Original Article

Assessment of risk factors for hospital readmission after kidney transplantation

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Abstract

Background and Purpose: Hospital readmission after kidney transplantation is a real challenge for both patients and healthcare systems. Assessment of the risk factors of readmission after kidney transplantation is vital and can reduce morbidity and cost in transplant recipients and donors. The aim of the current study was to determine the risk factors of hospital readmission in patients undergoing kidney transplantation in Montaserieh Hospital of Mashhad, northeast of Iran.

Materials and Methods: This retrospective study included 523 first kidney transplant patients between January 2013 and March 2019 from the Montaserieh Hospital Information System (HIS) of Mashhad, Iran. Every-time readmission was the study primary outcome. Donors and recipient's demographic data, recipient's comorbidities, reasons for end-stage renal disease (ESRD), panel reactive antibody (PRA) status, dialysis parameters, cold ischemic time, and delayed graft function (DGF) were the potential risk factors. Statistical analysis was done using Chi-square and Student's t-test.

Results: Data from 523 patients were assessed for potential eligibility. Based on the exclusion criteria, data from 479 patients were included in the final analysis. 174 (36.3%) patients were never readmitted, and 305 (63.7%) were readmitted at least once post-discharge. 39 (12.8%) were readmitted within the first-month post-discharge. Older age, sex, higher prevalence of comorbidities, diabetes and hypertension, duration of primary disease before transplantation, hemodialysis and duration of pre-transplant dialysis, mean pre-transplant platelet count, intraoperative complications, increased cold ischemic time, and delayed graft function were associated with a higher prevalence of readmission (p<0.05).

Conclusion Our results showed that different independent variables and patients' comorbidities were important risk factors for readmission after kidney transplantation. Early prediction of these risk factors could result in prevention from readmission in patients undergoing kidney transplantation.

***Keywords*:** Kidney transplantation; Readmission; Risk Factors; Comorbidity

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1. *Introduction*

Kidney transplantation is the treatment of choice for most patients with end-stage renal disease (ESRD) (1, 2). Readmission after kidney transplantation is a real challenge for both patients and healthcare systems. It has been reported that about 30% of all kidney transplant recipients were readmitted during the first month after discharge (3-5).

Rehospitalization is associated with a significant increase in cost, morbidity, graft failure, and even mortality (6-8). Unfortunately, registry-based of kidney transplant recipients are limited, so novel predictors are needed (9). About half of these readmissions could be preventable (10, 11). So, recognizing risk factors for readmission and their management could help to reduce the rate of readmission. Infections, rejection episodes, and surgical complications are the three main reasons for hospitalization after kidney transplantation. Surgical complications are more prevalent in early (the first month) post-transplant period, and infections are more common in late (after the first month) phase. However, acute and chronic rejections can be seen in both periods (10, 12). Furthermore, US national data shows that other factors associated with early hospital readmission are older age, African-American race, comorbidities, such as obesity, diabetes, heart disease, chronic obstructive pulmonary disease (COPD), as well as length of hospital stay and frailty (13). Donor risk factors including age, donation after death, and cold time are among the main risk factors for readmission. Moreover, transplantation process risk factors like human leukocyte antigen (HLA) mismatch, lack of induction therapy, waitlist time, and blood pressure are accounted for early hospital readmission in patients after kidney transplantations (13, 14).

Most studies have focused on the risk of early readmission in kidney transplantation. However, many patients have late or multiple readmissions (9). This study aimed to recognize risk factors for readmission during different intervals (early versus late) after kidney transplantation and assess the most important risk factors of multiple readmissions.

2. *Materials and Methods*

This study was a retrospective and single-center observational study that included all kidney transplantations in Mashhad between January 2013 and March 2019. We obtained the data from the Montaserieh Hospital Information System (HIS) and the paper files. Montaserieh hospital is the main solid organ transplant center in Mashhad, Northeast of Iran. All kidney transplant surgeries in Mashhad and their follow-ups are performed in this hospital. All first kidney transplant recipients from deceased donors in this center between January 2013 and March 2019 were assessed for eligibility (n= 523), with a minimum of one-year follow-up for readmissions. Graft loss or patient death during the first hospitalization (not readmission) were exclusion criteria. Also, patients with incomplete data or migration to other transplant centers were excluded. The flow diagram of this study is shown in Figure 1.

