Original Article

Optimal Hematocrit during Cardiopulmonary Bypass to Minimize Post-Operative Renal Dysfunction in Cardiac Surgery

Optimal Hematocrit during Cardiopulmonary Bypass

Abdul Wasay, Muhammad Asad Bilal Awan, Asmatullah Achakzai, Muhammad Mansoor, Muhammad Ishaq Khan and Muhammad Arif

ABSTRACT

Objective: The aim of our study is to identify the ideal hematocrit which must be maintained on CPB to minimize hemodilution induced renal dysfunction after cardiac surgery in our population.

Study Design: Prospective observational study.

Place and Duration of Study: This study was conducted at the Department of Cardiac surgery National Institute of Cardiovascular Diseases (NICVD) Karachi. Duration was 6 months from December 2020 to May 2021.

Materials and Methods: All patients with age between 18 and 80 years undergoing cardiac surgery(CABG, valvular, adult congenital) using CPB were included in study. Patients with preoperative renal failure ,Unstable hemodynamic state and Complex cardiac surgeries were excluded.

Patient's demographic data was obtained such as age (years), gender, height (cm), weight (kg), and BMI (kg/m^2). Hematocrit was recorded and all the patients were observed during their post-operative hospital stay and incidence of post-operative renal dysfunction was recorded. Data was entered and analysis using SPSS version-21.The receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cutoff value of hematocrit. Two sided p-value of ≤ 0.05 was taken as criteria of statistical significance.

Results: Total number of patients were 259 which were included in study. In our study mean age was 50.79 ± 13.31 years and mean body mass index was 25.3 ± 5.1 kg/m^2. Preoperative mean creatinine was 0.9 ± 0.2 ng/dL.The mean cardiopulmonary bypass time was 120.3 ± 32.6 minutes. Mean hematocrit maintained on pump was 26 ± 3.7. Post operatively only 3(1.2%) patients developed renal dysfunction and mean post-operative creatinine was 1 ± 0.3 ng/dL. Overall mortality was 1.2% (3). The area under the curve on ROC analysis was found to be 0.839 [0.691 to 0.986] and the optimal hematocrit level of 27.85 had sensitivity of 100% and specificity of 73% for the prediction of post-operative renal dysfunction.

Conclusion: Hematocrit during CPB affects the outcome after cardiac surgery. It has a direct effect on post-operative renal function. Further larger studies need to be carried out to find out the optimal hematocrit levels needed for best results in cardiac surgery patients.

Key Words: Hematocrit, CardioPumonary Bypass CPB, Renal Dysfunction

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INTRODUCTION

Cardiovascular diseases are the leading cause of death worldwide, with annual deaths of 17.9 million people. [1] Despite of recent advances in medical management and percutaneous interventions, many of these patients undergo open heart surgery using cardiopulmonary bypass. CPB is unique because blood exposed to foreign, non-endothelial surfaces is collected and continuously recirculated throughout the body. This contact with synthetic surfaces within the perfusion circuit, as well as open tissue surfaces within the wound trigger inflammatory response which initiates a powerful thrombotic stimulus and production, release and circulation of vasoactive and cytotoxic substances that affect every organ and tissue within the body.[2] Renal injury after CPB is one of the adverse outcome manifest as subclinical injury to established renal failure requiring dialysis.[3]

Renal blood and plasma flow, free water clearance, creatinine clearance and urine volume decreases without hemodilution.[4] Hemodilution dilutes plasma hemoglobin; improves flow to the outer renal cortex;

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improves total renal blood flow; increases creatinine, electrolyte and water clearance; and increases glomerular filtration and urine volume.[5] Furthermore, hemodilution during CPB decreases chances of red blood cell injury[6] which is an independent cause of renal injury.[7] Hemodilution also reduces the risk of hemoglobin precipitation in renal tubules during extracorporeal perfusion.[8]

Hemodilution during CPB results in reduced oxygen carrying capacity of blood and therefore put kidney at risk of ischemic injury.[9] However, due to hemodilution blood viscosity decreases which results in increased blood flow in both micro and macrocirculation which compensates for the reduced oxygen carrying capacity.[10] However optimal hematocrict level below which further hemodilution causes reduced oxygen delivery to tissues is indeterminate. On the other hand increasesd blood flow increase microembolic load to the kidney during CPB and hence raises possibility of renal injury.[9]

The optimal level of hemodilution on CPB for open heart surgery patients is an important question that need careful assessment. Although it is a known fact that severe hemodilution increases the risk of adverse renal outcomes but on the other hand several above discussed benefits necessitates low hematocrict on CPB. The proposed nadir hematocrit necessary to prevent hemodilution-induced renal dysfunction differ greatly, and different values of 22%, 24%, and 26% have all been reported.[11-13] A considerable dispute is still present regarding the optimal level of hematocrict to be maintained on CPB to minimize renal injury.

