doi: 10.5262/tndt.2016.1002.04

Acute Renal Failure and Its Impact on Survival Following Cardiac Transplantation

Kalp Naklini Takiben Akut Böbrek Yetmezliği ve Sağkalım Üzerine Etkisi

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ABSTRACT

OBJECTIVE: We evaluated the incidence and risk factors for acute renal failure (ARF) and also the associated hazard of death in recipients of cardiac transplants.

MATERIAL and METHODS: We included 25 patients in the study; 18 patients developed ARF (72%) and underwent continuous venovenous hemodiafiltration (Group I) and 7 patients had stable renal function (28%) (Group II). We retrospectively retrieved demographic variables; clinical, perioperative, postoperative complications and echocardiographic data; and biochemical parameters at the time of the surgery and six months later.

RESULTS: Cumulative survival was 72.2% after 6 months, 64.2% after 24 months, and 51.4% after 32 months for Group I and 50% after 32 months for Group II ($p>0.05$). A total of 8 patients died (32%); 1 (5.5%) from Group I and 7 (87.5%) from Group II. Risk factors for ARF were preoperative serum BUN, creatinine levels, and cardiopulmonary bypass time ($p<0.05$). Only one patient underwent chronic hemodialysis because of chronic renal dysfunction in Group I while there was no such patient in group II.

CONCLUSION: Preoperative serum BUN, creatinine value, and cardioopulmonary bypass time were found to be risk factors for ARF after cardiac transplantation. Postoperative renal dysfunction did not affect long-term renal function and survival.

KEY WORDS: Acute renal failure, Continuous veno-venous hemodiafiltration, Heart transplantation

ÖZ

AMAÇ: Kalp nakli adaylarında ölüm riski ile ilişkili akut böbrek yetmezliği (ABY) insidansı ve risk faktörlerini inceledik.

GEREÇ ve YÖNTEMLER: Çalışmaya 25 hasta (Erkek:19, Kadın:6) alındı, tüm hastaların 18'inde (%72) ABY gelişti ve sürekli veno-venöz hemodiyafiltrasyona alındı (Group I) ve 7 hasta (%28) stabil böbrek fonksiyonları gösterdi (Grup II). Retrospektif olarak demografik değişkenleri taradık; klinik, perioperatif, postoperatif komplikasyonlar ve ekokardiyografik veri; operasyon esnasındaki ve 6 ay sonraki biyokimyasal parametreleri değerlendirdik.

BULGULAR: Kümülatif hayatta kalım, Grup I'de 6 ay sonra %72,2, 24 ay sonra %64,2, 32 ay sonra %51,4 ve Grup II için 32 ay sonra %50 idi ($p>0,05$). Tüm hastalar dikkate alındığında 8 hasta öldü (%32); Grup I'den 1 (%5,5) hasta ve Grup II'den 7 (%87,5) hasta öldü. Kalp nakli sonrası ABY için risk faktörleri; preoperatif serum BUN ve kreatinin değerleri, kardiyopulmoner bypass süresi idi ($p<0,05$). Sadece Grup I'deki bir hasta kronik renal disfonksiyon nedeniyle kronik hemodiyalize gitmişken Grup II'de hiç biri gitmedi.

SONUÇ: Bizim çalışmamızda, akut böbrek yetmezliği kalp nakli yapılan hastalarda nadir değildi. Preoperatif daha yüksek serum BUN, kreatinin seviyeleri ve kardiyopulmoner bypass zamanı, kalp nakli sonrası akut böbrek yetmezliği için risk faktörüydü. Operasyon sonrası gelişen akut böbrek fonksiyon bozukluğu uzun dönem böbrek fonksiyonunu ve sağkalımı etkilememekteydi.

ANAHTAR SÖZCÜKLER: Akut böbrek yetmezliği, Sürekli veno-venöz hemodiafiltrasyon, Kalp nakli

Received : 08.02.2015
Accepted : 06.12.2015

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INTRODUCTION

Cardiac transplantation (CT) has become an important opportunity for end-stage cardiac failure in recent decades. As with other similarly complex cardiac surgery procedures, acute renal failure (ARF) is common after cardiac transplantation, and is associated with morbidity and mortality (1,2). Most researchers concentrate on long-term evolution of chronic renal failure, but the conciliations about ARF are less well investigated in cardiac transplantation patients (3). Risk and consequences of ARF after cardiac surgery have been well reported in the nontransplantation setting. However, information regarding risk factors of acute renal failure after cardiac transplantation is limited (4-7). In some studies, the main reason associated with renal failure after CT are the use of calcineurin inhibitors (cyclosporine and tacrolimus), diabetes mellitus, cardiopulmonary bypass time, transfusion requirements, albumin, donor age, ischemic heart disease, preoperatively impaired renal function, and low cardiac output after transplantation (2-5). Thus, the existing data regarding the risk for posttransplantation ARF are provided beneficial clinical decision. RIFLE criteria have been utilized for the evaluation of ARF. That classificated regulation contains separate criteria for creatinine and urine output. A patient with ARF can perform the criteria direct changes in serum creatinine, estimated glomerular filtration rate or urine output, this classification that pioneers to the worst possible classification should be used (5). There are a few studies about RIFLE-based ARF after CT and its risk factors (5,6). In the present study, we evaluated the incidence and risk factors for acute renal failure and also the associated hazard of death in recipients of cardiac transplant patients.

