# Impact of Preoperative Renal Replacement Therapy in Clinical Outcome of Heart Transplant Patients

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# Abstract

Although renal dysfunction is considered as a relative contraindication for heart transplantation (HTx), in real world, due to co-existing intrinsic renal dysfunction and/or cardiorenal syndrome, many patients with advanced heart failure (HF) experience worsening of renal function and some even require renal replacement therapy (RRT) by the time they undergo HTx We aimed to investigate the prognosis and clinical outcomes of heart transplant (HTx) patients who required renal replacement therapy (RRT) during the perioperative period.The Korean Organ Transplant Registry (KOTRY) is a nationwide organ transplant registry in Korea. A total of 501 HTx patients had been prospectively enrolled in the KOTRY registry during 2014-2018. Among the 501 patients, 13 underwent combined heart and kidney transplantation (HKTx). Patients who underwent isolated HTx were grouped according to their pre and postoperative RRT status. The primary outcome was progression to dialysis-dependent end-stage renal disease (ESRD) after HTx. The secondary outcome was all-cause mortality after HTx. The median follow-up was 22 months (9–39 months). Patients who needed preoperative RRT but free from postoperative RRT showed comparable overall survival and renal outcome to patients who were free from both pre and postoperative RRT. From multivariable analysis, preoperative RRT was not associated with progression to ESRD or all-cause mortality after HTx, however, postoperative RRT was a significant predictor for both progression to ESRD and all-cause mortality after HTx. Preoperative creatinine or estimated glomerular filtration rate (eGFR) were not predictive of progression to ESRD after HTx. The present analysis suggests that preoperative RRT requirement does not indicate an irreversible renal dysfunction in patients waiting for HTx. The survival and renal outcome was comparable to those who did not need perioperative RRT when renal function recovered after HTx. However, postoperative RRT was associated with progression to ESRD and mortality after HTx.


# Introduction

Renal dysfunction is often associated with advanced heart failure (HF) in patients listed for heart transplantation (HTx). The 2016 International Society of Heart and Lung Transplantation recommended that irreversible renal dysfunction (eGFR< 40mL/min/1.73m$^2$) is a relative contraindication for HTx alone.[1] A previous study using United Network of Organ Sharing (UNOS) data showed that pre-HTx eGFR was independently associated with the mortality and ESRD after HTx.[2]

In real world, due to co-existing intrinsic renal dysfunction and/or cardiorenal syndrome, many patients with advanced HF experience worsening of renal function and some even require renal replacement therapy (RRT) by the time they undergo HTx. Clinically, it is difficult to determine whether declining of renal function is going to be irreversible due to intrinsic renal dysfunction. In some patients, worsening of renal function which even result in temporary RRT before HTx may recover with improved cardiac function after HTx. However, there is no single laboratory test to determine irreversibility of renal function. A study from a single center reported a different result than previous UNOS data showing that pre-

transplantation glomerular filtration rates (GFR) was not predictive of mortality or ESRD after HTx.[3] This is because low GFR does not mean irreversible intrinsic renal dysfunction.

Although considered as a relative contraindication, in a real world, some advanced HF listed for HTx experience severe deterioration of renal function and even require preoperative RRT before HTx. The aim of this study was to analyze the prognostic significance of preoperative RRT in HTx patients in terms of the prevalence of future dialysis-dependent ESRD and overall mortality after HTx.

# Results

### Baseline characteristics

The median follow-up was 22 months (9–39 months). Among the 501 patients, 13 underwent combined HKTx; all of these patients were on dialysis preoperatively. Among the 488 patients who underwent isolated HTx, 74 were on either continuous renal replacement therapy (CRRT) (n=62) or conventional hemodialysis (HD) (n=12) before HTx (groups 2 and 4).

Table 1 shows the baseline characteristics of patients who underwent isolated HTx in relation to perioperative RRT status. Patients from group 1 had longest waiting list duration, while patients in group 2 and 4 had relatively short waiting list duration, suggesting patients in group 2 and 4 are likely to be more rapidly decompensated HF patients. Group 4 included more patients with ischemic heart disease and fewer patients with idiopathic dilated CMP than did the other groups. Patients who needed preoperative RRT (groups 2 and 4) were more likely to have diabetes mellitus (DM) compared to patients in the other groups, although this difference was not statistically significant. Patients who needed preoperative RRT (groups 2 and 4) were also more likely to need pre-HTx mechanical cardiac support ($p < 0.001$) and pre-HTx mechanical ventilator ($p < 0.001$) than patients in the other groups. Mean preoperative BUN and creatinine values were significantly higher in group 4 than in the other groups.

