Original Research Article

# PROCALCITONIN AS A BIOMARKER FOR ACUTE RESPIRATORY DISTRESS SYNDROME POST-CARDIOPULMONARY BYPASS

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**ABSTRACT**

**Background:** Acute respiratory distress syndrome (ARDS) is a serious postoperative complication following cardiac surgery under cardiopulmonary bypass (CPB), with systemic inflammation playing a pivotal role in its pathogenesis. Serum procalcitonin (PCT), a biomarker of inflammatory response, may have prognostic value in identifying patients at higher risk for ARDS in the postoperative period. The aim is to evaluate the association between elevated serum procalcitonin levels and the incidence of ARDS in patients undergoing cardiac surgery under cardiopulmonary bypass.
**Materials and Methods:** This prospective observational study was conducted on 160 adult patients undergoing elective cardiac surgery under CPB. Based on 24-hour postoperative serum PCT levels, patients were divided into two groups: Group A (PCT <7 ng/mL) and Group B (PCT >7 ng/mL), with 80 patients in each group. Clinical, intraoperative, and postoperative parameters were compared. ARDS was diagnosed using the Berlin definition. Data were analyzed using SPSS v25, with p <0.05 considered statistically significant.
**Results:** Group B patients had significantly longer CPB time (167.3 ± 80.1 min vs. 107.4 ± 34.6 min, p<0.001), higher incidence of ARDS (37.5% vs. 10%, p=0.001), and prolonged ICU stay (42.10 ± 33.2 hrs vs. 23.35 ± 3.7 hrs, p<0.001) compared to Group A. Mechanical ventilation time and hospital stay were also significantly increased. ROC analysis showed that a serum PCT level >10 ng/mL had an AUC of 0.891 for predicting ARDS, with 80.6% sensitivity and 76.1% specificity.
**Conclusion:** Elevated serum procalcitonin levels are significantly associated with higher incidence and severity of ARDS in patients undergoing cardiac surgery under CPB. Procalcitonin may serve as a useful biomarker for early risk stratification and targeted monitoring in the postoperative period.
**Keywords:** Procalcitonin, ARDS, Cardiopulmonary Bypass.

## INTRODUCTION

Acute Respiratory Distress Syndrome (ARDS) is a critical postoperative complication in patients undergoing cardiac surgery, particularly when cardiopulmonary bypass (CPB) is employed. ARDS is characterized by acute onset hypoxemia, bilateral pulmonary infiltrates, and non-cardiogenic pulmonary edema, often leading to significant morbidity and mortality in the intensive care setting.[1] Among patients undergoing cardiac procedures under CPB, the reported incidence of ARDS varies from 2% to 10%, with even higher rates in those with prolonged bypass time and perioperative inflammation.[2]

Cardiopulmonary bypass is known to trigger a systemic inflammatory response through a variety of mechanisms including blood contact with non-endothelial surfaces, ischemia-reperfusion injury, endotoxemia, and complement activation.[3] This systemic inflammation plays a central role in the pathogenesis of postoperative lung injury and ARDS. Identifying early biomarkers that can predict or correlate with the risk of ARDS following cardiac surgery remains a high-priority objective in perioperative critical care.

Procalcitonin (PCT), a 116-amino acid peptide and a precursor of calcitonin, has emerged as a promising inflammatory biomarker in both infectious and non-infectious inflammatory states. It is secreted in response to bacterial endotoxins and inflammatory cytokines, making it a sensitive marker for systemic inflammatory response and sepsis.[4] In the setting of cardiac surgery, elevated PCT levels have been observed postoperatively even in the absence of infection, reflecting the magnitude of the inflammatory reaction associated with CPB.[5]

Recent studies have reported associations between elevated PCT levels and postoperative complications such as low cardiac output syndrome, prolonged mechanical ventilation, and multi-organ dysfunction.[6] Moreover, some investigations have suggested a correlation between higher PCT concentrations and the incidence of pulmonary complications, including ARDS.[7] This association could be attributed to the fact that procalcitonin reflects the intensity of systemic inflammation, which is a known trigger for increased pulmonary capillary permeability and alveolar damage.

While C-reactive protein (CRP) and interleukins have traditionally been used to monitor inflammatory responses, procalcitonin has shown a more rapid rise and higher specificity in the context of post-surgical inflammation and sepsis.[8] Additionally, PCT levels can serve as a dynamic marker for risk stratification and early intervention in critically ill cardiac surgery patients. A study by Srisawat et al. found that persistently high levels of PCT within the first 48 hours after CPB were strongly associated with postoperative respiratory complications, including ARDS.[9]

Despite these findings, the predictive role of serum procalcitonin in the development of ARDS following CPB remains under-investigated, especially in prospective clinical studies. Understanding this relationship is crucial to improving early diagnosis, risk stratification, and potentially guiding perioperative interventions to reduce the incidence of ARDS and improve outcomes in cardiac surgery patients.[10]

This study was therefore undertaken to explore the association between elevated serum procalcitonin levels and the development of acute respiratory distress syndrome in patients undergoing cardiac surgery under cardiopulmonary bypass.

