Current Status of Kidney Transplant Outcomes: Dying to Survive

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Kidney transplantation is associated with improved survival compared with maintenance dialysis. In the United States, post-transplant outcomes have steadily improved over the last several decades, with current 1-year allograft and patient survival rates well over 90%. Although short-term outcomes are similar to those in the international community, long-term outcomes appear to be inferior to those reported by other countries. Differences in recipient case mix, allocation polices, and health care coverage contribute to the long-term outcome disparity. This review presents the current status of kidney transplant outcomes in the United States and compares them with the most recent outcomes from Australia and New Zealand, Europe, and Canada. In addition, early trends after implementation of the new kidney allocation system in the United States and its potential impact on post-transplant outcomes are discussed.

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Key Words: Allograft survival, Kidney transplant, Outcomes, Organ allocation, Patient survival

INTRODUCTION

ESRD is common in the United States and is associated with significant morbidity and mortality. Kidney transplantation is the treatment of choice for suitable candidates with ESRD. Since the advent of kidney transplantation in 1954, allograft and patient survival in the United States have markedly improved because of advances in surgical techniques and immunosuppression. Few studies have compared kidney transplant outcomes between the United States and other countries. Because of varying allocation policies, cultural differences influencing preferences for living vs deceased donation, and government-funded health care in some countries, it is possible that post-transplant outcomes are vastly different in other countries. The aim of this review was to describe the current status of kidney allograft and patient survival in the United States based on data from the 2014 Scientific Registry of Transplant Recipients (SRTR) Annual Data Report. These outcomes are compared with those from Australia and New Zealand (ANZ), Europe, and Canada, using the most recent published registry data. Finally, we comment on the early impact of the new deceased donation kidney allocation system (KAS) implemented in the United States in December 2014 on transplant outcomes.

This study used data from the SRTR. The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight of the activities of the OPTN and SRTR contractors.

KIDNEY TRANSPLANT OUTCOMES: UNITED STATES

Allograft Survival

A total of 17,814 adult kidney transplants were performed in the United States in 2014.[1] Of these, 12,279 were from deceased donors and 5535 were from living donors. Deceased donor allograft survival rates have improved over time. The most recent SRTR annual report showed long-term outcome data on recipients who underwent transplant from 1991 to 2014. From 2010 to 2014, the unadjusted 1-year allograft survival rate for recipients of a first deceased donor kidney transplant was 93.4% (Fig 1). For second or subsequent deceased donor transplants, the 1-year unadjusted allograft survival rate was comparable at 92.5%. Five-year unadjusted allograft survival rates for a primary deceased donor transplant and for retransplant were 72.4% and 71.6%, respectively, among transplant recipients from 2005 to 2009.

It is well established that living donor kidney transplants are associated with superior post-transplant outcomes compared with deceased donor transplants, and this was reflected in the SRTR data. In recipients undergoing a primary living donor kidney transplant, the 1-year unadjusted allograft survival rate was 97.2%. In those undergoing retransplant from a living donor (first transplant from deceased or living donor), 1-year allograft survival was similar at 97.3%. Five-year unadjusted allograft survival rates for a first living donor kidney transplant and a second or subsequent transplant were 84.6% and 81.4%, respectively. Despite better outcomes, numbers of living donor transplants in the United States have decreased over the past 10 years; the largest decrease was in living-related donor kidney transplants, from 4340 in 2004 to 2693 in 2014.[1] This underscores the ongoing need to encourage and support living donation.

Potential explanations for the decline in living kidney donation include an aging US population such that potential donors are older, often have more comorbidity, and

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may not be medically suitable, financial disincentives, changes in organ allocation and donor selection criteria, and inadequate public awareness about the benefits of living organ donation.[2,3] In particular, financial burdens have been identified as a major barrier. Although the recipient's health insurance covers the donor's donation-related medical expenses, it does not reimburse for other expenses (eg, travel to the transplant center for pre-donation testing and surgery, lodging, lost wages during the post-surgery recovery period, especially for self-employed or part-time workers, and higher premiums for health or life insurance or, difficulty obtaining it, after donation).[2,3] The average out-of-pocket cost incurred by patients after living donation is reported to be $5000.[4] In June 2014, the transplant community convened a Consensus Conference on Best Practices in Live Kidney Donation and issued several recommendations with the goal of making living donation financially neutral. Progress is being made as the Living Donor Protection Act was introduced in Congress in February 2016. This bill would prohibit life, disability, and long-term care insurance carriers from charging higher premiums or denying coverage to individuals based on previous kidney donation. Additionally, the legislation clarifies that donors are covered under the Family and Medical Leave Act and directs the Department of Health and Human Services to continue efforts to educate Americans about organ donation.

