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ORIGINAL PAPER

Kidney Transplantation in Elderly Recipients: Five-Year Experience

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ABSTRACT

Objectives: The prevalence of end-stage renal disease is rising among older adults worldwide. Despite kidney transplantation being considered the best renal replacement therapy, it presents unique challenges in elderly patients. This study aims to describe deceased donor kidney transplantation in our center, analyze outcomes namely delayed graft function (DGF), acute rejection, bacterial infections, and death-censored allograft loss in patients aged 65 years or older, and compare graft and patient survival with recipients younger than 65 years old. **Methods:** A single-center retrospective cohort study of kidney transplantation from a deceased donor between 2016 and 2020 was conducted. Data on donor, recipient, and transplant characteristics were collected, and outcomes after transplantation were analyzed. Univariate Cox regression was used to compare patient and death-censored allograft survival between older and younger patients. **Results:** Of the 294 deceased-donor transplants performed, 48 were allocated to recipients aged 65 years or older. These patients had a significantly higher prevalence of extended criteria donors (ECD) when compared to younger recipients ($p < 0.001$). The mean recipient age in the elderly group was 68 ± 2 years, with a median follow-up of 29 months (interquartile range [IQR] 18-49). During the 1st year, five (10.4%) patients were diagnosed with biopsy-proven acute rejection and 24 (50%) with bacterial infections. DGF was observed in 27 (56.3%) patients and was associated with a higher proportion of high-risk donors (ECD and uncontrolled circulatory death donors with normothermic regional perfusion) ($p = 0.034$), longer cold ischemic times ($p = 0.031$), and hospitalization duration ($p < 0.001$). Death-censored allograft survival at 1, 3, and 5 years was 89.1, 89.1, and 84.6%, respectively, which was not statistically different from the group of younger recipients ($p = 0.56$). Throughout follow-up, five patients died, three (60%) of whom had a functioning allograft. Patient survival at 1, 3, and 5 years was 100, 97.6, and 79.2%, respectively, again showing no notable differences compared to younger recipients ($p = 0.12$). **Conclusion:** Even though an individualized approach and careful pre-transplant evaluation are key for the success of kidney transplantation in the elderly population, our 1, 3, and 5-year death-censored allograft and patient survival in older patients were similar to younger recipients.

Descriptors: Kidney Transplantation; Elderly; Delayed Graft Function; Graft Survival; Patient Survival.

Transplante Renal em Idosos: Experiência de Cinco Anos

RESUMO

Objetivos: A prevalência de doença renal em estágio terminal está aumentando entre os adultos mais velhos em todo o mundo. Apesar de o transplante renal ser considerado a melhor terapia de substituição renal, ele apresenta desafios únicos em pacientes idosos. Este estudo pretende descrever o transplante renal com doador falecido em nosso centro, analisar os resultados, nomeadamente, função tardia do enxerto (FTE), rejeição aguda, infecções bacterianas e perda do aloenxerto censurada para a morte em pacientes com 65 anos ou mais, e comparar a sobrevida do enxerto e do paciente com receptores com menos de 65 anos. **Métodos:** Foi realizado um estudo de coorte retrospectivo em um único centro sobre transplante renal de doador falecido entre 2016 e 2020. Foram coletados dados sobre as características do doador, do receptor e do transplante, e os resultados após o transplante foram analisados. A regressão univariada de Cox foi usada para comparar a sobrevida do paciente e do aloenxerto censurada para a morte entre pacientes mais velhos e mais jovens. **Resultados:** Dos 294 transplantes de doadores falecidos realizados, 48 foram alocados para receptores com 65 anos ou mais. Esses pacientes tiveram uma prevalência significativamente maior de doadores com critérios estendidos (DCE) em comparação com receptores mais jovens ($p < 0,001$). A idade média dos receptores no grupo de idosos foi de 68 ± 2 anos, com um acompanhamento mediano de 29 meses (intervalo interquartil [IQR] 18-49). Durante o primeiro ano, cinco (10,4%) pacientes foram diagnosticados com rejeição aguda comprovada por biópsia e 24 (50%) com infecções bacterianas. A FTE foi observada em 27 (56,3%) pacientes e foi associada a uma proporção maior de doadores de alto risco (doadores com DCE e morte circulatória não controlada com perfusão regional normotérmica) ($p = 0,034$), tempos isquêmicos frios mais longos ($p = 0,031$) e maior duração de hospitalização ($p < 0,001$).

A sobrevida do aloenxerto censurado para a morte em 1, 3 e 5 anos foi de 89,1, 89,1 e 84,6%, respectivamente, o que não foi estatisticamente diferente do grupo de receptores mais jovens (p = 0,56). Durante o acompanhamento, cinco pacientes morreram, três (60%) dos quais tinham um aloenxerto funcional. A sobrevida dos pacientes em 1, 3 e 5 anos foi de 100, 97,6 e 79,2%, respectivamente, mais uma vez sem diferenças notáveis em comparação com os receptores mais jovens (p = 0,12). **Conclusão:** Embora uma abordagem individualizada e uma cuidadosa avaliação pré-transplante sejam fundamentais para o sucesso do transplante renal na população idosa, nossa sobrevida do aloenxerto e do paciente censurado para a morte em 1, 3 e 5 anos em pacientes idosos foi semelhante à dos receptores mais jovens.

