## ORIGINAL ARTICLE

# Complications of kidney transplantation with grafts from expanded criteria donors

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#### **Abstract**

*Purpose* The limited availability of kidneys for transplantation has been addressed by expanding the criteria for allowing a donor kidney to be transplanted, but this tendency may cause suboptimal kidneys to be implanted and could be associated with greater risk of complications.

Methods A retrospective study of 407 kidney transplantations was done to compare complications of transplantation with non-expanded (n=244) and expanded criteria donors (n=163). Expanded criteria donors were donors older than 60 years, or donors aged 50–60 years who had  $\geq 2$  of the following risk factors: hypertension, diabetes mellitus (type 2), creatinine >1.5 mg/dL, or death caused by stroke. Results Compared with transplant recipients from non-expanded criteria donors, transplant recipients from expanded criteria donors had significantly greater frequency of graft loss, delayed graft function, pneumonia, overall surgical complications, early reoperation, wound eventration, hydro-

nephrosis, postoperative hemorrhage, and wound infection. When analyzing surgical complications types, a significant greater frequency of urologic, wound, vascular, early and late surgical complications was found. In terms of severity, expanded donor criteria transplantation was related to Clavien I, III, and IV complications.

Conclusions Transplantation of kidneys from expanded criteria donors is associated with a significant higher risk of medical and surgical complications than kidneys from non-expanded criteria donors.

**Keywords** Transplant  $\cdot$  Renal failure  $\cdot$  Age  $\cdot$  Wound  $\cdot$  Survival

## **Abbreviations**

AV Arteriovenous BMI Body mass index

HLA Human leukocyte antigen

NA Not available NS Not significant UV Ureterovesical

Introduction

Kidney transplantation is the treatment that results in the best quality of life and survival for most patients with end-stage kidney disease [1, 2]. However, the availability of this treatment is limited by the increasing number of patients waiting for an available donor kidney. In the United States during 2007, there were more than 76,000 people waiting for a kidney transplant, an increase of 86% from the previous decade [3]. The limited availability of kidneys for transplantation has been addressed by expanding the criteria for allowing a donor kidney to be transplanted, but this

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tendency may cause suboptimal kidneys to be implanted, especially in countries with limited donor programs [4].

Studies of the functional outcomes of kidney transplantation with expanded criteria have shown greater frequency of delayed graft function and infection, and lower frequency of graft and recipient survival, than transplantation with grafts selected with stricter guidelines [5–9]. Furthermore, grafts from expanded criteria donors may be associated with higher rates of infectious and cardiovascular complications, longer and more complex hospital stays, and shorter survival periods than grafts from non-expanded criteria donors [5–12]. Nevertheless, transplantation with suboptimal grafts from expanded criteria donors may be justified to minimize the adverse effects of remaining on the dialysis and in those patients with limited life expectancy who may die before the graft fails [13–15].

Limited studies are available about the full effect of kidney transplantation with expanded criteria, including surgical complications, and the available information is controversial. Moreover, kidney transplantation with expanded criteria donors may increase the availability of kidney transplantation to a larger group of patients but may be associated with a greater frequency of complications and lower graft survival in comparison with non-expanded criteria donors. The purpose of this study was to evaluate the frequency of complications and graft survival associated with expanded and non-expanded criteria using a validated classification method [16, 17].

**Table 1** Classification of surgical complications in 407 consecutive recipients of kidney transplantation

142 transplant recipients had 182 surgical complications Adapted and modified from Clavien et al. [16]

<sup>a</sup> Different subtypes according to the type of anesthesia were

Grade	Effects of complication	Observed complications	No. (%) patients with complications
I	Alteration of the ideal postoperative course No threat to patient's life No reoperation; only bedside procedures necessary No increase in the hospital stay	Surgical wound infection	21 (5)
II	More medical treatment with drugs required (including transfusions and parenteral nutrition) No reoperation Potentially life threatening Limited residual disability	Perirenal hematoma	21 (5)
III	Surgery, endoscopy, or radiology required <sup>a</sup>	Wound eventration Lymphocele Hydronephrosis Vesicoureteral reflux Graft lithiasis Urinary fistula Vesicoureteral junction stenosis	106 (26)
IV	Life threatening Residual long-term disability (including resection of the organ transplant or persistence of life-threatening condition)	Renal vein thrombosis Arterial thrombosis Postoperative bleeding	34 (8)
V	Death	None	0 (0)

# Materials and methods

Subjects

This study was a retrospective evaluation of 407 consecutive kidney transplantations from deceased donors performed between 1994 and 2009.