CLINICAL SUMMARY

- Short-term kidney transplant outcomes in the United States are similar to those in other countries.
- Long-term kidney allograft and patient survival are worse in the United States than in Australia and New Zealand, Europe, and Canada.
- Differences in post-transplant insurance coverage, deceased donor allocation policy, and recipient comorbidity probably contribute to inferior long-term US outcomes.

Patient Survival

Recipients of living donor kidney transplants enjoy high survival rates, with little difference in outcomes for primary transplant and retransplant. The unadjusted 1-year patient survival rate was 97.0% for primary deceased donor transplant recipients from 2010 to 2014 and 97.2% for retransplant recipients. Patient survival at 5 years was 86.1% for first-transplant recipients and 88.9% for retransplant recipients who underwent deceased donor transplant from 2005 to 2009. For living donor transplant recipients, patient survival at 1 year and 5 years was 98.7% and 93.1% (primary transplant) and 99.0% and 92.9% (retransplant), respectively.

Although one might anticipate that retransplant would be associated with worse post-transplant outcomes since retransplant recipients are often highly sensitized and at higher risk for rejection, worse outcomes were not observed. This likely reflects selection bias during the evaluation for retransplant, when patients who were nonadherent (perhaps leading to allograft failure) or who have substantial comorbidity are usually not deemed candidates for retransplant.

Preemptive Transplant

Kidney transplant before dialysis initiation is associated with better post-transplant outcomes than transplant after dialysis initiation. Meier-Kriesche and colleagues[5] reported that less than 6 months of pretransplant dialysis was associated with a 17% higher risk of death-censored allograft loss compared with preemptive transplant. The risk of allograft loss increased with longer pretransplant dialysis time, although the relative increase after 3 years of dialysis was minimal. Similarly, these authors showed that 6 months or longer of dialysis pretransplant was linked to a higher risk of death post-transplant compared with preemptive transplant. Other advantages of preemptive transplant include lower rates of delayed graft function and lower overall ESRD treatment costs compared with maintenance dialysis.[6,7]

In 2014, 17.1% of US adult transplant recipients underwent a preemptive transplant.[1] As would be expected, preemptive transplant accounted for a smaller fraction of all deceased donor (10.6%) than of living donor (31.6%) transplants.[1] Although the proportion of preemptive living donor transplants increased from 23% in 1995 to 32% in 2014, growth has been stagnant since 2004 despite recognition of the benefits and new paradigms, such as the Kidney First Initiative.[1,7] Future research should focused on understanding reasons for this.

High Kidney Donor Profile Index Kidneys

Previously, deceased donor kidneys were classified as standard criteria donor (SCD) or expanded criteria donor (ECD). ECD kidneys were from donors aged 60 years or older or 50 to 59 years with 2 of the following: serum creatinine more than 1.5 mg/dL, history of hypertension, or death from a stroke.[8] ECD kidneys are associated with a 1.7 times higher risk for allograft failure compared with SCD kidneys.[9] Under the new KAS, the ECD and SCD classifications were supplanted by the kidney donor profile index (KDPI), which is computed using donor age; height; weight; race; and hypertension, diabetes, cause of death, serum creatinine, hepatitis C, and donation after circulatory death (DCD) status.[10] High KDPI kidneys are anticipated to have shorter allograft survival than lower KDPI kidneys. For US recipients who underwent transplant in 2009, unadjusted 1- and 5-year allograft survival was 84.4% and 60.0%, respectively, for a KDPI >85% kidney and 94.3% and 81.3% for a KDPI 20% or lower kidney.[1]

Transplant candidates may opt for KDPI >85% kidney offers, similar to opting for ECD kidneys under the previous allocation system. Given the shortage of donor kidneys and the high annual mortality on dialysis, some patients may benefit from accepting a high KDPI kidney rather than remaining on dialysis. Massie and others[11] demonstrated that after 19.8 months, even patients who accepted the "lowest quality" KDPI 91%-100% kidneys had higher cumulative survival than patients who stayed

