OPEN



Sandesh Parajuli[®], MD,^{1,2} Jacqueline Garonzik-Wang, MD, PhD,^{2,3} Brad C. Astor, PhD,^{1,4} Fahad Aziz, MD,^{1,2} Neetika Garg, MD,^{1,2} Bridget Welch, MHA/INF,^{2,3} Jon Odorico, MD,^{2,3} Joshua Mezrich, MD,^{2,3} Dixon Kaufman, MD, PhD,^{2,3} David P. Foley, MD,^{2,3} and Didier Mandelbrot, MD^{1,2}

Background. Kidney transplant outcomes have dramatically improved since the first successful transplant in 1954. In its early years, kidney transplantation was viewed more skeptically. Today it is considered the treatment of choice among patients with end-stage kidney disease. **Methods.** Our program performed its first kidney transplant in 1966 and recently performed our 12000th kidney transplant. Here, we review and describe our experience with these 12000 transplants. Transplant recipients were analyzed by decade of date of transplant: 1966–1975, 1976–1985, 1986–1995, 1996–2005, 2006–2015, and 2016–2022. Death-censored graft failure and mortality were outcomes of interest. **Results.** Of 12000 kidneys, 247 were transplanted from 1966 to 1975, 1147 from 1976 to 1985, 2194 from 1986 to 1995, 3147 from 1996 to 2005, 3046 from 2006 to 2015, and 2219 from 2016 to 2022 compared with 1966–1975, there were statistically significant and progressively lower risks of death-censored graft failure at 1 y, 5 y, and at last follow-up in all subsequent eras. Although mortality at 1 y was lower in all subsequent eras after 1986–1995, there was no difference in mortality at 5 y or the last follow-up between eras. **Conclusions.** In this large cohort of 12000 kidneys from a single center, we observed significant improvement in outcomes over time. Kidney transplantation remains a robust and ever-growing and improving field.

(Transplantation Direct 2024;10: e1575; doi: 10.1097/TXD.00000000001575.)

Since the first successful kidney transplantation between monozygotic twins by Dr Joseph Murray in 1954, kidney transplantation has modernized and improved significantly.^{1,2}

Accepted 12 November 2023.

- ² UW Health Transplant Center, Madison, WI.
- ³ Division of Transplantation, Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI.

⁴ Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health, Madison, WI.

This study was supported by an unrestricted research grant from the Virginia Lee Cook Foundation (D.M.).

The authors declare no conflicts of interest.

S.P. was involved in data collection, design, analysis, and article preparation. J.G.-W. was involved in concept and editing. B.C.A. was involved in analysis and editing. F.A., N.G., J.O., J.M., D.K., and D.F. were involved in editing. B.W. was involved in data collection and editing. D.M. was involved in concept, article preparation, and editing.

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantationdirect.com).

Correspondence: Sandesh Parajuli, MD, University of Wisconsin School of Medicine and Public Health, 4175 MFCB, 1685 Highland Ave, Madison, WI 53705. (sparajuli@medicine.wisc.edu).

Copyright © 2024 The Author(s). Transplantation Direct. Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

ISSN: 2373-8731

DOI: 10.1097/TXD.000000000001575

In the early years, kidney transplantation was viewed more skeptically rather than enthusiastically, mainly due to early immunologic risks, technical issues, adverse effects of immunosuppressive agents, and a relative shortage of available organs.³ Rennie,⁴ considered transplantation as only a temporary relief from the basic form of treatment, which is dialysis, despite having a better quality of life with transplantation. In 1967, "The Gottschalk Committee report" endorsed both dialysis and transplantation as established therapies among patients with kidney failure.5 After the implementation of Medicare funding for renal replacement therapy in 1972, long-term dialysis rapidly evolved as a first-line treatment.³ Simultaneously, the mid-1960s and early 1970s laid the groundwork for transplantation due to advances in organ preservation, immunosuppression, and histocompatibility, leading to better short-term outcomes, and that was further advanced with the introduction of cyclosporine in the early 1980s.⁶ In 2019, the federal government signed the Executive Order "Advancing American Kidney Health" intending to facilitate and promote kidney transplantation as the optimal modality for renal replacement therapy.7

Today, compared with dialysis, kidney transplantation offers a better quality of life, longer life expectancy, and costeffectiveness.⁸ In the past decades, improvement in outcomes after kidney transplantation has been mainly attributed to significant improvement in early graft survival.^{9,10} However, recent data suggest continuous improvement even in long-term outcomes.¹¹ At the University of Wisconsin, the first kidney transplant was performed in 1966, and in 2022, the 12 000th kidney transplant was completed. In this study, we present our experience with 12 000 kidney transplants with

Received 6 October 2023. Revision received 31 October 2023.

