Cardiovascular Topics

Comparison of early postoperative results in patients with and without diabetes with low ejection fraction and normal serum creatinine values who underwent coronary artery bypass operation

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Abstract

Background: Low left ventricular ejection fraction and renal insufficiency are factors that increase the risk of coronary artery bypass graft surgery in patients with diabetes mellitus. The aim of this study was to group patients with low left ventricular ejection fraction undergoing coronary artery bypass graft surgery according to the presence or absence of diabetes mellitus and to evaluate postoperative changes in serum creatinine levels and postoperative outcomes.

Methods: A total of 93 patients undergoing isolated coronary artery bypass grafting were included in this single-centre, retrospective, cohort study. Patients with a pre-operative low left ventricular ejection fraction of less than 35% were included in the study. Patients were divided into diabetic and non-diabetic groups and intra- and intergroup values were compared. Pre-operative, and postoperative days 2 and 5 serum creatinine levels of the patients were measured and compared.

Results: Of the 93 patients included in the study, 60 were in the diabetic group (group 1) and 33 were in the non-diabetic group (group 2). Postoperative 2- and 5-day creatinine levels were significantly higher in group 1 than in group 2 (p = 0.033 and p = 0.005, respectively). Postoperative 2- and 5-day creatinine levels were significantly higher than pre-operative creatinine levels in group 1 (p = 0.008 and p = 0.001, respectively). The intensive care unit stay was significantly longer in the diabetes mellitus group than in the group without diabetes mellitus (p = 0.031).

Conclusion: Following coronary artery bypass graft surgery in patients with low left ventricular ejection fraction, which is already a risk factor, creatinine levels were found to have increased in the diabetes mellitus group.

Keywords: cardiac surgery, acute kidney injury, diabetes mellitus, low left ventricular ejection fraction

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Coronary artery disease is one of the leading causes of death today.[1] Percutaneous and medical treatment can be listed among the treatments for this disease, and surgical treatment also has an important place in ischaemic heart disease.[2] Conditions such as low left ventricular ejection fraction (LLVEF < 35%), diabetes mellitus (DM) and renal failure are among the factors that increase mortality and morbidity rates in coronary artery bypass graft (CABG) surgery.[1] Despite these risks, surgical treatment may be preferred to medical treatment because complete revascularisation can be achieved.[3,4]

Renal failure is a risk factor for CABG surgery, and CABG surgery and extracorporeal circulation are known to cause renal failure.[5] Heart disease is associated with reduced renal function and progression of renal disease. The incidence of renal dysfunction after open-heart surgery is reported to be 30–50%, with 1–5% of these patients requiring permanent haemodialysis.[6] DM is also a major risk factor for renal failure.[7]

CABG surgery in patients with LLVEF is associated with a risk of renal failure. In this study, we analysed the postoperative serum creatinine level changes in this group of patients and divided the patients with normal pre-operative creatinine values into two groups according to DM status. We also aimed to evaluate postoperative creatinine level changes and early postoperative outcomes in these groups.

Methods

All patients who underwent CABG surgery under cardiopulmonary bypass (CPB) in our clinic between 2019 and 2021 were retrospectively reviewed. The presence of coronary artery disease suitable for revascularisation on angiography and an LLVEF ≤ 35%, as calculated by two-dimensional echocardiogram, were the selection criteria for the study group. Patients with previous CABG, left ventricular aneurysm, coronary artery disease not suitable for CABG, moderate-to-severe mitral regurgitation, concomitant valvular heart disease, pre-operative creatinine value of 1.4 mg/dl and above, and emergency and dialysis patients were excluded from this study.

Patients with DM were included in group 1 and those without DM (non-DM) were included in group 2. Demographic characteristics and pre- and postoperative data of the patients were compared.

Local ethical approval was obtained from Prof Dr Cemil Taşçıoğlu City Hospital (number 2021/434). An informed consent form were obtained from the patients for this retrospectively designed study.

Elective patients identified as CABG surgery candidates with a pre-operative creatinine level of less than 1.4 mg/dl were operated on under stable conditions. Patients were operated on at least two weeks after the angiography procedure. Pre-operatively, immediately after cardiac catheterisation, the Nephrology Department was consulted and patients were hydrated under appropriate conditions. Patients did not take any regular nephrotoxic medication before or after the procedure.

