Original Article

Impact of Serum Procalcitonin on Duration of Mechanical Ventilation and ICU Stay in Post-Cardiopulmonary Bypass Patients

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Abstract

Background: *Post-cardiopulmonary bypass (CPB) patients often experience systemic inflammatory responses, with serum procalcitonin (PCT) serving as a biomarker for postoperative complications.*

Objective: *To evaluate the impact of serum Procalcitonin (PCT) levels on mechanical ventilation duration and Intensive Care Unit (ICU) stay in patients undergoing Cardiopulmonary Bypass (CPB).*

Materials and Methods: *This prospective observational study was conducted in the Department of Cardiac Surgery, National Heart Foundation Hospital and Research Institute, Dhaka, Bangladesh, from September 2020 to August 2022. It included 140 patients who underwent cardiac surgery with cardiopulmonary bypass in the cardiac surgery department at the National Heart Foundation Hospital and Research Institute.*

Results: *In this study, patients were divided into two groups- group A included 70 patients with serum procalcitonin levels <7 ng/ml and group B included 70 patients with serum procalcitonin levels>7 ng/ml. On 1st postoperative day, serum procalcitonin levels were 1.36(±0.97) ng/ml and 27.09(±26.11) ng/ml in groups A &B respectively (p < 0.001).Group B had significantly prolonged mechanical ventilation time (18.0 ± 16.5 hours vs. 8.4 ± 2.0 hours, p < 0.001) and longer ICU stays (40.8 ± 32.7 hours vs. 23.1 ± 3.6 hours, p < 0.001) compared to Group A. Total hospital stay was also extended in Group B (8.5 ± 2.6 days vs. 7.2 ± 0.7 days, p < 0.001).*

Conclusion: *Elevated postoperative serum procalcitonin levels are associated with prolonged mechanical ventilation, extended ICU stays and longer hospitalization in CPB patients. Monitoring PCT levels may help predict recovery trajectories and guide early interventions to improve postoperative outcomes.*

Key words: *Post-Cardiopulmonary Bypass Patients, Serum Procalcitonin, Mechanical Ventilation, ICU Stay.*

Date of received: *19.11.2024*

Date of acceptance: *26.02.2025*

DOI: https://doi.org/10.3329/kyamcj.v16i01.80736

KYAMC Journal. 2025; 16(01): 03-08.

Introduction

Cardiopulmonary bypass (CPB) is an essential component of many cardiac surgeries but is associated with a systemic inflammatory response that can lead to complications such as prolonged mechanical ventilation and extended intensive care unit (ICU) stays. Postoperative inflammatory markers are commonly used to assess the severity of this response. Among them, procalcitonin (PCT) has gained attention as a potential biomarker for guiding clinical decisions in critically ill patients.

Although CPB enabled open heart surgery, saving hundreds of thousands of lives, blood circulation through an artificial extracorporeal circuit can cause systemic and pulmonary injury. Bronchial artery flow is maintained during CPB, but pulmonary arterial flow is significantly reduced. Concurrently, lung ventilation is usually stopped to improve surgical exposure and field stability. The lack of ventilation, combined with decreased blood flow to the lungs, may increase the risk of pulmonary injury. Cardiopulmonary bypass also triggers a severe systemic inflammatory cascade, which can result in pulmonary injury. During CPB, up to 60% of patients have increased pulmonary vascular permeability.[1]

Cardiac surgery with cardiopulmonary bypass (CPB) is a highly sterile procedure, but it can result in a systemic inflammatory

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response syndrome.[2] This systemic inflammatory response syndrome (SIRS) is caused by a variety of stimuli, including blood exposure to non-physiological surfaces, surgical trauma, myocardial ischemia-reperfusion due to aortic clamping, and endotoxin release, which can lead to acute respiratory distress syndrome.[3] In practice, all procalcitonin produced by thyroid C cells is converted to calcitonin, resulting in no procalcitonin being released into the circulation. During inflammation, procalcitonin is primarily produced by two pathways: a direct pathway induced by lipopolysaccharide (LPS) or another toxic metabolite from microbes, and an indirect pathway induced by various inflammatory mediators such as IL-6, TNF- α, etc. and others.