¹ Division of Nephrology, Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI.

a focus on the change in patient demographics over time, immunosuppression strategies, and improvements in graft and patient survival.

MATERIALS AND METHODS

This was a single-center study of all kidney transplant recipients at the University of Wisconsin from its inception in 1966 to 2022, when the 12 000th kidney transplant was performed. All recipients, including adult and pediatric, multiorgan transplants including a kidney, dual or en bloc kidneys were included. We excluded recipients who were transplanted at another transplant center but were followed at our center. For 12000 kidney outcomes, dual and en bloc were counted as 2 (outcomes based on the kidney). Next, the subgroup of kidney-only recipients (based on the recipient outcomes) was analyzed: here, the dual or en bloc kidney recipients were counted only once. En bloc or dual kidneys with multiorgan transplants were excluded (eg, kidney-pancreas recipient with en bloc kidney). Also, we further analyzed outcomes of kidney-only transplant recipients since 1994, which include some of the donor and immunologic risk factors. This study was approved by the University of Wisconsin Health Sciences Institutional Review Board (IRB protocol number: 2014-1072). This study was in adherence to the Declaration of Helsinki. The clinical and research activities being reported were consistent with the Principles of the Declaration of Istanbul as outlined in "The Declaration of Istanbul on Organ Trafficking and Transplant Tourism." Due to the nature of the study, informed consent from study patients pertinent to this study was not obtained.

The 12000 kidneys were transplanted in November 2022, and all patients had at least 3 mo of follow-up when data were analyzed in February 2023. Kidney transplants were categorized into 6 decades: 1966-1975, 1976-1985, 1986-1995, 1996-2005, 2006-2015, and 2016-2022. Death-censored graft failure (DCGF) and death within 1-y posttransplant, 5-y posttransplant, and at last follow-up were primary outcomes of interest. Patients were followed until DCGF or death (if those complications occurred) or until the end of data analysis in February 2023. DCGF was defined as a return to dialysis or retransplantation. All deaths were death with functioning grafts. Among kidney transplants in the 2016–2022 cohorts, for 1-y outcomes, only those transplanted before February 2022 were included, whereas for 5-y outcomes, only those transplanted before February 2018 were included. Most kidney transplant recipients continued to follow at our center for their posttransplant care, and their primary outcomes of interest were collected in our database. For those recipients who transferred their care to a different center, we queried the United Network of Organ Sharing Standard Transplant Analysis and Research database and identified recipients who had those primary outcomes of interest.

History of the University of Wisconsin Kidney Transplant Program

In July 1965, 3 faculty members at the University of Wisconsin, Dr Fritz Bach, with experience in mixed lymphocyte culture; Dr William Kisken, a general surgeon with interest in transplant and genetics; and Dr Richard Rieselbach, a nephrologist with a particular interest in transplantation, first met to pursue a dream of transplantation in the Midwest of the United States.¹² With this, the first kidney transplant from a deceased donor was performed in early 1966. In the same year, 7 kidneys were transplanted in 5 recipients, including one from a living donor. The program's volume gradually increased, and by the end of 1975, 247 kidneys had been transplanted. In 1974, Dr Folkert O. Belzer, who invented the University of Wisconsin preservation solution,¹³ joined the group and focused on further strengthening the program. In the last decade, approximately 250–300 kidneys are transplanted at University of Wisconsin annually.

Training

The University of Wisconsin has an active training program in both surgical and medical kidney transplantation. The surgical transplant fellowship was started in 1984 and the transplant nephrology fellowship in 1992. So far, >60 surgeons and nephrologists have been trained in the program and are practicing in the field both in the United States and internationally.

Database and Clinical Research Program

The Wisconsin Allograft Recipient Database (WisARD) was initiated in 1984 and prospectively collects information on all solid organ transplants performed at the University of Wisconsin. Available data include pretransplant details (eg, cause of disease, duration of disease, comorbidities), immediate posttransplant data (eg, all relevant medications, laboratory values, and in-hospital events), and follow-up information (graft survival, hospitalizations, procedures, and diagnoses). WisARD receives laboratory values for most recipients, along with major health events. Throughout the years WisARD has been a valuable resource for research studies performed by University of Wisconsin transplant faculty and trainees resulting in numerous publications on a broad array of transplantrelated issues. WisARD data was further refined in 1994 when an electronic medical record system was implemented and started collecting various other transplant-relevant information including some of the donor's information.

