Recipient Criteria Predictive of Graft Failure in Kidney Transplantation

Ernesto P. Molmenti, MD, PhD, MBA, FICA[1,2] Asha Alex, MD[1] Lisa Rosen, ScM[3] Mohini Alexander, MD[2] Jeffrey Nicastro, MD[1] Jingyan Yang, MHS[4] Eric Siskind, MD[1] Leesha Alex, BS[1] Emil Sameyah, MD[3] Madhu Bhaskaran, MD[2] Nicole Ali, MD[2] Amit Basu, MD[1] Mala Sachdeva, MD[2] Stergiani Agorastos, BS[1] Prejith Rajendran, MBBS[1] Prathik Krishnan, MBBS[1] Poornima Ramadas, MBBS[1] Leo Amodu, MD[1] Joaquin Cagliani, MD[1] Sameer Rehman, MD[1] Adam Kressel, MD[1] Christine B. Sethna, MD[5] Georgios C. Sotiropoulos, MD, PhD[6] Arnold Radtke, MD[7] George Sgourakis, MD[8] Richard Schwarz, MD[2] Steven Fishbane, MD[2] Alessandro Bellucci, MD[2] Gene Coppa, MD[1] Horacio Rilo, MD[1] Christine L. Molmenti, MPH, PhD[4]

[1] Department of Surgery, Hofstra North Shore-LIJ School of Medicine, New York
[2] Department of Medicine, Hofstra North Shore-LIJ School of Medicine, New York
[3] The Feinstein Institute for Medical Research, Hofstra North Shore-LIJ School of Medicine, New York
[4] Mailman School of Public Health, Columbia University, New York
[5] Department of Pediatrics, Hofstra North Shore-LIJ School of Medicine, New York
[6] Department of General, Visceral and Transplantation Surgery, University Hospital Essen, Essen, Germany
[7] Department of General and Visceral Surgery, University Hospital Muenster, Albert-Schweitzer-Campus, Muenster, Germany
[8] Department of General Surgery, Red Cross Hospital, Athens, Greece

Address for correspondence Ernesto P. Molmenti, MD, PhD, MBA, FICA, Transplant Center, 1554 Northern Boulevard, Manhasset, New York 11030 (e-mail: emolment@nshs.edu).

Int J Angiol 2016;25:29–38.

Abstract

Several classifications systems have been developed to predict outcomes of kidney transplantation based on donor variables.

This study aims to identify kidney transplant recipient variables that would predict graft outcome irrespective of donor characteristics.

All U.S. kidney transplant recipients between October 25,1999 and January 1, 2007 were reviewed. Cox proportional hazards regression was used to model time until graft failure. Death-censored and nondeath-censored graft survival models were generated for recipients of live and deceased donor organs. Recipient age, gender, body mass index (BMI), presence of cardiac risk factors, peripheral vascular disease, pulmonary disease, diabetes, cerebrovascular disease, history of malignancy, hepatitis B core antibody, hepatitis C infection, dialysis status, panel-reactive antibodies (PRA), geographic region, educational level, and prior kidney transplant were evaluated in all kidney transplant recipients.

Among the 88,284 adult transplant recipients the following groups had increased risk of graft failure: younger and older recipients, increasing PRA (hazard ratio [HR],1.03–1.06], increasing BMI (HR, 1.04–1.62), previous kidney transplant (HR, 1.17–1.26),

Keywords

- kidney transplant recipients
- outcomes predictors
- graft failure
- comorbidities
- patient education
- geographic disparities

published online
September 15, 2015

DOI http://dx.doi.org/10.1055/s-0035-1563605.
ISSN 1061-1711.

dialysis at the time of transplantation (HR, 1.39–1.51), hepatitis C infection (HR, 1.41–1.63), and educational level (HR, 1.05–1.42).
Predictive criteria based on recipient characteristics could guide organ allocation, risk stratification, and patient expectations in planning kidney transplantation.

Kidney transplantation represents the best alternative for survival and improved quality of life for eligible end stage renal disease patients. Although several classifications that estimate outcomes have been developed, they all involve donor features. The Kidney Donor Risk Index (KDRI) and Kidney Donor Profile Index (KDPI),[1,2] based on deceased donor age, height, weight, ethnicity, history of hypertension, history of diabetes, cause of death, serum creatinine, hepatitis C virus status, and donation after circulatory death, assess the relative risk of graft failure irrespective of recipient characteristics.

The objective of this study was to identify kidney transplant recipient variables that would predict graft outcome irrespective of donor characteristics. These recipient predictive criteria could constitute an instrument of great potential value and a relevant addition to the current allocation system. They would provide information on expected outcomes not only at the time of evaluation and during wait listing when no donor information is routinely available, but also at the time of organ allocation when they would be complemented by the already existing donor classifications.