### Clinical outcome

Postoperative clinical characteristics of 4 groups are described in supplementary table 1. Significantly more patients from group 4 experienced primary graft failure. Right ventricular systolic pressure were higher in patients who were supported with postoperative RRT (group 3 and 4) at 1 month after HTx.

After HTx, more patients in group 4 had dialysis-dependent ESRD ($p < 0.001$) than patients in the other groups (Figure 1). During the first 6 months of follow-up, most patients from group 4 developed dialysis-dependent ESRD. After the first 6 months, patient status in relation to dialysis-dependent ESRD stabilized. Among the patients who needed early post-HTx RRT (groups 2 and 4), those from group 2 were less likely to have dialysis-dependent ESRD (11.8%) than those from group 4 (36.8%, $p = 0.013$). A summary of renal outcome is described in supplementary Figure 1.

Table 2 shows the renal function of all patients who underwent isolated HTx at 6 months and 12 months post-HTx. BUN and creatinine levels were significantly higher in group 4 than in the other groups at both 6 months and 12 months post-HTx. None of patients who became dialysis dependent ESRD recovered to be dialysis free.

Table 3 shows univariate and multivariable analyses for progression to dialysis dependent ESRD after HTx. From multivariable analysis, insulin dependent DM and postoperative RRT were significantly associated with progression to ESRD after HTx. Preoperative RRT did not remain to be statistically significant after adjustment of other variables. Supplement table 2 show subgroup analysis to predict progression to ESRD after HTx according to preoperative RRT status. The significant clinical predictors for progression to ESRD differed between two subgroups. In a preoperative RRT (-) subgroup, the needs for preopertive mechanical ventilation, preoperative mechanical cardiac support, baseline eGFR, baseline creatinine, postoperative RRT, and primary graft failure were significant clinical factors in univariate analysis. However, in a preoperative RRT (+) subgroup, insulin dependent DM and early postoperative RRT were significant clinical predictors.

Univariate analysis showed that insulin-dependent DM, preoperative mechanical ventilation, preoperative mechanical cardiac support, preoperative RRT, preoperative eGFR, preoperative creatinine, cardiopulmonary bypass time, early postoperative RRT and primary graft failure were associated with post-HTx ESRD. However, after adjusting for confounding variables, insulin-dependent DM, and early postoperative RRT were the only variables that were independently associated with post-HTx dialysis-dependent ESRD.

### All-cause mortality after HTx

After HTx, patients in group 4 had significantly higher mortality than patients in the other groups (4-year survival rate = 51.9%) (Figure 2). Patients who underwent combined HKTx showed comparable survival (4-year survival rate = 92.3%) to patients in group 1 (4-year survival rate = 90.3%). Patients in group 2 also showed comparable survival to those in group 1 (4-year survival rate =: 94.1%). Univariate analysis revealed that preoperative DM, preoperative mechanical ventilation, preoperative mechanical cardiac support, preoperative RRT, and early postoperative RRT were significant independent predictors of all-cause post-HTx mortality (Table 3). However, preoperative eGFR and preoperative creatinine levels were not associated with all-cause mortality after HTx (Table 3). In multivariate analysis, preoperative DM and early postoperative RRT were the only independent predictors of all-cause mortality after HTx.

Table 4 summarizes the univariate and multivariate analyses for all-cause mortality after HTx. From multivariable analysis, postoperative RRT and primary graft failure the significant predictors of all-cause mortality after HTx. Supplement table 3 shows subgroup analysis according to preoperative RRT status. In preoperative RRT (-) group, from univariable analysis, early postoperative RRT, ESRD progression after HTx, and primary graft failure were statistically significant clinical predictors of all-cause mortality after HTx. From multivariate analysis, early postoperative RRT was the only significant clinical factor. In

preoperative RRT (+) group, early postoperative RRT and primary graft failure were significant predictors for mortality after HTx from multivariate analysis.

# Discussion

The main finding of this study is that preoperative RRT was not associated with progression to ESRD or all-cause mortality after HTx. However, requirement of post RRT was a significant predictor for progression to ESRD and all-cause mortality after HTx. Patients who required preoperative RRT but were free from postoperative dialysis, showed a comparable prognosis to patients who did not require pre- or postoperative RRT. Perioperative creatinine or eGFR were not predictive of progression to ESRD and all-cause mortality after HTx.