Immunosuppressive Agents

Both induction and maintenance immunosuppressive agents have evolved with time. We have utilized all available induction and maintenance immunosuppressive agents, starting from steroid-only induction, followed by anti-lymphocyte globulin, anti-thymocyte globulin, OKT3, daclizumab or basiliximab, and recently either rabbit anti-thymocyte globulin or alemtuzumab.¹⁴⁻¹⁷

Clinic Follow-up

We follow our kidney transplant recipients at either the University Hospital or various outreach regional clinics. After discharge from an initial kidney transplant admission, patients are typically seen at posttransplant times of 3 wk, 6 wk, 3 mo, 6 mo, 9 mo, 12 mo, 18 mo, 24 mo, and then annually, unless the recipient decides to transfer their care to a different transplant center. We have a busy transplant clinic with >12 000 clinic visits per year. As of the end of 2022, we were following 3106 kidney-only transplant recipients and a total of 3745 kidney transplant recipients (including simultaneous pancreas-kidney, liver-kidney, etc.) who were transplanted at our center. In 2011, we established a novel delayed graft function (DGF) clinic so that patients could be discharged once

3

Parajuli et al

recovered from surgery yet still requiring intermittent dialysis in the setting of DGF.¹⁸ Our clinic also follows several hundred recipients transplanted at other centers. Approximately 500 kidney biopsies are performed in the outpatient clinic per year.

Statistical Analyses

Baseline characteristics were compared using the chisquare test or *t* tests, as appropriate. Bivariable and multivariable logistic regression models and Cox proportional hazards regression models with a 95% confidence interval were used to assess primary outcomes with reference to those transplanted in 1966–1975. All variables from baseline characteristics were included in multivariable analyses. Kaplan-Meier survival analysis for each outcome was created by comparing all 6 groups. Additional models considered primary outcomes exclusively among kidney-only recipients. A *P* value of less than or equal to 0.05 was considered statistically significant. All analyses were performed using the MedCalc Statistical Software, Version 16.4.3 (MedCalc Software, Ostend, Belgium; https://www.medcalc.org; 2016).

RESULTS

Entire Cohort

A total of 12000 kidneys were transplanted between March 1966 and November 2022 (Table 1). Over time, the mean age of recipients at the time of transplant increased, as did body mass index (BMI). The proportion of non-White recipients (particularly African American and Asian), and previous transplant recipients also increased. The proportion of DGF and postoperative length of stay decreased (Table 2). Notably, the proportion of live donor kidney transplants did not change over time. Patient and graft survival at 1 y, 5 y, and the last follow-up continually improved throughout the study period (Figure 1).

The risk of DCGF at 1 y, 5 y, and at last follow-up was significantly lower over time in comparison with recipients during 1966–1975 (Table 3). While mortality was significantly lower at 1-y posttransplant, it was not significantly different at 5-y posttransplant (Figure 2). At last follow-up, unadjusted mortality was increased, but adjusted mortality was not (Table 4). The Kaplan-Meier curves for patient survival are shown in Figure 3.

Long-term Survival

As of 1997, 4142 kidneys had been transplanted, which provides at least 25 y of follow-up. At the last, follow-up, 565 (14%) recipients had the same kidney allograft for >25 y. Of these 565, 270 (48%) were recipients of a living kidney donor, 132 (23%) were simultaneous pancreas and kidney recipients and one was a simultaneous heart-kidney recipient.

Kidney-only Recipients

We also analyzed outcomes when including just kidney-only recipients. There were a total of 10 145 kidney-only recipients including 105 dual kidney recipients and 86 en bloc recipients. The first dual kidney transplant was performed in 1998 and en bloc in 1984 at our center. The outcomes were highly similar to the entire cohort of 12 000 kidneys and are shown in Tables S1–S3 (SDC, http://links.lww.com/TXD/A610) and Figures S1–S3 (SDC, http://links.lww.com/TXD/A610).

Kidney-only Recipients Since 1994

Since 1994, 7363 kidneys were transplanted at our center (Table S4, SDC, http://links.lww.com/TXD/A610). Similar to the previous findings, the age of the recipients continues to increase along with the BMI in the current era. Also, the proportion of kidneys from donation after circulatory death (DCD) was highest at 21% in the 2016–2022 era compared with 7% in 1994–1995 or 1996–2005. However, the proportion of living donor transplants peaked at 44% in the 1996–2005 era and has declined to 36% in the 2016–2022 era. Also, the rate of preemptive transplants has been declining and was only 14% in the recent era of 2016–2022. Similar to the recipient demographics, the donor's age and BMI have been continuously rising.

