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The impact of waiting time and comorbid conditions on the survival benefit of kidney transplantation

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The impact of waiting time and comorbid conditions on the survival benefit of kidney transplantation.

Background. Longer waiting times may limit the survival benefit of kidney transplantation in older patients or those with a high burden of comorbid disease.

Methods. We performed a longitudinal study of mortality among 63,783 transplant candidates who started dialysis between April 1995 and December 2000. We determined the relative risk (RR) of death and increase in life expectancy among subjects who received a first deceased donor transplant after different waiting times compared to subjects who had equivalent waiting times but remained on dialysis.

Results. Transplant recipients had a lower long-term RR of death and the risk reduction was greatest in recipients with longer waiting times (RR of death 12 months after transplantation for recipients with waiting times of 0, 1, 2, 3 years was 0.49, 0.43, 0.38, 0.34, $P = 0.0006$).The average increase in life expectancy in transplant recipients was 9.8 years and was lower in older recipients and recipients with comorbid conditions. Increased waiting times from 1 to 3 years only moderately decreased the overall survival benefit of transplantation from 7.1 to 5.6 years, and all subjects derived a survival benefit from transplantation with waiting times up to 3 years.

Conclusion. These findings do not support limiting access to transplantation for otherwise suitable candidates on the basis of longer anticipated waiting times.

Transplantation is the preferred treatment for patients with end-stage kidney disease. Compared to patients treated with dialysis, transplant recipients live longer, have improved quality of life, and consume fewer health care resources [1–3]. The survival benefit of transplantation compared to dialysis was demonstrated in a cohort of patients activated to the transplant waiting list in the United States between 1991 and 1996 [1]. Since that time, both waiting times for transplantation and the burden of comorbid disease in patients seeking transplantation have increased. In the current era, the shortage of available organs is the dominant issue. As of March 2005 there were 61,192 patients on the United Network of Organ Sharing waiting list for kidney transplantation [4]. By 2010, a projected 95,000 patients will be on the kidney waiting list in the United States, and waiting times of a decade or more are anticipated [5, 6]. The success of kidney transplantation has also contributed to the increased demand, and patients previously denied transplantation because of age or comorbid conditions now routinely seek and receive transplants. For example, between 1991 and 2001, the proportion of deceased donor kidney transplant recipients in the United States who were older than 50 years increased from 29.5% to 47.7% [7].

Previous work evaluating the survival benefit of transplantation compared to dialysis did not consider the impact of death or progression of comorbidity while awaiting transplantation and, hence, its applicability to the care of patients under current conditions is uncertain [1]. As the discrepancy between the supply and demand for kidney transplantation grows, pressure to preferentially allocate organs to patients with the greatest chance of benefit is likely to increase. The purpose of this study was to determine the impact of increased waiting time and comorbid disease on the survival benefit of transplantation in the current era.

METHODS

Data from the United States Renal Data System were used for this study. There were 361,254 subjects under the age of 75 years who began their first chronic dialysis treatment between April 1, 1995 and December 31, 2000. We studied the subset of 63,783 subjects who were also active on the kidney transplant waiting list. Descriptive

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statistics included the chi-square test or ANOVA as appropriate.

Survival was determined from the time of first activation to the transplant waiting list. Patients were followed until death, living donor, or multiorgan transplant, or the end of follow-up (December 31, 2000). Follow-up continued for subjects who were removed from the waiting list or had transplant failure. The relative risk of death in transplant recipients compared to subjects who remained on the waiting list with the same amount of waiting time was determined in a Cox regression analysis. Because mortality among transplant recipients increased sharply during the perioperative period and then declined below the rate observed in comparable subjects remaining on dialysis, the coefficient of the transplant status variable was allowed to vary with time after transplantation. We also permitted the risk of death after transplantation to differ in subjects with longer waiting times prior to transplantation with the use of time-varying coefficients. Analyses were adjusted for age, gender, race, cause of end-stage renal disease, comorbid conditions defined at the time of dialysis initiation (ischemic heart disease, congestive heart failure, stroke, peripheral vascular disease), duration of dialysis exposure prior to wait-listing, and year of placement on the transplant waiting list.

