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ORIGINAL PAPER

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Assessment of Short-term, Within Hospital Cardiovascular Complications After Renal Transplantation in Baqiyatallah Hospital

Mohsen Sadeghi Ghahrodi^{1,3}, Behzad Einollahi², Amir Baharvand^{1,3}, Mohammad Javanbakht²

¹Department of Cardiology, School of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran

²Nephrology and Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

³Atherosclerosis Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

Corresponding authors: Amir Baharvand and Mohammad Javanbakht, E-mail: tabiblor88@gmail.com and mhmvbt81@gmail.com, Tel: +2181262073, ORCID: <https://orcid.org/0000-0002-0837-9591>.

ABSTRACT

Introduction: Several studies have looked at cardiac complications in patients with end-stage renal disease (ESRD) after renal transplantation, but more attention has been paid to the long-term cardiovascular complications. **Aim:** The present study was designed to investigate the short-term cardiovascular complications of intrahospital hospitalization in post-renal transplant patients and related factors. **Methods:** In this retrospective cohort study, the medical records of all renal transplant patients in Baqiyatallah Hospital between 2015 and 2018 during the post-transplantation phase were investigated. Demographic data, transplantation type, cardiac risk factors, pre-operation cardiac consultation and para-clinical tests results were extracted from the patients' records. The frequency and factors influencing the need for re-visitation as well as its final diagnosis were analyzed. **Results:** A total of 982 patients with a mean age of 13.73 ± 45.33 years were studied (62.6% males). In 39.8% of patients, cardiology re-visitation was required; of these 391 visits, only 162 patients (41.4%) had heart problems. In multivariate analysis, patients' need for cardiac reconsideration was predicted by 7 variables; age, diabetes, history of CABG, ECG, echocardiography, angiography, and myocardial perfusion scan ($R^2 = 0.652, P < 0.001$). Furthermore, the five variables of first cardiology consultant, the first consultation physician, left ventricular hypertrophy, having history of angiography and myocardial perfusion scan, can predict the final diagnosis of cardiac problems in re-counseling ($R^2 = 0.188, P = 0.043$). **Conclusion:** Given the high prevalence of need for a patient's recurrent cardiac

visit, it seems that risk assessment prior to kidney transplantation needs to be more accurate. It is recommended that elderly patients with abnormal findings in electrocardiography and echocardiography, having diabetes, having a history of negative coronary angiography or myocardial perfusion scan be more closely monitored for heart disease.

Keywords: Kidney transplantation, Cardiac risk assessment, Electrocardiography, Echocardiography, Coronary Angiography, Stress Test.

1. INTRODUCTION

Kidney transplantation is the treatment of choice in a group of end-stage renal disease (ESRD) patients that has increased dramatically after advances in the production of immunosuppressive drugs (1, 2). Statistics show that the prevalence of coronary artery disease and its associated mortality is increasing worldwide (3). Cardiovascular diseases are common after kidney transplantation as a major cause of morbidity and mortality in these patients and nowadays kidney transplantation is considered as a risk factor for cardiovascular complications (1). Delville et al., investigated the prevalence and predictive factors of cardiovascular events after kidney transplantation, in which 62% of patients had more than 4 risk factors and preoperative screening tests for kidney transplantation were unpredictable in 6% of cases; At follow-up, 15% of patients experienced cardiovascular events on average 2 ± 2 days after transplantation such as ACS, increased troponin levels, and atrial fibrillation. No mortality was recorded

in these patients (4). Coronary angiography is a noninvasive test for the diagnosis of cardiovascular disease and is considered as a gold standard, but is not possible for all patients (5). Gowdak et al., have screened coronary heart disease in high-risk patients, and the results suggest that coronary artery disease is strongly associated with CAD in diabetic patients, patients with peripheral vascular disease (PAD), and patients a history of myocardial infarction; the prevalence of cardiovascular disease range from 26 to 100% in these patients. The incidence of death in diabetic patients, PAD and myocardial infarction is predicted to be 2-fold, 4-fold and in 6-fold respectively (6).

2. AIM

Therefore, we aimed to evaluate the short-term cardiovascular complications in ESRD patients after kidney transplantation and to prevent further morbidity and morbidity by timely treatment of these complications. Numerous studies have been performed in different countries in ESRD patients after kidney transplantation, which has been more focused on long-term cardiovascular complications. In Iran, despite extensive kidney transplantation, no comprehensive study has been performed to date. The purpose of this study was to evaluate the short-term cardiovascular complications of renal transplantation in order to help patients and physicians in preventing these complications and their treatment.

3. METHODS

This historical cohort study was performed on patients undergoing kidney transplantation in Baqiyatallah Hospital between 2015 and 2017. This study was performed as a census and all renal transplant patients were enrolled up to a maximum of 1000 patients

Inclusion criteria included all renal transplant patients at Baqiyatallah Hospital between 2015 and 2017.