There was a significant decrement in the length of stay after transplant in the current era of 2016–2022 with a mean of 5.4 d compared with 17.4 d in 1994–1995 (data not shown). Also, in the current era, the rate of DCGF and death has improved significantly.

The risk of DCGF at 1 y, 5 y, and at last follow-up was lower over time in comparison with recipients during 1994– 1955 (data not shown). While after adjustment of various recipient's and donor's characteristics, still, the risk of DCGF was lower over time at 1 and 5 y but not at the last follow-up. Mortality was not significantly lower in the adjusted model in the current era.

CONCLUSIONS

In this large retrospective cohort of 12000 kidneys transplanted from a single center, over more than 55 y, we demonstrate a significant improvement in 1-y graft and patient survival. We also highlight how baseline characteristics of transplant recipients have changed over time, with recipients getting older, the proportion of nonwhite recipients rising, the BMI increasing, and the postoperative length of stay shortening. Also, some of the donor's demographics have changed, and we are utilizing more DCD kidneys in the recent era. In the past, while 1-y graft survival was improving in the United States during the 1990s compared with the immediate postcyclosporine era (the early 1980s), long-term graft outcomes were felt to be significantly lagging.¹⁹ However, recent data show continuous improvement in long-term outcomes, similar to this study.¹¹ Also, positive reports like this, including data on prolonged graft survival, may open avenues for further research and learning opportunities for the providers.

Here, we demonstrate stepwise improvement in DCGF, with hazard ratio (HR) of 0.03 (P < 0.001) for 1-y graft failure in the current era of 2016–2022, compared with the historic era of 1966–1975 in an adjusted model. Similar, outcomes with HR of 0.11 (P < 0.001) for 5-y DCGF were found among recipients transplanted in the current era of 2016–2022, along with at last follow-up with a HR of 0.19 (P < 0.001). There has also been some improvement in the patient's mortality at 1 y, 5 y, and last follow-up, although that is not as profound as DCGF. The reason behind this could be related to the increasing age of the recipients, and as recipients in the new era are having functional grafts for a longer period, their risk of early DCGF is low, so they are likely to have mortality with functional graft, as all mortality in our cohort was with functional graft.

TABLE 1.

