

Acute Renal Failure Following Coronary Artery By-Pass Surgery: Perioperative Risk Factors

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ABSTRACT

Objective: Morbidity and mortality rates due to acute renal failure (ARF) developed in the postoperative period in patients undergoing coronary artery by-pass surgery (CABG), are increasing. After the determination of risk factors for the development of ARF in the perioperative period, treatment strategies to prevent the development of ARF can be implemented.

Methods: Three hundred and nine patients who had undergone isolated CABG between May 2005 and December 2006 were included in the study. Patients' data registered in the preoperative, intra-operative, and postoperative periods were collected in the electronic media. Factors possibly affecting the development of ARF in the postoperative period were determined by univariate analysis. Later, the independent risk factors affecting the development of ARF were determined by multivariate analysis.

Results: Univariate analysis showed that there was a relation between old age, low ejection fraction (EF) in the preoperative period, presence of COPD, high preoperative serum creatinine levels, long CPB duration, the requirement of intra-operative inotropic support, the amount of postoperative mediastinal drainage, peak creatinine levels, the amount of blood transfusions and postoperative ARF development. At the end of the evaluation of these factors with multivariate analysis; old age, high creatinine levels in the preoperative period, the requirement of inotropic support during the operation and increased amounts of postoperative mediastinal drainage were found to be independent risk factors for the development of ARF.

Conclusions: ARF development is found to be higher in patients with old age, low EF, impaired preoperative renal functions. We suggest that implementing a close follow up with appropriate measures for these patients can decrease the risk of ARF development postoperatively.

Key Words: Coronary artery bypass surgery, acute renal failure, ICU

ÖZET

Koroner Baypas Cerrahisi Sonrasında Görülen Akut Böbrek Yetmezliği: Perioperatif Risk Faktörleri

Amaç: Koroner Baypas cerrahisi sonrasında gelişen akut böbrek yetmezliğine (ABY) bağlı olarak mortalite ve morbidite oranı giderek artış göstermektedir. Perioperatif dönemde ABY gelişimine neden olabilecek risk faktörlerinin belirlenmesi ile ABY gelişiminin önlenmesi ve tedavisine yönelik stratejiler geliştirilebilmektedir.

Yöntemler: Mayıs 2005 – Aralık 2006 tarihleri arasında izole koroner baypas cerrahisi uygulanan 309 hasta çalışmaya dahil edildi. Operasyon öncesindeki, operasyon esnasındaki ve operasyon sonrasındaki hasta verileri bilgisayar kayıt sistemi ile toplandı. Postoperatif dönemde ABY gelişimine neden olabilecek faktörler univaryans analiz ile saptandı. Ardından ABY gelişimine neden olabilecek bağımsız risk faktörleri multivaryans analiz ile belirlendi.

Bulgular: Univaryans analiz sonucunda ileri yaş, ameliyat öncesindeki düşük ejeksiyon fraksiyonu, KOAH varlığı, serum kreatinin yüksekliği, Kardiyopulmoner baypas süresinin uzaması, ameliyat esnasında

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inotropik destek gereksinimi, ameliyat sonrasında mediastinal drenaj miktarı, pik kreatinin seviyesi, kan transfüzyon miktarı ile postoperative ABY gelişimi ilişkili bulunmuştur. Bu faktörlerin multivaryans analiz ile değerlendirilmeleri sonucunda ileri yaş, operasyon öncesindeki yüksek kreatinin düzeyi, ameliyat esnasındaki inotropik destek gereksinimi ve ameliyat sonrasında mediastinal drenaj miktarı ABY gelişiminde bağımsız risk faktörleri olarak belirlendi.

Sonuç: Operasyon öncesinde renal fksiyonları sınırdaki olan, ileri yaşta ve düşük ejeksiyon fraksiyonu olan hastalarda ABY gelişimi daha sık görülmektedir. Bu hastalarda uygun destek tedavileri ile ABY gelişiminin önüne geçilebileceğini düşünüyoruz.