The projected number of life years remaining was determined in time-dependent parametric survival analyses that included the same covariates in the Cox regression analysis described above. The projections of life years remaining in wait-listed dialysis subjects were based on follow-up from activation to the waiting list until live donor or multiorgan transplantation, death, or end of study, and therefore included the impact of death on dialysis during the wait-list period. These projections assumed a Weibull distribution for the survival times in subjects remaining on dialysis, and a log-normal distribution for the survival times in subjects who received a transplant, based on goodness of fit tests and graphical comparison of the parametric hazard curves with the empiric hazards. [8] All analyses were performed with SAS, version 8.2 (SAS Institute, Cary, NC, USA). The study was approved by our university hospital ethics review board.

RESULTS

Of the 63,783 wait-listed dialysis subjects studied, 19,666 received a first deceased donor kidney transplant after a median waiting time of 0.65 years (5th–95th percentile, 24 days–2.65 years). An additional 8568 received either live donor or multiorgan transplants, while 35,549 subjects did not receive transplants and remained on dialysis. Compared to subjects who remained on dialysis, recipients of first deceased donor kidney transplants were younger and more likely to be male and of white race ($P < 0.001$ for all group comparisons) (Table 1). Transplant recipients were also less likely to have diabetic kidney disease, ischemic heart disease, or congestive heart failure ($P < 0.001$ for all group comparisons) (Table 1). Among transplant recipients with waiting time $\leq$12 months, the proportion of recipients aged $\geq$60 years (20%), of white race (72%), with diabetic kidney disease (34%), history of ischemic heart disease (8%), peripheral vascular disease (5%), congestive heart failure (12%), or cerebrovascular accident (3%) was higher than among receipts with waiting times $\geq$36 months (11%, 51%, 23%, 6%, 3%, 9%, 2%; $P < 0.001$ for all group comparisons).

The relative risk of death in transplant recipients who received transplants after 0, 1, 2, or 3 years of waiting time compared to wait-listed subjects with equal waiting time who remained on dialysis is shown in Figure 1. All transplant recipients had an increased relative risk of death in the immediate posttransplant period. The relative risk of death then rapidly declined, and transplant recipients had a lower long-term relative risk of death. The unadjusted annual death rates and hazard for mortality in dialysis subjects increased with each additional year on the waiting list (Table 2, Fig. 2A). In contrast, the annual death rates and hazard for morality in transplant recipients were similar in subjects who received transplants after short or long waiting times (Table 2, Fig. 2B). Consequently, the relative risk of death among transplant recipients tended to decrease with increasing waiting times, compared with subjects who remained on dialysis (Fig. 1).

The projected years of life remaining for subjects who received transplants after different waiting times and subjects who remained on dialysis are shown in Table 3, as well as the projected benefit in life years for transplant recipients. The average projected benefit for subjects who received a transplant at any time during follow-up was 9.8 years. The benefit of transplantation was inversely related to subject age and was lower in subjects with comorbid conditions. For example, transplant recipients who were 0 to 19 years of age or $\geq$70 years at the time of activation to the waiting list derived a projected survival benefit of 17.2 and 3.7 additional life years, respectively, compared with subjects of similar age who remained on dialysis (Table 3).

The benefit of transplantation was greatest in subjects who received transplants with the shortest waiting time. However, the overall survival benefit associated with transplantation was only moderately reduced, from 7.1 years after a waiting time of 1 year to 5.6 years after a waiting time of 3 years (Table 3), and the survival benefit of transplantation was observed in all subject groups even after the maximum observed waiting time of 3 years. The magnitude of the benefit associated with shorter waiting time appeared most pronounced in younger subjects [i.e., transplant recipients aged 0–19 had a 2.6 year

Table 1. Characteristics of study subjects and comparison of transplant recipients and subjects who remained on dialysis during follow-up

	All subjects on the waiting list ($N = 63,783$)	Subjects who remained on dialysis during follow-up ($N = 35,549$)	Subjects who received a live or multiorgan transplant ($N = 8568$)	Recipients of a first deceased donor transplant ($N = 19,666$)
Age[a] *mean ± SD*	47 ± 14	49 ± 13	42 ± 13	46 ± 14
Male%	60	58	60	62
Race%				
White	61	55	75	68
Black	29	35	17	24
Asian	5	6	4	4
Native American	2	2	1	1
Other/unknown	3	3	2	2
Cause of ESRD[b]%				
Diabetes	37	40	38	31
Glomerulonephritis	25	22	30	28
Other	38	38	33	41
Comorbid conditions[a]%				
Ischemic heart disease	9	10	7	8
Peripheral vascular disease	5	6	4	5
Congestive heart failure	13	15	9	11
Cerebrovascular accident	3	3	2	3
Listed before or at start of dialysis%	14	11	20	15
Months from first dialysis to wait-listing[c] *mean ± SD)*	12 ± 10	14 ± 11	8 ± 8	12 ± 9

[a] Defined at time of activation to transplant waiting list.
[b] End-stage renal disease.
[c] Patients wait-listed after dialysis initiation only.