Current ISHLT guidelines establish that GFR < 40ml/min/1.73m$^2$ is a relative contraindication for HTx. A previous study on the prognostic value of perioperative renal function in HTx have produced conflicting results.[3] Preoperative measured GFR was not predictive of mortality or ESRD after HTx. This is because there is no single laboratory parameter can determine irreversibility of renal dysfunction. Our results showed that in patients who needed preoperative RRT, if renal function were recovered as a result of improved cardiac function after HTx, preoperative renal function was not predictive of mortality or renal outcome after HTx.

In a real world practice, it is very difficult to specify the etiology of renal dysfunction in advanced heart failure patients with deteriorating renal function. Not a small number of patients experience deterioration of renal function secondary to impaired to cardiac function while waiting for HTx. Our data suggest that postoperative RRT is a significant predictors for all-cause mortality and progression after HTx, while preoperative creatinine, eGFR, or RRT did not show any significant association. But clinicians need to make decisions about proceeding to HTx based on preoperative data. It would be very informative if we could distinguish group 2 patients (preoperative RRT (+)/postoperative RRT (-)) from group 4 patients (preoperative RRT (+)/postoperative RRT(+)) with preoperative clinical characteristics. Our results showed, however, baseline characteristics of group 2 and 4 patients were similar, except higher incidence of idiopathic dilated cardiomyopathy in group 2 compared to group 4.

The 3-month mortality rate on the transplant waiting list for advanced HF patients who are dialysis dependent is 21%, which is three times higher than the rate for non-dialysis dependent patients.[4] If physicians could determine that accompanied dialysis dependent renal dysfunction is irreversible, the best way to improve survival would be combine HKTx.[5,6] However, it is worth noting that the overall survival rate and renal outcome in group 2 was comparable to those who underwent combined HKTx. This finding suggest that in group 2, compromised renal function which led to RRT, was largely due to hemodynamic consequences of HF, so-called cardiorenal syndrome, which was reversible with HTx. In clinical practice, it is very difficult to differentiate the main cause of renal dysfunction and predict reversibility of renal dysfunction. Therefore, physician should be very careful when making decisions regarding combined HKTx, because although only a limited number, some patients show renal recovery

with HTx, even they were on preoperative RRT. Postoperative RRT was a significant predictor of poor survival and renal outcome after HTx. In patients who needed postoperative RRT, other interventions, such as delayed kidney transplantation may be considered to improve outcome.

This study had some limitations. We used estimated GFR, rather than measured GFR. The exact etiology of renal dysfunction or ESRD, detailed doses of preoperative inotropic drugs, or other markers of end-organ damages, such as lactate, were not available. In addition, exact duration of preoperative were not available. However, generally advanced HF patients who are on chronic dialysis (> 3 months) are listed for combined HKTx and in patients who underwent isolated HTx, most of patients who needed preoperative RRT were on CRRT (83%). Therefore, in patients who underwent isolated HTx, most of RRT were likely not chronic RRT. Although this is multi-center study, the follow-up period was relatively short. Because a relatively small number of patients finished more than 36 month follow up in group 2 and 4, this could infer a survival bias. In our cohort, high risk patients who needed preoperative ECMO or mechanical ventilators are included. These patients may not be considered eligible for HTx in other centers. Despite these limitations, there is few data describing clinical outcome of HTx patients who needed perioperative RRT. Our study is meaningful because our data show clinical outcome of HTx patients who needed perioperative RRT, who were not often represented in previous data. An important aspect of our study is that this study described a multi-center, nationwide cohort of HTx patients without selection bias that reflects the reality of clinical practice.

# Conclusion

Requirement of preoperative RRT was not associated with all-cause mortality or progression to ESRD after HTx. Patients who were supported with preoperative RRT but free of postoperative dialysis showed comparable survival rates to patients who did not require perioperative RRT. However, postoperative RRT was a significant predictor of progression to ESRD and all-cause mortality after HTx. Preoperative creatinine, eGFR, or RRT status were not associated with post-HTx renal and clinical outcome in preoperative RRT group. The present analysis showed that preoperative creatinine, eGFR or RRT requirement are not indicative of an irreversible renal dysfunction in patients waiting for HTx. Future studies are needed to determine how to predict reversibility of renal dysfunction in patients with advanced HF waiting for HTx.