## MATERIALS AND METHODS

This hospital-based prospective observational study was conducted in the Department of Cardiothoracic and Vascular Surgery, in collaboration with the Department of Anesthesiology and Critical Care, at a tertiary care center in India. The objective was to evaluate the association between postoperative serum procalcitonin (PCT) levels and the development of acute respiratory distress syndrome (ARDS) in patients undergoing cardiac surgery under cardiopulmonary bypass (CPB).

**Sample Size and Study Population**

A total of 160 adult patients undergoing elective cardiac surgery requiring cardiopulmonary bypass were enrolled in the study after obtaining informed written consent. Patients were recruited consecutively from the cardiothoracic surgical unit.

**Group Allocation**

Out of the 160 patients enrolled in the study, 140 patients with complete data and within predefined criteria were analyzed and divided into two groups based on their postoperative serum procalcitonin (PCT) levels measured within 24 hours of surgery:

- Group A: Included 70 patients with serum procalcitonin levels <7 ng/mL
- Group B: Included 70 patients with serum procalcitonin levels >7 ng/mL

The cutoff value of 7 ng/mL was chosen based on existing literature indicating a significantly elevated systemic inflammatory response beyond this threshold in post-cardiac surgical patients. Patients with borderline or intermediate PCT levels (n = 20) were excluded from comparative analysis to maintain clear group separation and statistical clarity.

**Inclusion Criteria**

- Patients aged ≥18 years undergoing elective cardiac surgery under CPB
- Preoperative hemodynamic stability
- Written informed consent obtained from the patient or legal guardian

**Exclusion Criteria**

- Patients with pre-existing pulmonary conditions (e.g., COPD, ILD)
- Preoperative sepsis or infection
- Emergency cardiac surgery or redo surgeries
- Hepatic or renal failure (serum creatinine >2.5 mg/dL or ALT >2× upper limit)
- Patients requiring prolonged mechanical ventilation >48 hours preoperatively

**Surgical and Anesthetic Management:** All surgeries were performed via median sternotomy using standard CPB protocols. A roller pump and membrane oxygenator were used. Heparin was administered to achieve activated clotting time >480 seconds. Moderate hypothermia (28–32°C) was maintained during CPB. After surgery, patients were transferred to the intensive care unit (ICU) for postoperative management.

**Procalcitonin Measurement:**

Serum procalcitonin levels were measured at the following intervals:

- Preoperatively (baseline)
- 6 hours postoperatively
- 24 hours postoperatively

Venous blood samples were collected and analyzed using a standardized immunoassay method (electrochemiluminescence immunoassay—ECLIA). A value >2 ng/mL within 24 hours postoperatively was considered elevated based on current literature and institutional thresholds.

**ARDS Assessment**

ARDS was diagnosed based on the Berlin definition, requiring all the following:

- Onset within one week of a known clinical insult
- Bilateral opacities on chest radiograph or CT
- Respiratory failure not fully explained by cardiac failure or fluid overload
- $PaO_2/FiO_2$ ratio ≤300 mmHg with PEEP ≥5 cm $H_2O$

**Outcome Measures**

- Primary Outcome: Incidence of ARDS in relation to elevated serum procalcitonin levels
- Secondary Outcomes: Duration of mechanical ventilation, ICU length of stay, in-hospital mortality

**Statistical Analysis:** Data were entered in Microsoft Excel and analyzed using SPSS version 25.0. Continuous variables were presented as mean ± SD and compared using Student's t-test. Categorical variables were expressed as percentages and analyzed using the Chi-square test or Fisher's exact test as appropriate. Correlation between PCT levels and ARDS was assessed using binary logistic regression. A p-value of <0.05 was considered statistically significant.

## RESULTS

[Table 1] compares the demographic variables between the two groups based on serum procalcitonin levels. The age distribution and gender ratio were comparable between groups with no statistically significant differences. Body mass index (BMI) categories and mean BMI were also similar in both groups, indicating that baseline physical profiles were matched and unlikely to influence outcome variation.

[Table 2] presents the comparison of preoperative clinical parameters, including white blood cell (WBC) count and NT-pro-BNP levels. Both values were slightly lower in Group B, but the differences were not statistically significant, suggesting comparable preoperative inflammatory and cardiac biomarker profiles.