Methods

Subjects

Data on 88,284 kidney transplants performed in the United States from October 25, 1999 to January 1, 2007 obtained from the United Network for Organ Sharing (UNOS) were considered in the analysis.

Selection Criteria

There were 119,979 transplants between October 25, 1999 and January 1, 2007. Several variables of interest (drug-treated hypertension, cerebrovascular disease, and angina) had collection end dates of January 1, 2007. Since then, they have become optional data fields and their reporting has been sparse. The start date was chosen because relevant donor-related variables (deceased donor – cardiac arrest post–brain death), although not of primary interest, had collection dates beginning October 25, 1999. Recipients listed for pancreas ($n = 3{,}629$) and kidney pancreas ($n = 6{,}719$) as well as those with no organ listed ($n = 16{,}173$) were excluded. Kidney recipients younger than 18 or with missing age were also excluded ($n = 3{,}857$). There were 1,317 adult kidney recipients with multiple transplants in our timeframe of interest. For purposes of our analysis, only the initial transplant between October 25, 1999 and January 1, 2007 was included. Body mass index (BMI) < 15 or > 55, live donor preoperative creatinine > 1.5, and deceased donor terminal creatinine > 6 were deemed unlikely and treated as unknown.

Primary Outcome Variable

The primary outcome considered was (death-censored and nondeath-censored) graft survival, as defined in previous studies.[3] In death-censored graft survival, graft survival was censored at the time of death (based on the assumption that death was unrelated to the transplant) or at the time of the last known patient status (if neither failure nor death occurred). In nondeath-censored graft survival, death with a functioning graft was treated as graft failure (under the assumption that death was related to the transplant).

Statistical Analysis

Cox regression was used to model time until graft failure. Recipient risk factors significantly associated with graft failure using univariable screening at the level of $p < 0.10$ were included in the final multivariable model. Transplant and donor variables known to be highly predictive of graft failure, while not of direct interest, were included in the multivariable model as covariates, regardless of statistical significance. Donor variables included human leukocyte antigen (HLA) mismatch and elements of the KDPI. Although backward elimination was also considered in building the final model, its results were similar to those of univariable screening and are not reported here. Separate models were used for recipients of live and deceased donors. Each model was analyzed using both definitions of graft survival, resulting in four multivariable models. The proportional hazards assumption was evaluated graphically by plotting the log-negative-log of the estimated survival function by the log of time.

Results

Demographics of the 88,284 subjects included in our final sample are detailed in ►**Table 1**.

Death-Censored Graft Survival

Recipients of Live Donors

►**Table 2** shows the death-censored multivariable Cox regression analysis for graft survival in recipients of live donors (3,667 graft failures). Younger and older recipients (quadratic term) had an increased risk of graft failure. Recipients with overweight or obese BMI, a previous kidney transplant, hepatitis C, increasing panel-reactive antibodies (PRA), dialysis at the time of transplant, and diabetes also had an increased risk of graft failure as compared to recipients

Table 1 Characteristics of kidney transplant recipients of live and deceased donors and all recipients

Factor	All recipients ($n = 88,284$)	Recipients of live donors ($n = 27,117$)	Recipients of deceased donors ($n = 61,167$)
Age, y	48.90 ± 13.26	46.03 ± 13.39	50.17 ± 13.00
Gender			
Male no. (%)	53,174 (60.23)	16,064 (59.24)	37,110 (60.67)
BMI			
Underweight, no. (%)	2,432 (2.75)	775 (2.86)	1,657 (2.71)
Normal weight, no. (%)	31,722 (35.93)	9,954 (36.71)	21,768 (35.59)
Overweight, no. (%)	28,464 (32.24)	8,677 (32.00)	19,787 (32.35)
Obese class I, no. (%)	15,349 (17.39)	4,648 (17.14)	10,701 (17.49)
Obese class II, no. (%)	4,998 (5.66)	1,491 (5.50)	3,507 (5.73)
Obese class III, no. (%)	1,497 (1.70)	476 (1.76)	1,021 (1.67)
Unknown	3,822 (4.33)	1,096 (4.04)	2,726 (4.46)
Previous kidney transplant			
Yes	9,467 (10.72)	2,528 (9.32)	6,939 (11.34)
No	78,817 (89.28)	24,589 (90.68)	54,228 (88.66)
Previous malignancy			
Yes	3,043 (3.45)	955 (3.52)	2,088 (3.41)
No	74,826 (84.76)	22,995 (84.80)	51,831 (84.74)
Unknown	10,415 (11.80)	3,167 (11.68)	7,428 (11.85)
Angina			
Yes	8,684 (9.84)	2,378 (8.77)	6,306 (10.31)
No	74,075 (83.91)	22,922 (84.53)	51,153 (83.63)
Unknown	5,525 (6.26)	1,817 (6.70)	3,708 (6.06)
Drug-treated hypertension			
Yes	68,902 (78.05)	21,341 (78.70)	47,561 (77.76)
No	14,887 (16.86)	4,383 (16.16)	10,504 (17.17)
Unknown	4,495 (5.09)	1,393 (5.14)	3,102 (5.07)
Peripheral vascular disease			
Yes	2,981 (3.38)	837 (3.09)	2,144 (3.51)
No	79,144 (89.65)	24,368 (89.86)	54,776 (89.55)
Unknown	6,159 (6.98)	1,912 (7.05)	4,247 (6.94)
Drug-treated COPD			
Yes	761 (0.86)	217 (0.80)	544 (0.89)
No	82,384 (93.32)	25,341 (93.45)	57,043 (93.26)
Unknown	5,139 (5.82)	1,559 (5.75)	3,580 (5.85)
Symptomatic cerebrovascular disease			
Yes	2,046 (2.32)	560 (2.07)	1,486 (2.43)
No	80,551 (91.24)	24,899 (91.82)	55,652 (90.98)
Unknown	5,687 (6.44)	1,658 (6.11)	4,029 (6.59)
Hepatitis B surface antigen			
Positive	1,475 (1.67)	395 (1.46)	1,080 (1.77)
Negative	75,098 (85.06)	23,451 (86.48)	51,647 (84.44)
Not done	1,949 (2.21)	562 (2.07)	1,387 (2.27)
Unknown/missing	9,762 (11.06)	2,709 (9.99)	7,053 (11.53)