Expanded criteria donors were defined as either donors older than 60 years or donors aged 50–60 years who had ≥2 of the following risk factors: hypertension, diabetes mellitus (type 2), serum creatinine >1.5 mg/dL, or death caused by stroke. Other donors were classified as non-expanded criteria donors. We have followed the Expanded Criteria Donor definition adopted on October 31, 2002, by the organ procurement and transplantation network/united network for organ sharing (OPTN/UNOS) [4].

Surgical complications were categorized as early (within 30 days after transplantation) or late complications (>30 days after transplantation). Wound complications included wound infections and wound eventrations. Collections consisted of lymphoceles and perirenal hematomas. Urologic complications included hydronephrosis with deterioration in renal function, urinary fistulas, ureterovesical junction stenosis, vesicoureteral reflux, and graft lithiasis. Vascular complications consisted of postoperative hemorrhage, renal vein thrombosis, renal artery thrombosis, and renal artery stenosis. All surgical complications were recorded and classified according to the modified Clavien classification (Table 1) [16, 17].



not recorded

Kidney transplantation was performed by the same 4 surgeons throughout the study period. In all transplantations, the renal artery and vein of the donor were anastomosed to the external iliac artery and vein of the recipient, respectively, with an end-to-side suture using monofilament 6-0. For ureteral reimplantation, the Campos-Freire technique was used, followed by routine ureteral catheterization. Ureterovesical anastomosis was completed using a polydioxanone (PDS) 6/0 absorbable braided suture, and bladder was closed in one layer [18].

## Data analysis

Data analysis was performed using statistical software (SPSS, version 15.0, SPSS Inc., Chicago, IL, USA). Comparisons were made using t test for continuous variables and  $\chi^2$  test (chi-square test) for categorical variables. The risk of developing surgical complications was calculated with univariate and multivariate binary logistic regression analyses. The Kaplan–Meier method and the log-rank test were used to evaluate graft survival. This analysis was performed censoring for death with a functioning graft. The primary end point of the study was graft failure, defined as the recurrence of end-stage renal failure (after transplantation) necessitating dialysis. The relation between clinical variables and graft survival was evaluated with a univariate Cox proportional hazards regression model.

Continuous data were reported as mean  $\pm$  SD and categorical data as number (%). Statistically significant differences were defined by  $P \leq 0.05$ .

# Results

Evaluation at a mean of 6 years after transplantation showed that 163 grafts (40%) proceeded from expanded criteria donors and 244 (60%) from non-expanded donors. In the expanded criteria donor group, 127 donors (77.9%) were older than 60 years and 36 (22.1%) were donors between 50 and 60 years with at least 2 risk factors. Expanded criteria donors had a significantly higher BMI, greater frequency of stroke resulting in death, arterial hypertension, and diabetes mellitus (type 2) than non-expanded criteria donors (Table 2).

Transplant recipients from expanded criteria donors were significantly older and had a higher BMI, longer dialysis duration, greater frequency of diabetes mellitus type 2, iliac vessel calcification, and use of tacrolimus than transplant recipients from non-expanded criteria donors (Table 2). A multivariate analysis was carried out with those recipient variables that were significant in previous univariate studies. Recipient age was the only factor with a significant and independent association with surgical

**Table 2** Clinical factors, medical problems, and treatment variables in donors and recipients of 407 kidney transplantations

1	, ,		
Donor selection criteria			
Variables	Non-expanded	Expanded	P <sup>a</sup>
No. (%) transplantations	244 (60)	163 (40)	
Donor			
Donor age (years)	$37 \pm 14$	$65 \pm 7^{\mathrm{b}}$	≤0.001
BMI (kg/m²) <sup>b</sup>	$25 \pm 3$	$26 \pm 5$	≤0.04
Serum creatinine (mg/dL)	$1.1 \pm 0.4$	$1.2\pm0.4$	NS
Stay in Intensive Care Unit (days)	$3 \pm 4$	$2 \pm 2$	≤0.006
Medical problems			
Stroke resulting in death	99 (41)	128 (79)	≤0.001
Arterial hypertension	12 (5)	80 (49)	≤0.001
Diabetes mellitus, type 2	1 (0.4)	23 (14)	≤0.001
Recipient			
Age (years)	$45 \pm 13$	$59 \pm 11$	≤0.001
BMI (kg/m²)	$25 \pm 4$	$26 \pm 4$	$\leq 0.002$
Dialysis time (months)	$26 \pm 32$	$42 \pm 57$	≤0.001
Cold ischemia time (h)	$14 \pm 5$	$15 \pm 5$	NS
HLA matches	$2.2 \pm 0.9$	$2.3 \pm 0.9$	NS
Medical problems			
Arterial hypertension	186 (76)	135 (83)	NS
Dyslipidemia	70 (29)	50 (31)	NS
Iliac vessel calcification <sup>c</sup>	36 (15)	47 (30)	≤0.001
Diabetes mellitus (type 1)	22 (9)	7 (4)	NS
Diabetes mellitus (type 2)	5 (2)	10 (6)	≤0.04
Treatment			
Main pharmacological drug			
Cyclosporine	130 (53)	71 (44)	
Tacrolimus	99 (41)	89 (55)	≤0.002
Monoclonal antibody induction	16 (7)	12 (7)	NS
Transplantation revision	28 (11)	17 (10)	NS