MATERIALS and METHODS

We included 25 (nineteen men and six woman) patients who underwent cardiac transplantation at Baskent University Hospital between 2005 and 2008. Of these patients, 18 (72%) developed ARF and underwent continuous veno-venous hemodiafiltration (CVVHDF) (Group I, mean age 36.8±17.2 years, mean post-transplant duration 27.7±20.5 months) and 7 patients (28%) had stable renal functions (Group II, mean age 24.3±12.3 months, mean post-transplant duration 25.2±14.9 months). Histidine-tryptophan-ketoglutarate (HTK) solution was used for protection of the donor heart. Orthotopic cardiac transplantation was performed using the biatrial anastomosis technique. The same surgical and anesthetic techniques were used in all patients. After the surgery, they stayed in the intensive care unit and the same treatment was applied to all patients by the same team. Hemofiltration was routinely used during the operations to prevent hemodilution and inflammatory responses. We retrospectively retrieved demographic variables; clinical, perioperative (cardiopulmonary bypass time, number of need replacement of erythrocyte suspension and fresh frozen plasma), postoperative complications (intensive care unit time, ARF, postoperative dialysis requirement) and echocardiographic data; biochemical parameters at the time of the operation and six months after the operation.

The postoperative ARF definition was based on the creatinine increase by the RIFLE classification, which corresponds to a 1.5 creatinine increase, two to three times, respectively, above the basal value**.** RIFLE defines three grades of increasing severity of acute kidney injury - risk (class R), injury (class I) and failure (class F) - and two outcome classes (loss and end-stage kidney disease). A unique feature of the RIFLE classification is that it provides three grades of severity for acute kidney injury based on changes in either serum creatinine or urine output from the baseline condition.

Acute renal failure was treated early by CVVHDF for renal replacement therapy and the dose of CsA and tacrolimus were reduced. Threshold creatinine level was determined as 1.5 mg/dl for long-term renal dysfunction. CsA level aim was 300 to 400 ng/ml following CT. The target was planned as 200 to 300 ng/ml in the first month and 150 to 250 ng/ml after the third month. Tacrolimus levels were planned between 5 and 20 ng/ml during the following period. Blood creatinine levels, tacrolimus, and CsA levels were also determined. Sirolimıs was started at 2 mg/day. The dosage was regulated to achieve a trough level of 5-10 mg/day.

Statistical Analyses

Statistical analyses were done with the SPSS for Windows (SPSS Inc., Chicago, IL, USA) statistics programme. All the numerical variables are expressed as mean ± SD. Normality of data was analyzed using the Kolmogorov-Smirnov Test. The Independent samples t test or the Mann-Whitney U test were used for comparing two groups. Chi-square test, student's t test were used in analyzing the difference between groups. Correlation analyses were done using the Pearson or Spearman tests according to homogeneity characteristics. Multiple linear regression analysis was performed to detect the potential predictors of ARF in patients. $P< 0.05$ was considered significant.

RESULTS

We followed up 25 transplantated patients for 6-57 months. There were no significant differences between two groups for age, smoking, diabetes mellitus, history of hypertension, arrhythmia, pleural effusion, or immunosuppressive therapy modalities ($p>0.05$). In group I 11 (61.1%) patients were using tacrolimus and 7 (38.9%) were using cyclosporin A. In group II 4 (57.1%) of the patients received tacrolimus and 2 (26.7%) of them received cyclosporin A and 1 patient received sirolimus (14.3%) and there were no significant differences. All of the recipients received steroids. Cumulative survival of Group I was 72.2% after 6 months, 64.2% after 24 months, 51.4% after 32 months and 50% for group II after 32 months ($p>0.05$). A total of 8 patients died (32%); 1 (5.5%) patient from Group I and 7 (87.5%) patients from group II.