(*Continued*)

Table 1 (*Continued*)

Factor	All recipients ($n = 88,284$)	Recipients of live donors ($n = 27,117$)	Recipients of deceased donors ($n = 61,167$)
Hepatitis C status			
Positive	4,875 (5.52)	799 (2.95)	4,076 (6.66)
Negative	72,795 (82.46)	23,554 (86.86)	49,241 (80.50)
Not done	6,253 (7.08)	1,592 (5.87)	4,661 (7.62)
Unknown/missing	4,361 (4.94)	1,172 (4.32)	3,189 (5.21)
Dialysis at transplant			
Yes	74,094 (83.93)	19,780 (72.94)	54,314 (88.80)
No	12,899 (14.61)	6,839 (25.22)	6,060 (9.91)
Unknown	1,291 (1.46)	498 (1.84)	793 (1.30)
Diabetes at registration			
Yes	25,270 (28.62)	7,144 (26.35)	18,126 (29.63)
No	61,130 (69.24)	19,434 (71.67)	41,696 (68.17)
Unknown	1,884 (2.13)	539 (1.99)	1,345 (2.20)
Current PRA (median [Q1, Q3])		0.0 (0.0, 0.0)	0.00 (0.00, 3.00)
Education			
No high school diploma or GED	4,765 (5.40)	994 (3.67)	3,771 (6.17)
High school diploma or GED	33,091 (37.48)	9,114 (33.61)	23,977 (39.20)
Attended college/technical school	17,389 (19.70)	5,951 (21.95)	11,438 (18.70)
Associate/bachelor's degree	10,811 (12.25)	4,176 (15.40)	6,635 (10.85)
Graduate degree	4,291 (4.86)	1,831 (6.75)	2,460 (4.02)
Unknown/missing	17,937 (20.32)	5,051 (18.63)	12,886 (21.07)
Region			
1	3,722 (4.22)	1,202 (4.43)	2,520 (4.12)
2	13,544 (15.34)	4,472 (16.49)	9,072 (14.83)
3	11,145 (12.62)	2,512 (9.26)	8,633 (14.11)
4	7,443 (8.43)	1,865 (6.88)	5,578 (9.12)
5	14,055 (15.92)	4,976 (18.35)	9,079 (14.84)
6	2,960 (3.35)	628 (2.32)	2,332 (3.81)
7	9,398 (10.65)	3,757 (13.85)	5,641 (9.22)
8	4,944 (5.60)	1,463 (5.40)	3,481 (5.69)
9	5,579 (6.32)	1,819 (6.71)	3,760 (6.15)
10	7,567 (8.57)	2,371 (8.74)	5,196 (8.49)
11	7,927 (8.98)	2,052 (7.57)	5,875 (9.60)

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; GED, general educational development; PRA, panel-reactive antibodies.

without these characteristics. Recipients with a high school (HS) diploma or general educational development (GED) had an increased risk of graft failure as compared to attendees of college, recipients of associate or bachelor's degrees and graduate degrees, with hazard ratio (HR) ranging from 1.14 to 1.42. Attendees of college had an increased risk of graft failure as compared to recipients of associate or bachelor's degrees (HR,1.13) and graduate degrees. Recipients in UNOS transplant region 2 had an increased risk of graft failure as compared to regions 1, 3, 4, 5, and 10, with HR ranging from 1.20 to 1.27. Malignancy, angina, drug-treated hypertension, drug-treated chronic obstructive pulmonary disease (COPD), peripheral vascular disease, and cerebral vascular disease were not statistically significant at $p < 0.10$ by univariable screen and were excluded from the final multivariable model.