Descritores: Transplante de Rim; Idoso; Função Retardada do Enxerto; Sobrevivência do Enxerto; Sobrevivência do Paciente

INTRODUCTION

Recently, the aging of the population has become a reality worldwide. Chronic kidney disease (CKD) is a common disease and older patients are the most prevalent group of end-stage renal disease (ESRD) patients.[1,2] Kidney transplantation (KT) is the best treatment for ESRD in all ages and is associated with better quality of life and long-term survival when compared to staying on dialysis.[3-7] However, elderly patients are often frail, typically have many comorbidities, and are more susceptible to infections and cardiovascular events than younger recipients.[8,9] Immunosuppression required for KT has potentially harmful effects in this group of patients, namely increased risk of malignancy and infectious complications, which need to be balanced against KT superiority in terms of long-term survival, justifying medical reluctance to include these patients on the KT waitlist.[2,9] Despite proven benefits, older patients still have prolonged waitlist times,[2,9] which has a significant impact on outcomes, particularly in elderly patients, who have a considerable risk of dying while on the waitlist.[10]

Furthermore, due to the shortage of organs, kidneys from expanded criteria donors (ECD) are increasingly used, especially in older patients,[4,11] which could be associated with more complications and worse long-term outcomes.[4]

Therefore, it is crucial to evaluate short and long-term complications to reduce the risks and improve the outcomes of this complex group of patients.

This study aimed to analyze major early and late complications after KT in patients aged 65 years or older transplanted in our center. Additionally, to evaluate the impact of age on KT outcomes, we compared patient and death-censored allograft survival in this group of patients with recipients younger than 65 years transplanted during the same period.

METHODS

Patients

This single-center retrospective cohort study included all KT from deceased donors performed at Unidade Local de Saúde de São João between January 1, 2016 and December 31, 2020. Patients were divided into two groups based on age (those aged 65 years and older [≥ 65 years old] and those younger than 65 years old [< 65 years old]) and were followed until death, allograft failure, or until June 30, 2021.

Demographic data of recipients, dialysis vintage, donor type, transplant-related variables (cold ischemic time (CIT), induction immunosuppression, and delayed graft function [DGF]), death-censored graft loss (DCGL), and the event of death were collected for both age groups. The group of patients aged ≥ 65 years old was specifically analyzed for comorbidities (including diabetes mellitus, hypertension, obesity, heart failure, myocardial infarction, and auricular fibrillation), Charlson comorbidity index (CCI), immunological data, maintenance immunosuppression, surgical and non-surgical complications after KT, biopsy proven acute rejection (BPAR) and infections during the 1st year post-KT, hospitalization duration, and cardiovascular complications and neoplasms during follow-up. CCI was stratified into four groups: low (< 4 points), intermediate (≥ 4 and < 7 points), and high (≥ 7 points).[12]

Donor type was classified as standard criteria donors (SCD), ECD, and uncontrolled circulatory death donors with normothermic regional perfusion (donor after cardiocirculatory death [DCD]). ECD was defined as a donor aged ≥ 60 years or 50 to 59 years with two of the following criteria: 1) cerebrovascular accident as the cause of death; 2) previous history of systemic hypertension; and 3) terminal serum creatinine > 1.5 mg/dL. DGF was defined as the need for hemodialysis in the 1st week post-KT, while primary non-function was defined as the absence of renal function recovery after KT, including surgical complications that resulting in allograft loss.

Regarding immunosuppression, all patients received induction therapy with either basiliximab or anti-T lymphocyte immunoglobulin (ATG) (Thymoglobulin® or ATG-Fresenius®). ATG was used in cases of DCD donors and high immunological risk patients, such as those with a repeat kidney transplant, panel reactive antibody (PRA) ≥ 20%, presence of donor-specific

antibodies (DSA), or when considered appropriate by the clinician due to specific clinical settings. In the majority of patients, maintenance immunosuppression consisted of prednisolone, a calcineurin inhibitor (mostly tacrolimus), and mycophenolate mofetil. All patients received prophylaxis for *Pneumocystis jirovecci* pneumonia with trimethoprim-sulfamethoxazole for 12 months. In patients at higher risk for cytomegalovirus (CMV) infection, prophylaxis with oral valganciclovir was given for 6 months (induction immunosuppression with ATG or those with donor CMV seropositive and receptor CMV seronegative).