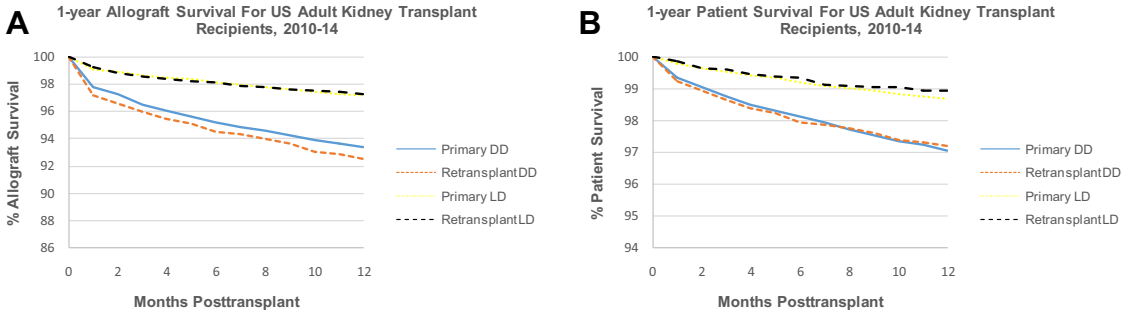

Figure 1. Unadjusted 1-year allograft (A) and patient (B) survival among US adult kidney transplant recipients by transplant type. Abbreviations: DD, deceased donation; LD, living donation.

on the waiting list or eventually received a lower KDPI kidney. Subgroup analysis showed that the patients aged older than 50 years who expected to remain on the waiting list for 33 months or longer were the most likely to experience a 5-year survival benefit from accepting a KDPI ≥ 81% kidney rather than continuing to wait.[11]

Donation After Circulatory Death

DCD kidneys are procured from a donor after the heart has stopped. In 2014, 17.1% of adult deceased donor recipients in the United States received a DCD organ.[1] The most recent SRTR data show that DCD and donation after brain death kidneys have similar short- and long-term allograft survival. Unadjusted 1- and 5-year allograft survival for DCD kidneys was 90.1% and 73.2%, compared with 91.6% and 74.2% for DBD kidneys.[1] Previous studies have confirmed this finding and also report similar short- and long-term patient survival.[12,13] However, the risk of delayed graft function is 1.5 to 2 times higher for DCD kidneys.[12,13]

KIDNEY TRANSPLANT OUTCOMES: ANZ

The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) is a robust database that tracks transplant outcomes in ANZ. In 2014, 1052 kidney transplants were performed in ANZ; living donation accounted for 32%.[14] Similar to the United States, the number of living donor transplants in Australia has decreased since 2008, whereas the number of deceased donor transplants has increased. In New Zealand, the numbers of living and deceased donor kidney transplants are relatively stable.

Table 1 lists unadjusted 1- and 5-year allograft and patient survival rates for ANZ deceased and living donor kidney transplant recipients. With the exception of 5-year primary allograft survival rates, which were better in Canada, ANZ appeared to have the best post-transplant outcomes compared with the other regions described.

The United States had relatively similar 1-year allograft and patient survival rates compared with ANZ in all categories, including living and deceased donor transplants and retransplants. However, all US long-term transplant outcomes were notably worse than ANZ long-term outcomes. For example, the 5-year allograft survival rate for a primary deceased donor transplant was 72.4% in the United States vs 81% in ANZ.[1,14]

KIDNEY TRANSPLANT OUTCOMES: EUROPE

The European Renal Association-European Dialysis and Transplant Association registry collects data on kidney transplant outcomes in Europe and comprises data from 49 national and regional registries including Spain, France, and the United Kingdom. The most recent annual report published in 2015 provides transplant outcome data for 2013. A total of 19,426 kidney transplants were performed, of which 68% (13,207) were from deceased donors, 31% (6002) were from living donors, and 1% (217) were from an unknown donor type.[15] Use of deceased donor kidneys varies greatly in Europe. In 2013, most kidney transplants performed in Spain, Estonia, Finland, and Belgium were

Table 1. International Comparison of Allograft and Patient Survival After Kidney Transplantation

