significance (log-rank test: $\chi^2 = 2.294$, $P = 0.129$). Death-censored graft survival at 5 years was also similar in the study and the control group (79.3 and 85%, respectively, at 5 years, $P = 0.19$). According to the 'acute' (group 'acute') and 'chronic' (group 'Chronic') criteria, the 5-year graft survival was 73.5 and 76.9%, respectively, in the 'acute' and the control groups ($P = 0.79$) and 66.2 and 75.9%, respectively, in the 'chronic' and the control groups ($P = 0.09$). As depicted in Figure 2, the 'chronic' parameter showed a tendency towards an inferior graft survival compared to the acute parameter, although the difference was not statistically significant ($P = 0.19$).

Fifty-nine patients from the study group either died or lost their transplant, including 20 deaths and 39 graft failures. Out of those 39 graft failures, chronic rejection was the cause of failure in 16 patients, acute rejection in six, surgical complications in two and miscellaneous causes in two. The 13 remaining patients of the study group (22%) had early graft failures, including six arterial thrombosis and seven primary non-functioning kidney. The grafts from these 13 patients came from marginal donors with (i) donor age >60 years old in 11 cases, (ii) donor with primary hypertension in eight cases, (iii) serum creatinine level >200 μmol in four cases, and (iiii) prolonged ischemia time (>32 h) in three cases.

In the control group of 'optimal' kidney recipients, 47 patients either died or lost their transplant, including 18 deaths and 29 graft failures. Out of those 29 graft failures,

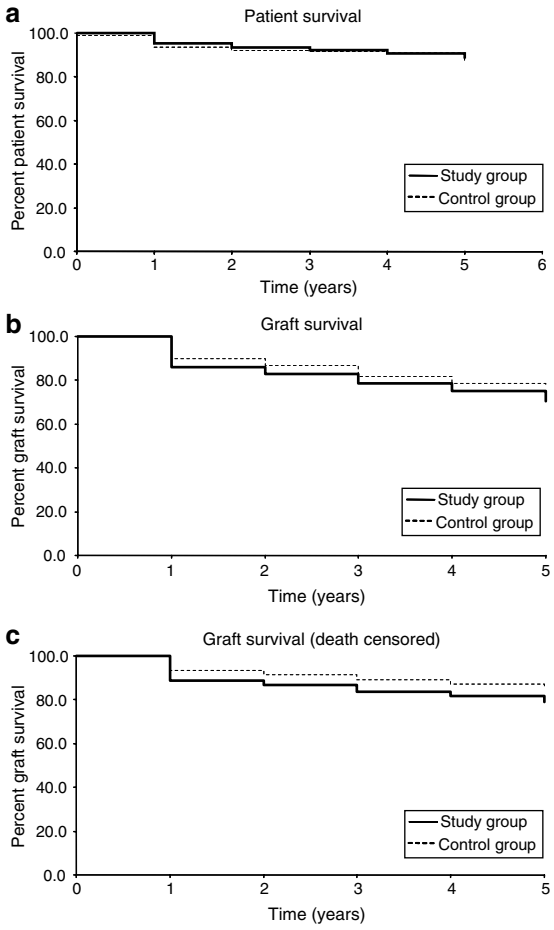

Figure 1 | Recipients of study and control kidney transplants have similar graft and patient survival up to 5 years post-transplant. Recipients of study and control grafts have similar patient and graft survival up to 5 years post-transplant. Kaplan–Meier survival curves between 0 to 5 years post-transplant are shown for, (**a**) patient survival, (**b**) overall graft survival, and (**c**) death-censored graft survival of patients from the study (solid lines) and the control group (dashed lines). For all three survival indices, no significant differences are present between the two groups (P = NS).

