SERBIAN ARCHIVES OF MEDICINE Est.1872

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Paper Accepted* **ISSN Online 2406-0895**

Original Article / Оригинални рад

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Cardiac surgery in patients with chronic renal failure

Кардиохирургија код болесника са хроничном бубрежном инсуфицијенцијом

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Received: October 25, 2016
Revised: March 21, 2017
Accepted: March 21, 2017
Online First: March 31, 2017
DOI: 10.2298/SARH161025097B

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SUMMARY

Introduction/Objective Patients with chronic renal failure (CRF) undergoing cardiac surgery are believed to have more postoperative complications and significantly higher mortality rate.

The aim of this work was to determine preoperative predictors of exacerbation of CRF and the outcome in patients with CRF submitted to cardiac surgery.

Methods A retrospective study included 169 patients hospitalized from 2012 to 2015 (age 67.71±8.46 years, 72.3% male). The analysis included numerous perioperative characteristics.

Results Preoperative stage I CRF was present in 62 (37%), stage II in 77 (46%) and stage III-V in 30 (17%) patients. Exacerbation of CRF was registered in 37 (21.9%) and the lethal outcome in 16 (9.5%) patients. Stage II of CRF (Odds ratio [OR] 4.76; 95% Confidence interval [CI] 1.31-17.28; p=0.018) and stage III-V of CRF (OR 11.39; 95% CI 2.87-45.14; p=0.001) were designated as predictors for exacerbation of CRF following cardiac surgery. In patients with CRF stage I and II, multivariate analysis designated previous cerebrovascular insult (OR 3.36; 95% CI 1.04-10.93; p=0.044) and ejection fraction ≤35% (OR 5.35; 95% CI 1.83-15.64; p=0.02) as predictors for exacerbation of CRF. The only predictor of postoperative dialysis requirement was higher stage of CRF (OR 5.81; 95% CI 1.22-27.81; p=0.028). CRF stage III-V was a predictor of lethal outcome (OR 7.64; 95% CI 1.49-39.27; p=0.015).

Conclusion Higher stage of CRF in patients submitted to cardiac surgery is a predictor of exacerbation of renal failure and the lethal outcome.

Keywords: chronic renal failure; cardiac surgeries; morbidity; mortality

САЖЕТАК

Увод/Циљ Сматра се да болесници са хроничном бубрежном инсуфицијенцијом (ХБИ) после кардиохируршких операција имају више оперативних компликација и знатно повећану смртност.

Циљ рада је био да се одреде преоперативни показатељи погоршања ХБИ и смртног исхода код болесника са ХБИ и кардиохируршким операцијама.

Методе Ретроспективно су анализиране периоперативне карактеристике код 169 болесника (старости 67,71±8,46 година, 72,3% мушкараца) лечених од 2012 до 2015.

Резултати рада Преоперативно, у I стадијуму ХБИ било је 62 (37%), у II – 77 (46%), а III-V стадијуму 30 (17%) болесника. Погоршање ХБИ регистровано је код 37 (21,9%), а смртни исход код 16 болесника (9,5%). II стадијум ХБИ (OR 4,76; 95% CI 1,31-17,28; п=0,018) и III-V стадијум ХБИ (OR 11,39; 95% CI 2,87-45,14; *p*=0,001) били су предиктори акутизације ХБИ. Код болесника са I и II стадијумом ХБИ, мултиваријантни предиктори акутизације ХБИ били су: претходни цереброваскуларни инзулт (OR 3,36; 95% CI 1,04-10,93; *p*=0,044) и ејекциона фракција≤35% (OR 5,35; 95% CI 1,83-15,64; *p*=0,02). Једини предиктор постоперативне дијализе је виши стадијум ХБИ (OR 5,81; 95% CI 1,22-27,81; *p*=0,028). III-V стадијум ХБИ био је предиктор смртног исхода (OR 7,64; 95% CI 1,49-39,27; *p*=0,015).

Закључак Тежи стадијум ХБИ код болесника подвргнутих кардиохируршким операцијама јесте предиктор погоршања бубрежне инсуфицијенције и смртног исхода.

Кључне речи: хронична бубрежна инсуфицијенција, кардиохирургија, морбидитет, морталитет

INTRODUCTION

There is a significant increase in the number of patients with chronic renal failure (CRF) who require cardiac surgery. Heart diseases are more frequent in this specific population compared to the general population [1]. Terminal renal failure is recognized as a significant risk factor for the outcome of cardiac surgery. The prognosis of patients diagnosed with cardiovascular disease and CRF is much worse than in patients without this associated morbidity. In patients with impaired renal function, cardiac surgery may cause aggravation of pre-existing renal failure or irreversible renal damage [1]. The problems these patients have are further complicated during open heart surgery when extracorporeal circulation is used.

