Continuous renal replacement therapy versus furosemide for management of kidney impairment in heart transplant recipients with volume overload

Seyed Mohsen Mirhosseini, Mohammad Fakhriv, Shadi Asadollahi, Zargham Hossein Ahmadi, Farin Rashid Farokhi, Mohammad Reza Boloursaz, and Mohammad Reza Masjedi

OBJECTIVES: It is unknown whether continuous renal replacement therapy or furosemide therapy is superior in heart transplant recipients who are in postoperative kidney insufficiency and volume overload. This prospective non-randomized, controlled trial investigated the efficacy of the two methods after transplantation.

METHODS: We assigned heart transplant recipients 18 years of age or older who were oliguric (urine output < 400 ml/day); had volume overload and estimated glomerular filtration rate < 60 ml/min/1.73 m² of body surface area calculated with the use of the Modification of Diet in Renal Disease equation, to designed initiation of intervention. We followed 30 patients for up to 30 days. The primary outcome was estimated glomerular filtration rate status after intervention.

RESULTS: Between January 2010 and April 2012, a total of 30 adults (mean age: 37 years; 18 men and 12 women) were assessed for entry in this trial. Continuous renal replacement therapy, when compared with furosemide, was associated with a significant increase in estimated glomerular filtration rate of patients after intervention 61 ± 4.5 vs 55 ± 8.5 ml/min/1.73 m² (P = 0.02). Moreover, the mean glomerular filtration rate at discharge time for the continuous renal replacement therapy group was 72 ± 7.3 and 58 ± 7.4 ml/min/1.73 m² for the furosemide group (P < 0.001). During the follow-up period, 6 of 15 patients in the continuous renal replacement therapy group (40%) and 4 of 15 in the furosemide group (26.6%) died (P = 0.43).

CONCLUSIONS: In this study, continuous renal replacement therapy in heart transplant recipients with reduced kidney function was associated with an improvement in estimated glomerular filtration rate status in comparison with furosemide.

Keywords: Continuous renal replacement therapy · Heart transplantation · Acute kidney injury · Glomerular filtration rate

INTRODUCTION

In 1967, Christiaan Barnard performed the first heart transplantation [1]. So far, more than 100,000 heart transplantations have been reported in the International Society for Heart and Lung Transplantation (ISHLT) through 2010 [2]. Significant developments in rejection prevention, immunosuppressant agents and infection control have improved heart transplant outcomes [3]. With the advent of optimal care for patients with heart transplant, the number of critically ill patients being admitted for transplantation has increased; nonetheless, it is often correlated to impaired renal function [4].

Acute kidney injury (AKI) following cardiac surgery contributes to high mortality and morbidity rates throughout the hospitalization period as a result of poor cardiac function [5]. Many strategies are recommended to manage AKI in post-cardiac surgery settings, including the use of diuretics, fluid therapy and high perfusion pressure [6]. Furosemide is a loop diuretic and vaso-dilator that may decrease oxygen consumption in the loop of Henle by inhibiting sodium transport, thus potentially lessening ischaemic injury. By increasing urinary flow, it may also reduce intratubular obstruction and back leak of filtrate. Based on these properties, furosemide might be expected to prevent AKI. However, there are only minimal data to support its use, and
some evidence of harm from prophylactic use. Additionally, some studies proposed that furosemide might be an effective element along with other methods in the prevention of AKI through gentle and continual diuresis [7].

On the other hand, it has been declared that morbidity and mortality in AKI might be improved through continuous therapies in contrast to intermittent haemodialysis (IHD) [8]. Continuous renal replacement therapy (CRRT) is one of the successful methods which has been evolved in the previous decade. CRRT is beneficial for patients with an unsteady haemodynamic condition or multi-organ failure since this method uses continuous and gradual removal of the solute [9].

In this study, we intend to compare the efficacy of CRRT with furosemide in the management of postoperative kidney injury in heart transplant patients.

**MATERIALS AND METHODS**

**Study design**

The objective of this single-centre, non-randomized, controlled trial was to evaluate kidney-protecting strategies with furosemide or CRRT in postoperative kidney injuries of heart transplant recipients. The study was conducted in the transplant centre of Masih Daneshtari Hospital between January 2010 and April 2012.

