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Deceased Donor Kidney Transplantation in Patients Aged 70 and Older: Is 70 the New 50?

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Abstract

Background: Deceased donor (DD) kidney transplantation (KT) outcomes in patients who are aged 70 years and older are understudied.

Methods: We retrospectively reviewed our single center DD KT outcomes in patients aged 70 years and older. All patients received antibody induction with tacrolimus, half-dose mycophenolate, ± steroids. Results: Over 10.75 years, we performed 114 KTs in 112 patients aged 70 and older (mean 73.8, range 70-84 years) including 42 patients who were aged 75 and older. The study group included 60 males/52 females and 79 Caucasians/28 African Americans/5 other with a mean waiting time of 16 months; 75 patients (66%) received kidneys from expanded criteria donors (ECDs) and 14 received dual KTs. Delayed graft function occurred in 27% and influenced graft but not patient survival. With a mean follow-up of 68 months, patient survival was 59% and uncensored kidney graft survival was 47%. Three year and death-censored kidney graft survival rates were 76% and 74%, respectively. Outcomes were similar in patients < or ≥ 75 years. Of 60 graft losses, death with a functioning graft (DWFG) accounted for 41 (68%). Of 46 deaths, 72% were due to cardio/cerebrovascular events, infection, or malignancy. At present, 54 of the 66 surviving patients (81.8%) have functioning grafts. The incidences of acute rejection and major infection were 14% and 45%, respectively.

Conclusions: Advanced recipient age has a modest effect on medium-term outcomes in appropriately selected elderly patients using predominantly ECD kidneys, which may not be appropriate for younger patients. However, medium-term outcomes are largely influenced by a higher incidence of DWFGs in the elderly, suggesting that matching strategies for kidney and patient longevity are warranted.

Keywords: Age-matching; Death with functioning graft; Dual kidney transplants; Elderly recipients; Expanded criteria donors; Outcomes; Recipient age

Abbreviations

BMI: Body Mass Index; CAN: Chronic Allograft Nephropathy; CRCL: Creatinine Clearance; DCD: Donation after Cardiocirculatory Death; DD: Deceased Donor; DGF: Delayed Graft Function; DKT: Dual Kidney Transplant; DWFG: Death With a Functioning Graft; ECD: Expanded Criteria Donor; ESRD: End Stage Renal Disease; GFR: Glomerular Filtration Rate; HLA: Human Leukocyte Antigen; KT: Kidney Transplantation; MDRD: Modification of Diet in Renal Disease; PRA: Panel Reactive Antibody; SCD: Standard Criteria Donor; SCR: Serum Creatinine; UNOS: United Network for Organ Sharing; US: United States; USRDS: United States Renal Data System

Introduction

In the recent past, advanced chronological age was a contraindication for kidney transplantation (KT) because older age was used as a surrogate for disease burden, functional status, co-morbidities, and risks for infection and hospitalization. However, similar to trends in the United States (US) general population, there has been an increasing yet disproportionate shift toward increasing numbers of older recipients in KT. The risk of end stage renal disease (ESRD) increases disproportionately with older age. At the end of 2012, chronic kidney disease affected 40% of people aged 70 and older in the US [1]. In 2012, 46% of the nearly 116,000 new (incident) ESRD patients were 65 years or older and the median age for new dialysis patients was 64.8 years. In the decade from 2001-2011, the overall size of the kidney waiting list in the US nearly doubled [2]. During this same interval, the actual number of candidates aged 65 and older (the so-called "elderly") who were placed on the waiting list nearly tripled and those aged 70 and older quintupled. In addition, the annual number of elderly patients actually receiving KTs doubled during this period [1-3].

