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Assessing Predictors of Early and Late Hospital Readmission After Kidney Transplantation

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Background. A better understanding of the risk factors of posttransplant hospital readmission is needed to develop accurate predictive models. **Methods.** We included 40 461 kidney transplant recipients from United States renal data system (USRDS) between 2005 and 2014. We used Prentice, Williams and Peterson Total time model to compare the importance of various risk factors in predicting posttransplant readmission based on the number of the readmissions (first vs subsequent) and a random forest model to compare risk factors based on the timing of readmission (early vs late). **Results.** Twelve thousand nine hundred eighty-five (31.8%) and 25 444 (62.9%) were readmitted within 30 days and 1 year postdischarge, respectively. Fifteen thousand eight hundred (39.0%) had multiple readmissions. Predictive accuracies of our models ranged from 0.61 to 0.63. Transplant factors remained the main predictors for early and late readmission but decreased with time. Although recipients' demographics and socioeconomic factors only accounted for 2.5% and 11% of the prediction at 30 days, respectively, their contribution to the prediction of later readmission increased to 7% and 14%, respectively. Donor characteristics remained poor predictors at all times. The association between recipient characteristics and posttransplant readmission was consistent between the first and subsequent readmissions. Donor and transplant characteristics presented a stronger association with the first readmission compared with subsequent readmissions. **Conclusions.** These results may inform the development of future predictive models of hospital readmission that could be used to identify kidney transplant recipients at high risk for posttransplant hospitalization and design interventions to prevent readmission.

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INTRODUCTION

Although kidney transplantation is recognized as the best treatment option for most patients with end-stage renal disease (ESRD) to improve both life expectancy and quality of life, it remains a complex treatment option for the nearly 200 000 patients living with a functioning graft in the United States.[1] Among the many challenges faced by patients and providers after kidney transplantation is the burden of hospital readmission. Around 30% of kidney transplant (kTx) patients are readmitted within the first 30 days after discharge from the hospital posttransplant,[2-5] a substantially higher rate than for patients undergoing other surgeries (4%–15%).[6] Early hospital admission among kTx recipients is associated with a 2-fold increase in graft failure, 3-fold increase in further readmissions, and 50%–75% increase in patient mortality.[7,8] Furthermore, posttransplant admissions are costly (average cost, >$10 000), representing 20% of all Medicare payments for transplantation.[2,9] Moreover, research suggests that up to 50% of these readmissions could be preventable[10-12] and early intervention post discharge in ESRD patients demonstrated their efficacy in reducing early readmission.[13] Thus, reliable tools to predict hospital readmission after kidney transplantation are needed.

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Although several studies have identified important risk factors for hospitalization following kidney transplantation, including demographic,[2] socioeconomic,[14-17] clinical,[2,8,18-20] transplant surgery, and utilization factors,[21,22] few studies have tried to predict posttransplant readmission, and the ones that did reported a low accuracy (c-statistics between 0.63 and 0.71).[2,7,19] One potential explanation of this poor accuracy is the variability in the causes and timing of readmission. Indeed, rejection-related or surgical complication–related readmissions have a higher incidence early posttransplant, while infections and other comorbidities-related readmissions are the most prevalent causes of readmission later posttransplant.[10,23] Finally, most studies examined the risk of first readmission posttransplantation, although an important group of transplant recipients experience multiple readmissions posttransplantation. We hypothesized that a better understanding of the risk factors of kTx readmission and how their respective importance vary over time may inform interventions to identify transplant recipients at high risk for posttransplant hospitalization target recipients at highest risk of readmission for targeted interventions.

The aim of this observational, retrospective study was to compare the importance of various risk factors in predicting posttransplant readmission among kTx recipients based on the timing of readmission (first 30 days post discharge vs 31–90 days vs 91–365 days) and number of readmissions (first readmission vs subsequent).

MATERIALS AND METHODS

Study Population

We obtained data from the United States renal data system (USRDS) database and considered inclusion of all patients in the United States who received a first kTx after the age of 18 years from January 1, 2005 to December 31, 2014 (N = 137 510) in order to have at least a 1 year of follow-up (through December 31, 2015) for hospital readmission. The USRDS standard analytical files (SAF). PATIENTS, SAF.MEDEVID, SAF.WAITLIST_KI, SAF.TX, SAF.HOSPITAL, and SAF.DEATH were used. In order to capture pre- and posttransplant readmissions, we included only patients with Medicare as the primary payer at the time of transplant and at least 1 year prior to transplantation (N = 40 810). The flowchart of our study inclusion and exclusion criteria can be found in Figure 1.

Study Variables

The main study outcome was readmission up to 1 year post discharge of kidney transplantation. All hospital readmissions within 1 year following discharge were extracted from the SAF HOSPITAL file.

Potential predictors extracted at the time of transplantation included ESRD-related risk factors (dialysis vintage, modality, etc.), recipients and donor demographics (age at transplant, race, ethnicity), recipient comorbidities, recipient socioeconomic factors (insurance), and transplant factors (cold ischemia type, number of mismatch). Overall, 30 variables were included in the first model studying factors associated with single versus multiple readmission and are presented in Table 1. In the second model, all the 131 variables available were included in the model.

