Recipient Age and Risk for Mortality After Kidney Transplantation in England

Asra Karim,[1] *Daniela Farrugia,*[1] *James Cheshire,*[2] *Sophia Mahboob,*[2] *Irena Begaj,*[3] *Daniel Ray,*[3] *and Adnan Sharif*[2,4]

Background. The aim of this study was to explore age-related mortality post-kidney transplantation in England over the last decade.

Methods. This study used data from Hospital Episode Statistics to select all kidney transplant procedures performed in England between April 2001 and March 2012. Demographics and medical comorbidities (based upon ICD-10 codes) were extracted at baseline. Data linkage analysis was performed with the Office for National Statistics to identify all deaths occurring among this study cohort.

Results. Data for 19,103 kidney transplant procedures was analyzed, with a median follow-up of 4.4 years (interquartile range 2.2–7.3 years). Categorization of age cohorts at time of transplantation were age below 50 (n=11,421, 59.8%), 50 to 59 (n=4,195, 22.0%), 60 to 69 (n=2,887, 15.1%), 70 to 79 (n=589, 3.1%), and 80 and above (n=11, 0.1%). There were 2,085 deaths that occurred among the study cohort during follow-up and mortality risk increased with age: below 50 (5.8%), 50 to 59 (14.2%), 60 to 69 (22.0%), 70 to 79 (31.9%), and 80 and above (45.5%). The three most common causes of deaths for recipients 70 and over were cardiac (21.2%), infection (21.2%), and malignancy (20.2%), respectively. Lower mortality was observed with the receipt of a living-donor kidney for recipients aged 70 and above. On Cox regression analysis, risk for death increased with each additional decade of recipient age over 50.

Conclusion. Increasing age is a strong, independent risk factor for death after kidney transplantation. Although lower mortality was observed with living kidney transplantation among elderly recipients, living-donor rates decrease with increasing recipient age. Pretransplant counseling and posttransplant tailored immunosuppression should be explored, the latter requiring targeted clinical trials.

Keywords: Age, Death, Survival, Mortality, Kidney transplantation.

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Increased age is not a contraindication for kidney transplant assessment but age-related comorbidity is and influences risk of mortality postoperatively. While caution must be exercised in the assessment and evaluation of the potential elderly kidney allograft recipient, age per se should not dissuade transplant clinicians to consider such individuals who are otherwise deemed suitably fit candidates. For the majority of older patients, it is clear that transplantation offers a survival advantage over remaining on dialysis (*1, 2*). In addition, there are potential improvements in quality-of-life parameters for older recipients that should be part of the initial assessment to determine the likely benefit from transplantation (*3–5*).

However, there are unique challenges with regards to transplantation in the older recipient that requires targeted evaluation and long-term management (*6*). Although it is widely accepted that increasing age relates to increased risk for mortality post-kidney transplantation, there is a paucity of literature in the contemporary era exploring this observation at a population-based level. In addition, the quantification and stratification of risk for older recipients by factoring in

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[1] Department of Nephrology and Transplantation, Renal Institute of Birmingham, Queen Elizabeth Hospital, Birmingham, UK.
[2] Medical School, University of Birmingham, Birmingham, UK.
[3] Department of Medical Informatics, Queen Elizabeth Hospital, Birmingham, UK.
[4] Address correspondence to: Adnan Sharif, M.D., Renal Institute of Birmingham, Queen Elizabeth Hospital, Edgbaston, Birmingham, B15 2WB, UK.
E-mail: adnan.sharif@uhb.nhs.uk

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TABLE 1. Comparison of demographics between kidney allograft recipients with malignancy-related death, non–malignancy-related death, and those alive