Anahtar Kelimeler: Koroner arter baypas cerrahisi, Akut böbrek yetmezliği, Yoğun bakım ünitesi

INTRODUCTION

Despite the advances in surgical techniques and better intensive care unit conditions, the development of acute renal failure after open heart surgery is still seen frequently (1,2). Due to this complication, 0.515% of the patients need dialysis treatment associated with prolongation of intensive care unit and hospital stays (3,4). Mortality rate reaches 70% in patients who receive dialysis treatment (1,4). Recently due to the advances in dialysis equipment and implementation techniques the mortality has decreased to 20% in some centers, but still has not declined to the levels acceptable for open heart surgery (5,6). When the risk factors for the development of acute renal failure (ARF) are evaluated, the results of many studies are seen to be different one from another. The reasons of the difference of ARF after open heart surgery and associated mortality and morbidity rates are the difference in the demographic features of the patients, creatinine value indicating renal failure, and fundamentals of dialysis implementation criteria. Generally, the accepted indications for dialysis are oliguria, fluid overload, azotemia and patient's clinical situation (1).

Among the factors which can be associated with renal failure in the postoperative period; the common results of some studies are old age, preexisting renal insufficiency, left ventricular dysfunction, prolonged cross clamp and cardiopulmonary bypass durations (7,8). As the development of ARF is a systemic event, the investigation of risk factors which can cause renal failure is very important. There are quite a lot of studies on this topic. However, factors affecting the development of ARF following open heart surgery are not well described. New clinical studies on this topic would especially help selecting patients at high risk for the development of ARF and such patients would receive appropriate preventive measures prior to surgery.

In this study, we aimed to determine perioperative risk factors for the development of postoperative renal failure in patients undergoing isolated coronary artery bypass surgery.

METHODS

Enrollment Of Patients And Data Collection

Three hundred and nine patients (251 male, 58 female) who had undergone isolated coronary bypass surgery between May 2005 and December 2006 were included in the study. Patients who were receiving dialysis previously, and patients with plasma creatinine level above 2 mg/dl, and patients who had extracardiac surgery in addition to coronary bypass surgery were excluded from the study.

Patients' data were retrospectively collected from their medical records and electronic media. Age, sex, body mass index, chief complaints on admission to the hospital, history of diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD), peripheral vascular disease, carotid artery disease, the list of medications, complete blood count and biochemical measurements including preoperative urea and creatinine levels, the requirement of inotropic assistance, the use of intraaortic balloon pump (IABP), the requirement of mechanical ventilatory assistance were all recorded. Total perfusion duration, cross clamp duration, distal anastomosis count, IABP usage, the requirement of inotropic assistance, the lowest body temperature during cardiopulmonary bypass (CPB), the lowest and mean perfusion pressures during operation were recorded from the charts.

Renal function tests, inotropic support, IABP usage, medications given, mediastinal drainage amount, extubation time, mobilization time, transfusion of whole blood and blood products, dialysis treatments; electrolytes and arterial blood gas values in the postoperative period were recorded. Hospital mortality rates and complication rates were calculated. Deaths which had occurred during the same hospitalization or in the first 30 days following operation were accepted as operative mortality. The 30% increase in the postoperative creatinine level in comparison with preoperative creatinine level or serum creatinine level above 2.0 mg/dl was used to determine ARF. Hemofiltration was not applied to the patients with borderline renal functions. When the symptoms of renal failure were seen like oliguria, acidosis, and hyperpotassemia medical treatments were implemented. These measures were a maintenance of a good fluid-electrolyte balance, an

avoidance of potassiumrich solutions in volume replacement, an avoidance of potassiumrich banked bloods, and an early use of balanced glucose-insulin solutions. In case of a failure of the medical management intermittent venovenous hemodialysis was applied.

Surgical Method

In all patients coronary artery bypass surgery was implemented with CPB method. Grafts which would be used were prepared following standard median sternotomy. Standard heparinization was applied following the opening of pericardium. After the aortic and right atrial cannulation, CPB was entered. CPB was continued under intermediate degree hypothermia ($\sim 32^{\circ}\text{C}$) and hemodilution (Htc $\sim 22\%$) with 2.22.4 L/m² flow speed. Mean perfusion pressure was held between 50-75 mmHg during CPB.

Myocardial protection was provided via hyperkalemic cold blood cardioplegia given from the aortic root. Cross clamp was removed after every distal anastomosis was accomplished and proximal anastomosis was made under side clamp. Heparin was neutralized with appropriate dose of protamine at the end of CPB.

