# Acute exacerbation in chronic kidney disease increases mortality after coronary artery bypass grafting

## *Böbrek yetersizliğinde alevlenme, koroner bypass greftleme sonrası mortaliteyi anlamlı olarak artırır*

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***Background:*** In this article we investigated short term results of patients who had chronic kidney disease before coronary artery bypass graft (CABG) surgery.

***Methods:*** The results of 360 patients who underwent elective CABG surgery between December 2006 and April 2008 were evaluated retrospectively. Two-hundred and sixty-seven of these patients underwent CABG surgery. Finally, we evaluated the results of 55 patients (23 females, 22 males; mean age 66.7±9.4 years; range 45 to 84 years) who had creatinine clearance values lower than 60 mg/kg/m$^2$.

***Results:*** Mortality occurred in two patients (8.6%) with mild glomerular filtration rate (GFR) decrease (0-25% decrease from preoperative GFR), in two patients (11.6%) with moderate decrease (25-50%) and in three patients (75%) with severe decrease (>50%). It was determined that GFR decrease in the postoperative period increased the likelihood of death (p=0.001). The odds ratio of death in the group with mild decrease in GFR increased 12.6 times, that in the group with moderate decrease increased 15.6 times and that in the group with severe decrease increased 35.2 times.

***Conclusion:*** If the renal function in patients with chronic renal disease can be kept at the levels of preoperative values, postoperative early results are affected mildly. However, if acute exacerbation occurs, it increases the risk of mortality. This data also indicates that every effort to save renal function will decrease postoperative mortality.

*Key words:* Chronic kidney disease; coronary artery bypass grafting; short term results.

***Amaç:*** Bu yazıda koroner bypass greftleme (KABG) ameliyatı öncesinde kronik böbrek yetersizliği olan hastaların kısa dönem sonuçları incelendi.

***Çalışma planı:*** Aralık 2006 ile Nisan 2008 tarihleri arasında elektif KABG ameliyatı uygulanan 360 hastanın sonuçları geriye dönük olarak incelendi. Bu hastaların 267'sine KABG ameliyatı uygulandı. Sonuçta kreatinin klirensi 60 mg/kg/m$^2$'nin altında olan 55 hastanın (23 kadın, 22 erkek; ort. yaş 66.7±9.4 yıl; dağılım 45-84 yıl) sonuçları değerlendirildi.

***Bulgular:*** Mortalite glomerüler filtrasyon oranı (GFR)'nda hafif derecede azalma olan (ameliyat öncesi döneme göre %0-25 azalma) iki hastada (%8.6), orta derecede azalma (%25-50) olan iki hastada (%11.6) ve ciddi azalma olan (>%50) üç hastada (%75) görüldü. Ameliyat sonrası dönemdeki GFR azalmasının ölüm riskini artırdığı (p=0.001) tespit edildi. Ölüm riski, glomerüler filtrasyon oranında hafif azalma olan grupta 12.6 kat, orta derecede azalma olan grupta 15.6 kat ve ciddi azalma olan grupta 35.2 kat arttı.

***Sonuç:*** Kronik renal yetersizlikli hastalarda eğer renal fonksiyonlar ameliyat öncesi değerlerinde korunabilirse, ameliyat sonrası erken dönem sonuçlar daha az etkilenmektedir. Bununla birlikte, meydana gelen bir alevlenme ölüm riskini artırmaktadır. Bu veriler böbrek fonksiyonlarını korumak için yapılacak her işlemin ameliyat sonrası mortaliteyi azaltacağını da gösterebilir.

*Anahtar sözcükler:* Kronik böbrek hastalığı; koroner arter bypass greftleme; kısa dönem sonuçlar.

