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ORIGINAL ARTICLE

DOES MEAN PERFUSION PRESSURE DURING CARDIOPULMONARY BYPASS AFFECT RENAL FUNCTION?

Ramesh Patel[1], Atul Solanki[2], Hasmukh Patel[3], Himani Pandya[4], Jignesh Patel[5], Sanjay Patel[6]

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ABSTRACT: BACKGROUND: After cardiac surgery acute kidney injury (AKI) is a common and serious condition carrying significant costs and is independently associated with increased morbidity and mortality. During cardiopulmonary bypass (CPB) surgery, modifiable factors may contribute to post-operative AKI. Their prevention might be a potential target for nephroprotection and any other morbidity after cardiac surgery. **METHODS AND MATERIAL:** The objective of the present study was to identify and determine whether intraoperative hypotension or any other cofactor are independent risk factors for postoperative AKI defined by the RIFLE (renal Risk, Injury, Failure, Loss of renal function and End-stage renal disease). On basis of this patients were divided into two groups according to rise in serum creatinine >0.3 mg/dl till 72 hrs postoperatively. Group B patients have developed AKI (n=34) and the remaining patients were in Group A. **RESULT:** In our study we have found that mean arterial pressure during CPB were less in group B patients compare to group A patients which was statistically significant ($p<0.001$). And in this group ICU stay and mortality rate were also high compare to group A patient who had not developed AKI. **CONCLUSION:** Lower MAP during CPB is associated with development of postoperative renal derangement, leads to increase ICU stay and mortality. Larger studies are required to further support the evidence.

KEYWORDS: Mean Perfusion Pressure, Cardio Pulmonary Bypass, Acute Kidney Injury.

INTRODUCTION: Acute kidney injury (AKI) is a common and major complication of cardiopulmonary bypass (CPB) and is independently associated with increased morbidity and mortality.[1,2] Cardiac surgery is now the second most common cause of AKI in critically ill.[3] Many risk factor for AKI after cardiac intervention has been identified but only some are modifiable. Despite target systemic mean arterial pressure (MAP) values of >55 or 60mmhg during CPB, more severe hypotensive episodes occur relatively frequently may be prolonged with MAP values below the optimal renal auto regulation threshold.[4,5]

Similarly bleeding or hemodilution can decrease arterial oxygen delivery and contribute to AKI.[6] Even minimal rise in serum creatinine postoperatively are associated with a substantial decrease in survival.[7] Despite of advances in bypass techniques, intensive care, and delivery of hemodialysis, mortality and morbidity associated with ARF have not markedly changed in last decade.[8] Off pump coronary artery bypass grafting, which eliminates the need for CPB, has been reported to be associated with a lower incidence of AKI.[9] Other studies did not confirmed this finding. Aim of the study was to determine the effect of MAP during cardiopulmonary bypass on postoperative renal derangement.

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MATERIAL AND METHODS: After taking approval from medical ethics committee of U. N. Mehta institute of cardiology and research centre, total one hundred twenty two patients undergoing CPB during cardiac surgery were enrolled for study. Written inform consent was taken from all the patients. Inclusion criteria were age> 18 years, without preoperative renal dysfunction. Patients with preoperative serum creatinine > 1.2 mg% were excluded from study. All patients were provided equal standard of anesthetic management as per institutional protocols.

For providing CPB a S3 heart-lung machine (Stockert Instrumente GmbH, Munich, Germany) with a roller pump and a heat exchange device (Stockert Instruments GmbH) was used for CPB. Standard cannulation and cardiopledgia protocol were used for all patients. During CPB mean perfusion pressure was maintained as near as 60 mmhg with mild hypothermia 34 to 34.5°C. Protamine sulphate 1mg/100unit was given at end of CPB to terminate heparin effect. Residual pump volume was transfused to patient. During CPB target Hb >7 gm% was maintained, while in postoperative ICU Hb >9 gm% was maintained.

Patient's demographic data and preoperative renal function test were recorded.