Postoperative FollowUp

Patients who were hemodynamically stable, awake enough to protect their airways, and without significant secretions were extubated when weaning parameters permitted. It was awaited until the drainage became serous and less than 10 cc/hour in order to remove thoracic and mediastinal drains. Hemodynamical parameters were continuously followed by monitors in the intensive care unit. All patients were monitored in the intensive care unit and on the floor during the first postoperative four days. In addition electrocardiograms were obtained daily on all patients.

Close followup and prompt treatment were applied to patients with chronic renal insufficiency or ARF to prevent volume depletion and electrolyte imbalance. Patients with increasing creatinine levels, increasing potassium levels in spite of balanced glucose/insulin infusion, oliguria, and fluid overload unresponsive to medical treatment were consulted by a nephrologist and dialysis was initiated when appropriate. All data were recorded in the patients' charts. All complications which had occurred in the intensive care unit (renal, respiratory, hemodynamic, and cerebral) were treated promptly and they were recorded with associated mortality rates.

Statistical Analysis

All continuous data were presented as "mean \pm SD". In the univariate analysis, categorical data were compared with chisquare test and Fischer's exact test, whereas continuous data were compared with independentsamples t test. Multivariate analysis

was performed with binary logistic regression (forward stepwise) analysis and Odds ratio (Ors) was computed at 95% confidential intervals (95% CI). A curve was drawn with receiver operating curve analysis and the correlation of the variations of renal functions with age was evaluated with the area under the curve. Area under the curve was taken into account for the predictive value of ROC curve. Differences were considered statistically significant when P value was < 0.05 . Data were analyzed by statistical software (SPSS for Windows 12.0; SPSS, Chicago, Illinois).

RESULTS

According to the previously defined criteria, postoperative ARF was determined in 58 (18.8%) of 309 patients included in the study. Hemodialysis was done on six of them. The patients' mean serum creatinine level was 0.95 ± 0.25 in the preoperative period while it was 1.23 ± 0.67 in the postoperative period.

A peak in the serum creatinine levels was observed on average on the postoperative second day (minimum:2daysmaximum:5 days). There was not a statistically significant difference between both groups in terms of creatinine peak time. The demographic features of the patients in the groups are given in Table 1. The average age of the patients with ARF was significantly higher than the average age of the patients without ARF, whereas mean EF percentage was clearly lower ($p < 0.001$, $p < 0.001$, respectively). COPD ratio in the group with ARF was higher than in the other group ($p < 0.05$). There was not a significant difference between the groups in term of the other factors (clinical features, medications used) ($p > 0.05$).

CPB duration in the patients with ARF was 109.29 ± 34.27 , while in patients without ARF it was 100.31 ± 26.96 (< 0.05). During the exit from CPB, the ratio of patients who received inotropic support was higher in patients with ARF ($p < 0.001$). Distal anastomosis count, cross clamp duration, minimum CPB temperature, mean blood pressure and the ratio of intraoperative IABP use were similar in both groups ($p > 0.05$). Intraoperative data of both groups are given in Table 2.

Postoperative amount of mediastinal drainage and the need for blood transfusions were clearly higher in the group with ARF in comparison with the group without ARF ($p < 0.001$, $p < 0.001$, respectively). There was a statistically significant association between the hospital and the intensive care unit stay, and renal failure. The time spent in the intensive care unit for patients with ARF was 64.48 ± 34.50 hours, while in the group without ARF it was 49.75 ± 16.38 hours ($p < 0.001$). While the 30day mortality rate in all patients was 3.2% ($n=9$), it was 10.3% ($n=6$) in the group with ARF and 1.2% ($n=3$) in the

Table 1: The comparison of preoperative data in the development of ARF with univariate analysis