Table 2 Death-censored graft survival in recipients of live donors and recipients of deceased donors

Factor[a]	Recipients of live donors[b,c] HR (95% CI) $n = 27,117$	Recipients of deceased donors[d,e] HR (95% CI) $n = 61,167$
Age	0.93 (0.92, 0.95)	0.94 (0.93, 0.94)
Age ×age	1.01 (1.00, 1.01)	1.00 (1.00, 1.01)
Gender		
Male	0.97 (0.91, 1.04)	1.07 (1.03, 1.11)
Female	Reference	Reference
BMI		
Underweight	1.05 (0.87, 1.26)	0.95 (0.85, 1.05)
Normal weight	Reference	Reference
Overweight	1.09 (1.00, 1.18)	1.11 (1.07, 1.16)
Obese class I	1.26 (1.14, 1.39)	1.27 (1.20, 1.33)
Obese class II	1.47 (1.28, 1.68)	1.37 (1.27, 1.47)
Obese class III	1.62 (1.32, 1.99)	1.61 (1.43, 1.82)
Previous kidney transplant		
Yes	1.25 (1.13, 1.39)	1.17 (1.11, 1.24)
No	Reference	Reference
Peripheral vascular disease		
Yes		1.13 (1.02, 1.25)
No		Reference
Hepatitis C status		
Positive	1.56 (1.33, 1.83)	1.44 (1.34, 1.54)
Negative	Reference	Reference
Not done	0.90 (0.75, 1.08)	1.04 (0.96, 1.13)
Dialysis at transplant		
Yes	1.43 (1.31, 1.56)	1.51 (1.41, 1.62)
No	Reference	Reference
Diabetes		
Yes	1.09 (1.00, 1.18)	1.02 (0.98, 1.06)
No	Reference	
Current PRA (in 10-percentage point increments)	1.06 (1.04, 1.08)	1.04 (1.03, 1.05)
Education		
No high school diploma or GED	1.33 (1.04, 1.70)	1.00 (0.89, 1.13)
High school diploma or GED	1.42 (1.20, 1.66)	1.12 (1.01, 1.23)
Attended college/technical school	1.24 (1.05, 1.47)	1.06 (0.96, 1.18)
Associate/bachelor's degree	1.09 (0.92, 1.31)	1.02 (0.92, 1.14)
Graduate degree	Reference	Reference
Region		
1	1.03 (0.86, 1.23)	1.07 (0.97, 1.19)
2	1.27 (1.11, 1.45)	1.37 (1.28, 1.47)
3	1.06 (0.91, 1.23)	1.12 (1.04, 1.21)
4	1.03 (0.87, 1.21)	1.18 (1.09, 1.28)
5	Reference	Reference
6	1.00 (0.78, 1.29)	0.94 (0.84, 1.05)

(*Continued*)

Table 2 (*Continued*)

Factor[a]	Recipients of live donors[b,c] HR (95% CI) $n = 27,117$	Recipients of deceased donors[d,e] HR (95% CI) $n = 61,167$
7	1.16 (1.02, 1.33)	1.11 (1.02, 1.20)
8	1.17 (0.99, 1.38)	1.05 (0.95, 1.15)
9	1.08 (0.90, 1.29)	1.27 (1.17, 1.39)
10	1.06 (0.91, 1.23)	1.13 (1.04, 1.22)
11	1.15 (0.99, 1.33)	1.35 (1.26, 1.46)

Abbreviations: BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; GED, general educational development; HR, hazard ratio; PRA, panel-reactive antibodies.

[a]Recipients of live/deceased donors: Unknown or missing categories are not presented in the table since valid inferences cannot be drawn from them.

[b]Recipients of live donors: Model is also adjusted for recipient hepatitis B surface antigen. However, the results are not displayed due to nonsignificance in the multivariable model.

[c]Recipients of live donors: Model is also adjusted for donor age, donor BMI, donor gender, donor ethnicity, HLA mismatch level, donor preoperative creatinine, and donor hepatitis C antibody.

[d]Recipients of deceased donors: Model is also adjusted for recipient angina status, cerebrovascular disease, and hepatitis B surface antigen. However, the results are not displayed due to nonsignificance in the multivariable model.

[e]Recipients of deceased donors: Model is also adjusted for donor age, donor BMI, donor gender, donor ethnicity, HLA mismatch level, donor terminal laboratory creatinine, donor hepatitis C antibody, donor history of diabetes, donor history of hypertension, donor cause of death, and donor cardiac arrest postbrain death.

