Acute Kidney Injury after Cardiac Surgery

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Background: Renal dysfunction is one of the most common complications after cardiac surgery. The major concern is that despite advances in bypass techniques, intensive care and delivery of hemodialysis, mortality and morbidity associated with renal failure have not markedly changed in the last decade. The purpose of this work was to study the incidence of renal dysfunction after cardiac surgery, analyzing the possible causes, associated risk factors and treatment methods used.
Material and methods: In this prospective observational study we analyzed patients undergoing open-heart surgery between October 1, 2010 – December 15, 2010 at the Clinic of Cardiac Surgery Târgu Mureş. Blood urea nitrogen and creatinine level were recorded for all patients before and after surgery, patients age, sex, type of surgical intervention, length of cardiopulmonary bypass, and the degree of intraoperative hypothermia, hemodilution and postoperative hemodynamic function were noted.
Results: In this period 89 patients underwent cardiac surgery. Renal dysfunction developed in 20.2% of the patients and was more common in patients with complex surgery with prolonged cardiopulmonary bypass ($p<0.0167$), in patients with intraoperative hemodynamic instability. Other intraoperative factors, such as hemoglobin level lower than 8 g/dl ($p=0.0103$), postoperative hemodynamic dysfunction and use of vasoconstrictor agents also influenced the development of renal dysfunction.
Conclusions. Cardiac surgery is associated with a relative high incidence of renal dysfunction. Risk factors for this syndrome are varied and involve hemodynamic and inflammatory changes, but factors such as the body temperature and hemoglobin level during extracorporeal circulation could have a significant contribution.

Keywords: renal dysfunction/failure, cardiac surgery, creatinine, urea, cardiopulmonary bypass

Introduction

Acute renal failure is one of the major postoperative complications after open heart surgery, with clinical manifestation ranging from a mild elevation in serum creatinine to anuric renal failure.

Depending on the definition, the incidence of acute renal failure after cardiac surgery varies between 7 to 30%. The incidence of severe kidney injury that requires dialysis is approximately 1–3% [1,2]. The major concern is that occurrence of postoperative renal failure is associated with a high mortality rate (24% to 70%), and despite advances in bypass techniques, intensive care, and delivery of hemodialysis, mortality and morbidity associated with acute renal failure have not markedly changed in the last decade [3,4].

In the preoperative period hemodynamic instability, occurred as a consequence of underlying diseases, renal hypoperfusion, use of nephrotoxic drugs, presence of systemic infections (endocarditis) can lead to subclinical lesions in the kidney. Intraoperatively patients are exposed to the artificial surface of the cardiopulmonary circuit, which can induce systemic inflammatory response. Also intraoperative hypovolemia, decreased cardiac output or microembolism can contribute to renal failure. Postoperative administration of nephrotoxic drugs, the occurrence of infections/sepsis, positive pressure mechanical ventilation, low cardiac output and use of vasoconstrictors may worsen hypoperfusion and systemic inflammatory reaction, which appears as important risk factors in renal dysfunction [3,4].

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The purpose of this study was to determine the incidence of renal dysfunction after cardiac surgery, analyzing the possible causes, associated risk factors and treatment methods used in our patient population. The aim is to select patients who are at high risk for postoperative kidney injury, to adopt strategies of renal protection.

Material and methods

In this prospective observational study we analyzed the development of renal injury in adult patients undergoing cardiac surgical interventions between October 1, 2010 – December 15, 2010 at the Târgu Mureş Clinic of Cardiovascular Surgery. Patients with chronic renal failure were excluded.

Renal dysfunction was diagnosed using RIFLE (Risk, Injury, Failure, Loss of function, End-stage renal disease) criteria. Blood urea nitrogen and serum creatinine were recorded preoperatively and in the second and fourth day in the postoperative period. We analyzed the incidence of renal dysfunction according to patients' age, sex, type of surgery, cardiopulmonary bypass time, intraoperative body temperature, degree of hemodilution, use of vasopressor agents and analgesics in the postoperative period.

Statistical analysis was made using Fisher's exact test and Tukey-Kramer test. We considered differences statistically significant, when $p<0.05$.

Results

In the studied period, 89 patients underwent cardiac surgical intervention, 66 (74%) male and 23 (36%) female. The mean age of patients was 58.4±11.4 years, range between 17–75 years.