Statistical Analysis

Comparison of Readmitted Versus Nonreadmitted Patients During the First Year Postdischarge

Patient characteristics are presented as means and standard deviation for continuous variables and counts and percentages

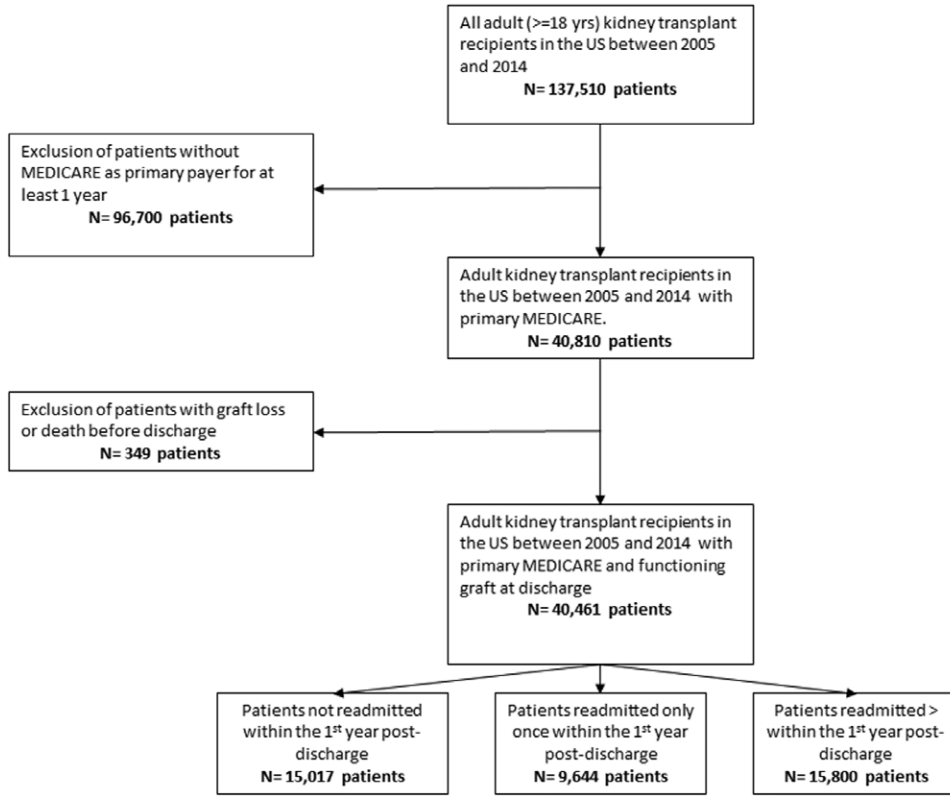

FIGURE 1. Inclusion and exclusion criteria of adult kTx recipients from the United States Renal Data System database, 2005–2014. kTx, kidney transplant; US, United States.

TABLE 1.

Recipients, donors, and transplants characteristics for first kidney transplant in the United States between 2005 and 2014, followed through 2015 by readmission status

Variable	Study cohort (N = 40 461)	Zero readmissions (N = 15 017)	One readmission (N = 9644)	Two or more readmissions (N = 15 800)
Recipient characteristics				
Age at Transplant[a]	53.12 (13.68)	51.74 (13.72)	52.64 (13.81)	54.71 (13.41)
<40 y	7343 (18.15%)	3101 (20.65%)	1836 (19.04%)	2406 (15.23%)
40–60 y	19 427 (48.01%)	7433 (49.50%)	4691 (48.64%)	7303 (46.22%)
>60 y	13691 (33.84%)	4483 (29.85%)	3117 (32.32%)	6091 (38.55%)
Recipient's gender[a]				
Females	15 381 (38.01%)	5484 (36.52%)	3688 (38.24%)	6209 (39.30%)
Males	25 080 (61.99%)	9533 (63.48%)	5956 (61.76%)	9591 (60.70%)
Recipient's race[a]				
White	22 556 (55.75%)	8497 (56.58%)	5325 (55.22%)	8734 (55.28%)
Black	13 730 (33.93%)	4792 (31.91%)	3308 (34.30%)	5630 (35.63%)
Native A	543 (1.34%)	202 (1.35%)	127 (1.32%)	214 (1.35%)
Asian	1754 (4.34%)	839 (5.59%)	423 (4.39%)	492 (3.11%)
Others	1284 (3.17%)	470 (3.13%)	327 (3.39%)	487 (3.08%)
Unknown/missing	594 (1.47%)	217 (1.45%)	134 (1.39%)	243 (1.54%)
Recipient ethnicity[a]				
Hispanic	7033 (17.38%)	2777 (18.49%)	1697 (17.60%)	2559 (16.20%)
Non-Hispanic	33 077 (81.75%)	12 103 (80.60%)	7868 (81.58%)	13 106 (82.95%)
Unknown/missing	351 (0.87%)	137 (0.91%)	79 (0.82%)	135 (0.85%)
Recipient's BMI at transplant[a]				
Obese	13 847 (34.22%)	4863 (32.38%)	3259 (33.79%)	5725 (36.23%)
Overweight	12 381 (30.60%)	4682 (31.18%)	3001 (31.12%)	4698 (29.73%)
Normal	12 623 (31.20%)	4911 (32.70%)	2973 (30.83%)	4739 (29.99%)
Underweight	1185 (2.93%)	415 (2.76%)	295 (3.06%)	475 (3.01%)
Missing	425 (1.05%)	146 (0.97%)	116 (1.20%)	163 (1.03%)
Diabetes at transplant[a]				
Yes	17 350 (42.88%)	5509 (36.69%)	3972 (41.19%)	7869 (49.80%)
No	23 111 (57.12%)	9508 (63.31%)	5672 (58.81%)	7931 (50.20%)
CHF at transplant[a]				
Yes	8120 (20.07%)	2510 (16.71%)	1873 (19.42%)	3737 (23.65%)
No	32 341 (79.93%)	12 507 (83.29%)	7771 (80.58%)	12 063 (76.35%)
Cerebral-vascular disease at transplant[a]				
Yes	2104 (5.20%)	646 (4.30%)	476 (4.94%)	982 (6.22%)
No	35 357 (64.80%)	14 371 (95.70%)	9168 (95.06%)	14 818 (93.78%)
Tobacco use current				
Yes	1722 (4.26%)	634 (4.22%)	407 (4.22%)	681 (4.31%)
No	36 573 (90.39%)	13 565 (90.33%)	8690 (90.11%)	14 318 (90.62%)
Missing	2166 (5.35%)	818 (5.45%)	547 (5.67%)	801 (5.07%)
COPD at transplant[a]				
Yes	3941 (9.74%)	1290 (8.59%)	896 (9.29%)	1755 (11.11%)
No	36 520 (90.26%)	13 727 (91.41%)	8748 (90.71%)	14 045 (88.89%)
Alcohol use				
Yes	364 (0.90%)	127 (0.85%)	78 (0.81%)	159 (1.01%)
No	37 928 (93.74%)	14 072 (93.71%)	9018 (93.51%)	14 838 (93.91%)
Missing	2169 (5.36%)	818 (5.45%)	548 (5.68%)	803 (5.08%)
Drug use[b]				
Yes	285 (0.70%)	100 (0.67%)	56 (0.58%)	129 (0.82%)
No	38 006 (93.93%)	14 099 (93.89%)	9040 (93.74%)	14 867 (94.09%)
Missing	2170 (5.36%)	8181 (5.45%)	548 (5.68%)	804 (5.09%)
Dialysis vintage (mo)[a]	50.29 (36.37)	47.21 (34.48)	50.75 (36.56)	52.92 (37.76)
Time on waiting list (mo)[a]	27.56 (23.81)	26.80 (23.29)	28.16 (24.33)	27.91 (23.97)
Primary cause of renal disease[a]				
Diabetes	11 822 (29.22%)	3616 (24.08%)	2713 (28.13%)	5493 (34.77%)
Primary GN	6720 (16.61%)	2900 (19.31%)	1630 (16.90%)	2190 (13.86%)
Secondary GN	1705 (4.21%)	657 (4.38%)	431 (4.47%)	617 (3.91%)
Cystic/hereditary/congenital/disease	2892 (7.15%)	1240 (8.26%)	721 (7.48%)	931 (5.89%)
Hypertension	9311 (23.01%)	3712 (24.72%)	2232 (23.14%)	3367 (21.31%)