During CPB MAP, aortic cross clamp time, CPB time, lowest hematocrit and pump flow rate were recorded. Postoperative urine output, serum creatinine, serum urea, hematocrit and creatinine clearance were measured till 3rd postoperative day. Postoperative requirement of dialysis and ICU stay also recorded.

We considered AKI when patients serum creatinine was raised ≥0.3 mg/dl within 48 hours or increase in serum creatinine ≥1.5 times baseline which is known or presumed to have occurred within prior 7 days or urine volume <0.5 ml/kg/hr for 6 hours according to KDIGO, AKI practice guideline.[10] On basis of this patients were divided into two groups according to rise in serum creatinine >0.3 mg/dl till 72 hrs postoperatively. Group B patients have developed AKI (n=34) and the remaining patients were in Group A.

STATISTICAL ANALYSIS: Statistical analysis was carried out using SPSS version 20.0 software (SPSS Inc, USA). The chi-squared test and independent sample t-test were used to compare categorical and continuous variables respectively. Data were presented as mean±SD or proportion as appropriate. The "p" value less than 0.05 was considered to be significant.

RESULTS: Aim of study was to evaluate the association between MAP during CPB and postoperative renal derangement. Total one twenty two patients were enrolled in this study.

In our study mean age of patients were 43 years. Baseline demographic and preoperative clinical characteristics patients were height (Group A 159.32±15.56 vs. Group B 160.05±11.44 p=0.804) weight (Group A 52.36±13.70 vs. Group B 56.67±12.41 p=0.113) BSA (Group A 1.50±0.23 vs. Group B 1.63±0.52 p=0.084) statistically non-significant in both groups (Table 1). In group A patients M= 46 and F=42 and group B patients M=21 and F= 13.

Variable	Group A ≤0.3 (88)	Group B >0.3 (34)	P value
Age	45.21±15.23	50.23±11.20	0.083
Height	159.32±15.56	160.05±11.44	0.804

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Weight	52.36±13.70	56.67±12.41	0.113
Sex	M=46 F=42	M=21 F=13	-
BSA	1.50±0.23	1.63 ± 0.52	0.084

Table 1: Demographic details

BSA: Body surface area.

In our study we have found that mean arterial pressure during CPB were less in group B patients compare to group A patients which was statistically significant ($p<0.001$). (Table 2) Intraoperative data were comparable between the groups were shown in Table 3. Intraoperative cardio pulmonary bypass time and cross clamp time were also statistically non-significant between the two groups ($p=0.8940$ & $p=0.8731$). (Table 4)

Variables	**Group A ≤0.3 (N=88) (No patients & %)**	**Group B >0.3 (N=34) (No patients & %)**
MAP >50 mm hg	81(92.04%)	21(61.76%)
MAP ≤50 mmhg	6(6.8%)	13(38.23%)

Table 2: Association between MAP and postoperative renal derangement

Variable	**Group A ≤0.3 (N=88) Mean±SD**	**Group B >0.3 (N=34) Mean±SD**	**P value**
CPB Time	112.26±74.12	116.23±46.89	0.772
AOX Time	79.92±39.23	80.14±33.93	0.976
Flow rate	3.75±0.60	3.869±0.46	0.313
Lowest HCT	26.24±3.90	25.68±3.44	0.468
Priming volume	1183.91±127.18	1205.88±88.56	0.358

Table 3: ACC, CPB, flow rate, priming volume, lowest hematocrit in two groups

CPB: Cardio pulmonary bypass, AOX: Aortic cross clamp, HCT: Hematocrit.

	Group A ≤0.3 (N=88) (No patients & %)	**Group B >0.3 (N=34) (No patients & %)**
CPB >90 minutes	54 (61.36%)	22 (64.70%)
CPB ≤ 90 minutes	34 (38.63%)	12 (35.29%)
ACC > 60 minutes	60 (68.18%)	23 (67.64%)
ACC ≤ 60 minutes	28 (31.81%)	11 (32.35%)

Table 4: Length of CPB and ACC time and renal derangement in two groups

CPB: Cardio pulmonary bypass, AOX: Aortic cross clamp.