	US[1]		ANZ[14]		Europe[15]		Canada[16]	
Outcome	Primary	Retransplant	Primary	Retransplant	Primary	Retransplant	Primary	Retransplant
Deceased donation								
1-y Allograft survival	93.4	92.5	95	94	90.7	N/A	94.9	N/A
5-y Allograft survival	72.4	71.6	81	83	77.8	N/A	81.4	N/A
1-y Patient survival	97.0	97.2	98	96	96.0	N/A	N/A	N/A
5-y Patient survival	86.1	88.9	90	96	87.1	N/A	N/A	N/A
Living donation								
1-y Allograft survival	97.2	97.3	98	98	95.8	N/A	97.7	N/A
5-y Allograft survival	84.6	81.4	90	83	86.9	N/A	90.8	N/A
1-y Patient survival	98.7	99.0	99	99	98.6	N/A	N/A	N/A
5-y Patient survival	93.1	92.9	95	94	94.3	N/A	N/A	N/A

Abbreviations: ANZ, Australia and New Zealand; NA, not applicable; US, United States.
All data are presented as percentages.

from deceased donors.[17] In Slovenia and the Castille and León region of Spain, 100% of the transplants were from deceased donors. Meanwhile, all transplants performed in Iceland and most performed in Bosnia and Herzegovina, Denmark, and The Netherlands were from living donors.[17]

The current unadjusted 1- and 5-year allograft and patient survival rates for kidney transplants in Europe are summarized in Table 1. The 1-year outcome data are from transplants performed from 2007 to 2011 and the 5-year outcome data are from transplants performed from 2004 to 2008. Data on retransplants are not published in the European Renal Association-European Dialysis and Transplant Association annual report. Compared with Europe, the United States had slightly better 1-year allograft and patient survival for primary living and deceased donor transplants but worse 5-year outcomes.

KIDNEY TRANSPLANT OUTCOMES: CANADA

The Canadian Organ Replacement Register tracks kidney transplant outcomes from the 25 active transplant centers in Canada. A total of 1224 kidney transplants (excluding multiorgan transplants) were performed in Canada in 2014, most from deceased donation.[16] Diabetic nephropathy was the cause of ESRD for 27.1% of deceased donor recipients and 15.4% of living donor recipients.[16] Data on allograft survival rates for retransplants and patient mortality are not published in the Canadian Organ Replacement Register. As listed in Table 1, the United States and Canada had similar unadjusted 1-year allograft survival for primary living donor transplants, but 5-year allograft survival was worse in the United States.

COMPARISON OF INTERNATIONAL OUTCOMES

Although there is a dearth of previous studies examining cross-country kidney transplant outcomes, our finding of worse long-term outcomes in the United States is consistent with previous findings. For example, international data on rates and outcomes of DCD transplants are not available.

Ojo and colleagues[18] found that the adjusted 10-year patient survival after deceased donor kidney transplant was 86% in Spain and 67% in the United States ($P < .001$) and that the hazard ratio (HR) for death was 2.35 in the United States compared with Spain. Kim and associates[19] compared US and Canadian kidney transplant recipients from 1991 to 1998 and found that although there was no statistically significant difference in mortality between the 2 countries in the first-year post-transplant (HR 1.09, $P = .30$), a difference developed for years 2 through 8 (covariate adjusted HR 1.53, $P < .005$). Using the Collaborative Transplant Study database, Gondos and others[20] showed that 5- and 10-year unadjusted deceased donor allograft survival rates were superior in Europe (77.0% and 56.5%, respectively) compared with the United States across all age and ethnic groups, and the difference was magnified in black recipients (white recipients, 71.3% and 45.7%; black recipients, 62.5% and 33.7%). The pattern was similar for living donor transplants.

Why are long-term kidney transplant outcomes worse in the United States? One possibility is the difference in how post-transplant care is paid for. In the United States, patients lose Medicare coverage for immunosuppression 36 months after transplant.[21] The high cost of these medications might create a financial burden that could lead to medication nonadherence and late allograft loss. In Canada and some European countries, no such barrier exists as transplant recipients have free access to immunosuppression through a nationalized health service, possibly contributing to the better long-term allograft and patient survival in those regions.

Comorbidity differences also factor into post-transplant outcomes. Multiple studies have shown a higher prevalence of recipient ESRD from diabetic nephropathy in the United States than in other countries (Ojo and colleagues, 24.1% US vs 5.6% Spain; Kim and others, 22.7% US vs 17.6% Canada; Gondos and colleagues, 26.0% US vs 8.3% Europe).[18-20] Given that diabetes is associated with cardiovascular morbidity and mortality, this may help explain worse long-term patient survival in the United States.