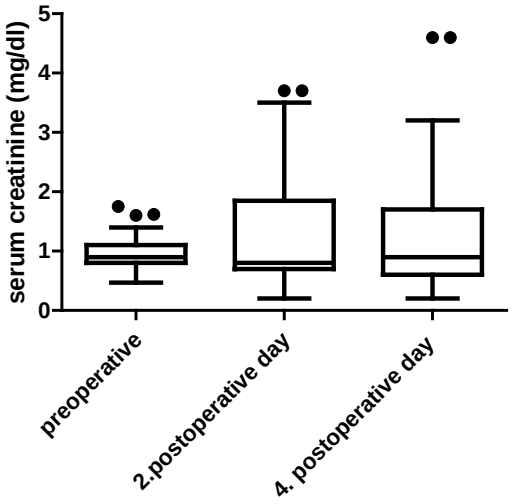

Fig. 1. Variation of serum creatinine level in patients undergoing cardiac surgery

In 34 cases valvuloplasty or valvular replacement was performed, in 49 cases coronary revascularization, in 4 cases simultaneous coronary revascularization and valvuloplasty/ valvular replacement was made and in 2 patients congenital heart diseases were corrected.

We analyzed in all patients included in this study the serum creatinine level in the preoperative and postoperative period. The serum creatinine level showed a slight increase in the second day after surgery in almost all patients, with a mean of 1.28 mg/dl, lowering for the fourth day in patients without postoperative complications and remaining high in those with renal injury (Figure 1).

According to the RIFLE criteria, the incidence of renal dysfunction/failure was 20.2% (2 patients with renal failure and 16 with renal dysfunction) and 10 more patients could be included in the high risk group.

In two patients continuous veno-venous hemodialysis was indicated because of high level of blood urea nitrogen, serum creatinine and potassium level, 16 received continuous perfusion with furosemide, in dosage between 2–10 mg/kg/day, the remaining were treated with furosemide in bolus doses of 40 mg 2–3 times daily. In 13 patients with

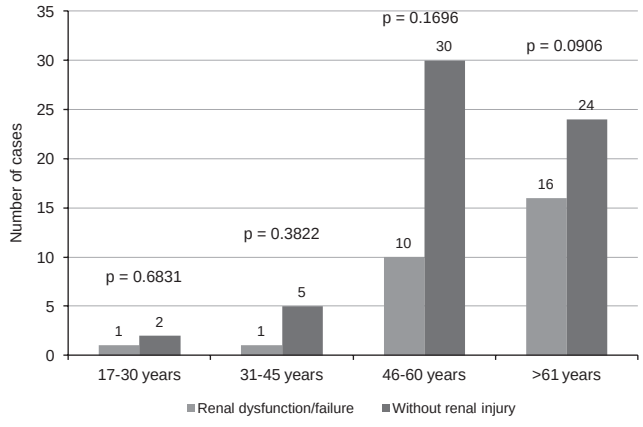

Fig. 2. Incidence of renal injury in relation to age

Table I. Patients characteristics (CABG – coronary artery bypass graft; CHD – congenital heart disease)

	Group 1 (no renal injury)	Group 2 (renal dysfunction)	p value
No. of patients	61	28	
Gender			
Male	45	21	0.5068
Female	16	7	
Mean age (years)	57.5±12 (17–75)	60.4±9.9 (28–74)	0.2688
Type of surgery			
CABG	34	15	0.5142
CABG + valvular replacement	2	2	0.3735
Valvular replacement	24	10	0.4660
CHD correction	1	1	0.5327

continuous furosemide perfusion, diuresis was maintained above 0.5 ml/kg/hour, but serum creatinine level remain elevated on the fourth postoperative day, with decline only after 7–10 days.

In order to identify factors for kidney injury and associated morbidity and mortality, we divided the patients in 2 groups: in Group 1 we enrolled patients without renal injury, in the Group 2 patients with renal dysfunction/ failure and those with high risk for renal injury (postoperative serum creatinine 1.5 fold higher than the preoperative value, oliguria for 6 hours). We didn't observe significant differences between the 2 groups as to the gender of the patients, mean age or type of surgery (Table I).

Even if the mean age wasn't significantly higher in kidney injury group, there was significant increase in the incidence of renal dysfunction after 61 years (Figure 2).

Cardiopulmonary bypass duration was significantly higher (p=0.0167 – Tukey-Kramer test) in patients with renal dysfunction (116.5±39.2 minutes vs. 91.4±47.4 minutes).