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TABLE 1. (Continued)

Variable	Study cohort (N = 40 461)	Zero readmissions (N = 15 017)	One readmission (N = 9644)	Two or more readmissions (N = 15 800)
Neoplasms/tumor	2386 (5.90%)	779 (5.19%)	560 (5.81%)	1047 (6.63%)
Other	5232 (12.93%)	1974 (13.15%)	1266 (13.13%)	1992 (12.61%)
Missing	393 (0.97%)	139 (0.93%)	91 (0.94%)	163 (1.03%)
Modality[a]				
Hemodialysis	31 884 (78.80%)	11 466 (76.35%)	7541 (78.19%)	12 877 (81.50%)
Auto HD	115 (0.28%)	57 (0.38%)	22 (0.23%)	36 (0.23%)
PD	5379 (13.29%)	2153 (14.34%)	1326 (13.75%)	1900 (12.03%)
Preemptive transplantation	3083 (7.62%)	1341 (8.93%)	755 (7.83%)	987 (6.25%)
Functional status[a]				
No activity limitations	28 679 (70.88%)	10 914 (72.68%)	6927 (71.83%)	10 838 (68.59%)
Some assistance	8454 (20.89%)	2858 (19.03%)	1935 (20.06%)	3661 (23.17%)
Total assistance	500 (1.24%)	136 (0.91%)	103 (1.07%)	261 (1.65%)
Missing/unknown	2828 (6.99%)	1109 (7.38%)	679 (7.04%)	1040 (7.38%)
Donor characteristics				
Donor age[a]	40.37 (15.63)	38.50 (15.22)	40.09 (15.43)	42.32 (15.92)
<40 y	18 344 (45.34%)	7679 (51.14%)	4388 (45.50%)	6277 (39.73%)
40–60 y	6303 (41.97%)	6303 (41.97%)	4438 (46.02%)	7542 (47.73%)
>60 y	1034 (6.89%)	1034 (6.89%)	818 (8.48%)	1981 (12.54%)
Missing	1 (0.00%)	1 (0.01%)	0 (0.00%)	0 (0.00%)
Donor sex[a]				
Females	18 208 (45.00%)	6549 (43.61%)	4412 (45.75%)	7247 (45.87%)
Males	22 253 (55.00%)	8468 (56.39%)	5232 (54.25%)	8553 (54.13%)
Donor race[a]				
White	32 806 (81.08%)	12 378 (82.43%)	7807 (80.95%)	12 621 (79.88%)
Black	6222 (15.38%)	2073 (13.80%)	1461 (15.15%)	2688 (17.01%)
Native A	202 (0.50%)	90 (0.60%)	44 (0.46%)	68 (0.43%)
Asian	1014 (2.51%)	391 (2.60%)	275 (2.85%)	348 (2.20%)
Others	217 (0.54%)	85 (0.57%)	57 (0.59%)	75 (0.47%)
Donor ethnicity[a]				
Hispanic	5869 (14.51%)	2232 (14.86%)	1460 (15.14%)	2177 (13.78%)
Non-Hispanic	33 099 (81.80%)	12 140 (80.84%)	7845 (81.35%)	13 114 (83.00%)
Unknown/missing	1493 (3.69%)	645 (4.30%)	339 (3.52%)	509 (3.22%)
Donor BMI[a]				
Obese	10 879 (26.89%)	3850 (25.64%)	2525 (26.18%)	4504 (28.51%)
Overweight	13 421 (33.17%)	5035 (33.53%)	3240 (33.60%)	5146 (32.57%)
Normal	14 221 (35.15%)	5366 (35.73%)	3450 (35.77%)	5405 (34.21%)
Underweight	1579 (3.90%)	596 (3.97%)	363 (3.76%)	620 (3.92%)
Missing	361 (0.89%)	170 (1.13%)	66 (0.68%)	125 (0.79%)
Donor type[a]				
Living	8482 (20.96%)	3694 (24.60%)	2117 (21.95%)	2671 (16.91%)
Deceased	31 979 (79.04%)	11 323 (75.40%)	7527 (78.05%)	13 129 (83.09%)
Expanded criteria donor[a]				
Yes	6271 (15.50%)	1671 (11.13%)	1384 (14.35%)	3216 (20.35%)
No	34 156 (84.42%)	13 332 (88.78%)	8252 (85.57%)	12 572 (79.57%)
Missing	34 (0.08%)	14 (0.09%)	8 (0.08%)	12 (0.08%)
Donor after cardiac arrest[a]				
Yes	4141 (10.23%)	1494 (9.95%)	957 (9.92%)	1690 (10.70%)
No	36 320 (89.77%)	13 523 (90.05%)	8687 (90.08%)	14 110 (89.30%)
Transplant characteristics				
Induction[a]				
Yes	35 251 (87.12%)	13 250 (88.23%)	8417 (87.28%)	13 584 (85.97%)
No	5210 (12.88%)	1767 (11.77%)	1227 (12.72%)	2216 (14.03%)
HLA Match[a]	1.73 (1.48)	1.82 (1.52)	1.72 (1.48)	1.65 (1.45)
Cold ischemia time[a]	15.12 (10.65)	14.30 (10.55)	15.16 (10.92)	15.87 (10.53)
>Median	18 501 (45.73%)	6399 (42.61%)	4416 (45.79%)	7686 (48.65%)
≤Median	20 405 (50.43%)	8070 (53.74%)	4890 (50.71%)	7445 (47.12%)
Missing	1555 (3.84%)	548 (3.65%)	338 (3.50%)	669 (4.23%)