These trends have occurred because of the convergence of demographic inevitability, medical advances and the natural history of chronic kidney disease. Current data demonstrate an escalating share of elderly patients in the ESRD population [1]. Aging is associated with

anatomic changes as well as the gradual loss of physiologic reserve in a number of organ systems, and dialysis may accelerate or exacerbate many of these chronologic perturbations [4,5]. Although loss of renal function may be associated with normal aging, the presence of ESRD in the elderly population is commonly associated with increased mortality risk and co-morbidities such as hypertension, diabetes mellitus, ischemic heart disease, peripheral vascular disease, cerebrovascular disease, dyslipidemia, frailty, dementia, depression, other organ disease/dysfunction and malignancy [5-17]. However, elderly patients are a heterogeneous group defined by chronological but not necessarily biological age. Outcomes of deceased donor (DD) KT in patient's ≥70 years of age are understudied. The purpose of this study was to review retrospectively our single center experience in DD KT in patients ≥70 years of age receiving contemporary immunosuppression in the new millennium, which spans the expanded criteria donor (ECD) era in the US.

Methods

Study design

We conducted a retrospective chart review of all DD KTs performed at our center from 10/1/01 through 7/1/12 (minimum 3.5 years follow-up). Standardized donor and recipient selection and management algorithms were followed during the period of study [18,19]. No specific upper age limit was an absolute contraindication to KT, as the oldest recipient in this series was 84 years.

Definitions

In addition to recipient age, outcomes were evaluated according to DD age and quality. ECD were defined by the standard United Network for Organ Sharing (UNOS) definition [20]. For purposes of this study, any DD not meeting ECD criteria was defined as a standard criteria donor (SCD). Delayed graft function (DGF) was defined as the need for dialysis for any reason in the first week post-transplant. Renal allograft loss was defined as death with a functioning graft (DWFG), transplant nephrectomy, return to dialysis, retransplantation, or return to the pretransplant serum creatinine (SCr) level in preemptively transplanted patients.

Donor evaluation and management

The Cockcroft-Gault formula was employed to estimate donor creatinine clearance (CrCl) to determine single or dual KT (DKT) into a single recipient as previously reported [21]. Whenever possible, ECD kidneys were placed on machine preservation to minimize ischemia-reperfusion injury, maintain functional reserve, and provide another means of assessment as previously reported [20]. Although pump parameters were not exclusively used to discard kidneys, a flow rate >80 ml/min and a resistance <0.40 mm Hg/ml/min after a minimum of 6 hours on machine preservation were considered as thresholds for utilization for single KTs. Standard serological evaluation for donors included testing for hepatitis B, hepatitis C, human immunodeficiency virus, cytomegalovirus, and Epstein-Barr virus.

Recipient evaluation and selection

All patients underwent a comprehensive pre-transplant medical, psychosocial, and financial evaluation, with emphasis placed on the cardiovascular system to determine operative risks and physiological age [18,19,21]. Non-contrast abdominal/pelvic computerized tomographic imaging (to assess iliac artery calcifications) and cardiac stress testing were performed in all patients. In general, elderly patients needed to be reasonably well compensated, active, functional, not have multiple comorbidities, and have a solid social support system. All patients aged 70 years and older also underwent carotid and iliac artery duplex ultrasonographic imaging, cardiology consultation, and heart catheterization. Standard serological evaluation for potential recipients included testing for hepatitis B, hepatitis C, human immunodeficiency virus, cytomegalovirus, and Epstein-Barr virus. Specific exclusion criteria in the elderly included the presence of dementia, nursing home residence, poor overall functional status or frailty, lack of adequate social support, advanced disease or organ failure in an extra-renal organ system, recent malignancy, severe cardiac or vascular disease, or projected life expectancy of <2 years. Patients were discussed at a multidisciplinary pretransplant selection committee meeting, with candidacy for placement on the waiting list determined by group decision. At this time, elderly patients were assigned as high risk from a wait list maintenance perspective (meaning that annual re-evaluations would occur in the absence of KT) and virtually all elderly patients (following informed consent) were listed as willing to accept an ECD kidney.

Patients were initially selected for KT according to UNOS guidelines. With marginal donor and ECD kidneys, however, recipient selection was not always by standard kidney allocation but based on older age (>55 years), smaller size (Body Mass Index <25 kg/m^2) matching, and identifying low immunological risk patients such as primary transplant, human leukocyte antigen (HLA) matching, low panel reactive antibody (PRA) level (usually 0%) and informed consent [18,19,21].