The body temperature during cardiopulmonary bypass was maintained usually around 35°C, but sometimes pati-

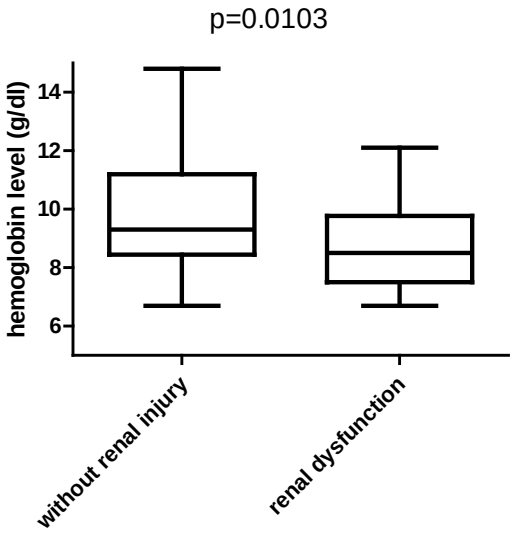

Fig. 3. Renal dysfunction in relation to the degree of hemodilution during cardiopulmonary bypass

Table II. Number of patients receiving inotropic and vasoconstrictor agents

	Patients without renal injury (61)	Patients with renal dysfunction (28)
Dopamine <5 µg/kg/min	6	7
Dopamine >5 µg/kg/min	3	11
Dobutamine <5 µg/kg/min	11	10
Dobutamine >5 µg/kg/min	8	7
Epinephrine <150 ng/kg/min	2	1
Epinephrine >150 ng/kg/min	1	3
Norepinephrine >50 ng/kg/min	1	5

ents became mildly hypothermic because the low temperature in the operating theatre. In patients with renal dysfunction the average body temperature was 33.6±1.2°C, slightly higher than in patients without renal impairment (33.4±0.8°C).

Hemodilution is used during cardiopulmonary bypass to reduce blood viscosity and peripheral vascular resistance. We observed that intraoperative hemoglobin level was significantly lower (8.8±1.5 g/dl) in patients with renal dysfunction compared to patients without compromised kidney function (9.8±1.9 g/dl) (Figure 3).

In patients with renal dysfunction low cardiac output was present in 16 patients (54.1%), two of them needing intraaortic balloon counterpulsation, comparing with patients without kidney injury, where heart failure was present only in 14 patients from 61 enrolled in this group (22.9%). Patients with cardiac failure were treated with inotropic agents and vasoconstrictors. We observed that in the group of renal dysfunction vasoconstrictors were used more frequently and at higher doses (Table II).

In the postoperative period patients received non-steroidal anti-inflammatory agents to relieve pain. Renal dysfunction occurred more frequently in patients who received ketoprofen (35.2%) than metamizole (15.8%) and less frequently in those who received only opioids (14.6%).

Discussions

Our study showed that renal dysfunction is frequent after cardiac surgical interventions. The kidney injury could be severe, requiring hemodialysis, but in most of the cases there were only mild elevation of serum creatinine and/or a reduction of diuresis, with rapid recovery under conservative therapy.

Most of the studies showed an increased risk of renal dysfunction in women and in patients over 70 years [5,6]. In our patients kidney injury developed at younger ages (after 61 years), but we couldn't found a higher incidence in female, and the most severe cases, requiring hemodialysis developed only in men. This could be due to more complex surgical interventions occurred in male patients comparing to females.

The incidence of renal dysfunction was higher in simultaneous coronary revascularization with valvuloplasty/valve replacement, probably due to prolonged cardiopulmonary bypass time and low cardiac output, more frequent in these cases.

In patients with prolonged cardiopulmonary bypass time renal injury was significantly higher. Some degree of renal injury is inevitable during cardiopulmonary bypass [7]; this was demonstrated in our study by the elevated serum creatinine level in the second postoperative day.

Cardiopulmonary bypass is associated with significant hemodynamic changes, which may lead to regional renal ischemia and cellular injury, these could either initiate acute renal dysfunction or extend pre-existing kidney injury. During cardiopulmonary bypass, renal blood flow may be reduced by periods of low perfusion, hypotension, vasoconstriction and microemboli [1,7].

Perfusion pressure during cardiopulmonary bypass is an important determinant of adequate O_2 and nutrient delivery to vascular beds. Perfusion pressure is determined by the interaction of blood flow and arterial resistance. Both are changing during cardiac surgery (vasomotor tone can be affected by anesthesia, hypothermia, vasoactive medication) and lead to changes in perfusion pressure. In general, it is recommended a mean perfusion pressure of 50 to 70 mmHg during extracorporeal circulation [1,7], but it is not known what are this affect renal perfusion and oxygen delivery. The majority of studies on autoregulation of regional blood flow during cardiopulmonary have suggested that mean arterial pressures above 70 mmHg lead to higher intraoperative creatinine clearances but without a change in postoperative renal function as compared with pressures between 50 and 60 mmHg [1]. Thus, it is likely that renal perfusion and autoregulation are also maintained as long as these hemodynamic goals are met. However, these values are the minimum blood flows that support normal organ function, and any perturbation may lead to ischemia and cellular damage. If there is any degree of pre-existing renal dysfunction, the autoregulatory capacity of the kidney may be lost and renal blood flow becomes linearly dependent on perfusion pressure. In these patients higher mean pressure may be required to maintain adequate renal perfusion [7].