Basal creatinine concentration was measured within the following seven days before surgery. After surgery, data were collected daily for seven consecutive days, including serum creatinine concentration and urine output. Urine output was measured at one-hour intervals during the first 72 hours postoperatively while the patient was in the post-operative care unit.

The day of surgery was defined as day 0. Patients were assessed for the development of acute kidney injury (AKI) from post-operative day 1 to day 7, based on changes in serum creatinine concentration. Pre-operative creatinine levels, and post-operative day 2 and day 5 creatinine values were compared in groups 1 and 2, taking into account the minimum increase in creatinine concentration within 48 hours and one week, as in the acute kidney injury network (AKIN) and kidney disease improving global outcomes (KDIGO) criteria.[8,9]

Although the AKIN criterion seems to be more applicable than the KDIGO criterion, as it suggests a shorter time interval for the time of diagnosis, it was planned to look at day 5 creatinine values in addition to day 2 values, as this may underestimate the severity of AKI.

Peri-operative outcomes were compared between the groups and post-operative complications were recorded. According to the AKIN classification, AKI was defined as an increase of ≥ 50% or 0.3 mg/dl in the pre-operative baseline creatinine level within 48 hours.[9] Post-operative AKI was compared in both groups.

All operations were performed on-pump by the same surgical team. There was no difference between coronary revascularisation techniques in the two groups.

After releasing the left internal mammary artery, standard cannulation was performed, followed by antegrade cardioplegia cannula placement and CPB was initiated. Moderate hypothermia was maintained, and a roller pump and membrane oxygenator were used during CPB. The perfusion rate was set at 50–75 ml/kg/min and mean arterial pressure at 60 mmHg and above. Myocardial protection was achieved with intermittent blood cardioplegia and topical cooling, following clamping of the aorta when appropriate conditions were provided. Distal anastomoses were made in cross-clamps and proximal anastomoses were made in side clamps.

Blood pressure, rhythm, amount of chest tube drainage, urine output, oxygenation profile, state of consciousness and pain control were closely monitored during intensive care unit (ICU) follow up. Mean arterial blood pressure was maintained at 60 mmHg and above by ensuring stable haemodynamics. Urine output was monitored hourly and blood gas, potassium and bicarbonate values were measured intermittently. Fluid support was provided so that urine output was 1 ml/kg/hour and above. The effect of cross-clamps, total perfusion time and the number of bypass vessels on the change in postoperative creatinine value were investigated in both groups.

Statistical analysis

Analysis of the data was done in the IBM SPSS 22.0 (SPSS Inc, Chicago, IL, USA) package program. Descriptive statistics are shown as mean (standard deviation) for normally distributed variables and median (minimum – maximum) for non-normally distributed variables. The differences between the groups were evaluated with the *t*-test when the assumption of normal distribution was provided, and with the Mann–Whitney *U*-test when the assumption of normal distribution was not provided. The Spearman correlation test was used since the normality assumption was not provided for the relationship between continuous variables. Pearson's chi-squared test was employed for intergroup comparison of categorical variables. For $p < 0.05$, the results were considered statistically significant.

No sample calculation was made before the study. All patient records were accessed. *Post hoc* power analysis was performed with Gpower 3.1. The power was calculated as 0.69 for creatinine on postoperative day 2 and 0.84 for creatinine on postoperative day 5.

Results

A total of 93 patients with LLVEF ≤ 35% who underwent isolated CABG were analysed. Among these patients, 60 were in the group with DM (group 1) and 33 were in the non-DM group (group 2). The demographic characteristics of the patients are given in Table 1. The pre-operative LLVEF was found to be 32% (2.1) in group 1, and 31% (2.0) in group 2, and no statistically significant differences were found between the groups. There were no differences between the groups in terms of other demographic data.

Although the peri-operative data of the patients (cross-clamp time, total perfusion time, number of bypass vessels) were numerically higher in group 1, this did not cause a statistically significant difference (Table 2).