Acute renal failure is a life threatening complication which can follow coronary artery bypass grafting (CABG) surgery. It occurs in 1% to 5% of patients following CABG. When dialysis is indicated, mortality rates can reach as high as 50%.[1] Even minimal changes in serum creatinine are associated with a considerable decrease in survival in the postoperative period.[2] Perioperative risk factors for developing acute renal injury are well documented.[3]

Chronic kidney disease (CKD) is associated with worse outcomes after CABG surgery. However, there are five different stages of chronic kidney disease

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according to the National Kidney Foundation.[4] As the stage progresses, mortality increases as well. Mortality rates for stages 1 to 4 are 0, 1.9, 4.3 and 33.3% respectively.[5] Dialysis-dependent CKD (stage 5) is associated with approximately 2.9 and 3.8-fold increases in odds of operative mortality following CABG surgery.[6] Careful perioperative planning and special management are the keys to minimize the risk of the patient as the stage increases.

In this report we would like to investigate short term results of patients who had CKD before CABG surgery.

## PATIENTS AND METHODS

### Design overwiev

In this retrospective study, we collected patient data from our dedicated software-based database. We wanted to evaluate the short term results of patients who had chronic kidney disease before CABG surgery. Therefore we investigated the results of the patients who had glomerular filtration rate (GFR) values less than 60 mL/min/1.73 $m^2$. The control group had GFR values higher than 90 mL/min/1.73 $m^2$. Glomerular filtration rate values were calculated by modification of diet in the renal disease (MDRD) formula as described in the literature.[7]

We performed the study at a tertiary care, teaching University Hospital.

### Participants

Adults undergoing elective CABG surgery between December 2006 and April 2008 were enrolled in the study. There were 360 patients operated on during this period. Two hundred and sixty seven patients underwent CABG surgery. We excluded patients who had off-pump CABG procedure (n=12). Patients who underwent concomitant procedures such as valve surgery, ascending and or arcus aorta surgery, carotid surgery and redo surgery were also excluded (n=105). Finally, we evaluated the results of 55 patients (23 females, 22 males; mean age 66.7±9.4 years; range 45 to 84 years) who had creatinine clearance values lower than 60 mg/kg/$m^2$. The study was approved by the ethics committee of our institution.

### Surgical technique

Radial and pulmonary arterial catheters were introduced under local anesthesia. After standard anesthesia, a median sternotomy was performed followed by routine aortic and right atrial two-stage cannulation. The standard cardiopulmonary bypass (CPB) technique was carried out using membrane oxygenators and under moderate systemic hypothermia (30 ºC). Mean arterial blood pressure was kept between 50 and 70 mmHg during CPB. Myocardial protection was achieved by antegrade and retrograde cold blood cardioplegia. Heparin was administered 3.0 mg/kg and was neutralized with protamine, in a ratio of 1:3, within 10 min. after the end of CPB.

Short term mortality was defined as death within 30 days of the operation or during the same hospitalization. Low cardiac output syndrome (LCOS) was defined as the need for postoperative intraaortic baloon support (IABP) and/or inotropic support, for any length of time, in the intensive care unit (ICU).

### Renal replacement therapy

We prefer to use continous venovenous hemodiafiltration (CVVHD) in renal replacement therapy since early and aggressive use of CVVHD is associated with better survival in severe acute renal failure (ARF) after cardiac operations.[8] Patients who were on a hemodialysis program before surgery had dialysis before and after surgery. Dialysis the day before was done for potential beneficial effects.[9] In two patients, hemodialysis was needed to immediatedly reduce potassium levels following surgery.

### Statistical analysis

We compared baseline patient characteristics and outcome variables across treatment groups, categorical variables by using Chi-square or Fisher's exact tests, and continuous variables by using T-tests or Wilcoxon rank-sum tests. The variables with a p value less than 0.10 at univariate analysis were entered in a stepwise multiple linear regression analysis to identify the independent predictors of mortality and ICU stay. We estimated odds ratios according to multivariate logistic regression analyses and considered two-sided p values less than 0.05 to be statistically significant. We used SPSS (Statistical Package for the Social Sciences), version 15.0 (SPSS Inc., Chicago, IL) for analyses.