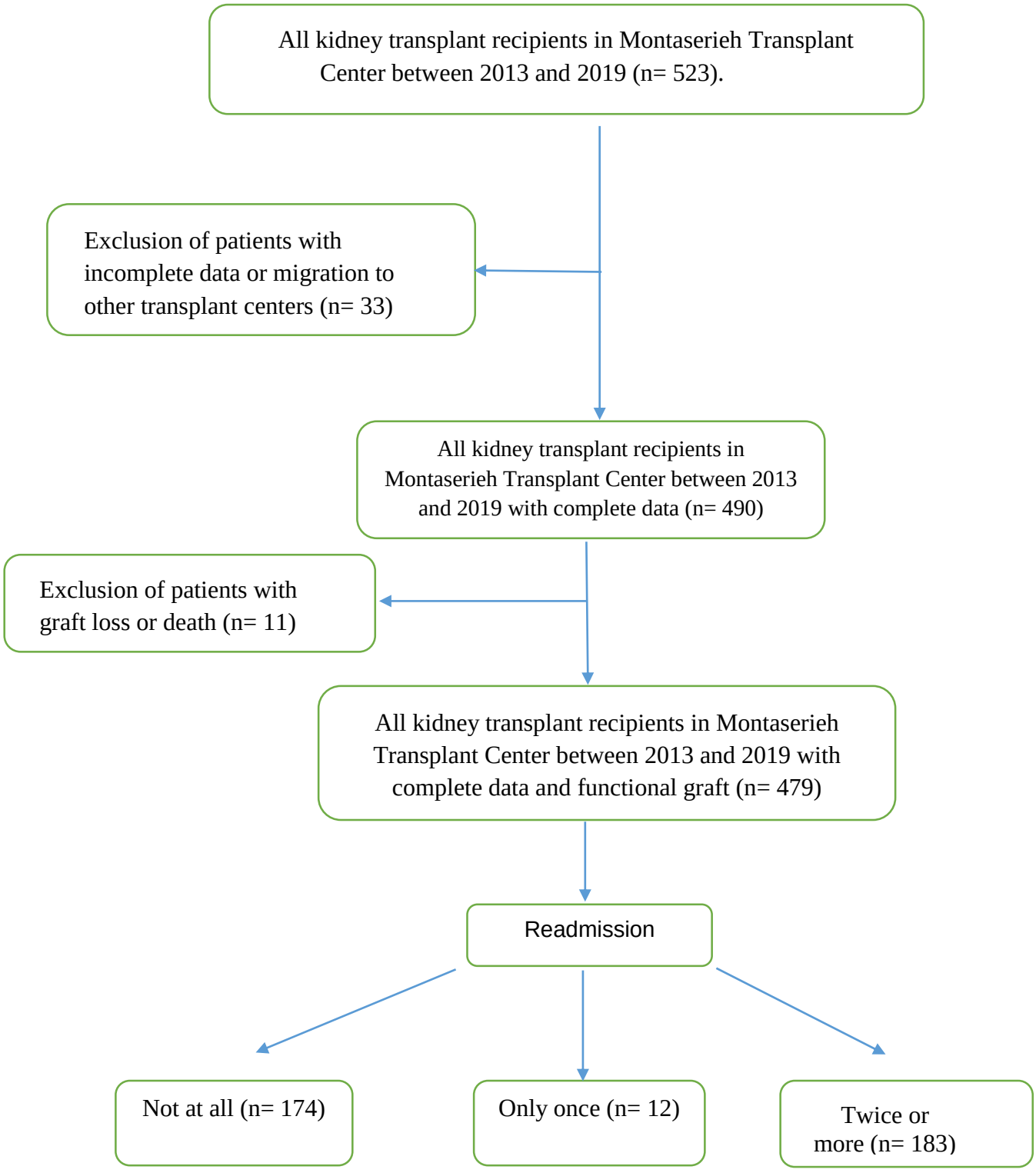

Figure 1. Flow diagram of inclusion-exclusion criteria in our study

Every-time readmission was the primary outcome of our study. The potential risk factors for transplant readmission, such as donors and recipient's demographics characteristics (age, sex, and BMI), recipient comorbidities, reasons of ESRD, dialysis parameters, cold ischemic time, panel reactive antibody (PRA) status, delayed graft function (DGF) are presented in Table 1.