Variable		<50	50–59	60–69	70+	P^a
Number (%)		11,421	4,195	2,887	600	—
Gender	Male (%)	6,842 (59.9%)	2,599 (62.0%)	1,820 (63.0%)	412 (68.7%)	<0.001
	Female (%)	4,539 (40.1%)	1,596 (38.0%)	1,087 (37.0%)	188 (31.3%)	
Ethnicity	White	8,109 (71.0%)	2,987 (71.2%)	2,142 (74.2%)	457 (76.2%)	0.001
	Black/black British	608 (5.3%)	191 (4.6%)	108 (3.7%)	27 (4.5%)	
	Asian/Asian British	988 (8.7%)	421 (10.0%)	254 (8.8%)	41 (6.8%)	
	Chinese	45 (0.4%)	18 (0.4%)	16 (0.6%)	2 (0.3%)	
	Mixed	117 (1.0%)	32 (0.8%)	16 (0.6%)	1 (0.2%)	
	Other	232 (2.0%)	74 (1.8%)	40 (1.4%)	4 (0.6%)	
	Unknown	1,322 (11.6%)	472 (11.3%)	311 (10.8%)	68 (11.3%)	
Socioeconomic deprivation (IMD 2010)	1 (most deprived)	2,791 (24.4%	832 (19.8%)	481 (16.7%)	99 (16.5%)	<0.001
	2	2,649 (23.2%)	855 (20.4%)	590 (20.4%)	103 (17.2%)	
	3	2,211 (19.4%)	869 (20.7%)	563 (19.5%)	122 (20.3%)	
	4	1,908 (16.7%)	827 (19.7%)	613 (21.2%)	142 (23.7%)	
	5 (least deprived)	1,862 (16.3%)	812 (19.4%)	640 (22.2%)	134 (22.3%)	
Donor	Living	4,631 (40.5%)	1,275 (30.4%)	799 (27.7%)	116 (19.3%)	<0.001
	Deceased	6,790 (59.5%)	2,920 (69.6%)	2,088 (72.3%)	484 (80.7%)	
Medical comorbidity	MI	109 (1.0%)	159 (3.8%)	180 (6.2%)	55 (9.2%)	<0.001
	CCF	52 (0.5%)	32 (0.8%)	26 (0.9%)	10 (1.7%)	<0.001
	PVD	64 (0.6%)	43 (1.0%)	40 (1.4%)	7 (1.2%)	<0.001
	CVA	95 (0.8%)	92 (2.2%)	80 (2.8%)	17 (2.8%)	<0.001
	Diabetes	1,636 (14.3%)	755 (18.0%)	497 (17.2%)	80 (13.3%)	<0.001
	Pulmonary disease	534 (4.7%)	205 (4.9%)	164 (5.7%)	23 (3.8%)	0.022
	Liver disease	30 (0.3%)	19 (0.5%)	10 (0.3%)	2 (0.3%)	0.461
	CT disease	262 (2.3%)	74 (1.8%)	40 (1.4%)	9 (1.5%)	0.014
	Peptic ulcer	30 (0.3%)	24 (0.6%)	18 (0.6%)	5 (0.1%)	0.005
	Cancer	18 (0.2%)	19 (0.5%)	22 (0.8%)	15 (2.5%)	<0.001

[a] Statistical comparison of categorical responses between age groups and variables.

medical or transplant-related variables has not been performed. To inform clinical practice, the authors undertook a population-based cohort analysis of all deaths occurring post-kidney transplantation in England over the last decade, focusing on age-related mortality risk determined at the time of transplantation.

RESULTS

A total of 19,688 kidney transplant procedures in England were recorded in the Hospital Episode Statistics (HES) data for adult (18,499) and pediatric (n=1,189) kidney allograft recipients. Excluding those with missing demographic data (n=585), this study had a cohort of 19,103 for further analysis (104,154 patient-years for entire study cohort).

The median age for the whole cohort at time of transplantation was 45 (interquartile range 34–55). Recipients were categorized into the following age cohorts: age below 50 (n=11,421, 59.8%), 50 to 59 (n=4,195, 22.0%), 60 to 69 (n=2,887, 15.1%), 70 to 79 (n=589, 3.1%), and 80 and over (n=11, 0.1%). There were 11,673 (61.1%) men in the study cohort, with 7,430 (38.9%) women. Ethnic breakdown of the study cohort comprised of white (13,695, 71.7%), black or black British (934, 4.9%), Asian or Asian British (1704, 8.9%), Chinese (81, 0.4%), mixed (166, 0.9%), other ethnic group (350, 1.8%), and unknown (2173, 11.4%). Socioeconomic deprivation quintiles were (from most to least deprived respectively) 1 (22.0%), 2 (22.0%), 3 (19.7%), 4 (18.3%), and 5 (18.0%). Living-donor transplantation occurred in 6,262 (32.8%) of all kidney transplant procedures reported. Diabetes mellitus classification was the most common medical comorbidity recorded in 2,968 (15.5%) of all kidney allograft recipients. Table 1 highlights significant differences among the age cohorts in relation to these baseline differences.

