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# Improvement in Severe Heart Failure Post-Successful Renal Transplantation: A Single-Centre Experience with Seven Cases

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**Abstract**

Heart failure is common in patients with chronic renal disease, either as a complication of renal failure or from shared risk factors, or is the major cause of death in patients on dialysis. At present, end stage renal disease (ESRD) patients who have systolic heart failure are considered high-risk for surgery; and nephrologists and cardiologists are reluctant to refer these patients for kidney transplant evaluation. It is unclear whether such patients should be accepted and waitlisted for transplantation. seven cases with end stage renal disease (ESRD) and severe heart failure with ejection fraction (EF) of less than 20% and newyork class 3 - 4, despite being on optimal treatment, who underwent renal transplant from nonrelative living donor at Shahid Moddaress hospital in Tehran, Iran during the July 2013 to December 2015, were retrospectively collected and analysed. The mean ± SD of patient's age was 32.7 ± 16 years, and about 72% of them were female. The left ventricle ejection fraction increased by 35% on an average after the renal transplantation. Renal transplantation significantly improved the LV systolic function and ejection fraction status and subsequently decreased the need for medical treatment and heart transplantation.

*Keywords:* Heart Failure, Kidney Failure, Transplantation

## 1. Introduction

Cardiovascular events are the frequent cause of morbidity and mortality in end-stage renal disease (ESRD) patients. Several studies have demonstrated that heart failure is 12 to 36 times more common in dialysis patients compared to the general population (1, 2). Also, the mortality in a dialysis patient increases by almost 50% after the diagnosis of heart failure is established, based on clinical signs and symptoms (3). Left ventricular hypertrophy, left ventricular dilatation and systolic or diastolic dysfunction have been reported as manifestations of chronic uraemia (4, 5). So, heart failure, arrhythmias and sudden death could be expected in these patients (5). A recent study revealed that more than 85% of dialysis patients will die three years after hospitalization from CHF (3). The mechanism of heart failure in a patient with end stage renal disease (ESRD) includes: Intradialytic volume overload and vascular access flow, anaemia due to decreased production of erythropoietin, hypertension and arterial wall stiffness (hypertension could be the reason, or ESRD), and valvular disease: Valvular calcifications mainly in mitral and aortic valve are indicators of poor prognosis in patients with ESRD. Vascular pathology: Several kinds of vascular pathology can play a role in uremic patients: Atherosclerosis, arteriosclerosis and vascular calcification and remodelling (6, 7) renal transplantation leads to an improvement in a number of factors predisposing to heart failure, including volume overload, uremic toxicity, anaemia, dyslipidaemia, calcium/phosphate metabolism, and hyperhomocysteinemia (8). It can reduce overall mortality by 68% (9). Although left ventricle systolic dysfunction was previously considered a contraindication to kidney transplant, some studies demonstrated reversals of cardiac dysfunction after transplant (10-12). Also, literatures showed a sensible reduction in the incidence of HF for diabetic patients following successful kidney transplantation (1, 10). The aim of this study is to present eight cases referring to Shahid Modarress Educational Hospital (The only governmental facility in north-western Tehran, Iran) with ESRD and symptomatic severe heart failure undergoing kidney transplantation during the July 2013 to December 2015.

## 2. Case Presentation

### 2.1. Case 1

A 53-year-old woman with ESRD secondary to uncontrolled hypertension was under haemodialysis for 7 years.

She had past medical history of longstanding type one diabetes mellitus (DM) and ischemic heart disease (IHD). She underwent CABG (coronary artery bypass grafting) seven months prior to a kidney transplant. After CABG, she was suffering from ongoing dyspnoea that was multifactorial, anaemia, and poorly controlled hypertension. She was on Asprin 100 mg daily, Rosuvastatin 5 mg daily, metoprolol 25 mg BD, methyldopa (250 mg /BD), calcium carbonate 500 mg BD, Rocaltrol 0.25 mcg orally BD, ALMGS (Aluminum / Magnesium / Simethicone 225/200/25 mg per 5 mL).

Echocardiographic evaluation demonstrated left ventricular ejection fractions (LVEF) of 15%, moderate mitral valve regurgitation (MR), pulmonary artery pressure (PAP) of 65 and septal wall hypokinesia. In the chest, CT scan evidence of pulmonary congestion was obvious, and pulmonary function test (PFT) showed evidence of lung-restrictive disease.

The patient underwent renal transplantation and initially commenced on Prednisolone, Cyclosporine and Mycophenolate. After 3 months, she had no pulmonary symptoms, and ejection fraction (EF) increased to 45%.

### 2.2. Case 2

A 38-year-old man, with unknown etiology of ESRD, was under haemodialysis through jugular catheter. He was admitted to hospital with sepsis, most likely secondary to catheter infection, and transesophageal echocardiography (TEE) rolled out infective endocarditis, but showed ejection fraction (EF) = 15%, moderate tricuspid regurgitation (TR), pulmonary artery pressure (PAP) = 43 mmHg, severe pleural effusion and dilated aortic root. His medication included, Calcium Carbonate (500 mg) BD, Digoxin 500 mcg / daily 5 days a week, Cholecalciferol 25 mcg/day, Furosemide 100 mg /BD and Eprex 4000 three times a week.