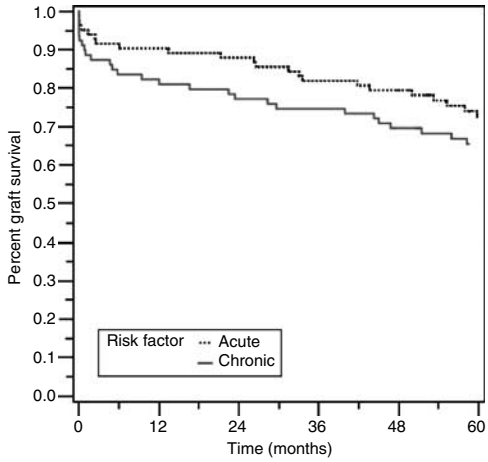

Figure 2 | Influence of the 'acute' and 'chronic' cause of graft refusal on the 5-year graft survival. The 'acute' and 'chronic' parameters did not influence significantly graft survival up to 5 years post-transplant ($P = 0.19$). Kaplan–Meier survival curves between 0 and 5 years post-transplant are shown for patients who received organs refused on the basis of 'acute' criteria (dashed lines) or 'chronic' criteria (solid lines).

Table 3 | Causes of graft failure in the study and the control group

Causes of graft failure	Study group (*n*=39)	Control group (*n*=29)	*P*-value
PNFK	13	3	0.01
Chronic rejection	16	13	NS
Acute rejection	6	6	NS
Surgical complications	2	1	NS
Miscellaneous complications	2	6	NS

PNKF=primary non-functioning kidneys.

chronic rejection was the cause of failure in 13 patients, acute rejection in six, surgical complications in one and miscellaneous complications in six. In the control group, only three early failures were recorded (6.3% of the total of failures), including two cases of arterial thrombosis and one primary non-functioning kidney. Causes of graft loss in both groups are listed in Table 3.

Analysis of renal function

Overall, mean creatinine clearance during the follow-up period (Figure 3) was significantly ($P<0.001$) lower in the study group patients compared to controls from day 7. In both groups, mean creatinine clearance progressively increased in a parallel manner from day 2 to month 3: 40.2 ml/min (95% confidence interval (CI) 36.9–43.6) in the study group patients and 52.3 ml/min (95% CI 49.2–55.4) in the controls had remained stable until 2 years post-transplant and then started to decline: 33.3 ml/min (95% CI 29.5–38.1) in the study group patients and 48.5 ml/min (95% CI 42.7–56.3) in the controls at 5 years. We also calculated mean creatinine clearance in the groups refused on the basis of acute and chronic injury at 5 years. The mean creatinine clearance was significantly higher in the 'acute' group compared with the 'chronic' group (38.9 ml/min, 96% CI 33.4–41.1 vs 28.5 ml/min, 95% CI 22.2–34.8) ($P = <0.001$).

DISCUSSION

During the study period, 170 transplantations, representing 5.2% of the total of the kidney transplantation activity in Ile de France, have been performed using grafts declined by two or more centers. Those grafts were refused by individual centers based on their assessment of the donors and grafts qualities. Analysis of the principal causes of kidney refusal reveals classical characteristics of marginal donor kidney (donor age, abnormal serum creatinine, donor medical history or prolonged ischemia time) but, interestingly, also includes other factors that do not meet the previously reported expanded donors' criteria such as donor atheroma, donor anatomic abnormalities and, chiefly, impaired donor hemodynamics.[6,8,9] This, however, accounts for real practice