The glomerular filtration rate was estimated (eGFR) using the equation Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) according to serum creatinine.[13]

Outcomes

In the group of patients aged ≥ 65 years old, we analyzed immediate post-KT surgical and non-surgical complications, hospitalization duration, BPAR, infectious complications, and kidney function during the 1st year. Additionally, malignancy, cardiovascular complications, patient death, and DCGL during the entire follow-up were analyzed. Finally, acute rejection, bacterial infections, and kidney function in the 1st year post-KT as well as patient and death-censored allograft survival (censored for death, loss of follow-up, or end of the inclusion period) at 1, 3, and 5 years after KT were compared between the two age groups.

Statistical analysis

Categorical variables were presented as absolute (n) and relative frequencies (%), while continuous variables were expressed as mean ± standard deviation (SD) or as medians (interquartile ranges [IQR]), depending on data distribution. To evaluate between-group differences chi-square or Fisher exact tests were used in categorical variables, while a student *t* test or Mann-Whitney *U* test were used to assess between-group differences in continuous variables. Kaplan-Meier curves were used to evaluate death-censored allograft and patient survival and univariate Cox regression was utilizes to compare the two groups according to the patient age. Statistical analyses were performed using SPSS version 27 and $p < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics according to age group

From 2016 until 2020, 294 deceased-donor transplants were performed in our center, 48 of which were in recipients aged ≥ 65 years old. Patients were followed for a median of 29 months (IQR 18-49), ranging from 1-64 months. Baseline characteristics of patients aged < 65 years old versus those aged ≥ 65 are presented in Table 1.

There were no differences between the groups concerning recipient gender, dialysis vintage, cold ischemic time (CIT), or the occurrence of DGF. However, in the younger group, a higher percentage of patients received induction immunosuppression with ATG compared to patients aged ≥ 65 years old (140 of 246 [56.9%] vs. 20 of 48 [41.7%], p = 0.017). Furthermore, the donors of the patients aged ≥ 65 years old were more commonly ECD, while the proportion of DCD and SCD was higher in the younger group (p < 0.001) (Table 1).

Table 1. Baseline characteristics according to age group.

Baseline characteristics	< 65 years (n = 246)	≥ 65 years (n = 48)	p-value
Recipient characteristics			
Age (years), mean ± SD	51 ± 9	68 ± 2	< 0.001
Gender, n (%)			0.196
Female	88 (35.8)	21 (43.8)	
Male	158 (64.2)	27 (56.2)	
Dialysis vintage (months), mean ± SD	58 ± 36	56 ± 26	0.657
Donor type, n (%)			< 0.001
SCD	107 (43.4)	10 (20.8)	
ECD	65 (26.4)	28 (58.3)	
DCD	74 (30.0)	10 (20.8)	
Transplant related			
Cold ischemic time (hours), mean ± SD	15 ± 4	16 ± 5	0.708
Induction immunosuppression, n (%)			0.017
Basiliximab	106 (43.1)	28 (58.3)	
ATG	140 (56.9)	20 (41.7)	
DGF	112 (45.5)	27 (56.3)	0.292

Source: Elaborated by the authors.

Analysis of patients aged ≥ 65 years old

Baseline patient characteristics

In this group of patients, the most frequent comorbidity was hypertension (n = 40, 83.3%), followed by diabetes (n = 21, 43.8%). As shown in Table 2, 13 (27.1%) patients had heart disease (history of myocardial infarction [n = 6, 12.5%], heart failure [n = 4, 8.3%], and auricular fibrillation [n = 3, 6.3%]). The mean CCI was 3 ± 1 points (lowest CCI of 2 and highest of 6).

Only one patient had PRA > 20% and the median number of human leucocyte antigen A, B, and DR mismatches (HLA ABDR MM) was 4 (IQR, 3-5). No patient had a history of previous KT and two had DSA. Most patients (n = 28, 58.3%) received basiliximab as induction therapy and triple maintenance immunosuppression with prednisolone, tacrolimus, and mycophenolate mofetil was administered in the majority of patients (n = 43, 89.5%) (Table 2).

Table 2. Clinical and immunological characteristics of recipients aged ≥ 65 years old.

Characteristics	
Patients, n	48
Comorbidities, n (%)	
Hypertension	40 (83.3)
Diabetes mellitus	21 (43.8)
Myocardial infarction	6 (12.5)
Heart failure	4 (8.3)
Auricular fibrillation	3 (6.3)
Obesity (body mass index ≥ 30)	3 (6.3)
CCI (points), mean ± SD	3 ± 1
Transplant characteristics	
PRA > 20%, n (%)	1 (2.1)
HLA ABDR MM, median (IQR)	4 (3-5)
Induction immunosuppression, n (%)	
Basiliximab	28 (58.3)
ATG	20 (41.7)
Maintenance immunosuppression, n (%)	
PDN/MMF/TAC	43 (89.5)
PDN/MMF/CsA	1 (2.1)
PDN/EVR/TAC	1 (2.1)

Source: Elaborated by the authors. CsA = cyclosporine; EVR = everolimus; MMF = mycophenolate mofetil; PDN = prednisolone; TAC = tacrolimus.