Data reported as mean  $\pm$  SD or number (%) patients. Mean follow-up (all patients combined) was 73  $\pm$  54 months

BMI, body mass index; HLA, human leukocyte antigen

complications appearance (OR: 1.03, 95% CI: 1.01–1.04; P = 0.002).

Transplant recipients from expanded criteria donors had significantly greater frequency of hospitalization because of respiratory or cardiovascular problems and greater frequency of graft loss, delayed graft function, and pneumonia, than transplant recipients from non-expanded criteria donors (Table 3).



<sup>&</sup>lt;sup>a</sup> NS not significant (P > 0.05)

<sup>&</sup>lt;sup>b</sup> For expanded criteria donors, 127 donors (78%) were older than 60 years and 36 donors (22%) were aged 50–60 years

<sup>&</sup>lt;sup>c</sup> Determined by radiography

Table 3 Medical and surgical complications in 407 consecutive recipients of kidney transplantation

Donor selection criteria								
Complication	Non-expanded	Expanded	Odds ratio	95% Confidence interval	$P^{a}$			
No. (%) transplantations	244 (60)	163 (40)						
Hospitalization because of								
Infection	111 (45)	87 (53)	1.4	0.9–2.0	NS			
Respiratory problem	44 (18)	45 (28)	1.7	1.1–2.7	≤0.03			
Cardiovascular problem	37 (15)	40 (25)	1.8	1.1–3	≤0.02			
Digestive problem	25 (10)	26 (16)	1.6	0.9–2.9	NS			
Specific medical complications								
Overall acute rejection	116 (48)	63 (39)	0.6	0.4–1	NS			
Acute rejection during first year	92 (38)	53 (33)	0.3	0.5–1.2	NS			
Urinary tract infection	89 (36)	79 (48)	0.8	0.5-1.2	NS			
Graft pyelonephritis	44 (18)	22 (13)	0.7	0.4-1.2	NS			
Graft loss	43 (18)	47 (29)	1.9	1.1–3	≤0.008			
Delayed graft function	36 (15)	40 (25)	2.9	1.2–3.1	≤0.007			
Chronic rejection	34 (14)	21 (13)	0.9	0.5-1.6	NS			
Pneumonia	25 (10)	30 (18)	2	1.1–3.5	≤0.02			
Neoplasm	20 (8)	23 (14)	1.8	0.9-3.4	NS			
Recipient death	16 (7)	16 (10)	1.5	0.7–3.1	NS			
Overall surgical complications	65 (27)	77 (47)	2.4	1.6–3.7	≤0.001			
Specific surgical complications <sup>b</sup>								
Lymphocele	19 (8)	10 (6)	0.9	0.4-2.0	NS			
Early reoperation	18 (7)	22 (13)	1.9	1.0-3.7	≤0.05			
Wound eventration	15 (6)	19 (12)	2.1	1.1-3.9	≤0.03			
Hydronephrosis <sup>c</sup>	13 (5)	21 (13)	2.6	1.2–5.4	≤0.009			
Urinary fistula	13 (5)	6 (4)	0.4	0.2-1.8	NS			
Hematoma	10 (4)	11 (7)	1.6	0.7–4.0	NS			
Postoperative hemorrhage	8 (3)	15 (9)	2.9	1.2–7.2	≤0.02			
Wound infection	7 (3)	14 (9)	3.1	1.2-8.0	≤0.02			
UV junction stenosis	5 (2)	9 (6)	2.7	0.9–8.5	NS			
Renal vein thrombosis	4(2)	8 (5)	3.1	0.9–10.4	NS			
AV revision anastomosis	2 (0.8)	6 (4)	4.6	0.9-23.2	NS			
Graft lithiasis	1 (0.4)	3 (2)	4.5	0.5-44.1	NS			
Types of surgical complications								
Collections <sup>d</sup>	28 (11)	22 (13)	1.2	0.6-3.2	NS			
Urologic	25 (10)	28 (17)	1.8	1.0-3.2	≤0.05			
Wound (all)	20 (8)	29 (18)	2.4	1.3-4.4	≤0.004			
Vascular	13 (5)	23 (14)	2.9	1.4–5.9	≤0.003			
Timing of complications								
Early complications	24 (10)	27 (17)	1.8	1.0-3.2	≤0.05			
Late complications	45 (18)	48 (29)	1.8	1.1-2.9	_ ≤0.01			
Grade (severity) of complication <sup>e</sup>	. /	` '			_			
I	7 (3)	14 (9)	3.1	1.2-8.0	≤0.02			
П	10 (4)	11 (7)	1.6	0.7–4.0	NS			
III	53 (22)	53 (32)	1.7	1.1–2.7	≤0.02			
IV	12 (5)	22 (13)	3	1.5–6.2	≤0.003			

