Evaluation of myocardial perfusion and function after kidney transplantation by Gated SPECT myocardial perfusion scintigraphy

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ABSTRACT

Introduction: The aim of this study was to evaluate the effect of successful kidney transplantation (KT) on myocardial perfusion and left ventricular function by both qualitative (visual) interpretation and semiquantitative parameters, using myocardial perfusion scintigraphy with gated-single photon emission computed tomography (gated-SPECT) in patients suffering from end-stage renal disease.

Methods: From a total of 38 patients who were candidates of KT, twenty-six patients (16 female, 10 male, mean age: 47.5 yr, range: 24-64 yr) who had successful KT were included. Myocardial perfusion scintigraphy was performed by Gated Single Photon Emission Computed Tomography (Gated-SPECT) method, before and after surgery (mean: 24 months). Perfusion and function status was evaluated by qualitative and semiquantitative parameters.

Results: Our data showed qualitative evidence of perfusion and functional abnormality in pre-transplant scans as follows: Abnormal perfusion in left anterior descending (LAD), left circumflex (LCX) and right coronary artery (RCA) territories in 42.5%, 53.8% and 65.4% of cases, respectively; dilation in 57.7% and inhomogenity of uptake in 53.8% of cases. However no statistically significant change was noted after transplantation, i.e. p value for all semiquantitative values including summed stress score (SSS), summed rest score (SRS) and summed difference score (SDS), summed motion score (SMS), summed thickening score (STS), ejection fraction (EF), end diastolic volume (EDV), end systolic volume (ESV), and stroke volume (SV) was greater than 0.05.

Conclusion: Renal transplantation may not have considerable long term effect on myocardial perfusion and function in patients with chronic renal failure. This could be due to either non-reversible myocardial changes or continuing effect of degrading factors on the myocardium.

Key words: Kidney transplantation; Myocardial perfusion; Myocardial function; Gated-SPECT

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INTRODUCTION

Chronic renal failure is a complex metabolic syndrome, and the uremic status can influence contractile function of myocardium [1]. It has also been shown that these patients might already have a large number of structural and functional peripheral vascular and cardiac abnormalities and the resultant myocardial ischemia may lead to left ventricular (LV) dysfunction that can persist even after the return of normal perfusion. This prolonged dysfunction is known as myocardial stunning [2].

It is suggested that kidney transplantation (KT) can resolve many of the cardiac abnormalities associated with chronic kidney failure [3,4].

Myocardial perfusion scintigraphy in gated SPECT mode is a sensitive and specific method that can effectively assess both cardiac perfusion and function [5,6]. We used this method before and after renal transplantation, to assess pre-transplantation myocardial perfusion and function in patients with end-stage renal disease, and subsequently to evaluate the probable effect of KT on improving perfusion and function status of myocardium.

METHODS

Thirty-eight patients with chronic renal failure who were candidates for renal transplantation were enrolled in the study. Twelve patients were excluded because of unsuccessful transplantations or refusal to undergo the second scan after receiving transplant. A total of 26 patients (mean age: 47.5 yr, range: 24-64 yr), 16 female and 10 male, were included in the study.

For every patient myocardial perfusion scans, performed in gated SPECT mode before and after transplantation, were compared qualitatively and semi-quantitatively. The average interval between the two scans was 24 months and the average time between transplantation and the post-transplantation scan was 20 months.

This study was approved by the institutional ethics committee of Tehran University of Medical Sciences and written informed consent was obtained from all patients.

Image acquisition

For myocardial perfusion imaging the patients were instructed to fast at least 4 hrs before the study. Possible interfering medications with dipyridamole study mainly xanthine containing drugs were stopped 48 hrs before the stress phase. Also caffeine containing foods and beverages were avoided for at least 24 hrs. A commercial sestamibi kit (AEOI, Tehran, Iran) was used and the labeling and quality control procedures were performed according to the manufacturer's instructions. A dose of 666-814 MBq of Tc-99m sestamibi was given 4 min following the standard pharmacological stress with intravenous injection of 0.56 mg/kg dipyridamole over 4 min period. In the presence of dipyridamole side effects such as vertigo, chest pain, headache and electrocardiographic changes, 250 mg aminophylline was slowly injected intravenously 5 min after radiotracer injection. Single photon emission tomography (SPECT) with standard acquisition protocol was performed about 60 min after radiotracer injection, using a rotating, dual head gamma camera (Solus, ADAC, Milpitas, CA) equipped with a low-energy high resolution parallel hole collimator.