Immunosuppression

Nearly all DD KT patients received depleting antibody induction with either multi-dose rabbit antithymocyte globulin or single dose alemtuzumab 30 mg intravenous as a single intra-operative dose [22]. Maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil, and either rapid tapering doses of steroids or early steroid withdrawal based on immunological risk stratification [22]. Target 12 hour tacrolimus trough levels were 6-8 ng/ml for elderly recipients, who also received only half dose mycophenolate mofetil (1 gm/day) in 2 divided doses. Early steroid withdrawal was performed in low-risk patients whereas steroids were continued in high immunological risk patients such as patients receiving retransplants, patients with a current PRA level >20%, and patients experiencing DGF [22].

Post-transplant management

All patients received surgical site prophylaxis with a first-generation cephalosporin for 24 hours, anti-fungal prophylaxis with nystatin or fluconazole for 1 month, and anti-pneumocystis prophylaxis with sulfamethoxazole-trimethoprim (dapsone if allergic to sulfa) for at least 12 months. Antiviral prophylaxis consisted of oral valganciclovir for 3-6 months, depending on donor and recipient cytomegalovirus serologic status. Specifics regarding drug dosing and duration have been published previously [18,19,21,22].Most patients received aspirin prophylaxis or other types of anti-platelet or anti-coagulation therapy. The diagnosis of renal allograft rejection was suggested by an unexplained rise in SCr level of >0.3 mg/dl or a 25% increase from baseline level and confirmed by ultrasound-guided percutaneous biopsy. Major infection was defined as requiring hospital readmission

for evaluation and management. Post-transplant renal allograft function was evaluated by measuring SCr levels as well as calculating glomerular filtration rate (GFR) using the abbreviated modification of diet in renal disease (MDRD) formula.

Statistical analysis

Data were compiled from both prospective and retrospective databases, with confirmation by medical record review in accordance with Institutional Review Board guidelines and approval. Categorical data were summarized as proportions and percentages and continuous data were summarized as means and standard deviations. Univariate analysis was performed by the unpaired t test for continuous variables, the chi-square test for categorical variables, and Fisher's exact test when data were sparse. Actual patient and graft survival, death-censored graft survival, and actuarial survival rates were determined. Survival curves were computed using the Kaplan-Meier method and compared using the log-rank test. A two-tailed p value of <0.05 was considered to be significant.

Results

Over a 10.75 year period, we performed 114 KTs in 112 patients aged ≥70 (mean 73.8 years, range 70-84). Septuagenarians comprised 12.2% of our overall adult DD KT activity although their annual proportion increased from 3%-16% during the period of study. The recipient group included 52 women and 60 men (79 white, 28 black, 5 other) with a mean waiting time of 16 months. A total of 70 patients were 70-74 years of age (mean 71.9) while the remaining 42 (2 transplanted twice) were ≥75 years of age (mean 76.8, oldest 84 years). Demographic and transplant characteristics of patients 70-74 and ≥75 years of age are displayed in Table 1.

Variable Mean ± SD	70-74 years of age (n=70)	≥75 years of age (n=44 KTs in 42)	P-value
Age (years)	71.9 ± 1.5	76.8 ± 1.9	<0.05
Males	37 (53%)	23 (55%)	NS
African American	14 (20%)	14 (33%)	0.12
Recipient BMI (kg/m2)	26.7 ± 4.2	26.0 ± 4.0	NS
Duration of dialysis (months)	37.3 ± 26.5	32.0 ± 24.2	NS
Time on waiting list (months)	17.5 ± 17	13 ± 12.8	NS
Renal replacement therapy pretransplant			
-Hemodialysis	49 (70%)	31 (74%)	NS
-Peritoneal dialysis	13 (19%)	6 (14%)	
-Preemptive transplant (no dialysis)	8 (11%)	5 (12%)	
Retransplant	3 (4.3%)	3 (6.8%)	NS
Cytomegalovirus (CMV) Donor +/Recipient -	14 (20%)	4 (9%)	0.19
Expanded criteria donor (ECD)	45 (64%)	30 (68%)	NS
Kidney Donor Profile Index (KDPI, %)	74 ± 22	73 ± 25	NS
Dual KT	9 (12.9%)	5 (11.4%)	NS
Cause of ESRD			
Diabetes	27 (39%)	19 (43%)	NS
Hypertension	19 (27%)	14 (32%)	
Other	24 (34%)	11 (25%)	
Cold ischemia (hours)	25.4 ± 7.8	26.4 ± 7.8	NS

