ORIGINAL PAPERS

Adv Clin Exp Med 2015, **24**, 5, 845–850
DOI: 10.17219/acem/23463

ISSN 1899–5276

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Does the Stage of Chronic Kidney Failure Influence the Outcome in Cardiac Surgery?

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article

Abstract

Background. The number of patients with chronic kidney failure requiring cardiac surgery is continuously increasing. Additionally, significant worsening in the overall risk profile of this group of patients is noted.
Objectives. To investigate the effect of chronic renal dysfunction both in non-dialysis-dependent renal failure and end-stage renal failure patients, on early mortality – morbidity and late survival in a series of cardiac surgery patients at our institution.
Material and Methods. 1344 patients who had open heart surgery at our university hospital between 2010 and 2013 were retrospectively reviewed. Chronic renal dysfunction was defined according to preoperative glomerular filtration rate. Patients selection (n = 80). Group 1 mild – (GRF 59–30 mL/min), Group 2 moderate – (GFR 29–15 mL/min), Group 3 end stage – (GFR < 15 mL/min) renal failure.
Results. Chronic renal dysfunction was present in 5.95 % of all patients studied. Group 1 – 55 (68.75%), Group 2 – 16 (20%), Group 3 – 9 (11.25%). No difference between the groups in the need for heart inotropic support was noted; however the use of these medications was necessary in 60.6% of all studied patients. Forty nine percent in Group 1, 87.5% in Group 2 and 77% in Group 3, respectively. Renal replacement therapy in the early postoperative period was needed in 12 patients, with significance between the groups (p = 0.001). The overall hospital mortality was 2.5%. Follow-up was completed with a mean of 1.4 years (range 2 months to 4 years). There were 6 (7.5%) late deaths.
Conclusions. Our observations do not exhibit large variations in postoperative complications and deaths in patients with chronic renal failure, depending on the degree of preoperative renal function impairment. It seems that renal failure regardless of the degree of impairment is a factor aggravating the intra and post-operative course in cardiac surgery patients (**Adv Clin Exp Med 2015, 24, 5, 845–850**).

Key words: chronic kidney failure, cardiac surgery, glomerular filtration rate.

Chronic renal failure is commonly associated with coronary atherosclerotic disease and valvular heart disease [1]. Cardiovascular disorders are the leading cause of death in this group of patients [2, 3]. High perioperative risk in chronic renal dysfunction patients is the result of many associated factors such as anemia, hypertension, volume overload and the growth of calcium phosphate products, resulting from hyperparathyroidism secondary to uremia [4]. Structural and functional changes in the heart muscle (left ventricular hypertrophy) in these patients, and progressive changes in the vascular wall are other cardiovascular risk factors.

In recent years the number of patients with impaired renal function requiring cardiac surgery is continuously increasing. In addition to the growing number of these patients, there has been a significant worsening in the overall risk profile of patients referred for cardiac surgery, and the findings of previous studies may therefore not be reliably applicable. The relationship between mild-to-moderate renal insufficiency and post -operative clinical outcomes after cardiac surgery

has been most assessed based on the serum creatinine levels and not the glomerular filtration rate (GFR). Serum creatinine levels are affected by several factors in the body and may not be reliable enough on their own because kidney lesions and decreased glomerular filtration may also be present in individuals with normal serum creatinine values.

It is well known that end-stage renal failure (ESRF) requiring dialysis negatively impacts the early and late outcome of patients undergoing cardiac surgery. Data with respect to non-dialysis-dependent renal failure patients (NDRF) is more limited, and additionally, these studies have provided limited information regarding long-term survival and its predictors in this population [5, 6].

This study was designed to investigate the effect of chronic renal dysfunction both in NDRF and ESRD on early mortality and morbidity as well as late survival in a series of patients who underwent cardiac surgery at our institution.

Methods

Patients

The records of all 1344 patients who had open heart surgery performed at our University Hospital between January 2010 and December 2013 were retrospectively reviewed. Chronic renal dysfunction was defined according to the level of kidney function (glomerular filtration rate [GFR]), irrespective of diagnosis according to the National Kidney Foundation, K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Based on this criteria, we selected 80 patients, fulfilling the criteria of renal failure: mild – (GRF 59–30 mL/min), moderate – (GFR 29–15 mL/min), ESRD – (GFR < < 15 mL/min). Outcomes were compared between the three groups of patient cohorts for perioperative mortality, morbidity and long-term survival. The three groups were unevenly matched as this was not a randomized study, but a case control study.

All patients with ESRD were on maintenance hemodialysis prior to surgery.

Surgical Procedures

All surgeries were performed using median sternotomy with standard techniques with either cardiopulmonary bypass with systemic normothermia, using a Dideco Compacflo membrane oxygenator (Sorin Group) and the roller pump with non-pulsatile blood flow 2, 2-2, 4 L/m^2/min. mounted on the CPB unit Stoeckert S3 (Stoeckert, Munich, Germany) or off pump coronary artery bypass (OPCAB) for patients undergoing isolated coronary artery bypass surgery.