Patients were in a supine position during the image acquisition. Thirty-two azimuth images, 30 s/projection, were obtained in a 180-degree circular orbit, beginning from 45 degrees right anterior oblique to 135 degrees left posterior oblique with step and shoot acquisition on a 64×64 matrix and 38.5 cm detector mask (1.22 zoom). Rest images were obtained on the following day using the same imaging protocol. No attenuation correction was used in the imaging process.

Image analyses and interpretation

Reconstruction of the images was carried out by Pegasys software (ADAC system). An expert nuclear physician used the cine-display of the rotating planar projections to assess sub-diaphragmatic activities, attenuations and patient motion to optimize the technical quality of the images.

The raw data were prefiltered by ramp and subsequently by Butterworth filters with frequency cut-off of 0.45 and order of 9.0. Also the data were semiquantitatively processed using Auto-QUANT software package (Cedars-Sinai Medical Center, Los Angeles, CA, USA) based on 20 segment analysis. Semiquantitative values, including EF, TID, LHR, SSS, SRS, SDS, SMS, STS, EDV, ESV and SV were also compared by statistical methods before and after renal transplantation.

The patients were stratified in four groups according to SSS, including normal (SSS≤3), mildly abnormal (4≥SSS>8), moderately abnormal (9≥SSS>11), and severely abnormal (SSS≥12).

Qualitative interpretation of scans, including homogeneity of uptake, visual perfusion status of myocardial walls, ventricular dilation and transient ventricular dilation (TID) was performed by two nuclear medicine physicians; in cases of disagreement a third opinion was also obtained.

Statistical analysis

We used SPSS statistical software (SPSS version 17.0) for statistical analysis. To compare semiquantitative values before and after renal transplantation, including EF, TID, LHR, SSS, SRS, SDS, SMS, STS, EDV, ESV and SV, wilcoxon signed rank test was used. To evaluate the qualitative data of pre and post transplantation measurements, Chi-Square test was used. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Considering cardiac risk factors, from the total of 26 patients, 7 cases (26.9%) were hyperlipidemic, 14 (53.8%) hypertensive, 3 (11.5%) smoker and 5 (19.2%) were diabetic.

In assessing the perfusion status of pre-transplantation hearts by qualitative measure (visual interpretation), abnormal perfusion was noted with a frequency of 11 (42.5%) in LAD, 14 (53.8%) in LCX, and 17 (65.4%) in RCA territory. Visual dilation was noted in 15 (57.7%) and transient right ventricle visualization was seen in 6 (23.1%) of cases.

The post-transplantation scans were somehow more homogeneous than the pre-transplantation images,

though the value was considered insignificant (p=0.08).

The difference in visual interpretation of perfusion in LAD territory (perfusing anterior and anteroseptal walls), LCX territory (perfusing anterolateral and inferolateral walls) and RCA territory (perfusing inferior and inferoseptal walls), before and after transplantation were insignificant (p values, 0.5, 0.1 and 1.0, respectively).

Regarding visual assessment, the frequency of left ventricular dilation, transient left ventricular dilation (TID), and transient right ventricle visualization were not different after transplantation compared to pre-transplantation studies (p=1.0 , p=0.1, p=0.1, respectively). Semiquantitative data in pre- and post-transplatation scans are shown in Table 1.

In assessing SSS, from 21 patients who were within normal range (SSS≤3), 19 patients (90.5%) remained in this group after transplantation, while only two patients were relocated as mildly abnormal group (8≥SSS>4). Mildly abnormal group (8≥SSS>4) included only one patient showing no change after transplantation. There were four patients in the severely abnormal group (SSS≥12) from whom 3 patients remained in the same group, while one was changed to the medium risk group (11≥SSS>9).

Table 1. Comparison of semiquantitative perfusion and function data before and after renal transplantation.

Scintigraphic Parameter		Pre-transplantation	Post-transplantation	p value*
SSS	Median (range)	5 (0-22)	5 (0-21)	0.915
SDS	Median (range)	5 (0-7)	0 (0-11)	0.323
SRS	Median (range)	0 (0-18)	0 (0-21)	0.256
TID ratio	Mean (SD)	0.99±0.15	1.01±0.09	0.554
LHR	Mean (SD)	0.33±0.05	0.33±0.06	0.585
SMS	Median (range)	4.5 (0-69)	4 (0-70)	0.180
STS	Median (range)	0 (0-46)	0 (0-46)	0.311
ESV	Mean (SD)	33.50±23.05	33.72±23.36	0.482
EDV	Mean (SD)	77.04±34.26	78.28±36.35	0.530
EF	Mean (SD)	60.37±16.11	60.56±14.95	0.878

* Wilcoxon Signed Ranks Test

SSS: summed stress score, SRS: summed rest score, SDS: summed difference score, TID ratio: transient ischemic dilation ratio, LHR: lung heart ratio, SMS : summed motion score, STS: summed thickening score, ESV: end systolic volume, EDV: end diastolic volume, EF: ejection fraction