Table 1: Demographic and transplant characteristics among recipients 70-74 compared to ≥75 years of age.

With a mean follow-up of 68 months (range 45-173 months), overall patient survival was 59%. One, three, and five year actual patient survival rates were 94.6%, 85.7%, and 78.6%, respectively. Of the 46 deaths, 13 (28%) occurred within 2 years, 11 (24%) within 2-5 years, and 22 (48%) more than 5 years following KT. Causes of death included cardiovascular [17], infection or malignancy (6 each), respiratory or cerebrovascular (4 each), and other or unknown causes [9].

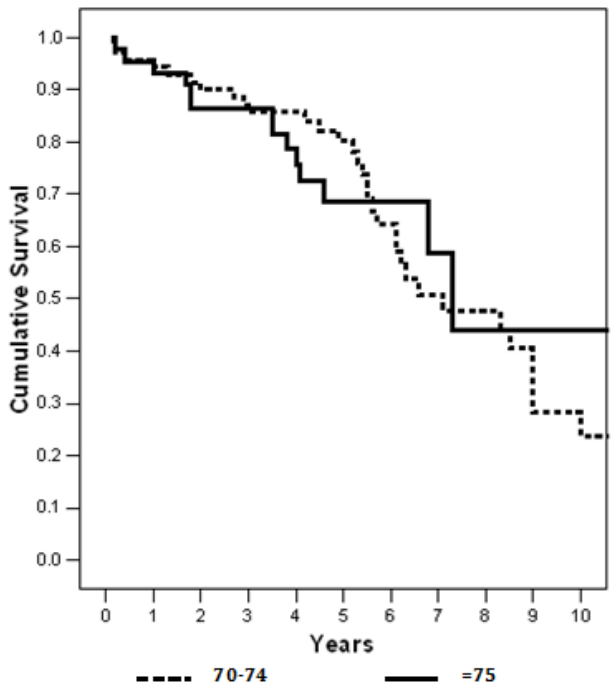

Figure 1: Actuarial patient survival according to recipient age group (70-74 versus ≥75, p=NS).

Causes of death were equally distributed at different time intervals following KT and nearly half of deaths occurred more than 5 years following KT. Cardio/cerebrovascular events, infection, or malignancy accounted for 72% of deaths. Actuarial patient survival was no different in patients ≥75 compared to those 70-74 years of age (Figure 1).

Uncensored and death-censored overall kidney graft survival rates were 47% and 74%, respectively. One, three, and five years uncensored and death-censored actual kidney graft survival rates were 90.4% and 95.4%, 76.3% and 86.1%, and 67.5% and 81.1%, respectively. Of the 60 graft losses, 23 (38.3%) occurred within 2 years, 14 (23.3%) within 2-5 years, and 23 (38.3%) more than 5 years following KT.

DWFG accounted for 41 (68%) of the graft losses. A total of 11 DWFGs (27%) occurred within 2 years, 8 (19%) within 2-5 years, and 22 (54%) more than 5 years following KT. Of the remaining 19 graft losses, causes were primary non-function [5], chronic allograft nephropathy (CAN) or acute rejection (3 each), chronic rejection or acute kidney injury (2 each), and other or unknown causes [4].

A total of 12 (63%) of death-censored graft losses occurred within 2 years, 6 (32%) within 2-5 years, and only 1 (5%) more than 5 years following KT. Of the 23 graft losses occurring more than 5 years following KT, all but 1 was secondary to DWFG. The uncensored (50% *versus* 45.7%) and death-censored actual (71% *versus* 76.2%) and actuarial (Figures 2 and 3, p=NS) kidney graft survival rates were no different in patients 70-74 compared to those ≥75 years of age (Table 2).