In order to reduce perioperative risk, an optimal perioperative strategy is required. Most published studies emphasize the importance that preoperative clinical status has on postoperative

mortality and morbidity in this category of patients, but little is known about the predictive factors for long-term survival. In patients with mild to moderate reduction of glomerular filtration rate (GFR), there is quite consistent evidence that surgical revascularization is a better therapeutic option compared to percutaneous coronary intervention (PCI) [2]. This especially applies to patients with CRF caused by diabetes mellitus, who are recommended "off pump" surgery [3,4]. In patients with the terminal phase of the renal disease, there is no such clear evidence in favor of surgical approach. Better long-term results in these patients are being achieved with the surgical approach, but with the higher rate of intra-hospital events and complications, whereas *vice versa* is true for PCI comparing to coronary artery bypass grafting (CABG).

Only 15 years ago, patients with CRF were believed to have unacceptably high operative risk and only a rare underwent cardiac surgery [5,6]. Perioperative treatment strategy of these patients in intensive care units is constantly improving. Based on the research results and improving clinical practice results, the attitude towards candidates for cardiac surgery with CRF has been dramatically changed.

In our study, we sought to determine: 1) Present preoperative clinical CRF patient profile; 2) Examine occurrence of postoperative morbidity and mortality in patients with CRF who underwent cardiac surgery.

METHODS

This retrospective analysis included 169 patients with CRF who underwent cardiac surgery (coronary, valvular, and combined) during the period 2012-2015, at the Institute of Cardiovascular Diseases Vojvodina. Patients with CRF were divided into three groups according to the creatinine clearance (CC) values [1]. The first group was comprised of patients with CC ≥ 90 mm/min/1.73 m^2, the second group – patients with CC 60-89 mm/min/1.73 m^2, and the third group – patients with CC 15-59 mm/min/1.73 m^2. The third group included all the patients with CRF stage III, IV and V, considering the small number of patients in each stage separately. Following comorbidities and patient characteristics were assessed: high blood pressure (>140/90 mmHg), diabetes, blood lipid levels, chronic obstructive pulmonary disease, peripheral arterial occlusive disease, cerebrovascular insult, myocardial infarction, heart failure (HF) class using New York Heart Association (NYHA) III/IV classification, left ventricle ejection fraction (EF) ≤ 35%. Following postoperative complications were assessed: new onset of myocardial infarction, heart rhythm disturbances, cerebrovascular insult, sepsis, sternal infection, return to the intensive care unit, respiratory insufficiency, pericardial effusion, exacerbation of renal failure and lethal outcome.

Heart surgeries were performed using extracorporeal circulation, in moderate hypothermia and perfusion pressure >50 mmHg. Heart was stopped using the cold antegrade St Thomas' Hospital cardioplegia (with 40 mmol/l K^+). Intraoperative and postoperative monitoring included ECG,

transesophageal echocardiography, oxygen saturation (pulse oximetry), diuresis, continual measurement of arterial, central venous and pulmonary arterial pressure.

Criteria for the diagnosis of HF were defined as the need to ensure hemodynamic support with the inotrops: adrenaline, dobutamine (>5 mg/kg) and/or high doses of dopamine longer than 24 hours, and the value of cardiac index <2.0 l/min/m^2 [2].

Postoperative myocardial infarction was defined as an increase of cardiac enzymes following the surgery (troponin and CK-MB) more than 10 times compared to reference levels [5]. Heart rhythm disturbances were defined as the new onset of arrhythmia - atrial fibrillation or ventricular tachycardia. Cerebrovascular event was defined as an isolated neurological deficit after the surgery. Respiratory failure was defined as a requirement for mechanical ventilation longer than 24 hours. Septic attack was diagnosed on the basis of sepsis criteria (white blood cell count, body temperature, respiratory rate, inflammatory mediators: CRP, fibrinogen, procalcitonin, and positive blood cultures). Pericardial effusion was defined as the presence of abnormal amount of fluid in pericardial cavity - more than 100 ml. Exacerbation of renal failure was defined as significant increase of nitrogenous substances in blood comparing to preoperative values [4]. Hospital mortality was defined as any death that occurred during index hospitalization.

