
Dual Kidney Transplantation from Donors at the Extremes of Age



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- BACKGROUND:** The study purpose was to analyze outcomes in recipients of pediatric dual en bloc (PEB) kidneys from small pediatric donors (SPDs, age ≤ 3 years) and dual kidney transplants (KTs) from adult marginal deceased donors (DDs) in the context of the Kidney Donor Profile Index (KDPI).
- STUDY DESIGN:** This was a single center retrospective review. Recipient selection included primary transplant, low BMI, low immunologic risk, and informed consent. All patients received antibody induction with FK/MPA/ \pm prednisone.
- RESULTS:** From 2002 to 2015, we performed 34 PEB and 73 adult dual KT. Mean donor ages were 17 months for the PEB and 59 years for the dual KT; mean KDPIs were 73% for PEB and 83% for dual KT, and mean cold ischemia times were 21.0 hours for PEB and 26.5 hours for dual KT. Adult dual KT recipients were older (mean age 38 years for PEB and 60 years for dual KT) and had shorter waiting times (mean 25 months for PEB and 12 months for dual KT). With a mean follow-up of 7.6 years, actual patient survival (88% for PEB and 62% for dual KT) and graft survival (71% for PEB and 44% for dual KT) rates were higher in PEB compared with dual KT. Death-censored kidney graft survival rates were 77% for PEB and 58% for dual KT. Delayed graft function (DGF) rates were 15% for PEB and 23% for dual KT; incidences of DGF in single kidney transplantations from SPDs and adult nonmarginal DDs were 20% and 32%, respectively. Based on actual 5-year graft survival rates, the adjusted KDPIs for dual PEB and dual KT were 3% and 60%, respectively.
- CONCLUSIONS:** Acceptable mid-term outcomes are associated with PEB and adult dual KT, which may expand the donor pool and prevent kidney discard. The KDPI is inaccurate for predicting outcomes from either PEB from SPDs or dual KT from adult marginal DDs, which may prevent acceptance of these organs. (J Am Coll Surg 2019;228:690–705. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)
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The need to expand the organ donor pool remains a formidable challenge in kidney transplantation (KT). One strategy to increase donor potential by reducing organ wastage at the extremes of donor age is the transplantation of 2 kidneys from the same donor into a single

recipient.¹⁻⁵ For small pediatric donors (SPDs) age 3 or younger, it is estimated that there are 800 unrealized potential donors per year in the United States.^{2,6} The notion of pediatric dual en bloc (PEB) KT dates back to the pioneering studies of Carrel⁷ in 1908, and the first successful dual PEB KT performed in an adult recipient was reported in 1972.⁸ At present, dual PEB KT account for only 2% of all deceased donor (DD) KT in the US, representing about 200 to 300 cases per year.⁹ At the other end of the age spectrum, either performing adult dual KT from expanded criteria donors (ECDs) or marginal DDs represents another approach to improving kidney use in situations in which kidney discard rates are high because of concerns regarding overall quality, limited functional capacity, and lower projected life span of these singly transplanted organs.^{3-5,10-16} The practice of dual KT

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Abbreviations and Acronyms

AKI	= acute kidney injury
DCD	= donation after cardiocirculatory death
DD	= deceased donor
DGF	= delayed graft function
ECD	= expanded criteria donor
GFR	= glomerular filtration rate
KAS	= Kidney Allocation System
KDPI	= Kidney Donor Profile Index
KT	= kidney transplantation
PEB	= pediatric en bloc
PNF	= primary nonfunction
SCD	= standard criteria donor
SPD	= small pediatric donor
UNOS	= United Network for Organ Sharing

from older adult DDs dates back to the mid-1990s, with initial experiences reported by the Stanford and Maryland groups.^{3,17-19} In March 1997, the United Network for Organ Sharing (UNOS) introduced policy specific to “double kidney allocation.” At present, nearly 3% of adult DDs in the US are eligible for double allocation, yet only 0.5% of DD KT_s (about 60) are performed as dual KT_s annually.⁹ For DD kidneys meeting double allocation criteria, >50% are ultimately not transplanted. Deceased donors with marginal renal functional capacity represent a large proportion of potential kidneys doomed to either discard or nonrecovery.^{3-5,9-16}

Because of comprehensive (and controversial) efforts that spanned more than a decade, the new Kidney Allocation System (KAS) for DD kidneys was implemented in December 2014 in the US.^{20,21} Some of the goals of the new KAS were to improve utility and equity by matching donor and recipient projected outcomes while reducing differences in access for specific patient populations. Central to the paradigm of the new KAS was the Kidney Donor Profile Index (KDPI), which is a derivative of the Kidney Donor Risk Index (KDRI).²²⁻²⁸ The Kidney Donor Risk Index is an estimate of graft longevity based on a multivariable analysis of risk factors for graft loss after DD KT.²²⁻²⁴ When the concept of the Kidney Donor Risk Index model for DD kidneys was first developed, the authors identified human leukocyte antigen match, cold ischemia time, en bloc, and dual kidney coefficients as significant factors in addition to the 10 variables that were ultimately included in the KDPI score. However, when the KDPI was implemented into DonorNet in 2012, it omitted these 4 variables without recalculating the model because these variables may not be known at the time of the match run. In other words, the KDPI score is exclusive to single KT and is not meant to be

predictive of (or even used for) dual KT. Unfortunately, use of the KDPI has become an important tool in both donor assessment and decision-making regarding kidney use. The purpose of this study was to analyze outcomes in recipients of dual PEB kidneys from SPDs and dual KT_s from adult marginal DDs in the context of the KDPI scoring system.

METHODS

Study design

We conducted a retrospective chart review of all primary adult DD KT_s performed at our center, from 2002 to 2015. During this study period, 1,259 primary DD KT_s were performed, including 733 from standard criteria donors (SCDs), 420 from ECDs, 73 dual KT_s from adult marginal DDs, and 33 dual PEB KT_s. An additional dual PEB KT was performed as a retransplant and is included in the analysis. Standardized donor and recipient selection and management algorithms were followed during the period of study.^{5,29-37} In general, we followed United Network for Organ Sharing (UNOS) criteria for dual KT allocation, which stipulate that kidneys from DDs 18 years of age or older must be offered singly unless the donor meets at least 2 of the following conditions and the local organ procurement organization would not otherwise use the kidneys singly: 1. DD \geq 60 years of age; 2. Estimated DD creatinine clearance (creatinine clearance) $<$ 65 mL/min based on serum creatinine level on admission; 3. Rising serum creatinine level ($>$ 2.5 mg/dL) at time of retrieval; 4. History of medical disease in DD (defined as either longstanding hypertension or diabetes mellitus); and 5. Adverse DD kidney histology (defined as moderate to severe glomerulosclerosis $>$ 15% and $<$ 50%).⁵

Definitions

For the purpose of this study, SPDs were defined as 3 years of age or younger. Dual PEB KT was classified as keeping both donor kidneys attached to the aorta and inferior vena cava, which are then used as arterial and venous conduits for the subsequent transplant into a single recipient. Marginal DDs were characterized by estimated kidney function (see below). Expanded criteria donors were defined by the UNOS definition as all DDs 60 years old or older and DDs 50 to 59 years of age with any 2 of the following criteria: history of DD hypertension; cerebrovascular cause of brain death; or DD terminal serum creatinine level $>$ 1.5 mg/dL.^{10,11} Standard criteria donors were defined as all DDs not meeting the criteria for ECD. Donation after cardio-circulatory death

(DCD) donors were identified as organ recovery after declaration of death by cardio-circulatory arrest in the setting of voluntary withdrawal of life support.³⁰ Delayed graft function (DGF) was defined as the need for dialysis (for any reason) in the first week post-KT. Primary non-function (PNF) was defined as the failure to render the patient dialysis-free after KT, absence of a decline in serum creatinine level in a pre-emptively transplanted patient, or early allograft nephrectomy post-KT. Renal allograft loss was determined as death with a functioning graft, allograft nephrectomy, resumption of dialysis, kidney retransplantation, or return to the pretransplant serum creatinine level in a pre-emptively transplanted patient.

The KDPI is a national scoring system that was developed to rank order the quality of kidneys, as defined by an aggregate population relative risk.²⁰⁻²⁸ The KDPI explicitly incorporates 10 donor factors (age, height, weight, ethnicity, hypertension, diabetes, cause of death, serum creatinine level, hepatitis C status, and DCD status) to assign an overall score (0% to 100%) in which a lower score describes a kidney with a projected longer lifespan. A KDPI \geq 85% delineates lower quality kidneys that were categorized as ECD kidneys in the previous binary system of classification (ECD vs SCD). The KDPI was introduced in 2012 and then fully implemented in December 2014 as part of the new national KAS, and it projects long-term graft survival. Implementation of the KDPI in the context of the new KAS was expected to improve kidney use by matching patient and graft longevity. For purposes of this study, KDPI projections were based on UNOS data as of April 4, 2014 (that included primary adult deceased donor kidney transplants from 2004 to 2011), which approximates the study period.