Donors' and recipients' clinical characteristics were shown as Mean±SD for continuous variables and counts (with percentages) for categorical variables. We classified patients in two ways, first readmitted versus never readmitted, and the second was early versus late readmission. We used chi-square test for categorical variables analysis. Continuous variables were analyzed using the t-test. *P*-value < 0.05 was considered as the level of significance.

This study has been approved by the Ethics Committee of Mashhad University of Medical Sciences, Mashhad, Iran (IR.MUMS.fm.REC.1396.818).

3. *Results*

A total of 479 first-time kidney transplant recipients were included in our study. All donors were brain dead deceased donors. Among these, 174 (36.3%) were never readmitted, and 305 (63.7%) were readmitted at least once post-discharge. Among readmitted patients, 122 (40%) were readmitted once, and 183 (60%) were readmitted twice or more. 39 (12.8%) of the patients were readmitted within the first-month post-discharge. The average age of our study population was 36.9±13.6 years old. The mean age was 40.3±13.1 in the readmitted group and 30.9±12.5 in the patients who were never readmitted, which was statistically significant ($p<0.001$). Moreover, in our study, older age, higher prevalence of comorbidities, diabetes, hypertension, duration of primary disease before transplantation, hemodialysis, and duration of pre-transplant dialysis was associated with a higher prevalence of readmission ($p < 0.05$). Mean pre-transplant platelet count, intraoperative complications, increased cold ischemic time, and delayed graft function (defined as the need for dialysis during the first week after transplant surgery) were also associated with a higher prevalence of readmission ($p < 0.05$) (Table 1& 2).

Table 1. Clinical characteristics of kidney transplants included in our study

Variable	Never readmitted 174 (36.3%)	Readmitted once or more 305 (63.7%)	*P-value*
Recipient characteristics			
Age	30.9 ± 12.5	40.3 ± 13.1	***p* < 0.001**
Sex: Male (%)	87 (50%)	191 (62.6%)	***p* = 0.007**
Female (%)	87 (50%)	114 (37.4%)	
Primary cause of ESRD			
Diabetes mellitus (%)	62 (35.6%)	161 (52.8%)	***p* < 0.001**
Hypertension (%)	29 (16.7%)	63 (20.7%)	***p* < 0.001**
Glomerulonephritis (%)	69 (39.7%)	74 (24.3%)	***p* < 0.05**
Others (%)	14 (8%)	7 (2.3%)	***p* < 0.001**
Duration of primary disease (%)	6.43 ± 2.44	8.26 ± 2.74	***p* < 0.001**
Dialysis parameters			
Hemodialysis (%)	122 (70.1%)	213 (69.8%)	***p* = 0.942**
Peritoneal dialysis (%)	52 (29.9%)	92 (30.2%)	***p* = 0.902**
Duration of dialysis (year)	3.12 ± 1.69	4.29 ± 1.91	***p* < 0.001**
Donor characteristics			
Age	30.81 ± 9.57	31.35 ± 9.13	***p* = 0.540**
Sex: Male (%)	97 (56%)	162 (53%)	***p* = 0.578**
Female (%)	77 (44%)	143 (47%)	
Delayed graft function (%)	16 (5.2%)	289 (94.8%)	***p* = 0.002**
Transplant characteristics			
Panel reactive antibody	<5%	<5%	***p* = 0.182**
Cold ischemic time	**34.71 ± 5.20**	**36.56 ± 6.13**	***p* < 0.001**

Data are presented as means ± SDs. *p* < 0.05 is considered as statistically significant.