Procalcitonin (PCT) is a 116-amino acid polypeptide that serves as a potential marker for infection. The level of procalcitonin in the blood of healthy people is below the clinical assay limit of detection (0.05 ng/mL). Procalcitonin levels rise in response to a pro-inflammatory stimulus, particularly one of bacterial origin. LPS, microbial toxins, and inflammatory mediators such as IL-6 or TNF- induce the CALC-1 gene in adipocytes during inflammation, but procalcitonin is never cleaved to produce calcitonin. In a healthy person, procalcitonin is produced by CALC-1 in endocrine cells in response to increased calcium levels, glucocorticoids, CGRP, glucagon, or gastrin, and is cleaved to form calcitonin, which is released into the bloodstream.[4] Procalcitonin increases within 4 hours of response to infection or injury, showing a peak level at approximately 12–16 hours after the initial stimulus, and the half-life is approximately 20 – 24 hours blood and returns to baseline in 2–3 days.[4] The inflammatory response is activated during cardiopulmonary bypass (CPB), which may lead to acute respiratory distress syndrome (ARDS) and procalcitonin (PCT) increases during this inflammatory response.[5]

Therefore, in this study, we aimed to evaluate the impact of serum PCT levels on mechanical ventilation duration and ICU stay in patients undergoing CPB.

Materials and Methods

This was a prospective observational study conducted in the Department of Cardiac Surgery, National Heart Foundation Hospital and Research Institute, Dhaka, Bangladesh from September 2020 to August 2022. This study included 140 patients who underwent cardiac surgery with cardiopulmonary bypass in the cardiac surgery department at the National Heart Foundation Hospital and Research Institute. Patients were divided into two groups- group A included 70 patients with serum procalcitonin levels <7 ng/ml and group B included 70 patients with serum procalcitonin levels >7 ng/ml.

These are the following criteria to be eligible for enrollment as our study participants:

Inclusion Criteria

a) Patients aged more than 18 years;
b)Patients with elective cardiac surgery under cardiopulmonary bypass;
c) Patients being free from active preoperative infection or inflammatory disease;
d) Patients with leukocyte count <12x10^9 /L, and body temperature < 37.5 ˚C were included in the study.

Exclusion Criteria

a) Patients with a previous history of lung surgery;
b) Patients with emergency and redo cardiac surgery;
c) Patients with any history of acute illness (e.g.,renal or pancreatic diseases, ischemic heart disease, asthma, COPD etc.);
d) Patients who were not willing to participate were excluded from our study.

Surgical procedure:All patients included in this study were operated on through a median sternotomy approach and using a cardiopulmonary bypass. A standard CPB circuit was used and a mean arterial pressure was kept 50 to 60 mm of Hg. Myocardial protection was achieved with intermittent antegrade cold blood cardioplegia with moderate systemic hypothermia (300C to 320C). After completing the operating procedure, protamine sulfate (100:1 ratio) was used to reverse the heparin effect at completion of the surgical procedure. Following the surgical procedure, all the patients were brought to the Cardiac Intensive Care Unit (CICU) where they were monitored until the patients were extubated.

Data collection procedure: A thorough history and physical examination were performed and recorded on the questionnaire. Informed consent was taken from each subject before enrollment. Detailed history, clinical examination, and relevant investigation reports of all patients were recorded in the data collection sheet preoperatively.Demographic data were noted. Type of surgery, duration of operation, CPB time, aortic Cross clamp time, blood transfusion, and FFP transfusion during the operation were recorded. Serum concentration of procalcitonin on 1st postoperative day was recorded. Patients were divided into two groups; group A included 70 patients with serum procalcitonin level <7 ng/ml and group B included 70 patients with serum procalcitonin level >7 ng/ml according to serum procalcitonin level on the 1st postoperative day with a cut-off value of 7.0 ng/ml. Patients were followed daily upto the 7th postoperative day to determine whether the patient developed ARDS.Blood gas analysis was tested at least once per day when the patients were in the CICU. All data were collected, summarized, and statistically analyzed.