Clinical information and outcomes were obtained 24 h before intervention and daily during the ICU stay and the hospital stay, until death or hospital discharge.

The authors designed and supervised the trial in collaboration with the staff of the National Research Institute of Tuberculosis and Lung Disease (NRITLD), Masih Daneshtari Hospital.

The entire study protocol of this trial has been reviewed and approved by the Ethics Committee of Shahid Beheshti University of Medical Science, and informed consent was obtained from all patients.

**Study population**

Of the 46 screened patients who underwent first bicaval orthotopic heart transplantation, participants who were between 18 and 80 years of age were eligible if they were oliguric (urine output <400 ml/day); showed evidences in accordance with volume overload (right atrial pressure >12 mmHg, peripheral oedema or pulmonary congestion) and postoperative kidney dysfunction.

Serum creatinine (SCr) was used to calculate eGFR based on the Modification of Diet in Renal Disease (MDRD) formula [10]. Kidney dysfunction was considered if eGFR was <60 ml/min/1.73 m² and SCr was ≥0.3 mg/dl based on risk, injury, failure, loss and end-stage kidney disease criteria [11]. Of these, 30 patients (65.2%) were eligible, and 15 each were assigned to the CRRT group and the furosemide group. In our study, random assignment to treatment condition was impractical, owing to physician's discretion based on CRRT advantage in precise volume control and imitation of the external excretory renal function in intensive care. Additional factors that influenced the non-randomized design and assigning of patients to the CRRT group were critically severe kidney impairment, haemodynamic instability in some post-transplant patients and availability of the CRRT machine.

Administration of loop diuretics is a commonly used method in the postoperative period and in the early management of acute renal dysfunction; at least in selected populations of patients such as patients with volume overload and/or oliguria [12]. Additionally, continuous infusions vs high boluses of loop diuretics have been revealed to be potentially superior regarding effectiveness and toxicity [6]. Hence, this study used furosemide as the second study arm to be compared with CRRT in the management of AKI after heart transplantation.

The study population consisted of 18 men (60%) and 12 women (40%), with a mean age of 37 ± 12.4 years and body mass index (BMI) of 23 ± 4 kg/m². Further demographic and clinical characteristics are shown in Table 1.

The exclusion criteria were pre-existing clinical and/or laboratory evidence of acute or chronic renal failure at the time of recruitment, multiorgan transplantation, BMI over 35 kg/m² and patients who were on furosemide therapy before recruitment.

Of the 16 patients who were not enrolled in this study, 6 were excluded from participation because of exclusion criteria, 5 declined to participate and 5 were omitted owing to their physicians’ decision.

**Intervention**

Patients were categorized into two treatment groups, which were stratified by demographic characteristics and associated co-morbid features (diabetes mellitus, myocardial infarction, hypertension, stroke and arteriosclerotic vascular disease). Patients who were assigned to furosemide therapy received sustained infusions of furosemide (20 mg/h). Patients in this group were omitted for the final analyses if their clinical setting (hypotension, electrolyte imbalance etc.) required cessation or an increase in predefined furosemide dosage. The CRRT group underwent continuous venovenous haemofiltration modality. The vascular access was established by percutaneous placement of a double lumen catheter into either the subclavian, internal jugular or femoral veins. The procedure was done through a high-flux membrane, and its settings, including the flow rate of the replacement fluid (1–2 l/h) and blood stream (50–200 ml/min), were established according to patients’ states by the nephrologists’ decision. Filters were replaced only when they were occluded and did not function properly. The CRRT procedure was conducted by a renal-care specialist team consisting of a nephrologist, dialysis nurses and certified technicians.

Medical measures for correction of fluid, electrolyte and acid–base disorders were instituted in all patients routinely. Postoperative care of the patients was followed according to the established standards of care of heart transplant surgical patients.