MATERIALS AND METHODS

This prospective observational study was conducted at the Department of Cardiac surgery National Institute of Cardiovascular Diseases (NICVD) Karachi for 6 months from December 2020 to May 2021.

Sample size: A study conducted by Karkouti K et al. [9] reported that the adjusted odds ratio for acute renal failure necessitating dialysis support with severe hemodilution (nadir hematocrit concentration <21%) was 2.34, and for mild hemodilution (nadir hematocrit concentration >25%) it was 1.88 (95% confidence interval, 1.02-3.46). At 5% level of significance, 80% power of test, with an expected frequency of acute renal failure in high risk patients as 10% and taking odds ratio of 1.8 the minimum required sample size for the study was calculated to be n=247. Sample size for the study was calculated using G*Power 3.1.9.2.

Sample selection:

- **Inclusion criteria**
  1. All patients with age between 18 and 80 years
  2. Either male or female
  3. Patients undergoing cardiac surgery(CABG, valvular, adult congenital) using CPB
  4. CPB time up to 180 minutes
- **Exclusion criteria**
  1. Patients with age above 80 years
  2. Preoperative renal failure
  3. Anemia
  4. Unstable hemodynamic state (IABP, Inotropes, hypotensive (mAP <60 mmHg))
  5. Redo cardiac surgeries
  6. Complex cardiac surgeries
  7. LVEF <30%

Study Variables and Operational Definition

Pre-Operative Renal Failure: Preoperative renal failure is considered when preoperative creatinine level is above 1.4mg/dl.

Post-Operative Renal Injury: Patients was labelled As renal injury when meeting the following criteria:
Creatinine = 2 Times normal.
Urine output= < 0.5 ml /Kg/hour For 12 hours.

Comorbids:

Diabetic Mellitus (DM): patient with documented history of DM and on anti-diabetic medication for at least 6 months

Hypertension (HTN): patient with documented history of HTN and on anti-hypertensive medication for at least 6 months

Smoking: patient currently or has history of smoking 10 or more cigarettes per day for at least 1 year.

Data Collection: The study was started after approval of the ethical review committee of NICVD. For this study we included consecutive patients undergoing cardiac surgery (CABG, valvular, adult congenital) using CPB criteria at cardiac surgery department of NICVD and fulfill the inclusion. Prior to inclusion the purpose, and benefits of the study was explained and verbal informed consent regarding their inclusion in research study and publication of their data while maintaining confidentiality along with written informed consent for the surgery was obtained. Patient's demographic data was obtained such as age (years), gender, height (cm), weight (kg), and BMI (kg/m^2). History of the patients was taken regarding comorbid conditions such as diabetic mellitus, hypertension, and smoking was taken. All the surgeries was performed by cardiac surgeons. Patients with above 80 years of age, preoperative renal failure, anemia, unstable hemodynamic state (IABP, Inotropes, hypotensive (mAP <60 mmHg)), and LVEF <30% were excluded. Patients undergoing redo cardiac surgeries or complex cardiac surgeries was also excluded. Hematocrit was recorded and all the patients were observed during their post-operative hospital stay and incidence of post-operative renal dysfunction was recorded as per the operational definition.

All the collected data was recorded on predesigned proforma. Patient information was kept secured and available to authorized person only. And no patient identification such as name, MR number, CNIC number, or mobile number etc. was not disclosed during the reporting and publication of results.

Data Analysis: Data was entered and analysis using SPSS version-21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Quantitative (continuous) variables were expressed using appropriate descriptive statistics such as mean ± SD, median (IQR), maximum and minimum. Frequency and percentages were calculated for categorical variables. Patients were categorized into two groups based on post-operative renal dysfunction and appropriate t-test or Mann-Whitney and chi-square test or fisher exact test was applied to assess the differences and associations. Post-operative renal dysfunction was assessed for the various levels of hematocrit. A U-shaped relationship between the hematocrit and post-operative renal dysfunction has been reported in some of the past studies, hence, incidence of post-operative renal dysfunction was assessed by three groups namely low, moderate, and high hematocrit. Logistic regression analysis was performed taking post-operative renal dysfunction as dependent and other characteristics, including hematocrit, as independent variables and adjusted and unadjusted odds ratio (OR) and 95% confidence interval was reported. The receiver operating characteristic (ROC) curve analysis will be performed to determine the optimal cutoff value of hematocrit. Two sided p-value of ≤ 0.05 was taken as criteria of statistical significance.

