# Differences in heart rate variability parameters before and after kidney transplantation in patients with renal failure

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**Abstract:** Introduction: Heart Rate Variability(HRV) is defined as R-R interval changes over time and is used in assessment of sympathetic and Vagal nerve effects on sinus node and thus on the heart rate. It has been seen that HRV abnormalities is reversible after normalization of renal function in kidney transplantation even in patients with long term dialysis, the kidney transplantation had normalized the HRV. Methods: In a cross–sectional and analytical study, we evaluated the HRV changes before and after kidney transplantation in 20 patients with chronic renal failure after, changes in HRV 20 patients with chronic renal failure after achieving the inclusion criteria. The patients were followed for 6 months and the results were assessed for HRV changes and other paraclinical factors. Results: In total, 11(61.1%) of patients were male and 7 (38.9 %) were female. Mean age of patients was 42.7±25 which was in the range of 25-59 years. Between parameters of HRV in patients, only the increase in the VLF and ULF was significant which had a statistically meaningful changes in comparison with the pre transplantation period (P=0.05, P=0.01). The changes in the other parameters were not statistically significant. Conclusion: With regard to the findings of this study we can defend the theory of inhibited HRV return in hemodialysis patients after the kidney transplantation, but there is need for studies with more cases to prove and confirm this theory.
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**Keywords:** Chronic renal failure; Heart rate variability; Kidney transplantation

## 1. Introduction

The changes in the R-R interval which is called Heart rate variability is used for evaluation of the sympathetic and Vagus nerve on the sinus node and as a result on the heart rate (Tulppo and Huikuri, 2004) this can be helpful in finding the patients which are at the risk of cardiovascular disease or mortalities(Malik, 2000).

HRV is measured by two methods: Time Domain Method and Frequency domain method. The signal changes in a period of time are called Time domain method and the frequency domain method measures the signal sin frequency bond (Malik, 2000).

The both of above methods can be used for evaluating the HRV but the periodical analysis can evaluate the sympathetic and parasympathetic activity in a more accurate way (Zipes and Jalife, 2004).

There are several factors that impact on heart rate variability (HRV) including cardiovascular disease (Karcz, 2003). Other affecting factors include Body mass index (BMI), increased blood sugar, high blood pressure and certain health conditions such as kidney disease (Huikuri and Makikallio, 2001).

The autonomic system dysfunction is the predominant feature of the uremic situation. Autonomic neuropathy associated with renal failure can cause sympathetic and parasympathetic involvement and is also associated with peripheral neuropathy (Campese, 1981).

One of the most important presentations of autonomic dysfunction caused by uremia is the abnormal control of the cardiovascular system which has a major role on hypertensive attacks during hemodialysis specially in diabetic patients (Travis and Henrich, 1989).

There are several studies about HRV in patients with chronic renal failure (CRF) which most of them is about patients under hemodialysis.

In the studies on the patients under hemodialysis the sizable decrease in all frequencies and specially low frequencies was seen.

It is concluded that the HRV abnormalities is a reversible situation after normalizing the renal function with renal transplantation (Axelrod, 1987).

Even in patients under long term hemodialysis the renal transplantation can normalize the HRV (Dvora, 1999).

In other studies the autonomic function reverse is reported after the renal transplantation (Heidbreder, 1985).

This reverse in autonomic function is suggestive of the opinion that autonomic control of the heart rate in renal failure is a result of uremic wastes (Tamura, 1998).

With regarding to the fact that there are no previous studies in this issue and with considering the importance of this matter the aim of this study is the evaluation of the HRV changes in patients before and after renal transplantation in patients with CRF.

## 2. Material and Methods

In a cross sectional descriptive-analytic study that performed in cardiovascular disease department of Tabriz university of medical sciences on patients with chronic renal failure candidate for kidney transplantation, we measured the Hart rate variability parameters before and after the transplantation.

We enrolled 20 patients to the survey upon inclusion and exclusion criteria.

The complete cardiac evaluation (Trans thoracic echocardiography, and Electrocardiogram (ECG)), HRV (with 24 hours holter monitoring) and laboratory tests such as Urea, Creatinine, Hemoglobin and hematocrit was done for patients before kidney transplantation, patients was evaluated for HRV changes and Urea and Creatinine 6 months after transplantation.

Exclusion criteria:

1-History of cardiac failure as 2 and 3 function class

2-Unsuccessful kidney transplantation

3- Patients not referring 6 months after transplantation

4 - Lack of consent to participate in the study.

The obtained data was coded and then entered into a computer and statistically analyzed by SPSS software. T-Test and chi-square test were used for data analysis. Significance level for tests was determined as 95% ($P< 0.05$).