Recipients of Deceased Donors

►**Table 2** shows the death-censored multivariable Cox regression analysis for graft survival in recipients of deceased donors (13,361 graft failures). Younger and older recipients had an increased risk of graft failure. Males, recipients with overweight or obese BMI, a previous kidney transplant, peripheral vascular disease, hepatitis C, increasing PRA, and dialysis at the time of transplant also had an increased risk of graft failure as compared to recipients without these characteristics. Recipients with a HS diploma or GED had an increased risk of graft failure as compared to recipients without a HS diploma, attendees of college, recipients of associate or bachelor's degrees, and graduate degrees, with HR ranging from 1.05 to 1.12. Region 5 and 6 recipients had a reduced risk of graft failure as compared to all other regions, excluding region 8, with HR ranging from 0.68 to 0.90. Region 2 recipients had an increased risk of graft failure as compared to all other regions, excluding 9 and 11, with HR ranging from 1.16 to 1.46. Region 9 recipients had an increased risk of graft failure as compared to regions 1, 3, 5, 6, 7, 8, and 10, with HR ranging from 1.13 to 1.36. Malignancy, drug-treated hypertension, and drug-treated COPD were not statistically significant at $p < 0.10$ by univariable screen and were excluded from the final multivariable model.

Nondeath-Censored Graft Survival

Recipients of Live Donors

►**Table 3** shows the noncensored multivariable Cox regression graft survival analysis for recipients of live donors (6,026 graft failures, inclusive of recipients who died with functioning grafts). Younger and older recipients had an increased risk of graft failure. Recipients with underweight or obese BMI, a previous kidney transplant, malignancy, drug-treated COPD, angina, peripheral vascular disease, cerebral vascular disease, hepatitis C, increasing PRA, dialysis at the time of transplant, and diabetes also had an increased risk of graft failure as compared to recipients without these characteristics. Recipients without a HS diploma or GED had an increased risk of graft failure as compared to recipients of associate or bachelor's degrees (HR,1.22) and graduate degrees. Recipients with a HS diploma or GED had an increased risk of graft failure as compared to attendees of college, recipients of associate or bachelor's degrees, and graduate degrees with HR ranging from 1.11 to 1.36. Attendees of college had an increased risk of graft failure as compared to recipients of associate or bachelor's degrees (HR,1.14) and graduate degrees. Gender was not statistically significant at $p < 0.10$ by univariable screen and was excluded from the final multivariable model.

Recipients of Deceased Donors

►**Table 3** shows the noncensored multivariable Cox regression graft survival analysis for recipients of deceased donors (23,231 graft failures inclusive of patients who died with a functioning graft). Younger and older recipients had an increased risk of graft failure. Males and recipients with overweight or obese BMI, a previous kidney transplant, malignancy, angina, peripheral vascular disease, hepatitis C, increasing PRA, dialysis at the time of transplant, and diabetes also had an increased risk of graft failure as compared to recipients without these characteristics. Recipients with a HS diploma or GED had an increased risk of graft failure as compared to attendees of college, recipients of associate or bachelor's degrees and graduate degrees, with HR ranging from 1.06 to 1.15. Attendees of college had an increased risk of graft failure as compared to recipients of associate or bachelor's degrees (HR,1.08) and graduate degrees. Recipients from regions 5, 6, and 8 had a reduced risk of graft failure

Table 3 Nondeath-censored graft survival in recipients of live donors and recipients of deceased donors

Factor[a]	Recipients of live donors[b,c] HR (95% CI) $n = 27,117$	Recipients of deceased donors[d,e] HR (95% CI) $n = 61,167$
Age	0.92 (0.91, 0.93)	0.93 (0.93, 0.94)
Age ×age	1.01 (1.00, 1.01)	1.00 (1.00, 1.01)
Gender		
Male		1.12 (1.09, 1.15)
Female		Reference
BMI		
Underweight	1.19 (1.02, 1.38)	1.07 (0.98, 1.16)
Normal weight	Reference	Reference
Overweight	1.01 (0.95, 1.08)	1.04 (1.01, 1.07)
Obese class I	1.10 (1.02, 1.38)	1.17 (1.12, 1.21)
Obese class II	1.32 (1.18, 1.47)	1.21 (1.14, 1.28)
Obese class III	1.46 (1.23, 1.73)	1.54 (1.40, 1.69)
Previous kidney transplant		
Yes	1.26 (1.15, 1.37)	1.19 (1.14, 1.24)
No	Reference	Reference
Malignancy		
Yes	1.28 (1.13, 1.44)	1.10 (1.03, 1.18)
No	Reference	Reference
Drug-treated COPD		
Yes	1.54 (1.24, 1.92)	1.10 (0.97, 1.25)
No	Reference	Reference
Angina		
Yes	1.11 (1.02, 1.21)	1.18 (1.13, 1.23)
No	Reference	Reference
Peripheral vascular disease		
Yes	1.27 (1.12, 1.43)	1.30 (1.22, 1.38)
No	Reference	Reference
Cerebral vascular disease		
Yes	1.21 (1.04, 1.41)	1.05 (0.97, 1.14)
No	Reference	Reference
Hepatitis C status		
Positive	1.63 (1.44, 1.84)	1.41 (1.33, 1.49)
Negative	Reference	Reference
Not done	0.95 (0.82, 1.10)	1.02 (0.95, 1.08)
Dialysis at transplant		
Yes	1.46 (1.36, 1.56)	1.39 (1.32, 1.46)
No	Reference	Reference
Diabetes		
Yes	1.42 (1.34, 1.50)	1.32 (1.28, 1.36)
No	Reference	Reference
Current PRA (in 10-percentage point increments)	1.05 (1.04, 1.07)	1.03 (1.03, 1.04)
Education		