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Ventilation and postoperative hospital stay was high in group B patients which was statistically significant the incidence of mortality were also higher in Group B (17.64%) patients as compare to Group A (1.13%). (Table 5)

Variables	Group A ≤0.3 (N=880)	Group B >0.3 (N=34)	P value
ICU stay	3.17±1.78	4.79±4.11	0.004
MVT	7.42±11.27	11.76±12.24	0.083
Mortality	01(1.13%)	06(17.64%)	0.0021

Table 5: ICU stay and renal derangement

DISCUSSION: We performed prospective study on 122 patients who underwent CPB during cardiac surgery. We analysed the effect of MAP during CPB on postoperative acute kidney injury.

In our study we followed patients for renal derangement till 3rd postoperative day. Out of 122 patients 34 patients developed renal derangement till 72 hrs postoperatively. Maximum number of patients had renal derangement on first postoperative day. Patients whose serum creatinine rise >0.3 mg/dl than preoperative value till 72 hrs postoperatively were in group B and serum creatinine rise <0.3 mg/dl than preoperative value were in group A.

In our study we followed RIFLE criteria to diagnose kidney injury.(11)

1) **Risk:** serum creatinine rise to more than 1.5 mg% or urine output less than 0.5 ml/kg/hour for 6 hours.
2) **Injury:** serum creatinine rise to more than 2 mg% or urine output less than 0.5 ml/kg/hour for 12 hours.
3) **Failure:** serum creatinine rise to more than 3mg% or urine output less than 0.5 ml/kg/hour for 24 hours or anuria for 12 hours.

Renal blood flow begins to decline at MAP less than 50 mm hg, autoregulation of GFR occurs at higher pressure (70-80) mm hg. Kidney receives 20% of total cardiac output, 90% of renal blood flow supplies cortex and creates tissue oxygen tension of approximately 50 mm hg versus 8 to 10 mm hg in medulla. Preferential blood flow leads to medullary thick ascending limb of Henle being extremely vulnerable to hypoperfusion induced ischemia, and explains why acute renal failure can be induced as little as a 40 % decrease of renal blood flow. Prevention of AKI during cardiopulmonary bypass is therefore dependent on adequate blood flow rate, MAP and as well as reducing oxygen demand.

Nuzhat et al concluded in their study that MAP < 50 mm hg and low flow during CPB is one of the risk factors for acute kidney injury even in patients with normal serum creatinine.(12) Their study showed significant association of low mean arterial perfusion pressure with cardiac surgery associated kidney injury.

Similar findings were found in our study where MAP of patient having renal derangement were lower (<50 mmhg) as compared to those of patients not having renal derangement. Statistically difference of MAP was significant between two groups (p<0.001).

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Murphy GS et al, in their study found that the optimal MAP to ensure adequate tissue perfusion during CPB has not been established.[13] Lower limit of safe perfusion pressure is uncertain, with investigators advocating lower (50-60 mmhg) and higher(70-80 mm hg) mean perfusion pressure during routine CPB.

At many cardiac centres, clinicians maintain MAP of 50-60 mm Hg during CPB in the majority of adult patients undergoing bypass. Other data support higher MAPs (70 mm Hg) during CPB. More recent investigations have demonstrated that the lower limit of autoregulation may be much higher than 50 mm Hg. In a study of 511 patients undergoing CPB by Slogoff S et al, MAPs_50 mm Hg (expressed as absolute values or intensity-duration units) were not predictors of postoperative renal or neurologic dysfunction.[14]

In contrast, Reich et al, identified hypotension during bypass (defined as a MAP <50 mm Hg) as a significant predictor of mortality in a cohort of 2149 CABG patients.[15] Fisher et al. observed that patients who developed acute renal failure had longer periods of bypass at pressures 60 mm Hg than control patients with normal postoperative renal function.[16]