# Methods

### Study design and population

The Korean Organ Transplant Registry (KOTRY) is a web-based, nationwide, organ transplant registry in Korea that was established in 2009.[7,8] The KOTRY consists of 59 solid organ transplantation centers, coordinated by medical research coordinating center, which validate the data quality and regular surveillance of the data collecting process with support from Korean National Research Institute of Health.[9] For HTx, data were collected from 4 nationally representative hospitals. Each participating

centers acquired the approval from their institutional ethic review board for the study protocol and prospective acquisition of patient data (Institutional review board of Samsung Medical Center, Yonsei University College of Medicine, Seoul National University College of Medicine, Asan Medical Center, and Seoul National University Bundang Hospital). HTx patients have been prospectively enrolled in the KOTRY registry since 2014. The registry includes baseline demographic data of patients, including risk factors, etiology of HF, echocardiographic data, laboratory results, and medications, as well as follow-up data, including comorbidities, rejections, hospitalizations, and mortality. Longitudinal follow-up data including posttransplant laboratory results, comorbidities, and mortalities were obtained. Follow-up records were tracked up to the patients' deaths. To minimize follow-up loss and for the quality of longitudinal data collection, posttransplantation comorbidity and mortality data is collected on regular annual interval with periodic feedback on each center's data transfer quality. All methods were carried out in accordance with relevant guidelines and regulations. Informed consent was obtained from all patients and from legally authorized representatives/next of kin for dead patients.

Between January 2014 and December 2018, a total of 501 HTx patients were registered. Among the 501 patients, 13 underwent combined HKTx. All patients were followed up until death and last follow up date was June 2019. The remaining patients were grouped according to pre- and post-HTx renal function, as follows: group 1, patients with pre- and post-renal eGFR > 30 ml/min/1.73m$^2$ who did not require perioperative RRT; group 2, patients who required preoperative RRT but not postoperative RRT; group 3, patients who required postoperative RRT but not preoperative RRT; and group 4, patients who required both pre- and postoperative RRT.

### Renal function estimation

Index creatinine was used to calculate the eGFR by using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[10] Creatinine and blood urea nitrogen (BUN) were measured preoperatively and at 1 month, 6 months, 1 year, and 2 years after HTx. Preoperative BUN, creatinine, and eGFR were assessed a day before HTx.

### Definition and outcomes

Perioperative RRT was defined as a need for dialysis (continuous renal replacement therapy [CRRT] or conventional hemodialysis [HD]). RRT was initiated on the physician's decision when transplanted patients experienced oliguria (≤ 0.5 mL/kg/hr), refractory fluid overload, severe metabolic acidosis (pH < 7.1), or symptoms/signs of uremia. Primary graft dysfunction after HTx was defined as the use of mechanical support within 24 hours after the surgery. The primary outcome was progression to dialysis-dependent end-stage renal disease (ESRD) after 3 month post-HTx. The secondary outcome was all-cause mortality after HTx.

### Statistical analysis

Continuous data were expressed as mean ± standard deviation, and categorical variables were expressed as absolute number (percent). Differences in continuous variables between groups were analyzed with Student *t*-tests and Mann-Whitney tests. Differences in categorical values were assessed with Fisher's exact tests. The proportion of patients who did not develop post-HTx ESRD and posttransplant survival rates were analyzed with the Kaplan-Meier method. Multivariate Cox regression analysis was used to identify independent prognostic factors for all-cause mortality.

All analyses were performed with IBM SPSS Statistics version 25 (SPSS Inc., Chicago, IL, USA). Two-tailed $P$ values < 0.05 were considered significant.

# Declarations

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### Contributions

J.O.C, Y.H.C, K.S, J.O, H.J.C, S.H.J, H.Y.L, J.J.P, D.J.C, S.M.K, J.J. K and E.S.J coordinated the collection of multi-center data. J.O.C participated in conceptualization and editing the manuscript. D.K participated in data analysis and writing manuscript. All authors reviewed the manuscript.

### Ethics declarations

The authors declare no competing interests.