Based on ISHLT guidelines for the care of heart transplant recipients [13], continuous infusion of inotropic drugs with the minimum effective dose was utilized to maintain haemodynamic stability and adequate tissue perfusion without causing adverse effects postoperatively. Once stabilized, the patients were rapidly weaned off the inotropes. The following therapies were applied: isoproterenol 1–10 µg/min, dobutamine 1–10 µg/kg/min, dopamine 1–10 µg/kg/min, milrinone 0.375–0.75 µg/kg/min and α-adrenergic agonists including norepinephrine or epinephrine (1–10 µg/min) to maintain adequate mean arterial pressure.

The initial dosage of tacrolimus was 0.05 mg/kg in two divided amounts to maintain a trough blood level around 10–15 ng/ml.
within the first 6 months post-transplantation and 3–5 ng/ml thereafter.

### Trial outcomes

The primary outcome was eGFR changes due to its precision in estimating and detecting renal function failure. It has long been well known that SCr, as a measure of kidney function, is insufficient by itself for the early detection of chronic disease. The GFR calculated via Cockcroft–Gault equation as the conventional measure of renal function appears to be no better than SCr for the prediction of kidney failure. The MDRD equation is considered to afford adequate estimates of GFR for most kidney patients as in clinical practice and research; both SCr and MDRD eGFR continue to be used for evaluation of heart transplant patients. Indeed, MDRD eGFR is a simple function of SCr, age, sex and race. This estimation in patients receiving heart transplantation has been assessed in several studies, and the accuracy of this method has been confirmed for such populations [14]. However, the MDRD formula accuracy is far from perfect; nonetheless, this formula is thus certainly the best among other creatinine-based formulae to estimate the GFR in heart transplant patients with renal failure. Thus, we calculated the eGFR based on four-variable MDRD equation

\[
186 \times \text{SCr}^{-1.154} \times \text{age}^{0.203} \times \text{sex} \times \text{race}
\]

where SCr is in mg/dl, Age is in year, sex is 0.742 if female and 1 if male, and race is 1.21 if black and 1 otherwise.

Secondary outcomes of the present study were early mortality rate at 30 days after initiation of intervention; ultimate eGFR within 30 days; and time to discharge (hospital admission to discharge time). Patients’ early mortality was reported by hospital discharge records and causes of death were classified as cardiac (sudden cardiac arrest, myocardial infarction), sepsis and coagulopathies.

### Statistical analysis

We used a time-to-event analysis to compare the proportion of patients with primary and secondary outcomes in the two groups. Summaries of continuous variables are presented as means ±SD for normally distributed data; categorical variables are presented as frequencies (percentages). Continuous variables were compared with the use of Student’s t-test or the Mann-
Whitney U-test (for non-parametric data), and categorical data with the use of chi-square tests. All patients were followed until death or the end of the trial. The statistical analyses were performed with the use of IBM SPSS software, version 20.0 (SPSS, Inc., Chicago, IL, USA). All statistical tests were two tailed, a P-value <0.05 was considered statistically significant.

RESULTS

Study population

Of the 30 patients who were enrolled, 15 were assigned to CRRT and 15 to furosemide therapy between January 2010 and April 2012 (Fig. 1). The study groups were statistically similar with respect to demographic characteristics, prevalence of comorbidities, operative characteristics and estimated GFR before intervention. Baseline and clinical parameters are summarized in Table 1.

The two groups did not differ significantly with respect to pharmacological interventions, which were prescribed according to the standard post-transplant protocol of the centre during the trial period (Table 2).

Intervention

At the time of the initiation of the therapies, the mean eGFR, as calculated with the use of the MDRD equation, was 50 ± 7.2 ml/min/1.73 m² for the CRRT group, and 52 ± 7.0 ml/min/1.73 m² for the furosemide group (mean difference: −2.3 ml/min/1.73 m², 95% confidence interval [CI]: −7.6 to 3, P = 0.4). Among the patients who were assigned to the CRRT group, 40% had eGFR of <50 ml/min/1.73 m². This proportion was 26.6% for the furosemide group (P = 0.4).