Gold et al, compared two strategies of blood pressure management during CPB and concluded that high MAP may improve outcomes, but this finding could not be subsequently validated either.[17]

Jinu Joseph et al, reported that higher mean arterial pressures help to maintain sufficient glomerular filtration pressures, whereas lower MAP could not be defined.[18]

Murphy GS, et al, observed that there is insufficient evidence at the present time to recommend an optimal MAP for all patients undergoing CPB.[13] Despite the publication of numerous clinical trials, several questions remain unanswered. In particular, MAP may be influenced by multiple variables including flow, blood viscosity (Temperature and hematocrit), depth of anesthesia, anesthetic used, and perioperative inflammation. MAP can be increased or decreased by altering flow rate or blood viscosity (i. e., hematocrit) and by the administration of vasoactive Medications. The impact of these various factors on outcomes Complicates interpretation of studies assessing optimal MAP.

We didn't find any statistically significant difference in two groups for flow rate, priming volume and lowest hematocrit.

In Our study, mean CPB time in group A was 111.6±73.91 min and in group B was 116.23±46.89 min with & mean ACC time in group A was 79.43±39.27 min and in group B was 80.14±33.93 min. ACC time and CPB time were not statistically significant in two groups.

Nuzhat et al, reported aortic cross clamp time more than 40 minutes, bypass time more than one hour, low flow during CPB and age above 50 years showed significance at level of 5%.[12] Various other studies have reported higher renal dysfunction, morbidity and mortality in Patients undergoing cardiac surgery with longer cardiopulmonary bypass.[19,20]

Our study did not observed any significant correlation between longer CPB time (>90 min) and longer ACC time (>60 min) among those having post-operative renal derangement as compared to those not having post-operative renal derangement. We didn't find increase duration on mechanical ventilation (MVT) associated with postoperative renal dysfunction.

We observed requirement of longer duration of ICU stay in patients who developed renal dysfunction in 72hrs postoperatively (p=0.004). A significant association between renal dysfunction and mortality was observed in our study (p=0.0021).

CONCLUSION: Lower MAP during CPB is associated with development of postoperative renal derangement, leads to increase ICU stay and mortality. Larger studies are required to further support the evidence.

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AUTHORS:

1. Ramesh Patel
2. Atul Solanki
3. Hasmukh Patel
4. Himani Pandya
5. Jignesh Patel
6. Sanjay Patel

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Cardiac Anesthesia, U. N. Mehta Institute of Cardiology & Research Center, (Affiliated to B. J. Medical College) New Civil Hospital Campus, Asarwa, Ahmedabad.
2. Chief Perfusionist, Department of Perfusion, U. N. Mehta Institute of Cardiology & Research Center, (Affiliated to B. J. Medical College) New Civil Hospital Campus, Asarwa, Ahmedabad.
3. 2nd Year Resident DM Cardiac Anesthesia, U. N. Mehta Institute of Cardiology & Research Center, (Affiliated to B. J. Medical College) New Civil Hospital Campus, Asarwa, Ahmedabad.
4. Research Associate, Department of Research, U. N. Mehta Institute of Cardiology & Research Center, (Affiliated to B. J. Medical College) New Civil Hospital Campus, Asarwa, Ahmedabad.
5. Perfusionist, Department of Perfusion, U. N. Mehta Institute of Cardiology & Research Center, (Affiliated to B. J. Medical College) New Civil Hospital Campus, Asarwa, Ahmedabad.
6. Research Assistant, Department of Research, U. N. Mehta Institute of Cardiology & Research Center, (Affiliated to B. J. Medical College) New Civil Hospital Campus, Asarwa, Ahmedabad.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Ramesh Patel,
Associate Professor,
Department of Cardiac Anesthesia,
U. N. Mehta Institute of Cardiology & Research Center,
(Affiliated to B. J. Medical College)
New Civil Hospital Campus,
Asarwa, Ahmedabad.
E-mail: dr.ramesh33@gmail.com

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