## 3. Results

In a cross sectional descriptive –analytic study, we evaluated the HRV changes in 20 patients with chronic renal failure candidate for renal transplantation before and after renal transplantation. We excluded 1 patient because of transplanted kidney rejection and another patient for not referring 6 months after transplantation. At the end the analysis is presented upon data taken from 18 patients.

11 of patients (61.1%) was male and 7 (38.9%) was female. the mean age of the patients' was 42.7±12 years in the range of 25 to 59 years of old. The demographic findings of patients are shown in table 1.

2 of patients (11.1%) had a simultaneous coronary artery disease. 94.4% of patients had normal sinus rhythm and the AF rhythm was present in 5.6% of patients. 27.8% of patients had Left Ventricular Hypertrophy (LVH) in their ECG. There was no the branch blocks and other types of block in studied patients and there was ST-T changes in 1 patient.

**Table 1:** Demographics characteristics of patients

| Variable | Mean ± SD | Range |
|---|---|---|
| Height(*cm*) | 164±0.05 | 150-172 |
| Weight(*Kg*) | 63.6 ± 6.9 | 44-74 |
| BMI( $^{Kg}/_{m^2}$) | 23.6 ± 2.6 | 16.3-27.3 |
| SBP(*mmHg*) | 138.8 ± 19.9 | 100-165 |
| DBP(*mmHg*) | 84.4 ± 12.1 | 60-110 |
| HB | 12.2 ± 6.5 | 8.3-16.1 |
| HCT | 30.9 ± 6.3 | 22.1-37.4 |
| BUN | 104.3 ± 9 | 41-150 |
| Cr | 8.7 ± 2.4 | 5.3-12.8 |
| Ejection Fraction | 55.8 ± 12.1 | 30-75 |

HRV for patients before and after the transplantation is shown in table 2. The laboratory findings of patients are also shown in table 3. There was a significant reduce in BUN and Cr of patients before and after transplantation (P=0.0001). Distributions of HRV parameters in before and after the transplantation are shown in Chart 1 and 2.

**Table 2:** HRV of patient's in Pre Transplantation and post Transplantation

| Variable | Pre Transplantation (N=18) | Post Transplantation (N=18) | P |
|---|---|---|---|
| SDNN | 110.7±50.6 | 122.2±2.8 | 0.41 |
| SDANN | 118.6±82.4 | 104.7±41.8 | 0.34 |
| RMSSD | 65.7±6.1 | 57.1±4.1 | 0.60 |
| HRV | 39.1±4.3 | 39.5±4.1 | 0.89 |
| ULF | 108.8±43.9 | 123.9±10.4 | 0.05 |
| VLF | 233±90.3 | 295.3±100 | 0.01 |
| LF | 129.4±51.5 | 132.7±63.3 | 0.76 |
| HF | 125.5±45.9 | 115±34.5 | 0.25 |
| LF/HF | 1.3±0.6 | 1.4±0.6 | 0.23 |

**Table 3:** Laboratory finding in pre and post transplantation

| | Mean ± Std Deviation | Range |
|---|---|---|
| Admission HB | 12.3 ± 6.6 | 8.3 -38.1 |
| Admission HCT | 30.9 ± 6.4 | 12.1 - 37.4 |
| Admission Creatinine | 8.53 ± 2.45 | 5.30 - 12.80 |
| Admission BUN | 104.35 ± 37.32 | 41 – 150 |
| Creatinine after | 1.32 ± .21 | 1.00 - 1.70 |
| Bun after | 43.33 ± 5.27 | 36 – 56 |

## 4. Discussions

There are several factors that impact on HRV including cardiovascular disease (Karcz, 2003). Other affecting factors include BMI, increased blood sugar, high blood pressure and certain health conditions such as kidney disease (Huikuri and Makikallio, 2001).

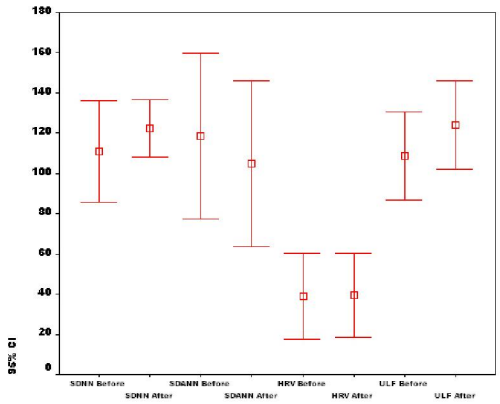


Chart 1. Distribution of SDNN, SDANN, HRV and ULF of patients in before and after the transplantation

This reverse in autonomic function is suggestive of the opinion that autonomic control of the heart rate in renal failure is a result of uremic wastes (Tamura, 1998).