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TABLE 1. (Continued)

Variable	Study cohort (N = 40 461)	Zero readmissions (N = 15 017)	One readmission (N = 9644)	Two or more readmissions (N = 15 800)
CMV risk[a]				
High	6495 (16.05%)	2166 (14.42%)	1535 (15.92%)	2794 (17.68%)
Medium	27 363 (67.63%)	10 232 (68.14%)	6523 (67.64%)	10 608 (38.77%)
Low	4721 (11.67%)	1945 (12.95%)	1138 (11.80%)	1638 (10.37%)
Unknown/missing	1882 (4.65%)	674 (4.49%)	448 (4.65%)	760 (4.81%)
Length of stay (days)[a]	7.92 (11.39)	6.88 (13.01)	7.60 (9.81)	9.09 (10.51)
<1 wk	28 447 (70.31%)	11 798 (78.56%)	6899 (71.54%)	9750 (61.71%)
>1 wk	12 014 (29.69%)	3219 (21.44%)	2745 (28.46%)	6050 (38.29%)

[a]$P \leq 0.01$.
[b]$P \leq 0.05$.
BMI, body mass index; CHF, congestive heart failure; CMV, Cytomegalovirus; COPD, chronic obstructive pulmonary disease; HD, hemodialysis.

for categorical variables. We compared recipient, donor, and transplant characteristics between patients readmitted versus those never readmitted using χ^2 tests for categorical variables and *t* tests for continuous variables. We performed 2 types of analysis. The aim of the first analysis was to compare factors associated with the risk of first versus subsequent readmission; the aim of the second analysis was to compare the predictors of early versus late readmission.

Comparison of First Versus Subsequent Readmissions

In the first analysis, we used Prentice, Williams and Peterson Total time model to study the association of various predictors with first and multiple readmission. The Prentice, Williams and Peterson model is an extension of the Cox proportional Hazard model for noncensoring events. Indeed, since readmission is not a censoring event, this model allows for studying not only the first but also the subsequent readmissions occurring within the 1-year follow-up period.[24] Given the low rate of missing data (<2%), we performed a complete case analysis.

Comparison of Early Versus Late Readmissions

In the second analysis, we built 3 predictive models with the outcome of hospital readmission within 1–30 days post discharge (Model 1), 31–90 days post discharge (Model 2), and 91–365 days post discharge (Model 3). We used the Random Forest model to predict readmission using all the selected variables from the SAF analytics files. We used 3-fold cross-validation to assess the validity of our model. Predictive accuracy was assessed by calculating the area under the receiver operating curve. Predictors were then categorized into 6 groups: recipient demographics, recipient medical, recipient socioeconomic status, donor demographic, donor medical, and transplant factors. In order to compare the contribution of each group of predictors over time, we summed the weight of each predictor by group.

Statistical analyses were performed using SAS, R and Python, and a *P*-value < 0.05 was considered statistically significant.

RESULTS

Comparison of Readmitted Versus Nonreadmitted Patients

Among 40 461 first-time kTx recipients included in our study, 12 985 (31.8%) were readmitted within 30 days post discharge, 25 444 (62.9%) were readmitted within 1 year post discharge, and 15 800 (39.0%) were readmitted more than once. Mean age of our population was 53.1 (SD 13.7) years old and included 62% male and 55.7% Caucasians. Table 1 describes the main recipient, donor, and transplant characteristics by readmission status. Overall, patients who were readmitted at any time during follow-up were older, had a higher prevalence of comorbidities (diabetes, obesity, congestive heart failure, cerebrovascular disease, and chronic obstructive pulmonary disease), and had a poorer functional status (needed partial or total assistance). African American race was associated with a higher prevalence of readmission and Asian race with a lower prevalence compared with patients who were not readmitted. Dialysis vintage and renal replacement therapy modality prior to transplant were also associated with a higher prevalence of readmission. Although hemodialysis (HD) was the most prevalent renal replacement therapy modality in all groups, the prevalence of HD was higher among readmitted patients while peritoneal dialysis and preemptive transplantation were more prevalent among nonreadmitted patients.