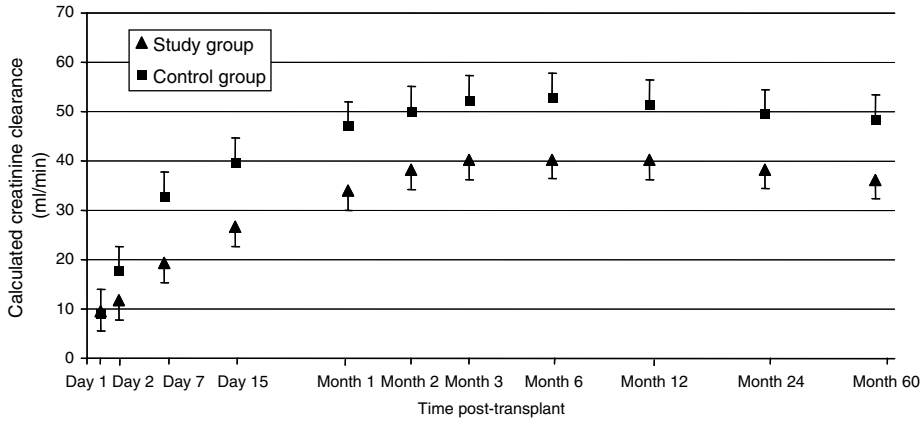

Figure 3 | Recipients of study donor kidney transplants have lower average serum creatinine clearance compared to recipients of control donor kidney transplants. Serum creatinine clearances calculated by the Cockcroft and Gault formula are shown for recipients of marginal (▲) and control (■) kidney transplants. Results are shown between day 1 to months 60 and expressed as mean ± s.d. $P < 0.01$ for marginal donor recipients (study group) vs control donor recipients (control group).

of several transplant centers in France. The main causes of kidney refusal as stated by each transplant center in the Etablissement Francais des Greffes registry are listed in Table 1. We cannot exclude that, in several cases, refusal was indeed justified by more than a single criterion. For instance, we report that in 15% of cases, cause of refusal was advanced donors age and in 14%, donors atheroma. It is likely that most patients from these subgroups are sharing both criteria.

The potentially important question, whether this assessment was accurate or not, might be answered by evaluating whether the utilization of these initially refused organs had a negative impact on long-term post-transplant outcome.

Our study showed that acceptable long-term graft survival (i.e. 70.4% at 5 years) was achieved using discarded kidneys. The 170 recipients of optimal kidneys from the control group had a 6.7% better 5-year graft survival rate compared with the study patients, although this difference was not statistically significant. Furthermore, transplantation of kidneys from the study group was not associated with a significantly increased mortality. Historical reports on marginal kidney transplantation, essentially from elderly donors, have shown that greater donor age was associated with lower graft survival.[9–11] In 2001, Ojo *et al.*[8] reported a significantly lower 5-year graft survival in a group of marginal donor kidney recipients, compared with optimal donor kidney recipients (53 and 67%, respectively). Further analyses have suggested, however, that post-transplant outcome of marginal kidneys was not necessarily poor, and depended on several factors, including donor risk factors associated with atherosclerosis, factors associated with the allocation process, CIT and finally all parameters involved in the post-transplant period, such as quality and timing of immunosuppressive combination protocol, and occurrence and severity of post-transplant rejection episodes.[12–14] Our data are in accordance with studies[15,16] reporting acceptable survival rates using kidneys that would otherwise be discarded, or using kidneys from donors with established risk factors such as age, hypertension history, or severe histological damages.[17,18]

Graft survival was also analyzed according to the cause of graft refusal ('acute' and 'chronic'). Although the difference did not reach statistical significance, the results suggest that patients who received grafts discarded because of events occurring just before donation (potentially reversible) have a better graft survival than patients who received grafts with (or probably with) chronic lesions. This tendency is confirmed by the significantly higher mean serum creatinine clearance in recipients of kidney initially refused on the basis of acute criteria. This suggests that the influence of acute renal dysfunction on the decision to accept or to decline a marginal renal transplant should be minimized. In contrast, marginal kidneys with possible chronic renal damage may require specific evaluation and allocation before they can be considered for transplantation. This includes a large recommendation of renal biopsy before transplantation, the use of the 'old for old' strategy for organs distribution in case of elderly donors and recipients and the use of dual transplants. Moreover, recipients should be more systematically informed before transplantation on the possible inferior outcome of those kidneys.