Statistical Analysis: All data were recorded systematically in preformed data collection form. Quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was done with independent Student's t-test for continuous data, Chi-square for categorical data, and Mann-Whitney U test for nonparametric data. A p-value <0.05 was considered as significant.Statistical analysis was performed using SPSS 26 (Statistical Package for Social Sciences) for Windows version 10.The study was approved by the Ethical Review Committee of National Heart Foundation Hospital and Research Institute.

Results

Table I: Age distribution of the study patients between two groups (n=140)

Age group (years)	Group A (n=70)	Group B (n=70)	p-value
18 -27	11(15.7%)	9(12.9%)	
28 -37	18(25.7%)	10(14.3%)	
38 -47	13(18.6%)	17(24.3%)	
48 -57	17(24.3%)	17(24.3%)	
>57	11(15.7%)	17(24.3%)	
Mean±SD	43.20±13.18	46.61±13.75	0.136

Table I presents the age distribution of participants in Group A and Group B. In Group A, the largest proportion of participants falls within the 28-37 age range (25.7%), followed by the 48-57 age group (24.3%).In Group B, the highest percentage is seen in 38-47, 48-57 and >57 age groups (24.3% each). The mean age for Group A is 43.20 ± 13.18 years, while for Group B, it is slightly higher at 46.61 ± 13.75 years. The p-value is 0.136, indicating no statistically significant difference (NS) in age distribution between the two groups.

Table II: Gender distribution of the study patients between two groups (n=140)

Gender	Group A (n=70)	Group B (n=70)	p-value
Male	29(41.4%)	37(52.9%)	0.176
Female	41(58.6%)	33(47.1%)	

Table II shows that in group A, 41.4% of patients were male and 58.6% were female; in group B, 52.9% were male and 47.1% were female. The male-female ratio was 1:1.41 and 1.12:1 in Group A and Group B, respectively.

Table III: Comparison of preoperative, perioperative, and postoperative clinical parameters between the two groups (n=140)

Pre - operative variables	Group A (n=70)	Group B (n=70)	p-value
Preoperative WBC (per mm^3 of blood)	8477.14 ± 1295.72	8251.43 ± 1336.74	0.312
Preoperative NT-pro-BNP (pg/ml)	251.86 ± 205.16	217.01 ± 157.55	0.262
Per - operative variables			
Total operative time (hrs)	4.46 ± 0.98	5.56 ± 1.80	<0.001
CPB time (min)	105.01 ± 33.95	164.04 ± 78.67	<0.001
Aortic cross-clamp time (min)	69.03 ± 27.54	95.83 ± 34.11	<0.001
Blood transfusion (unit)	1.89 ± 0.67	2.07 ± 0.89	0.166
FFP transfusion (unit)	1.90 ± 0.30	2.00 ± 0.42	0.107
Post-operative variables			
Serum procalcitonin level on 1st postoperative day (ng/ml)	1.36 ± 0.97	27.09 ± 26.11	<0.001
1st postoperative day fluid balance (ml)	-300.7 ± 100.9	-309.9 ± 109.9	0.554
Postoperative NT-Pro BNP (pg/ml)	316.6 ± 204.2	264.54 ± 138.28	0.286