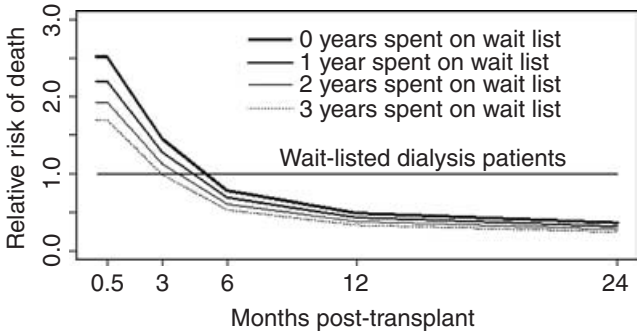

Fig. 1. The relative risk of death at different times after transplantation in transplant recipients with progressively longer waiting times compared to subjects who waited the same duration of time but remained on dialysis is shown. Values were adjusted for recipient age, gender, race, cause of end-stage kidney disease, comorbid conditions defined at the time of dialysis initiation (ischemic heart disease, congestive heart failure, stroke, peripheral vascular disease), duration of dialysis exposure prior to transplantation, and year of placement on the transplant waiting list.

decrease in the anticipated survival benefit with an increase in expected waiting time from at least 12 to 36 months compared to a decrease of 0.6 years in recipients aged ≥70 years (Table 3)].

DISCUSSION

In this longitudinal study of transplant candidates in the United States, we found that transplant recipients had a lower relative risk of death compared to wait-listed dialysis patients with similar waiting times. Increased waiting times were not characterized by a diminished benefit of transplantation, but instead were associated with a lower relative risk of death compared with remaining on dialysis. The increased risk reduction among transplant recipients with longer waiting times was the result of high mortality among subjects who remained on dialysis for long time periods and the consistent reduction in mortality after transplantation that was not attenuated by increased waiting times. Although the overall survival benefit of transplantation was decreased with increased waiting times, this decrement was small and subjects in all age groups and with a variety of comorbid conditions derived a survival advantage with transplantation up to the maximum observed waiting time of 3 years. Our findings do not support limiting access to transplantation based on a perceived decrease in survival benefit with increased waiting time and identify the need to improve the survival of patients who remain on dialysis awaiting transplantation for prolonged periods.

As originally reported by Wolfe et al, we found that the relative risk of death in transplant recipients compared to wait-listed dialysis subjects was higher in the immediate postoperative period but decreased rapidly thereafter, resulting in a long-term survival advantage associated with transplantation [1]. Notably, we found that the relative risk of death at any time point after transplantation continued to decrease with longer waiting times, relative to those who remained on dialysis. There were 2 factors that contributed to this unanticipated finding. First, there was a predictable increase in the absolute risk of death with time among subjects who remained on dialysis. This

Table 2. Unadjusted annual death rates[a] among wait-listed patients during different waiting periods and among transplant recipients[b] with different waiting times prior to transplantation