The incidence of acute rejection was in fact high in both groups (35.9 and 30.6% in the control and the study groups, respectively), especially since half of the patients received induction therapy. However, this study was conducted from 1992 to 1998, and at this time, diagnosis of acute rejection was not systematically confirmed by renal biopsy, suggesting that acute rejection diagnosis could be overestimated. We also found that organs from the study group were significantly associated with an increased risk of post-transplant anuria, an increased incidence of delayed graft function, and a relatively poorer graft function in the first 2 years post-transplant in comparison with recipients of paired optimal transplants. It is of importance that 13 transplants from the study group experienced primary non-function compared to

three controls. These findings could not be attributed to a bias in recipient selection, because all parameters known to affect renal function recovery were matched in both groups. Utilization of allografts from marginal donors has been associated with inferior performance in a number of reports.[19,20] The achievement of improved utilization has been attempted by the transplantation of selected marginal kidneys in dual transplantation protocols.[21–23] However, there are currently no established guidelines to determine in which case dual transplantation should be performed. Various criteria and scoring systems have been proposed,[24,25] but never validated in controlled studies. Therefore, this policy remains to be evaluated in the long term, and controlled studies should be designed in order to compare dual procedure with transplantation of single marginal kidneys. Lack of clear benefits provided by dual procedure could strongly challenge the dual transplantation policy in the context of graft scarcity. Our data support the utilization of separate kidneys from marginal donors for transplantation, yielding comparable overall long-term survival to that obtained by transplantation of optimal kidneys. Thus, the undeniable increased risk of early complications should not prevent the systematic use of kidneys from donors with risk factors. As previously implemented by the Eurotransplant allocation system of the 'old for old' strategy for organs distribution, we suggest that in the context of organ shortage, these 'marginal' kidneys should be preferentially attributed to recipients with a significant decrease in life expectancy, including old recipients and patients with compromised access to transplantation.

An important issue is preventing additional injuries that have been proven to enhance the deleterious effects of donor risk factors, that is, prolonged ischemia time, immunological injuries[26,27] and the nephrotoxicity of immunosuppressive drugs. Fifty percent of patients in our study received induction protocols with delayed introduction of anticalcineurin drugs, and the acute rejection incidence was lower in one-third of patients. On the other hand, because of the lack of tailored policies for the allocation and transplantation of kidneys from donors presenting with criteria of poor quality, a relatively prolonged mean CIT (>28 h) was unfortunately recorded in both groups of our study. This fact could be, in part, responsible for the poor functional recovery in the study group. The implementation in the Eurotransplant allocation system of a short ischemia time,[28] and this latter policy should be encouraged. However, data from the Collaborative Transplant Study[29] showing that a very short CIT was associated with a worse graft survival than donors kidney exposed to 7–36 h of CIT indicates that the critical length of CIT is still far from being established.

CONCLUSION

The main objective of our study was to evaluate the outcome of kidney grafts, defined as marginal according to an operational strategy, that is, the refusal by at least two centers, and to validate or not the transplant centers' attitude. Our data showing an increased incidence of delayed graft function and primary non-functioning kidney as well as decreased mean creatinine clearance values retrospectively confirm that our study group was indeed composed of marginal kidneys and, therefore, strengthen primary clinical evaluation. This study, however, demonstrates that such discarded grafts can provide acceptable survival rates, suggesting that in numerous situations, the decision to refuse them may be unjustified and that marginal donor kidneys should be more rigorously defined to minimize the discard of transplantable kidneys. However, according to the 'chronic' or 'acute' origins of renal damage, our results also suggest that a note of caution is needed before suggesting the use of kidney from marginal donors with possible chronic lesions.