DISCUSSION

Chronic renal failure is a complex metabolic syndrome, and the uremic status can have adverse effect on myocardium [1]. This influence can be on myocardial blood supply or functional status of myocardium [2-4]. Uremia is likely to induce specific changes in the relaxation properties of the myocardium. These changes are responsible for the impaired diastolic function independent of blood pressure, degree of hypertrophy, and metabolic changes, suggesting the existence of a specific cardiomyopathy [7]. Prolonged exposure to uremic toxins has been shown to influence myocardial contractility. Although the mechanism of action of such toxins is not well established, several potentially negative inotropic and chronotropic factors have been verified in uremic plasma [8,9]. Exposure to these agents in long run can result in fibrosis of myocytes and eventually fatal cardiac event [10,11]. These patients might develop a specific cardiomyopathy, secondary to their specific metabolic, biochemical, hormonal, and even due to hemodynamic compromise (atrioventricular fistula) [12]. Cardiotoxic substances produced during uremia can adversely affect the myocardial function by slowing down its contraction and relaxation [13].

To evaluate cardiac perfusion and function in patients with chronic renal failure and to assess the effect of KT on cardiac status, electrocardiographically gated myocardial perfusion SPECT (GSPECT) method is the ideal method and was used in our study. This is a state-of-the-art technique for the combined evaluation of myocardial perfusion and left ventricular function within a single study. It is currently one of the most commonly performed cardiology procedures in nuclear medicine departments. Automation of the image processing and quantification has made this technique highly reproducible, practical and user friendly in the clinical setting. In patients with coronary artery disease, gating enhances the diagnostic and prognostic capability of myocardial perfusion imaging, providing incremental information over the perfusion data, and has shown potentials for myocardial viability assessment and sequential follow-up after therapy [5,14].

By this objective gateway method, myocardial perfusion, hypokinesia, dyskinesia, and functional parameters (left ventricular ejection fraction and systolic wall thickening) are well established and potentially useful to establish diagnostic, prognostic, and therapeutic indications [15].

Several studies have utilized Gated-SPECT as a valuable method in assessing prognosis after renal transplantation [4,16-19].

As renal transplantation causes significant improvement in azotemic condition, it is to be expected to induce improved cardiac status. Different studies have shown that renal transplantation can improve functional status of congestive heart failure [3,4,20,21], and increases survival [4]. Stokkel et al's study showed the systolic left ventricular dysfunction in terms of LVEF, wall motion, and wall thickening significantly improved 6 months after KT in patients with end-stage kidney disease [20]. Evaluation of heart function by echocardiography showed that after renal transplantation, myocardial hypertrophy was diminished and left ventricular systolic and diastolic function improved [3]. Parfrey showed improvement of LV systolic function, by an improvement in LV fraction shortening [21].

Our study however, didn't show such a trend. Although there was some evidence of improved perfusion after renal transplantation, the statistical evaluation did not show significant improvement in either perfusion or functional status of myocardium by qualitative or semiquantitative parameters. These parameters included visual interpretation of perfusion, dilation, transient RV visualization (qualitative assessment), TID, LHR, SSS, SRS, SDS, STS, SMS, EDV, ESV, SV, and EF (semiquantitative assessment), demonstrating p values persistently> 0.05. These findings could be due to long-standing uremic condition affecting cardiac perfusion and functioncausing irreversible changes of myocardium [2-4,7-11]. Another explanation for observation of coronary artery disease related abnormalities even after transplantation could be the possibility of increased risk of coronary artery calcification and coronary ischemia in renal transplant recipients [22]. This cardiovascular morbidity might also be caused by events related to surgical intervention and allograft function [23]. Also, the time interval after transplantation in our study (mean: 20 months) was longer than previous studies which showed functional improvement. We assumed the longer time interval after transplantation likely led to disappearance of the earlier improving cardiac effects explaining the findings in pre and post transplantation images in our study.

Also cardiac risk factors which might seem to have continuing influence on myocardium after transplantation were not interfering factors in our study considering their frequencies (hyperlipidemia: 26.9%, hypertension: 53.8%, smoking: 11.5% and diabetes: 19.2%).

The very similar findings in pre and post transplantation studies of our semiquantitative parameters (which are exclusively objective), while surprising, strongly confirmed our qualitative interpretations. More studies with larger sample size

are needed to further investigate these unexpected findings.

CONCLUSION

Renal transplantation may not have considerable long term effect on myocardial perfusion and function in patients with chronic renal failure. This could be due to either non-reversible myocardial changes or continuing effect of degrading factors on the myocardium.

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