[Table 3] illustrates perioperative variables such as operative time, cardiopulmonary bypass (CPB) time, aortic cross-clamp time, and transfusion requirements. Operative time, CPB time, and aortic cross-clamp time were significantly higher in Group B, reflecting increased intraoperative complexity or systemic inflammation. Transfusion volumes were marginally higher in Group B, but the differences were not statistically significant.

[Table 4] compares postoperative variables. Serum procalcitonin levels were significantly higher in Group B as per study design. Fluid balance and postoperative NT-pro-BNP values were statistically comparable, indicating that other postoperative metabolic markers did not differ significantly between the groups.

[Table 5] outlines the severity distribution of ARDS among the groups. Group B had a markedly higher incidence of ARDS, including moderate and severe forms. This difference was statistically significant and supports the hypothesis that elevated procalcitonin is associated with higher ARDS risk postoperatively.

[Table 6] presents outcome variables, including mechanical ventilation time, ICU stay, and hospital stay. All three parameters were significantly prolonged in Group B, suggesting worse postoperative recovery and higher morbidity in patients with elevated serum procalcitonin.

[Table 7] provides the ROC analysis for serum procalcitonin in predicting ARDS. The area under the curve (AUC) was 0.891, indicating excellent discriminatory power. A cutoff value of 10 ng/mL offered 80.6% sensitivity and 76.1% specificity, demonstrating strong predictive capability for identifying high-risk patients.

**Table 1: Comparison of Demographic Variables Between Groups (n=160)**

| Demographic Variables | Group A (n=80) | Group B (n=80) | P value |
|---|---|---|---|
| Age group (in years): 18–27 | 13 (16.3%) | 11 (13.8%) | 0.421NS |
| 28–37 | 20 (25%) | 15 (18.8%) | – |
| 38–47 | 15 (18.8%) | 20 (25%) | – |
| 48–57 | 18 (22.5%) | 18 (22.5%) | – |
| >57 | 14 (17.5%) | 16 (20%) | – |
| Mean Age (years) ± SD | 43.80 ± 12.9 | 46.98 ± 13.6 | 0.117NS |
| Gender: Male | 36 (45%) | 42 (52.5%) | 0.239NS |
| Gender: Female | 44 (55%) | 38 (47.5%) | – |
| BMI: Underweight (<18.5) | 10 (12.5%) | 9 (11.3%) | 0.786NS |
| BMI: Normal (18.5–24.99) | 44 (55%) | 40 (50%) | – |
| BMI: Overweight (25–29.99) | 18 (22.5%) | 21 (26.3%) | – |
| BMI: Obese (>30) | 8 (10%) | 10 (12.5%) | – |
| Mean BMI ± SD | 23.42 ± 4.12 | 23.61 ± 4.38 | 0.755NS |

**Table 2: Comparison of Preoperative Clinical Parameters (n=160)**

| Preoperative Variables | Group A (n=80) | Group B (n=80) | P value |
|---|---|---|---|
| WBC (per mm³) | 8492.5 ± 1290.6 | 8274.2 ± 1355.4 | 0.276NS |
| Range | (5700–11200) | (5100–12000) | |
| NT-pro-BNP (pg/mL) | 254.1 ± 209.3 | 219.7 ± 158.2 | 0.248NS |
| Range | (20–875) | (25–778) | |

**Table 3: Comparison of Perioperative Variables (n=160)**

| Variables | Group A (n=80) | Group B (n=80) | P value |
|---|---|---|---|
| Total operative time (hrs) | 4.53 ± 1.05 | 5.62 ± 1.82 | <0.001S |
| Range | (3.0–9.3) | (3.3–15.0) | |
| CPB time (min) | 107.4 ± 34.6 | 167.3 ± 80.1 | <0.001S |
| Range | (48–252) | (43–660) | |
| Aortic cross-clamp time (min) | 70.8 ± 28.1 | 97.2 ± 34.5 | <0.001S |
| Range | (26–180) | (19–244) | |
| Blood transfusion (units) | 1.92 ± 0.69 | 2.10 ± 0.88 | 0.142NS |
| Range | (1–4) | (1–8) | |
| FFP transfusion (units) | 1.91 ± 0.32 | 2.02 ± 0.44 | 0.092NS |
| Range | (1–2) | (1–4) | |

**Table 4: Comparison of Postoperative Variables (n=160)**

| Variables | Group A (n=80) | Group B (n=80) | P value |
|---|---|---|---|
| Procalcitonin Day 1 (ng/mL) | 1.38 ± 1.01 (0–5.4) | 27.6 ± 26.5 (8–94.5) | <0.001S |
| 1st Post-op Day Fluid Balance (ml) | -305.2 ± 101.6 | -311.1 ± 110.4 | 0.542NS |
| NT-pro-BNP (pg/mL) | 319.4 ± 207.6 | 268.1 ± 139.4 | 0.272NS |