Table 1. Demographic characteristics of the groups

Demographics	*DM group (n = 60) n (%)*	*Non-DM group (n = 33) n (%)*	p-*value**
Age (years)	67.7 (9.9)	54.6 (6.3)	0.87
Gender			
Female	33 (55)	19 (57.5)	0.91
Male	27 (45)	14 (42.5)	0.94
Hypertension	18 (30)	10 (30.3)	0.80
BMI	27.0 (3.1)	26.71 (4.3)	0.61
COPD	15 (25)	8 (24.2)	0.44
Smoking	30 (50.0)	17 (51.5)	0.31
Ejection fraction	32 (2.1)	31 (2.0)	0.48
EuroSCORE (mean)	1.8 (0.6)	1.40 (0.4)	0.46

BMI: body mass index; COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus. *Mann–Whitney *U*-test.

Table 2. Peri-operative data

	DM group (n = *60*)		*Non-DM group* (n = *33*)		
Peri-operative data	*Mean (SD)*	*Median (min–max)*	*Mean (SD)*	*Median (min–max)*	p-*value**
Cross-clamp time (min)	76.97 (22.09)	72 (43–115)	65.12 (16.38)	59 (44–109)	0.41
Total pump time (min)	123 (29.2)	113 (80–175)	119 (24.3)	112 (80–175)	0.81
Bypass numbers	4.5 (0.5)	4.00 (2–5)	4.01 (0.7)	4.00 (2–5)	0.91

SD: standard deviation, min: minumum, max: maximum, DM: diabetes mellitus.
*Mann–Whitney *U*-test.

When comparing the two groups, no significant differences were found between the pre-operative creatinine values (p = 0.294). The postoperative creatinine values on days 2 and 5 were significantly higher in group 1 compared to group 2 (p = 0.033 and p = 0.005 respectively). Pre- and post-operative data are shown in Table 3.

When both groups were evaluated, the post-operative creatinine levels at days 2 and 5 were significantly higher than the pre-operative levels in group 1 (p = 0.008 and p = 0.001, respectively) (Fig. 1). Post-operative creatinine levels increased in group 2, but not to a statistically significant level (Table 4).

The creatinine level increased above 2.0 mg/dl in two patients in the DM group on the second postoperative day. Since the urinary output was less than 0.5 ml/kg/hour, furosemide was given at a dose of 0.5 mg/hour for 12 hours in one patient and 24 hours in the other in order to provide cardiovascular stability. No patient required haemodialysis in the study groups.

The incidence of AKI in the entire patient group was found to be 29%, according to the AKIN criteria. When comparing the patients who developed AKI in the two groups, 21 patients in group 1 and six patients in group 2 developed AKI. This difference was not statistically significant (p = 0.081) (Fig. 2).

The correlation of cross-clamp times and total perfusion times with creatinine change was also examined in the study. In the DM group (group 1), a negative correlation was found between the postoperative creatinine increase on day 5 and the total perfusion time (R = –0.294, p = 0.023).

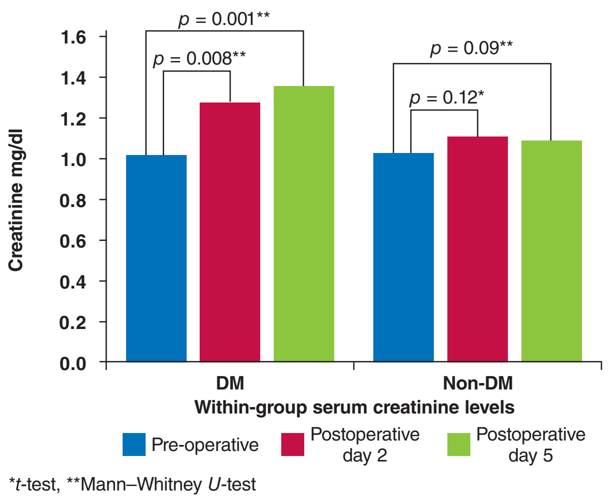

Fig. 1. Within-group serum creatinine levels.