(*Continued*)

Table 3 (*Continued*)

Factor[a]	Recipients of live donors[b,c] HR (95% CI) $n = 27,117$	Recipients of deceased donors[d,e] HR (95% CI) $n = 61,167$
No high school diploma or GED	1.32 (1.10, 1.57)	1.05 (0.97, 1.15)
High school diploma or GED	1.36 (1.21, 1.53)	1.15 (1.07, 1.23)
Attended college/technical school	1.23 (1.09, 1.39)	1.08 (1.01, 1.17)
Associate/bachelor's degree	1.08 (0.95, 1.23)	1.00 (0.93, 1.09)
Graduate degree	Reference	Reference
Region		
1	1.04 (0.91, 1.20),	1.07 (0.99, 1.15)
2	1.18 (1.07, 1.31)	1.22 (1.16, 1.29)
3	1.09 (0.97, 1.23)	1.13 (1.07, 1.19)
4	0.98 (0.80, 1.19)	1.16 (1.10, 1.23)
5	Reference	Reference
6	0.98 (0.80, 1.19)	0.97 (0.90, 1.06)
7	1.11 (1.00, 1.23)	1.13 (1.06, 1.20)
8	1.09 (0.95, 1.24)	1.05 (0.98, 1.12)
9	1.07 (0.93, 1.23)	1.18 (1.11, 1.26)
10	1.08 (0.97, 1.21)	1.16 (1.10, 1.24)
11	1.20 (1.07, 1.34)	1.27 (1.20, 1.35)

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CI, confidence interval; GED, general educational development; HR, hazard ratio; PRA, panel-reactive antibodies.

[a]Recipients of live/deceased donors: Unknown or missing categories are not presented in the table since valid inferences cannot be drawn from them.

[b]Recipients of live donors: Model is also adjusted for recipient drug-treated hypertension and hepatitis B surface antigen. However, the results are not displayed due to nonsignificance in the multivariable model or significance in the unknown category.

[c]Recipients of live donors: Model is also adjusted for donor age, donor BMI, donor gender, donor ethnicity, HLA mismatch level, donor preoperative creatinine, and donor hepatitis C antibody.

[d]Recipients of deceased donors: Model is also adjusted for recipient drug-treated hypertensionand hepatitis B surface antigen. However, the results are not displayed due to nonsignificance in the multivariable model or significance in the unknown category.

[e]Recipients of deceased donors: Model is also adjusted for donor age, donor BMI, donor gender, donor ethnicity, HLA mismatch level, donor terminal laboratory creatinine, donor hepatitis C antibody, donor history of diabetes, donor history of hypertension, donor cause of death, and donor cardiac arrest postbrain death.

compared to all other regions, excluding 1, with HR ranging from 0.76 to 0.93. Recipients from region 2 had an increased risk of graft failure compared to regions 1, 3, 5, 6, 7, and 8, with HR ranging from 1.08 to 1.26. Recipients from region 11 had an increased risk of graft failure compared to all other regions, excluding 2, with HR ranging from 1.08 to 1.31. All variables were statistically significant at $p < 0.10$ by univariable screen and all were included in the final multivariable model.

Discussion

Our series identified recipient age, increasing PRA, BMI, prior transplant, dialysis at the time of transplantation, hepatitis C infection, and education as variables associated with increased risk for graft failure in adult kidney transplant recipients regardless of survival definition or donor type.

