



The influence of mean arterial blood pressure during cardiopulmonary bypass on post-operation acute kidney injury in hypertensive patients

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ABSTRACT

Introduction: Over a period of time, kidney blood vessels will be damaged in those patients suffering from hypertension.

Objectives: This study aimed to investigate the effect of mean arterial pressure during cardiopulmonary bypass (CBP).

Patients and Methods: The present observational prospective study was conducted on 90 high risk patients, having records of hypertension and being candidates for open heart surgery. Patients divided into three groups based on their mean arterial pressure (MAP), lower than 60 mmHg (first group), between 60 to 70 mm Hg (second group) and higher than 70 mm Hg (third group) respectively during cardiopulmonary bypass. Clinical outcomes being studied included cardiac surgery-associated acute kidney injury (CSA-AKI) (RIFLE class), serum creatinine levels, glomerular filtration rate (GFR) and urinary output up to 24 hours after the surgery.

Results: Data related to 90 case-patients have been analyzed. There was no difference between the groups in terms of demographic information. Prevalence of AKI in preliminary course after cardiac surgery was different among the groups. AKI occurred in six patients (15%) of the first group, five patients (12.5%) of the second group and two patients (5%) of the third group ($P=0.03$). There have been no differences in terms of serum creatinine levels, GFR and urinary output during 24 hours after cardiac surgery, among the groups. However, delta creatinine level and delta GFR were significant in those groups with MAP of lower than 60 mm Hg and also between 60-70 mm Hg.

Conclusion: This study showed that MAP level during CBP directly affects occurrence of AKI in patients after open heart surgery. High risk patients such as those suffering from hypertension have to be constantly monitored during CBP regarding their MAP. We concluded that MAP drops to lower than 70 mm Hg has to be prevented in hypertensive patients.

Implication for health policy/practice/research/medical education:

In a prospective study on 90 high risk patients, we found that mean arterial pressure value during CPB directly affects post-operative occurrence of AKI in patients undergoing cardiac surgery. Thus, high risk patients such as those already suffering from hypertension have to be constantly monitored in terms of MAP during cardiopulmonary bypass; therefore, decrease of MAP lower than 70 mm Hg should be prevented.

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Introduction

Acute kidney injury (AKI) is one of complications often observed after cardiac surgery. Its occurrence is sometimes serious in more than 30% of patients conducting coronary artery bypass grafting (CABG) surgery through cardiopulmonary bypass (CPB) (1). Death toll in those

patients required hemodialysis treatment because their cardiac surgery-associated acute kidney injury (CSA-AKI) has been estimated to be 60% to 70% (2). In fact, post-CPB kidney complications occur due to the two following reasons: effect of nephrotoxins resulted from activation of inflammatory systems and reduction of blood flow to

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kidney tissues resulted from hypoperfusion during CPB (3, 4).

Twenty percent of the heart output is received by kidneys, however in case of more than 40% reduction in blood flow to the kidneys, hypoxia will occur which creates a background for occurrence of AKI. Therefore, it becomes of dual importance since mean arterial pressure (MAP) could play an important role in the establishment of proper perfusion pressure in kidney tissues (5). On the other hand, in patients suffering from hypertension, the kidney vessels will be damaged, resulting in reduction of blood flow to the kidney tissues more (6).

Objectives

Based on the above explanations, keeping MAP within a normal range during CPB seems to prevent occurrence of serious damages to vital organs such as kidneys. In this study, the effect of MAP during CPB was studied.

Patients and Methods

Study protocol

In this observational prospective study, patients who underwent the CABG procedure (July 2017 until May 2018) in Rajaie cardiovascular medical and research center, Tehran enrolled in the study. Inclusion criteria were: having high blood pressure, bypass time of 60 to 120 minutes, cross-clamp time of 45 to 90 minutes, patients' weight to be between 50 to 90 kg, lack of severe anemia history, lack of diabetes or having controlled diabetes, ejection fraction (EF) of higher than 30%, lack of such diseases as chronic kidney failure, severe urinary tracts infection (UTI), prostate hypertrophy and polycystic kidney and also record of urological surgeries or having only one kidney.