Adverse events

During initial hospitalization after KT

Surgical complications occurred in 13 (27.1%) patients, including five (10.4%) vascular complications, six (12.5%) urologic complications, and two (4.2%) wound-related complications. There were three cases of primary nonfunction, all due to surgical vascular complications (one due to hemorrhagic shock from renal artery anastomosis, and two secondary to graft thrombosis – one arterial and one venous thrombosis). All cases of PNF occurred in recipients of ECD. Regarding medical complications, 11 (22.9%) patients had bacterial infections, with urinary tract infections being the most common (n = 9, 18.8%). Cardiovascular events occurred in seven (14.6%) patients, namely ischemic events and auricular fibrillation (Table 3). During the inpatient stay, 12 (25%) non-diabetic patients had post-transplantation hyperglycemia, two of whom developed post-transplant diabetes mellitus in the 1st year after KT.

A high proportion of patients (n = 27, 56.3%) had DGF (Table 3). When analyzing associated factors, cold ischemic time (CIT) was significantly higher in patients with DGF when compared with those without DGF (16 [IQR 12-19] vs. 11 [IQR 10-19], p = 0.031). Furthermore, the proportion of high-risk donors (ECD and DCD) was higher in patients with DGF (24 of 27 [88.9%] vs. 11 of 18 [61.1%], p = 0.034). No statistically significant differences were observed between patients with and without DGF concerning the donor age (59 ± 10 vs. 63 ± 9, p = 0.285), dialysis vintage (50 [IQR 34-66] months vs. 52 [IQR 37-81] months, p = 0.750), recipient CCI (3 ± 1 vs. 3 ± 1, p = 0.165), or the median number of HLA ABDR MM (4 [IQR 3-5] vs. 4 [IQR 3-5], p = 0.420).

Regarding initial hospitalization duration after KT, the median time was 13 days (IQR 9-25) (Table 3), with patients with DGF having a statistically significant longer hospital stay than patients without DGF (22 [IQR 13-33] days vs. 9 [IQR 7-10] days, p < 0.001).

Table 3. Complications during the 1st year after KT and short-term complications.

Complications	
Patients, n	48
During initial hospitalization	
Surgical complications, n (%)	13 (27.1)
Vascular	5 (10.4)
Renal artery stenosis	2 (4.2)
Renal artery thrombosis	1 (2.1)
Renal vein thrombosis	1 (2.1)
Hemorrhagic shock (arterial anastomosis)	1 (2.1)
Urologic	6 (12.5)
Urinary leak	2 (4.2)
Lymphocele	2 (4.2)
Obstructive uropathy	2 (4.2)
Wound related complications	2 (4.2)
Surgical wound infection	1 (2.1)
Wound dehiscence	1 (2.1)
Non-surgical complications, n (%)	
Post-transplantation hyperglycemia	12 (25)
Infections	11 (22.9)
Urinary tract infection	9 (18.8)
Other infections	2 (4.2)
Cardiovascular events	7 (14.6)
Immunosuppression-related cytopenias	3 (6.3)
Delayed graft function, n (%)	27 (56.3)
Primary nonfunction, n (%)	3 (6.3)
Initial hospitalization duration (days), median (IQR)	13 (9-25)
Acute rejection, n (%)	5 (10.4)
TCMR	3 (6.3)
Borderline	2 (4.2)
TCMR IA	1 (2.1)
ABMR	1 (2.1)
Mixed rejection	1 (2.1)
Infections, n (%)	
Bacterial infections	24 (50.0)
CMV infection	15 (31.2)
Readmission, n (%)	18 (37.5)
Total duration of hospitalizations (days), median (IQR)	17 (10-50)

Source: Elaborated by the authors.

Rejection and infections during the ıst year post-KT

During the 1st year of follow-up, five (10.4%) patients were diagnosed with BPAR, based on Banff criteria. In the group of younger patients, 36 (17.1%) were diagnosed with BPAR, but no statistically significant difference was found between the two groups (p = 0.648). The majority (n = 4, 80%) of BPAR cases in elderly patients occurred within the first 3 months post-KT. Three patients had T-cell mediated rejection (TCMR), including two borderline rejections and one TCMR IA, which were all treated with pulses of methylprednisolone. One patient was diagnosed with antibody-mediated active rejection (ABMR) and one was diagnosed with mixed rejection (TCMR IA and ABMR). Both were treated with pulses of methylprednisolone, intravenous immune globulin, and plasma exchange. In all cases, treatment was successful with improved kidney function (Table 3).