Table 3. Pre- and postoperative data

	DM group (n = *60*)		*Non-DM group* (n = *33*)		
Pre- and postoperative data	Mean (SD)	Median (min–max)	Mean (SD)	Median (min–max)	p-*value*
Pre-operative creatinine (mg/dl)	1.02 (0.17)	1.05 (0.70–1.34)	1.03 (0.18)	0.95 (0.70–1.34)	0.294*
Postoperative day 2 creatinine (mg/dl)	1.28 (0.37)	1.26 (0.49–2.3)	1.11 (0.35)	1.0 (0.62–1.93)	0.033**
Postoperative day 5 creatinine (mg/dl)	1.24 (0.34)	1.36 (0.69–1.63)	1.07 (0.24)	1.09 (0.69–1.63)	0.005*
Drainage amount (ml)	568.78 (198.33)	574.98 (450–630)	514.48 (155.00)	500.00 (450–650)	0.279*
Erythrocytes used	3.3 (0.12)	3 (2–5)	3.12 (0.14)	3 (2–5)	0.897*
Length of stay in ICU (day)	3.65 (1.16)	4 (2–6)	3.12 (0.96)	3 (2–5)	0.031*
Length of stay in hospital (day)	8.50 (1.93)	8 (6–12)	8.48 (1.5)	8 (6–12)	0.960*

DM: diabetes mellitus, min: minimum, max: maximum, ICU: intensive care unit, SD: standard deviation.
*Mann–Whitney *U*-test, ***t*-test.

Table 4. Within-group serum creatinine levels via pre- and postoperative 2nd and 5th days

	Pre-operative creatinine (mg/dl) (P1)		*Postoperative day 2 creatinine (mg/dl) (P2)*		*Postoperative day 5 creatinine (mg/dl) (P5)*	
Groups	*Mean (SD)*	*Median (min–max)*	*Mean (SD)*	*Median (min–max)*	*Mean (SD)*	*Median (min–max)*
DM	1.02 (0.17)	1.05 (0.70–1.34)	1.28 (0.37)	1.26 (0.49–2.3)	1.24 (0.34)	1.36 (0.69–1.63)
Non-DM	1.03 (0.18)	0.95 (0.70–1.34)	1.11 (0.35)	1.0 (0.62–1.93)	1.07 (0.24)	1.09 (0.69–1.63)

DM group: P2 > P1, p = 0.008, P5 > P1, p = 0.001.

The length of stay in the ICU was significantly longer in the DM group than in the non-DM group (p = 0.031). No patient required ultrafiltration in the peri-operative period. With the exception of erythrocyte suspension, no blood product was used in any of the patients in the pre-, intra- or postoperative period. The amount of post-operative drainage and the use of erythrocyte suspension did not differ between the groups (Table 3).

One patient in the DM group developed a saphenous vein infection and three in each group developed atrial fibrillation. These patients returned to sinus rhythm with amiodarone treatment. No in-hospital mortality was observed in the study.

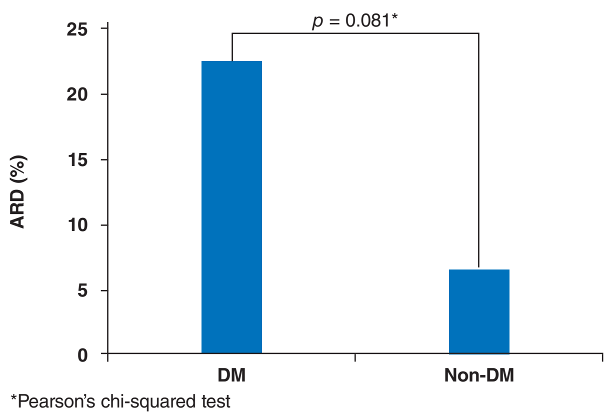

Fig. 2. Intergroup acute renal disease. ARD: acute renal disease, DM: diabetes mellitus.

Discussion

DM is a common disease worldwide and is among the leading causes of cardiovascular diseases. It increases the risk of coronary artery disease and heart failure, and these conditions themselves may increase the risk of kidney failure. In addition, independently of these, DM itself can cause kidney failure. DM is responsible for approximately half of all end-stage renal disease in the United States of America.[10] Approximately half of coronary artery disease patients also have DM.[11]

One of the main treatment options for coronary artery disease is CABG surgery. It has been found that 30% of patients undergoing this operation have DM.[12] DM, LLVEF and renal dysfunction are some of the most important factors that increase mortality and morbidity rates in patients undergoing CABG surgery.