Differences in deceased donor allocation are another potential explanation for the difference in long-term outcomes. The Eurotransplant Senior Program (ESP) was launched in 1999 in an attempt to improve longevity matching of deceased donor organs and reduce discard rates of organs from elderly donors, while maintaining adequate allograft and patient survival. Under this allocation scheme, organs from donors aged 65 years or older are allocated to local recipients aged 65 years or older. Frei and colleagues[22] showed that the number of elderly donors increased and waiting time for elderly recipients decreased. Five-year patient and allograft survival were similar under ESP allocation and under the regular policy except for slightly higher rates of acute rejection.[22] A primary benefit of the ESP is that it reduces the transplantation of older kidneys into younger recipients, which has been associated with the worst outcomes.[23] Before implementation of the new KAS, nothing prevented such an allocation in the United States, which might also have contributed to inferior outcomes.

Deceased donor organ assessment also varies between the United States and other countries. In the United States, approximately 17% of kidneys procured are discarded.[24] Procurement biopsies are obtained for more than half of all deceased donor kidneys and the number one reason given for discard is the biopsy result. In 2014, the discard rate was 29.8% for biopsied and 6.6% for non-biopsied organs, despite lack of convincing evidence that the procurement biopsy predicts kidney allograft outcomes.[1] In a recent study, Kasiske and colleagues[25] compared the biopsy reports of kidneys that were discarded but had contralateral kidneys that were transplanted. They found that most biopsy results were incomplete and frequently missing comment on the amount of tubular atrophy or the presence of acute tubular necrosis, possibly due to most procurement biopsies being read by nonrenal pathologists usually outside daytime hours at the local hospital where the procurement occurred. In addition, only 33%

Table 2. Deceased Donor Kidney Transplant Rates Before and After the New Kidney Allocation System

	Pre-KAS		Post-KAS		Change After KAS	
Recipient Category	*n*	%	*n*	%	% Change	*P*
Age, y						
0-17	463	4.2	443	3.9	−8.5	.17
18-34	957	8.8	1460	12.8	45.9	<.0001
35-49	2627	24.1	3181	27.9	15.8	<.0001
50-64	4354	39.9	4245	37.2	−6.7	<.0001
≥65	2500	22.9	2068	18.1	−20.9	<.0001
cPRA 95%-98%	380	3.5	393	3.4	−1.1	.88
cPRA 99%-100%	267	2.4	1528	13.4	447.0	<.0001
Race/ethnicity						
Black	3438	31.5	4191	36.8	16.6	<.0001
White	4553	41.8	4030	35.4	−15.3	<.0001
Hispanic	1857	17.0	2119	18.6	9.1	.0024
Asian	796	7.3	777	6.8	−6.6	.16
Dialysis duration, y						
Preemptive transplant	946	8.7	647	5.7	−34.6	<.0001
<1	1199	11.0	917	8.0	−26.8	<.0001
1-<5	5430	49.8	4688	41.1	−17.4	<.0001
5-<10	2858	26.2	3980	34.9	33.2	<.0001
>10	468	4.3	1165	10.2	138.1	<.0001

Abbreviations: cPRA, calculated panel reactive antibody; KAS, kidney allocation system.
Comparison periods are December 4, 2013, to December 3, 2014, for pre-KAS and December 4, 2014, to December 3, 2015, for post-KAS.

of kidneys discarded had more than 20% global glomerulosclerosis, which is often considered synonymous with severe kidney damage and frequently used by transplant surgeons as the threshold for declining offers. The authors concluded that procurement biopsies should be abandoned in the United States, similar to what was done in Europe, and that this may help reduce waiting time to transplant by increasing the supply of useable organs.

EARLY TRENDS AFTER KAS IMPLEMENTATION

In December 2014, OPTN implemented a new allocation policy for deceased donor kidneys.[10] The goals of the new KAS were to increase the utility of transplanted organs by improving longevity matching and to increase transplant opportunities for highly sensitized candidates with high calculated panel reactive antibody (cPRA) scores. As described earlier, deceased donors are stratified by KDPI. Meanwhile, candidates are characterized by an estimated post-transplant survival (EPTS) score, which is determined by age, dialysis duration, diabetes status, and number of previous organ transplants. A higher EPTS is associated with shorter post-transplant patient survival. Under the KAS, deceased donor kidneys with a KDPI 20% or lower are preferentially allocated to candidates with an EPTS 20% or lower. In other changes, under the KAS, waiting time begins at the listing date or the start of dialysis (whichever is earlier), and additional priority points are given to patients with cPRA 20% or higher. Full details of the KAS are beyond the scope of this review, and readers are directed to the summary by Israni and colleagues.[10]