## RESULTS

Perioperative descriptives are in table 1. Only two patients were on a regular hemodialysis program. Perioperative renal functions were replaced by three different methods including ultrafiltration during CPB (n=15; 27.2%), CVVHD (n=30; 54.5%), hemodialysis (n=5; 9%).

Age (66.2±9.6 vs. 62.1±17.3 years; p=0.001) was higher, extubation time (8.4±12.6 vs. 6.2±6.6 hours; p=0.01) was longer, ICU stay (64.4±42.5 vs. 44.2±14.2 hours; p=0.02) was longer, and discharge time (9.95±5.56 vs. 7.64±4.3 days; p=0.01) was longer in CKD patients.

Major perioperative morbidities are included in table 2. Five of eight patients who had low cardiac output syndrome (LCOS) received intra-aortic balloon

**Table 1. Perioperative descriptives**

| Variable | CKD (n=55) | Range | Non-CKD (n=200) | Range | *p* |
|---|---|---|---|---|---|
| Age (years) | 66.2±9.6 | (45-84) | 62.1±17.3 | (22-86) | 0.001 |
| Graft # | 2.98±1.06 | (1-5) | 2.94±1.05 | (1-6) | 0.374 |
| EF % (mean) | 52±6.4 | (45-65) | 53.6±5.5 | (40-70) | 0.56 |
| LVEDD (mm) | 56.7±5.4 | (49.4-60.9) | 55.8±4.4 | (48.7-61.4) | 0.98 |
| LVESD (mm) | 39.6±3.3 | (35.4-44.3) | 38.7±2.2 | (36.2-47.4) | 0.76 |
| Mild MR (n) | 12 | 21.8% | 27 | 13.5% | 0.02 |
| Moderate-severe MR (n) | None | – | None | – | – |
| Extubation time (hour) | 8.4±12.6 | (6-28) | 6.2±6.6 | (1-14) | 0.01 |
| ICU stay (hour) | 64.4±42.5 | (19-207) | 44.2±14.2 | (24-184) | 0.02 |
| Preoperative GFR | 48.2±11.3 | (11.47-59.45) | 89.2±24.5 | (60.14-134.23) | <0.001 |
| Postoperative GFR | 38.8±13.9 | (9.54-70.34) | 76.4±18.4 | (45.2-127.7) | <0.001 |
| ACCT (min) | 77.9±33.7 | (31-189) | 75.8±24.3 | (27-164) | 0.38 |
| TPT (min) | 116.2±52.7 | (46-378) | 109.2±60.1 | (34-244) | 0.49 |
| Discharge time (day) | 9.95±5.56 | (6-33) | 7.64±4.33 | (5-17) | 0.01 |

CKD: Chronic kidney disease; EF: Ejection fraction; LVEDD: Left ventricular end diastolic diameter; LVESD: Left ventricular end systolic diameter; MR: Mitral regurgitation; ICU: Intensive care unit; GFR: Glomerular filtration rate; ACCT: Aortic cross clamp time; TPT: Total perfusion time.

pump (IABP) support and two of them had perioperative myocardial infarction. There was no deep sternal wound infection and no bleeding that required revison as well (Table 2).

Seven patients died in the early postoperative period. The most common causes of early death were LCOS (5%), multisystem organ failure (MOF) (5%) and perioperative myocardial infarction (3.6%; Table 3). When compared to patients with no CKD (stage 3 and higher), the mortality rate was higher in the CKD group (7% vs 2.5%; p<0.001). All morbidity and mortality parameters were higher in the CKD group, however inotrop usage (p=0.03), prolonged intubation (p=0.02), IABP usage (p=0.03) were statistically higher. According to postoperative GFR, patients were classified in three subgroups: patients who had mild GFR decrease (0-25% decrease from preoperative GFR), moderate (25-50%) and severe (>50%; Table 4). As noted in the table 4, GFR decrease in postoperative period directly increased the likelihood of death. There were two deaths in the mild group which had an odds ratio of 12.6. A moderate decrease in GFR resulted in an odds ratio of 15.6, while a severe decrease increased the likelihood of death 35 times. Three patients died in the severe decrease group which represents 75% of patients in that subcategory.