**Table 5: Comparison of Severity of ARDS (n=160)**

| Severity of ARDS | Group A (n=80) | Group B (n=80) | P value |
|---|---|---|---|
| No ARDS | 72 (90%) | 50 (62.5%) | 0.001S |
| Mild ARDS | 5 (6.3%) | 14 (17.5%) | |
| Moderate ARDS | 2 (2.5%) | 7 (8.8%) | |
| Severe ARDS | 1 (1.3%) | 9 (11.2%) | |

**Table 6: Comparison of Postoperative Outcomes (n=160)**

| Variables | Group A (n=80) | Group B (n=80) | P value |
|---|---|---|---|
| Mechanical ventilation (hrs) | 8.52 ± 2.01 | 18.45 ± 16.9 | <0.001S |
| ICU stay (hrs) | 23.35 ± 3.7 | 42.10 ± 33.2 | <0.001S |
| Hospital stay (days) | 7.23 ± 0.7 | 8.58 ± 2.65 | <0.001S |

**Table 7: ROC Curve – Serum Procalcitonin for Predicting ARDS**

| Test Variable | AUC | SE | Cut-off (ng/mL) | Sensitivity | Specificity | P value | 95% CI (Lower–Upper) |
|---|---|---|---|---|---|---|---|
| Serum Procalcitonin | 0.891 | 0.036 | 10.0 | 80.6% | 76.1% | <0.001 | 0.820 – 0.9 |

## DISCUSSION

This study highlights a strong association between elevated serum procalcitonin (PCT) levels and the incidence as well as severity of acute respiratory distress syndrome (ARDS) in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB). Patients with serum procalcitonin levels >7 ng/mL (Group B) demonstrated significantly higher rates of ARDS, prolonged mechanical ventilation, longer ICU stays, and extended hospitalization compared to those with lower PCT levels.

The pathophysiology behind this observation likely lies in the intense systemic inflammatory response triggered by CPB. Contact of blood with artificial surfaces, ischemia-reperfusion injury, and surgical trauma result in the release of inflammatory mediators that contribute to endothelial damage and pulmonary capillary leakage.[11] Procalcitonin, a precursor of the hormone calcitonin, is known to rise in response to systemic inflammation even in the absence of infection. Elevated postoperative PCT levels may therefore serve as a surrogate marker for systemic inflammatory burden and endothelial dysfunction following CPB.[12]

Our findings are consistent with prior studies that identified PCT as an early predictor of adverse respiratory outcomes in critically ill patients. A multicentric prospective study by Nobile et al. demonstrated that PCT levels >10 ng/mL within the first 24 hours after cardiac surgery were associated with a significantly increased risk of postoperative ARDS and prolonged ventilation.[13] Similarly, PCT kinetics have been shown to outperform traditional markers like CRP or leukocyte count in predicting both infectious and non-infectious complications post-CPB.[14]

Interestingly, although the groups in our study had similar preoperative WBC counts and NT-proBNP levels, the intraoperative variables such as CPB time and cross-clamp time were significantly longer in patients with higher PCT levels. This suggests that extended surgical duration may amplify systemic inflammation and subsequent PCT elevation, predisposing patients to ARDS. These findings align with the study by Schuetz et al., which concluded that both operative stress and hemodilution during CPB contribute to transient immunosuppression and proinflammatory responses.[15]

The ROC analysis in our study further supports the diagnostic accuracy of serum procalcitonin, with an AUC of 0.891 and a cutoff value of 10 ng/mL providing strong sensitivity and specificity for predicting ARDS. While PCT is not specific to pulmonary injury, its rapid rise, ease of measurement, and strong correlation with clinical severity make it a promising biomarker for risk stratification in cardiac surgical patients.

Despite its strengths, our study is limited by a single-center design and lack of serial PCT monitoring beyond the first postoperative day. Future multicentric trials with larger cohorts and inclusion of additional inflammatory markers may provide a more comprehensive picture of the inflammatory cascade leading to ARDS.

## CONCLUSION

Elevated serum procalcitonin levels in the immediate postoperative period are significantly associated with a higher incidence and severity of ARDS in patients undergoing cardiac surgery with cardiopulmonary bypass. Procalcitonin not only correlates with the inflammatory response but also serves as a useful predictive marker for postoperative pulmonary complications. Incorporating PCT measurements into routine postoperative monitoring may help in early identification of high-risk patients, allowing timely intervention and potentially improving clinical outcomes.

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