	Time after activation to waiting list				Waiting time prior to transplantation			
	0–12.0 months	12.1–24.0 months	24.1–36.0 months	≥36.0 months	0–12 months	12–24 months	24–36 months	≥36 months
All patients	4.5	8.0	9.3	11.2	4.1	4.1	4.0	5.4
	4.3–4.6	7.6–8.3	8.8–9.9	10.3–12.0	3.8–4.4	3.7–4.5	3.3–4.7	4.2–6.8
Age								
0–19	1.8	2.2	1.6	2.2	1.1	2.6	0.9	0
	1.2–2.8	1.2–4.0	0.5–5.0	0.7–6.8	0.7–1.8	1.6–4.6	0.1–6.6	
20–39	2.9	4.8	5.3	5.6	1.9	1.5	2.1	1.2
	2.6–3.2	4.2–5.3	4.5–6.2	4.6–6.9	1.6–2.3	1.1–2.0	1.3–3.3	0.5–2.9
40–59	4.6	8.0	9.2	12.1	4.4	4.6	3.3	6.8
	4.3–4.9	7.5–8.5	8.5–10.0	10.9–13.3	4.0–4.8	4.0–5.3	2.6–4.3	5.1 -9.1
60–64	6.3	10.6	15.2	18.3	7.0	7.5	9.5	11.7
	5.7–7.1	9.3–12.0	13.1–17.7	15.1–22.3	6.0–8.3	5.8–9.8	6.4–14.1	6.5–21.2
65–69	6.3	15.0	16.1	18.6	8.5	7.4	15.1	9.8
	5.5–7.2	13.2–17.0	13.3–19.4	14.5–23.9	7.1–10.2	5.2–10.4	9.8–23.2	4.1 -23.6
>70	8.7	18.6	23.1	25.2	9.9	8.7	12.1	26.1
	7.1–10.7	15.1–22.9	17.3–31.0	16.6–38.3	7.4–13.2	4.8–15.7	3.9–37.5	3.7–185
Gender								
Female	4.6	7.5	8.8	11.1	4.2	4.0	2.6	6.1
	4.3–4.9	7.0–8.1	7.9–9.7	9.9–12.4	3.8–4.7	3.4–4.8	1.8–3.6	4.2–8.8
Male	4.3	8.3	9.8	11.2	4.0	4.1	4.9	4.9
	4.1–4.6	7.8–8.8	9.0–10.6	10.1–12.4	3.7 -4.4	3.6–4.6	4.0–6.0	3.6–6.8
Race								
white	5.0	9.6	11.5	15.3	4.3	3.9	4.3	6.0
	4.7–5.2	9.1–10.1	10.7–12.4	13.9–16.8	4.0–4.6	3.5–4.5	3.5–5.3	4.4–8.1
black	3.8	6.3	7.1	7.1	3.8	4.6	3.6	5.4
	3.5–4.2	5.7–6.8	6.3 -,8.0	6.1–8.2	3.3–4.4	3.7–5.5	2.6–5.2	3.6–8.2
Asian	3.0	4.5	6.2	5.9	3.3	2.8	1.1	2.4
	2.4–3.7	3.6–5.7	4.7–8.3	4.0–8.6	2.3 4.7	1.6–4.9	0.3–4.2	0.6 -,9.4
Native American	4.2	6.7	9.2	12.0	5.2	3.7	7.1	0
	2.9–5.9	4.7–9.7	6.1–14.0	7.6–18.8	3.0–9.2	1.4–9.9	2.3–22.0	
Cause of ESRD								
Diabetes	7.0	13.7	15.8	20.2	6.0	7.0	6.5	10.3
	6.6–7.4	12.9–14.6	14.6–17.2	18.2–22.4	5.5–6.6	6.0–8.1	4.9–8.6	7.1–15.0
Glomerulonephritis	2.4	4.2	5.6	6.2	2.8	2.4	3.1	3.2
	2.2–2.7	3.7–4.8	4.8–6.5	5.2–7.6	2.4–3.2	1.9–3.1	2.2–4.4	1.8–5.6
Other	3.4	5.3	6.5	7.9	3.6	3.4	3.2	4.6
	3.1–3.6	4.9–5.8	5.8–7.3	6.9–9.1	3.2–4.0	2.9–4.0	2.4–4.3	3.2–6.6
Comorbid conditions								
None	3.6	6.4	7.4		3.4	3.5	3.3	4.9
	3.4–3.8	6.0–6.8	6.8–8.0		3.2–3.7	3.1–3.9	2.7–4.1	3.7–6.4
Ischemic heart disease	7.6	15.6	18.1	19.9	7.7	8.1	7.2	4.3
	6.8–8.5	14.0–17.4	15.6–21.0	16.3–24.2	6.5–9.1	6.0–10.9	4.3–12.2	1.4–13.4
Peripheral vascular disease	8.7	18.5	17.4	21.4	6.5	8.9	11.3	14.4
	7.6–9.9	16.2–21.1	14.2–21.3	16.6–27.6	5.1 -8.2	6.2–12.7	6.3–20.4	6.0–34.5
Congestive heart failure	7.7	13.5	16.6	17.3	8.1	7.6	9.4	6.1
	7.0–8.4	12.3–14.9	14.6–18.9	14.6–20.6	7.0–9.3	5.9–9.8	6.3–14.0	2.7–13.5
Cerebrovascular accident	8.4	13.0	17.3	18.0	6.7	9.2	6.0	11.4
	7.0–10.0	10.6–16.0	13.3–22.5	12.4–26.0	4.9–9.1	5.9–14.3	2.2–15.9	3.7–35.5