Comparison of First Versus Subsequent Readmissions

Among recipient characteristics, older age, female gender (hazard ratio [HR]: 1.07; 95% confidence intervals [CI], 1.05-1.10), diabetes (HR: 1.12; 95% CI, 1.08-1.17), congestive heart failure (HR: 1.11; 95% CI, 1.08-1.15), chronic obstructive pulmonary disease (HR: 1.08; 95% CI, 1.05-1.13), and low functional status were independently associated with both the first and subsequent posttransplant readmission (Table 2). Asians had a constant lower risk of readmission when the risk of African American did not significantly differ from Caucasians (HR: 0.99; 95% CI, 0.96-1.02) for the first readmission and was slightly lower for the subsequent ones (HR: 0.97; 95% CI, 0.95-0.99) after adjusting for donors and transplant characteristics. Similarly, Hispanic ethnicity was consistently associated with a lower risk of readmission. Patients treated with home HD or peritoneal dialysis had a lower risk of readmission compared with patients on HD. Each additional year of dialysis treatment was associated with a 3.6% increased risk of readmission (HR: 1.04; 95% CI, 1.02-1.04). Preemptive transplantation was also independently associated with a lower risk of readmission for both first (HR: 0.94; 95% CI, 0.89-0.99) and subsequent readmissions (HR: 0.94; 95% CI, 0.89-0.99). Living (vs deceased) donor transplant was associated with a lower risk of subsequent readmission

TABLE 2.

Adjusted hazard ratio of first and subsequent readmission post discharge in recipients of a first kidney transplantation in the United States between 2005 and 2014, followed through 2015 (N = 39 742)

	First readmission			Subsequent readmission total time model		
Variables	**HR**	**95% CI**		**HR**	**95% CI**	
Recipient characteristics						
Age at transplant						
<40 vs >60	0.935	0.897	0.975	0.931	0.9	0.964
40–60 vs >60	0.912	0.886	0.939	0.916	0.896	0.937
Recipient's gender						
Female vs male	1.074	1.046	1.102	1.054	1.033	1.076
Recipient's race						
Black vs White	0.988	0.956	1.021	0.969	0.945	0.994
Native A vs White	0.912	0.816	1.018	0.971	0.893	1.056
Asian vs White	0.721	0.671	0.774	0.854	0.803	0.909
Others vs White	1.02	0.948	1.097	0.902	0.848	0.959
Recipient ethnicity						
Hispanic vs Non-Hispanic	0.897	0.862	0.933	0.945	0.916	0.975
Recipient's BMI at transplant						
Obese vs normal	1.039	1.007	1.073	0.997	0.972	1.022
Overweight vs normal	0.99	0.959	1.023	0.992	0.967	1.018
Underweight vs normal	1.055	0.978	1.137	1.011	0.953	1.074
Diabetes at transplant						
Yes vs no	1.124	1.083	1.167	1.084	1.054	1.116
CHF at transplant						
Yes vs no	1.112	1.078	1.147	1.06	1.036	1.085
Cerebral-vascular disease at transplant						
Yes vs no	1.087	1.03	1.147	1.03	0.99	1.072
Tobacco use current						
Yes vs no	1.012	0.95	1.077	1.046	0.996	1.097
COPD at transplant						
Yes vs no	1.089	1.045	1.134	1.073	1.04	1.107
Alcohol use						
Yes vs no	1.067	0.93	1.223	1.078	0.975	1.191
Drug use						
Yes vs no	1.046	0.898	1.218	1.068	0.953	1.197
Dialysis vintage (mo)	1.003	1.002	1.003	1.001	1.001	1.001
Time on waiting list (mo)	0.999	0.999	1	0.999	0.999	1
Primary cause of renal disease						
Diabetes vs hypertension	1.156	1.105	1.208	1.07	1.034	1.107
Primary GN vs hypertension	0.993	0.952	1.037	0.982	0.948	1.018
Secondary GN vs hypertension	1.093	1.021	1.17	1.044	0.987	1.105
Cystic/hereditary/congenital/disease vs hypertension	0.988	0.933	1.046	0.933	0.889	0.98
Neoplasms/tumor vs hypertension	1.168	1.103	1.236	1.014	0.97	1.061
Others vs hypertension	1.077	1.03	1.126	1.02	0.984	1.057
Modality						
Auto HD vs HD	0.831	0.642	1.076	1.159	0.967	1.388
PD vs HD	0.955	0.92	0.992	0.941	0.912	0.971
Preemptive transplantation vs HD	0.943	0.891	0.998	0.925	0.882	0.971
Functional status						
Some assistance vs no activity limitations	1.092	1.059	1.127	1.063	1.038	1.088
Total assistance vs no activity limitations	1.302	1.16	1.46	1.086	0.998	1.181
Donor characteristics						
Donor age						
<40 vs >60	0.796	0.751	0.844	0.886	0.848	0.925
40–60 vs >60	0.926	0.878	0.975	0.948	0.913	0.984
Donor sex						
Female vs male	1.035	1.009	1.062	1.006	0.985	1.026

Continued next page

TABLE 2. (Continued)