Preoperative data	ARF developed patients (n=58)	ARF not developed patients (n=251)	P value
Age (years)	70.50 ± 8.08	63.45 ± 7.92	0.000
Sex (female/male)	6 / 52	52 / 199	NS
EF (%)	47.06 ± 10.62	51.46 ± 7.38	0.000
Unstable angina	15 (%25.9)	62 (%24.7)	NS
Previous MI	24 (%41.4)	99 (%39.4)	NS
Peripheral arterial disease	11 (%19)	36 (%14.3)	NS
IABP	1 (%1.17)	1 (%0.4)	NS
DM	19 (%32.8)	70 (%27.9)	NS
HT	29 (%50.9)	146 (%58.2)	NS
COPD	19 (%17.2)	18 (%7.2)	0.02
Serum creatinine	1.11 ± 0.20	0.91 ± 0.24	0.000
Hematocyte (%)	37.08 ± 7.15	39.16 ± 6.24	NS
Emergent surgery	4 (%6.9)	13 (%5.2)	NS
LMCA	20 (%34.5)	69 (%27.5)	NS

EF : Ejection fraction, MI: Myocardial infarct, IABP: Intra aortic balloon pump, DM: Diabetes Mellitus, HT: Hypertension, COPD: Chronic obstructive pulmonary disease, LMCA: Left main coronary arterial involvement.

NS: not significant

Table 2: The comparison of intraoperative data in the development of ARF with univariate analysis

Intraoperative data	ARF developed patients (n=58)	ARF not developed patients (n=251)	P value
Distal anastomosis	2,96	3,11	NS
CPB stay (minute)	109.29 ± 34.27	100.31 ± 26.96	0.03
Cross clamp duration (minute)	72.67 ± 19.72	72.10 v 21.43	NS
Minimum body temperature (°C)	31.48 ± 1.71	31.92 ±2.16	NS
Mean TA	55.77 ± 7.88	55.05 ± 7.58	NS
Inotropic support (%)	29 (%50)	61 (%24.3)	0.000
IABP usage (%)	6 (%10.3)	18 (%7.2)	NS

CPB: Cardiopulmonary by-pass, TA: Arterial blood pressure, IABP: Intra aortic balloon pump, NS: not significant

group without ARF ($p < 0.001$). The postoperative data of both groups are given in Table 3.

Factors shown to play a role in the development of ARF in the postoperative period by univariate analysis (age, EF percentage, preoperative serum creatinine level, CPB duration, intraoperative inotropic support, the amounts of mediastinal drainage, and blood transfusions) were evaluated by multivariate analysis (logistic regression). At the end of the multivariate analysis; old age, high creatinine levels in the preoperative period, the requirement of inotropic support during the operation and increased mediastinal drainage were found to be independent risk factors for the development of ARF in the postoperative period. The correlation of the variations of renal functions with age was shown with receiver operating curve analysis ($p < 0.05$, the area under the curve: 0.752).

DISCUSSION

The development of ARF in the postoperative period of patients undergoing coronary bypass surgery

is a serious complication. Many studies aimed to determine the factors affecting the development of ARF, whose etiology is thought to be multifactorial and whose mechanism is not well described, have been done. Old age, high ASA class, intake of radioopaque substance, history of DM, peripheral vascular disease, COPD, congestive heart failure, the requirement of IABP, the need for combined coronary and valve surgery, impaired cardiac functions, prolonged CPB duration, renal impairment in the preoperative period were suggested as independent risk factors (2,913).

Generally acute renal failure with progressive oliguria or anuria, and resulting from a low cardiac output may improve by itself in the first 48 hours after cardiac surgery, but electrolyte imbalance and fluid overload worsened during this period can trigger other complications. Thus prompt treatment of these disturbances is very important. Especially in the case of acute renal failure with progressive oliguria, preservation of normal cardiac output and

Table 3: The comparison of postoperative data in the development of ARF with univariate analysis

Postoperative data	ARF developed patients (n=58)	ARF not developed patients (n=251)	P value
Extubation duration	13.39 ± 8.32	11.42 ± 6.77	NS
Mediastinal drainage	919.91 ± 484.99	680.27 ± 297.47	0.000
Peak creatinine value (mg/dL)	2.20 ± 0.95	1.01 ± 0.28	0.000
Creatinine peak time	2.32 ± 0.47	2.29 ± 0.57	NS
Blood transfusion	2.24 ± 1.54	1.31 ± 1.14	0.000
Revision (%)	6 (%10.3)	12 (%4.8)	NS
ICU stay (hour)	65.48 ± 34.50	49.70 ± 16.38	0.000
Mortality	7 (%12.1)	3 (%1,2)	0.000

ICU: Intensive care unit stay, NS: not significant

Table 4: Multivariate analysis of independent risk factors associated with ARF development.