[a] Per 100 patient years, point estimate, and 95% CI.
[b] Death rate at any time after transplantation in patients who received deceased donor kidney transplants after different waiting times.

increase (Fig. 2) was nearly linear but did plateau over time, suggesting a survivor effect among wait-listed subjects with longer waiting times. This increase in the risk of death on dialysis may result from progressive cardiovascular disease in this population [9–11]. Our analysis was designed to help clinicians decide whether to activate a particular patient on the waiting list. Therefore, to avoid bias, subjects were included in analyses even if they were removed from the waiting list. Therefore, some of the increase in the absolute risk of death in dialysis subjects over time may have been contributed by those who were no longer active transplant candidates. Similarly, reliable information regarding wait-listed patients placed "on hold" was not available and was not incorporated in our analysis. Our findings suggest that as waiting times for transplantation continue to increase, monitoring and maintaining the medical fitness of transplant candidates will become increasingly difficult.

The second factor contributing to the lower relative risk of death in transplant recipients with longer waiting times was the fact that the absolute risk of peri-transplantation death appeared to be independent of waiting time. We

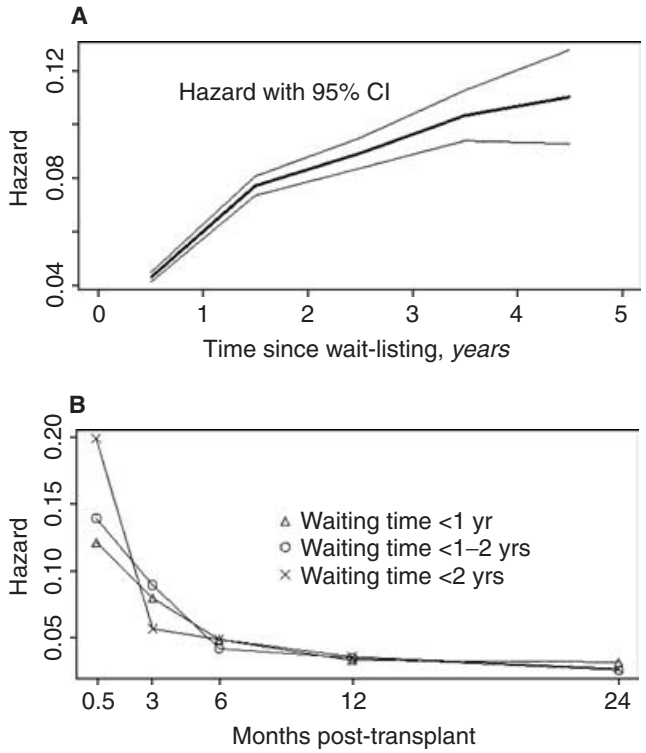

Fig. 2. (*A*) The hazard and 95% CI for mortality among subjects who remained on dialysis as a function of time since activation to the waiting list. (*B*) The hazard for mortality at different time points after transplantation for recipients who received first deceased donor kidney transplants after different waiting times. Although the hazard for mortality was higher during the immediate postoperative period among patients with longer waiting times, overall the hazards were very similar among transplant recipients with different waiting times.

hypothesized that the posttransplant risk of death would be higher in subjects who received transplants after longer waiting times due to progression of comorbid disease on dialysis, and therefore allowed the risk to vary with waiting time. The finding that increased waiting times did not increase the absolute risk of death after transplantation suggests that there may be systematic differences between the subjects who received transplants after prolonged waiting times and those who remained on dialysis that are unaccounted for in our multivariate analysis. A selection bias is supported by the finding that the proportion of transplant recipients ≥60 years and recipients with diabetes or comorbid conditions decreased as waiting times increased (Table 2).