Data Accuracy

To verify the quality of the HES data, information was extracted from the UK National Transplant database to determine the number of transplants performed during the same time frame. During the time from April 2001 to March 2012, 19,405 kidney transplant procedures were registered (19,241 kidney alone, 49 en bloc kidneys, and 115 double kidneys transplants). This identifies a small discrepancy of 283 kidney transplant alone procedures that have been over-reported in the HES data in comparison to UK National Transplant Database records (concordance 98.6% between both data sets).

Mortality risk ratio of transplant versus general population (age stratified)

Study or Subgroup	Transplant population Events	Transplant population Total	General population Events	General population Total	Weight	Risk Difference M-H, Random, 95% CI
0-50	662	11421	43871	34782563	25.4%	0.06 [0.05, 0.06]
50-59	595	4195	47358	6397087	25.3%	0.13 [0.12, 0.14]
60-69	635	2887	111148	5680431	25.2%	0.20 [0.19, 0.22]
70+	193	600	886966	6152375	24.1%	0.18 [0.14, 0.21]
Total (95% CI)		19103		53012456	100.0%	0.14 [0.06, 0.22]
Total events	2085		1089343			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 610.53$, df = 3 ($P < 0.00001$); $I^2 = 100\%$
Test for overall effect: Z = 3.45 (P = 0.0006)

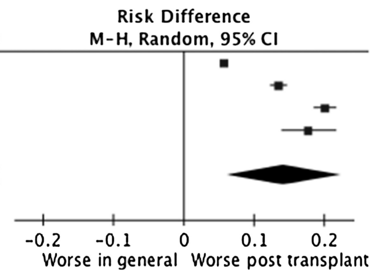


FIGURE 1. Mortality risk ratio of transplant versus general population (age stratified) comparing transplant cohort (2001–2012) to general population in England (2001–2011). As 2012 mortality data is not currently available for England, 2011 data was extrapolated to 2012.

Risk of Death

HES data was cross-referenced with official death certification registered with the Office for National Statistics (ONS) to determine differences in cause of death dependent upon recipient age. This study identified 2,085 deaths that occurred post-kidney transplantation with median a follow-up of 4.4 years (interquartile range 2.2–7.3 years, 104,154 patient-years). It was observed that there was an increased risk of death as age of kidney allograft recipients at time of transplantation increased: below 50 (5.8%), 50 to 59 (14.2%), 60 to 69 (22.0%), 70 to 79 (31.9%), and 80 and over (45.5%). A similar increasing risk can be identified for death within the first year post-kidney transplantation: below 50 (1.5%), 50 to 59 (3.8%), 60 to 69 (5.9%), 70 to 79 (11.9%), and 80 and over (9.1%). Because of the low numbers of kidney allograft recipients aged 80 and over, this cohort was incorporated into the 70 and over subgroup of recipients for all subsequent analyses.

Mortality rates were compared in the transplant cohort with the general population in England over the same period and observed significantly higher mortality rates in the transplant population for each age bracket (see Fig. 1).

Figure 2 highlights change in mortality at the arbitrary cut-off age placed at 70 years. While the risk for death was 32.2% among kidney allograft recipients aged 70 or more (at median follow-up of 4.4 years post-kidney transplantation), it can be seen that the risk could be substantially altered dependent upon the presence or absence of additional factors. The lowest risk of mortality for kidney allograft recipients aged 70 and over was in the context of a living kidney donor (20.7% at median follow-up). This is an important observation in the context of findings from Table 1 that highlights lower rates of living kidney transplants as recipient age increases.

Living Kidney Transplantation and Age-Related Mortality

This study further explored the link between age-related mortality and receipt of living versus deceased kidneys. Recipients under 70 who received a live kidney had lower mortality at median follow-up (5.7% vs. 12.8%, $P<0.001$) and within the first year (1.6% vs. 3.3%, $P<0.001$) compared to receiving a deceased donor kidney, respectively. Under seventies also had lower risk of mortality from cardiovascular causes (1.0% vs. 2.8%, $P<0.001$), infection (1.0% vs. 2.8%, $P<0.001$), and malignancy (1.2% vs. 2.2%, $P<0.001$) comparing living versus deceased kidney transplantation, respectively.