Factors	Ba	P value	Exp(B)b	95% CI for Exp(B)
Age	0.099	0.001	1.104	1.043-1.168
Inotropic support	0.832	0.015	2.298	1.174-4.497
Preoperative creatinine	2.447	0.007	11.554	1.978-67.500
Mediastinal drainage	0.002	0.000	1.002	1.001-1.002

a Logistic regression equation predicts the log odds, the coefficients (column entitled B) represent the difference between the log odds, a log odds ratio.

b The antilog of the coefficients, column entitled Exp(B), is an odds ratio. CI, Confidence interval.

the prevention of fluid overload are tried. In case of progressive impairment of renal functions despite of well fluid and electrolyte management and adequate diuretic treatment, if metabolic acidosis, progressive increase in plasma potassium and body fluid volume occur, dialysis treatment is provided (15,16).

In the postoperative period, ARF developed in 58 of 309 patients undergoing coronary artery bypass surgery. Slight renal function impairment is seen after cardiac surgery almost in all patients. However, there is no consensus regarding the definition of ARF (17). In this situation, different centers accepted different cutoff values of serum creatinine for the definition of ARF. In different studies, criteria like 0.5 mg/dL increase in creatinine level from the basal level, 50% reduction in creatinine clearance and dialysis requirement were accepted (18,19). In our study, as an indicator of renal damage, the increase of preoperative creatinine level more than 30% in the postoperative period or serum creatinine level higher than 2.0mg/dl were accepted (20). For patients in whom ARF developed in the postoperative period with oliguria, acidosis, and hyperkalemia which are not responding to medical therapy, a dialysis treatment was started.

In this study, renal function impairment in older patients was more frequent in comparison with the younger ones. Additionally, in the multivariate

analysis, old age factor was shown to be an independent risk factor for the development of ARF. In our study, the mean age of the patients with renal function impairment was determined to be 70.50 ± 8.08 years while in the other group it was 63.45 ± 7.92 years. The advances in the areas of cardiac surgery and anesthesia have provided the chance of operating older patients.

However, with increasing age some complications are seen more frequently. With the increase in age renal tissue gets older too, and it brings to structural and functional alterations. Due to these alterations, kidney can not easily deal with electrolyte imbalance, rapid volume alterations and hemodynamic impairments (21, 22). Although the older patients are more predisposed to the development of ARF, they do not benefit from the supportive therapies as much as the younger patients (23). Close follow up and life expectation in patients with renal insufficiency in every age is very important.

In our study, there was a statistically important correlation between preoperatively measured serum creatinine levels and ARF development. Additionally, multivariate analysis showed that preoperative creatinine level is a powerful risk factor for the development of ARF. This finding is supported by many studies in the literature (7,12,13,24). In patients with preoperative high serum creatinine levels, ARF development ratio and dialysis require-

ment in the postoperative period were found to be 41% and 29%, respectively (25,26).

Even a slight increase in the preoperative creatinine level paves the way to ARF development in post-cardiac surgical intervention. Especially highly predisposed to inflammatory and oxidative damage in the preoperative period, these patients are frequently seen in the cardiac surgery units (2,13,27). For that reason, applying preventive measures used in patients with low creatinine clearance to the patients with slightly increased preoperative creatinine level may quite decrease the development of ARF. CPB duration was longer in patients with ARF in comparison with patients without ARF ($p < 0.05$). Different mechanisms are suggested for the development of ARF following CPB. In patients undergoing coronary artery bypass surgery via CPB method, a decrease in the blood flow by 2575% during CPB and a decrease in creatinine clearance by 20% in the postoperative period were shown to play a role (2830).