Variables	First readmission HR	95% CI		Subsequent readmission total time model HR	95% CI	
Donor race						
Black vs White	1.141	1.1	1.183	1.062	1.033	1.091
Native A vs White	0.849	0.702	1.027	1.086	0.944	1.25
Asian vs White	1.063	0.978	1.155	0.964	0.899	1.034
Others vs White	1.004	0.845	1.192	1.073	0.932	1.234
Donor ethnicity						
Hispanic vs non-Hispanic	1.058	1.017	1.1	1.005	0.974	1.037
Donor BMI						
Obese vs normal	0.996	0.964	1.028	1.023	0.997	1.049
Overweight vs normal	0.982	0.952	1.012	0.996	0.972	1.02
Underweight vs normal	1.082	1.011	1.157	1.034	0.98	1.093
Donor type						
Living vs deceased	0.966	0.927	1.007	0.948	0.916	0.98
Expanded criteria donor						
Yes vs no	1.126	1.075	1.179	1.059	1.024	1.096
Donor after cardiac arrest						
Yes vs no	1.054	1.01	1.099	1.016	0.983	1.05
Transplant characteristics						
Induction						
Yes vs no	0.91	0.877	0.945	0.963	0.936	0.99
HLA match	0.978	0.969	0.987	0.995	0.988	1.002
Cold ischemia time						
>Median vs ≤Median	1.063	1.033	1.095	1.012	0.99	1.036
CMV risk						
Medium vs low	1.04	0.997	1.085	0.987	0.954	1.021
High vs low	1.129	1.075	1.185	1.04	1	1.081
Length of stay (days)	1.003	1.002	1.003	1.004	1.004	1.005
>1 vs <1 wk	1.422	1.385	1.461	1.17	1.146	1.194

BMI, body mass index; CHF, congestive heart failure; CI, confidence intervals; CMV, Cytomegalovirus; COPD, chronic obstructive pulmonary disease; HD, hemodialysis; HR, hazard ratio.

(HR: 0.95; 95% CI, 0.92-0.98) but was not significantly associated with the risk of first readmission. Receiving a transplant from an expanded donor criteria (vs standard criteria donor) was associated with an increased risk of readmission. Finally, higher HLA matching and receiving induction therapy were associated with a decreased risk of readmission, whereas longer length of stay at transplant admission and a high risk of cytomegalovirus infection were associated with an increased risk of readmission (Table 2).

Figure 2 compared the HR of first versus subsequent readmission. Overall, the association between recipient characteristics and posttransplant readmission was consistent between the first and subsequent readmissions. On the contrary, the association between donor characteristics and readmission was stronger with the first readmission than with the subsequent readmissions. The same was true with transplant characteristics although some characteristics such as length of stay at transplant admission remained strongly associated with subsequent readmission (HR = 1.17; 95% CI, 1.15-1.19).

Comparison of Early Versus Late Readmissions

The predictive accuracy of our predictive models were 0.61 (0.60–0.63), 0.62 (0.61–0.64), and 0.63 (0.62–0.64) for models 1 (1–30 days), 2 (31–90 days), and 3 (91–365 days), respectively. The list of the predictors and their weights in each model is presented as a heat map in Figure S1 (**SDC**, http://links.lww.com/TXD/A215). After categorizing the predictors into the 6 groups, transplant factors remained the main predictive group for early and late readmission (all 3 models). However, the importance of transplant-related predictors decreased with time from 50% of the prediction at 30 days to 29% at 1 year. Recipients' medical factors were the main predictors accounting for 26%, 27%, and 29% of the prediction at 30, 90, and 365 days, respectively. Both recipients' demographics and socioeconomic factors accounted for 2.5% and 11%, respectively, of the prediction at 30 days (Model 1), their contribution to the prediction of later readmission (Model 3) increased to 7% and 14%, respectively. Donor demographics accounted for 5% to 10% of the prediction within the 3 models. Donor medical characteristics and socioeconomic factors remained relatively poor predictors of hospital readmission at all times (Figure 3).

DISCUSSION

This study confirms the high burden of hospital readmission in the year following kidney transplantation among adult kTx recipients and that predicting hospital readmission in this population remains challenging. The development of electronic medical records and innovative analytical methods allows the extraction of new potential predictors of readmission. This study underlines the need to carefully select potential risk factors in light of each specific study outcome since predictors' importance vary based on the timing