He underwent renal transplantation after the infection came under control. Echocardiography after one month demonstrated moderate LVH and severe left ventricular systolic dysfunction (EF = 25%), severe diastolic dysfunction, mild to moderate right ventricle size and severe right ventricle systolic dysfunction, no aortic stenosis (AS), trivial aortic insufficiency (AI), mild MR (mitral valve regurgitation), moderate tricuspid regurgitation (TR), PAP = 40, moderate left ventricular hypertrophy, and small pleural effusion. Echocardiography 4 months post-transplant showed ejection fraction of 45% and mild tricuspid regurgitation.

### 2.3. Case 3

A 30-year-old woman with unknown etiology of end stage renal disease (ESRD) had background history of asthma, hypertension during pregnancy, seizure since age of 22 and mitral valve replacement at the age of 25 due to mitral stenosis secondary to rheumatic fever. She was on haemodialysis for 3 years. Echocardiography revealed MILD MR (mitral valve regurgitation), EF = 15% and PAP = 80. She was on folic acid1mg/d, Enalapril 5 mg/bd, Warfarin 2.5 mg/daily, Calcium Carbonate 500/BD and Frusemide 40 mg/BD.

She underwent renal transplantation and LVEF improved to 20% after one month and then to 40% after 3 months.

### 2.4. Case 4

A 15-year-old girl from a remote area was on haemodialysis for 2 years; she was suffering from dyspnoea, high blood pressure, and anaemia. The cause of end stage renal disease was not clear to us. Echocardiographic findings included mitral regurgitation, aortic insufficiency, tricuspid regurgitation (TR), and severe cardiomegaly with LVEF (about 15% - 20%). After starting heart failure management, her LVEF improved to 20% - 25%.

Three months after successful kidney transplantation, the patient was asymptomatic, and echocardiographic findings showed improvement in LVEF, mitral regurgitation, aortic insufficiency, tricuspid regurgitation, and moderate cardiomegaly. Her LVEF one year after surgery was near 65%.

### 2.5. Case 5

A 54-year-old woman with ESRD since 4 years ago, and hypertension since the age of 40. Type 2 diabetes mellitus, ischemic heart disease and ischemic cardiomyopathy. She underwent CABG two years prior to transplant. She had left ventricular ejection fractions = 15% before transplantation. She was on Atorvastatin 40 mg/daily, Amlodipine 5 mg/daily, losartan 25/daily, Asprin 80 mg/daily, Metoprolol 25 mg/BD, and Nitrocontin 2.6 mg/BD. One month later, her left ventricular ejection fractions improved to 20%. She underwent renal transplantation. Three months after surgery, her LVEF was reported as 50%.

### 2.6. Case 6

A 39-year-old woman, with poorly controlled hypertension, ESRD and heart failure, was on haemodialysis for about 18 months. Her drug history included Carvedilol 6.25/BD, Losartan 25 mg/BD, Amlodipine 10 mg, Aspirin 100mg daily and Rosuvastatin 5 mg daily. He LVEF before renal transplantation was 15%.

Echocardiography 6 months after kidney transplant revealed LVEF = 60% with normal left ventricular size, mild diastolic dysfunction, normal right ventricle (RV) size and

good systolic function, trivial mitral valve regurgitation, trivial tricuspid regurgitation and pulmonary artery pressure (PAP) = 27 mmHg).

*2.7. Case 7*

A 13-year-old boy from a remote area with a 4-year-long history of ESRD predialysis state was referred with signs and symptoms of heart failure of unknown cause. Echocardiography revealed left ventricular ejection fractions = 10%, pulmonary artery pressure = 50, moderate tricuspid regurgitation and moderate mitral regurgitation.

Echocardiography 3 months after transplantation revealed LVEF=30% - 35% and six months later, it improved to 60%, with no clinical evidence of heart failure.

Patient's EF and other cardiac clinical disorder such as trivial mitral valve regurgitation, trivial tricuspid regurgitation and pulmonary artery pressure were measured using the Transesophageal Echocardiography. Also Two measurements of systolic and diastolic blood pressures (SBP and DBP, respectively) were taken using a standardized mercury sphygmomanometer (calibrated by the Iranian Institute of Standards and Industrial Researches) on the right arm after a 15-minute rest in a sitting position; mean of the two measurements was considered as subject's blood pressure. Hemoglobin levels were measured as a part of the routine complete blood count (CBC) test for patients. Also, in this case series the patient's EF was considered as main variable. Table 1 addresses the baseline and echocardiographic characteristics for reported cases.