Statistical analysis was performed using the SPSS 19 (Statistical Package for Social Science). A p value of <0.05 was considered statistically significant. The Kolmogorov–Smirnov test was used for determination of quantitative data distribution. Differences of mean values were tested by the independent samples t-test or Mann-Whitney U test and results are presented as mean (standard deviation). The relations between categorical variables were tested using the chi-square (χ^2) test and the results are presented as frequencies and percentages. Univariate and multivariate binary logistic regression were performed to determine the effects of all the factors on the dependent variable. Only variables designated as significant by a univariate analysis were entered into multivariate regression analysis.

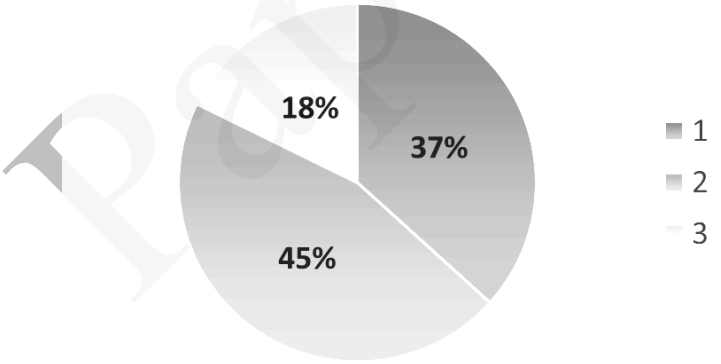

Figure 1. Representation of patients with CRF based on creatinine clearance. 1–Patients with creatinine clearance ≥ 90 mm/min/1,73m^2 ; 2– Patients with creatinine clearance 60-89 mm/min/1,73m^2 ; 3–Patients with creatinine clearance 15-59 mm/min/1,73m^2.

RESULTS

The study was conducted on 169 CRF patients, mean age 67.71±8.46 years, of whom 125 patients (73.9%) were males. The number and percentage of patients according to the CRF stage is presented in the Figure 1. Majority of patients were classified into CRF stage II (45%).

High blood pressure was detected

in 166 patients (98.2%). There was no statistically significant difference between the number of patients with high blood pressure within different stages of renal failure (p> 0.05). Diabetes mellitus was present in 64 (37.8%) patients. There was no statistically significant difference in the incidence of diabetes mellitus throughout renal failure stages (p>0.05).

Significant difference was noted in the incidence of patients with HF (p=0.018), NYHA III/IV stage (p=0.032) and EF≤35% according to the renal failure stage. Comparing patients with the stage II CRF to those with the stage I, there was statistically significant difference in the incidence of patients with NYHA III/IV stage (p=0.017) and EF≤35% (p=0.013). There was statistically significant difference in the incidence of patients with HF (p=0.005), NYHA III/IV (p=0.022) and EF≤35% (p=0.026) when comparing patients with the stage III-IV CRF to those with the stage I.

Table 1. Preoperative characteristics of patients with CRF.

	Renal failure stage			*p*
	1	2	3	
	n (%)	n (%)	n (%)	
SEX (male)	49 (79%)	51 (66,2%)	25 (73,5%)	0,242
HBP	60 (96,8%)	76 (98,7%)	34 (100,0%)	0,473
DM	19 (30,6%)	32 (41,6%)	13 (38,2%)	0,410
HLP	45 (72,6%)	56 (72,7%)	25 (73,5%)	0,995
COPD	12 (19,4%)	11(14,3%)	6 (18,2)	0,712
PAOD	4 (6,5%)	3 (3,9%)	1 (2,9%)	0,677
CVI	7 (11,3%)	16 (20,8%)	5 (14,7%)	0,309
MI	28 (45,2%)	36 (46,8%)	19 (55,9%)	0,579
HF	19 (30,6%)	32 (41,6%)	20 (60,6)	0,018
NYHA III/IV	8 (12,9%)	23 (29,9%)	11 (32,4%)	0,032
EF≤35	7 (11,3%)	22 (28,6%)	10 (29,4%)	0,030

HBP – high blood pressure, **DM**-diabetes mellitus, **HLP** - hyperlipoproteinemia, **COPD** – chronic obstructive pulmonary disease, **PAOD** –peripheral arterial occlusive disease, **CVI** – cerebrovascular insult, **MI** – myocardial infarction, **HF** – heart failure, **NYHA** – New York Heart Association, **EF** – ejection fraction.

