

## MEAN ARTERIAL PRESSURE AND PULSE PRESSURE, INFLUENCE ON POSTOPERATIVE RENAL AND NEUROLOGICAL OUTCOMES IN ELDERLY PATIENTS UNDERGOING CORONARY REVASCULARIZATION

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### **Contribution**

All the authors contributed significantly to the research that resulted in the submitted manuscript.

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### **ABSTRACT**

**Objectives:** To observe the impact of both MAP and PP for the postoperative renal and neurological outcomes in patients undergoing CABG.

**Methodology:** This prospective double blinded observational study of patients undergoing CABG, at Cardiac Surgery department, Punjab Institute of Cardiology, Lahore Pakistan, was conducted from January 2011 to November 2011. Preoperatively urea, creatinine, ultrasound kidney, X-Ray abdomen and Carotid Doppler study was performed. Postoperatively RIFLE criteria was used for Acute Renal Injury. Patients with neurological deficit and seizures underwent CT and EEG. Data was analyzed by using SPSS 20.  $P \leq 0.05$  was considered as significant.

**Results:** Total number of patients included were 115. Co morbid conditions found in patients with high MAP and PP were hypertension (34.8%;  $p=0.612$ ), diabetes mellitus (39.1%;  $p=0.305$ ), obesity (65.2%;  $p= 0.001$ ) and COPD (21.7%;  $p=0.001$ ). Acute Kidney injury was in patients with pulse pressure between 31-40 mmHg & mean arterial pressure between 71-90 mmHg. The only association of ARI was found with hypertension ( $p=0.050$ ). Stroke, RIND, TIA, coma and seizures had no association with pulse pressure  $<30$ mmHg and Mean arterial pressure of  $<70$ mmHg.

**Conclusion:** For post CABG patients MAP and PP are good markers for the neurological deficit but not for renal disease.

**Key Words:** Mean Arterial Pressure, Pulse Pressure, Neurological Deficit, Renal Disease, CABG

## INTRODUCTION

For coronary artery disease (CAD) one of the standard treatment options is coronary artery bypass grafting surgery (CABG), utilizing cardiopulmonary bypass (CPB). CABG prolongs life among patients with severe triple vessel (TVD) or left main coronary artery (LMS) disease.

Over the past decade coronary artery bypass grafting surgery (CABG) significantly improved the survival and reduced the 30-days outcome in term of mortality and morbidity.<sup>1-4</sup> Although mortality after CABG is very low, morbidity resulting from neurological and renal complications have been relatively high.

Increased arterial blood pressure (BP) is an independent predictor for in-hospital-outcomes. Several methods have been suggested to predict these events with raised systolic BP (SBP), diastolic BP (DBP), pulse pressure (PP, the difference between SBP and DBP) and mean arterial pressure (MAP).<sup>5,6</sup> Among them MAP & PP have gained more popularity as powerful predictors of cardiovascular and non-cardiovascular events. Mitchell GF et al, for example, have found that increase in PP linked with post MI in patients with LV dysfunction.<sup>5</sup> Moreover, Vaccarino V et al, found a 10–mm Hg rise in PP was significantly associated with increased risk of coronary heart disease as 12%, CHF as 14% and death as 6%.<sup>6</sup> A large MAP is, as shown by Kanji HD et al, an independent early postoperative risk for AKI.<sup>7</sup>

Previous literature observed that pulse pressure (PP) is an independent risk factor which is associated with cardiovascular diseases and death, but after CABG whether PP increases outcomes, it was unclear.<sup>8</sup>

Routinely MAP during CPB has been maintained in the range of 50 mm Hg, and several studies have suggested that there was no adverse impact at this MAP, once it is within auto regulatory range.<sup>9-12</sup> Current data suggested the importance of PP over other regular procedures for BP, in order to recognize the threat for early adverse outcomes.<sup>13-19</sup>

Looking at such diversity in literature, where MAP and PP were examined in different population samples, we demonstrated this study to see the impact of both MAP and PP for the postoperative renal and neurological outcomes in population undergoing CABG.