Data reported as number (%) patients

UV, ureterovesical; AV, arteriovenous

<sup>&</sup>lt;sup>e</sup> Adapted and modified from Clavien et al. [16]



<sup>&</sup>lt;sup>a</sup> NS, not significant (P > 0.05)

<sup>&</sup>lt;sup>b</sup> Renal artery stenosis and renal artery thrombosis each were noted in 1 patient with non-expanded criteria and 1 patient with expanded criteria. Vesicorenal reflux was noted in 1 patient with non-expanded criteria and not in any patient with expanded criteria

<sup>&</sup>lt;sup>c</sup> Hydronephrosis causing functional impairment

<sup>&</sup>lt;sup>d</sup> Collections consisted of lymphoceles and perirenal hematomas

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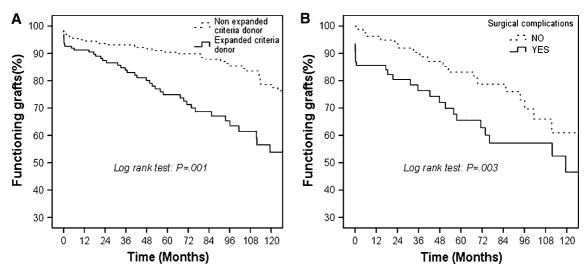


Fig. 1 a Relation between donor selection criteria and graft survival in 407 kidney transplantations, **b** Relation between surgical complications and graft survival in 163 patients who had transplantation of kidneys from extended criteria donors

A total of 142 (35%) recipients had a surgical complication, and most complications were treated with an invasive procedure involving surgery, endoscopy, or radiology (Clavien grade III) (Table 1). Compared with transplant recipients from non-expanded criteria donors, transplant recipients from expanded criteria donors had significantly greater frequency of overall surgical complications, early reoperation, wound eventration, hydronephrosis, postoperative hemorrhage, and wound infection. When analyzing surgical complications types, a significant greater frequency of urologic, wound, vascular, early and late surgical complications was found. In terms of severity, expanded donor criteria transplantation was related to higher risk of minor complications (Clavien grade I) and potentially lifethreatening risk events (Clavien grades III and IV) (Table 3).

For the sake of analyzing more precisely the impact of donor characteristics on surgical complication appearance, we adjusted for recipient age by selecting recipients older than 50 years in non-expanded criteria donor group. This cut-off point was selected according to univariate analysis that showed 50 years as a surgical complication risk factor (OR: 2.2; 95% CI, 1.5–3.4; P < 0.001). We considered nonexpanded criteria donor grafts implanted in recipients older than 50 years as control group (N = 82), and we compared it with the expanded criteria donor group (N = 163). No difference was found in recipient ages (58.7 years  $\pm$  5 SD vs. 58.91 years  $\pm$  10 SD; P > 0.05) between non-expanded and expanded criteria donors groups. Furthermore, there was no difference in terms of wound eventration (OR: 0.9, 95% CI: 0.4–2.1; P > 0.05), wound infection (OR: 1.1, 95% CI: 0.4–3.2; P > 0.05), or early reoperation (OR: 2.4, 95% CI: 0.8-6.5; P > 0.05). However, recipients from expanded criteria donors still had a greater frequency of vascular complications (OR: 3.2, 95% CI: 1.07–9.5; P = 0.04) and hydronephrosis (OR: 3.8, 95% CI: 1.1–13.4; P = 0.03).