Information on the impact of the new KAS on post-transplant outcomes has been eagerly awaited. A recent study by Stewart and colleagues[26] highlighted the 12-month post-implementation trends (Table 2). The number of deceased donor transplants increased by 4.6%. Transplants in patients with cPRA 99%-100% increased sharply, from 2.4% pre-KAS to 13.4% post-KAS, although these patients make up only 8% of the waiting list. Statistically significant increases in transplant rates also occurred for

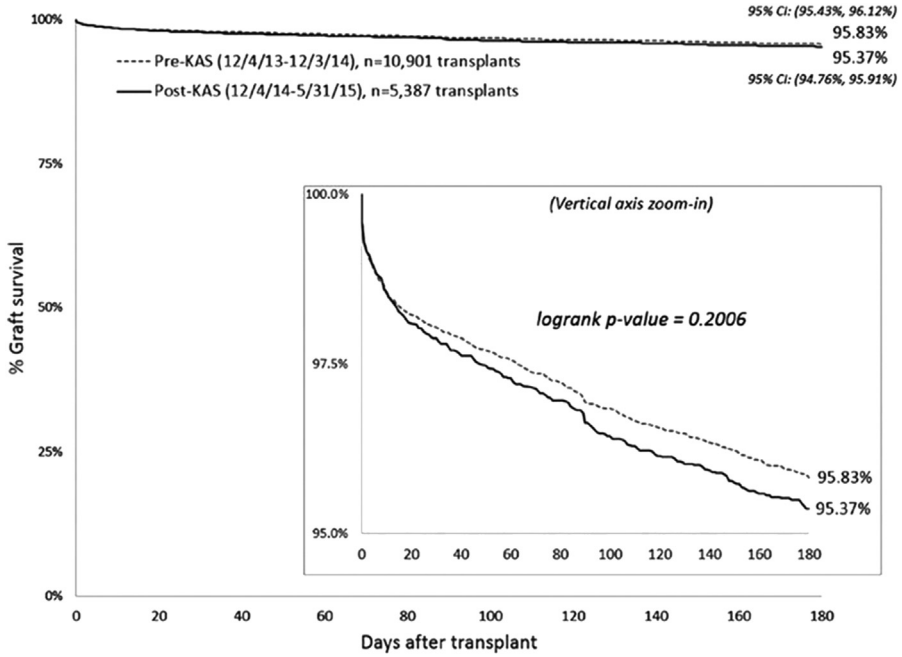

Figure 2. Comparison of 6-month all-cause allograft survival before and after implementation of the KAS. Abbreviation: KAS, kidney allocation system. Reprinted with permission from Stewart et al.[26]

black recipients (31.5% pre-KAS, 36.8% post-KAS) and for patients with more than 10 years on dialysis (4.3% pre-KAS, 10.2% post-KAS). Meanwhile, the transplant rate for patients aged 65 years or older decreased by 20.9%. Waitlist mortality was unchanged after the KAS, but more kidneys are being discarded (2850 pre-KAS and 3161 post-KAS).

Better donor-recipient longevity matching has been observed under the KAS, with a 7.7% increase in the number of transplants in which donor and recipient age are within 10 years of each other and a 22.6% decrease in transplants in which the age difference is more than 30 years. Although the rate of delayed graft function increased from 24.4% to 29.2% post-KAS, there was no statistically significant difference in the 6-month all-cause allograft survival rate (95.4% post-KAS, 95.8% pre-KAS, $P = .20$; Fig 2). The KAS is predicted to improve long-term allograft and patient survival in the United States, but whether these measures become more in line with those observed in other countries remains to be seen.

CONCLUSIONS

Compared with ANZ, Europe, and Canada, the United States has similar 1-year post-transplant outcomes, but 5-year and long-term outcomes appear to be worse. However, without proper risk adjustment of other countries' data, it is difficult to draw firm conclusions. Moreover, there is no standardization among international kidney transplant registries in the outcomes tracked or published. In light of these possibly worse outcomes, it is reassuring that adjusted 1- and 5-year kidney transplant outcomes for all US transplant programs are published online (http://www.srtr.org/csr/current/Centers/TransplantCenters.aspx?organcode=KI), allowing programs to monitor their outcomes relative to the rest of the country.

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