Donor evaluation and management

For SPDs, we relied mainly on donor body weight and actual kidney size and anatomy, either to determine whether to use the kidneys for dual PEB, single KT, or to refuse the offer.³⁷ In our dual PEB KT experience, the youngest donor age was 5 months (7.7 kg body weight) and the lowest donor weight was 6.8 kg (7 months of age). Donor age was less useful than either donor weight or kidney size in our decision-making for kidney use because we usually refused kidneys from donors $<$ 8 kg or kidneys $<$ 6 cm in length. In comparison, for marginal DDs, the Cockcroft-Gault formula was used to estimate adult DD creatinine clearance, using both the admission and terminal donor serum creatinine level and adjusted body weight to calculate a range of DD kidney function in order to determine single or dual KT

into a single recipient.^{5,17,29-36,38} If the estimated DD creatinine clearance was $>$ 65 mL/min, then a single KT was usually performed. If the estimated DD creatinine clearance was 30 to 65 mL/min, then an adult dual KT was performed, preferably into an older recipient with a BMI $<$ 30 kg/m².^{5,29-36} If the estimated DD creatinine clearance was $<$ 30 mL/min (in the absence of acute kidney injury [AKI]), then the kidney(s) were not accepted for transplant at our center. However, over time and with increased experience, some of the above criteria were liberalized in the setting of dual KT. The oldest donor in this experience was 78 years. Other marginal DD "contraindications" for DKT included the presence of disseminated intravascular coagulation or rhabdomyolysis, extremely large kidneys ($>$ 13 cm in length, because of space considerations in the recipient), presence of complex vascular or urologic anatomy (multiple vessels or ureters), glomerulosclerosis $>$ 35%, and projected prolonged cold ischemia time because of logistical issues. In most cases, both kidneys were accepted on "full waivers," as many of these kidneys were targeted for discard in the absence of our use for dual KT. A "waiver" implies that a kidney acquisition charge does not have to be paid by the accepting center if the kidney(s) are not transplanted, on condition that documentation is provided as to why the kidneys were not used (for example, poor pump parameters or unexpected anatomic findings). However, with application of the above donor selection criteria, it was unusual (probably $<$ 5%) that accepted kidneys were discarded, although we do not specifically track these data.

Kidney preservation

Kidneys from SPDs were managed with cold storage preservation. Whenever possible, however, adult marginal DD kidneys were placed on machine preservation to minimize preservation injury, maintain functional reserve, and provide another means of assessment.³⁵ Although pump parameters were not exclusively used to discard kidneys, a flow rate $>$ 60 mL/min and a resistance $<$ 0.50 mm Hg/mL/min after a minimum of 6 hours on machine preservation were considered thresholds for dual KT use.^{5,35} If the kidneys were pumping well, cold ischemia times \geq 36 hours were considered acceptable. If the pump flows were $<$ 60 mL/min or resistances were $>$ 0.5 mm Hg/mL/min, then the kidneys were not transplanted at our center. In addition, the logistics of transplanting both kidneys with an acceptable ($<$ 40 hours) cold ischemia time was a consideration, particularly if the kidneys were being imported from another donor service area and not initially placed on machine preservation locally. Because most of the kidneys were not initially offered as

"2 for 1" and many were imported from other organ procurement organizations, prolonged cold ischemia time was not uncommon. Consequently, *ex vivo* assessment of the kidneys based on pump parameters was an important part of the management algorithm. However, dual kidney discard based on poor pump parameters exclusively was rare. Although dual kidney discard was not specifically tracked, the primary reasons for dual kidney discard were unexpected anatomic findings or damage to the kidneys.

Histologic assessment

Donor kidney biopsy was used to assist in the evaluation of pre-existing and terminal renal parenchymal injury in adult marginal DDs but not in SPDs. Renal cortical wedge biopsies for frozen section were performed and evaluated for the presence and degree of glomerulosclerosis, interstitial fibrosis, chronic interstitial inflammation, tubular atrophy, and vascular hyalinosis or sclerosis.^{29,39-44} Moderate to severe vascular or interstitial changes, tubular atrophy, or glomerulosclerosis $\geq 35\%$ were a contraindication to kidney use. For paired kidney biopsies displaying disparate histologic results, a mean of the 2 biopsies was estimated to assist in the determination of dual kidney use or refusal. Although DD kidney biopsies were performed in most cases of dual KT, a histologic score was not specifically determined because many biopsies were performed at the donor hospital, and specimens were not available for our own pathologist to review.

Recipient evaluation and selection

At our center, no specific upper age limit was an absolute contraindication to dual KT; the oldest DKT recipient in this series was 79 years. All patients underwent a comprehensive pre-transplant medical, psychosocial, and financial evaluation, with emphasis placed on the cardiovascular system to determine operative risks and physiologic age.^{5,29-36,45} Specific exclusion criteria in the elderly included the presence of dementia, nursing home residence, poor overall functional status or frailty, lack of social support, advanced disease or organ failure in an extra-renal organ system, recent malignancy, limited life expectancy, or severe cardiac or vascular disease.^{5,29-36,45} Patients approved for KT were stratified by risk, and a decision was made whether or not to list the patient as willing to accept a dual kidney based on the medical assessment and discussions with the patient and his or her referring physician. In particular, the predicted ability to tolerate a longer and more complicated operative

procedure with perhaps a higher incidence of DGF were important considerations.

For dual PEB KT, recipient selection followed UNOS guidelines (the "match run"), but was also based on younger age (but not pediatric patients). However, similar to donor assessment, body weight was more useful in adult recipient selection than age. We attempted to select recipients weighing less than 200 lbs in order to avoid large mismatches between kidney and recipient size. In addition, we selected low immunologic risk patients, including primary transplants with a low panel reactive antibody (PRA) level (usually 0%), human leukocyte antigen-matching, and negative T and B cell flow cytometric crossmatches.³⁷ All KTs from SPDs were performed with informed consent from the recipient. Finally, severe hypertension, presence of an abnormal urinary bladder (either anatomically or functionally), high risk for recurrent kidney disease, and history of thrombophilia or need for anticoagulation were considered contraindications to dual PEB KT from SPDs.

For adult dual KT, whenever possible, marginal DD kidneys were used by matching estimated renal functional capacity to recipient need.^{5,29-36} With marginal DD kidneys, recipient selection was usually not by standard UNOS kidney allocation, but based on older age (>50 years) and smaller size (weight < 200 lbs and BMI < 30 kg/m²), matching and identifying low immunologic risk patients such as primary KT, human leukocyte antigen matching, low panel reactive antibody level, and informed consent.^{5,29-36} Other recipient characteristics unique to adult marginal DD dual kidney consideration were adequate space in the pelvis (extremely small stature or presence of large polycystic kidneys were relative contraindications), favorable vascular anatomy (no severe long segment concentric iliac atherosclerosis), adequate bladder capacity (to accommodate 2 ureteral anastomoses), no chronic anticoagulation (warfarin or clopidogrel) or history of thrombophilia, adequate cardiac function and reserve (ejection fraction $> 40\%$ to 50% , no atrial fibrillation or significant valvular disease), absence of either significant pulmonary hypertension or systemic hypotension, and no history of previous pelvic surgery or irradiation.^{5,32,33}

During the period of study, no other transplant centers in our donor service area were actively performing adult dual KTs from marginal DDs. Consequently, we were able to select an appropriate candidate for adult dual KT who typically was lower on our match run list because all patients at other centers had been "coded out" for either single or dual kidney use.

Operative technique for dual pediatric en bloc and dual kidney transplantation

Small pediatric donor kidneys were recovered en bloc with aorta, inferior vena cava, and bilateral ureters in continuity; no attempt was made to perform any dissection along the aorta, vena cava, or renal hila in the donor.³⁷ Back bench preparation of the PEB specimen included oversewing the supra-renal aorta and vena cava with careful, meticulous dissection of the infra-renal aorta and vena cava, with individual ligation of lumbar and mesenteric branches. Minimal dissection was performed in the renal hila in order to preserve any accessory vessels. Perinephric fat was left on the kidneys so that suture fixation of the upper poles antero-medially could be performed to maintain correct graft orientation. The PEB allograft was transplanted extraperitoneally with end-to-side anastomoses between the distal vena cava and aorta to the distal right external iliac vein and artery, respectively. Separate parallel extravesical ureteroneocystostomies over 2 indwelling stents were performed to the dome of the bladder, attempting to make the ureters as short as possible. Pediatric en bloc allografts were affixed to either the lateral pelvic wall or retroperitoneum using perinephric fat or capsule in order to avoid torsion.

Dual kidneys from adult marginal DDs were procured in the usual fashion, separated at the time of procurement, preserved as mentioned previously, prepared separately on the back table, and then transplanted sequentially, either through a lower midline intraperitoneal ($n = 10$), lower midline extraperitoneal ($n = 5$), bilateral extraperitoneal ($n = 4$), or unilateral extraperitoneal approach ($n = 54$). Since 2008, we have exclusively used the unilateral extraperitoneal approach, which decreases operating time by at least 1 hour compared with the bilateral procedure.^{5,32,33} Standard end-to-side vascular anastomoses to the iliac vessels were performed followed by separate dual anterior extravesical ureteroneocystostomies over 2 separate ureteral stents. The most common scenario involved vascular implantation of the donor left kidney, first to the common iliac vessels followed by vascular implantation of the donor right kidney second, and more distally on the external iliac vessels. After confirmation of vascular patency and hemostasis, the kidneys were then positioned “piggyback” to avoid torsion, twist, or tension to any of the vascular anastomoses. At this point, the ureters were cut to length and separate urologic implantations to the bladder were performed over ureteral stents. The dual KT procedure usually lasted 1 to 2 hours longer than a conventional single KT from an adult DD.

Immunosuppression

All recipients received depleting antibody induction with either multidose rabbit antithymocyte globulin or alemtuzumab 30 mg intravenous as a single intraoperative dose.^{5,37,46} Maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil (2 g/day), and either rapid tapering doses of steroids or early steroid withdrawal based on immunologic risk stratification. Target 12-hour tacrolimus trough levels were 6 to 10 ng/mL for all recipients; recipients aged 60 years and older received a half dose mycophenolate mofetil (1 g/day) in 2 divided doses.^{5,29-36,46} Early steroid withdrawal was performed in low-risk patients; steroids were continued in high immunologic risk patients such as patients receiving retransplants, patients with a current panel reactive antibody level $> 20\%$, and patients experiencing DGF.⁴⁶ Steroids were also maintained in patients already on prednisone, those at risk for recurrent disease, and in young African-American recipients.