Table III compares preoperative, intraoperative, and postoperative variables between Group A and Group B. The mean white blood cell (WBC) count was higher in Group A (8477.14 ± 1295.72 per mm³) compared to Group B (8251.43 ± 1336.74 per mm³), but the difference was not statistically significant (p = 0.312). Similarly, preoperative NT-pro-BNP levels were higher in Group A (251.86 ± 205.16 pg/ml) than in Group B (217.01 ± 157.55 pg/ml), but the difference was not significant (p = 0.262).The total operative time was significantly longer in Group B (5.56 ± 1.80 hours) compared to Group A (4.46 ± 0.98 hours, p < 0.001). Cardiopulmonary bypass (CPB) time was also notably longer in Group B (164.04 ± 78.67 minutes) than in Group A (105.01 ± 33.95 minutes, p < 0.001). Aortic cross-clamp time was significantly longer in Group B (95.83 ± 34.11 minutes) compared to Group A (69.03 ± 27.54 minutes, p < 0.001). Serum procalcitonin levels on the first postoperative day were dramatically higher in Group B (27.09 ± 26.11 ng/ml) compared to Group A (1.36 ± 0.97 ng/ml), with a highly significant difference (p < 0.001). Postoperative NT-pro-BNP levels were slightly lower in Group B (264.54 ± 138.28 pg/ml) compared to Group A (316.6 ± 204.2 pg/ml), but the difference was not statistically significant (p = 0.286).

Table IV: Comparison of mechanical ventilation time, duration of ICU stays, and postoperative hospital stay between two groups (n=140)

Variables	Group A (n=70)	Group B (n=70)	p-value
Mechanical ventilation time (hours)	8.4±2.0	18.0±16.5	<0.001
Duration of ICU stay (hours)	23.1±3.6	40.8±32.7	<0.001
Postoperative hospital stays (days)	7.2±0.7	8.5±2.6	<0.001

Table IV compares postoperative recovery parameters between Group A and Group B, each with 70 patients. Mechanical ventilation time was significantly longer in Group B (18.0 ± 16.5 hours), compared to 8.4 ± 2.0 hours in Group A (p < 0.001). ICU stay duration also showed a significant difference, with Group B patients staying in the ICU for an average of 40.8 ± 32.7 hours, whereas Group A had a much shorter stay of 23.1 ± 3.6 hours (p < 0.001). Total postoperative hospital stay was also prolonged in Group B (8.5 ± 2.6 days) compared to Group A (7.2 ± 0.7 days, p < 0.001). However, patients in Group B experienced a significantly longer recovery period, requiring more time on mechanical ventilation, in the ICU and the hospital compared to Group A.

Discussion

The mean age of the patients was 43.20±13.18 years and 46.61±13.75 years in group A and group B respectively. In group A, 41.4% of patients were male and 58.6% of patients were female and in group B, 52.9% of patients were male and 47.1% of patients were female. There were no statistically significant (p > 0.05) differences observed in age and sex between the two groups. These results were similar to the study conducted by Cheng and Chen, 2020.[5]
However, significant differences were observed in total operative time, cardiopulmonary bypass (CPB) time, and aortic cross-clamp time, with group B experiencing longer durations for all parameters (p < 0.05). These findings are consistent with Cheng and Chen (2020), who also reported prolonged operative and CPB times in patients with elevated procalcitonin levels.[5] Prolonged CPB and cross-clamp durations are known to exacerbate systemic inflammation, potentially leading to worse postoperative outcomes, including prolonged mechanical ventilation and ICU stay.

This study found that in group A mean serum procalcitonin level on 1st postoperative day was 1.36±0.97 ng/ml with a minimum of 0.0 ng/ml to a maximum of 5.3 ng/ml and in group B mean(±SD) serum procalcitonin level on 1st postoperative day was 27.09(±26.11) ng/ml with a minimum of 8.0 ng/ml to a maximum of 94.0 ng/ml. There was a statistically significant (p < 0.05) difference observed in serum procalcitonin level on 1st post-operative day between the two groups. These findings were consistent with the study conducted by Cheng and Chen, 2020, where procalcitonin concentration was 16.23 ± 5.9 ng/mL in the procalcitonin elevated cohort, and 2.70 ± 1.43 ng/mL in the procalcitonin control cohort (p < 0.001).[5]