Exclusion criteria were: off-pump or concomitant open-chamber surgery, postoperative intra-aortic balloon pump and extra-corporeal membrane oxygenation, hypothermia lower than 32°C, using thermal-coronary-angiography (TCA) technique and cardiac arrest before undergoing bypass pump.

Upon entrance of the samples into the operating room, their files have been reviewed accurately based on inclusion criteria. After obtaining their informed consent, the patients have been entered into the study as the research sample.

For patients, electrocardiography and pulse oximetry was conducted too. In addition to a peripheral intravenous line, an arterial line was specified through placement of a catheter with the size proportionate to weight of patients, mostly in one of radial arteries of one of upper limbs; hence, arterial blood pressure could be monitored. Around 10 mL/kg of Ringer's crystalloid solution was received by all patients before starting the surgery. Anesthesia induction was administered through 10-15 µg/kg fentanyl and 0.1 mg/kg of body weight midazolam.

Around 0.1 mg/kg pancuronium was injected in form of bolus as a muscle relaxant for facilitating endotracheal intubation. Anesthesia was maintained through fentanyl (5 µg/kg/h) and midazolam (1 µg/kg/min). In case of more drug required to maintain proper depth of anesthesia, sevoflurane has been used before and after CPB. Using an anesthesia machine with tidal volume of 10 mL against each 1 kg of body weight and adjusted with proper respiratory rhythm (between 30 to 35 mm Hg of PaCO₂), patients were subjected to mechanical ventilation.

After induction of anesthesia, an appropriate Foley catheter was used to monitor diuresis level. Hypotension and hypertension during CPB were preferably treated by phenylephrine and TNG respectively. In case of using any kind of inotropic or vasopressor drugs, their dosages have been recorded. Heparin (300 IU/kg) was administered as the anticoagulant after reaching activated clotting time over 480 seconds, then cannulation and CPB were authorized.

In those patients with low-hemoglobin and hematocrit levels before surgery, fresh packed blood in required amounts was added to prime solution to reach a hematocrit level of 25-30%

during surgery. Volume of added blood was also recorded as mL/kg. Mean hypothermia by the temperature of 32-34°C was used. However, in some of the samples, body temperature has not been reduced due to the surgeon's view. Arterial blood gas analysis and arterial blood pressure also were monitored in addition to urinary output.

Prime solutions including venofundin etherified starches (6%) equal to 15 mL/kg, Ringer's lactate serum and heparin (3 IU against 1 mL of prime solution) and also mannitol solution (0.5 g/kg) in form of infusion were added until CPB being disconnected.

CPB was administered via roller pumps in form of non-pulsatile blood flow (2.4 L/m²). Bypass machines used in the study were Stockert S5, S3 heart lung machine and oxygenators such as QUADROX-Adult manufactured by Maquet Company, CAPIOX FX25 manufactured by Trumo Corporation and Affinity Fusion manufactured by Medtronic Company were used.

After establishment of CPB pulsatile blood flow will be changed to non-pulsatile or linear blood flow. Hence when pump is connected, the monitored blood pressure shows MAP too. According to various factors, MAP fluctuates within one range during pumping thus MAP was recorded at each 10 minutes time intervals during pumping. After the end of CPB, the mean arterial blood pressure value was assessed for every patient. Then patients were categorized in one of the three groups based on MAP during pumping. The mean values of arterial pressure have been lower than 60 mm Hg, between 60-70 mm Hg and higher than 70 mm Hg, respectively for the first, the second and the third groups. After the end

of surgery and when stable hemodynamic was achieved, CPB was disconnected while heparin was neutralized by protamine.

Urine volumes of samples were recorded during surgery, 6 hours, 12 hours and 24 hours after disconnection of CPB. Serum creatinine level before surgery and the day after surgery was recorded from patients' files. Likewise, before and post-surgery glomerular filtration rate (GFR) was assessed based on Cockcroft and Gault formula (CG).