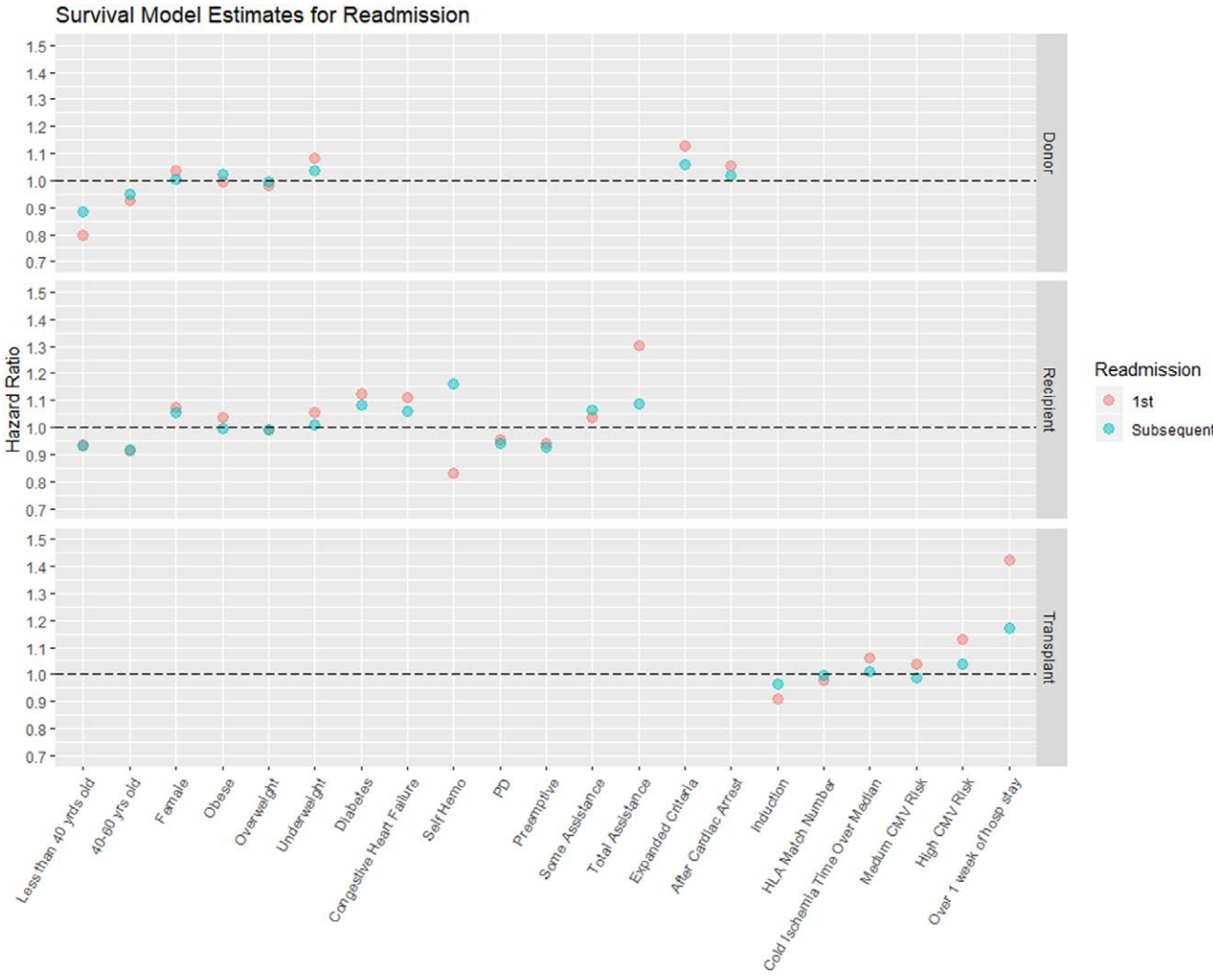

FIGURE 2. Comparison of adjusted hazard ratio of first vs subsequent readmission by groups of predictors (donor, recipient, and transplant factors). CMV, Cytomegalovirus.

of readmission and whether we consider the first versus the subsequent readmissions.

Indeed, readmission after surgery has been increasing over the last decade in the United States.[25,26] In general surgery, early hospital readmission rates vary by procedure and have been reported to be as high as 22% for some procedures.[27] kTx recipients present with a high incidence of early hospital readmission, with previously reported incidence varying between 11%[19] and 48%[2] across transplant centers. In addition, a recent report from Canada did not find any improvement in the rate of readmission over the last decade among kTx recipients.[28] Accordingly, we found that the national incidence of readmission within our study period was 31.8% within 30 days post discharge and 62.9% within the first year.

Moreover, posttransplant readmission is associated with graft failure, patient mortality, and medical expenditure.[2,7-9] Therefore, predicting posttransplant readmission is of great interest for both clinicians and healthcare institutions. In surgery in general, Kansagara et al[3] reviewed 30 studies with readmission prediction models yielding fairly poor discriminatory abilities with c-statistics ranging within 0.50–0.60 and few above 0.70. Previously described large national cohorts of hundreds of thousands of patients undergoing heterogeneous surgeries using elaborate prediction models also yielded limited predictive accuracy.[6,29] What is most notable about these studies is that even with the size of the cohort and complexity of information available to predict readmissions at the time of discharge, researchers were unable to attain an adequate model predicting readmission. Although, prediction accuracy greatly improved after the inclusion of post discharge data, the use of such models in clinical practice might be limited especially when trying to prevent early readmission.

To date, studies on readmission among kTx recipients have mostly focused on risk factor identification. Important risk factors for hospitalization previously identified include demographic factors (older age and African American race),[2] socioeconomic factors (lower education and Medicaid insurance),[14,15] clinical factors (high body mass index and various comorbidities), transplant surgery factors (longer length of stay, receipt of a deceased [vs Living] donor, older donor age, and surgical complications), utilization factors (pretransplant hospitalization),[21,22] and adherence to medication.[30] However, only 1 study published a posttransplant-specific predictive model.[19] In this study, Taber et al[19] first designed a model including fixed pretransplant predictors and transplant characteristics that remained modestly predictive (area under the curve, 0.63; 95% CI, 0.58-0.69). The predictive accuracy significantly improved to 0.73; 95% CI, 0.67-0.79 after including