Baseline demographics of 12000 kidney transplant

Year of transplant	1966-1975	1976–1985	1986–1995	1996-2005	2006-2015	2016-2022	Р
Volume	247	1147	2194	3147	3046	2219	Total = 12 000
Male (%)	146 (59)	709 (62)	1331 (61)	1846 (59)	1858 (61)	1395 (63)	0.06
Mean age at transplant (y, SD)	33.5 ± 13.1	35.5 ± 1.7	40.7 ± 2.8	45.5 ± 13.9	50.3 ± 13.6	52.7 ± 13.8	<0.001
Age range at transplant (y)							<0.001
<18	36 (15)	65 (6)	74 (3)	104 (3)	42 (1)	35 (2)	
18–45	156 (63)	830 (72)	1343 (61)	1362 (43)	958 (32)	572 (26)	
>45–65	55 (22)	251 (22)	720 (33)	1472 (45)	1598 (53)	1187 (54)	
>65	0	1	57 (3)	254 (8)	448 (15)	425 (19)	
Race (%)							<0.001
White	236 (96)	1084 (95)	1990 (91)	2776 (88)	2473 (81)	1653 (75)	
African American	8 (3)	49 (4)	141 (6)	208 (7)	316 (10)	317 (14)	
Native American	2 (1)	7 (1)	26 (1)	50 (2)	62 (2)	29 (1)	
Asian	1	1	24 (1)	101 (3)	185 (6)	205 (9)	
Unknown/declined/other	0	5	16 (1)	12	10	15 (1)	
Mean BMI at transplant (kg/m ²)	21.0 ± 3.4	21.7 ± 3.5	24.3 ± 4.6	26.3 ± 5.4	27.6 ± 5.2	28.0 ± 5.4	<0.001
Living donor (%)	89 (36)	414 (36)	593 (27)	1091 (35)	1007 (33)	676 (31)	<0.001
Cause of ESKD (%)							<0.001
Diabetes	6 (2)	347 (30)	912 (42)	1158 (37)	947 (31)	753 (34)	
Hypertension	11 (5)	78 (7)	143 (7)	250 (8)	312 (10)	287 (13)	
Specified glomerulonephritis	38 (15)	186 (16)	350 (16)	544 (17)	630 (21)	441 (20)	
Chronic glomerulonephritis	97 (39)	148 (13)	168 (8)	140 (4)	63 (2)	32 (1)	
Polycystic kidney disease	17 (7)	77 (7)	167 (8)	283 (9)	376 (12)	239 (11)	
Other/unknown	78 (32)	311 (27)	454 (21)	772 (25)	718 (24)	467 (21)	
Types of transplant							<0.001
Kidney only	247 (100)	1145 (100)	1783 (81)	2558 (81)	2673 (88)	1930 (87)	
Kidney, pancreas		2	396 (18)	540 (17)	302 (10)	213 (10)	
Kidney, liver			11 (1)	29 (1)	68 (2)	63 (3)	
Kidney, heart			3	17 (1)	3	11 (1)	
Kidney, lung			0	0	0	2	
Kidney, heart, pancreas			1	0	0	0	
Kidney, liver, pancreas, intestine			0	3	0	0	
Number of kidney/s (%)							<0.001
Single	247 (100)	1139 (99)	2186 (100)	3037 (97)	2896 (95)	2093 (94)	
Dual		0	0	32 (1)	104 (3)	76 (3)	
En bloc		8 (1)	8	70 (2)	46 (2)	42 (2)	
En bloc, kidney-pancreas		0	0	8	0	8	
Previous transplant (%)	36 (15)	165 (14)	254 (12)	560 (18)	606 (20)	360 (16)	<0.001
No. of previous transplants (%)							<0.001
0	211 (85)	982 (86)	1940 (88)	2587 (82)	2440 (80)	1856 (84)	
1	34 (14)	149 (13)	213 (10)	447 (14)	495 (16)	291 (13)	
2	2 (1)	14 (1)	34 (2)	92 (3)	97 (3)	54 (2)	
3	0	2	6	19 (1)	12	14 (1)	
4	0	0	1	1	2	0	
5	0	0	0	1	0	1	
Preemptive transplant (%)	13 (5)	118 (16)	582 (27)	845 (27)	753 (25)	313 (14)	<0.001
Induction immunosuppression							<0.001
ALG	33 (13)	188 (16)	705 (32)	0	0	0	
ATG	4 (2)	269 (23)	78 (4)	446 (14)	0	0	
rATG	0 Ó	0	0	224 (7)	518 (17)	696 (31)	
OKT3	0	2	1082 (49)	57 (2)	0	0	
Alemtuzumab	0	0	0	886 (28)	214 (7)	401 (18)	
Basiliximab	0	0	0	1103 (35)	2235 (73)	461 (21)	
Daclizumab	0	0	0	140 (4)	0	0	
Other/unknown/none	210 (85)	688 (60)	329 (15)	271 (9)	78 (3)	643 (29)	

Bold values indicate statistically significant with P<0.05. ALG, anti-lymphocyte globulin; ATG, anti-thymocyte globulin; BMI, body mass index; ESKD, end-stage kidney disease; rATG, rabbit anti-thymocyte globulin.

Kidney transplant outcomes depend upon various factors, including center volume and experience.^{20,21} In 1 study among 285 US transplant centers from 2006 to 2016, comparing

outcomes among high-volume centers and low-volume centers, even among high-risk recipients (defined as age > 70 y, higher BMI > 35 kg/m^2 , receiving kidney with higher kidney

Outcomes of 12000 kidney transplants

Year of transplant	1966–1975	1976-1985	1986–1995	1996-2005	2006-2015	2016-2022	Р
Delayed graft function (%)	129 (52)	348 (30)	243 (11)	457 (15)	582 (19)	309 (14)	<0.001
Length of stay after transplant (d)	28.5 ± 18.2	27.5 ± 13.2	23.3 ± 14.7	11.3 ± 9.8	7.0 ± 6.1	6.6 ± 8.4	<0.001
Death censored graft failure at 1 y (%)	85 (34)	266 (23)	191 (9)	148 (5)	93 (3)	33 (2)/2009	<0.001
Death with functional graft at 1 y (%)	13 (5)	55 (5)	54 (3)	86 (3)	76 (3)	50 (3) /2009	<0.001
Death censored graft failure at 5 y (%)	106 (43)	370 (32)	387 (18)	444 (14)	273 (9)	47 (5)/746	<0.001
Death with functional graft at 5 y (%)	44 (18)	224 (20)	394 (18)	614 (20)	373 (12)	75 (10)/746	<0.001
Death censored graft failure at last follow-up (%)	165 (67)	626 (55)	979 (45)	1007 (32)	568 (19)	93 (4)	<0.001
Death with functional graft at last follow-up (%)	73 (30)	415 (36)	893 (41)	1214 (39)	851 (28)	224 (10)	<0.001

Bold values indicate statistically significant with P < 0.05.