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# Tables

**Table 1. Pre and postoperative characteristics of patients who underwent isolated HTx according to periop RRT support.**

| n=488 | Group 1 (n=361) | Group 2 (n=17) | Group 3 (n=53) | Group 4 (n=57) | P |
|---|---|---|---|---|---|
| | PreRRT (-) PostRRT (-) | PreRRT (+) PostRRT (-) | PreRRT (-) PostRRT (+) | PreRRT(+) PostRRT(+) | |
| Age, year | 55 (44-62) | 56 (49-65) | 53 (40-60) | 54 (46-61) | 0.283 |
| Male, n(%) | 247 (67.9) | 40 (74.1) | 19 (79.2) | 43(72.9) | 0.448 |
| Height | 167 (150-171) | 167 (163-176) | 168 (160-172) | 168 (160-172) | 0.738 |
| Weight | 61.7 (53.8-68.3) | 62.9 (55.1-70.0) | 61.1(53.7-70.0) | 63.4 (55.0-76.5) | 0.674 |
| Body mass index | 22.2 (20.0-24.5) | 22.1 (19.8-24.3) | 23.1(20.3-24.5) | 23.5 (19.4-25.8) | 0.649 |
| ***Etiology of Cardiomyopathy*** | | | | | |
| Ischemic | 65 (18.0) | 2 (11.8) | 10 (18.9) | 19 (33.3) | 0.045 |
| Idiopathic dilated | 205 (56.8) | 10 (58.8) | 27 (50.9) | 21(36.8) | 0.041 |
| Hypertrophic | 24 (6.6) | 0 (0) | 5 (9.4) | 0 (0) | 0.104 |
| Valvular heart disease | 16 (4.4) | 0 (0) | 2(3.8) | (1.8) | 0.644 |
| ***Comorbidities*** | | | | | |
| Hypertension | 107 (29.6) | 4 (2.7) | 16 (30.2) | 21 (36.8) | 0.660 |
| Diabetes mellitus | 95 (26.3) | 6 (35.3) | 15 (28.3) | 22 (38.6) | 0.078 |
| Insulin requiring diabetes mellitus | 20 (5.5) | 2 (11.8) | 5 (9.4) | 7 (12.3) | 0.194 |
| Preoperative echocardiography | | | | | |
| LV EF, % | 23.5 (18.0-30.0) | 24.5(18.3-31.7) | 21.1 (18.0-32.0) | 19.5 (15.0-26.0) | 0.922 |
| LV EDD, mm | 58 (48-67) | 64 (54-71) | 67 (49.6-76.1) | 61.6 (52.0-73) | 0.586 |
| LA volume index, ml/m$^2$ | 72 (53-95) | 61 (50-76) | 77.0 (58.5-94.5) | 67.0 (41.0-83.0) | 0.586 |
| Septal E/e' | 18.3 (12.8-24.2) | 23.2 (12.6-34.4) | 17.8 (14.9-23.0) | 20.5 (16.6-29.3) | 0.322 |
| RVSP | 39 (27-51) | 46 (33-56) | 47 (34.0-63) | 44.0 (29.0-55.0) | 0.015 |

| | | | | | |
|---|---|---|---|---|---|
| PreHTx mechanical cardiac support | 77 (21.2) | 14 (82.4) | 20 (37.2) | 44 (77.2) | <0.001 |
| ECMO | 70 (19.4) | 13 (76.5) | 20 (37.7) | 43 (75.4) | <0.001 |
| LVAD | 6 (1.7) | 0 (0) | 0 (0) | 1 (1.8) | 0.755 |
| IABP | 1(0.3) | 1 (5.9) | 0 (0) | 0 (0) | 0.004 |
| PreHTx mechanical ventilator | 42 (11.6) | 12 (70.6) | 19 (35.8) | 42 (73.7) | <0.001 |
| Waiting time since HTx enlisting (days) | 80 (32-170) | 18 (7-56) | 39 (13-175) | 19 (7-55) | 0.004 |

RRT, renal replacement therapy; DM, Diabetes mellitus; LV, left ventricle eGFR, estimated glomerular filtration rate; HTx, heart transplantation;LV, left ventricle; EF, ejection fraction, EDD, end-diastolic dimension; LA, left atrium; E, early mitral inflow velocity; e', early mitral tissue Doppler velocity; RVSP, right ventricular systolic pressure; ECMO, extracorporeal membrane oxygenation; LVAD, left ventricular assisting device; IABP, intra-aortic balloon pump; RRT, renal replacement therapy; EF, ejection fraction; LV, left ventricle; EDD, end –diastolic dimension