Among kidney allograft recipients aged 70 and over, it was observed that there was a decreased risk for death at median follow-up for recipients of living versus deceased kidneys donors (20.7% vs. 34.9%, respectively, $P=0.002$), but no difference in mortality within the first year (11.2% vs. 12.0%, respectively, $P=0.481$). In addition, there was no difference in risk for mortality from cardiovascular causes (5.2% vs. 7.2%, $P=0.228$), infection (5.2% vs. 7.2%, $P=0.228$), and malignancy (6.9% vs. 6.4%, $P=0.492$) comparing living versus deceased kidney transplantation, respectively.

Causality of Death

The three most common causes of deaths for recipients who were aged 70 and over were cardiac (21.2%), infection (21.2%), and malignancy (20.2%), respectively. Cardiovascular causes (cardiac, cerebrovascular, and vascular) accounted for 30.5% of all deaths among kidney allograft recipients aged 70 and over (see **Table S1, SDC,** http://links.lww.com/TP/A911).

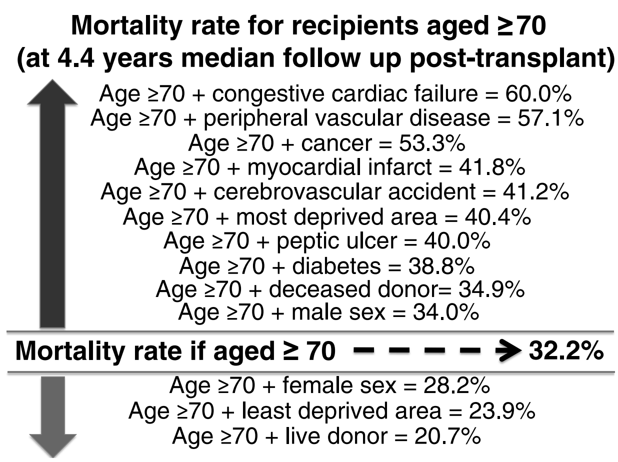


FIGURE 2. Risk of death for kidney allograft recipients aged 70 and over (at 4.4 years median follow-up post-transplantation), with risk adjustment in presence of a single additional covariable at the time of transplantation. This schema allows appropriate counseling regarding mortality risk for potential kidney allograft recipients aged 70 and over before transplantation.

Regression and Survival Analysis for Age-Related Mortality

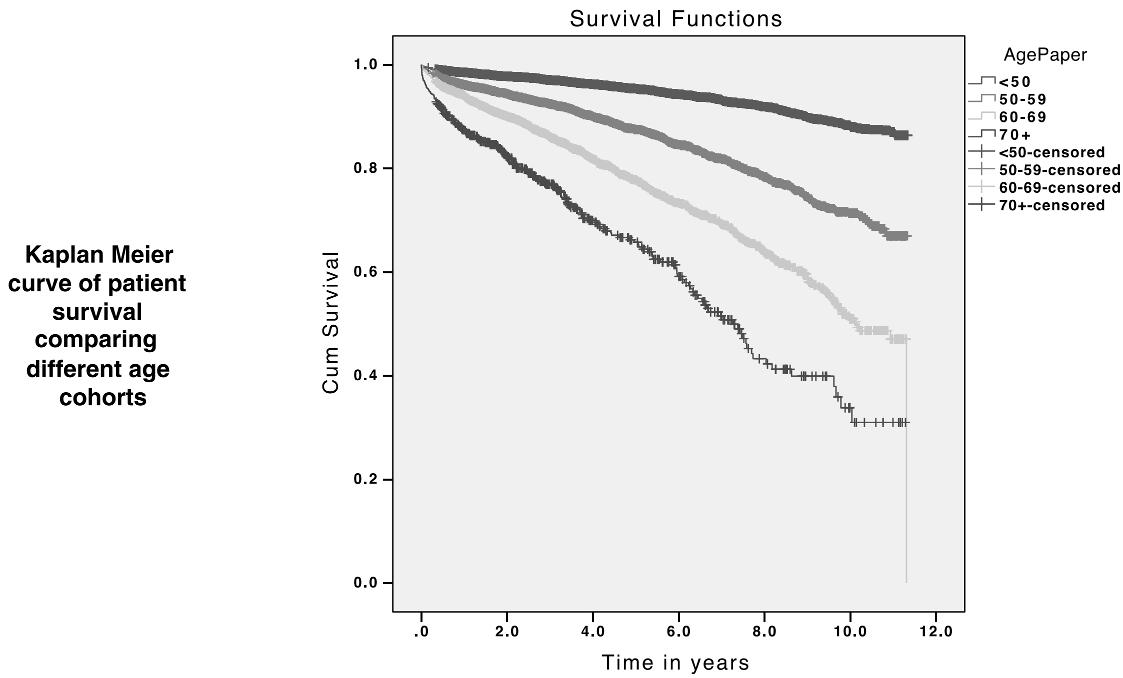
Figure 3 demonstrates unadjusted Kaplan-Meier survival curves for the risk of death after kidney transplantation dependent upon recipient age bracket. Using Cox proportional hazard models, the authors were able to demonstrate older allograft recipients over the reference age of below 50 had increasing hazard ratios for death post-kidney transplantation independent of other variables (see **Table S2, SDC,** http://links.lww.com/TP/A911).