When analyzing rejection-related variables, no significant differences were observed in the proportion of patients with ATG induction (3 of 5 [60%] vs. 14 of 40 [35%], p = 0.34), high-risk donors (DCD and ECD) (3 of 5 [60%] vs. 30 of 40 [75%], p = 0.28), or in the median number of HLA ABDR MM (5 [IQR 3-6] vs. 4 [IQR 3-5], p = 0.74) when patients with AR were compared with those without AR, respectively. However, a higher proportion of patients with AR experienced DGF when compared with those without AR (4 of 5 [80%] vs. 23 of 43 [53.4%], p = 0.56), even though no statistically significant difference was found.

After initial hospitalization, 24 (50%) patients were diagnosed with bacterial infections, 15 (62.5%) of which were urinary tract infections. The majority of these infections (n = 14, 58.3%) required hospitalization. In fact, 25 (52%) patients had bacterial infections, including during initial hospitalization and 1-year follow-up. CMV infection was diagnosed in 15 (31.2%) patients (Table 3). When comparing bacterial infections in these patients with the younger group, a statistically significant difference was detected, since elderly patients had a higher proportion of events (24 of 48 [50%] vs. 50 of 246 [20.3%], p < 0.001).

When elderly patients with bacterial infections were compared with elderly patients without bacterial infections, no statistically significant differences were observed in the proportion of pre-transplantation diabetes (12 of 24 [50%] vs. 6 of 21 [28.5%], p = 0.21), ATG induction (12 of 24 [50%] vs. 6 of 21 [28.6%], p = 0.12), or the occurrence of BPAR (4 of 24 [16.7%] vs. 1 of 21 [4.8%], p = 0.22), respectively.

During the 1st year post-KT, 18 (37.5%) patients were readmitted, in most cases (n = 12, 66.7%) due to infectious complications, and the median total duration of hospitalization (including the initial) was 17 days (IQR 10-50) (Table 3).

Malignancy and cardiovascular disease during follow-up

During follow-up, and after initial hospitalization, 12 patients (25%) suffered a cardiovascular event and no patient had cerebrovascular events. Regarding malignancy, seven patients (14.6%) were diagnosed with neoplasms (Table 4).

Table 4. Complications during the entire follow-up.

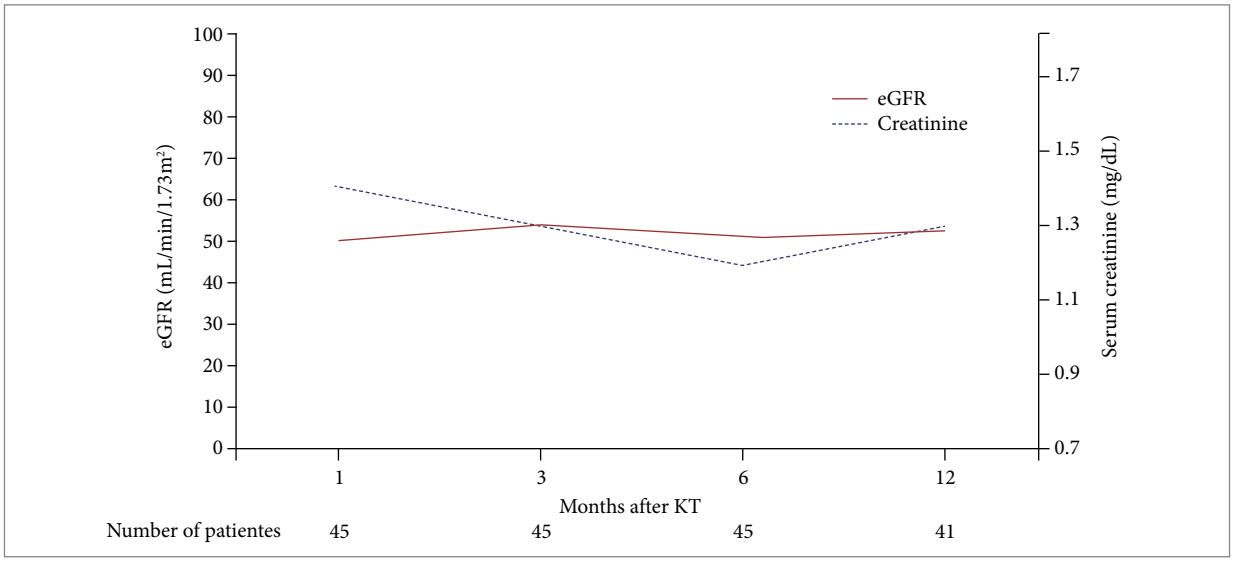
Complications	
Patients, n	48
Malignancy, n (%)	7 (14.6)
Renal cell carcinoma	2 (4.2)
Basal cell carcinoma	1 (2.1)
Squamous cell carcinoma	1 (2.1)
Lung adenocarcinoma	1 (2.1)
Kaposi sarcoma	1 (2.1)
Follicular thyroid cancer	1 (2.1)
Cardiovascular disease, n (%)	12 (25.0)
Myocardial infarction	5 (10.4)
Heart failure	4 (8.3)
Auricular fibrillation	3 (6.3)
Graft-loss, n (%)	9 (18.8)
Death-censored graft loss, n (%)	6 (12.5)
Primary nonfunction	3 (6.3)
Chronic allograft dysfunction	2 (4.2)
Rejection	1 (2.1)
Death, n (%)	5 (10.4)

Source: Elaborated by the authors.