Primary outcomes

After a 37 ± 22.5 h period of CRRT and 48 h of furosemide therapy, patients had a mean eGFR of 61 ± 4.5 and 55 ± 8.5 ml/min/1.73 m² for each group, respectively (mean difference: 5.7 ml/min/1.73 m², 95% confidence interval [CI]: 0.6–10.8, P = 0.02). Although the CRRT duration is individualized for each patient according to his/her clinical setting, our analysis demonstrated no statistically significant difference between the patients in this regard (P > 0.05). CRRT improved the eGFR, 50 ± 7.2 ml/min/1.73 m² before vs 61 ± 4.5 ml/min/1.73 m² after (P = 0.02).

Secondary outcomes

Mean eGFR at discharge time for the CRRT group demonstrated a significant improvement, when compared with the furosemide group, 72 ± 7.3 vs 58 ± 7.4 (mean difference: 13.4 ml/min/1.73 m², 95% confidence interval [CI]: 7.9–18.9, P < 0.001) (Table 2 and Fig. 2).

No significant difference was observed between the two groups in early mortality in the first 30 days as its rate was 40% in the CRRT group and showed to be 26.6% (P = 0.43) in those who received furosemide. The cause of death was similar for the patients in both groups (Table 3).

Table 2: Properties of drugs used post-heart transplant

<table>
<thead>
<tr>
<th>Drugs</th>
<th>CRRT group (n = 15)</th>
<th>Furosemide group (n = 15)</th>
<th>Total (n = 30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotic medications, number (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meropeneme</td>
<td>13 (86.6)</td>
<td>12 (80.0)</td>
<td>28 (93.3)</td>
<td>0.6</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>14 (93.3)</td>
<td>12 (80.0)</td>
<td>25 (83.3)</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Antifungal medications, number (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nystatine</td>
<td>15 (100)</td>
<td>15 (100)</td>
<td>30 (100)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Antiviral medications, number (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ganciclovir</td>
<td>11 (73.3)</td>
<td>14 (93.3)</td>
<td>25 (83.3)</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>Transplant medications, number (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anthymocyte globulin</td>
<td>15 (100)</td>
<td>15 (100)</td>
<td>30 (100)</td>
<td>1</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>15 (100)</td>
<td>15 (100)</td>
<td>30 (100)</td>
<td>1</td>
</tr>
<tr>
<td>Inotropes, number (%)</td>
<td>15 (100)</td>
<td>15 (100)</td>
<td>30 (100)</td>
<td>1</td>
</tr>
<tr>
<td>5% dextrose in water (500 ml/m²) plus KCl (10 meq/m²)</td>
<td>15 (100)</td>
<td>15 (100)</td>
<td>30 (100)</td>
<td>1</td>
</tr>
</tbody>
</table>

CRRT: continuous renal replacement therapy; KCl: potassium chloride
Based on International Society of Heart and Lung Transplantation grading (>3A), no biopsy-proven acute rejection was observed during the follow-up time.

**DISCUSSION**

This prospective, non-randomized, controlled trial was designed to compare the efficacy of CRRT and furosemide in the preservation of renal function in patients with post-heart transplantation with volume overload. To the best of our knowledge, there are no reports to support any potent treatment recommendations regarding the comparison of CRRT with furosemide in these patients. To achieve this goal, the two study groups were matched for sex, age and baseline aetiology for heart transplantation to avoid potential confounding factors. Renal function was evaluated by means of the MDRD study equation, which has been validated as an accurate indicator [10].

The status of renal function prior to heart transplantation has variably been suggested to predict the need for postoperative AKI requiring renal replacement therapy. A retrospective review of 622 adults who underwent 627 consecutive orthotopic heart transplants between 1994 and 2001 revealed that of 531 patients with a pretransplant creatinine clearance (CrCl) of >40 ml/min, 9% (49/531) required postoperative renal replacement therapy (lHD, CRRT or peritoneal dialysis) compared with 32% (31/96) of those with CrCl of <40 ml/min (P < 0.001) [15]. Similarly, in a small retrospective study of 56 recipients of cardiac transplant, operative creatinine-based approximation of GFR has been shown to be an important predictor of postoperative kidney injury requiring CRRT (median CrCl for those who required CRRT vs those who did not require CRRT was 44 vs 59 ml/min; P = 0.04) [16].