**Table 2. Renal function after isolated HTx according to periop RRT support.**

**A. All patients who underwent isolated HTx (n=488)**

| | Group 1 | Group 2 | Group 3 | Group 4 | P |
|---|---|---|---|---|---|
| | PreRRT (-)<br>PostRRT (-) | PreRRT (+)<br>PostRRT (-) | PreRRT (-)<br>PostRRT (+) | PreRRT(+)<br>PostRRT(+) | |
| BUN at 6-month post-HTx | 22.0 (17.0-27.4) | 29.0 (24.3-34.8) | 26.0 (19.5-32.9) | 32.0(20.0-44.1) | <0.001 |
| Creatinine at 6-month post-HTx | 1.08 (0.90-1.36) | 1.35 (1.13-1.57) | 1.33 (1.03-1.69) | 1.67 (1.10-2.21) | 0.001 |
| eGFR at 6-month post-HTx | 66.2 (51.0-85.6) | 75.2 (58.3-89.3) | 63.4 (49.3-82.5) | 56.6 (37.2-74.3) | 0.010 |
| BUN at 12-month post-HTx | 19.9 (15.4-24.0) | 28.2 (21.5 39.8) | 22.0 (17.0-2.76) | 28.4 (21.4-38.3) | <0.001 |
| Creatinine at 12-month post-HTx | 1.07 (0.87-1.27) | 1.50 (1.13-1.69) | 1.12 (0.90-1.46) | 1.89 (1.23-3.05) | <0.001 |
| eGFR at 12 month post-HTx | 69.5 (53.3-88.8) | 72.1 (57.8-89.9) | 64.2 (45.0-88.9) | 53.1 (32.1-76.4) | 0.004 |

**B. Patients who underwent isolate HTx and free from dialysis**

| | Group 1 | Group 2 | Group 3 | Group 4 | P |
|---|---|---|---|---|---|
| | PreRRT (-)<br>PostRRT (-) | PreRRT (+)<br>PostRRT (-) | PreRRT (-)<br>PostRRT (+) | PreRRT(+)<br>PostRRT(+) | |
| BUN at 6-month post-HTx | 22.0 (17.0-27.4) | 29.0 (24.3-34.8) | 24.7 (19.0-30.8) | 27.6 (19.9-39.6) | 0.007 |
| Creatinine at 6-month post-HTx | 1.08 (0.90-1.36) | 1.35 (1.13-1.57) | 1.27 (0.96-1.49) | 1.33 (1.11-1.98) | 0.002 |
| eGFR at 6-month post-HTx | 76.0 (50.9-85.1) | 79.2 (61.4-89.5) | 67.4 (52.3-87.1) | 56.8 (36.0-75.6) | 0.021 |
| BUN at 12-month post-HTx | 19.9 (15.4-24.0) | 28.2 (21.5 39.8) | 21.0 (17.1-25.8) | 27.0 (21.0-34.5) | 0.001 |
| Creatinine at 12-month post-HTx | 1.07 (0.87-1.27) | 1.50 (1.13-1.69) | 1.05(0.91-1.40) | 1.36 (1.08-1.81) | 0.001 |
| eGFR at 12-month post-HTx | 79.3 (53.3-88.0) | 82.1 (61.0-90.2) | 67.9 (45.0-88.9) | 54.8 (36.0-75.6) | 0.098 |

BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate

**Table 3. Univariable and multivariable analysis to predict progression to dialysis dependent ESRD after HTx.**

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| Variables | HR | 95% CI | p | HR | 95% CI | p |
| Age | 1.016 | 0.988-1.046 | 0.265 | 1.009 | 0.987-1.054 | 0.385 |
| Male gender | 1.107 | 0.518-2.367 | 0.794 | | | |
| Diabetes mellitus | 1.551 | 0.758-3.173 | 0.230 | | | |
| Insulin dependent diabetes mellitus | 4.866 | 2.013-11.764 | <0.001 | 2.479 | 1.085-5.665 | 0.031 |
| Preoperative mechanical ventilation | 4.416 | 2.188-8.912 | <0.001 | 0.801 | 0.296-2.169 | 0.663 |
| Preoperative mechanical cardiac support | 4.072 | 1.992-8.322 | <0.001 | 1.612 | 0.570-4.558 | 0.368 |
| Preoperative RRT | 15.108 | 7.091-32.186 | <0.001 | 2.327 | 0.969-5.648 | 0.062 |
| Preoperative eGFR | 0.971 | 0.957-0.985 | 0.001 | 0.994 | 0.980-1.008 | 0.410 |
| Preoperative creatinine | 2.852 | 1.844-4.411 | <0.001 | 1.191 | 0.883-1.608 | 0.252 |
| Cardiopulmonary bypass time | 1.006 | 1.000-1.011 | 0.040 | 1.001 | 0.995-1.007 | 0.735 |
| Cold ischemia time | 1.000 | 1.012-1.023 | 0.956 | | | |
| Postoperative RRT | 3.750 | 1.694-8.299 | <0.001 | 8.982 | 2.928-27.552 | <0.001 |
| Primary graft failure | 2.945 | 1.373-6.316 | 0.006 | 0.890 | 0.374-2.115 | 0.791 |