Ethical issues

The research followed the tenets of the Declaration of Helsinki. All patients signed a written informed consent form to participate in the study. This project was also approved by the Ethics committee of Rajaie Cardiovascular Medical and Research Center (registration code# RHC.AC.IR.REC.1396.44). This study was extracted from the MD thesis of Mohammad Reza Foroutan (Thesis # 93055).

Statistical analysis

Data collected in the research were analyzed through SPSS 20. To describe research units' specifications in each of the three groups, descriptive statistics including

measures of central tendency and dispersion (mean and standard deviation) and frequency distribution were used. For statistical analysis of results, chi-square, Wilcoxon, Kruskal-Wallis and

ANOVA statistical methods were used. *P* values below 0.05 were interpreted as statistically significant for all tests.

Results

Table 1 shows the results from frequency distribution based on gender. Based on the results, 28 (70%), 18 (45%) and 19 (47.5%) of patients were male in the first, second and third groups, respectively. Mann-Whitney U test was applied to compare the three groups because no significance level has been specified ($P=0.06$).

Age, weight, gender and body surface area of patients in all of the three groups were compared by one-way ANOVA test which showed no significant difference between the groups ($P>0.05$) too.

In the first, second and third group 37 (92.5%), 39 (97.5%) and 35 (87.5%) of patients have been already under treatment with blood pressure medication, respectively. Number of patients using antihypertensive medicines separately in each group is provided in Table 2. Based

Table 1. Demographic data of patients in the three groups studied

Variables	MAP < 60 (n = 40)	MAP(60-70) (n = 40)	>70 MAP (n = 40)	P Value
Gender, No. (%)				
Male	28 (70%)	18 (45%)	19 (47.5%)	0.6
Female	12 (30%)	22 (55%)	21 (52.5%)	
Age (y)	61.55±8.25	62.63±9.46	60.65±9.28	0.6
Weight (kg)	65.34±9.65	71.84±8.47	68.51±6.58	0.35
Height (cm)	171.65±15.36	168.76±13.12	164.59±15.47	0.61
BSA (m ²)	1.75±0.30	1.77±0.24	1.73±0.19	0.43
Pre. Op. LVEF (%)	49.12±5.12	45.25±7.92	44.25±8.28	0.7
Diabetes, No. (%)	25 (62.5)	20 (50)	17 (42.5)	0.45

Table 2. Comparison of patients' information during the operation in the three groups

Variables	MAP <60 (n=40)	MAP 60-70 (n=40)	MAP >70 (n=40)	P value
Cardiopulmonary Bypass time (min)	73.80±25.40	69.03±18.59	77.52±2.33	0.15
Cross clamp time (min)	39.52±15.60	37.80±10.44	44.70±15.69	0.06
Flow (cc.min)	4205.58±214.56	4249.63±276.51	4156.58±197.86	0.45
Hypothermia during surgery (°C)				0.42
32°C	29 (72.5%)	28 (70%)	26 (65%)	
34°C	11 (27.5%)	11 (27.5%)	13 (32.5%)	
35°C and more	0 (0%)	1 (2.5%)	1 (2.5%)	
Usage of hemofiltration	16 (53%)	14 (46%)	12 (40%)	0.46
Volume of hemofiltration (cc)	958.63±254.84	1023.95±235.57	912.61±249.63	0.33

on chi-square test, no significant difference between the groups was seen ($P>0.05$).

Among the first group, 25 (62.5%) of patients suffered from diabetes. The number of diabetic patients in the second and the third groups were 20 (50%) and 17 (42.5%), respectively. No significant difference was detected between the three groups as per Mann-Whitney U test ($P>0.05$).

Heart EF pre- and post-operatively was reviewed in all of the three groups. Using Kruskal-Wallis test, we found no significant difference between the groups ($P=0.7$). Pre- and post-operative mean values of heart EF were 49.12% (5.12), 45.25% (7.92) and 44.25% (8.28), respectively for the first, second and third groups.

Additionally, CPB time and aortic cross-clamp time in all of the three groups had no significant differences based on Kruskal-Wallis test. CPB mean time in the first, second and third groups was 73.80 (25.40), 69.03 (18.59), and 77.52 (24.33) minutes, respectively. Cross-clamp mean time was also 39.52(15.60), 37.80 (10.44) and 44.70 (15.69) minutes, respectively for the first, second and third groups.