Finally, the multivariate analysis of all possible risk factors related with surgical complications (donor and recipient age, dialysis duration, vascular calcifications, BMI, and diabetes mellitus type 2) revealed that expanded criteria donors transplantation was the only significant and independent risk factor (OR: 2.4; 95% CI, 1.5-3.7; P < 0.001).

In the whole series of 407 transplantations, graft survival was significantly lower for the expanded criteria donors (5-year survival rate: non-expanded criteria donors, 90% [95% CI, 88-92%]; expanded criteria donors, 74% [95% CI, 70–78%]; P < 0.001) (Fig. 1a). At the end of the study, there were 43 events in transplantations with non-expanded criteria donors (82% survival) and 47 events in transplantations with expanded criteria donors (71%). Univariate analysis adjusted for recipient age also showed significantly lower graft survival with expanded than non-expanded criteria donors (HR: 3.1; 95% CI: 1.8–5.7; P < 0.001). Furthermore, in the transplantations with extended criteria donors, surgical complications were associated with significantly lower graft survival (5-year survival rate: no surgical complications, 83% [95% CI, 79–87%]; surgical complications, 65% [95% CI, 59–71%]; *P* < 0.003) (Fig. 1b).

### Discussion

The present results showed that, compared with non-expanded criteria donors, kidney transplantation with expanded criteria donors was associated with greater frequency of medical and surgical complications, including urologic, wound, and vascular complications, greater frequency of more severe surgical complications, and lower



graft survival (Table 3; Fig. 1a). However, when considering recipient age, the risk of some complications was no different between non-expanded and expanded criteria donors. Therefore, transplantation of kidneys from expanded criteria donors, even those with suboptimal characteristics, is an acceptable alternative to remaining on the dialysis for older patients or patients for whom a non-extended criteria donor kidney is unavailable. Nevertheless, patient and graft survival may be limited when transplantation is performed in high-risk patients [19], and transplantation with non-expanded criteria donors may offer the best results for graft and recipient survival [4, 19, 20].

After adjusting for recipient age, there was no increased risk of wound eventration, wound infection, or early reoperation, but there was an increased risk of vascular complications and hydronephrosis in patients with expanded compared with non-expanded criteria donors. This finding suggests that recipient characteristics such as age may be primary determinants for wound complications, but graft or donor characteristics may be primary risk factors for vascular complications and hydronephrosis. Previous studies had shown that kidney transplantation from older donors may have lower survival rates than younger donors [19, 21]. Furthermore, older donor age is a risk factor for increased risk of surgical complications after kidney transplantation [22], and the present results confirmed that older recipient age also is a risk factor for complications.

The present study provided a broader description of different surgical complications than previously available, with the classification of severity using the Clavien system (Tables 1,3). Previous studies typically had evaluated only 1 type of complication, such as wound, urologic, or vascular complications, or reported data on overall surgical survival rates, but no previous studies had reported severity of complications with a standardized classification system such as the Clavien system [23–30]. Furthermore, conflicting data had previously been reported about surgical complications with expanded criteria donors. A greater incidence of vascular complications had been reported with donors and recipients that had vascular disease, including a higher frequency of arterial embolism and graft loss after manipulation of arteriosclerotic vessels [23], and an increased frequency of surgical complications was reported with transplants from expanded criteria donors (albeit with no increased frequency of graft loss, delayed graft function, or prolonged hospital stay) [24]. However, other studies had shown no increased frequency of surgical complications with expanded criteria donors including specific complications such as lymphocele, urinary fistula, thrombosis, hematoma, and urinary tract infections [25-27]. The analysis of the Eurotransplant Senior Program (ESP) also offers disparate results. Some authors assess that ESP transplantation is related with a greater incidence of overall surgical complications, lymphoceles, and late surgical complications [28, 29]. Oppositely, other studies did not find significant differences between ESP and Eurotransplant Kidney Allocation System (ETKAS) groups [30].

Nevertheless, although some studies did not demonstrate differences in the surgical complication rates between sub-optimal donors and non-expanded criteria donors, the present study confirms the results of others that surgical complications are frequent in cases with expanded criteria donors [29].

Limitations of the present study include the retrospective design and long study period, which spanned 15 years. However, a sample size of 407 transplantations helped address limitations of previous studies that had smaller study population, enabling the characterization of the different subtypes of surgical complications (Table 3). Furthermore, most previous studies included shorter follow-up periods than the present study [25–28], and longer follow-up is crucial because some surgical complications, such as ureterovesical stenosis, hydronephrosis, and wound complications, may develop more than a year after surgery.

**Conflict of interest** The authors declare that they have no conflict of interest.

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