The corresponding incidences of DWFG were 40% in patients 70-74 compared to 31% in those ≥75 years of age (p=NS). In the 19 surviving pts with GL, 2 were retransplanted (one of whom died 4 years later), 5 died (at mean of 13 months) after resuming dialysis, and 12 are alive on dialysis (for a mean of 38 months, none of whom are back on the waiting list for retransplant).

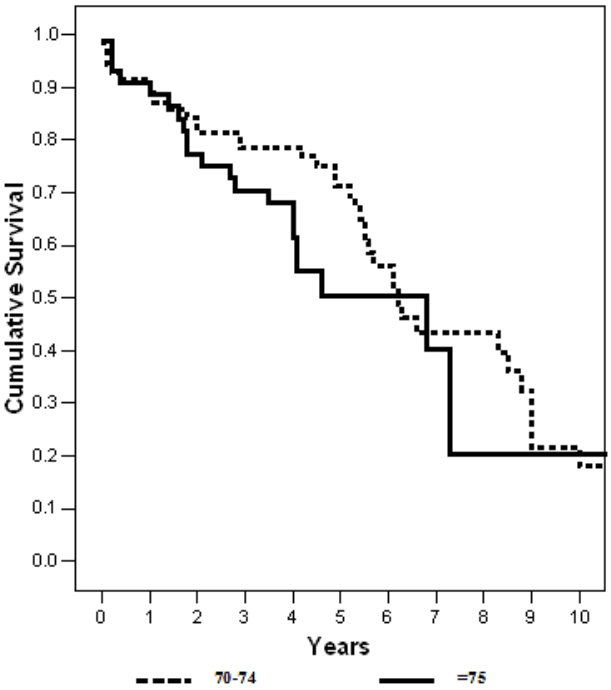

Figure 2: Actuarial graft survival according to recipient age group (70-74 versus ≥75, p=NS).

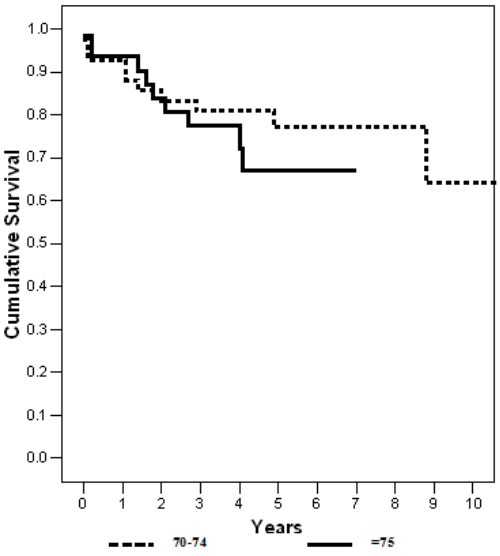

Figure 3: Actuarial death-censored graft survival according to recipient age group (70-74 versus ≥75, p=NS).

At present, 54 of the 66 surviving patients (81.8%) have functioning grafts. The incidence of DWFG in patients with diabetes was 39% compared to 34% in those without diabetes (p=NS).

Fourteen patients underwent DKT (11 from ECD and 3 from donation after cardiocirculatory death [DCD] donors). Mean waiting time for these patients was 12.6 months. Overall patient and graft survival rates were both 71.4% with a mean follow-up of 54 months. All 4 graft losses were DWFGs, occurring at a mean of 34 months post-transplant. One-year and death-censored actual graft survival rates were both 100%. The incidence of DGF was 14.3% following DKT compared to 29% for the remaining patients undergoing single KT (p=NS).