B P

Patient survival



*2016-2022 era, actual numbers of recipient with 1 or 5 years follow up only included

FIGURE 1. Graft and patient survival. Continuous improvement in actual graft survival (A) and patient survival (B), among 12000 kidney transplants.

TABLE 3.

Risk of graft failure (DCGF): all cohort

Complications		Unadjusted	Adjusted		
	HR (95% CI)	Р	HR (95% CI)	Р	
1-y DCGF					
1966–1975	Ref	Ref	Ref	Ref	
1976–1985	0.61 (0.48-0.78)	<0.001	0.55 (0.25-1.20)	0.13	
1986–1995	0.21 (0.16-0.27)	<0.001	0.26 (0.12-0.55)	<0.001	
1996–2005	0.11 (0.08-0.14)	<0.001	0.12 (0.06-0.26)	<0.001	
2006–2015	0.07 (0.05-0.09)	<0.001	0.07 (0.03-0.15)	<0.001	
2016–2022	0.04 (0.02-0.05)	<0.001	0.03 (0.01-0.07)	<0.001	
5-y DCGF					
1966–1975	Ref	Ref	Ref	Ref	
1976–1985	0.65 (0.53-0.81)	<0.001	0.51 (0.27-0.98)	0.04	
1986–1995	0.31 (0.25-0.39)	<0.001	0.38 (0.21-0.70)	0.002	
1996–2005	0.24 (0.20-0.30)	<0.001	0.30 (0.16-0.56)	<0.001	
2006–2015	0.15 (0.12-0.19)	<0.001	0.18 (0.10-0.34)	<0.001	
2016–2022	0.08 (0.06-0.11)	<0.001	0.11 (0.06-0.21)	<0.001	
DCGF at last follow-up					
1966–1975	Ref	Ref	Ref	Ref	
1976–1985	0.79 (0.67-0.94)	0.008	0.51 (0.31-0.84)	0.008	
1986–1995	0.59 (0.50-0.70)	<0.001	0.52 (0.33-0.84)	0.008	
1996–2005	0.58 (0.49-0.68)	<0.001	0.58 (0.36-0.93)	0.03	
2006-2015	0.42 (0.35-0.49)	<0.001	0.45 (0.28-0.72)	0.001	
2016-2022	0.15 (0.12-0.19)	<0.001	0.19 (0.11-0.31)	<0.001	

Bold values indicate statistically significant with *P* <0.05. Adjusted for sex, age, BMI, living donor transplant, diabetes as cause of ESKD, multiorgan transplant, previous transplant, preemptive transplant, use of depleting induction, and kidney DGF.

BMI, body mass index; CI, confidence interval; DCGF, death-censored graft failure; DGF, delayed graft function; ESKD, end-stage kidney disease; HR, hazard ratio; Ref, reference.





В





FIGURE 2. Death censored graft failure. Kaplan-Meier survival curve of death censored graft failure at 1 y (A), at 5 y (B), and last follow-up (C) among 12000 transplants.

TABLE 4.

Risk of death: all cohort

	U	Adjusted			
Complications	HR (95% CI)	Р	HR (95% CI	Р	
1-y death with functioning graft					
1966–1975	Ref	Ref	Ref	Ref	
1976–1985	0.90 (0.49-1.64)	0.72	0.94 (0.51-1.75)	0.86	
1986–1995	0.46 (0.25-0.85)	0.01	0.39 (0.20-0.76)	0.006	
1996–2005	0.49 (0.28-0.89)	0.02	0.32 (0.17-0.60)	<0.001	
2006–2015	0.47 (0.26-0.84)	0.01	0.24 (0.13-0.45)	<0.001	
2016–2022	0.46 (0.25-0.84)	0.01	0.22 (0.12-0.46)	<0.001	
5-y death with functioning graft					
1966–1975	Ref	Ref	Ref	Ref	
1976–1985	1.18 (0.85-1.65)	0.31	1.31 (0.40-4.29)	0.65	
1986–1995	1.07 (0.78-1.47)	0.68	1.27 (0.40-3.99)	0.68	
1996–2005	1.17 (0.86-1.60)	0.31	1.30 (0.42-4.08)	0.65	
2006–2015	0.73 (0.53-1.01)	0.053	0.73 (0.23-2.29)	0.59	
2016–2022	1.36 (0.98-1.90)	0.07	1.05 (0.33-3.31)	0.94	
2016–2022	0.15 (0.12-0.19)	<0.001	0.19 (0.11-0.31)	<0.001	
Death with functioning graft at last follow-up					
1966–1975	Ref	Ref	Ref	Ref	
1976–1985	1.51 (1.70-1.96)	<0.001	0.86 (0.27-2.76)	0.80	
1986–1995	1.79 (1.39-2.30)	<0.001	1.11 (0.35-3.49)	0.86	
1996–2005	2.90 (2.25-3.73)	<0.001	1.45 (0.46-4.57)	0.53	
2006–2015	3.17 (2.45-4.10)	<0.001	1.28 (0.41-4.05)	0.67	
2016–2022	2.72 (2.04-3.62)	<0.001	0.97 (0.31-3.12)	0.97	

Bold values indicate statistically significant with *P* <0.05. Adjusted for sex, age, BMI, living donor transplant, diabetes as cause of ESKD, multiorgan transplant, previous transplant, preemptive transplant, use of depleting induction, and kidney DGF.