Cardiopulmonary bypass induces a systemic inflammatory response syndrome. Contact of blood components with the artificial surface of the bypass circuit, ischemia-reperfusion injury, endotoxemia, surgical trauma, nonpulsatile blood flow, heparin-protamin complexes and pre-existing left ventricular dysfunction all are possible causes of the activation of inflammatory mediators [8,9].

The end result of this generalized inflammatory response within the kidney is not known. In animal the pathologic role of interstitial inflammation and the release of proinflammatory cytokines and reactive oxygen species in the production of tubular injury have been demonstrated, and it is likely that cardiopulmonary bypass-induced inflammation has significant deleterious effects on the kidney through similar mechanisms [1,7].

Other factors that might have an impact on renal hemodynamics include hemodilution (oxygen delivery capa-

city), hypothermia (oxygen consumption) and the absence of pulsatile perfusion. Hemodilution dilutes plasma hemoglobin, improves flow to the outer renal cortex, improves total renal blood flow, increases creatinine, electrolyte and water clearance, increases glomerular filtration and urine volume, but excessive hemodilution reduces oxygen delivery, and hemoglobin concentrations below 8 g/L cause organ dysfunction at temperatures above 30°C [7].

In our study intraoperative hemoglobin level was significantly lower in patients with renal dysfunction.

Hypothermia is considered a good organ preservation strategy, but in the last several years the trend in cardiac surgery is to maintain normothermia during cardiopulmonary bypass. This shortens the extracorporeal circulation time, lessen the postoperative bleeding and increase hemodynamic stability in patients, but raised the question about safety meaning organ and tissue preservation [2]. In our study we didn't observe significant difference in the development of renal injury in patients with intraoperative mild hypothermia or normothermia.

Renal dysfunction occurred more frequently in patients with postoperative cardiac failure and in those who needed high doses of vasoconstrictors to maintain cardiac output and blood pressure. In the postoperative period hemodynamic instability, low cardiac output, use of vasoactive agents, exposure to nephrotoxic medications, volume depletion, and sepsis are critical events that can lead to kidney injury [10,11]. Kidneys, already compromised by preoperative disease and the cardiopulmonary bypass induced injury, are particularly sensitive to ischemic injury secondary to low cardiac output and hypotension. Thus perioperative management includes efforts to maximize cardiac output using dopamine or dobutamine if necessary, avoiding renal arterial vasoconstrictive drugs. Some drugs that increase cardiac output and improve renal blood flow in lower dose, in higher doses (epinephrine in doses over 1.5 μg/kg/min and dopamine over 12 μg/kg/min) cause renal vasoconstriction and reduce renal cortical blood flow [12, 13]. If perioperative low cardiac output and hypotension do not occur, the healthy kidney has sufficient functional reserve to provide adequate renal function during and after operation [2,7].

Renal dysfunction occurred more frequently in patients who received non-steroid anti-inflammatory drugs as analgesic in the postoperative period. Non-steroid anti-inflammatory drug administration decrease renal plasma flow and glomerular filtration rate within hours, and if analgesic administration continue, there is a risk for acute tubular necrosis and permanent damage to the kidney [14].

Conclusions

Cardiac surgery with the use of cardiopulmonary bypass is associated with high risk for renal dysfunction. The pathogenesis is complex and involves hemodynamic, inflammatory and other mechanisms that interact at cellular level. In our study it was more frequent in elderly, after complex surgical interventions and prolonged cardiopulmonary bypass, in patients with excessive hemodilution. Low cardiac output and the use of vasoconstrictor agents influence the development of kidney injury, as well as the use of non-steroid anti-inflammatory agents to relieve postoperative pain. We observe no differences in the incidence of renal dysfunction in patients with normothermia or mild hypothermia.

Postoperative acute renal failure remains a serious complication of cardiac surgery that does not seem to have been influenced yet by any strategies designed to prevent it, possible because its etiology is multifactorial. More research needs to be conducted to identify patients who are most susceptible to acute renal failure and to identify the most effective strategies to prevent it.

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