A total of 75 patients (66%) received kidneys from ECDs including 8 DCD donors. The remaining 39 patients (34%) received kidneys from SCDs including 10 DCD donors. Mean cold ischemia time for all cases was 25.8 hours including 15 (13.2%) with cold ischemia times of ≥36 hours. Machine preservation was deployed for various periods of time in 84 (74%) cases with a mean pump time of 12.4 hours. Machine preservation was used in 100% of DCD donor, 78% of ECD, and 48% of SCD kidneys (p<0.01). The incidences of DGF were 66.7% for DCD, 16.4% for ECD, and 27.6% for SCD KT (p=0.0001). The overall incidence of DGF was 27.2% (including 5 cases of primary non-function) and did not correlate with either subsequent patient survival or DWFG. However, the presence of DGF did correlate with subsequent kidney graft loss. Actual (35.5% with *versus* 51.8% without DGF, p=0.14) and death-censored graft survival (52.4% with *versus* 82.7% without DGF, p=0.016) rates were lower in patients with DGF. Actual patient survival (50% DCD *versus* 53.7% ECD *versus* 75.9% SCD, p=0.048) was higher following SCD KT. Actual graft survival (33.3% DCD *versus* 41.8% ECD *versus* 69% SCD, p=0.009) likewise exhibited a stepwise improvement favoring SCD KT. The incidences of DWFG were 38.9%, 41.8%, and 20.7% (p=0.07) in DCD, ECD, and SCD KT recipients, respectively. Death-censored graft survival rates were 54.5%, 71.8%, and 87% (p=NS) in DCD, ECD, and SCD KTs, respectively. The incidences of acute rejection and major infection were 14% and 45%, respectively.

Discussion

The aging donor and recipient populations have led to new challenges in KT. An increasing proportion of elderly patients are receiving renal replacement therapies for ESRD and this age group represents the fastest growing population being placed on the kidney waiting list [1]. Although being placed on the waiting list has become more common for the elderly ESRD population, it remains reserved for the relatively few. For example, of prevalent dialysis patients in 2010, 40.5% of those aged 18-44 were placed on the waiting list compared to 13.7% of those aged 65-74 and 1.6% of those aged 75 and older [1-3]. For elderly patients on the waiting list, both their mortality and their willingness to accept a kidney from an ECD were 1.5 times higher than the remainder of younger patients on the waiting list [1-3]. In 2016, >100,000 candidates are on the kidney waiting list yet the total annual number of KTs (both living and DD) performed in the US for the past several years has remained flat at about 17,000. Because of the increasing disparity between the growing number of KT candidates and stagnant organ supply, median waiting times and mortality on the kidney waiting list have doubled in the new millennium [1-3]. Data from the United States Renal Data Systems (USRDS) report show that within 3 years of listing, older patients are more likely than younger patients to receive a DD KT, less likely to receive a living donor KT, and more likely to die before receiving any KT [1,2]. Median (national) waiting times to transplant for the elderly (≥ age 65) are 3.9 years compared to almost 5 years for patients aged 18-49 in the US. Median waiting times are dependent on a number of factors including not only age but blood type, geographic location, level of sensitization, availability of a living donor, and willingness to accept a kidney from an older (expanded criteria) donor. However, one study demonstrated that 46% of KT candidates ≥60 years of age placed on the waiting list will actually die before receiving a DD KT [22]. In 2013, 3101 patients aged 65 and older received KTs in the US, which represented nearly 18% of overall KT activity. The corresponding numbers a decade ago were 1687 patients and 11% of activity, respectively [1,2].

Older donor and recipient age are important prognostic factors in KT. Recipient age remains a major risk factor for mortality following transplant, with the risk of death increasing proportionately with advanced age and specific age-related co-morbidities [6-9,11-14,16-19]. Unlike younger patients, DWFG is the primary cause of graft failure in the elderly. However, biological age is clearly more important that chronological age, so identification and optimization of modifiable risks is of paramount magnitude in the elderly. In addition, minimization of waiting time is of critical import, particularly for the elderly patient who is already on dialysis. On the other hand, up to 50% of ECD kidneys are discarded [2]. Consequently, a number of strategies have been proposed including donor and recipient matching by age, projected longevity, medical risks, serology, histocompatibility, size, and nephron mass [23-31]. Because recipient age has been shown to be an independent risk factor for graft loss in older patients secondary to DWFG and CAN, many studies have demonstrated that death-censored graft survival in older patients is comparable to or even greater than survival rates seen in younger patients [16-19,23-31].