## METHODOLOGY

This prospective double blinded observational study was conducted at Department of Cardiac Surgery, Punjab Institute of Cardiology, Lahore Pakistan, from January 2011 to November 2011. All elderly patients (>60 years age) planned to undergo CABG electively were included for this study. All cases were operated at the same clinic and by the same operating team. Patients for Emergency surgery, redosurgery, additional surgical procedures (Valvular or

congenital), carotid artery endarterectomy, preoperative neurological disease, chronic renal failure, on dialysis, reoperation for bleeding, and sternal fractures, and preoperative MAP <70mmHg or >90mmHg and PP of <40 or >60 mmHg, postoperative arrhythmias, were excluded from the study. Informed consent was obtained for the surgical procedure and its outcomes.

Preoperatively, for the detection of renal pathology, urea, creatinine, ultrasound kidney and X-Ray abdomen, were performed. Pre-CABG Carotid Doppler study was performed in all patients above 60 years of age, with previous history of stroke and Left main coronary artery lesion.

All the surgeries were performed using cardiopulmonary bypass (CPB) and after cooling to 28-32°C. Cardiac diastolic arrest was made by intermittent antegrade blood cardioplegia with potassium.

Once received in ICU, patients were monitored for 3 days. Urea & creatinine were performed daily. AKI/ARI, according to RIFLE criteria, was classified as follows; patient at RISK - when serum creatinine rises 1.5 times normal; patient with injury when serum creatinine rises two times the normal; and patient with failure if serum creatinine rises markedly to three times normal upper limit. ARI was used for injury while word ARF (Acute renal failure) was used for failure category, in RIFLE classification.

During post-CABG ICU stay, all early neurologic complications were diagnosed by the attending neurologist and prospectively entered into our database. All patients evaluated for onset of neurologic deficit and seizures, underwent cranial computed tomography (CT) and Electroencephalogram (EEG). For each new postoperative neurologic complication, the time of appearance and duration of symptoms were recorded. The major postoperative neurological complications were defined as follows.<sup>21</sup>

A stroke is any confirmed neurological deficit of abrupt onset caused by a disturbance in blood flow to the brain, when the neurologic deficit does not resolve within 24 hours. A reversible ischemic neurologic deficit (RIND) is the symptomatic neurological deficit for at least 24 hours after onset, with complete reversibility of function within 72 hours. A transient ischemic attack (TIA) is the temporary loss of neurological function resulting from temporary occlusion of blood flow in a cerebral artery, but without resulting in permanent brain injury. Most symptoms last less than 5 minutes but may last up to 24 hours.

Seizure is a paroxysmal episode, caused by abnormal electrical conduction in the brain, resulting in the abrupt onset of transient neurologic symptoms such as involuntary muscle movements, sensory disturbances and altered consciousness. In clonic seizure there are generalized

clonic contractions without a preceding tonic phase. Tonic seizure is one characterized by tonic but not clonic contractions. Generalized tonic-clonic seizure the seizure of grand mal epilepsy, consisting of a loss of consciousness and generalized tonic convulsions followed by clonic convulsions. Partial seizure is any seizure due to a lesion in a specific, known area of the cerebral cortex. Simple partial seizure is partial seizure without loss of consciousness. Complex partial seizure is associated with disease of the temporal lobe and characterized by variable impairment in consciousness and automatisms with amnesia. We analyzed variables of age, gender, diabetes, previous cardiac intervention, preoperative IABP support requirement, postoperative mean arterial and pulse pressures (every day for 3 days at 9, 14 & 20 hours of the day; a mean was taken for last calculations), CPB & cross clamp time, number of red blood cell (RBC) units given in the operating room, postoperative urea, creatinine, postoperative hepatic failure (LFTs), & neurological complications.

Data was analyzed by using SPSS (Statistical Package for Social Sciences) version 20. Qualitative variables were expressed as mean  $\pm$  S.D, while quantitative variables were expressed in the form of frequencies, percentages. Variables like (MPA, PP, AKI and ARF) were compared with patient characteristics using Chi-square test. Logistic regression will be applied to estimate the association between neurological and post-operative renal undergoing CABG with predictors. Level of significance was considered  $\leq 5\%$ . All tests applied were two tailed.