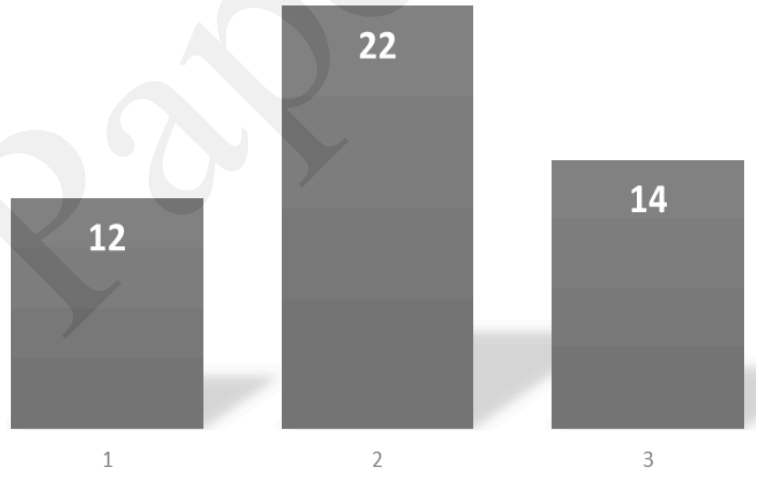

Figure 2. Representation of patients with postoperative HF according to CRF stage (1 – Patients with creatinine clearance ≥ 90 mm/min/1,73m^2 ; 2 – Patients with creatinine clearance 60-89 mm/min/1,73m^2 ; 3 – Patients with creatinine clearance 15-59 mm/min/1,73m^2).

Previous myocardial infarction (MI) was present in 83(49.1%) patients. There was no significant difference in the incidence of MI throughout the stages of renal failure (p>0.05) (Table 1).

The number of patients who underwent coronary surgery was 90 (53.2%), valvular surgery 36 (21.3%) and combined surgery 43 (25.5%). Mean duration of extracorporeal circulation was 88.23±35.52 min.

There was no significant difference in the incidence of patients with the new onset of MI in regard to the CRF stage (p>0.05). New onset of MI was a rare complication after surgery in patients with CRF. There was no significant difference in the incidence of patients with arrhythmias, CVI and sepsis rate in regard to the CRF stage (p>0.05).

Significant difference in the incidence of respiratory failure with regard to the CRF stage (p=0.049) was noted, and it was most notable between CRF stage I and stages III-IV (p=0.016). Postoperative occurence of HF – defined as the need to ensure hemodynamic support with the inotrops (adrenaline, dobutamine >5 mg/kg, and/or high doses of dopamine longer than 24 hours), and the value of cardiac index <2.0 l/min/m^2 – is presented in Figure 2 (p<0.0001).

Highly significant difference was present in the incidence of acute exacerbation of renal failure with regard to the CRF stage (p<0.01) – between the CRF stages I and II (p=0.011), II and III-V(p=0.016) and between the CRF stages I and III-V (p<0.01). Also, there was significant difference in the mortality rate in regard to the CRF stage (p=0.021) – between the CRF stages I and III-V (p=0.006) (Table 2).

Table 2. Postoperative complication in patients with CRF.

Postoperative complications	Renal failure stage			*p*
	1	2	3	
	n (%)	n (%)	n (%)	
NOMI	0	2 (2,6%)	2 (5,9%)	0,185
NOHA	24 (38,7%)	35 (45,5%)	15 (44,1%)	0,716
NOCVI	2 (3,2%)	4 (5,2%)	0	0,383
SEPSIS	2 (3,2%)	3 (3,9%)	1 (2,9%)	0,690
STERINF	2 (3,2%)	4 (5,2%)	1 (2,9%)	0,788
RET to ICU	6 (9,7%)	10 (13,0%)	7 (20,6%)	0,320
RESP FAIL	4 (6,5%)	9 (11,7%)	8 (23,5%)	0,049
PER EFF	5 (8,1%)	12 (15,6%)	5 (14,7%)	0,387
AC RF	3 (4,8%)	15 (19,5%)	14 (41,2%)	0,000
Mortality	2 (3,3%)	7 (9,1%)	7 (20,6%)	0,021

NOMI – new onset of myocardial infarction, **NOHA** – new onset of heart arrhythmias, **NOCVI** – new onset of cerebrovascular insult, **STERNINF** – sternal infection, **RET to ICU** – return to the intensive care unit, **RESP FAIL** – respiratory failure, **PER EFF** – pericardial effusion, **AC RF**- acute exacerbation of renal failure.