Younger and elderly recipients had an increased risk of graft failure. A higher degree of immune responsiveness, immunosuppressive medication noncompliance, financial, and social factors have been postulated to contribute to a greater incidence of early graft loss in the young.[4–6] Previous studies reported elderly recipients to have a high incidence of comorbidities, frailty, and death with functioning grafts, as well as a greater impact of rejection on graft loss.[7]

PRA is an immunological test that quantifies the percentage of the population against which an individual reacts via preformed antibodies. Recipients with PRA $\geq$ 80% have a higher risk of acute rejection leading to graft failure, and are given additional points in the organ allocation algorithm.[8]

BMI is a measure of body fat based on height and weight.[9] Patients with BMI $\geq$ 30 (obese classes I, II, and III) had an increased risk of graft failure when compared with those with lower BMI. An analysis of adult renal transplant patients registered in U.S. Renal Data System had demonstrated that BMI $<$ 18 and $>$ 36 were associated with worse patient and graft survival.[10] Surgical-site infections, delayed graft function, prolonged hospitalization, acute rejection, and decreased overall graft survival had previously been found to be more prevalent in obese individuals.[11,12]

Prior smaller studies had reported conflicting results on retransplantation outcomes.[13–15] In our series retransplantation was associated with decreased graft survival.

The process of dialysis is associated with micro- and macrovascular pathologies, malnutrition, chronic systemic inflammation, and decreased renal clearance.[16] Studies have shown that patients who are preemptively transplanted have improved graft survival.[17] Longer transplant wait times while on dialysis negatively impact posttransplant graft function.[16] End-stage renal disease and chronic dialysis can be associated with up to a 72% increase in mortality risk.[16]

Our study demonstrated that recipients with a diagnosis of hepatitis C before transplantation had an increased risk of graft failure, an observation consistent with prior reports.[18] This finding was consistent in all four models. Chronic active hepatitis and cirrhosis should be thoroughly evaluated prior to kidney transplantation.[19]

Previous studies showed that education could have an association with improved outcomes.[20–22] We observed increased graft survival among HS graduates irrespective of definition or donor type.

Prior malignancy, peripheral vascular disease, angina, and diabetes were associated with an increased risk of graft failure in recipients of both live and deceased donors only when using the nondeath-censored definition (that treats all deaths as graft failures). This difference could potentially be attributable to deaths associated with malignancies, cardiovascular disease, and diabetic complications.[23,24] UNOS and the Organ Procurement and Transplantation Network (OPTN) facilitate organ procurement, allocation, and transplantation by dividing the nation into 11 regions that loosely correspond to U.S. census regions.[25] Variations in waiting list times, availability of organs, and transplant rates have been previously reported[26] and could account for some of the regional geographic differences observed.

The timeframe of October 25, 1999 through January 1, 2007 was chosen because some variables of interest had a collection end date of January 1, 2007. These variables are currently optional data fields and become very sparse in more recent years. Additionally, important donor-related variables, while not of primary interest for this study, had collection dates that began on October 25, 1999. Certain assumptions were made in regard to plausible values for BMI and creatinine. Specifically, BMI < 15 or > 55, live donor preoperative creatinine > 1.5 and deceased donor terminal creatinine > 6 were deemed unlikely values due to common donor selection practices and were interpreted as missing or unknown. Some important predictors of graft failure were excluded due to large amounts of missing data, such as warm and cold ischemia times. With limitations related to quality control, variables which were found to be nonsignificant may not have been appropriately registered or followed up over time in the database and should be considered further in detail. Donor variables for inclusion in the multivariable model were based on HLA mismatch and on the KDPI. Since KDPI addresses only deceased donors, variables such as diabetes, cause of death, and cardiac arrest postbrain death were not relevant for live donors.

Conclusions

We propose a model based on the recipient characteristics, and independent of donor variables. Age, increasing PRA, BMI, prior transplant, dialysis at the time of transplantation, hepatitis C infection, and education were found to be associated with an increased risk for graft failure in adult kidney transplant recipients regardless of survival definition and donor type. These recipient predictive criteria could further optimize outcomes and organ allocation[27] by providing information not only at the time of evaluation and during wait listing when no donor information is routinely available, but also at the time of organ allocation when they would be complemented by the already existing donor grading classifications.

Acknowledgments

The authors of this article have no conflicts of interest to disclose. This work was supported in part by Health Resources and Services Administration contract 231–00–0015. The content is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government. Lisa Rosen, ScM, Feinstein Institute of Medical Research, conducted the data analysis, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the analysis. The authors would like to acknowledge Bruce Shepperson, SAS analyst at UNOS, for his assistance with all data-related queries. We would also like to thank Mr. John Raggio and Dr. Donna Kesselman, the Janet and John Raggio Nephrology Institute, and the Michael and Jamie Mazzei family for their kind support.