Among the treatment modalities that are available for patients with ESRD, KT is preferred and confers the highest benefit because it is associated with an improved life expectancy, better quality of life, and is cost-effective both for patients and payers [4,8,10,12,32-42]. However, with the increasing disparity between the steadily rising number of potential transplant candidates and relatively static number of available organs, ethical concerns have been expressed that providing elderly ESRD patients with scarce DD kidneys may not represent a worthwhile investment [39,40]. Because one of the primary goals of renal replacement therapy is to maximize patient survival, and transplantation of older patients has an inherently higher mortality risk, diverting more kidneys to the ever-increasing older ESRD population may result in significant limitations imposed on the useful life of donor organs. However, studies have demonstrated that KT offers both a cost and survival benefit to virtually all patients with ESRD irrespective of age [4,8,10,12,32-42]. In the new millennium, a changing landscape of KT has occurred with increasing numbers of older donors and recipients, a more liberal window of acceptable risk, gradually improving outcomes, and a steadily burgeoning disparity between organ supply and demand.

According to USRDS data, the presence of ESRD is associated with a 75-80% decrease in years of remaining life expectancy at every age compared to the non-ESRD population although the absolute number of years lost is obviously less at more advanced ages [1]. For example, the mean expected remaining lifespan for the general population who are aged 70-74 years is 13.9 years, with women living approximately 2 years longer than men [43]. For those in the 75-79 age group, the mean expected remaining lifespan is 10.7 years. For patients with ESRD on

dialysis, mean expected lifespans in these same age groups are 3.6 and 3.1 years, respectively [1]. In comparison, the mean expected remaining lifespans for KT recipients who are aged 70-74 years and 75-79 years are 9.8 and 8 years, respectively. A previous review of SRTR data revealed that KT recipients who are aged ≥70 years had a 41% lower overall risk of death compared to candidates on the wait list in the same age group [37]. USRDS data demonstrate that the 1-, 3-, and 5-year patient survival rates for dialysis patients on the waiting list for KT in the 70-74 year age group were 73.3%, 54.3%, and 27.1%, respectively [1]. In our study, the corresponding 1-, 3-, and 5-year patient survival rates for septuagenarians following KT were 94.6%, 85.7%, and 78.6%, respectively. Nearly half of the deaths and >50% of the DWFGs occurred more than 5 years following KT. Using UNOS data, for all patients age 70-74 years who underwent DD KT in the US between 11/1/02 and 10/31/2007, 1-, 3-, and 5-year patient survival rates were 90.2%, 78.9%, and 66.1%, respectively [44]. The corresponding rates for patients 75-79 years of age were 86.9%, 73.8%, and 59.9%, respectively. In other words, KT in septuagenarians conservatively doubles their mean expected remaining lifespan although it does not achieve the mean expected remaining lifespan of the general population.

Variable **Mean ± SD**	**70-74 years of age (n=70)**	**≥75 years of age (n=44 KTs in 42)**	**P-value**
Patient survival	26 (79%)	31 (94%)	0.15
Kidney graft survival	21 (64%)	22 (67%)	NS
Follow-up (months)	60 ± 24	58 ± 22	NS
2-year patient survival	32 (97%)	31 (94%)	NS
2-year kidney graft survival	30 (91%)	27 (82%)	NS
Death-censored graft survival	21/26 (81%)	22/32 (69%)	0.37
Death with a functioning graft	7 (21%)	1 (3%)	0.05
Delayed graft function	11 (33%)	8 (24%)	NS
Length of initial hospital stay (days)	6.4 ± 2.0	5.9 ± 2.4	NS
Acute rejection	6 (18%)	3 (9%)	NS
Major infection	7 (21%)	5 (15%)	NS
Surgical complications	3 (9%)	0	NS
Re-admissions	14 (42%)	10 (30%)	NS
Serum creatinine (mg/dl)			
1 month	1.8 ± 1.0	1.8 ± 0.9	NS
12 months	1.5 ± 0.9	1.7 ± 0.9	NS
aMDRD GFR (ml/min)			
1 month	43 ± 16	46 ± 21	NS
12 months	50 ± 17	50 ± 22	NS

Table 2: Outcomes in recipients 70-74 compared to ≥75 years of age.