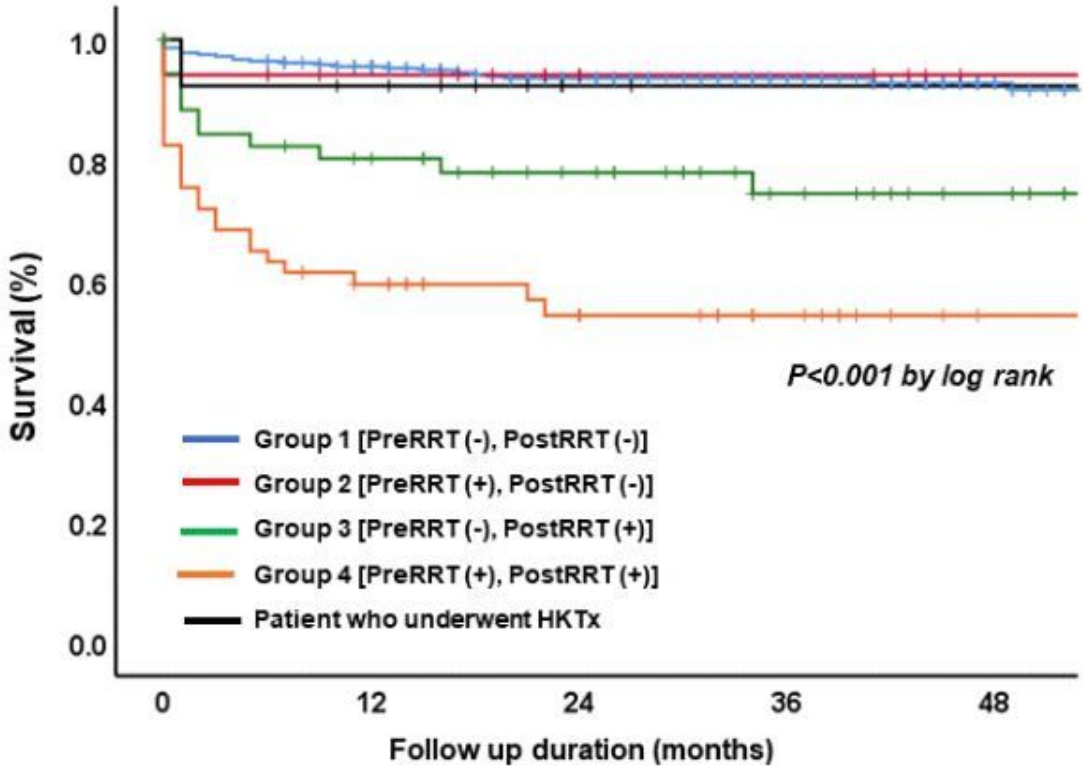
RRT, renal replacement therapy; eGFR, estimated glomerular filtration rate; HTx, heart transplantation; ESRD, end-stage renal disease

**Table 4. Uni and multivariate analysis to predict all-cause mortality after HTx.**

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | p | HR | 95% CI | p |
| Age | 1.022 | 0.999-1.039 | 0.075 | 1.018 | 0.988-1.029 | 0.295 |
| Male gender | 1.193 | 0.703-2.023 | 0.514 | | | |
| DM | 1.843 | 1.136-2.979 | 0.013 | 1.749 | 0.942 - 2.670 | 0.083 |
| Insulin dependent DM | 1.742 | 0.723-4.164 | 0.217 | | | |
| Preoperative mechanical ventilation | 2.874 | 1.782-4.630 | <0.001 | 1.394 | 0.674-2.879 | 0.893 |
| Preoperative mechanical cardiac support | 2.742 | 1.705-4.410 | <0.001 | 1.510 | 0.743-3.048 | 0.437 |
| Preopertive RRT | 2.743 | 2.302-6.084 | <0.001 | 1.306 | 0.723-2.359 | 0.515 |
| Preoperative eGFR | 0.993 | 0.992-1.005 | 0.588 | | | |
| Preoperative creatinine | 1.044 | 0.882-1.297 | 0.753 | | | |
| Postoperative RRT | 6.413 | 3.949-10.417 | <0.001 | 4.396 | 2.469-7.828 | <0.001 |
| ESRD after HTx | 5.142 | 2.464-10.725 | <0.001 | 1.142 | 0.708-2.814 | 0.327 |
| Primary graft failure | 2.955 | 1.373-6.316 | 0.006 | 2.434 | 1.407-4.213 | 0.001 |