Patient and allograft outcomes

In the 1st year post-KT, and after excluding PNF and graft loss, the median serum creatinine and eGFR beyond 1 month remained relatively stable, and at 12 months were 1.3 (IQR 1.0-1.8) mg/dL and 53 (IQR 42-71) mL/min/1.73 m^2, respectively (Fig. 1). Even though no statistically significant difference was found in the median serum creatinine when compared with the younger group (1.3 mg/dL [IQR 1.0-1.8] mg/dL vs. 1.2 [IQR 1.0-1.6] mg/dL, p = 0.960), the eGFR was statistically higher in the younger group (53 [IQR 42-71] mL/min/1.73 m^2 vs. 62 [IQR 45-78] mL/min/1.73 m^2, p = 0.035).

At 6 months after KT, 20% (n = 9) of elderly patients had eGFR ≤ 30 mL/min/1.73 m^2, including patients with graft loss and PNF. For interpretation of creatinine and eGFR, dropouts due to PNF (n = 3), graft loss (n = 1), and patients with less than 1 year of follow-up (n = 3) must be taken into account.



Source: Elaborated by the authors.

Figure 1. Evolution of kidney function during the 1st year post-KT.

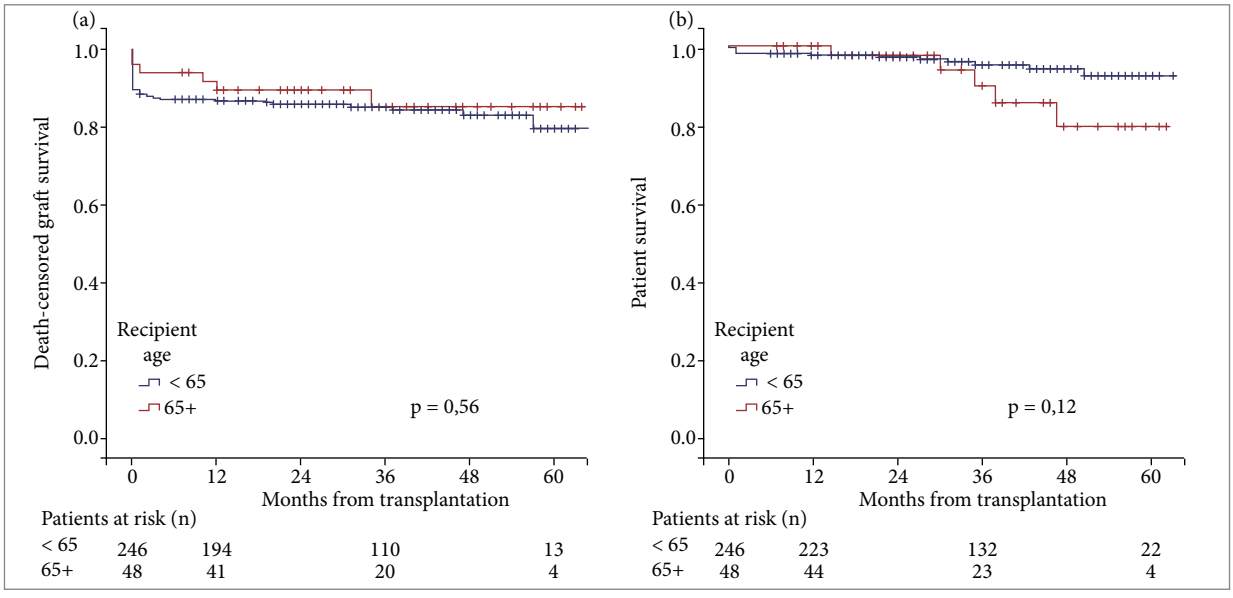
During follow-up, five (10.4%) patients died (Table 4) after a median time of 33 months (IQR 22-49; range 15-39 months) from KT, three (60%) of whom had a functioning allograft.

Graft loss was observed in nine (18.8%) patients. In three (6.3%) patients it was due to death with a functioning graft. DCGL was the main cause of graft failure and was observed in six (12.5%) patients. One patient suffered chronic rejection and two developed chronic allograft dysfunction without evidence of a specific etiology (Table 4). Excluding PNF, three of the remaining 45 patients lost graft function between 10 and 34 months after KT.

Death-censored allograft and patient survival

In the group of patients aged ≥ 65 years old, death-censored allograft survival at 1, 3, and 5 years was 89.1, 89.1, and 84.6%, respectively. When compared to the death-censored allograft survival in younger recipients (86.6, 85.6, and 79.4%, respectively), no statistically significant differences were found, HR 0.77 (95% confidence interval [95%CI] 0.33-1.83), p = 0.56 (Fig. 2A).