In our study (in which 2/3rds of recipients received ECD kidneys), 1-, 3-, and 5-year uncensored graft survival rates were 90.4%, 76.3%, and 67.5%, respectively. DWFG accounted for 2/3rds of the graft losses, and nearly all of the late graft losses were secondary to DWFGs. Cardio/cerebrovascular events, infection, or malignancy accounted for 72% of deaths. Actuarial graft survival was no different in patients 70-74 compared to ≥75 years of age. At present, 54 of the 66 surviving patients (81.8%) have functioning grafts. These results compare favorably with registry data and support the contention that appropriately selected septuagenarians are acceptable transplant candidates and may be better served with an ECD kidney than a younger population [38]. Moreover, because the mean expected graft lifespan of an ECD kidney is 6-8 years, one might contend that transplanting an ECD kidney into a septuagenarian matches graft and patient longevity [39-41].Consequently, in the new millennium, the annual number of DD KTs performed in patients who are ≥70 years of age in the US has increased from 291 in year 2000 to >700 per year since 2007 [1,43,44].

A total of 14 septuagenarians underwent DKT, which was associated with a 50% reduction in DGF, a nearly 50% reduction in waiting time, and good outcomes (100% one-year and 71% 4.5-year patient and graft survival rates). The presence of DGF was associated with an increased rate of graft loss but not mortality, whereas DD category exhibited a

stepwise improvement in outcomes for DCD (lowest), ECD (intermediate) and SCD (highest) KTs [45-47].

Based on this experience, because biological age is more important than chronological age, we believe that there exists a cohort of relatively low risk septuagenarians who predictably may do well with an ECD kidney if it results in shorter waiting (or dialysis) time. Donor and recipient age-matching is logical because it provides a physiological match (nephron mass demand and supply), an immunological match (immunogenicity/immune response), a logistical match (prevention of deaths on the waiting list and organ discard), and a longevity match (limited life and graft expectancy). One might contend that an important goal of KT is to have the transplanted organ "outlive" the patient. In other words, DWFG could be considered the ultimate endpoint of transplantation with the caveat that death was neither accelerated nor related to the consequences of transplantation and the requisite chronic immunosuppression. However, another important objective is to avoid large "mismatches" of donor kidney and recipient longevity so as to not lose kidney graft life-years. There is no question that a spectrum of DD kidney quality exists and that many recovered kidneys are discarded because of concerns about both initial graft function as well as expected kidney lifespan [2,3]. Unfortunately, predictive tools and scoring systems are not always reliable and therein lies the challenge of determining not only the "usability" of a given kidney but also choosing the most appropriate recipient. In addition, what is missing from our study is an accurate, objective and reproducible pretransplant assessment of function, social support, and global health status in the elderly, which may be better defined and captured in future studies with the application of frailty instruments to the candidate KT population. However, age by itself is not an adequate predictor of overall risk, and some elderly patients may not predictably do well with an ECD (or SCD) kidney regardless of waiting time. Understanding the factors that determine outcomes in the elderly is essential to optimize not only recipient selection and management but also choice of donor organ as well.

In summary, our single-center study supports the contention that KT is a viable therapeutic modality for elderly ESRD patients, particularly with marginal donor kidneys that may not necessarily be appropriate for younger recipients who have greater projected long-term survival. A highly organized pre-transplant screening, selection, and waitlist monitoring process coupled with a robust immunosuppressant protocol and intensive post-transplant surveillance ensures that kidneys transplanted into the elderly are used to their full potential and truly enhance quality of life and life expectancy without necessarily compromising graft life-years. We no longer consider advanced chronological age to be a contraindication to either organ donation or transplantation.

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