There is no similar study in Iran evaluating the role of kidney transplantation in patients with CRF, the effect of some other treatments like replacement therapy on HRV such as hemodialysis is studied so far .and this can be suggestive for the innovation of our study.

Fukuta and colleague in 2003 have stated that reductions in some parameters of HRV including those presenting the long term changes in HRV in patients under chronic hemodialysis is independent predictors for cardiovascular events (Fukuta, 2003).

Giordano and colleague in 2001 have shown that patients with CRF and Diabetes under chronic hemodialysis show severe impairments in HRV that can be a result of diabetes caused autonomic neuropathy and chronic renal failure. Whereas the HRV parameters is reversible in non diabetic patient's in comparison with diabetic patient's after the hemodialysis (Giordano, 2001).

In the study of Axelord and colleague on hemodialysis patients there seemed a significant reduce in all frequencies specially in low frequencies regarding to the HRV parameters. They reported a reverse in HRV impairments after normalizing the kidney function (Axelrod, 1987).

In our study despite the findings of Axelord study, there was not a significant changes in LF parameter in patients after the renal transplantation (p=0.76).

In our study there was a history of receiving Calcium channel blocker agents in 14 cases(82.4%) and beta blockers in 17(94.4%) of patients.

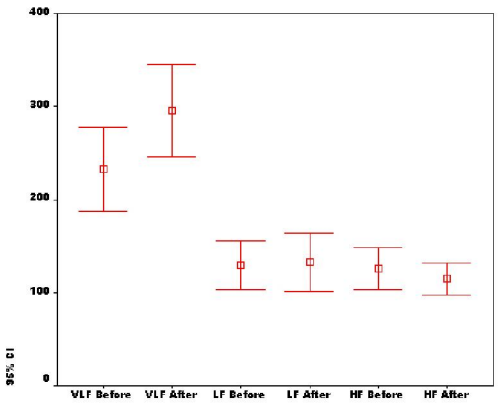


Chart 2. Distribution of VLF, LF and HF of patients in before and after the transplantation

In a similar study by Ondocin et al in USA, the ACEs effect on HRV was studied on hemodialysis patients and stated that despite normal population, in patients with ESRD, ACEs can increase the sympathetic activity in patients leading in severe changes in HRV (Ondocin and Narsipur 2006).

In the study of Ondocin, the mean age of patients was 50.6 years and the causes of ESRD in 4 patients (36%) was diabetes and in 5 cases (45%) the underlying cause was the HTN (Ondocin and Narsipur 2006).

In our study the risk factor was an above and the underlying disease was similar to study above, diabetes and hypertension was the most common causes of end stage renal disease(ESRD) ,there was also simultaneous coronary artery disease in 2 (11.1%) of patients.

In study of Ondocin and his colleague the most HRV parameters which was affected from HRV was SDNN and SDANN (Ondocin and Narsipur 2006).

Isaline and colleagues have stated that the circadian rhythm of the HRV in patients with ESRD can normalize after renal transplantation the sudden cardiac death in patients with ESRD can be associated with autonomic dysfunction lead in decrease in HRV (Isaline, 2005).

In the study of Brodde and his colleague it is stated that autonomic dysfunction in hemodialysis patient was improved after renal transplantation and sympathetic and parasympathetic function is also

improved specially in primary levels (Brodde and Daul, 1984).

In 2001 Agelink and colleagues studied the effect of age and gender on HRV in patient with CRF and showed that there is a significant decrease in ULF and LF/HF in young women comparing to the young men in the same age, its also stated that women have a more rest Heart rate than similar aged men (Agelink, 2001).

Ranpuria and colleague have stated that HRV parameters changes can be used to predict cardiovascular events in patients under chronic hemodialysis and these events can be prevented with effective treatment of coronary artery diseases and reducing the HRV impairments, considering the point that coronary artery disease can be of most common causes of death in ESRD patients (Ranpuria, 2008).

**Conclusion:**

With regard to the findings of this study we can defend the hypothesis of the inhibited HRV reverse in patients under hemodialysis after renal transplantation, but the certification of this hypothesis needs multicenter studies with more cases.

**Suggestions:**

There were some limitation in our study and we can propose some suggestion with eliminating them:

1-conducting a similar study with more cases and comparing the HRV parameters changes in patients after transplantation and its relationship with duration of illness.

2-conducting a similar study on patients with ESRD in the form of two groups, patients who underwent renal transplantation and patients under chronic hemodialysis and assessing the above modalities on HRV parameters

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