No significant difference between the three groups was detected (Mann-Whitney U test; $P=0.46$) for hemofiltration during CPB. Therefore, for 16 (53%), 14 (46%) and 12 (40%) of patients in the first, second and third groups, respectively, hemofiltration was used. No Filtered volume had no significant difference between the groups regarding ($P>0.05$).

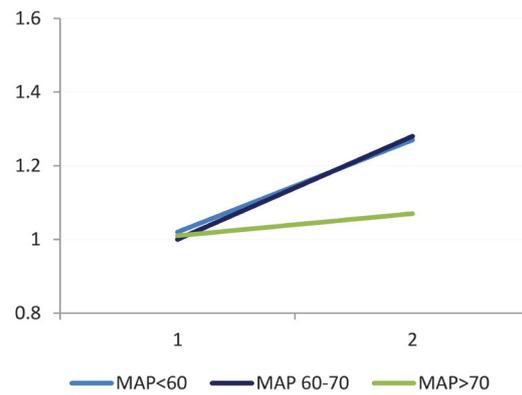


Figure 1. Serum creatinine changes before and after surgery in three groups

No significant difference of hypothermia level between three groups (Mann-Whitney U statistical test) was detected (Table 3; $P>0.05$).

Serum creatinine level (sCr) and GFR before surgery and 24 hours after surgery had no significant differences between the groups ($P>0.05$; Figures 1 and 2). Differences in creatinine serum levels before surgery and after that (Δ sCr) and also differences between GFRs before and after surgery (Δ GFR) in each group were studied by intergroup Wilcoxon statistical test. We found a significant statistical difference between Δ sCr and Δ GFR in those groups with MAP of lower than 60 mm Hg and also between 60-70 mm Hg. However, there was no significant difference

Table 3. Comparison of patients' renal function and the incidence of acute renal injury in the three groups

Variables	MAP <60 (n=40)	MAP 60-70 (n=40)	MAP >70 (n=40)	P value
SCr (mg.dL)				
Before operation	1.02±0.19	1±0.22	1.01±0.19	0.58
24h after operation	1.27±0.30	1.28±0.34	1.07±0.29	0.37
(Δ SCr)	0.25±0.11	0.27±0.12	0.06±0.10	0.49
GFR				
Before operation	79.16±31.60	76.61±22.81	73.92±24.33	32/·
24h after operation	66.16±33.89	64.32±32.16	71.21±30.39	0.61
(Δ GFR)	-13.00±2.29	-12.29±15.70	-2.71±6.06	0.17
Urine Volume (cc)				
During CPB	548.47±158.24	604.20±187.32	578.37±164.18	0.21
Until 6h after operation	1233.75±387.19	1252.14±352.09	1152.51±294.59	0.54
Until 12h after operation	1988.75±511.84	1928.74±411.04	1961.25±447.57	0.67
Until 24h after operation	3223.56±650.93	3114±555.06	3213.73±591.17	0.18
AKI				
Risk	6 (15%)	5 (12.5%)	2 (5%)	0.03*
Injury	4 (10%)	4 (10%)	2 (5%)	
Failure	2 (5%)	0	0	
Loss of kidney function	0	0	0	
End-stage renal disease	0	0	0	

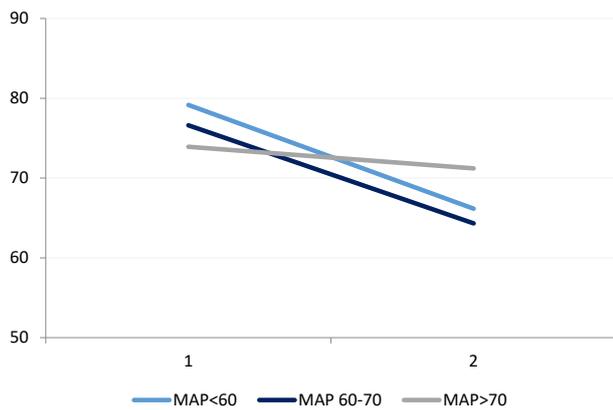


Figure 2. Changes in glomerular filtration rate before and after surgery in three groups.