BMI, body mass index; CI, confidence interval; DGF, delayed graft function; ESKD, end-stage kidney disease; HR, hazard ratio; Ref, reference.

donor profile index > 85%, acute kidney injury or hepatitis C +ve), Merzkani et al²² reports that in high-risk recipient subgroups, low-center volume (compared with high-center volume) was associated with a higher risk of death in the elderly (age \geq 70 y) and higher risk of graft failure in obese recipients $(BMI \ge 35 \text{ kg/m}^2)$ at short- and long-term follow-up. This may be related to higher volume centers presumably having more experience, a more extensive multidisciplinary teams, and broader resources for management and follow-up. The impact of a large, specialized network of transplant coordinators Α

95

90

244



FIGURE 3. Patient mortality. Kaplan Meier survival curve of patient mortality at 1 y (A), at 5 y (B), and at last follow-up (C) among 12000 transplants.

123

15 20 25

117 87 71 48 32

632 451 305

1472 1018 672 367 175 39

1856 1143 512 143 15

697 573 2211

0 0

also helps manage and follow-up with patients with tailored protocols that are needed to improve patient and graft survival. In addition, high-volume centers are more likely to have increased availability of other advanced specialties such as transplant cardiology, transplant infectious disease, and oncology that may help optimize outcomes. High-volume centers for each specific high-risk group might have a lower threshold to accept these populations and take a risk.

Similar to our study, in 2001, Matas et al²³ presented their experience of 2500 living donor kidney recipients, showing the outcome of living donor transplants has continued to improve. Overall, graft and patient survival have improved over time despite various suboptimal recipient and donor factors including older recipient age, higher BMI, frequency of diabetes, longer dialysis time, older donor age, DCD, and many more.²⁴ Among deceased donor kidney recipients, the 10-y overall graft survival rate was 42.3% from 1996 to 1999 and increased to 53.6% from 2008 to 2011. The 10-y patient survival rate increased from 60.5% during the 1996-1999 period to 66.9% during the 2008-2011 period.24

With these improvements, it is not unusual for some of our kidney recipients to have prolonged graft survival of >20 or 30 y. This is demonstrated in increasing reports on patients transplanted in the 1980s or early 1990s.^{25,26} We have previously reported "Characteristics and Outcomes of Kidney Transplant Recipients with a Functioning Graft for More than 25 Years."25 This study of 112 recipients found that despite prolonged graft survival, not everyone had an ideal posttransplant course. Only 66% received living donor kidneys, and 18% of recipients had previous kidney transplants. Also, 24% had acute rejection, 44% had malignancy, predominantly skin cancers, and 77% had some form of infectious complications, particularly urinary tract infections. At last follow, the majority of recipients had hypertension and hyperlipidemia. Likely, due to close

follow-up in a dedicated transplant clinic, they had excellent graft function with a mean estimated glomerular filtration rate of 53.2 ± 14 , even after a mean of 29.8 ± 4.0 y posttransplant.

Our study has the expected limitations of a single-center observational study, reflecting our specific population and clinical approach, which has evolved with time. Our findings are reflective of our specific practice, and this should be factored into the interpretation. However, our large center experience and granular clinical registry provide a useful basis for estimating risks and reporting outcomes. Another potential advantage of our single-center data is that it reflects a more homogeneous clinical approach to patient selection, surgical technique, and medical management, in contrast to registry data involving multiple centers.

In conclusion, this is the first study from a single center with 12000 kidney transplants assessing various outcomes. Kidney transplantation remains a robust and ever-growing and improving field. This type of data may continue to help motivate the patients and the providers dedicated to the field of transplant. With close follow-up and appropriate management, it is possible not only to increase the quantity of kidney transplant volume but also the quality as assessed by the prolonged graft survival.