DM, diabetes mellitus; RRT, renal replacement therapy; eGFR, estimated glomerular filtration rate; HTx, heart transplantation; ESRD, end-stage renal disease

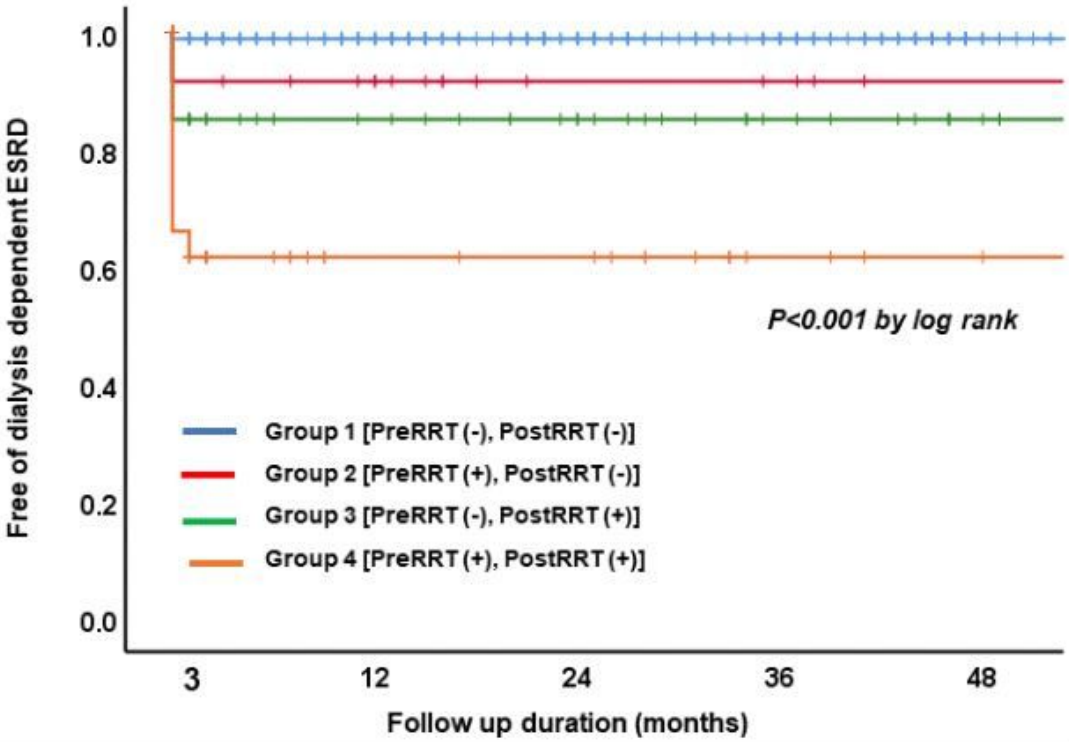
# Figures




| # at risk | Baseline | 12M | 24M | 36M | 48M |
|---|---|---|---|---|---|
| Group 1 | 361 | 356 | 241 | 155 | 73 |
| Group 2 | 17 | 12 | 7 | 5 | 2 |
| Group 3 | 53 | 35 | 26 | 16 | 6 |
| Group 4 | 57 | 24 | 19 | 8 | 4 |

## Figure 1

Proportion of patients who developed dialysis-dependent ESRD after HTx for patients in the 4 groups. ESRD = end-stage renal disease, RRT = renal replacement therapy.




| # at risk | 3M | 12M | 24M | 36M | 48M |
|---|---|---|---|---|---|
| Group 1 | 361 | 277 | 191 | 130 | 53 |
| Group 2 | 17 | 11 | 7 | 5 | 2 |
| Group 3 | 53 | 31 | 24 | 15 | 7 |
| Group 4 | 57 | 16 | 16 | 6 | 3 |

**Figure 2**

Kaplan Meier survival curves showing overall survival for patients in the four groups and those who underwent combined HKTx. RRT =r enal replacement therapy, HKTx = heart and kidney transplantation.

# Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supF1ver1.3.jpg
- supTablever1.5.docx