MATERIALS AND METHODS

Patients

Between January 1992 and December 1998, 3 258 cadaveric renal transplants were performed in eight transplant centers located in the French regional area of Ile de France. We retrospectively selected for this case-controlled study 170 patients (study Group) who have received during this period a 'marginal kidney', and 170 paired patients (control Group). A 'marginal kidney' was defined as a kidney accepted for transplantation in a transplant center after having been refused because of a perceived increased risk of poor renal function by at least two other centers from the same regional area. The decision of centers to accept or decline kidneys was made on a case-by-case basis, taking into account the available information, including donor's medical history, cause of death, initial pre-harvesting serum creatinine, urine output, hypotension and cardiac arrest episodes, anatomy and the general aspect of the kidney and other variables. In the course of the selection for the study group, living donors, multiple organ transplants, pediatric recipients and transplants performed after refusal for technical or logistical meanings were excluded. We have also excluded kidneys that were turned down because graft was believed not to be appropriate for a specified potential recipient, for immunological or any other reasons. The control group was formed by selecting the patients who had undergone kidney transplantation immediately before or after each study group patient at the same transplant center, with a kidney that no center has refused.

Demographic, medical, monitoring and procurement data of the donors, routine yearly follow-up, graft failure and patient death were reported to the Registry of the Etablissement Français des Greffes. The following data were retrieved and compared between both groups: donor age, cause of death, pre-harvesting serum creatinine, episodes of severe hypotension and cardiac arrest, CIT, recipient demographic characteristics, panel-reactive antibody level (0–4, 5–80 and >80%) and mean human leukocyte antigen mismatching. We have also compared variables characterizing immediate functional transplant outcome: incidence of delayed postoperative diuresis (urine output lower than 500 ml/day during the first 24 h after transplantation), incidence of delayed graft function defined by the need for post-transplantation hemodialysis or peritoneal dialysis during the first 7 days after transplantation, and the incidence of primary non-functioning kidneys defined as graft that had never functioned. We have also compared the following variables: immunosuppressive protocol (immediate or delayed treatment with

anticalcineurin drug, induction or not with polyclonal antiglobulins), incidence of post-transplant acute rejection episodes and duration of initial hospitalization. In most cases (85%), acute rejection was documented by a renal biopsy. The renal function was assessed in both groups by comparing creatinine clearance calculated by the Cockcroft and Gault formula at days 1, 2, 7 and 15, 1 month, 3 and 6 months, and 1- and 5-year post-transplant, respectively. Graft and patient survivals were assessed until 5-year post-transplant.

Statistical analysis

All statistical analyses were performed using the SAS software package version 8.1 (SAS Institute Inc., Cary, NC, USA). Data are expressed as mean $\pm$ s.d., unless indicated otherwise. Differences in donors and recipients variables were evaluated using the unpaired Student's *t*-test for continuous variables and the χ^2 test for nominal variables. Graft survival was defined as an alive patient with a functioning graft, the end point being defined as either death or graft failure. The Kaplan–Meier survival estimator was used to determine graft and patient survival. A two-sided *P*-value of 0.05 was considered statistically significant, as dependent variable on allograft survival.

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Appendix A1

The data reported here have been supplied by the following kidney transplantation centers from the Groupe Coopératif de Transplantation d'Ile de France (GCIF) (listed in alphabetic order): Créteil – Hôpital Henri-Mondor (Dr Dahmane, Pr Lang), Le Kremlin-Bicêtre – Hôpital Bicêtre (Dr Hiesse, Pr Charpentier), Paris – Hôpital Européen Georges Pompidou (Dr Antoine, Pr Glotz), Paris – Hôpital Necker (Dr Morelon, Pr Kreis), Paris – Hôpital de la Pitié (Dr Barrou, Pr Bitker), Paris – Hôpital Saint-Louis (Dr Bedrossian, Pr Legendre), Paris – Hôpital Tenon (Pr Rondeau, Pr Sraer), Suresnes – Hôpital Foch (Dr Aubert, Dr Delahousse). Donor's data have been supplied by local procurement units, and collected by the Service de Régulation et d'Appui of Région Ile-de-France – Centre – Les Antilles (Dr Claquin, Dr Atinault).