Post-transplant management

All patients received surgical site prophylaxis with a first-generation cephalosporin for 24 hours, antifungal prophylaxis with nystatin or fluconazole for 1 month, and anti-Pneumocystis prophylaxis with sulfamethoxazole-trimethoprim (dapson if allergic to sulfa) for at least 12 months. Antiviral prophylaxis consisted of oral valganciclovir for 3 to 6 months, depending on donor and recipient cytomegalovirus serologic status. Specifics regarding drug dosing and duration have been published previously.^{5,29-37,46} Most patients received aspirin prophylaxis. Because of 2 ureteral implantations into the bladder, the urethral catheter usually remained in place for a minimum of 4 to 5 days. Treatment of hypertension, hyperlipidemia, anemia, diabetes, and other medical conditions was initiated as indicated, aiming to maintain the blood pressure $< 140/90$ mm Hg, fasting serum cholesterol < 200 mg/dL, hematocrit $> 27\%$, and fasting blood sugar < 126 mg/dL. Post-transplant renal allograft function was evaluated by measuring serum creatinine levels as well as calculating glomerular filtration rate 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

Table 1. Donor, Preservation, Transplant, and Recipient Characteristics

Variable	Dual KT (n = 73)	PEB (n = 34)
Donor age, y, mean ± SD	59.4 ± 11.5	1.4 ± 0.8
Donor age ≥65 y, n (%)	30 (41)	0
Donor weight, kg, mean ± SD	75.9 ± 18.5	11.0 ± 2.6
Donor sex, male, n (%)	28 (38.4)	17 (50)
Donor race: African-American, n (%)	16 (22)	13 (38)
Donor BMI, kg/m ² , mean ± SD	26.4 ± 5.75	17.3 ± 2.8
ECD, n (%)	46 (63)	0
DCD donor, n (%)	17 (23)	6 (17.6)
Calculated creatinine clearance, mL/min, mean ± SD	66 ± 36	99 ± 50
Pre-retrieval serum creatinine, mg/dL, mean ± SD	1.3 ± 0.6	0.37 ± 0.26
Terminal serum creatinine ≥ 2.0 mg/dL, n (%)	11 (15)	0
Imported kidney, n (%)	32 (43.8)	17 (50)
Machine preservation, n (%)	63 (86)	0
Pump time, h, mean ± SD	12.4 ± 6.0	
Pump flow, mL/min, mean ± SD	98 ± 29	
Pump resistance, mm Hg/mL/min, mean ± SD	0.31 ± 0.13	
Cold ischemia time, h, mean ± SD		
First or only kidney	25.8 ± 8.6	21.0 ± 7.8
Second kidney	27.2 ± 8.6	
Cold ischemia time ≥ 36 h, n (%)	13 (18)	1 (2.9)
Human leukocyte antigen-mismatch, mean ± SD	4.1 ± 1.3	4.2 ± 1.4
0% Panel reactive antibody, n (%)	58 (79.5)	30 (88)
Panel reactive antibody ≥10%, n (%)	11 (15)	2 (5.9)
Cytomegalovirus donor+/recipient-, n (%)	13 (18)	5 (14.7)
Kidney Donor Profile Index, mean ± SD	83 ± 18	73 ± 9
Recipient age, y, mean ± SD	60 ± 11	38 ± 12
Recipient age ≥ 65 y, n (%)	26 (36)	1 (2.9)
Recipient weight, kg, mean ± SD	73.1 ± 14.6	72.2 ± 14.7
Recipient sex, male, n (%)	29 (39.7)	21 (62)
Recipient race, African American, n (%)	32 (43.8)	17 (50)
Recipient: diabetes, n (%)	28 (38)	6 (17.6)
Recipient BMI, kg/m ² , mean ± SD	26.2 ± 4.4	25.8 ± 5.3
Duration of dialysis pretransplant, mo, mean ± SD	25 ± 21	41 ± 27
Waiting time, mo, mean ± SD	12 ± 12	25 ± 14
Retransplant, n (%)	0	1 (2.9)

DCD, donation after cardiocirculatory death; ECD, expanded criteria donor; KT, kidney transplant; PEB, pediatric en bloc.

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, actuarial, and death-censored survival rates were determined. Survival curves were computed and compared using the Kaplan-Meier method and the log-rank test. A 2-tailed value of *p* < 0.05 was considered significant.

RESULTS

From 2002 to 2015, we performed 34 dual PEB and 73 adult dual KTs; 17 dual PEB (50%) and 32 adult dual

marginal DD kidneys (44%) were imported from other donor service areas. Of the 73 dual KTs, 46 were from ECDs, 17 from DCD donors, and 10 from adult SCDs; 7 kidneys were transplanted from adult donors with AKI (Table 1). Nearly all marginal DD kidneys were refused by multiple centers and many were targeted for discard. Mean estimated marginal DD creatinine clearance was 66 mL/min; 50 marginal DDs (68%) had an estimated creatinine clearance < 65 mL/min and 11 (15%) had a terminal serum creatinine level ≥ 2.0 mg/dL. Mean donor ages were 17 months for SPD and 59 years for marginal DD, mean donor weights were 11.0

Table 2. Operative Results

Variable	Dual KT (n = 73)	PEB (n = 34)
Overall patient survival, n (%)	45 (61.6)	30 (88.2)
Patient survival, n (%)		
1-y	70 (95.9)	34 (100)
5-y	57/71 (80.3)	26/28 (92.9)
Overall graft survival	32 (43.8)	24 (70.6)
Graft survival, n (%)		
1-year	66 (90.4)	32 (94.1)
5-year	49/71 (69)	22/28 (78.6)
Follow-up, mo, mean ± SD	92 ± 44	91 ± 40
Death-censored graft survival, n (%)	32/55 (58.2)	24/31 (77.4)
Death-censored graft survival, n (%)		
1-y	66/70 (94.3)	32/34 (94.1)
5-y	49/62 (79)	22/26 (84.6)
Death with a functioning graft, n (%)	18 (24.7)	3 (8.8)
Dialysis-free rate in survivors, n (%)	32/45 (71.1)	24/30 (80)
Delayed graft function, n (%)	17 (23)	5 (14.7)
Primary non-function/thrombosis, n (%)	2 (2.7)	1 (2.9)
Days to serum creatinine < 3.0 mg/dL, mean ± SD	7.1 ± 7.8	4.7 ± 4.5
Initial length of stay, d, mean ± SD	7.1 ± 5.7	5.4 ± 2.9
Acute rejection in first year, n (%)	11 (15)	2 (5.9)
Major infection in first year, n (%)	19 (26)	7 (20.6)
Surgical complications, n (%)	10 (13.7)	1 (2.9)
Readmissions in 1 st year, n (%)	30 (41)	14 (41.2)
Serum creatinine, mg/dL, mean ± SD		
12 mo	1.5 ± 0.6	1.2 ± 0.3
24 mo	1.5 ± 0.5	1.1 ± 0.8
Glomerular filtration rate, mL/min/1.73m ² , mean ± SD		
12 mo	53 ± 25	72 ± 18
24 mo	50 ± 22	75 ± 24

PEB, pediatric en bloc; KT, kidney transplant.

kg for SPD and 75.9 kg for marginal DD, and proportions of male donors were 50% for SPD and 38% for marginal DD (Table 1). Mean donor serum creatinine levels were 0.37 for SPD and 1.3 mg/dL in marginal DD, mean cold ischemia times were 21.0 for SPD and 26.5 hours for marginal DD (including 24 with a cold ischemia time \geq 30 hours and 13 with a cold ischemia time \geq 36 hours), and mean KDPIs were 73% for SPD and 83% for marginal DD (Table 1).

Adult dual KT recipients were older (mean age 38.0 years in PEB and 60 years in dual KT), less frequently male (62% in PEB and 40% in dual KT), and had shorter waiting times (mean 25 months in PEB and 12 months in dual KT) and time on dialysis (mean 41 months in PEB and 25 months in dual KT, Table 1). One PEB and no dual KTs were performed as retransplants, and 82% of recipients had a panel reactive antibody level of 0%. Other

donor, preservation, transplant, and recipient characteristics are listed in Table 1.

With a mean follow-up of 7.65 years, actual patient survival (88% for PEB and 62% in dual KT) and graft survival (71% in PEB and 44% in dual KT) rates were higher in PEBs compared to dual KTs (Table 2). Death-censored kidney graft survival rates were 77% in PEB and 58% in dual KT. Actuarial patient, graft, and death-censored kidney graft survival rates for PEB and dual KT are shown in Figures 1 to 3. The longest surviving grafts after PEB and dual KT at our center are 15 and 16 years, respectively. Rates of DGF were 15% for PEB and 23% for dual KT; there was 1 case of thrombosis after PEB KT (secondary to fulminant recurrence of focal segmental glomerulosclerosis at 2 days post-KT in a pediatric recipient) and 2 cases of PNF with adult dual KTs (1 thrombosis, 1 PNF in dual kidneys from a

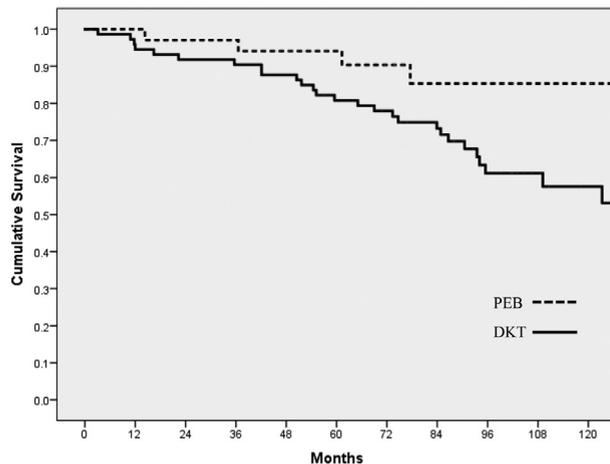


Figure 1. Actuarial patient survival rates of pediatric en bloc (PEB) and dual kidney transplant (DKT) recipients.