## RESULTS

In our study a total of 115 patients undergoing CABG were included. Of them 56 (48.69%) patients were diabetic while hypertension, obesity (BMI  $> 30 \text{ kg/m}^2$ ), smoking and COPD were found in 35 (27.83%), 42 (36.52%), 44 (38.26%) and 6 (5.2%) patients respectively. Left Internal mammary artery was harvested in 71 (77.17%) patients, while it was not harvested in others secondary to bad bony quality of sternum, or when the distal grafting of LAD or its diffuse disease nature was anticipated.

Acute Renal injury was found in 12 patients while ARF developed in 7 patients and urine output dropped to  $< 1 \text{ ml/kg/hr}$  in 7 patients with pulse pressure between 31-40 mmHg & mean arterial pressure between 71-90 mmHg. In patients who had MAP  $< 70 \text{ mmHg}$  and PP of  $< 30 \text{ mmHg}$ , there was no relation with drop in urine output, ARI and ARF ( $p > 0.110$ ). The ARF was associated with rise in age ( $p = 0.044$ ). Both AKI and ARF were highly associated with decrease in temperature of  $< 30^\circ\text{C}$ . There was no relation found with the cross clamp and bypass times in our study. No relation of AKI & CPB was found with ICU stay, time on ventilation, and mortality (Table 1). Stroke, RIND, TIA, coma and seizures had no association with pulse pressure  $< 30 \text{ mmHg}$  and Mean arterial pressure of  $< 70 \text{ mmHg}$ .

**Table 1: Distribution of the Clinical, Intra Operative and Post-Operative Characteristics in Acute Kidney Injury and Acute Renal Failure**

Variables		AKI	ARF
Gender	Male	8(61.5%)	6(60.0%)
	Female	5(38.5%)	4(40.0%)
Obesity		5(38.5%)	3(30.0%)
Diabetes		5(38.5%)	7(70.0%)
Hypertension		1(7.7%)	2(20.0%)
Mean Arterial Pressure (50-70 mmHg)		0	0
Pulse Pressure (30 mmHg)		0	0
Intra Operative Variables			
Cardiopulmonary Bypass time (min)		77.31 $\pm$ 8.240	70.60 $\pm$ 8.249
Cross Clamp time (min)		47.00 $\pm$ 14.059	43.20 $\pm$ 11.331
Side biting Clamp		12(92.3%)	10
Temperature $< 30^\circ\text{C}$		8(61.5%)	6(60.0)
Post-Operative			
ICU duration ( $> 3$ days)		9(69.2%)	7(70.0%)
Time on Ventilator ( $> 8$ hours)		1(7.7%)	2(20.0%)
Mortality		0	0

However the relationship exists for higher pulse pressures and mean arterial pressures as shown in Table 2. Association of different levels of MAP and PP with Cerebrovascular accidents (CVA) and seizures are shown in Table 2.

Binary logistic regression results indicated that male (OR: 1.15, CI 95%: 0.387- 3.38;  $p = 0.807$ ), diabetes mellitus (OR: 2.38, CI 95%: 0.908- 6.21;  $p = 0.078$ ), hypertension (OR: 3.81, CI: 95%, 0.79-18.35), ICU stay (OR: 1.699, CI: 95%, 0.433-1.128,  $p = 0.001$ ), MPA ( $< 50 \text{ mmHg}$ ) (OR: 4.77, CI 95%: 0.40-7.23;  $p = 0.010$ ) and cross clamp time (OR: 1.06, CI: 95%, 1.0-1.09,  $p = 0.023$ ) were significantly associated with both renal and neurological complications

**Table 2: Post-Operative Renal and Neurologic Complications and their Relation with Different Pulse Pressures (PP), Mean Arterial Pressures (MAP)**