Our projections of the survival benefit of transplantation account for both the waiting time for transplantation and death prior to transplantation. Our projections differ from the projections of life expectancy with transplantation provided by Wolfe et al, which were based on a subgroup of patients who had survived the wait-list period to receive a transplant [1]. Because our projections capture the impact of death on the waiting list, they can be used by clinicians to establish candidacy for transplantation at the time patients seek activation to the waiting list. This information is needed because of the significant cost and workload related to activating and maintaining patients on the waiting list [6, 12]. The magnitude of the anticipated survival benefit can be used to provide patients seeking transplantation with a reasonable expectation of outcome, and may influence patient preference for transplantation. Additionally, some patients may reasonably be excluded from consideration if the anticipated waiting time exceeds the projected life expectancy on dialysis.

We found that the increase in life years with transplantation was greatest in transplant recipients with the shortest waiting time. Importantly, the increased survival benefit among transplant recipients with the shortest waiting times was largely due to the progressive increase in mortality among patients who remained on the waiting list, rather than increased mortality among those who received transplants after longer waiting times. Indeed, we did not find a consistent increase in crude death rate among transplant recipients with longer waiting times (Table 2). These findings seem to differ from studies which have shown an increased relative risk of graft loss and or death [13, 14] among transplant recipients with longer waiting times. It is difficult to compare the crude death rates in our study to the risk ratios from a multivariate analysis used in these other studies. However, the apparent differences between our findings and those in other studies [13, 14] could be explained by the selection of healthier patients for transplantation after longer waiting times evident in our analysis. Since a relatively large proportion of subjects received a transplant after a waiting time of less than 1 year, the largest projected benefit was seen in subjects who received a transplant at any time during follow-up (after wait time of 0–3 years). The impact of increased waiting time was variable with a larger decrement in survival benefit among younger transplant recipients and recipients with nondiabetic kidney disease. Nonetheless, an apparent survival benefit of transplantation was observed in all subgroups and in subjects with waiting times of as long as 3 years (Table 3).

When interpreting our findings, readers should consider the inherent limitations of observational studies. Our assessment of comorbid conditions was performed when patients began their first treatment for end-stage kidney disease and not at the time of transplantation, and thus our analysis does not account for progression of comorbid conditions that may have occurred during the wait list period. It is plausible that progression of comorbid conditions may be different among patients who did and did not receive transplants, such differences may impact the survival benefit associated with transplantation and would not be captured in our analysis. Nonetheless, we believe the inclusion of comorbid conditions in our analysis increases the understanding of the anticipated survival benefit of transplantation compared to earlier

Table 3. Expected life years[a] with[b] and without[c] transplantation and benefit[d] of transplantation