DISCUSSION

In this study, it was demonstrated that increasing age remains a major risk factor for mortality after kidney transplantation, with risk for death increasing proportionally with age at time of transplantation. The risk of death can be further risk stratified among older kidney allograft recipients by the presence or absence of concomitant risk factors. Despite this, it was demonstrated that the majority of kidney allograft recipients in each age bracket remain alive at median follow-up post-kidney transplantation (even in the most extreme older recipient cases). In addition, it was found that living-donor kidney transplantation attenuates the risk of death in all age brackets (although it was reciprocally found that living-donor rates decline with increasing recipient age).

Registry data confirms elderly patients are more likely to receive a kidney allograft in the contemporary era (*7, 8*), and accurate assessment of biological versus chronological age is essential. Frailty, a measure of physiologic reserve, has been widely utilized in the surgical literature (*9*) and could be a valuable tool to assess the suitability of older potential kidney allograft recipients. It is acknowledged as an independent risk factor for adverse postoperative complications (*10*) and early readmission post-kidney transplantation (*11*). Further research in the utility of frailty assessment pre-kidney transplantation should be encouraged, as it could be a simple tool to allow mortality risk stratification among older kidney allograft candidates.

This study demonstrated lower rates of living-donor kidney transplantation as age of potential recipients increased, despite well-documented survival advantages for recipients of living-donor kidneys (*6, 12, 13*). Gill and colleagues demonstrated, in contrast to deceased donor transplantation, that living-donor transplantation eliminated or dramatically reduced the time to equal survival between transplant recipients and waitlist candidates for recipients aged 65 years and over (*14*). Therefore, expanding living-donor kidney options among elderly kidney transplant candidates would be a



Time (years)	0	1	2	3	4	5	6	7	8	9	10	11
Age < 50	11,421	10,471	9,307	8,106	6,915	5,771	4,637	3,616	2,706	1,792	982	290
Age 50-59	4,150	3,701	3,185	2,648	2,143	1,736	1,365	1,068	784	531	278	60
Age 60-69	2,887	2,438	1,973	1,542	1,193	920	691	518	342	223	103	21
Age ≥ 70	600	479	365	258	178	142	103	65	42	24	11	3

FIGURE 3. Unadjusted Kaplan-Meier survival curves of mortality after kidney transplantation stratified by different age cohorts.

TABLE 2. Cox regression proportional hazards model analysis of mortality post-kidney transplantation for allograft recipients by age

Variable		Hazard ratio	95% confidence interval	*P*
Cox regression output (time tailored at 5 years)				
Age	<50	1.00	—	—
	50–59	2.52	2.19–2.90	<0.001
	60–69	4.45	3.88–5.11	<0.001
	70+	7.62	6.30–9.29	<0.001

Variables incorporated into Cox proportional hazards model were age, gender, donor type (living vs. deceased), area of socioeconomic deprivation, ethnicity, year of transplant, and selected medical comorbidities (history of myocardial infarction, peripheral vascular disease, cerebrovascular disease, congestive cardiac failure pulmonary disease, liver disease, peptic ulcer, previous cancer, and diabetes).

sensible strategy to attenuate risk for mortality and should be actively explored.