In the group aged ≥ 65 years old, patient survival at 1.3 and 5 years was 100, 97.6, and 79.2%, respectively. Similarly, there were no statistical differences when compared with the patient survival in recipients aged < 65 years old (97.5, 96.5, and 92.3%, respectively), HR 2.29 (95%CI 0.81-6.5), p = 0.12 (Fig. 2B).



Source: Elaborated by the authors.

Figure 2. (a) Death-censored graft survival after KT in recipients aged ≥ 65 vs. < 65 years old. (b) Patient survival in recipients aged ≥ 65 vs. < 65 years old.

DISCUSSION

In recent years, there has been an increase in the number of older patients with ESRD worldwide, with a growing number of elderly patients receiving KT.[1,2] In Portugal, the number of transplant recipients aged ≥ 65 years has increased substantially during the last decade. While in 2013 8% (n = 36) of the total kidney transplant recipients were patients aged ≥ 65 years, the percentage went up to 17. 2% (n = 84) in 2022.[14]

KT is considered the best treatment for ESRD across all ages.[3-6] In fact, Wolfe et al.[7] demonstrated reduced long-term risk of mortality in patients aged 60 to 74 years who were transplanted versus those who remained on the waitlist. In our study of elderly kidney transplant recipients, we found good patient survival up to 5 years after KT, despite a significant proportion of ECD. Indeed, several studies have shown that in elderly patients KT of ECD improves recipient survival,[4,11,15] despite it being lower when compared to kidneys from younger donors.[16,17]

A higher comorbidity burden in older patients increases the risk of postoperative complications.[18] Increased age, DGF, and time on dialysis have been identified as risk factors for surgical complications in older kidney transplant recipients.[19] In our study, a significant proportion of patients (31.2%) suffered surgical complications. Similarly, other studies in older kidney transplant recipients also reported significant rates of surgical complications,[15,19] although different characteristics of the donor pool and the definition of surgical complications limit comparison between studies. Of note, all cases of PNF in our study were due to surgical vascular complications, which probably reflects the impact of donor and recipient age on surgical outcomes due to peripheral vascular disease.[20]

DGF is common in deceased donor transplantation and is associated with worse outcomes, namely prolonged hospitalization, higher morbidity, worse graft function, and graft loss.[21,22] Moreover, the impact of DGF on graft failure may be more pronounced in suboptimal grafts probably related to their lower functional reserve and recovery capacity to damage.[20] Donor-related variables, such as donor age, ECD, and DCD, are recognized risk factors for DGF.[22,23] Additionally, transplant-related factors, such as CIT, also promote higher rates of DGF.[22,23] The prevalence of DGF in older patients varies according to studies. Recent studies reported rates between 27.6 and 60%,[1,15,19] probably reflecting, at least in part, differences in CIT and donor-related variables such as donor age and type. In our older cohort, the proportion of DGF was 56.3%. Prolonged CIT and a considerable proportion of high-risk donors, including uncontrolled DCD donors, may have contributed to the proportion of patients with DGF since these patients had higher CIT and an increased proportion of high-risk donors when compared with patients without DGF. Importantly, DGF was associated with prolonged hospitalization duration, demonstrating its impact on patient morbidity and transplant costs. Therefore, reducing CIT should be a priority in these elderly patients, who more often receive kidneys from ECD to decrease the rate of DGF. Various mechanisms are thought to be involved in the impact of DGF on graft loss, including higher rates of acute rejection and ischemia-reperfusion injury.[23,24] However, the limited number of cases prevented us from being able to evaluate the association between DGF and acute rejection.

Bacterial infections were particularly common, occurring in 52% of patients in the 1st year after KT. Moreover, they motivated hospital readmission in the majority of the patients. In the study of Lemoine et al.[1] on kidney transplant recipients older than 70 years, an even greater proportion of patients had bacterial infections in the 1st year after KT. This high incidence of infectious complications highlights the impact of immunosuppression on this elderly population.

On the contrary, the incidence of BPAR was only 10.4%. This is supported by the literature, which demonstrates that immunosenescence in elderly patients reduces the prevalence of acute rejection while increasing the risk of infectious complications. With aging, the innate and adaptive immune system undergoes alterations that include signal pathways and cytokine release paralleled by modifications in drug metabolism, namely changes in renal and hepatic drug clearance.[2,25] Consequently, the use of less aggressive induction immunosuppression in this frail group of patients could be considered to reduce the risk of infections. In our study, the proportion of BPAR was higher in the younger group, even though not reaching statistical significance, which might be explained by the reduced number of events. However, concerning bacterial infections, there was a statistically higher proportion of events in older recipients. Half of elderly patients with bacterial infections during the 1st year received induction immunosuppression with ATG, but no statistically significant association could be established between the type of induction immunosuppression and bacterial infections. Additionally, the prevention of infectious complications should be a priority, including pre-transplant identification of patients at higher risk of infectious complications, timely vaccination as well as post-transplant prophylactic measures, namely prolonged use of prophylactic antibiotics whenever justified.