Aouifi et al., 1999 studied 36 patients prospectively, where they found peak procalcitonin was 1.79 (1.64) ng/ ml in SIRS patients vs 0.34 (0.32) ng/ ml in patients without SIRS. Serum procalcitonin concentrations in these patients ranged from 6.2 to 230 ng/ml. 3 Additionally, a study by Hensel et al. reported serum PCT concentrations ranging from 5.1 to 14.3 ng/ml on the first postoperative day in nine patients who developed acute lung injury. This suggests that PCT levels exceeding 5 ng/ml may strongly indicate postoperative complications.[6]

There were statistically significant (p < 0.001) differences observed in mechanical ventilation time (18.0 ± 16.5 vs 8.4 ± 2.0 hours), duration of ICU stays (40.8 ± 32.7 vs 23.1 ± 3.6 hours), and postoperative hospital stay (8.5 ± 2.6 vs 7.2 ± 0.7 days) between the two groups. These findings were consistent with the studies conducted by Cheng and Chen, 2020, where mechanical ventilation duration (2.6 ± 3.0 days versus 1.4 ± 0.9 days, p = 0.002) and longer ICU stay (3.3 ± 4.3 days versus 1.7 ± 1.4 days, p < 0.001) in the procalcitonin elevated cohort than in the procalcitonin control cohort.[5]

Aouifi et al. reported that cardiopulmonary bypass (CPB) duration and aortic cross-clamp time are significantly longer in valvular surgery with the CPB group (100 ± 29 min and 78 ± 31 min, respectively) compared to the other groups (p < 0.05). Mechanical ventilation duration varies, with valvular surgery with CPB Group requiring the longest duration (median 20 hours, range 6–40 hours), followed by valvular surgery with CPB Group (12 hours, range 6–21 hours). ICU stay is also slightly longer in valvular surgery with CPB Group (median 3 days, range 2–5 days) compared to valvular surgery with CPB Group (3 days, range 3–5 days).[3]

Additionally, the study by Meisner et al. (2002) reported that patients with PCT levels above 2 ng/ml within the first two postoperative days had a significantly higher incidence (95%) of postoperative abnormalities compared to those with lower PCT levels (59%).[7] This further supports the role of PCT as a marker of systemic inflammation and its potential impact on post-surgical outcomes.

Aouifi et al. determined that a PCT level above 1 ng/ml could predict bacterial infections, while levels exceeding 10 ng/ml were associated with septic shock.[8] Similarly, Jebali et al. reported a significant rise in PCT levels in infection cases as early as the second postoperative day.[9]

Limitations of the study

This study was a single-center study. We took a small sample size due to the short study period, so it does not represent a whole community. After evaluating those patients, we did not follow up with them for the long term and did not know other possible interference that may happen in the long term with these patients.

Conclusion

This study shows the significant impact of elevated postoperative serum procalcitonin (PCT) levels on patient recovery following cardiopulmonary bypass (CPB). Patients with higher PCT levels experienced significantly longer durations of mechanical ventilation, extended ICU stays, and prolonged overall hospitalization compared to those with lower PCT levels. Additionally, longer operative times, cardiopulmonary bypass durations, and aortic cross-clamp times were observed in the high-PCT group. These findings suggest that postoperative PCT levels could serve as a valuable biomarker for identifying patients at risk of delayed recovery and complications.

So further study with a prospective and longitudinal study design including a larger sample size needs to be done to validate the findings of our study.

Acknowledgement

I express my heartfelt gratitude to Prof. Dr.Farooque Ahmed, Professor, Department of Cardiac Surgery, NHFH & RI Dhaka, for his permission,constant and careful guidance, without which this work would not have been possible. I would like to express my deepest regards and gratitude to Associate professor Dr. Md. Hafizur Rahman and Assistant Professor Dr. Abdul Gafur and other Unit Head, Department of Cardiac Surgery, NHFH & RI, for their co-operation and directions during the study period.I would like to special thanks to biochemistry department for their co-operation. I want to give special thanks to the hospital authority and ethical committee for allowing me to conduct the study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: This study was approvedby the ethical review committee

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