RESULTS

Total number of patients were 259 which were included in study. In our study male ratio was predominant 69.5% (180) while there were 30.5% (79) females. Mean age was 50.79 ± 13.31 years and mean body mass index was 25.3 ± 5.1 kg/m^2. Most of the patients were in NYHA class II 55.2% (143). Type of cardiac surgery ; CABG were 69.9% (181), valvular were 23.9% (62) and adult congenital were 6.2% (16). Preoperative Left ventricle ejection fraction (LVEF) of these patients was 50.4 ± 8.6%. Preoperative mean creatinine was 0.9 ± 0.2 ng/dL. All pre-existing co- morbid conditions are also shown in Table 1. The mean cardiopulmonary bypass time was 120.3 ± 32.6 minutes. Mean hematocrit maintained on pump was 26 ± 3.7. Post operatively only 3(1.2%) patients developed renal dysfunction and mean post-operative creatinine was 1 ± 0.3 ng/dL. Overall mortality was 1.2% (3). Post-operative stay in ICU and hospital is shown in Table 1. The analysis of patient pre-operative and per-operative characteristics with post-operative renal dysfunction showed significant relationship with hematocrit and post-operative creatinine (p<0.001) as shown in Table-2.

Table No.1: Baseline clinical characteristics and post-operative outcomes

Characteristics	Total
Total (N)	259
Gender	
Male	69.5% (180)
Female	30.5% (79)
Age (years)	50.79 ± 13.31
≤ 50 years	40.9% (106)
50 to 70 years	56% (145)
>70 years	3.1% (8)
Body mass index(kg/m^2)	25.3 ± 5.1
NYHA	
I	39% (101)
II	55.2% (143)
III	5.8% (15)
IV	0% (0)
Type of surgery	
CABG	69.9% (181)
Valvular	23.9% (62)
Adult Congenital	6.2% (16)
Co-morbids	
Diabetes mellitus	50.2% (130)
Hypertension	49.6% (128)
Smoking	34.4% (89)
Obesity	6.2% (16)
AF	7.8% (20)
Cardiopulmonary bypass time (minutes)	120.3 ± 32.6
LVEF (%)	50.4 ± 8.6
Pre-operative creatinine	0.9 ± 0.2
Hematocrit	26 ± 3.7
Post-operative creatinine	1 ± 0.3
Outcomes	
Renal dysfunction	1.2% (3)
Mortality	1.2% (3)
Intensive care unit stay (hours)	72.6 ± 20.7
< 72 hours	30.1% (78)
≥ 72 hours	69.9% (181)
Length of hospital stay (days)	9.99 ± 4.33
< 7 days	13.1% (34)
≥ 7 days	86.9% (225)

The receiver operating characteristic (ROC) curve analysis of hematocrit for the prediction of post-operative renal dysfunction is shown in Figure 1. The area under the curve on ROC analysis was found to be 0.839 [0.691 to 0.986] and the optimal hematocrit level of 27.85 had sensitivity of 100% and specificity of 73% for the prediction of post-operative renal dysfunction.

Table No.2: Baseline clinical characteristics and post-operative outcomes stratified by the post-operative renal dysfunction

Characteristics	Renal Dysfunction		P-value
	Yes	No	
N	3 (1.2%)	256 (98.8%)	-
Gender			
Male	66.7%(2)	69.5% (178)	>0.999
Female	33.3% (1)	30.5% (78)	
Age (years)	48.67 ± 19.63	50.81 ± 13.27	0.782
≤ 50 years	33.3% (1)	41% (105)	0.906
50 to 70 years	66.7% (2)	55.9% (143)	
>70 years	0% (0)	3.1% (8)	
Body mass index	25.31 ± 3.09	25.29 ± 5.1	0.993
NYHA			
I	100% (3)	38.3% (98)	0.093
II	0% (0)	55.9% (143)	
III	0% (0)	5.9% (15)	
IV	0% (0)	0% (0)	
Type of surgery			
CABG	66.7% (2)	69.9% (179)	0.113
Valvular	0% (0)	24.2% (62)	
Adult Congenital	33.3% (1)	5.9% (15)	
Co-morbids			
Diabetes mellitus	33.3% (1)	50.4% (129)	0.622
Hypertension	66.7% (2)	49.4% (126)	0.621
Smoking	0% (0)	34.8% (89)	0.553
Obesity	0% (0)	6.3% (16)	>0.999
AF	0% (0)	7.9% (20)	>0.999
Cardiopulmonary bypass time (minutes)	89 ± 30.45	120.64 ± 32.46	0.094
LVEF (%)	50 ± 17.32	50.44 ± 8.56	0.931
Pre-operative creatinine	1 ± 0.3	0.9 ± 0.2	0.412
Hematocrit	30.45 ± 3.61	26 ± 3.67	0.038*
Post-operative creatinine	1.72 ± 0.73	1.02 ± 0.27	<0.001*
Intensive care unit stay (hours)	64 ± 13.86	72.75 ± 20.75	0.468
< 72 hours	33.3% (1)	30.1% (77)	>0.999
≥ 72 hours	66.7% (2)	69.9% (179)	
Length of hospital stay (days)	14.33 ± 4.62	9.94 ± 4.31	0.081
< 7 days	0% (0)	13.3% (34)	>0.999
≥ 7 days	100% (3)	86.7% (222)	