Data Collection and Follow-Up

Preoperative data collection included: patient demographics, preoperative risk factors, left ventricular ejection fraction (EF), NyHA class status, preoperative medications, concomitant diseases, type and mode of indication for surgery, intraoperative variables and postoperative complications.

Additionally, the following parameters were analyzed: hemoglobin (Hb), leukocytes (L), platelets (PLT), troponin I (TnI), C-reactive protein (CRP), procalcitonin (PCT), aspartate transaminase (AST), alanine transaminase (ALT).

Perioperative data collection included: time of surgery, cardiopulmonary bypass time, aortic cross-clamp time, postoperative ICU stay and duration of hospitalization. We evaluated the need for early postoperative inotropic support of cardiac function, and the need for intra-aortic balloon support and all cause complications.

The elected parameters were evaluated at three time points: 0 – before surgery, 1 – the first day after surgery, 2 – before discharge from the hospital.

Post-hospital discharge follow-up occurred through hospital visits, telephone calls, and use of an administrative database of death records. Patients with no death record as of January 2014 were considered to be alive. Death was defined as all--cause mortality.

The patient follow-ups covered the period from 1–3 years, and will be continued in the subsequent years.

Statistical Analysis

All data was entered into an Excel spread sheet and was transferred to STATISTICA 10.0 for further statistical analysis. Categorical variables were reported using number and percent of observations, while continuous variables were reported as mean ± standard deviations. The Shapiro-Wilk test applied at the beginning rejected the hypothesis of normal distribution of the variables tested; thereby further study used non-parametric tests. Categorical variables were compared using the Pearson chi square as proper. The non-parametric ANOVA Kruskal-Wallis test for multiple comparisons of average ranks (test *post hoc*) was used.

Results

Patient Presentation

From a total of 1344 patients operated on at our institution in the reporting period, according to the established criteria, chronic renal dysfunction was present in 80 (5.95 %) patients. Mild NDRF (group 1) – 55 (68.75%) patients, moderate NDRF (group 2) – 16 (20%) patients, and ESRD (group 3), 9 (11.25%) patients. Among the patients who were followed in this study, one patient was operated on with emergency indications, the remaining 79 were given elective cardiac surgery. Within this group, 52 (65%) patients had surgical myocardial revascularization, 15 (18.75%) replacement surgery of one or two valves and 13 (16.25%) combined surgery. The three studied groups were similar with respect to the type of surgical procedure (Table 1).

The mean age of patients in group 3 (ESRD) was significantly lower (p = 0018) when compared to group 2 and group 1 (Table 2).

Table 2 shows the distribution of co-morbid risk factors across patients with renal dysfunction in selected groups.

Diabetes was present in 26.2% of patients without significant differences in the groups, and hypertension in 90.0% of patients. Cigarette smokers were 10% of the studied population. 82.5% patients were on statins and 90% on beta-blocker treatment preoperatively.

Hemoglobin concentration was significant lower in ESRD patients (group 3) when compared to other groups, in the entire time of observation (Hb 1-p = 0.01, Hb 2-p = 0.006). Similar differences were observed in hematocrit values. It was evident, however, taking into account the increasing degree of renal impairment underlying the breakdown into groups.

Hospital Morbidity

No significant differences between the groups were noted in the serum concentration of CRP, leukocytes, thrombocytes, procalcitonin, troponin I, AST, and ALT in the entire time of observation. There were also no differences between groups in the incidence of atrial fibrillation, hypertension, use of beta blockers and converting enzyme inhibitors (data not shown).

The operative data and type of surgery performed are presented in Table 3. No matter the numerical values, there were also no significant differences between groups in duration time of cardiopulmonary bypass and aortic cross-clamp time.

There was also no difference between the groups in the need for heart inotropic support and the use of intra-aortic balloon pump. It should be noted, however, that the use of these medications was necessary in 60.6% of all studied patients, 49% in group 1, 87.5% in group 2 and 77% in group 3, respectively.