Table 2. Frequency and causes of readmissions

Diagnosis	Final Diagnosis		Number (%)	Total %
Infection (n= 163)	Acute gastroenteritis		64 (39.3%)	21%
	Upper respiratory tract infection	Urinary	46 (28.2%)	15.1%
	tract infections		40 (24.5%)	13.1%
	Pneumonia		8 (5%)	2.6%
	Herpes virus		5 (3%)	1.6%
Non-infection (n= 142)	Renal failure		65 (45.8%)	21.3%
	CVA/ IHD*		46 (32.4%)	15.1%
	Surgical complications		16 (11.3%)	5.2%
	Malignancies		15(10.5%)	4.9%

***Abbreviations. CVA: cerebrovascular accidents; IHD: ischemic heart disease**

In our study, a total of 305 patients were readmitted during seven years' follow-up, 39 patients (12.8%) in the early phase, and 266 (87.2 %) in the late phase after kidney transplantation. Renal failure and medical comorbidities were significantly associated with the late phase rehospitalization. In patients with comorbidities, 12 (8.5%) were

readmitted in the early-phase, and 129 (91.5%) in the late-phase (p=0.03) after kidney transplantation. Besides, lower platelet count was associated with early-phase readmission ($p < 0.05$). Delayed graft function and cold ischemic time did not differ significantly in the early versus late readmission in our study. The frequency and causes of readmissions regarding infection are presented in Table 2.

4. *Discussion*

Our results showed that about 63.7% of the patients after kidney transplantation would be readmitted at least once after transplantation in our hospital. Readmission after kidney transplantation was higher than many other surgical procedures. Post-surgical readmission was associated with increased cost, graft failure, and even mortality (1, 6, 7). As a result, the risk assessment of post-transplant readmission was critical, and the need for a reliable prediction model was of great significance. Most studies have focused on pre-operative and intra-operative characteristics of recipients and donors. However, the readmission rate could be influenced by many post-transplant risk factors (15). In the current study, older age, recipient comorbidities, hemodialysis, and its duration before transplantation, surgical and medical complications, lower pre-operative platelet counts, increased cold ischemic time, and delayed graft function was associated with an increased readmission rate. Similar to our results, Haugen et al. in a cohort study on 108830 kidney transplant patients from December 1, 1999 - December 31, 2014 in USA showed that older kidney transplant recipients were more prone to experience hospital readmission and also had a greater risk of graft loss after transplantation (13). Compatible with our results, Kim et al. showed that delayed graft functioning, diabetes, and glomerulonephritis were among the main causes of hospital readmission after kidney transplantation (16).

Furthermore, Covert et al. showed that diabetes and prolonged time on hemodialysis prior to kidney transplantation were significantly associated with increased risk of hospital readmission. This finding was in line with the findings of the present study (17).

Moreover, only comorbidities and low platelet count were correlated with the early-phase (Vs. the late phase) readmission (p<0.05). Although cold ischemic time was associated with increased readmission in our study, there was no significant difference between the early versus late readmission rates. In our study, only brain death donors were included; moreover, organ harvest and transplantation were performed in the same center. As a result, cold ischemic time was meager in all patients (36.5 ± 6.1 minutes). Finally, a reliable prediction model was needed considering many pre-operative, intra-operative, and post-operative variables to assess the real risk factors (7).

While pre- and intra-operative variables are more important in early readmission, it seems that post-operative variables could be more critical in predicting late readmission (9). Overall, demographic characteristics of recipients and donors, recipients comorbidities and functional status, primary renal failure reason, kind and duration of renal replacement therapy, immunologic factors, perioperative surgical and medical complications, quality of hospital care, drug toxicity, psychosocial

and economic status of the recipients, familial support, patient education, and compliance were among the most critical risk factors to be considered in a predicting model (18, 19).

Early prediction could result in effective prevention from readmission. Many different independent variables should be considered in a reliable predictive model. Donors and recipients clinical characteristics, perioperative problems, recipient age, sex, prevalence of comorbidities of the recipient should be included in the final predictive model. More accurate electronic healthcare records are needed to help to design such accurate models in the future.

Limitation

Our study had a few limitations. Frist, it was a retrospective study and due to its nature, hampered our ability to accredit any direct causality to the significant risk factors identified in the study. Second, it was a single-center cohort study which limited its generalizability. Third, assessment of readmission was narrowed to the Montaserieh Transplant Hospital, and we were unable to ascertain if patients were re-admitted elsewhere.

Conflicts of Interest

The authors declare that they have no conflict of interest related to this manuscript.

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