## 3. Discussion

This study showed significant improvements in left ventricular function after the renal transplantation in patients with ESRD and severe symptomatic heart failure. In addition, the left ventricle ejection fraction increased by 35% in average and was associated with an improvement in NYHA functional status after the renal transplantation.

Although the presence of baseline LV systolic dysfunction was associated with poorer overall long-term outcomes following kidney transplantation, improvement of LVEF $\geq$ 10 percentage points following kidney transplantation in patients with underlying LV systolic dysfunction was associated with better long-term events.

Patients with a history of long-time haemodialysis have a greatly increased adjusted incidence and prevalence rate of coronary heart disease as well as mortality after myocardial infarction compared to the general population (13). Some studies have demonstrated regression of left ventricular hypertrophy (LVH) and improvement of left ventricle function after successful renal transplantation (14).

During the last decade, there has been a steady trend of an increase in the prevalence of LVEF to < 55%, subsequent to the improvement in the patients with diabetes, kidney disease from CKD Stage 3, to the final stage. The percentage of LVEF in CKD patients is reported as 69.9 $\pm$ 10.4% in Stage 3; 68.2 $\pm$ 10.3% in Stage 4; and 67.1 $\pm$ 11.0% in Stage 5 pre-dialysis patients (all these values were statistically different). This suggests a monotone increase in the risk for CHF that corresponds to the stage of progression of CKD (15).

The hypothesis of an improvement in heart failure after kidney transplantation has been explored in small case series (16) and in a study utilizing data from the US renal data system, which included 1,369 patients with end stage renal disease (ESRD). The mechanism is most likely due to a decrease in the level of uremic toxins (3). ESRD is a complex metabolic syndrome and uraemia would affect heart function by influencing myocardial contractility and function (11). This improvement in CHF was independent of changes in volume status, hematocrit, and MAP. This suggests that volume alone does not account for changes in ejection fraction in patients with ESRD. On the other hand, in the kidney transplant patients, not only conventional factors that may have an effect on the general population, but also a number of atherogenic risk factors related to previous dialysis, abnormal renal function, and use of immunosuppressive and other drugs are frequently present and can affect the development of cardiovascular problems (17). By considering its availability and practicality, echocardiography remains an important clinical and research tool when assessing these parameters. Although, severe heart failure diagnosis made by echocardiography and patients follow-up had been complete but the results of this study should be interpreted with due consideration of its limitations, including small numbers of patients, lack of a control group, and long period of time during which patients were included. Prospective studies are needed to help to further define the details of therapy in this setting and more personalized renal transplantation protocols.

We concluded that kidney transplantation should be considered the treatment of preference for ESRD patients with systolic heart failure, because a longer period of dialysis in these patients may result in progressive and permanent myocardial dysfunction.

## Footnote

**Conflict of Interest:** None declared.

**Table 1.** Baseline Characteristics and Echocardiographic Data Before and After the Transplantation

| | | Age | Gender | Past Medical History | Haemoglobin | EF | Mitral Regurgitation | Aortic Regurgitation | Tricuspid Regurgitation | Blood Pressure |
|---|---|---|---|---|---|---|---|---|---|---|
| **Case 1** | Preop | 58 | Female | DM type 1, IHD, HTN | 70 mg/L | 15% | Moderate | Moderate | Moderate | 180/90 mmHg |
| | Postop | | | | 83 mg/L | 45% | Mild | Mild | Mild | - |
| **Case 2** | Preop | 38 | Male | Sepsis, endocarditis | 60 mg/L | 15% | Mild | Moderate | Moderate | 160/90 mmHg |
| | Postop | | | | - | 45% | Mild | Mild | Mild | - |
| **Case 3** | Preop | 30 | Female | Asthma, Seizure, Rheumatic Fever | 83 mg/L | 15% | Mild | Moderate | Mild | 120/80 mmHg |
| | Postop | | | | 87 mg/L | 40% | No MR | Mild | No TR | 120/70 mmHg |
| **Case 4** | Preop | 15 | Female | Dyspnoea, HTN | 60 mg/L | 25% | Moderate | Moderate | Moderate | 180/100 mmHg |
| | Postop | | | | - | 50% | Mild | Mild | Mild | - |
| **Case 5** | Preop | 54 | Female | Type 2 diabetes mellitus, IHD, CABG | 75 mg/L | 15% | Severe | Moderate | Mild | 130/80 mmHg |
| | Postop | | | | 80 mg /L | 50% | Mild | Mild | No | 120/80 mmHg |
| **Case 6** | Preop | 39 | Female | HTN | 60 mg/L | 15% | Moderate | Moderate | Moderate | 130/80 mmHg |
| | Postop | | | | 116 mg/L | 60% | Mild | Mild | Mild | 130/80 mmHg |
| **Case 7** | Preop | 13 | Male | Heart failure | 720 mg/L | 10% | Moderate | Moderate | Mild | 90/55 mmHg |
| | postop | | | | - | 60% | Mild | Mild | No | 100/60 mmHg |

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