	Without transplant	Transplant at any time during follow-up[e]		Transplant after minimum waiting time of 1 year		Transplant after minimum waiting time of 2 years		Transplant after minimum waiting time of 3 years	
	Expected life years	Expected life years	Benefit	Expected life years	Benefit	Expected life years	Benefit	Expected life years	Benefit
All patients	7.9 (7.5,8.2)	17.7 (16.7,18.7)	9.8	15.0 (14.2,15.8)	7.1	13.9 (13.1,14.6)	6	13.5 (12.7,14.2)	5.6
Age									
0–19	12.0 (9.2,14.7)	29.2 (23.8,34.6)	17.2	20.7 (16.6,24.9)	8.7	19.0 (15.0,23.0)	7	18.1 (14.3,21.9)	6.1
20–39	9.5 (8.8,10.1)	24.3 (22.4,26.1)	14.8	19.5 (18.0,21.0)	10	17.5 (16.2,18.9)	8	16.9 (15.6,18.2)	7.4
40–59	7.6 (7.3,8.0)	17.0 (16.0,18.0)	9.4	14.7 (13.8,15.5)	7.1	13.6 (12.8,14.4)	6	13.2 (12.4,14.0)	5.6
60–64	6.5 (6.1,6.9)	12.7 (11.7,13.7)	6.2	11.4 (10.5,12.3)	4.9	10.8 (9.9,11.6)	4.3	10.6 (9.8,11.4)	4.1
65–69	5.8 (5.4,6.2)	11.1 (10.1,12.1)	5.3	10.1 (9.2,11.0)	4.3	9.6 (8.8,10.5)	3.8	9.5 (8.7,10.4)	3.7
≥70	4.5 (4.0,4.9)	8.2 (7.1,9.2)	3.7	7.5 (6.5,8.5)	3	7.1 (6.2,8.0)	2.6	7.0 (6.1,7.9)	2.5
Male	7.9 (7.5,8.3)	18.2 (17.2,19.3)	10.3	15.4 (14.5,16.3)	7.5	14.2 (13.3,15.0)	6.3	13.8 (13.0,14.6)	5.9
Female	7.8 (7.4,8.1)	16.9 (15.9,18.0)	9.1	14.5 (13.6,15.4)	6.7	13.4 (12.6,14.3)	5.6	13.0 (12.2,13.8)	5.2
Race									
White	7.1 (6.7,7.4)	16.3 (15.4,17.2)	9.2	13.6 (12.8,14.4)	6.5	12.5 (11.8,13.2)	5.4	12.1 (11.4,12.8)	5
Black	9.1 (8.6,9.6)	19.5 (18.2,20.8)	10.4	17.0 (15.9,18.1)	7.9	16.0 (14.9,17.0)	6.9	15.5 (14.5,16.6)	6.5
Asian	10.4 (9.3,11.5)	24.1 (21.1,27.1)	13.7	20.8 (18.2,23.3)	10.4	19.2 (16.8,21.5)	8.8	18.4 (16.2,20.7)	8
Native American	9.7 (8.3,11.2)	21.4 (17.4,25.4)	11.7	19.0 (15.4,22.5)	9.3	17.6 (14.4,20.8)	7.9	17.2 (14.0,20.4)	7.5
Cause Of ESRD[f]									
Diabetes	5.4 (5.2,5.7)	11.4 (10.7,12.0)	6	9.6 (9.1,10.2)	4.2	9.1 (8.6,9.6)	3.7	8.8 (8.3,9.3)	2.4
Glomerulo-nephrititis	10.3 (9.6,11.0)	24.4 (22.6,26.3)	14.1	20.8 (19.2,22.4)	10.5	19.0 (17.5,20.5)	8.7	18.4 (17.0,19.8)	8.1
Other	9.3 (8.7,9.8)	21.6 (20.2,23.1)	12.3	18.3 (17.1,19.5)	9	16.8 (15.6,17.9)	7.5	16.2 (15.1,17.3)	6.9
Ischemic heart disease	7.0 (6.5,7.4)	14.9 (13.7,16.2)	7.9	12.8 (11.7,13.9)	5.8	12.0 (11.0,13.0)	5	11.6 (10.6,12.6)	4.6
Peripheral vascular disease	6.7 (6.2,7.2)	14.6 (13.2,16.1)	7.9	12.2 (11.0,13.4)	5.5	11.4 (10.3,12.5)	4.7	11.1 (10.0,12.2)	4.4
Congestive heart failure	6.8 (6.4,7.2)	13.5 (12.5,14.5)	6.7	11.8 (10.9,12.7)	5	11.0 (10.1,11.8)	4.2	10.7 (9.9,11.5)	3.9
Cerebrovascular accident	6.4 (5.8,7.0)	13.4 (11.8,15.1)	7	11.4 (10.0,12.8)	5	10.6 (9.3,11.9)	4.2	10.4 (9.1,11.6)	4

[a] Projected from the time of activation to the transplant waiting list. Projections based on a time-dependent parametric multivariate survival model. Point estimate and 95% CI in years are shown.
[b] Assuming a log-normal distribution for graft failure times.
[c] Assuming a Weibull distribution for graft failure times.
[d] The difference in expected life years with and without transplantation.
[e] Includes $N = 10{,}985$ (56% of all transplant recipients during follow-up) who received transplants with waiting times of ≤1 year.
[f] End-stage renal disease.

studies regarding this subject, which did not include adjustment for comorbid conditions [1].

The limitations of projections based on incomplete follow-up data have been highlighted recently in the transplant literature [15]. Nonetheless, it is clear that projections remain a necessary and valuable component of transplant-related research [16]. In making our projections we used goodness of fit tests and graphical comparisons in order to achieve the best approximation between the parametric hazards and the empiric hazards. Nonetheless, our projections are ultimately based on assumptions regarding the distribution of survival times in patients with relatively short follow-up and should be interpreted with this understanding.

CONCLUSION

We demonstrate that the survival benefit of transplantation is maintained with waiting times of up to 3 years in all transplant candidates irrespective of age and comorbid

disease status. These findings do not support limiting access to transplantation for otherwise suitable candidates on the basis of longer anticipated waiting times.

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