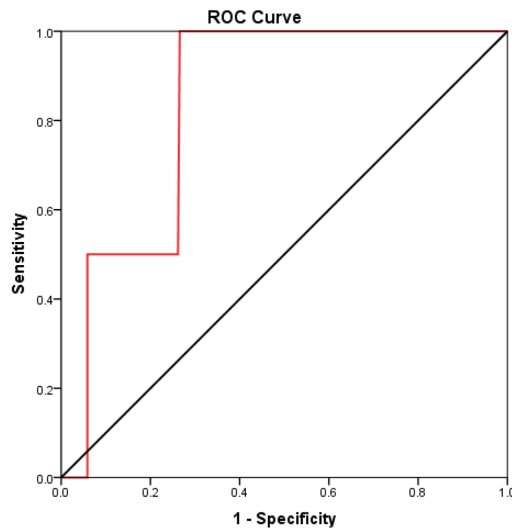

Figure No.1: The receiver operating characteristic (ROC) curve analysis of hematocrit for the prediction of post-operative renal dysfunction

DISCUSSION

It is still unclear that what should be the best value of hematocrit during cardiopulmonary bypass (CPB) to avoid the complications related to hemodilution during cardiac surgery. A study conducted by Ravi Ghatanatti in India on 200 patients documented effects of hemodilution on kidney function. Ravi divided patients according to degree of hemodilution into mild (>25%), moderate (21%–25%), and severe (<21%) and concluded that severe hemodilution(hematocrit of< 21%) is critical during CBP and is associated with significant decrease in creatinine clearance($P \leq 0.0001$) , while there was no significant decrease in creatinine clearance in mild and moderate group[3].This study results indirectly support our study which showed optimal hematocrit of 27.85% to avoid renal dysfunction.

Ranucci et al in a single-center retrospective cohort study analyzed data between 2000 to 2013. He included all patients (20,368 patients) undergoing cardiac operations on pump, and concluded that hemodilution during CPB is an independent risk factor for acute kidney injury (AKI). During these years, changes were made to CPB management to decrease the level of hemodilution by reducing the length of the circuit and by reducing priming volume. He also mentioned other independent risk factors causing AKI which include eGFR, left ventricular ejection fraction, diabetes, redo operations, non-elective operations, nonisolated coronary operations, preoperative IABP use, age, duration of CPB, the timing of angiography, and the HCT value during CPB[14].Where as in our study we could not find any significant relationship between post-operative renal dysfunction and factors like CPB time, age, diabetes mellitus and LVEF.

The association between the degree of hemodilution during CPB and renal dysfunction leading to acute renal failure (ARF) and requiring dialysis is supported by literature. In postmortem findings, most common etiologies for ARF after CPB are acute tubular necrosis(ATN) which is caused by insufficient oxygen delivery and renal infarctions due to microemboli.[15,7] A study done on 9080 patients showed that 1.5% patients (n = 134) developed acute renal failure requiring dialysis. This study showed independent, nonlinear relationship between hematocrit concentration during cardiopulmonary bypass and acute renal failure requiring dialysis .This showed hematocrit concentration 21%-25% was associated with the lowest risk of acute renal failure requiring dialysis. Compared with this the adjusted odds ratio for acute renal failure requiring dialysis was higher in hematocrit concentration <21% and >25%. Conclusion of this study was same as all above studies supporting an independent association between the degree of hemodilution during cardiopulmonary bypass and perioperative acute renal failure requiring dialysis. It also suggested that during cardiopulmonary bypass hematocrit should be kept within optimal range[9].

CPB management updates suggest that if Hb <7.5 g/dL (or hematocrit <22 percent), it should be managed by removal of fluid by ultrafiltration (hemoconcentration)[16]. Packed red blood cells (RBCs) transfusion is another option[17]. The decision to transfuse RBCs should be made based on individual characteristics of the patient[18,19]. In cases of severe anemia, first step is transfusion of available salvaged blood , second step is reinfusion of blood units harvested via normovolemic hemodilution, and as a last option allogenic RBCs should be transfused to maintain optimal hematocrit.In our study Optimal Hct is 27.85%, and has sensitivity of 100% and specificity of 73% to avoid from renal dysfunction in all those patient who are undergoing on-pump cardiac surgery. It include all types of cardiac surgeries i-e CABG, Valvular and Adult congenital surgeries.

CONCLUSION

Hematocrit during CPB affects the outcome after cardiac surgery. It has a direct effect on post-operative renal function. Further larger studies need to be carried out to find out the optimal hematocrit levels needed for best results in cardiac surgery patients.

Author's Contribution:

Concept & Design of Study:	Abdul Wasay
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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