Table 1. Demographic data of studied groups (n = 80)

	Group 1 (n = 55)	**Group 2 (n = 16)**	**Group 3 (n = 9)**
Age (years) ± SD	70.6 ± 8.79	66.0 ± 8.79	60.0 ± 6.96
Female gender	20 (36.36%)	6 (37.50%)	2 (22.22%)
Arterial hypertension	50 (90.91%)	15 (88.24%)	8 (88.89%)
Diabetes mellitus	15 (27.27%)	4 (25.00%)	2 (22.22%)
Smoking	7 (12.73%)	0	1 (11.11%)
Preoperative medications			
Statins Beta blockers ACEI	47 (85.45%) 40 (89.09%) 35 (63.64%)	12 (75%) 15 (93.75%) 6 (37.50%)	7 (77.78%) 8 (88.89%) 3 (33.33%)
EF before operation (%) NYHA Class I NYHA Class II NYHA Class III NYHA Class IV Elective surgery Emergency surgery	53.0% 44 11 0 0 54 1	51.2% 4 12 0 0 16 0	58.0% 0 5 4 0 9 0

Table 2. Surgical procedures performed (n = 80)

Procedure	Group 1 (n = 55)	Group 2 (n = 16)	Group 3 (n = 9)
AVA	3 (5.45%)	1 (6.25%)	1 (11.11%)
AVB	4 (7.27%)	1 (6.25%)	1 (11.11%)
MVA	0	2 (12.50%)	2 (22.22%)
MVB	2 (3.64%)	1 (6.25%)	1 (11.11%)
MVP	10 (18.18%)	2 (12.50%)	1 (11.11%)
TVP	5 (9.09%)	3 (18.75%)	1 (11.11%)
CABG	36 (65.4%)	9 (56.2%)	3 (33.33%)
CABG + AVR or MVP or TVP	7 (12.7%)	6 (37.5%)	0

AVA – aortic valve replacement artificial, AVB – aortic valve replacement biological, MVA – mitral valve replacement artificial, MVB – mitral valve replacement biological, MVP – mitral valve plastic reconstruction, TVP – tricuspid valve plastic reconstruction, CABG – coronary artery bypass grafting.

Table 3. Perioperative data of studied groups (n = 80)

	Group 1 (n = 55)	Group 2 (n = 16)	Group 3 (n = 9)
CPB time (min)	98.77 ± 39.86	109.71 ± 42.25	117.88 ± 30.93
Clamp time (min)	51.42 ± 24.39	61.14 ± 24.38	61.44 ± 24.81
Operation time (min)	221.72 ± 57.20	223.125 ± 65.57	256.11 ± 55.04
ICU (days)	3.037 ± 2.78	4.31 ± 4.94	3.37 ± 3.73
LOS (days)	16.83 ± 6.66	26.31 ± 19.52	14.44 ± 6.80
Complications			
IABP catheter insertion	1 (1.96%)	3 (17.65%)	1 (12.50%)
Inotropic agents	27 (49.0%)	14 (87.%)	7 (77.7%)
Blood transfusion	14 (25.45%)	4 (25.00%)	3 (33.33%)
Repeat thoracotomy	3 (5.45%)	1 (5.88%)	1 (11.11%)
FAC	12 (21.82%)	5 (31.25%)	0
FAP	6 (10.91%)	1 (6.25%)	0
RRT	2 (3.64%)	4 (25.00%)	6 (66.67%)
Mortality			
Early	2 (11.76 %)	0	0
Late	1 (1.81%)	2 (12.5%)	1 (11.11%)
Total	3 (5.45%)	2 (12.5%)	1 (11.11%)

EF – left ventricular ejection fraction, CPB – cardiopulmonary bypass time in min, Clamp time – clamping of aorta time in min, ICU – length of stay in the postoperative intensive care unit, LOS – length of stay in the hospital, IABP – intra-aortic balloon pump, FAC – continuous atrial fibrillation, FAP – paroxysmal atrial fibrillation, RRT – renal replacement therapy.

The study groups did not differ in the amount of blood transfusions and the need to re-open the chest.

The need for renal replacement therapy (RRT) in the early postoperative period was noted in 12 patients, with significance between the groups (p = 0.001). Two patients in group 1 (3.64%) and 4 (25%) in group 2 required RRT in ICU. Only one patient from group 2 was selected for the chronic dialysis program. In group 3, RRT was performed in 6 (66.67%) patients. Patients from this group returned to their mother dialysis centers after surgery for further treatment.

The average stay in ICU was 3.4 days, with no significant differences between the groups.

The length of hospital stay in the whole study group averaged 19.2 days and did not differ significantly between groups.

Hospital Mortality

The overall hospital mortality was 2.5% (2 patients from group 1). Causes of death were low cardiac output syndrome and multiple organ failure.

The relatively low mortality in the study group makes it impossible for statistical evaluation of the risk factors of death.

Long-Term Survival

Follow-up data was completed for all discharged patients with a mean of 1.4 years (range 2 months to 4 years). There were 4 (5%) late deaths. During follow-up, 1 (1.8%) patient in NDRF group 1 died within 3 months after surgery with MI diagnosis, 2 (11.76%) patients in NDRF group 2 died one year after surgery, both after combined CABG/valve surgery and 1 (11.1%) patient in ESRD group 3 died 2 years after surgery (mitral valve replacement due to infective endocarditis).