References

1 Rao PS, Schaubel DE, Guidinger MK, et al. A comprehensive risk quantification score for deceased donor kidneys: the kidney donor risk index. Transplantation 2009;88(2):231–236
2 Akkina SK, Asrani SK, Peng Y, Stock P, Kim WR, Israni AK. Development of organ-specific donor risk indices. Liver Transpl 2012;18(4):395–404
3 Hariharan S, Johnson CP, Bresnahan BA, Taranto SE, McIntosh MJ, Stablein D. Improved graft survival after renal transplantation in the United States, 1988 to 1996. N Engl J Med 2000;342(9):605–612
4 Joosten SA, Sijpkens YW, van Kooten C, Paul LC. Chronic renal allograft rejection: pathophysiologic considerations. Kidney Int 2005;68(1):1–13
5 Andreoni KA, Forbes R, Andreoni RM, Phillips G, Stewart H, Ferris M. Age-related kidney transplant outcomes: health disparities amplified in adolescence. JAMA Intern Med 2013;173(16):1524–1532
6 Kasiske BL, Cangro CB, Hariharan S, et al; American Society of Transplantation. The evaluation of renal transplantation candidates: clinical practice guidelines. Am J Transplant 2001;1 (Suppl 2):3–95

7 Furian L, Rigotti P. Transplantation: Optimizing outcomes in elderly kidney transplant recipients. Nat Rev Nephrol 2013;9(7):382–384
8 Organ Procurement and Transplantation Network (OPTN). Allocation calculators. Available at: http://optn.transplant.hrsa.gov/converge/resources/allocationcalculators.asp?index=75. Accessed August 26, 2013
9 The World Health Organization (WHO). Global database on body mass index. Available at: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html. Accessed August 26, 2013
10 Meier-Kriesche H-U, Arndorfer JA, Kaplan B. The impact of body mass index on renal transplant outcomes: a significant independent risk factor for graft failure and patient death. Transplantation 2002;73(1):70–74
11 Lynch RJ, Ranney DN, Shijie C, Lee DS, Samala N, Englesbe MJ. Obesity, surgical site infection, and outcome following renal transplantation. Ann Surg 2009;250(6):1014–1020
12 Gore JL, Pham PT, Danovitch GM, et al. Obesity and outcome following renal transplantation. Am J Transplant 2006;6(2):357–363
13 Ott U, Busch M, Steiner T, Schubert J, Wolf G. Renal retransplantation: a retrospective monocentric study. Transplant Proc 2008;40(5):1345–1348
14 Wang D, Xu TZ, Chen JH, et al. Factors influencing second renal allograft survival: a single center experience in China. Transpl Immunol 2009;20(3):150–154
15 Horovitz D, Caumartin Y, Warren J, et al. Outcome of third renal allograft retransplants versus primary transplants from paired donors. Transplantation 2009;87(8):1214–1220
16 Meier-Kriesche HU, Port FK, Ojo AO, et al. Effect of waiting time on renal transplant outcome. Kidney Int 2000;58(3):1311–1317
17 Meier-Kriesche H-U, Kaplan B. Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: a paired donor kidney analysis. Transplantation 2002;74(10):1377–1381
18 Morales JM, Aguado JM. Hepatitis C and renal transplantation. Curr Opin Organ Transplant 2012;17(6):609–615
19 Carbone M, Mutimer D, Neuberger J. Hepatitis C virus and nonliver solid organ transplantation. Transplantation 2013;95(6):779–786
20 Schaeffner ES, Mehta J, Winkelmayer WC. Educational level as a determinant of access to and outcomes after kidney transplantation in the United States. Am J Kidney Dis 2008;51(5):811–818
21 Waterman AD, Barrett AC, Stanley SL. Optimal transplant education for recipients to increase pursuit of living donation. Prog Transplant 2008;18(1):55–62
22 Goldfarb-Rumyantzev AS, Koford JK, Baird BC, et al. Role of socioeconomic status in kidney transplant outcome. Clin J Am Soc Nephrol 2006;1(2):313–322
23 Morath C, Mueller M, Goldschmidt H, Schwenger V, Opelz G, Zeier M. Malignancy in renal transplantation. J Am Soc Nephrol 2004;15(6):1582–1588
24 Kasiske BL, Zeier MG, Chapman JR, et al. Kidney Disease: Improving Global Outcomes. KDIGO clinical practice guideline for the care of kidney transplant recipients: a summary. Kidney Int 2010;77(4):299–311
25 Organ Procurement and Transplantation Network (OPTN). Regions. Available at: http://optn.transplant.hrsa.gov/converge/members/regions.asp. Accessed August 26, 2013
26 Ellison MD, Edwards LB, Edwards EB, Barker CF. Geographic differences in access to transplantation in the United States. Transplantation 2003;76(9):1389–1394
27 Ross LF, Parker W, Veatch RM, Gentry SE, Thistlethwaite JR Jr. Equal Opportunity Supplemented by Fair Innings: equity and efficiency in allocating deceased donor kidneys. Am J Transplant 2012;12(8):2115–2124