Factors that are associated with mortality and ICU stay were identified with logistic regression analysis (Table 5). Preoperative creatinine values were not associated with longer ICU stay and early mortality, however postoperative renal indexes such as increased creatinine and decrease of GFR were associated with longer ICU stay and early mortality. The most significant factor affecting prolonged ICU stay and early mortality was postoperative GFR decrease (p=0.001).

## DISCUSSION

Renal dysfunction is one of the most serious complications of CABG surgery. It appears to be common in

**Table 2. Perioperative morbidity and mortality**

| | CKD (n=55) | % | Non-CKD (n=200) | % | *p* |
|---|---|---|---|---|---|
| Inotropes | 11 | 20 | 24 | 12 | 0.03 |
| Low cardiac output syndrome | 8 | 14.5 | 16 | 8 | 0.06 |
| Atrial fibrillation | 8 | 14.5 | 25 | 12.5 | 0.744 |
| Prolonged intubation | 6 | 10.9 | 8 | 4 | 0.02 |
| Intraaortic balloon pump | 5 | 9 | 6 | 3 | 0.03 |
| Peroperative myocardial infarction | 2 | 3.6 | 2 | 1 | 0.43 |
| Infection | 2 | 3.6 | 2 | 1 | 0.43 |
| Bleeding | 0 | – | 2 | 1 | 0.28 |
| Deep sternal wound infection | 0 | – | 0 | – | – |
| Stroke | 0 | – | 0 | – | – |
| Exitus | 7 | 12.7 | 5 | 2.5 | 0.001 |

CKD: Chronic kidney disease

**Table 3. Early mortality**

| No | Sex/age | Cause of death | Postoperative day | Preoperative GFR | Postoperative GFR |
|---|---|---|---|---|---|
| 1 | M/66 | Perioperative MI | 5 | 11.47 | 9.50 |
| 2 | M/58 | Perioperative MI | 0 | 29.56 | 14.02 |
| 3 | F/75 | MOF, LCOS | 13 | 46.55 | 20.92 |
| 4 | M/61 | LCOS | 4 | 53.44 | 26.22 |
| 5 | F/67 | MOF | 12 | 58.78 | 34.17 |
| 6 | M/57 | LCOS | 8 | 51.27 | 28.43 |
| 7 | M/52 | MOF | 9 | 56.56 | 35.43 |

GFR: Glomerular filtration rate (mL/dk/1.73 $m^2$); MI: Myocardial infarction; MOF: Multi organ failure; LCOS: Low cardiac output sydrome.

**Table 4. Glomerular filtration rate decrease**

| Stage | n | % | Mortality (n) | Mortality (%) | OR | 95% CI |
|---|---|---|---|---|---|---|
| Mild (0-25%) | 23 | 41.8 | 2 | 8.6 | 12.6 | 1.3-108.3 |
| Moderate (25-50%) | 18 | 32.7 | 2 | 11.1 | 15.6 | 1.8-122.1 |
| Severe (25-50%) | 4 | 7.2 | 3 | 75 | 35.2 | 2.9-422 |

OR: Odds ratio; CI: Confidence interval.

patients undergoing cardiac surgery with CPB. Acute renal failure occurs in up to 30% of all patients who undergo cardiac surgery.[10] Many more patients suffer from occult, subclinical and transient renal injury without requiring dialysis. These patients have a high mortality, a more complicated hospital course, and a higher risk for infectious complications.[11,12]

Mild renal disfunction is an important independent predictor of in-hospital and late mortality in adult patients undergoing elective cardiac surgery including CABG and valve operations.[13] The mechanism in by which renal dysfunction contributes to postoperative mortality is unknown. In-hospital deaths were directly secondary to cardiovascular causes in two patients. Decreased GFR may be a marker of a more advanced cardiovascular disease including increased levels of inflammatory mediators and hypercoagulability, endothelial dysfunction, arterial stiffness or calcificatio and left ventricular hypertrophy.[9]