REFERENCES

- 1. Harrison JH, Merrill JP, Murray JE. Renal homotransplantation in identical twins. Surg Forum. 1956;6:432-436.
- 2. Starzl TE. The landmark identical twin JAMA. case. 1984;251:2572-2573.
- 3. Abecassis M, Bartlett ST, Collins AJ, et al. Kidney transplantation as primary therapy for end-stage renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/ KDOQITM) conference. Clin J Am Soc Nephrol. 2008;3:471-480.
- 4. Rennie D. Home dialysis and the costs of uremia. N Engl J Med. 1978:298:399-400

- Hanna KE. Origins of the Medicare kidney disease entitlement: the Social Security Amendments of 1972. In: *Biomedical Politics*. National Academies Press (US); 1991.
- Morris PJ, Chapman JR. The evolution of kidney transplantation. In: Chapman JR, Turner NN, Turner NN, et al, eds. Oxford Textbook of Clinical Nephrology: Three-Volume Pack. Oxford University Press; 2015.
- Thomas E, Milton J, Cigarroa FG. The Advancing American Kidney Health Executive Order: an opportunity to enhance organ donation. *JAMA*. 2019;322:1645–1646.
- Parajuli S, Clark DF, Djamali A. Is kidney transplantation a better state of CKD? Impact on diagnosis and management. *Adv Chronic Kidney Dis*. 2016;23:287–294.
- Hariharan S, Johnson CP, Bresnahan BA, et al. Improved graft survival after renal transplantation in the United States, 1988 to 1996. N Engl J Med. 2000;342:605–612.
- Sayegh MH, Carpenter CB. Transplantation 50 years later—progress, challenges, and promises. N Engl J Med. 2004;351:2761–2766.
- Poggio ED, Augustine JJ, Arrigain S, et al. Long-term kidney transplant graft survival-making progress when most needed. *Am J Transplant*. 2021;21:2824–2832.
- Sollinger HW, Becker YT, Burlingham W, et al. The history of the University of Wisconsin transplant program. *Clin Transpl*. 2007;271:287.
- Southard JH, van Gulik TM, Ametani MS, et al. Important components of the UW solution. *Transplantation*. 1990;49:251–257.
- Cunningham KC, Hager DR, Fischer J, et al. Single-dose basiliximab induction in low-risk renal transplant recipients. *Pharmacotherapy*. 2016;36:823–829.
- Schadde E, D'Alessandro AM, Knechtle SJ, et al. Alemtuzumab induction and triple maintenance immunotherapy in kidney transplantation from donors after cardiac death. *Transpl Int.* 2008;21:625–636.

- Parajuli S, Joachim E, Alagusundaramoorthy S, et al. Subclinical antibody-mediated rejection after kidney transplantation: treatment outcomes. *Transplantation*. 2019;103:1722–1729.
- Stratta RJ, Armbrust MJ, Lorentzen DF, et al. Cadaveric renal transplantation in the cyclosporine and OKT3 eras: the University of Wisconsin-Madison experience. *Clin Transpl.* 1987;183:193.
- Muth BL, Astor BC, Turk J, et al. Outpatient management of delayed graft function is associated with reduced length of stay without an increase in adverse events. *Am J Transplant*. 2016;16:1604–1611.
- Meier-Kriesche HU, Schold JD, Srinivas TR, et al. Lack of improvement in renal allograft survival despite a marked decrease in acute rejection rates over the most recent era. *Am J Transplant*. 2004;4:378–383.
- Sonnenberg EM, Cohen JB, Hsu JY, et al. Association of kidney transplant center volume with 3-year clinical outcomes. *Am J Kidney Dis*. 2019;74:441–451.
- Barbas AS, Dib MJ, Rege AS, et al. The volume-outcome relationship in deceased donor kidney transplantation and implications for regionalization. *Ann Surg.* 2018;267:1169–1172.
- Merzkani M, Chang SH, Murad H, et al. The association of center volume with transplant outcomes in selected high-risk groups in kidney transplantation. *BMC Nephrol.* 2023;24:61.
- Matas AJ, Payne WD, Sutherland DE, et al. 2,500 living donor kidney transplants: a single-center experience. Ann Surg. 2001;234:149–164.
- Hariharan S, Israni AK, Danovitch G. Long-term survival after kidney transplantation. N Engl J Med. 2021;385:729–743.
- Parajuli S, Mandelbrot DA, Aziz F, et al. Characteristics and outcomes of kidney transplant recipients with a functioning graft for more than 25 years. *Kidney Dis (Basel)*. 2018;4:255–261.
- Reimann AV, Nilsson J, Wuethrich RP, et al. Entering the third decade after kidney transplantation: excellent graft function refers to superior graft but not patient survival. *Transpl Int*. 2022;35:10675.