24-year-old donor with AKI and disseminated intravascular coagulation). Mean 2-year serum creatinine levels were 1.1 mg/dL in PEB and 1.5 mg/dL in dual KT; 2-year calculated GFR levels were 75 mL/min/1.73 m² in PEB and 50 mL/min/1.73 m² in dual KT.

One-year patient and graft survival rates were 100% and 94% for PEB compared with 96% and 90% dual KT, respectively (Table 2). In patients with a minimum follow-up of 5 years (n = 28 PEB and n = 71 dual KT), 5-year patient and graft survival rates were 93% and 79% in PEB compared with 80% and 69% in dual KT, respectively. Five-year death-censored kidney graft survival rates were 85% after PEB and 79% after dual KT (Table 2). Based on actual 5-year graft survival rates, the recalculated KDPIs for dual PEB and dual KTs were 3% and 60%, respectively.

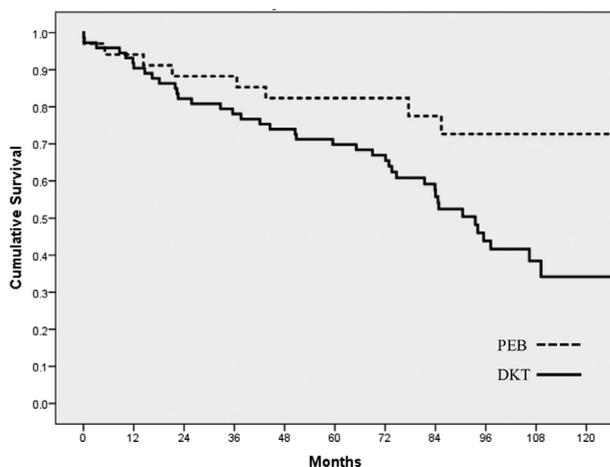


Figure 2. Actuarial kidney graft survival rates of pediatric en bloc (PEB) and dual kidney transplant (DKT) recipients.

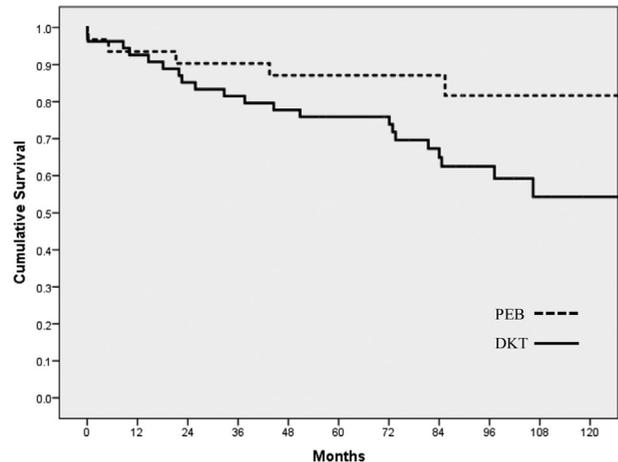


Figure 3. Actuarial death-censored kidney graft survival rates of pediatric en bloc (PEB) and dual kidney transplant (DKT) recipients.

In the PEB KT recipient group, there were 4 deaths and 10 graft losses. Patients #3 and #4 in our PEB KT experience were both teenagers who developed early graft failure (at 5 months secondary to noncompliance and at 2 days secondary to thrombosis/primary nonfunction, as noted previously, respectively). Patient #3 subsequently died 5 years later secondary to a hemorrhagic stroke (in the absence of retransplantation because of a high panel reactive antibody level). The only other deaths in the PEB KT group were adult males who experienced death with a functioning graft at 15 months, 37 months, and 78 months post-transplant (causes of death were unknown). The remaining 5 graft losses in the PEB KT group occurred at a mean of 84 months post-transplant and included 3 secondary to acute rejection and 2 patients with chronic allograft nephropathy and chronic rejection. Other than the 2 teenagers above, all remaining PEB KT recipients were adults.

Twenty-eight patients died at a mean of 64 months post-DKT. Eighteen patients experienced death with a functioning graft at a mean of 59 months post-transplant; the incidence of death with a functioning graft after DKT was 25%. An additional 10 patients died at a mean of 16.6 months after graft loss (and a mean of 75 months post-transplant). Fourteen of the deaths were secondary to cardiovascular, 2 infectious, 2 uremic, 2 malignancy, 2 respiratory failure, and 6 unknown causes. In addition to 18 deaths with a functioning graft, 23 patients experienced graft loss (n = 41 total) at a mean of 52 months post-DKT. Death with a functioning graft accounted for 44% of graft losses. Causes of graft loss independent of death included acute and chronic rejection (n = 7), chronic allograft nephropathy (n = 7), unknown (n = 3), primary nonfunction (n = 2), acute tubular

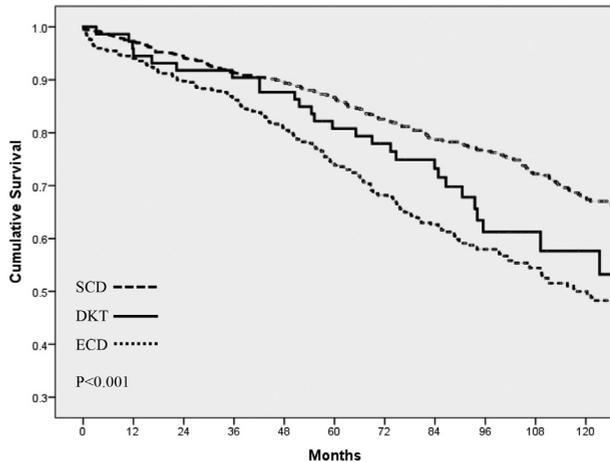


Figure 4. Actuarial patient survival rates of expanded criteria donor (ECD), standard criteria donor (SCD), and dual kidney transplant (DKT) recipients.

necrosis ($n = 2$), and 1 case each of malignancy and chronic pyelonephritis. Both patients who received kidneys with $>35\%$ glomerulosclerosis on donor kidney biopsy experienced early graft loss.

During the study period, we performed 420 primary single ECD KT; mean recipient age was 62 years (compared to 60 years in dual KT recipients) and mean KDPI was 83% (same as dual KT donors). With a mean follow-up of 7.5 years, actual patient (55% single ECD vs 62% dual KT) and kidney graft survival (37% single ECD vs 44% dual KT) rates were comparable. Death-censored kidney graft survival rates (52% single ECD vs 58% dual KT) were likewise similar. We also performed 733 primary single SCD KT during the period of study; mean recipient age was 52 years and mean KDPI was 47%. With a mean follow-up of 7.8 years, the actual patient and kidney graft survival rates were 72% and 54%, respectively; the death-censored graft survival rate was 67.5% (all $p < 0.0001$ compared with single ECD; all $p = \text{NS}$ compared with dual KT). Actuarial patient, graft, and death-censored graft survival rates for ECD, SCD, and dual KT are shown in Figures 4 to 6. However, the patient survival (72% with single SCD vs 88% with PEB KT, $p = 0.047$), kidney graft (54% with single SCD vs 71% with PEB KT, $p = 0.07$), and death-censored graft survival (67.5% single SCD vs 77% PEB KT, $p = 0.32$) rates were slightly higher after PEB KT compared with single SCD KT. For patients with a minimum follow-up of 5 years, actual 5-year graft survival rates after single SCD ($n = 620$) and single ECD ($n = 355$) KT were 74% and 58%, respectively, which translates to a KDPI of 46% (compared to 47% expected) for single SCD KT and a KDPI of 90% (compared to

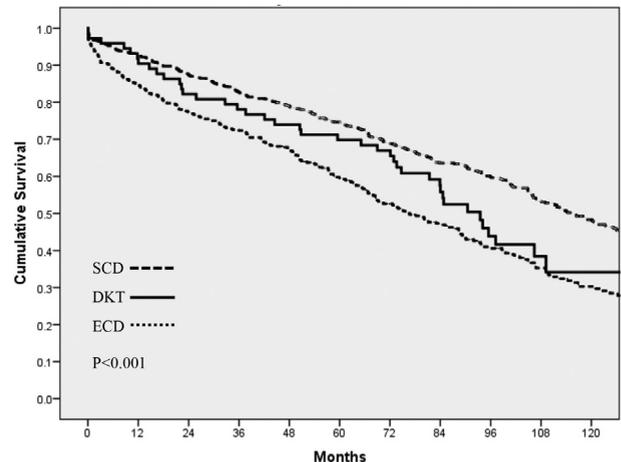


Figure 5. Actuarial kidney graft survival rates of expanded criteria donor (ECD), standard criteria donor (SCD), and dual kidney transplant (DKT) recipients.

83% expected) for single ECD KT. Five-year death-censored graft survival rates were 81% for single SCD KT (compared to 85% for PEB) and 69% for single ECD KT (compared to 79% for dual KT, $p = 0.09$). The incidences of DGF were 15% for PEB, 23% for dual KT, 27% for single ECD, and 36% for single SCD KT, respectively. The overall surgical complication rate after adult dual KT (14%) compared favorably with concurrent ECD (15.5%) and SCD (14.7%) single KT recipients, and the incidence of urologic complications was similar.