Exclusion criteria: Patients younger than 15 years.

Patients' information including demographic information, nature of transplantation, cardiac risk factors (e.g., diabetes, hypertension) preoperative cardiac consultation and requested paraclinic (cardiology, echocardiography, nuclear heart scan, angiography and exercise test), extracted from medical records of patients. Furthermore, the need for cardiac re-consultation, the complaint leading to the request for re-consultation, the requested paraclinic and its final diagnosis were extracted and recorded. Frequency and factors affecting the need for cardiac re-consultation and final cardiac diagnosis of patients were analyzed. The number of cases of mortality and the causes of mortality were also described.

Statistical analysis

Mean, standard deviation was used for quantitative variables and qualitative variables expressed as percentages and frequency.

Chi-square test was used to compare the qualitative variables between the two groups with /without need of counseling and also between the two groups with and without cardiac causes. Fisher exact test was used if necessary conditions were not available. Quantitative variables were compared between groups using t-test and nonparametric

tests. K-S test was used to check the normality of the data. Binary logistic regression statistical test was used to design the regression model to predict the need for re-counseling and the presence of cardiac causes in re-counseling. Significance level was set at 0.05.

4. RESULTS

A total of 982 patients with mean age of 45.33 ± 13.73 years were studied. The minimum age of patients was 18 years and the maximum age was 78 years. Furthermore, study population consisted of 615 (62.6%) male and 367 (37.4%) female. Transplant recipients were corpses for 526 (53.6%) and live donors was recorded as 456 (46.4%). Preoperative consultation was performed for 44 patients (4.5%) by the faculty members of Baqiyatallah, followed by other faculty members (62 patients, 6.3%) and non-faculty member physicians (876 persons, 89.2%).

Cardiac re-consultation after transplantation

Overall, 391 (39.8%) patients needed cardiac re-consultation after transplantation. The main complaints in 258 (66%) patients were dyspnea and chest discomfort, as well as arrhythmia (133, 34%).

Impact of age, sex, and type of transplant on the need for cardiac re-consultation after transplantation

The mean age of patients requiring cardiac resuscitation was significantly higher than those who did not require re-consultation after surgery ($P < 0.001$). There was no significant difference in sex distribution between the two groups of patients in need and without counseling ($P = 0.337$).

Frequency of transplantation from cadaver donor in patients requiring re-consultation was significantly higher than patients without requiring re-consultation ($P < 0.001$).

Variable	Need for re-consultation (N=391)	No need for re-consultation (N=591)	P value
Age (Year)	10.56 ± 55.00	11.65 ± 38.86	< 0.001
Sex			0.337
Male	(64.5%) 252	(61.4%) 363	
Female	(35.5%) 139	(38.6%) 228	
Transplant donor			< 0.001
The corpse	(62.4%) 244	(47.7%) 282	
Live person	(37.6%) 147	(52.3%) 309	

Table 1. Influence of age, sex, and type of transplant on the need for cardiac re-consultation after transplantation

Cardiovascular risk factors and patients' need for heart re-consultation after transplantation

Comparison of cardiac risk factors in the two groups showed that the frequency of hypertension, diabetes, and history of CABG surgery was significantly higher in those who needed cardiac re-consultation ($P < 0.001$).

The frequency of left ventricular hypertrophy (LVH) was not significantly different between the two groups ($P = 0.105$).

The history of coronary angiography (both positive and negative angiography results) was significantly higher in the group requiring cardiac re-consultation than patients who did not require cardiac re-consultation ($P < 0.001$).

Variable	Need for re-consultation (N=391)	No need for re-consultation (N=591)	P value
Hypertension	(91.8%) 359	(63.6%) 376	< 0.001
Diabetic	(49.4%) 193	(8.5%) 50	< 0.001
Left ventricular hypertrophy	(57.5%) 225	(52.3%) 309	0.105
CABG practice history	(5.9%) 23	(0.0%) 0	< 0.001
History of angiography			< 0.001
No	(75.2%) 294	(94.6%) 559	
Yes-Negative	(7.2%) 28	(4.2%) 25	
Yes-Positive	(17.6%) 69	(1.2%) 7	

Table 2. Cardiovascular risk factors and patients' need for heart re-consultation after transplantation

Confirmation of the heart and the need for a heart transplant after transplantation

Among patients requiring cardiac re-consultation after transplantation, cardiac approval was performed in 83.1% via nonmembers of university, while 16.9% of cases was confirmed by faculty members; of these, 27.3% were faculty affiliated with Baqiyatallah and 27.3% with other universities.

Among patients who did not need consultation after transplantation, 93.2% of the cases were approved by nonmembers of university and 6.8% by faculty members, among which 65% were faculty affiliated with Baqiyatallah University and 35% affiliated with other universities.