Discussion

The choice of glomerular filtration rate (GFR), instead of more simple serum creatinine concentrations, seems to be a more sensitive parameter in the assessment of renal function. Serum creatinine is influenced by many factors, among others: muscle mass and diet which cause an observed diversification of its levels especially depending on age, race or geographical conditions [7]. There are also observations indicating that in elderly patients, serum creatinine is not always adequate when assessing renal function [8, 9].

There is general agreement that in patients with chronic renal dysfunction, cardiac surgery leads to significantly more postoperative complications including prolonged mechanical ventilation, frequent need for renal replacement therapy, and consequently a longer postoperative ICU stay.

Our study did not demonstrate significant differences between the groups in the initial risk factor assessments such as hypertension, diabetes, left ventricular ejection fraction, use of angiotensin-converting enzyme inhibitors, beta-blocking agents and statins in the 3 groups of patients with different degrees of renal insufficiency. There were also no differences between the groups in the operating time indices: cardiopulmonary bypass and aortic cross-clamping time – the factors influencing further stay in the ICU and the duration of mechanical ventilation. Our study did not confirm this observation similarly to Simon's, Mangano's and O'Connor's observations [10–12].

There are a number of observations indicating that duration of cardiac surgery increases in line with the decline of the preoperative glomerular filtration rate in this patient population. Similar observations were noted in our study, but regardless of the numerical values that could confirm these opinions, there was no such relationship in the statistical analysis.

ICU length of stay was longer in group 2 and 3 when compared to group 1 but again this was not statistically significant. These results explain the specificity of individual patients and it is not always dependent on preoperative glomerular filtration rate.

Inotropic circulatory support was necessary in 27 patients (49%) in group 1, 14 patients (87.5%) in group 2 and in 7 patients (77.7%) in group 3.

Renal replacement therapy in the ICU was required by 66.67% of patients in group 3, 25% of patients in group 2, and 3.64% in group 1. One patient (in group 2) had exacerbation of renal failure major enough that he had to be sent to the chronic dialysis program.

Group 3 was significantly younger than the other groups, and all groups were dominated by men. According to Diez et al., among many factors, age over 65 years, female gender, surgery on the thoracic aorta, and preoperative atrial fibrillation are associated with worse prognosis after cardiac surgery [13].

All cause postoperative mortality was 7.5%. with the prevalence of late mortality 30 days after hospitalization. Death occurred more frequently in patients undergoing combined procedures (CABG plus valve replacement/reconstruction). In Poland, according to the National Register of cardiac surgery from the period 2006–2009 in-hospital mortality of patients after isolated CABG surgery was 2.86% and 5.57% after valvular surgery [14]. According to other European databases, perioperative mortality after cardiac surgery in patients with end-stage renal failure is much higher and increases depending on the type of operation: isolated CABG is 8.9%, isolated valve replacement is 19.3% and the procedure combining CABG + valve surgery, 39.5% [15].

These results suggest that patients with chronic renal insufficiency undergoing valvular and complex surgery should be in worse condition than the isolated CABG patients. Our results do not confirm these findings, especially in early hospital observation.

The main causes of death in patients with preoperative renal insufficiency are, according to Diez et al., low cardiac output, myocardial infarction, organ failure, sepsis, severe stroke, and pulmonary embolism. In our patients, the most common cause of death was low cardiac output and multiple organ failure.

Long term, up to 3 years' follow up of our patients showed that 4 patients (3 men and 1 woman) out of 6 died more than 30 days after hospitalization, one of them in the chronic hemodialysis program.

Most of the scientific reports with a risk factor assessment of late mortality after cardiac surgery in patients with chronic renal failure indicate that renal failure is an independent risk factor for late mortality, similar to age above 70 years, hypertension, COPD and diabetes mellitus.

Chronic renal dysfunction is an important independent predictor of postoperative early and late mortality in patients undergoing cardiac surgery. It increases the risk of postoperative complications in patients undergoing particularly complex revascularization surgery and valve replacement. Decreased preoperative levels of glomerular filtration rate is a simple marker of increased risk of infection, clotting disorders, impaired vascular endothelial function, stiffness and calcification of blood vessels, and left ventricular hypertrophy. All this results in the frequent need for the use of inotropic agents and cardiac assist devices in the early postoperative period. Our observations do not exhibit large variations in postoperative complications and deaths in patients with chronic renal failure, depending on the degree of renal function impairment. It turns out that mere renal failure regardless of the degree of impairment is a factor aggravating the intra- and post-operative course in cardiac surgery patients.

This study indicates the importance of the problem appearing with the increasing number of heart operations performed in this group of patients. It seems that a carefully-designed perioperative strategy, and the different approaches to renal protection techniques, should reduce morbidity and mortality among this population of patients.

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Conflict of interest: None declared

Received: 20.02.2014
Revised: 22.04.2014
Accepted: 24.06.2014