During the period of study, we performed 59 KT from pediatric donors 5 years old or less, including 34 PEB and 25 single KT. With a mean follow-up of 7 years in single KT recipients, actual patient survival (88% for PEB vs

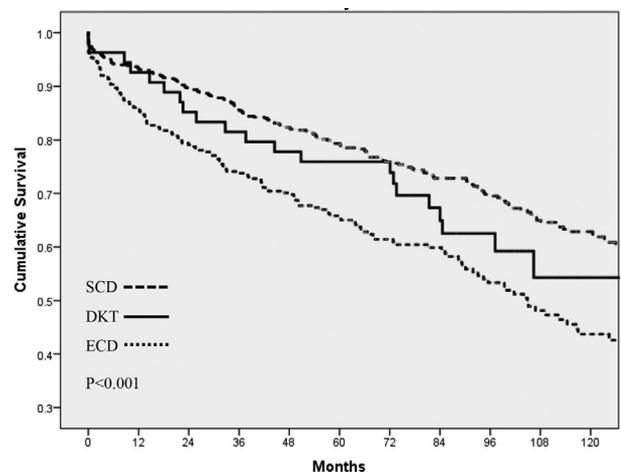


Figure 6. Actuarial death-censored kidney graft survival rates of expanded criteria donor (ECD), standard criteria donor (SCD), and dual kidney transplant (DKT) recipients.

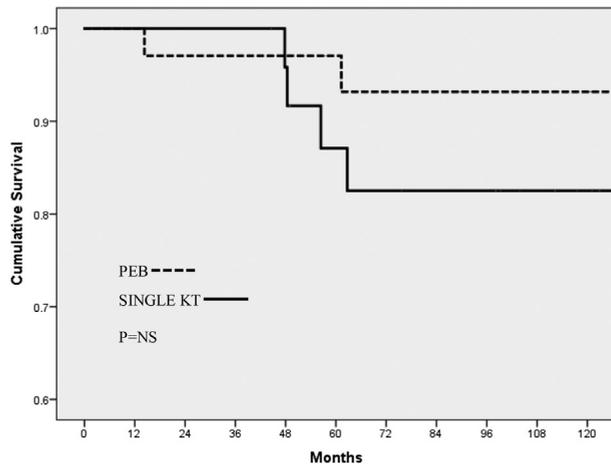


Figure 7. Actuarial patient survival rates of pediatric en bloc (PEB) and single kidney transplantation (KT) recipients from pediatric donors ≤ 5 years of age. NS, not significant.

76% for single KT) and graft survival (71% for PEB vs 56% for single KT) rates were slightly higher ($p = \text{NS}$) numerically in PEB compared with single KT recipients, respectively. Death-censored kidney graft survival rates were 77% PEB and 67% single KT, respectively. Survival rates were similar up to 4 years follow-up in the 2 groups, after which time graft survival declined more steeply in the single KT group. Actuarial patient, graft, and death-censored graft survival rates for PEB and single KT are shown in Figures 7 to 9. There was no influence of recipient sex or ethnicity on outcomes.

There was 1 case of thrombosis resulting in graft loss in each group. The incidence of DGF (15% for PEB vs 20% for single KT, $p = \text{NS}$) was similar. Mean length of hospital stay (5.4 vs 5.6 days) and the 1-year incidences of

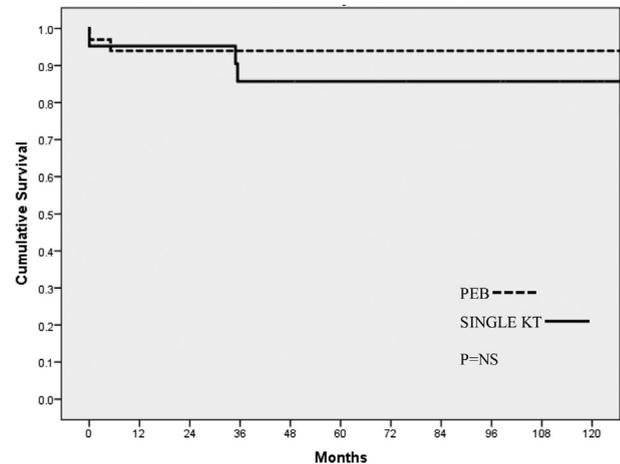


Figure 9. Actuarial death-censored kidney graft survival rates of pediatric en bloc (PEB) and single kidney transplantation (KT) recipients from pediatric donors ≤ 5 years of age.

surgical complications (3% vs 4%), acute rejection (6% vs 16%), and major infection were comparable in the PEB and single KT groups, respectively (all $p = \text{NS}$). Mean 12-month serum creatinine and abbreviated Modification of Diet in Renal Disease levels were 1.2 vs 1.35 mg/dL and 72 vs 60 mL/min (both $p = \text{NS}$) in the PEB and single KT groups, respectively.

From 2008 to 2015, we performed 180 living donor KT in 179 patients with a mean age of 47.4 years. At 5 years of follow-up, actual patient and graft survival rates were 91% ($p = \text{NS}$ compared with PEB [93%]) and 86% ($p = \text{NS}$ compared with PEB [79%]), respectively. The 5-year, death-censored kidney graft survival rate after living donor KT was 93% ($p = \text{NS}$ compared with PEB [85%]).

Adult dual KT outcomes did not differ by DD category or recipient age. Renal function after adult dual KT was comparable to single SCD KT (2-year mean serum creatinine levels were 1.5 mg/dL for dual KT vs 1.6 mg/dL for SCD, 2-year mean GFR levels were 50 mL/min/1.73 m² for dual KT vs 52 mL/min/1.73 m² for SCD) and superior to single ECD KT (2-year mean serum creatinine level 1.9 mg/dL, GFR level 40 mL/min/1.73 m²). In the absence of DGF or acute rejection, the proportion of total renal function (12-month estimated recipient GFR/estimated DD creatinine clearance $\times 100$) transplanted from adult DD to dual KT recipients was 77% compared to 56% for patients receiving single KTs from either adult SCDs or ECDs.

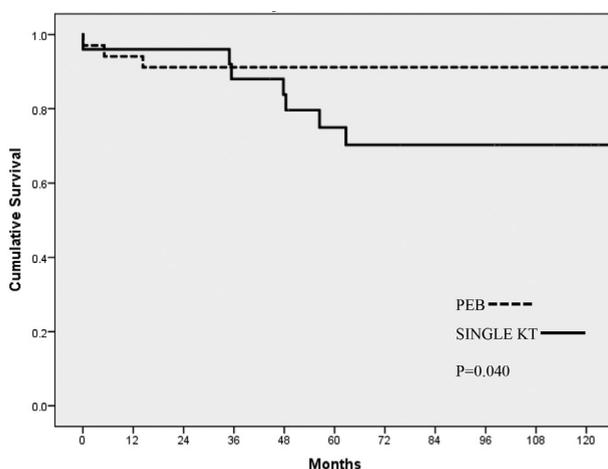


Figure 8. Actuarial kidney graft survival rates of pediatric en bloc (PEB) and single kidney transplantation (KT) recipients from pediatric donors ≤ 5 years of age.

DISCUSSION

The critical shortage of donor organs is one of the major challenges in organ transplantation today. The increasing

disparity between kidney supply and demand has fueled efforts to expand criteria for acceptable organs at both extremes of the donor age scale.¹⁻⁶ Due to the burgeoning crisis between organ supply and demand, national initiatives, such as the Organ Donor Breakthrough Collaborative, were established in order to expand the size of the donor pool.^{10,11,47,48} Commensurate with initiatives to expand the donor pool, the annual proportion of recovered DD kidneys that were subsequently discarded increased from 10% in 1998 to 19% in 2017.^{4,9-16} The kidney discard rate is directly related to KDPI score; ranging from 40% discard for a KDPI score of 80% to 60% discard for a KDPI score of 95%.^{4,9,13-16,49} For DDs 70 years of age or older, in fully half of cases, neither kidney is transplanted. At the highest KDPI scores (95% to 100%), discard rates approach 70% to 80%.^{4,9,13-16,49} For all donors with a KDPI $\geq 90\%$, in nearly 60% of cases, both kidneys are discarded. At present, more than 3,500 recovered kidneys from DDs are discarded annually in the US, of which half are from the high KDPI donor category.^{9,16,49}

Historically, kidneys from donors at the extremes of age have been considered marginal organs for KT because of concerns regarding limited nephron mass, technical complications, and long-term functional outcomes.⁵⁰ Nonetheless, most of the recent expansion in organ donation has occurred at the older extreme of age.¹⁰⁻²⁹ However, unlike kidneys from older donors, kidneys transplanted from SPDs into adult recipients have the capacity to grow to a normal adult renal size within a few months of KT and clearly represent an underused resource in the US.⁵¹ Both conversion (the proportion of potential organ donors for whom organ recovery is actually performed) and use (the proportion of recovered kidneys that are actually transplanted) rates are lower with donors at the extremes of age compared with donors of other ages.^{1,2,4-6,9,12-16,52}

For SPDs weighing ≤ 5 kg, most of the kidneys are discarded and for those that are used, virtually 100% are transplanted as PEB; for SPDs weighing 6 to 12 kg, approximately 80% are transplanted PEB, and for SPDs weighing 13 to 16 kg, about 50% are transplanted PEB.^{2,9,37,52-54} However, for potential SPDs < 10 kg, the kidney nonrecovery rate is $>40\%$, and for those kidneys that are recovered, the nonuse rate is $>30\%$. Nonrecovery and discard rates for SPDs weighing 10 to 15 kg are 20% and 15%, respectively.^{2,9,37,52-54} Retrospective analysis of all dual PEB KTs performed in the US in the new millennium revealed that $>80\%$ of these DDs had KDPI scores between 50% and 90%.^{9,55,56}

Analysis of all adult dual-eligible kidney marginal DDs revealed that nearly 75% had a KDPI score $\geq 85\%$.^{4,9,14,16,57,58} However, of all dual KTs performed

annually in the US, only 60% actually have a KDPI score $\geq 85\%$. Although the annual number of PEB KTs has remained stable (albeit lower than expected) with implementation of the new KAS, an unintended consequence has been a reduction in the number of dual KTs performed in the US.^{9,14,21,58} This decline in dual KT may be related in part to the "negative labelling effect" of high KDPI because the score is inappropriately applied to double kidney offers.²⁸ Because dual KT and high KDPI transplants are disproportionately performed more often in older recipients, expanding the use of dual KT with high KDPI DD kidneys may serve the dual purpose of counterbalancing the modest decline in access for older patients and the modest increase in discard for high KDPI DD kidneys that has occurred commensurate with the new KAS.