The differences between the two groups were statistically significant ($P < 0.001$).

In other words, out of 106 visits by faculty members, 66 (62%) needed re-counseling, while out of 876 visits by non-faculty members, 325 (37.1%) required cardiac re-counseling.

On the other hand, out of 44 visits by faculty members affiliated with Baqiyatallah University, 18 (40.9%) needed cardiac re-counseling, while out of 62 cardiac visits by faculty members of other universities, 48 (77.4%) needed a heart re-consultation.

The above points to the fact that the need for heart consultations was higher in visits by academic staff members than visits by non-academic staff members. There was also a need for heart consultations in the visits made by other faculty members of universities more than the faculty members affiliated with Baqiyatallah University (Table 3).

Variable	Need for heart consultation (N=391)	No need for heart consultation (N=591)	P value
Confirmation of heart by			< 0.001
Non-academic staff	(83.1%) 325	(93.2%) 551	
Academic staff	(16.9%) 66	(6.8%) 40	
Faculty affiliation			< 0.001
Baqiyatallah	(27.3%) 18	(65.0%) 26	
Other centers	(72.7%) 48	(35.0%) 14	

Table 3. The physician confirming the heart and the need for cardiac consultation after transplantation

Paraclinical data and the need for cardiac consultation after transplantation

Of those requiring cardiac re-consultation, 78.5% had a normal ECG and 21.5% had abnormal ECG findings. Among patients without requiring cardiac re-consultation, this distribution was found to be 94.4% for normal ECG and 5.6% for at least one abnormal ECG finding. Abnormal heart rate was significantly higher in patients requiring cardiac re-consultation ($P < 0.001$).

In addition, abnormal findings in echocardiography were significantly higher in patients requiring cardiac re-consultation than patients without cardiac re-consultation requirement ($P < 0.001$). The rate of exercise test request and its positive and negative result were significantly lower in patients requiring cardiac re-consultation as compared to patients without cardiac re-consultation requirement ($P < 0.001$).

However, the rate of request for cardiac nuclear scan and its positive and negative result was significantly higher in patients requiring cardiac re-consultation compared with patients without cardiac re-consultation requirement ($P < 0.001$). These are detailed in Table 4.

Variable	Need for heart consultation (N=391)	No need for heart consultation (N=591)	P value
Electrocardiogram (ECG or EKG)			< 0.001
Normal	(78.5%) 307	(94.4%) 558	
Abnormal	(21.5%) 84	(5.6%) 33	
Echocardiography			< 0.001
Normal	(82.6%) 323	(98.6%) 583	
Abnormal	(17.4%) 68	(1.4%) 8	
Sport test			< 0.001
No	(96.2%) 376	(85.3%) 504	
Yes-Negative	(3.6%) 14	(13.7%) 81	
Yes-Positive	(0.3%) 1	(1.0%) 6	
Perfusion scan			< 0.001
No	(55.2%) 216	(82.1%) 485	
Yes-Negative	(42.7%) 167	(16.9%) 100	
Yes-Positive	(2.0%) 8	(1.0%) 6	

Table 4. Required paraclinics and the need for cardiac re-consultation after transplantation

Sensitivity and specificity of exercise and scan testing in predicting the need for cardiac re-consultation

A total of 181 cardiac perfusion scans were performed in patients with a sensitivity of 4.57% and specificity of 94.34% to predict the need for cardiac re-consultation in patients. Furthermore, positive and negative predictive values for heart perfusion scan were determined as 57.14% and 37.45%.

The accuracy of a heart perfusion scan for predicting the need of heart re-consultation was determined to be 38.43%.

A total of 102 exercise tests were performed on patients. This test showed a sensitivity of 6.67% and specificity of 93.1% to predict the need for cardiac re-consultation in patients. Its positive and negative predictive values were calculated as 14.29% and 85.26%.

Moreover, the accuracy of the exercise test for predicting the need or lack of need of cardiac re-consultation was 80.39%.

Predicting the need for heart re-consultation in patients by regression model

Logistic regression using Forward Wald method, showed that patients' need for heart re-consultation could be predicted by 7 variables of age, diabetes, CABG history, ECG, echocardiography, angiography and nuclear heart scan ($R^2 = 0.652$, $P < 0.001$). The input and output variables in this regression model are presented in Table 5.