To further exacerbate this complex interplay, while rarer, acute rejection seems to induce more deleterious consequences in older patients.[25] Furthermore, the use of kidneys from ECD or DCD and with longer cold ischemic time imposes greater immunogenicity and, consequently, a higher risk of rejection.[2,25,26] In our population, even though all patients with acute rejection received kidneys from high-risk donors, no association could be established due to the limited number of events.

Authors are increasingly recognizing the need to individualize immunosuppression in elderly patients, according to recipient and donor characteristics. However, there are limited data on the management of immunosuppression in this population.[25,27] Since many elderly patients die with a functioning graft, less intensive immunosuppressive regimens, namely with steroid-sparing, seem to be beneficial.[27] Nevertheless, given the deleterious effects of rejection in this group of patients, in high immunologic risk recipients the use of lymphocyte-depleting agents such as ATG may be more appropriate, but more studies are required.[25]

In our population, during follow-up, 12 patients (25%) had cardiovascular events and seven (14.6%) were diagnosed with neoplasia. Likewise, the study of Cabrera et al.[15] in kidney transplant recipients aged ≥ 75 years found similar proportions of these complications. Older KT recipients are more likely to die from cardiovascular events, infections, and neoplasia, making cardiovascular disease screening before transplantation extremely important in this group of patients.[9,18]

Despite the limitations inherent to the restricted number of patients and time of follow-up, in our study, patient survival did not significantly differ between recipients aged ≥ 65 years when compared to younger recipients. To assess the comorbidities of our older cohort, we used CCI, which may identify patients with a higher risk of death.[2,12,28] Erlandsson et al.[12] studied patients aged > 60 years with a median CCI of 3 who were followed up to 10 years and found that a high CCI identified patients with a higher risk of death after KT. In our study, the mean CCI was 3 and no patient had a high CCI. However, the median dialysis vintage, which has also been shown to be a risk factor for mortality,[27] was 52 months, higher than in other series.[1,16,20,29] When comparing with other studies that analyzed patients aged ≥ 65 years, our 1 and 5-year patient survival was similar to the study of So et al.,[30] and 5-year patient survival was better than in the study of Faravardeh et al.,[20] although this comparison has its limitations. Patient survival in older adults has improved over time,[8] and the observed differences between our study and the study of Faravardeh et al.[20] may be explained by the transplant period, as in their study the median transplant year in patients aged ≥ 65 years was 2004. Given the increasing age of kidney transplant recipients, a tool to better evaluate patient comorbidities could help in the selection of elderly patients who would benefit most from KT.

As previously mentioned, older recipients have a significant cardiovascular, infectious, and neoplastic burden and, in most cases, die from these complications with a functioning allograft.[26,29] Comparable findings were observed in our population, as five (10.4%) patients died during follow-up and the majority (60%) had a functioning allograft. DCGL, including PNF, occurred in 12.5% of the older patients and, contrary to other studies,[1,15] DCGL was the main cause of graft loss. However, 5-year death-censored graft survival was over 80% and compares well to other studies in patients aged ≥ 65 years,[19,20,31] although different donor and transplant characteristics as well as the era of transplantation limits comparison between studies. Even though eGFR after 12 months of follow-up was statistically lower in the older group, we found no significant differences when the death-censored graft survival of our older cohort was compared to the younger group.

The present study has limitations inherent to its retrospective nature. Additionally, the restricted number of patients may have limited the analysis. However, it describes the characteristics and outcomes of KT in elderly recipients, who have particular specificities and require individualized management and therapy, and that, despite increasingly transplanted, are frequently not included in a scientific investigation.

In conclusion, KT is the best treatment option for ESRD, regardless of the recipient's age. Older recipients have specific characteristics, which should promote an individualized approach and a careful selection of the appropriate candidate for KT, including cardiovascular disease screening, timely vaccination as well as immunosuppression adjustment. Importantly, in our study no differences were found concerning 1, 3 and 5-year death-censored graft survival or 1, 3, and 5-year patient survival, when compared with younger recipients transplanted during the same period. Therefore, we advocate for selected elderly patients to be included in the waitlist for KT.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Paulo N, Fernandes V, Cerqueira A, Bustorff M, Sampaio S, Pestana M; **Conception and design:** Paulo N, Cerqueira A; **Data analysis and interpretation:** Paulo N, Pinho A; **Article writing:** Paulo N; **Critical revision:** Fernandes V, Cerqueira A, Bustorff M, Sampaio S, Pestana M; **Final approval:** Cerqueira A, Bustorff M, Sampaio S, Pestana M.

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