In our own experience, we have observed that SPDs subsequently used for dual PEB KTs are assigned relatively high scores in the new KAS because of the negative cumulative impact of reduced donor height, weight, and age in the calculation.^{55,56} Unfortunately, many of the KDPI variables do not "fit" for SPDs, particularly in the setting of dual PEB KT. For example, the mean KDPI in our dual PEB KT group was 73%, which translates roughly to an expected graft survival rate at 5 years follow-up of 66%. However, our observed graft survival rate at 5 years of follow-up in this group was 79%, which corresponds to a KDPI of 3%. Moreover, our dual PEB KT outcomes from SPDs were comparable to concurrent living donor KTs and superior to SCD single KTs at our center during the period of study, both from a functional and a survival perspective.

Similarly, the mean KDPI in dual KT recipients from marginal DDs in this study was 83%, which translates roughly to an expected 5-year graft survival rate of 61%. However, our observed 5-year graft survival rate was 69%, which corresponds to a KDPI of 60%. Moreover, renal function after adult DKT was comparable to concurrent SCD single KTs and superior to ECD single KTs at our center during the period of study. In addition, we have previously demonstrated that inadequate nephron mass does not seem to be a major issue for adult DKT recipients.^{5,32,33} Dual KTs from older donors may have a fixed nephron mass due to senescence that stabilizes at approximately 77% of the calculated donor creatinine clearance over time. Interestingly, in our concurrent experience with single KTs from either SCDs or ECDs, we found that renal function eventually stabilizes at approximately 56% of the calculated donor creatinine clearance. Consequently, one might contend that the KDPI is not applicable and a new predictive algorithm is needed for any type of dual KT.

Growing acceptance and use of marginal DD kidneys with limited renal functional capacity have been tempered by concerns that these kidneys have an increased susceptibility to ischemia-reperfusion injury leading to higher rates of PNF, DGF, and acute rejection, all of which may affect resource use, kidney graft survival, and projected life span.^{10-13,17-29,32-45,57-70} In addition, kidneys from older DDs have a reduced repair capacity and display increased immunogenicity.⁷¹ In this study, each pair of transplanted kidneys was from a “marginal” adult DD based on older age, pre-existing medical disease, abnormal renal function/anatomy/histopathologic findings, injury related either to warm ischemia (AKI or DCD donor) or cold ischemia (prolonged cold ischemia time, poor pump parameters), and absence of acceptance by multiple centers. The mean calculated adult DD creatinine clearance (66 mL/min) in these donors was well below a level considered normal for a kidney donor, and the majority (68%) met the creatinine clearance threshold considered acceptable for UNOS double kidney allocation. These concerns have fueled initiatives to qualitatively assess marginal DD kidneys before KT by examining associated risk factors, refining selection criteria, and using *ex vivo* biopsies and machine preservation parameters to predict outcome.^{4,5,10-13,17,35,38-44,57,68,69,72} An unintended consequence of these initiatives has been an increased risk of kidney discard associated with the use of either kidney biopsy (because of borderline histopathologic findings) or machine preservation (because of sub-optimal pump parameters) assessments. Poor renal function in a DD is second only to kidney biopsy findings as the main reasons given for kidney nonuse, and it represents the number 1 reason given for kidney nonrecovery.^{4,5,9-17,21-31,58}

A number of recent reports have demonstrated that the incidence of DGF after adult dual KT is not only acceptable, but is predictably lower than one might expect based on the overall quality of the kidneys.^{4,5,17-19,32,33,38-43,57,62-69,73,74} In this study, the incidence of DGF after adult dual KT was 23%, which was similar to the incidence of DGF (27%) that we experienced with single KT from ECDs, in which we followed similar algorithms and decision-making. Somewhat paradoxically, the incidence of DGF with single KT from SCDs (36%) was significantly higher, which may, in part, be related to both a lower rate of machine preservation and more DCD donors in this latter category. However, analogous to our experience in DCD and AKI donor KTs, and in contrast to our experience with single KT from either brain-dead ECDs or SCDs, the presence of DGF after dual KT did not adversely influence either patient or kidney graft survival rates.^{5,29-37,75}

In an effort to use adult DD kidneys that are not considered suitable for single KT for whatever reasons, the application of DKT has evolved in lieu of organ discard.^{4,5,17-19,32,33,38-43,57,62-69,73,74} Multiple studies of short- and long-term success with adult dual KT have been reported since the mid-1990's, at which time the primary indication for adult dual KT was insufficient nephron mass.^{3,17-19,32-40,62,63} At present, the decision to perform an adult dual KT vs either a single kidney or discard both kidneys is multifactorial and usually occurs when both kidneys have been refused for single KT by multiple centers and have accrued prolonged cold ischemia time.^{4,5,17-19,32,33,38-43,57,62-69,73,74} In our experience, only a minority of adult dual KTs actually occur in the setting of intentional dual kidney allocation according to UNOS criteria. Another confounding factor is that most ECD kidney offers meet the UNOS criteria for dual kidney allocation, yet the optimal use of kidneys from a utilitarian perspective is to perform 2 single KTs instead of 1 adult dual KT.

Pediatric en bloc and dual KTs have been shown to be effective when appropriate donors and recipients are chosen, even though these procedures may involve greater inherent anesthetic and surgical risks. In addition to donor organ quality, the greatest potential risk factor for inferior outcomes in adult dual KT is poor recipient selection. Early in our experience, we specifically excluded recipients 60 years of age or older from adult dual KT because of concerns regarding greater perioperative risks associated with longer operating times in the elderly, as well as their ability to tolerate predicted higher rates of DGF and surgical complications. In addition, by excluding older patients, we avoided patients with severe vascular disease, which likewise could jeopardize the overall success of adult dual KT. Wait list candidates with a BMI > 30 kg/m² were excluded from adult dual KT, as these patients likely would not receive an adequate “nephron dose.” Moreover, performing an adult dual KT in a patient with a high BMI would be technically more challenging and could be associated with a longer operating time and higher surgical complication rate. However, with time and experience, we liberalized recipient selection to include patients well into their 70s. This change in philosophy was determined, in part, by the realization that DGF and surgical complications were not a greater problem after adult dual KT and coincided with our transition to the unilateral extraperitoneal approach, which, in our experience, dramatically reduced the operating time and overall morbidity of the adult DKT procedure. Consequently, in the past 6 years, two-thirds of the adult dual KT recipients were aged 60 years or older and 29% were aged 70 years or older.

In an effort to minimize immunologic risk, 82% of recipients chosen for either PEB or adult dual KT in this study had a panel reactive antibody level of 0%, and only 1 (PEB) was a second transplant. Additional factors used to reduce the incidence of acute rejection included the use of flow crossmatch methodology and depleting antibody induction therapy. Eleven adult dual KT patients (15%) experienced an episode of acute rejection, which is nearly equivalent to our 15% incidence of acute rejection in our overall single ECD KT experience, and slightly lower than the 18% incidence documented in our single SCD KT experience. At our center, the majority of elderly patients (by design) receive either adult dual KTs or single kidneys from DCD or ECDs. It is well established that kidneys from these so-called "marginal" donors are particularly susceptible to ischemia-reperfusion injury, which may manifest as a higher incidence of DGF and be associated with enhanced immunogenicity.^{70,71,76} For these reasons, we endorse depleting antibody induction in all of our recipient groups in order to reduce the risk of early acute rejection and improve long-term graft survival outcomes, irrespective of donor or recipient age. By providing an immunosuppressive umbrella of protection against early acute rejection, depleting antibody induction may permit moderation in maintenance immunosuppressive regimens (including early steroid elimination) to reduce the overall risk of infections and malignancy while preserving renal function and preventing rejection. Lower calcineurin inhibitor target levels, reduced dose antimetabolite administration, and steroid-free maintenance immunosuppressive regimens are not only possible, but preferred, in adult dual KT recipients in the absence of acute or chronic rejection in order to prevent graft loss secondary to chronic allograft nephropathy.

Inadequate nephron mass does not seem to be a major issue for adult dual KT recipients. Without the benefit of adult dual KT, however, many of these patients would likely remain on the waiting list to this day. In patients receiving adult dual KT, the mean waiting time was 12 months, which was 7 months less than concurrent single ECD and 14 months less than concurrent single SCD KT recipients at our center. Renal allograft function and survival after adult dual KT were similar to those in concurrent single SCD and superior to those in single ECD KT recipients. Early in our experience, we noted 2 dual graft losses associated with transplanting kidneys that demonstrated >35% glomerulosclerosis on initial donor kidney biopsies. Based on these cases, we subsequently lowered our threshold for dual kidney use to <35% glomerulosclerosis on donor wedge kidney biopsies. Using the above

donor and recipient selection criteria and management strategies, adult dual KT recipients exhibit good graft function, with a mean serum creatinine of 1.5 mg/dL and a GFR of 50 mL/min/1.73m² at 24 months follow-up.