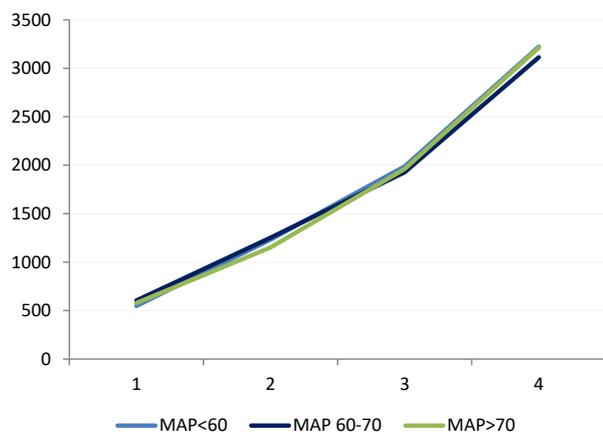


Figure 3. Changes in urinary output during and after surgery up to 24 hours after surgery in three groups.

between two groups with mean arterial blood pressure of higher than 70 mm Hg ($P > 0.05$).

Urine volumes related to the following time intervals also studied, during surgery and 6, 12 and 24 hours after that, we found no significant difference between the three groups at these time intervals ($P > 0.05$; Figure 3).

As far as AKI occurrence is concerned and according to RIFLE criteria, the three groups were compared with each other. Accordingly, a significant difference between the three groups regarding the occurrence of AKI was detected. It was also specified that in those groups with MAP of lower than 60 and between 60 to 70 mm Hg, AKI occurrence is more probable statistically than the group with higher mean arterial blood pressure than 70 mm Hg (Figure 4).

Discussion

AKI resulted from changes in serum creatinine levels compared to that of before heart surgery has been recognized as one of predictive factors, causing increase of

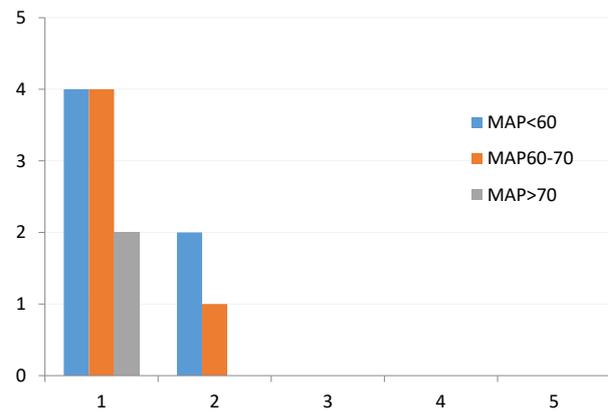


Figure 4. Comparison of the incidence of acute renal injury after surgery in three groups.

patients' death toll in hospitals. Among numerous factors predicting probability of AKI occurrence following heart surgery a number of them could not be adjusted. Among them, some factors are age, gender and previous kidney failure as well as associated illnesses such as hypertension (7). The results from present study showed that lower than 70 mm Hg MAP during CPB is associated with increase of AKI in those patients underwent open heart surgery. According to the study by Aronson et al and similar to our results, blood pressure drop during surgery compared to that of before surgery is independently related to increase of AKI occurrence within the post-operative period. Additionally post-operative complication's risk of occurrence when patients are hospitalized in CCU would be increased (8). AKI could cause reduction of kidney perfusion when blood pressure is low. This affects kidney function and imposes damage to renal tissue, resulting in some risks related to kidney performance. According to the study conducted on high risk candidates of open heart surgery by Kanji et al, those patients with more than 26 mm Hg MAP drop during the pumping compared to that of before bypass pumping independently have been faced with 2.8 times higher risk of occurrence of AKI, in comparison to other patients (2). Using cerebral blood flow monitoring device and recording MAP of patients going under CPB, it was declared by Ono et al that, patients with MAP lower than cerebral auto-regulation level (lower than 60 mm Hg) are independently faced with occurrence of AKI and post-open heart surgery. The difference between our study and the study by Ono et al regarding patients' selection, could be considered as the reason for them to believe MAP lower than 60 mm Hg is independently related to AKI occurrence. It seems that maintenance of MAP higher than 70 mm Hg during CPB is mandatory; therefore, occurrence of AKI would be somehow prevented (5). Similarly, in other articles also emphases have been made on blood pressure drop to lower than 60 mm Hg during bypass pumping as one of the risk factors related to AKI occurrence after heart