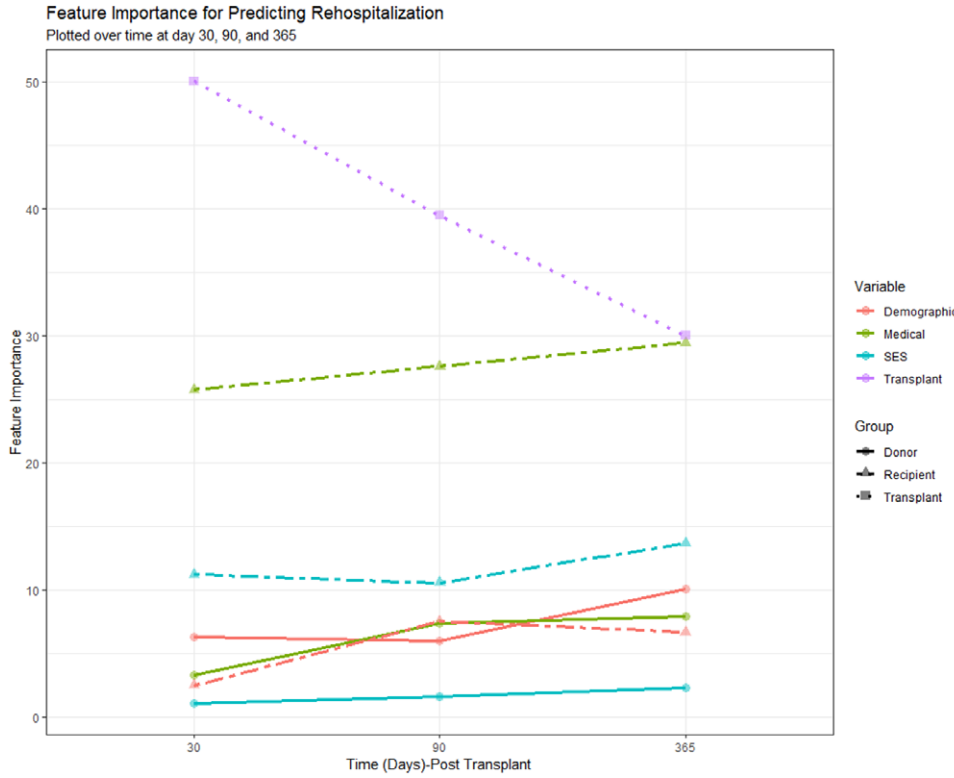

FIGURE 3. Respective contribution of the 6 groups of predictors or features (recipient demographics, recipient medical, recipient SES, donor demographic, donor medical, and transplant) to the prediction of readmission with time posttransplant. SES, socioeconomic status.

posttransplant but predischarge dynamic factors such as the systolic blood pressure slope during transplant admission. Thus, the development of more accurate predictive models of readmission after kidney transplantation will likely require the collection and inclusion of more granular data found in electronic healthcare records than those usually available in transplant registries. These data include socioeconomic data (eg, familial support, transportation issues) not typically included in standard databases but could be found in clinical notes and data, such as labs values or vitals collected by healthcare institutions. The adoption of electronic health records in most healthcare institutions, the development of advanced analytical infrastructure able to manage and extract useful predictors from large structured and unstructured data such as clinical notes, and utilization of advanced machine learning techniques such as Natural Language Processing may enable the improvement of risk stratification for posttransplant readmission. Recently, Srinivas et al[31] successfully applied this type of approach to the prediction of graft loss and mortality after kidney transplantation and reported high accuracies of their models of 0.87; 95% CI, 0.81-0.94 for 1-year graft loss and 0.84; 95% CI, 0.80-0.89 for 3-year mortality.[31] However, the main improvement in the predictive accuracy was provided by the inclusion of predictors collected post discharge (up to 90 days for 1 y prediction and up to 365 days for 3 y predictions). To prevent readmission and specifically early readmission requires early prediction, ideally before hospital discharge to allow the implementation of preventive measures and remains an unmet need. Finally, the extraction of new predictors based on previously reported risk factors and clinical input of transplant experts is a complex and time-consuming process and may be difficult to generalize outside of a single institution. Our study provides valuable information for researchers by guiding the selection of potential risk factors based on the timing of readmission. Indeed, when building a predictive model for early readmission, researchers should focus on including features related to transplant characteristics while, for building a predictive model for late readmission, researchers should focus on including features related to patients' comorbidities and socioeconomic characteristics. This result is supported by the selection of 6 transplant-related predictors (transplant number, delayed graft function, induction type, systolic blood pressure, diastolic blood pressure, and transplant stay cost) out of 9 predictors included in the 30-day readmission predictive model previously published by Taber et al.[19] Similarly, transplant factors also remain important predictors of late or subsequent readmission, recipients' clinical and socioeconomic characteristics predictive ability increases when looking at late readmission and do not vary when considering first or subsequent readmission. A potential explanation of these findings is the differential distribution of the causes of readmission over time. Indeed, surgical complications have been reported to be the first cause of early readmission after kidney transplantation accounting for 36% of all readmissions, followed by infection.[2] This explains why transplant factors are major predictors of early readmission. Similarly, while the incidence of surgical complications and infections decreases with time after transplant, the share of hospitalizations related to recipient comorbidities or transplant rejection increases. It is thus not surprising to observe an increasing importance of recipients' pretransplant medical characteristics and recipients' socioeconomic status in the prediction of late readmission.

Our study has several limitations. This study is based on USRDS data and lacking important predictive factors that are not available in national databases as well as accurate collection of causes of readmissions. This explains the relatively

low predictive accuracy of our model, similar to what has been previously reported in other studies. However, the aim of our study was not to build a better predictive model but to explore the respective contribution of various groups of predictors in order to guide the development of future predictive models based on more detailed databases or direct extraction from patients' electronic medical records. In addition, because we restricted our analyses to patients with Medicare claims data to obtain readmission dates, our results may not be generalizable to patients who do not have Medicare as the primary payer.

CONCLUSION

Highly accurate predictive models of posttransplant readmission are needed to guide the implementation of targeted interventions aiming at reducing the burden of posttransplant readmission after kidney transplantation. However, accurate predictive models that could be applied at the time of discharge are lacking. Collection of more granular data from patients' electronic healthcare records, selected based on the type and timing of readmission they aim to predict, is needed in order to build more accurate models. With improvements in predictive capacity, these models could eventually be useful in clinical practice by allowing for risk stratification of patients at high risk for readmission who would benefit from interventions prior to discharge from transplant surgery.

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