CONCLUSIONS

In summary, we report herein our single center retrospective cohort analysis with dual kidney transplants and conclude that the organ donor pool can be safely expanded from selected donors at the extremes of age. With appropriate donor and recipient selection, acceptable mid-term outcomes can be achieved with either dual PEB from SPDs or adult dual KTs from marginal DDs, which may expand the limited donor pool, prevent kidney discard, and offer a viable option to counteract the growing shortage of acceptable single kidneys. By performing PEB and adult dual KTs, DD transplant activity at our center increased by 8%. Outcomes are optimized when a systematic approach based on careful assessment of donor and kidney quality is implemented. With time and experience, we have liberalized our selection criteria to include DCD and AKI donors, smaller donors, and older recipients. In addition, kidneys with suboptimal pump parameters (flows 60 to 80 mL/min, resistances 0.4 to 0.5 mm Hg/mL) and longer cold ischemia times (>40 hours) are now considered acceptable if other donor characteristics are favorable. With dual PEB KTs from SPDs, outcomes comparable to living donor KTs can be attained. With adult dual KT from marginal DDs, satisfactory medium-term functional and survival outcomes can be realized that are similar to those for concurrent single SCD and superior to outcomes of concurrent single ECD kidney recipients. In addition, waiting times can be reduced in a predominantly older recipient population. It is important to note that dual kidneys should be transplanted in carefully selected recipients (low immunologic risk and body weight, favorable anatomy, and medical history) with informed consent. By calculating donor creatinine clearance and using donor kidney biopsy and pulsatile perfusion parameters, a reasonably accurate projection of kidney function and viability can be made. Transplantation of dual kidneys appears to lower the incidence of DGF compared with single kidneys of similar quality. Moreover, the KDPI is overestimated and is not accurate for predicting outcomes from either dual PEB from SPDs or dual KT from adult marginal DDs, which may prevent centers from otherwise accepting these organs for dual KT. Ultimately, longer-term follow-up is needed to determine the utility of this unconventional technique in expanding the donor pool.

Author Contributions

Study conception and design: Rogers, Farney, Orlando, Reeves-Daniel, Jay, Stratta

Acquisition of data: Rogers, Stratta

Analysis and interpretation of data: Rogers, Farney, Orlando, Reeves-Daniel, Jay, Stratta

Drafting of manuscript: Rogers, Farney, Orlando, Harriman, Reeves-Daniel, Jay, Doares, Kaczorski, Gantreaux, Stratta

Critical revision: Rogers, Farney, Orlando, Harriman, Reeves-Daniel, Jay, Doares, Kaczorski, Gantreaux, Stratta

REFERENCES

- Sanchez-Fructuoso AI, Prats D, Perez-Contin MJ, et al. Increasing the donor pool using en bloc pediatric kidneys for transplant. *Transplantation* 2003;76:1180-1184.
- Dharnidharka VR, Stevens G, Howard RJ. En-bloc kidney transplantation in the United States: An analysis of United Network of Organ Sharing (UNOS) data from 1987 to 2003. *Am J Transplant* 2006;5:1513-1517.
- Johnson LB, Kuo PC, Schweitzer EJ, et al. Double renal allografts successfully increase utilization of kidneys from older donors within a single organ procurement organization. *Transplantation* 1996;62:1581-1583.
- Tanriover B, Mohan S, Cohen DJ, et al. Kidneys at higher risk of discard: Expanding the role of dual kidney transplantation. *Am J Transplant* 2014;14:404-415.
- Stratta RJ, Farney AC, Orlando G, et al. Dual kidney transplants from adult marginal donors successfully expand the limited deceased donor organ pool. *Clin Transplant* 2016;30:380-392.
- Pelletier SJ, Guidinger MK, Merion RM, et al. Recovery and utilization of deceased donor kidneys from small pediatric donors. *Am J Transplant* 2006;6:1646-1652.
- Carrel A. Transplantation in mass of kidneys. *J Exp Med* 1908;10:98-140.
- Meakins JL, Smith EJ, Alexander JW. En bloc transplantation of both kidneys from pediatric donors into adult patients. *Surgery* 1972;71:72-75.
- Organ Procurement and Transplantation Network (OPTN) Data 2018. Available at: <https://optn.transplant.hrsa.gov/data/view-data-reports/>. Accessed January 18, 2019.
- Port FK, Bragg JL, Metzger RA, et al. Donor characteristics associated with reduced graft survival: An approach to expanding the pool of kidney donors. *Transplantation* 2002;74:1281-1286.
- Metzger RA, Delmonico FL, Feng S, et al. Expanded criteria donors for kidney transplantation. *Am J Transplant* 2003;3 [suppl 4]:114-125.
- Sung RS, Christensen LL, Leichtman AB, et al. Determinants of discard of expanded criteria donor kidneys: Impact of biopsy and machine perfusion. *Am J Transplant* 2008;8:783-792.
- Hall IE, Schroppel B, Doshi MD, et al. Associations of deceased donor kidney injury with kidney discard and function after transplantation. *Am J Transplant* 2015;15:1623-1631.
- Bae S, Massie AB, Luo X, et al. Changes in discard rate after the introduction of the Kidney Donor Profile Index (KDPI). *Am J Transplant* 2016;16:2202-2207.
- Reese PP, Harhay MN, Abt PL, et al. New solutions to reduce discard of kidneys donated for transplantation. *J Am Soc Nephrol* 2016;11:317-323.
- Stewart DE, Garcia VC, Rosendale JD, et al. Diagnosing the decades-long rise in the deceased donor kidney discard rate in the U.S. *Transplantation* 2017;101:575-587.
- Alfrey EJ, Lee CM, Scandling JD, et al. When should expanded criteria donor kidneys be used for single vs dual kidney transplants? *Transplantation* 1997;64:1142-1146.
- Stratta RJ, Bennett L. Preliminary experience with double kidney transplants from adult cadaveric donors: Analysis of UNOS data. *Transplant Proc* 1997;29:3375-3376.
- Lu AD, Carter JT, Weinstein RJ, et al. Excellent outcome in recipients of dual kidney transplants. *Arch Surg* 1999;134:971-976.
- Formica RN Jr, Friedewald JJ, Aeder M. Changing the kidney allocation system: A 20-year history. *Curr Transpl Rep* 2016;3:39-44.
- Stewart DE, Kucheryavaya AY, Klassen DK, et al. Changes in deceased donor kidney transplantation one year after KAS implementation. *Am J Transplant* 2016;16:1834-1847.
- Rao PS, Schaubel DE, Guidinger MK, et al. A comprehensive risk quantification score for deceased donor kidneys: The Kidney Donor Risk Index. *Transplantation* 2009;88:231-236.
- Woodside KJ, Merion RM, Leichtman AB, et al. Utilization of kidneys with similar kidney donor risk index values from standard versus expanded criteria donors. *Am J Transplant* 2012;12:2106-2114.
- Philippe E, Lee APK, Bracke B, et al. Does kidney donor risk index implementation lead to the transplantation of more and higher-quality donor kidneys? *Nephrol Dial Transplant* 2017;32:1934-1938.
- Massie AB, Luo X, Chow EKH, et al. Survival benefit of primary deceased donor transplantation with high-KDPI kidneys. *Am J Transplant* 2014;14:2310-2316.
- Rege A, Irish B, Castleberry A, et al. Trends in usage and outcomes for expanded criteria donor kidney transplantation in the United States characterized by kidney donor profile index. *Cureus* 2016;8:e887.
- Jay CL, Washburn K, Dean PG, et al. Survival benefit in older patients associated with earlier transplant with high KDPI kidneys. *Transplantation* 2017;101:867-872.
- Stewart DE, Garcia VC, Aeder MI, Klassen DK. New insights into the alleged kidney donor profile index labeling effect on kidney utilization. *Am J Transplant* 2017;17:2696-2704.
- Stratta RJ, Rohr MS, Sundberg AK, et al. Intermediate-term outcomes with expanded criteria deceased donors in kidney transplantation. *Ann Surg* 2006;243:594-601.
- Farney AC, Hines MH, Al-Geizawi S, et al. Lessons learned from a single center's experience with 134 donation after cardiac death donor kidney transplants. *J Am Coll Surg* 2011;212:440-453.
- Farney AC, Rogers J, Orlando G, et al. Evolving experience using kidneys from deceased donors with terminal acute kidney injury. *J Am Coll Surg* 2013;216:645-655.