	Variable	P Value	Exp. (B)
Remaining in the regression	Patients age	0.001 >	1.115
	Abnormal ECG	0.002	0.386
	Abnormal echocardiography	0.001 >	0.022
	Diabetes	0.001 >	0.227
	CABG history	0.998	0.001
	Angiography (Negative result)	0.001 >	0.097
	Angiography (Positive result)	0.005	0.189
	Perfusion scan (negative result)	0.094	3.313
	Perfusion scan (positive result)	0.008	7.144
	Removed	Gender (male)	0.493
Donor (live)		0.005	-
Heart endorsement by academic staff		0.544	-
Hypertension		0.936	-
Left ventricular hypertrophy		0.595	-
Exercise Test (Negative Result)		0.461	-
Exercise Test (Positive result)		0.645	-

Table 5. Regression model predicting the need for heart remediation in patients

5. DISCUSSION

In the present study, 982 patients undergoing kidney transplantation were evaluated in Baqiyatallah Hospital, study population consisted of 615 (62.6%) male and 367 (37.4%) female with a mean age of 54.33 years. Overall, 39.8% of patients needed heart re-consultation.

Multivariate analysis revealed that patients' need for cardiac re-consultation could be predicted by 7 variables including age, diabetes, CABG history, ECG, echocardiography, angiography, and nuclear heart scan. Abnormal findings by ECG, echocardiography, diabetes, CABG and abnormal angiographic findings were more frequent in patients visited by non-faculty member's physicians. Patients who were visited by faculty members were more likely to be in worsen condition than those visited by non-faculty members.

Dunn et al., 2019 designed a model of cardiac risk assessment in patients undergoing kidney transplantation based

on age, sex, diabetes, cancer, donor type (live / corpse), duration of ESRD, and cardiovascular comorbidities (7).

In our study, two predictive models of the need for cardiac re-consultation and the presence of cardiac causes in cardiac re-consultation were designed. Predictive models of need for cardiac reassessment included patient age factors, diabetes, CABG history, ECG, echocardiography, angiography, and nuclear heart scan.

The model predicting cardiac etiology at re-consultation included factors of ECG in first consultation, the first consultation physician, left ventricular hypertrophy, history of angiography, and nuclear heart scan.

Ciftci in 2018 found that fragmented QRS in standard 12-lead electrocardiogram have a high ability to detect ischemia in cardiac perfusion scans and severe blockage in coronary angiography (8).

In our study, abnormal findings in preoperative cardiac electrocardiogram were greater in those requiring cardiac re-consultation, but these abnormal findings were less in those with cardiac causes than those with non-cardiac causes for second consultation.

In a study by Sharma, stress echocardiography showed sensitivity, specificity, positive predictive value and negative predictive value as 94%, 88% 86% and 95%, respectively, in the diagnosis of coronary artery disease in ESRD patient's candidate for transplantation. Furthermore, serum troponin T level demonstrated sensitivity, specificity, positive and negative predictive values as 54%, 62%, 40%, and 74% (9). However, the Jafari in a study showed that none of the cardiac biomarkers of troponin I, T, CK and CK-MB had the necessary ability to diagnose coronary artery disease in these patients (10). In the present study, serum troponin levels could not correctly differentiate cardiac causes from non-cardiac causes.

Malyszko reported a prevalence of 2% for atrial fibrillation arrhythmia in the general population, whereas this prediction was up to 24% in patients with coronary heart failure. The presence of AF arrhythmias in kidney transplant recipients increases the risk of myocardial infarction, transplant rejection, and post-transplant mortality (11). In our study, 132 post-transplant patients developed cardiac arrhythmias including AF, PVC, and supraventricular tachycardia and bradycardia. A number of studies have investigated the effect of kidney transplantation on cardiac events in patients.

A study in 2018 showed that the incidence and severity of coronary artery disease in renal recipient patients were significantly lower than ESRD patients in the transplant waiting list (12). Furthermore, there was a significant improvement in echocardiographic findings in patients after preoperative kidney transplantation (13).

6. CONCLUSION

According to the results of the present study and the need of cardiac re-examination after kidney transplantation in 40% of patients, it seems that preoperative risk assessment in these patients requires more precision. According to the regression model predicting the need for re-visitations in patients, it is recommended that elderly patients with abnormal findings in electrocardiography

and echocardiography, diabetic patients with a history of negative coronary angiography or cardiac perfusion scan should be more carefully monitored for reducing cardiac reassessment in these patients

On the other hand, only 41% of people who needed a heart reassessment eventually received a cardiac diagnosis. Regarding the predictive regression model of cardiac causes in these patients, it is recommended that abnormal findings on ECG, heart confirmation by the non-faculty members, presence of left ventricular hypertrophy and a history of angiography and myocardial perfusion scan should be carefully assessed to prevent heart problems after transplant surgery.

- **Author's contribution:** MSGH, BE, AB, and MJ gave a substantial contribution to the conception and design of the study. MSGH, BE, AB, and MJ gave a substantial contribution of data. MSGH, BE, AB, and MJ gave a substantial contribution to the acquisition, analysis, or interpretation of data for the work. MMJ, MSGH, BE, AB, and MJ had a part in article preparing for drafting or revising it critically for important intellectual content. All authors gave final approval of the version to be published.
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