Total ischemic period was respectively 213.8±76.9 and 224.4±90.9 minutes (respectively range, 108 to 359, 120 to 347) ($p>0.05$) minutes) in group I and II. In the early echocardiographic

evaluation, mean ejection fraction was respectively 54±9.6% and 56±7.5% (range, 33 to 67, 32 to 66) (p>0.05), and in the last echocardiographic evaluation mean ejection fraction was respectively 59±4.5% and 58±3.7 % (respectively range, 52 to 64, 51 to 63) in group I and II (p>0.05). In the early initiation period the mean peak value of CsA was respectively 471±201.2 and 478±210.5 ng/mL (respectively range, 221 to 827, 224 to 819 ng/mL) (p>0.05); in the first month, respectively 249±94.1, 253±95.3 ng/mL (respectively range, 122 to 441, 125 to 446 ng/mL) (p>0.05) in group I and II. The mean preoperative BUN and creatinine levels were respectively; 25.2±11.3, 15.8±3.1 mg/dL (respectively; range 2 to 48, 11 to 21 mg/dL) (p<0.05) in group I and II.

Risk factors for acute renal failure after cardiac transplantation operation were preoperative serum BUN, creatinine levels, cardioopulmonary bypass time (p<0.05). Only in one patient renal function did not improve and the patient underwent a chronic hemodialysis programme in group I.

DISCUSSION

This single-center study showed that ARF was a highly prevalent complication and occurrence of ARF was not associated with cumulative survey in cardiac transplant patients. ARF risk factors were preoperative serum BUN, preoperative serum creatinine levels, and cardioopulmonary bypass time.

The RIFLE criteria were recently developed to standardize the diagnosis of ARF. This classification has been proposed to encompass minor changes to the requirement of renal replacement therapy. In fact, insignificant small variations in renal function in cardiac surgery patients are very important and greatly influence short- and long-term results (5). The RIFLE criteria have been newly used in a few heart transplantation studies[5,6] and we have also used it.

Acute renal failure is major and common problem of cardiac transplantation. Some studies have shown an overall incidence of ARF in the range of 6%-70.4% (2,3,8). We used the RIFLE criteria for the diagnosis of ARF in cardiac transplant patients. Escoresca et al demonstrated 70.4% rate of acute kidney failure during the first week after transplantation (2). We found the same result with this study (72%). Some studies have shown that ARF is associated with survival (9,10), but in our study cumulative survival was not associated with ARF. In our study one patient was died in group I, seven patients died in group II. This result showed that existence of ARF was not associated with the mortality rate.

In cardiac transplant patients postoperative ARF risk factors are found previous cardiac operation, blood transfusion, troponin I release >10, and length of ischemic time (3). In a recent study, Turker at al reported 61% of heart transplant recipients developed ARF and older, had a higher body mass index, more frequently had history of hypertension, smoking, and preoperative higher creatinine levels, had intraoperative higher mean arterial pressures, had higher frequency of intraoperative acidosis, and higher lactate levels as independent risk factors (6). In another study Gude et al showed that intravenous cyclosporine, donor age, and preoperative cardiac output were independent risk factors (1), Boyle et al reported that serum albumin and creatinine levels, insulin requiring diabetes, and cardiopulmonary bypass time were risk factors (7). Similar to these studies, we have also demonstrated cardiopulmonary bypass time, preoperative serum BUN, and creatinine levels as major risk factors for development of ARF after CT. There was no significant difference between ARF after CT and age, smoking, diabetes mellitus, history of hypertension, arrhythmia, and pleural effusion in our study. These conditions depend on small number of patients. Poor preoperative renal function and per-operative hemodinamic instability time may also predispose heart transplant recipients to the development of ARF. This means that it is very important to define risk factors to prevent, diagnose, and treat ARF earlier to improve patients' outcome.

Renal dysfunction occurs in patients waiting for cardiac transplanataion with severe cardiac failure due to low cardiac output and hormonal instability (11,12). In our study the early-last echocardiographic evaluation was similar in both groups.

Longer ischemic periods in cardiac transplantation, and higher morbidity and mortality have been evaluated (13). In cardiac transplantation the accepted time is 4 to 5 hours. In our study the total ischemic period was similar in both groups. HTK solution was used for protection of donor heart in two groups. Some studies showed that donor-recipient selection, hemodynamic stability, and using HTK solution are very important for cardiac transplantation patients (14,15) . In our study we used HTK solution and selected hemodynamically stable donor-recipient too.

Acute nephrotoxic effects of CsA are the result of constriction of afferent renal arterioles and generally reversible while the chronic nephrotoxic effects result from anatomic changes that are generally irreversible interstitial fibrosis, tubular atrophy, and arteriolar hyalinosis (4,16,17). One of the main factors for renal failure after cardiac transplantation may be the use of immunosuppressive drugs (18). However, in our study there were no differences in immunosuppressive therapy modalities in the two groups.

Study Limitations

This study was a retrospective, single-center, and had a small number of patients. There was no control group in the study, and a control group was formed by dividing patients into study groups.

CONCLUSION

In our study acute renal failure was not rare. Higher preoperative serum BUN, creatinine, and time for cardiopulmonary bypass were risk factors for acute renal failure after cardiac transplantation. Renal dysfunction for a limited time does not affect long-term renal function and survey.

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