The Eurotransplant Senior Program has adopted a dynamic and successful deceased-donor allocation approach to transplant elderly candidates, where kidneys from donors aged 65 or more have been allocated to recipients aged 65 or more within a narrow geographic area and regardless of HLA matching (*15*). More recently, Boesmueller and colleagues (*16*) have reported upon their experience within the Eurotransplant Senior Program allocation scheme of kidney allograft recipient aged 70 or more. Patient survival at 1 and 5 years posttransplantation was 95% and 67%, respectively, similar to the survival figures found in this analysis. Although this study did not identify cardiac failure to be the most common cause of death like Boesmueller et al., a pre-existing diagnosis of cardiac failure was found to be the most significant prognosticator of mortality after transplant among allograft recipients aged over 70 in the analysis. This clearly represents a high-risk group and careful assessment and risk stratification (e.g., annual echocardiograms) for such candidates should be explored.

One of the current limitations with the available clinical evidence base is a significant proportion of clinical trials (16.0%) excluded kidney transplant recipients over 65 years of age (*17*). This leaves a gap in the literature with regards to the optimal immunosuppressant regimen among the elderly. Adaptive and innate immunity decreases with age (*18*), and older kidney allograft recipients may not require the same level of immunosuppression as given per standard. This is especially important in the context of age being a strong risk factor for both malignancy (*19*) and infection (*20*) after kidney transplantation. However, caution should be exercised to ensure that immunosuppression for elderly kidney allograft recipients is attenuated but sufficient to avoid the risk of rejection (*21*). Heldal et al. (*22*) demonstrated acute rejection in the first 90 days after kidney transplantation was the strongest risk factor for death (more so than pretransplant comorbidity as classified by Charlson comorbidity index). Therefore, a fine balance is required and targeted clinical trials in the elderly are necessary to guide clinical management.

A key strength of this study is the unique linking between HES and ONS data streams. The completeness and national coverage of mortality data by ONS, and the ability to perform data linkage analysis, ensures comprehensive data is generated regarding mortality numbers and death certificate registration. Limitations include the absence of unmeasured or incompletely measured covariates, or both, that are not accounted for in the analysis (e.g., deaths not occurring in England, allograft failure, donor and recipient data). The ability for registry data streams to be combined would enhance the robustness of observational cohort studies; for example, linking HES and ONS data sets with both the Renal Registry and the National Transplant database in the United Kingdom should be explored. It would also facilitate suitable comparative cohorts for analysis; for example, comparing survival of this study's population cohort with similarly aged patients (with similar comorbidities) on the national kidney waiting list or on dialysis, or both, will determine the added life-years associated with transplantation. Finally, there were no quality-of-life or patient-reported outcome measures to demonstrate any advantage of kidney transplantation in the elderly cohort.

To conclude, this study has shown increased age at time of transplantation is a strong risk factor for mortality after kidney transplantation. For recipients aged 70 and over, the risk of death increases with concomitant medical comorbidities and decreases with female gender, living kidney allograft, and residence in an area of low socioeconomic deprivation. It is believed that the results should not dissuade transplantation assessment for the older kidney transplant candidate but should allow a tailored risk stratification to weigh up the "benefit versus risk equation" for each individual patient. In addition, living-donor kidney transplantation should be encouraged as the treatment of choice for all suitable older patients with end-stage kidney disease.

MATERIALS AND METHODS

Study Design

This was a retrospective observational cohort study, performed on prospectively registered national data sets. This study included all kidney transplant procedures performed at any English kidney transplant center (adult and pediatric) between April 2001 and March 2012. Combined organ transplants (kidney with another organ) were excluded from the analysis (n=1,255). During this time period, 19,688 kidney transplant procedures were recorded in the HES data (635 recipients had repeat transplant performed during the 11-year period but only original transplant factored into Cox regression analysis). Five hundred eighty-five were excluded because of the lack of completeness in relation to demographic information (age, gender, or socioeconomic deprivation), leaving a final cohort of 19,103 recipients for analysis.

Data Sources

Data was obtained from Hospital Episode Statistics (HES) (*23*), an administrative data warehouse containing admissions to all National Health Service hospitals in England, and it contains detailed records relating to individual patient treatments. This data is collected during a patient's time at hospital and is submitted to allow hospitals to be paid for the care they deliver. HES data is designed to enable secondary use, for example non-clinical purposes, and data extraction is facilitated utilizing codes on procedural classifications (Office of Population Censuses and Surveys Classification of Interventions and Procedures, 4th revision [OPCS-4]) (*24*) and medical classifications (World Health Organization International Classification of Disease, 10th revision [ICD-10]) (*25*). For this analysis exploring kidney transplantation, the following OPCS-4 codes were utilized to identify all kidney allograft recipients: M01 to M05, M08, and M09.