So what happens to patients with risk factors such as DM and LLVEF? There is a wealth of data that can be used to draw beneficial conclusions for patients. Guidelines recommend that CABG surgery should be performed in appropriate patients with the above risk factors, as total revascularisation can be achieved.[13]

As mentioned above, patients with LLVEF are at risk of renal failure, and CABG surgery in these patients increases this risk. It is well known that renal hypoperfusion and inflammatory damage caused by CPB via complex mechanisms are the causes of renal failure.[5] The reported incidence of AKI associated with cardiac surgery varies between five and 42%, depending on the population studied.[14] In patients undergoing CABG surgery, AKI developed in 26% of patients with LLVEF, and this is of course much more common in patients with DM.[15]

In the present study, serum creatinine levels were found to increase in the postoperative period in all patients undergoing CABG surgery in patients with pre-operative LLVEF < 35%. The study compared DM and non-DM control groups and although the percentage of AKI was numerically higher in the DM group, this did not reach statistical significance. However, there was a statistically significant increase in creatinine level change on days 2 and 5 postoperatively in the DM group.

AKI is a common complication after cardiac surgery, prolonging ICU stay and hospitalisation.[16] In their study of 1 881 patients undergoing open-heart surgery, Bastin *et al.*[17] reported that AKI developed in 25.9% of patients, according to the AKIN classification. Sampaio *et al*.[18] found that AKI developed in 51%, according to the AKIN classification.

In the present study, the rate of AKI was found to be 29% in all patients, which is consistent with the literature. In addition, the length of stay in ICU was found to be statistically significantly longer in the DM group, with markedly higher serum creatinine levels than in the control group. This is also in line with the literature. Renal dysfunction and atrial fibrillation, which require balanced postoperative haemodynamics, fluid management, and good treatment and monitoring, were considered to be factors prolonging the ICU stay of patients in our study.

DM is an independent risk factor for renal failure. The need for haemodialysis in the postoperative period, and mortality and morbidity associated with renal complications in diabetic patients ranged from 28–63% in various studies and were significantly higher than in non-DM patients.[19] In the present study, the percentage of AKI was found to be higher in the DM group, in line with the literature. However, this rate was not statistically significant when compared to the control group.

Cross-clamp times are prolonged in DM patients because of the high number of bypassed vessels. Although studies have shown a correlation between cross-clamp times and creatine elevation, no correlations were found between cross-clamp time and postoperative creatinine elevation in our study.[20] We believe that the reason for this is the limited number of patients.

Excessive amounts of blood transfusion, which is also considered to be tissue transplantation, causes more renal dysfunction and, of course, high morbidity and mortality rates. In a study comparing off- and on-pump CABG surgery, it was found that post-operative haematocrit levels were lower and amount of transfused blood products were higher in the on-pump group, associated with haemodilution, significant changes in intravascular volume, mechanical trauma to blood cells and more blood loss due to impaired coagulation status as a result of hypothermia.[21] However, in the same study, although the number of patients who developed acute renal failure was higher in the on-pump group, no statistically significant difference was found between the two groups.

In our study, there was no difference between the groups in terms of drainage and blood product replacement. Therefore, it is not possible to say that drainage and blood products were effective in terms of creatinine elevation in this study. Further studies with larger numbers of patients are needed.

Changes in serum creatinine levels are the most widely used method of monitoring renal dysfunction.[22] One of the major limitations of our study was that renal function was followed by only serum creatinine monitoring. More detailed studies on this topic are underway. The small number of patients and the inclusion of isolated CABG surgery patients are further limitations of this study.

Conclusion

It is well known that DM is one of the causes of kidney failure. This study showed that creatinine levels increased in the DM group after CABG surgery was performed in patients with LLVEF, which is also a risk factor for kidney failure. We believe that careful postoperative follow up in this group of patients could reduce the risk of permanent haemodialysis. It is predicted that minimal changes in creatinine levels after surgery, which means a small impairment in renal function, may have a negative effect on the outcome. Efficient follow up in the early postoperative period, recognising these changes, and taking precautions may lead to positive results.

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