Moreover, the present study showed the rate of acute kidney failure in the postoperative period after heart transplantation to be high (65.2%). AKI following orthotopic heart transplant has also been reported to appear at variable rates of incidence [17]. In the Escoresca Ortega et al. [18] observational study, a high incidence of AKI (70.4%) was found in the postoperative period among 54 patients who underwent heart transplantation. However, when followed over time, the rate of kidney failure among surviving patients was significantly reduced.

Our results revealed a significant difference between CRRT and furosemide therapy in controlling patients’ renal failure. There was a consistent and considerable advantage of CRRT over furosemide with respect to the improvement of eGFR status throughout the follow-up period. This result is in conformity with the Stevens et al. [16] study, which has described the management strategies regarding immunosuppressive therapy and the short-term prognosis in heart transplant recipients. CrCl has been used as the main predictor of renal failure and the patients who underwent CRRT had lower first 2-week postoperative CrCl than those who did not.

![Figure 2: Bar plots comparing mean estimated glomerular filtration rate (eGFR) by Modification of Diet in Renal Disease (MDRD) formula at the time of post intervention and discharge in patients were assigned to CRRT and furosemide group.](https://academic.oup.com/icvts/article-abstract/16/3/314/683331)

**Table 3: Primary and secondary outcomes**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>CRRT group (n = 15)</th>
<th>Furosemide group (n = 15)</th>
<th>Total (n = 30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR after intervention (ml/min/1.73 m²)</td>
<td>61 ± 4.5</td>
<td>55.7 ± 8.5</td>
<td>58 ± 7.3</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR at the time of discharge (ml/min/1.73 m²)</td>
<td>72 ± 7.3</td>
<td>58 ± 7.4</td>
<td>65 ± 9.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Early mortality, number (%)</td>
<td>6 (40.0)</td>
<td>4 (26.6)</td>
<td>10 (33.3)</td>
<td>0.43</td>
</tr>
<tr>
<td>Coagulopathies</td>
<td>3 (20)</td>
<td>1 (6.6)</td>
<td>4 (13.3)</td>
<td>0.2</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1 (6.6)</td>
<td>1 (6.6)</td>
<td>2 (6.6)</td>
<td>1</td>
</tr>
<tr>
<td>Sudden cardiac arrest</td>
<td>1 (6.6)</td>
<td>2 (13.3)</td>
<td>3 (10.0)</td>
<td>0.5</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 (13.3)</td>
<td>0 (0.0)</td>
<td>2 (6.6)</td>
<td>0.1</td>
</tr>
<tr>
<td>Alive, number (%)</td>
<td>9 (60.0)</td>
<td>11 (73.4)</td>
<td>20 (66.7)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

Plus–minus values are means ± SD.

CRRT: continuous renal replacement therapy; eGFR: estimated glomerular filtration rate.
Most previous studies did not compare the efficacy of CRRT with another treatment modality in the management of AKI. This study proposed furosemide as the control group. It has been stated that furosemide might be beneficial for GFR preservation in patients at different clinical settings. In one study, the trial of furosemide on seven healthy subjects who were on salt-restricted diets demonstrated an increase in the calculated GFR [19]. In another study, a significant decline in CrCl was detected after intravenous furosemide administration to edematous patients with symptomatic heart failure [20]. As there are inconsistencies with regard to the use of furosemide in patients with AKI, our study recruited patients with concurrent AKI and volume overload to ensure the benefit of the patients in the control group.

In the current study, high dose of furosemide were administered through intravenous infusions (20 mg/h), although it was not supposed to be associated with considerable side effects on renal function and other organs. This presumption is in agreement with the results of Cantarovich et al’s controlled trial [21] that enrolled 338 consecutive participants with acute renal failure. They analysed the effect of furosemide on the survival and renal recovery of 166 patients who received 25 mg/kg/day intravenous treatment or 35 mg/kg/day orally. Consequently, high-dose furosemide does not have an impact on the study outcomes, and no result in terms of side effects was reported. Nevertheless, furosemide administration may require caution in patients with AKI.