32. Moore PS, Farney AC, Sundberg AK, et al. Experience with dual kidney transplants from donors at the extremes of age. *Surgery* 2006;140:597–606.
33. Moore PS, Farney AC, Sundberg AK, et al. Dual kidney transplantation: A case-control comparison with single kidney transplantation from standard and expanded criteria donors. *Transplantation* 2007;83:1551–1556.
34. Stratta RJ, Sundberg AK, Rohr MS, et al. Optimal utilization of older donors and recipients in kidney transplantation. *Surgery* 2006;139:324–333.
35. Stratta RJ, Moore PS, Farney AC, et al. Influence of pulsatile perfusion preservation on outcomes in kidney transplantation from expanded criteria donors. *J Am Coll Surg* 2007;204:873–884.
36. Al-Shraideh YA, Farooq U, Farney AC, et al. Influence of recipient age on deceased donor kidney transplant outcomes in the expanded criteria donor era. *Clin Transplant* 2014;28:1372–1382.
37. Al-Shraideh Y, Farooq U, El-Hennawy H, et al. Single versus dual (en bloc) kidney transplants from donors <5 years of age: A single center experience. *World J Transplant* 2016 March 24;6:239–248.
38. Snanoudj R, Ranant M, Timsit MO, et al. Donor-estimated GFR as an appropriate criterion for allocation of ECD kidneys into single or dual kidney transplantation. *Am J Transplant* 2009;9:2542–2551.
39. Remuzzi G, Ruggenenti P. Renal transplantation: Single or dual for donors aging ≥ 60 years? *Transplantation* 2000;69:2000–2001.
40. Remuzzi GR, Cravedi P, Perna A, et al. Long-term outcome of renal transplantation from older donors. *N Engl J Med* 2006;354:343–352.
41. Kayler LK, Mohanka R, Basu A, et al. Single versus dual renal transplantation from donors with significant arteriosclerosis on pre-implant biopsy. *Clin Transplant* 2009;23:525–531.
42. Fernandez-Lorente L, Riera L, Bestard O, et al. Long-term results of biopsy-guided selection and allocation of kidneys from older donors into older recipients. *Am J Transplant* 2012;12:2781–2788.
43. Sefora PE, Silvio S, Nicola DF, et al. Optimizing utilization of kidneys from deceased donors over 60 years: Five-year outcomes after implementation of a combined clinical and histological allocation algorithm. *Transplant Int* 2013;26:833–841.
44. Escofet X, Osman H, Griffiths DFR, et al. The presence of glomerular sclerosis at time zero has a significant impact on function after cadaveric renal transplantation. *Transplantation* 2003;75:344–346.
45. Farooq U, Al-Shraideh Y, Katari R, et al. Single center experience with deceased donor kidney transplantation in patients aged 70 and older: A matched-pair cohort study. *J Transplant Tech & Res* 2014;4:1–7.
46. Farney AC, Doares W, Rogers J, et al. A randomized trial of alemtuzumab versus antithymocyte globulin induction in renal and pancreas transplantation. *Transplantation* 2009;88:810–819.
47. Shafer TJ, Wagner D, Chessare J, et al. US organ collaborative increases organ donation. *Crit Care Nurse* 2008;31:190–210.
48. Khan AS, Shenoy S. What did we really learn from the Collaborative? Is it in our best interest to use “every organ every time” in kidney transplantation. *Curr Transpl Rep* 2016;3:139–144.
49. Mohan S, Chiles MC, Patzer RE, et al. Factors leading to the discard of deceased donor kidneys in the United States. *Kidney Int* 2018;94:187–198.
50. Alexander JW, Vaughn WK. The use of “marginal” donors for organ transplantation: The influence of donor age on outcome. *Transplantation* 1991;51:135–141.
51. Nghiem DD, Hsia S, Schlosser JD. Growth and function of en bloc infant kidney transplants: a preliminary study. *J Urol* 1995;153:326–329.
52. Maluf DG, Carrico RJ, Rosendale JD, et al. Optimizing recovery, utilization and transplantation outcomes for kidneys from small, ≤ 20 kg, pediatric donors. *Am J Transplant* 2013;13:2703–2712.
53. Kayler LK, Magliocca J, Kim RD, et al. Single kidney transplantation from young pediatric donors in the United States. *Am J Transplant* 2009;9:2745–2751.
54. Sureshkumar KK, Patel AA, Arora S, Marcus RJ. When is it reasonable to split pediatric en bloc kidneys for transplantation into two adults? *Transplant Proc* 2010;42:3521–3523.
55. Parker WF, Thistlethwaite JR, Ross LF. Kidney donor profile index does not accurately predict the graft survival of pediatric deceased donor kidneys. *Transplantation* 2016;100:2471–2478.
56. Nazarian SM, Peng AW, Duggirala B, et al. The kidney allocation system does not appropriately stratify risk of pediatric donor kidneys: Implications for pediatric recipients. *Am J Transplant* 2018;18:574–579.
57. Klair T, Gregg A, Phair J, Kayler LK. Outcomes of adult dual kidney transplants by KDRI in the United States. *Am J Transplant* 2013;13:2433–2440.
58. Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2016 annual data report. *Kidney* 2018;18[S1]:18–113.
59. Ojo AO, Hanson JA, Meier-Kriesche H, et al. Survival in recipients of marginal cadaveric donor kidneys compared with other recipients and wait-listed transplant candidates. *J Am Soc Nephrol* 2001;12:589–597.
60. Merion RM, Ashby VB, Wolfe RA, et al. Deceased-donor characteristics and the survival benefit of kidney transplantation. *JAMA* 2005;294:2726–2733.
61. Pascual J, Zamora J, Pirsch JD. A systematic review of kidney transplantation from expanded criteria donors. *Am J Kidney Dis* 2008;52:553–586.
62. Dietl KH, Wolters H, Marschall B, et al. Cadaveric “two-in-one” kidney transplantation from marginal donors: Experience of 26 cases after 3 years. *Transplantation* 2000;70:790–794.
63. Tan JC, Alfrey EJ, Dafeo DC, et al. Dual-kidney transplantation with organs from expanded criteria donors: A long-term follow-up. *Transplantation* 2004;78:692–696.
64. Gill J, Cho YW, Danovitch GM, et al. Outcomes of dual adult kidney transplants in the United States: An analysis of the OPTN/UNOS database. *Transplantation* 2008;85:62–68.
65. Salifu MO, Norin AJ, O’Mahony C, et al. Long-term outcomes of dual kidney transplantation—a single center experience. *Clin Transplant* 2009;23:400–406.
66. Ekser B, Furlan L, Broggiato A, et al. Technical aspects of unilateral dual kidney transplantation from expanded criteria donors: Experience of 100 patients. *Am J Transplant* 2010;10:2000–2007.

67. De Serres SA, Caumartin Y, Noel R, et al. Dual-kidney transplants as an alternative for very marginal donors: Long-term follow-up in 63 patients. *Transplantation* 2010;90:1125–1130.
68. Rigotti P, Capovilla G, Di Bella C, et al. A single-center experience with 200 dual kidney transplantations. *Clin Transplant* 2014;28:1433–1440.
69. Mallon DH, Riddiough GE, Summers DM, et al. Successful transplantation of kidneys from elderly circulatory death donors by using microscopic and macroscopic characteristics to guide single or dual implantation. *Am J Transplant* 2015;15:2931–2939.
70. Perico N, Cattaneo D, Sayegh MH, Remuzzi G. Delayed graft function in kidney transplantation. *Lancet* 2004;364:1814–1827.
71. Oberhuber R, Ge X, Tullius SG. Donor age-specific injury and immune responses. *Am J Transplant* 2012;12:38–42.
72. Sonnenday CJ, Cooper M, Kraus E, et al. The hazards of basing acceptance of cadaveric renal allografts on pulsatile perfusion parameters alone. *Transplantation* 2003;75:2029–2033.
73. Snanoudj R, Timsit MO, Rabant M, et al. Dual kidney transplantation: Is it worth it? *Transplantation* 2017;101:488–497.
74. Mendel L, Albano L, Bentellis I, et al. Safety of dual kidney transplantation compared to single kidney transplantation from expanded criteria donors: A single center cohort study of 39 recipients. *Transplant Int* 2018;31:1110–1124.
75. Singh RP, Farney AC, Rogers J, et al. Kidney transplantation from donation after cardiac death donors: Lack of impact of delayed graft function on post-transplant outcomes. *Clin Transplant* 2011;25:255–264.
76. Tullius SG, Tran H, Guleria I, et al. The combination of donor and recipient age is critical in determining host immunoresponsiveness and renal transplant outcome. *Ann Surg* 2010;252:662–674.

Discussion



DR MARK H DEIERHOI (Birmingham, AL): Transplant programs are in a constant struggle between 2 competing issues. On the one hand, there is the ubiquitous and ever-increasing organ shortage. With a national kidney wait list numbering greater than 100,000, many patients will never receive a transplant, and there is constant pressure to use as many retrieved organs as possible. On the other hand, all solid organ programs are under the constant scrutiny of the regulatory bodies that govern transplantation, namely, the United Network for Organ Sharing (UNOS) and the Centers for Medicare & Medicaid Services.

As a result, every program must keep an eye on their observed-to-expected outcomes in the various transplant metrics, and the potential for adverse outcomes with the use of organs at the margins of acceptability therefore exert pressure to make programs risk averse. Of course, there are also the devastating problems for individual patients who receive a marginal organ and have an unacceptable outcome.

The Winston-Salem group has a long history of exploring the use of these difficult donors and has added greatly to our understanding of donor selection and transplant management. This paper

adds to their experience with a review of their use of dual transplants from donors at the extremities of age. They describe their assessment of these donors and the management of the recipients and demonstrate very acceptable outcomes.

The technical aspects of the vascular anastomoses for the young donors are largely mitigated by performing en bloc transplants, with the aorta and cava as conduits. Many of these kidneys have very small ureters. Do you have any special techniques for the ureteral implants and have there been any urologic complications in these donors? How do you negotiate with outside organ procurement organizations for the sharing of dual transplants? In my experience, some organ procurement organizations (OPOs) are very reluctant to consider this option if there is any chance of single organ allocation.

Given that many of these organs are still being discarded, do you feel that there's any utility in UNOS identifying centers that have a history of using these donors and expediting allocation to them to affect the discard rate? I've not been particularly impressed that the current system for allocating high kidney donor profile index (KDPI) donors, for example, has significantly affected this usage rate. Would there be any benefit in designating the donors at the very margins of the risk pool, such as donors with a KDPI of 100% or potentially dual donors, as exempt from the standard assessment of outcomes for a center, such as was done initially with the exemption of dual kidney plus other organ transplants from calculations of liver and heart outcomes?

DR ROBERT C HARLAND (Tucson, AZ): This study from the Wake Forest transplant program is particularly relevant because it addresses the fact that donors and recipients who we see are all getting older, not to mention the surgeons that are seeing them. And we increasingly are trying to figure out how to use these organs in the more than 100,000 patients who are waiting for a kidney transplant. This year, somewhere between 15,000 and 20,000 deceased donor kidneys will be available for transplant, and we are trying to figure out how to find the right home for each one of those organs.

This group has consistently pushed the envelope and tried to maximize organ use for the last 15 years. If you look at their data, they are routinely using nonstandard donors for almost half of their primary kidney transplants; 45% of their first-time kidney transplants are from something other than a standard criteria donor. It is something they are very adept at.

Despite this stance and this practice, the outcomes are very good. It is especially important as the manuscript looks at death censored graft survival, which is particularly crucial as the older recipients have comorbidities, and death with a functioning graft is a common occurrence.

The results of this study show excellent results in pediatric en bloc kidney recipients, with a much lower thrombosis rate than has been reported in previous series. Now, only 1 graft thrombosis was noted in that. Similarly, transplantation of both donor kidneys from older or otherwise challenged donors demonstrates better-than-expected graft survival and function that is similar to that seen with standard criteria, single-donor kidneys, and better than that with older single-donor kidneys.

This presentation and the manuscript represent a practical guide to the successful use of kidneys from the very young as well as older