A total of 16 deaths was registered. Thereof, 7 patients underwent coronary surgery, 6 underwent combined surgery and 3 patients underwent valve surgery. Seven patients were in the CRF stage III–V, seven patients were in the CRF stage II, and two patients were in the CRF stage I.

Univariate analysis designated CRF stage as a predictor of the occurrence of respiratory failure after surgery (OR=2.1; 95% CI 1.12-4.07; p=0.021) and CRF stage III-V (OR=4.46; 95% CI 1.23-16.15; p=0.023). CRF stage was also the predictor of in-hospital mortality (OR=2.72; 95% CI 1.27-5.08; p=0.009) and CRF stage III-V (OR=7.64; 95% CI 1.49-39.27; p=0.015). Preoperative CRF stage was the predictor of acute exacerbation of renal failure following surgery (OR=3.14; 95% CI 1.69-5.79; p<0.01), stage II (OR=4.76; 95% CI 1.31-17.28; p=0.018) and CRF stage III-V (OR=11.39; 95% CI 2.87- 45.14; p=0.001).

In patients with the CRF stage I and II, the univariate predictors of acute exacerbation of CRF were preoperative CVI (OR=3.06; 95% CI 1.01–9.25; p=0.048), NYHA III/IV (OR=4.5; 95% CI 1.60–12.64; p=0.004), EF≤35% (OR=5.05; 95% CI 1.78–14.30; p=0.002) and CRF stage (OR=4.76; 95% CI 1.31–17.28; p=0.018). In patients with the CRF stage I and II, the multivariate predictors of acute exacerbation of CRF were previous CVI (OR=3.36; 95% CI 1.04–10.93; p=0.044) and EF≤35% (OR=5.35; 95% CI 1.83–15.64; p=0.02).

DISCUSSION

The global number of cardiac surgery procedures performed in patients with CRF is constantly increasing [2,3]. According to the available data, adverse cardiovascular events are the most important cause of death in patients with CRF. Development of exacerbation of CRF is correlated with substantial short- and long-term morbidity and mortality. The pathogenesis is multifactorial. Hemodynamic, inflammatory, metabolic and nephrotoxic factors are involved and overlap each other, which lead to further aggravation of renal failure. Preoperative risk factors include advanced age, impaired left ventricular function or congestive HF, diabetes, chronic obstructive pulmonary disease and the urgency of the operation [7,8].

In large studies that have addressed this issue, the most commonly described postoperative morbidity included: respiratory failure, arrhythmias, acute exacerbation of renal insufficiency, pericardial effusion. Most of these complications might be explained, to an extent, through hypervolemic state developed early after the surgery (inadequate fluid management). Contrary to our findings, the need for dialysis was over 15% [9].

The high frequency of postoperative arrhythmias can be compared with the results of other studies as a result of electrolyte imbalance in the perioperative period [10-15]. The tendency to infection is a common feature for these patients, due to reduced chemotaxis, lymphopenia, decreased cell-mediated immunity and reduction functions of monocytes. In our study, patients underwent antibiotic protection so no significant occurrence of infection was recorded compared to other studies where the presence of sternal infection was around 8% [16-19].

A retrospective analysis of patients undergoing CABG at Cleveland Clinic found that level of creatinine over 168 mmol/l results in a higher perioperative morbidity (2.8%) and mortality (3.7%). Hospital mortality in patients with CRF submitted to cardiac surgery goes up to 36.7% as reported in large multicenter studies [20-23]. Our results are in line with the reports of cardiovascular centers around the world, and also with the largest multi-center study performed so far in which the mortality was 12.5% [24]. Our analyses designated the following factors as predictors of postoperative mortality of CRF patients: COPD and diabetes. Isolated coronary surgery is associated with the lowest incidence of acute exacerbation of CRF, followed by valvular and combined operations as is the case with our group of patients [25].

In terms of prevention of acute exacerbation of renal failure after surgery, a proper preoperative patient management is required especially those on chronic dialysis, patients with pulmonary diseases and metabolic disorders (diabetes). As our understanding of the pathogenesis of renal injury following cardiac surgery grows, better preventive and therapeutic strategies will arise. Current approaches include deferring elective surgery, until there is adequate recovery following pre-existing renal injury, careful pre-operative risk stratification of patients and consideration of less invasive procedures in those at greatest risk [26].

CONCLUSION

Preoperative chronic renal failure leads to an increased morbidity and mortality in patients submitted to cardiac surgery. Therefore, a careful preoperative evaluation is warranted as well as optimal perioperative management and treatment strategy for the purpose of risk reduction.

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