With regards to outcome analysis, HES data alone has the limitation of only capturing deaths occurring in a hospital setting. To obtain the complete mortality list, the study cohort was cross-referenced with mortality data from the ONS, which collects information on all registered deaths in the United Kingdom. Combining sources via this data linkage process is robust and creates a complete and comprehensive dataset with regards to mortality, which was the endpoint of interest in this analysis.

Study Variables

Data was extracted from each kidney transplant procedure performed in England in relation to patient demographics at time of transplant; age, gender, donor type (living vs. deceased), ethnicity (white, black or black British, Asian or Asian British, Chinese, mixed, other, and unknown), medical comorbidities (acute myocardial infarct, congestive heart failure, peripheral vascular disease, cerebral vascular accident, pulmonary disease, connective tissue disorder, peptic ulcer, cancer, liver disease, and diabetes mellitus), and socioeconomic deprivation (based upon Index of Multiple Deprivation [IMD] 2010) (*26*). Determination of socioeconomic deprivation was based upon the Index of Multiple Deprivation (2010), a multiple deprivation model calculated at the local level area. The model is based upon assessment of distinct domains of deprivation that can be individually recognized and measured: (1) Income Deprivation, (2) Employment Deprivation, (3) Health Deprivation and Disability, (4) Education Skills and Training Deprivation, (5) Barriers to Housing and Services, (6) Living Environment Deprivation, and (7) Crime. Individual domains are measured in isolation and subsequently combined (utilizing appropriately judged weighting) into a single composite. On the Index of Multiple Deprivation quintile scale, 1 represented the most deprived and 5 the least deprived area, respectively.

This study did not require institutional review board approval because of the pseudo-anonymized nature of the data retrieved—data was linked by NHS Informatics utilizing a special HES ID code and avoided patient-identifiable codes. This observational study was registered with a clinical trials registry (NCT01798524).

Data Quality

As an observational study, the authors adhered to the principles of the STROBE statement and have reported this article in keeping with the recommended guidance (*27*). In addition, data accuracy was checked from the HES database regarding transplant activity by corroborating HES data with the UK Transplant National Transplant database (where all transplant activity must be mandatorily reported). Transplant activity over the same dates as the study period was crosschecked between both databases to ascertain any discrepancy between data sets.

Classification of Death

Because of the subjective nature of death classification and heterogeneity of terms utilized in the death certificates, all deaths were classified into broad systems-based categories (including malignancy). Three authors (A.K., D.F., J.C.) converted all causes of death from ONS data from string into numerical data, with a third author independently verifying the data (A.S.). Any discrepancy on classification was resolved by discussion.

Statistical Methods

The primary study outcome was mortality post-kidney transplantation, with a focus upon data stratification by age. SPSS (version 20.0, Chicago, IL) was utilized for data analysis unless otherwise stated. Difference between groups was assessed with chi-square or two-sided Fisher exact test for categorical variables. A *P* value less than 0.05 and 0.001 in the statistical analysis was considered significant and highly significant, respectively.

Cox proportional hazards model was utilized as survival analysis. The proportionality assumption was checked for each variable and the whole model—for the main analysis, the proportionality assumption is true for all variables except cancer. Variables incorporated into the model were age, gender, donor type (living vs. deceased), area of socioeconomic deprivation, ethnicity, year of transplant, and all medical comorbidities. Review Manager 5 was utilized to generate risk difference Forest plots to compare malignancy death rates between transplant versus general populations. Relative survival analysis was performed against life tables published by the Office of National Statistics. Data was available for 2001 to 2011 (no 2012 data currently available) and therefore 2011 values were utilized as a proxy for 2012. Stata/IC 12 was utilized for this analysis and excess mortality was modeled using a full likelihood approach (*28*), implemented by Dickman (*29*).

With the assumption that data was missing at random, the authors performed listwise deletion and excluded the missing values from the analysis. Other missing data (e.g., ethnicity) was adjusted for as dummy variables in the models as required.