surgery (9). In a similar study conducted by Sirvinskas et al, the contradictory results have been obtained. They denied independent effect of MAP level during CPB on the occurrence of post-operative AKI. The difference between results of the two studies seems to be stemmed from selecting patients with various age ranges.

In fact, very limited number of articles rejected the effect of MAP lower than 60 mm Hg as a risk factor for the occurrence of post-operative AKI. However, these studies have been performed in small size or conducted through observation, since their results have been unsuccessful in showing effect of low MAP on the occurrence of AKI (10-12). Various studies reported the concept of low blood pressure's effect on damaging vital body organs. For example, Gottesman et al found that patients with more MAP drop during bypass pumping are more prone to post-operative neurological problems (13). Additionally, as concluded by Lombardi et al, low-MAP during bypass pumping is independently related to the occurrence of AKI in patients (14). We found, the increase in serum creatinine and reduction of GFR in those patients with MAP lower than 70 mm Hg during surgery occurred in a significant number of cases. According to the study by Song et al, acute coronary artery injury is more probable in cases with elevated serum creatinine levels in patients who are going to conduct CPB (15). Based on a three-year retrospective study performed by Rettig et al in patients performing CABG, a significant post-operative increase in occurrence of AKI in those patients with MAP lower than 50 mm Hg for at least 10 minutes during bypass pumping was found. Furthermore, preoperative creatinine level was higher in patients suffering from AKI. Post-operative creatinine levels in these patients showed up to more than 26 $\mu\text{mol/L}$ increase during 48 hours after surgery or the post-operative increase level was more than 150% during seven days after surgery compared to the base level(16). In an observational research performed on 157 patients being candidate for various open heart surgeries with similar preoperative creatinine levels, an increase in creatinine level during five days after surgery was observed, which is significantly higher in patients suffering from AKI. Serum creatinine levels in individuals with AKI were at least 25% higher than its base level in all conditions. Based on our study, post-operative serum creatinine levels of patients in groups with MAPs between 60 mm Hg and 70 mm Hg and/or lower than 60 mm Hg showed about 25% increase compared to the base status. This could be considered as a symptom of probable occurrence of AKI in these patients(2).

In our study particular attention could be made to comparison of results of urinary output levels during bypass pumping and within 24 hours after the surgery in CCU. In neither of these time periods significant difference was observed in terms of urinary output level. In a retrospective research (2009-2011) on the

patients affected by post-operative AKI, no independent relationship was found regarding overall effect of patients' urinary output level during CPB on occurrence of post-operative AKI. However, after dividing patients into two subgroups with urinary output levels of higher or lower than 4 mL/kg/h during bypass pumping, it was found that patients with urinary output level of lower than 4 mL/kg/h have been more prone to post-operative AKI(15).

Conclusion

In this study we found that MAP value during CPB directly affects post-operative occurrence of AKI in patients undergoing cardiac surgery because high risk patients such as those already suffering from hypertension have to be constantly monitored in terms of MAP during CPB; therefore, decrease of MAP lower than 70 mm Hg should be prevented.

Limitations of the study

We only assessed the patients until discharge from ICU and did not follow up them. Thus, larger studies with longer follow up is recommended.

Conflicts of interest

The authors declared no competing interests.

Authors' contribution

SA and MZ conducted the research. HS and RA prepared the manuscript. MF, AAGh, MS, MV, YNR and MA collected the data and managed the patients. BGh performed statistical analyses. All authors read and signed the final paper.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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