Outcome		<30PP	>51PP	<70MAP	>91MAP	Group 1	Group 2
Neurological outcome	Stoke	0	1(14.3%)	0	3(13.0%)	0	5(4.3%)
	Rind	0	1(14.3%)	0	1(4.3%)		
	TIA	0	1(14.3%)	0	1(4.3%)		
	Dementia	0	1(14.3%)	0	1(4.3%)		
	Confusion	1(5%)	1(14.3%)	1(5.9%)	1(4.3%)		
	Complete seizure	0	0	0	3(13.0%)		
	P-value	0.657	.000	0.658	0.000		
Stoke	0	3(42.9%)	0	5(21.7%)	0	3(42.9%)	
Seizures	0	0	0	3(13%)	0	7(16.4%)	
AKI	0	1(14.3%)	0	1(4.3%)	0	1(14.3%)	
ARF	0	2(28.6%)	0	3(13.0%)	0	2(28.6%)	
Creatinine	0	3(42.9%)	0	4(17.4%)	0	3(42.9%)	

postoperatively.

## DISCUSSION

Post-coronary artery revascularization morbidity is long being discussed and come up with various solutions to early diagnose and even prevent them from happening. The most studied of these morbidity are postoperative renal failure and neurological complications.

In our study 20% of patients developed renal disease post CABG, the range in literature being between 5-30%.<sup>22,23</sup> When it occurs, AKI after cardiac surgery with cardiopulmonary bypass (CPB) is considered a terrible complication with high morbidity & mortality.<sup>24,25</sup> Severe AKI requiring renal replacement therapy (RRT) after cardiac surgery is uncommon, nevertheless, has been associated with a 7.9 times increment in risk of death.<sup>26</sup> In our study the highest level of creatinine reached was 5.5%, but did not required RRT. However, even relatively mild increments of creatinine in serum during post-operative period have been associated with decline in survival, strangely our study did not show any mortality in AKI & ARF groups, it might be due to prompt recognition of progressing renal disease and its appropriate management strategy at our institute.<sup>27-29</sup>

Kanji et al found that AKI is present in 41% of patients postoperatively in early period, this is because their study

targeted only those patients who were at higher risk for AKI.<sup>28</sup> Present study demonstrated the incidence of AKI was only 11.3%, and ARF in 8.6%, but the high risk patients were not included in the study. In two other observational studies of cardiac surgery associated AKI, the incidence of AKI ranged between 3.7-9%.<sup>28,29</sup> Kanji et al also observed that those patients who were obese (with BMI (> 25 kg/m<sup>2</sup>) and those in whom side-biting aortic clamp was used, were at marked risk for early post-operative AKI, however our study failed to find such an association.<sup>30</sup> Recently a study by Aronson et al detected that raised blood pressure preoperatively and a rise in PP are linked with AKI, present results also confirms it.<sup>31</sup> The study by Sirvinskas et al established insignificant association between a MABP of 48-80 mm of Hg and postoperative renal failure in patients who had undergone CABG.<sup>32</sup> We totally agree with Sirvinskas et al, as we also found the similar results.

In the 1960s (5% to 9%) stroke was a common morbidity after surgery in past.<sup>33</sup> Although the advanced developments in procedures for surgery and cardioplegia, membrane oxygenators and in-line filtration, the stroke rate remain a persistent threat with CABG.

Post-operative stroke is significantly associated with short and long term outcome after CABG.<sup>34</sup> It is associated with a rise in hospital mortality, longer in-hospital stays, and increased cost for hospital and rehabilitative support.

Secondary to improvement in surgical techniques, and an increasing patient age, more patients with  $\geq 1$  comorbidities are opting for CABG. After surgery risk of post-operative stroke was reported from 1 to 5%, our study has 6% incidence of stroke, despite the fact that all major risk factor were excluded before including the patients in this study.<sup>35</sup>

### LIMITATIONS

Our study has a couple of limitations. This study is conducted only in a single center, and has comparatively smaller number of patients enrolled, and design is observational in nature making it amenable to bias. Additionally, our study may fall into selection bias. To add, the reduced sample size and relatively much accurate diagnosis for AKI used in our study, with shorter post-operative study time, has markedly limited our statistical power and refrained us from identifying potentially meaningful variations in clinical outcomes.

### CONCLUSION

We thus conclude that though the MAP and PP are good markers for the neurological deficit they are not as good with renal disease post CABG.

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