REFERENCES

1. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a cadaveric transplant. *N Engl J Med* 1999; 341: 1725.
2. Rao PS, Merion RM, Ashby VB, et al. Renal transplantation in elderly patients older than 70 years of age: results from the Scientific Registry of Transplant Recipients. *Transplantation* 2007; 83: 1069.
3. Laupacis A, Keown P, Pus N, et al. A study of the quality of life and cost-utility of renal transplantation. *Kidney Int* 1996; 50: 235.
4. Humar A, Denny R, Matas AJ, et al. Graft and quality of life outcomes in older recipients of a kidney transplant. *Exp Clin Transplant* 2003; 1: 69.
5. Cornella C, Brustia M, Lazzarich F, et al. Quality of life in renal transplant patients over 60 years of age. *Transplant Proc* 2008; 40: 1865.
6. Knoll GA. Kidney transplantation in the older adult. *Am J Kidney Dis* 2013; 61: 790.
7. US Renal Data System. USRDS 2011 Annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States. *Am J Kidney Dis* 2012; 59(Suppl 1): e1.
8. Schaeffner ES, Rose C, Gill JS. Access to kidney transplantation among the elderly in the United States: a glass half full, not half empty. *Clin J Am Soc Nephrol* 2010; 5: 2109.
9. Partridge JS, Harari D, Dhesi JK. Frailty in the older surgical patient: a review. *Age Ageing* 2012; 41: 142.
10. Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. *J Am Coll Surg* 2010; 210: 901.
11. McAdams-Demarco MA, Law A, Salter ML, et al. Frailty and early hospital readmission after kidney transplantation. *Am J Transplant* 2013; 13: 2091.
12. Gill J, Bunnapradist S, Danovitch GM, et al. Outcomes of kidney transplantation from older living donors to older recipients. *Am J Kidney Dis* 2008; 52: 541.
13. Levey AS, Danovitch G, Hou S. Living donor kidney transplantation in the United States—looking back, looking forward. *Am J Kidney Dis* 2011; 58: 343.
14. Gill JS, Schaeffner E, Chadban S, et al. Quantification of the early risk of death in elderly kidney transplant recipients. *Am J Transplant* 2013; 13: 427.
15. Frei U, Noeldeke J, Machold-Fabrizii V, et al. Prospective age-matching in elderly kidney transplant recipients—a 5-year analysis of the Eurotransplant Senior Program. *Am J Transplant* 2008; 8: 50.
16. Boesmueller C, Biebl M, Scheidl S, et al. Long-term outcome in kidney transplant recipients over 70 years in the Eurotransplant Senior Kidney Transplant Program: a single center experience. *Transplantation* 2011; 92: 210.
17. Blosser CD, Huverserian A, Bloom RD, et al. Age, exclusion criteria, and generalizability of randomized trials enrolling kidney transplant recipients. *Transplantation* 2011; 91: 858.
18. Martins PN, Pratschke J, Pascher J. Age and the immune response in organ transplantation. *Transplantation* 2005; 79: 127.

19. Gallagher MP, Kelly PJ, Jardine M, et al. Long-term risk of immunosuppressive regimens after kidney transplantation. *J Am Soc Nephrol* 2010; 21: 852.
20. Meier-Kriesche HU, Ojo AO, Hanson JA, et al. Exponentially increased risk of infectious death in older renal transplant recipients. *Kidney Int* 2001; 59: 1539.
21. de Fijter JW. The impact of age on rejection in kidney transplantation. *Drugs Aging* 2005; 22: 433.
22. Heldal K, Hartmann A, Leivestad T, et al. Clinical outcomes in elderly kidney transplant recipients are related to acute rejection episodes rather than pretransplant comorbidity. *Transplantation* 2009; 87: 1045.
23. Hospital Episode Statistics online. (Accessed on June 12, 2013; www.hesonline.nhs.uk).
24. OPCS-4 Classification—NHS Connecting for Health. (Accessed on June 12, 2013; www.connectingforhealth.nhs.uk).
25. World Health Organization: International Classification of Diseases (ICD). (Accessed on June 5, 2013; www.who.int/classifications/icd/en).
26. Department for Communities and Local Government. The English Indices of Deprivation 2010. (Accessed on June 17, 2013; https://www.gov.uk/government/publications/english-indices-of-deprivation-2010).
27. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007; 370: 1453.
28. Esteve J, Benhamou E, Croasdale M, et al. Relative survival and the estimation of net survival: elements for further discussion. *Stat Med* 1990; 9: 529.
29. Dickman PW, Coviello E, Hills M. Estimating and modelling relative survival. Accessed on July 19, 2013 at: www.pauldickman.com/survival/strs.pdf.