A hypoperfusion of the renal medulla is a factor triggering the development of ARF. Due to the vasoconstriction of renal arteries under low perfusion pressure, blood flow redistribution in the renal tissue is seen (31). Tissue edema following CPB, microembolization, endothelial dysfunction and inflammatory response are other factors playing a role in the development of ARF (3234). Myocardial dysfunction is another factor causing a renal hypoperfusion. In this situation, inotropic agents are used and when needed IABP support is given. ARF development is seen more frequently in patients with low EF (35). In our study the necessity of inotropic support was also more common in patients with ARF during the disconnection from CPB ($p < 0.001$). Renal perfusion is disturbed in patients with unstable cardiac functions and low cardiac output. Similarly patients with preoperative low EF are quite at risk for the development of ARF following cardiac surgery (36). In our study the effect of preoperative low EF on ARF development was only seen in the univariate analysis.

In our clinic we aim to keep hematocrite level above 25% in hemodynamically stable patients after operations made with CPB. Blood transfusion is applied according to the variations in hematocrite in addition to the amount of mediastinal drainage. The amount of mediastinal drainage in our patients with ARF was found to be an independent risk factor as shown with multivariate analysis. Renal perfusion decreases due to hypovolemia and hypotension caused by hemorrhage. In addition, volume and K^+ are acquired after bank blood transfusion. Due to increased mediastinal drainage in patients with ARF we needed to give more blood transfusions. Habib et al (37) demonstrated negative effects of blood transfusion on renal functions. Possible explanation of this relation is that transfu-

sed blood products have an artificially shortened lifespan, and their hemolysis leads to an increase in circulating free Fe which contributes to impairment of renal functions (38). In addition, in case of usage of stored red blood cells the smaller capillary is can be obstructed because of their less suppleness and deformability. This can result in increased organ ischemia (39).

In patients in whom ARF develops following open heart surgery, in addition to renal impairment other organs are also affected. Especially due to failure of vascular and respiratory systems, implementation of additional treatments is required. Renal functions are awaited to return to normal levels before hospital discharge. As a result, the patients' intensive care unit and hospital stays prolong, various systemic complications are seen and mortality risk increases. In our study, the intensive care unit stay of patients with renal insufficiency was prolonged by a mean of 15 hours due to various reasons. In addition, the mortality rate of patients with ARF was found to be quite high.

With the beginning of the impairment of renal functions in the postoperative period, a close follow up and a careful fluid and electrolyte management must be done. The aim is to stop the deterioration of renal functions further and to restore the normal functions. The reason is that if the measures are taken promptly, their long term survival rates are similar to those without ARF. The level of increase of creatinine postoperatively does also directly affect long term mortality. Indeed in two studies, both early and long (mean 100 months) term mortality rates of patients undergoing open heart surgery were found to be related to degree of postoperative increase in serum creatinine levels (40,41). In our study the mortality rate of patients with ARF was found to be 12.1% while it was 1.2% in the rest of patients.

In the presence of risk factors for the development of ARF following operations in centers doing cardiac surgery, strategies appropriate to the patient can be implemented. It should be kept in mind that the risk of development of ARF in the elderly patients with preoperative renal insufficiency and a low EF is quite high. A thorough evaluation of such patients by a team consisted of a heart surgeon, a cardiologist, an anesthesiologist, and a nephrologist is very important.

Measures to prevent renal dysfunction such as an adequate hydration, discontinuation of drugs adversely affecting renal function, improvement of hemodynamic status with inotropic agents, and prevention of renal insufficiency associated acid-base imbalance in the preoperative period, must be undertaken. The need for dialysis treatment may be decreased by taking similar preventive measures for patients with impaired renal functions in the postoperative period. In that way, the adverse

effects of dialysis on hemodynamics and bleeding diathesis can be avoided.

Limitations of The Study

As the patients' preoperative, intraoperative and postoperative data were collected retrospectively from medical records, patient charts, and electronic media, only patients whose data were available for the aforementioned periods, were included in the study. Patients whose data were not available during any of the aforementioned periods were excluded from the study. Serum creatinine level increase commonly used in the literature was preferred as renal dysfunction criterion. This increase can show glomerular filtration rate indirectly as it is expressed as a ratio. Although the measurement of serum creatinine level is quite practical, it is affected by age, sex, muscle mass, body fluid amount and body surface area. The measurement of creatinine clearance as an indicator of glomerular filtration rate could increase the power of the study. However, as the creatinine clearance was not routinely measured in our hospital, we evaluated the ratio of increase in serum creatinine level for development of ARF.

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