In isolated CABG series, CKD was an important predictor of in-hospital death as well. Zakeri et al.[14] found that the higher the preoperative creatinine levels, the higher the mortality rates were. They found that the mortality rate for GFR 90 mL/min per 1.73 $m^2$ was 1.0% (17 of 1707); GFR 60 to 89 mL/min per 1.73 $m^2$ was 2.1% (40 of 1922); GFR 30 to 59 mL/min per 1.73 $m^2$ was 7.1% (45 of 631) in their large (n=4403) series.

Our postoperative data shows that major complications following CABG such as inotrope usage, LCOS, AF, IABP usage and mortality rates are higher than the elective non-CKD patient population. Mortality rate is 12.7%, which is a very high rate for non-CKD operations, but reasonable for a series of CKD patients.

It was found that the patients had different characteristics based on their decrease in clearance. Mortality rates for the groups were 8.6% for the first group, and 11.1% and 75% for the second and third groups respectively. The odds ratio for mild, moderate and severe decrease in clearence had an odds ration of 12.6, 15.6 and 35.2 respectively. This analysis shows that acute worsening of kidney functions of patients who had chronic kidney disease increases mortality directly related to remaining renal functions. A severe decrease in creatinine clearence increases mortality rates up to 35.2 times, and has a mortality rate of 75%. However, if there is no difference or a minimal change in GFR, mortality rate is significantly lower.

Factors affecting mortality and prolonged ICU stay were related to renal indexes such as postoperative

**Table 5. Factors for ICU stay (>48 hours) and early mortality**

| | ICU stay | Early mortality |
|---|---|---|
| Age >65 year | 0.135 | 0.234 |
| Male gender | 0.208 | 0.09 |
| Preoperative creatinine | 0.08 | 0.65 |
| Postoperative creatinine | 0.02 | 0.001 |
| Postoperative GFR decrease | 0.001 | 0.001 |
| LVD (Preoperative) | 0.74 | 0.931 |
| Inotropes following surgery | 0.43 | 0.74 |
| IABP (Postoperative) | 0.03 | 0.91 |
| Peroperative MI | 0.001 | 0.001 |
| COPD | 0.02 | 0.44 |
| Diabetes mellitus | 0.09 | 0.07 |

ICU: Intensive care unit; GFR: Glomerular filtration rate; LVD: Left ventricular dysfunction; IABP: Intraaortic balloon pump; MI: Myocardial infarction; COPD: Chronic obstructive pulmonary disease.

creatinine and postoperative GFR decrease (both p=0.001). The other factor related to early mortality was perioperative myocardial infarction.

Chronic kidney disease is a well known and established risk factor for early complications and death following CABG surgery. If the renal functions would be kept as the levels of preoperative values, the impact of CKD on early results are mild, however if acute exacerbation occurs, it is strongly related to death. This data also indicates that, every effort to save any renal function after surgery has to be done perioperatively in order to reduce postoperative mortality.

### Limitations

There was no bleeding which required revision in operating room, deep sternal wound infection and stroke in our series. This may be related to small number of patients in our study. Only one surgical team performed all the operations; this may also be a very important factor for reducing bleeding and infectious complications.

Since CKD is a risk factor for all postoperative short term outcomes, this study does not indicate that morbidity and mortality rates are decreased. If the kidney functions remain unchanged like the 0-25% GFR decrease group, the mortality rates is still higher than the normal population at 8.6%.

Fifty-five patients who had GFR lower than 60 mL/min per 1.73 is a small series of patients from a single center. This may under or over estimate the rates of complications and results. More reliable results could be achieved by increasing the number of patients. However all patients were operated on by the same surgeon and team, so we believe this small series can demonstrate a result to show up the effect of renal function on early results.

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