In consideration of early mortality rate as the secondary outcome, there was no significant difference between the CRRT and furosemide groups; however, a high incidence of mortality outcome in the CRRT group was noted. Potential factors have been suggested to play a contributory role in postoperative renal failure, which was significantly greater in this group. Intraoperative risk factors including cardiopulmonary bypass time, number of blood transfusion requirement [5], higher frequency of established atherosclerotic vascular disease [17], postoperative acute tubular necrosis (ATN) [22] and immunosuppressive medication have been shown to be important predictors of acute postoperative renal failure. Therefore, it is conceivable that patients were selectively assigned to mechanical kidney support based on severity of kidney impairment and also, availability of CRRT equipment, discretion of nephrologist and availability of trained nursing staff. Furthermore, the superiority of CRRT in preventing impending renal injury includes continuous volume control and avoidance of intravascular volume reduction and hypotension throughout the CRRT period, which may prevent associated renal injury reported during standard IHD, and has influence on physician’s judgment.

The rate of death has been assessed in several studies that compared the CRRT method with IHD.

A meta-analysis of 13 studies [23] was conducted by Kellum et al. between 1977 and 98, which included 1400 patients treated with IHD or CRRT. They reported that in-hospital mortality did not differ in patients undergoing either of the two methods; however, after adjusting for study quality and severity of illness, mortality was lower in patients undergoing CRRT.

In our investigation, Tacrolimus, a calcineurin inhibitor, was applied as an immunosuppressive agent for the prevention of cardiac allograft rejection in all patients. Tacrolimus was associated with lower incidence of renal failure and improving graft survival than cyclosporin-based immunosuppression in heart transplant patients [24]. Hence, the tacrolimus tolerability profile, efficacy and safety of the present study outcomes support a preference for using it instead of conventional treatments in our study groups.

In this study, we also used the discharge eGFR in defining renal function improvement, owing to the commonly observed patient instability of the primary days with variations in support with inotropics and immunosuppressive drugs. Consequently, we observed a significant difference between both groups regarding eGFR within 30 days.

In summary, the GFR status through several methods of calculation for patients with a variety of clinical situations was evaluated, and to the best of our knowledge, this is the first study comparing CRRT and furosemide in patients with post-heart transplantation.

However, our study has certain limitations. The single-centre design and non-randomized feature of the study might have impaired our conclusions. Additionally, our sample size was small and the follow-up period was not prolonged enough to achieve any definitive conclusions on the survival and prevalence of recurring renal failure in heart transplant recipients. Furthermore, we used the MDRD equation to evaluate the renal function of our study groups, which is the recommended method by the National Kidney Foundation, but this method has some limitations [25]. It is based on the Scr concentration, which may differ in relation to the patient’s haemodynamic state or be affected by the patients’ medication. It also uses the patients’ weight, which in the transplant population rises gradually post-transplantation, possibly with a lower muscle mass-to-fat ratio as a result of steroid therapy. Overall, creatinine and eGFR are only surrogate markers of kidney function, and these data must be interpreted with caution. This may principally be true for critically ill patients. Furosemide was used as the sole loop diuretic, so we cannot make any decision on the relative effectiveness or disadvantage of other loop diuretics. The exact role of renal failure in contributing to death and co-existing interfacing causes of death was not analysed.

This controlled trial of heart transplant recipients with impending renal failure studied the outcome in terms of eGFR status. Postoperative renal failure is a significant complication in heart transplant recipients. Renal failure secondary to heart failure and acute renal failure requiring renal replacement therapy should be proactively and aggressively treated, because early therapy is associated with better renal function recovery within the first-year post-heart transplantation.

In conclusion, we found that patients who underwent CRRT had more improved renal recovery and clinical outcomes than those on furosemide therapy. Much work and multi-centric RCTs with larger sample size will be required to compare the efficacy of either CRRT or IHD vs other diuretics in the management of these patients.

ACKNOWLEDGEMENTS

We acknowledge the members of the renal care team; clinicians and nursing staff at the Masih Daneshvari Hospital, Tehran, Iran, for their valuable contribution and dedication to this project which has set the standard for CRRT care and set the stage for future fundamental trials.
**FUNDING**

This work was supported by the Transplantation Department of National Research Institute of Tuberculosis and Lung Diseases.

**Conflict of interest:** none declared.

**REFERENCES**


