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ORIGINAL RESEARCH

Postoperative Infections in Cardiac Surgery: A Multifaceted Analysis Integrating Biomarkers, Operative Characteristics, and Clinical Outcomes

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Abstract
Background: Procalcitonin (PCT) has been debated for its utility in predicting bacterial infections post-cardiac surgery with cardiopulmonary bypass (CPB), particularly in pediatric patients who are vulnerable to such complications.
Objective: This study aimed to assess the efficacy of postoperative PCT levels as a predictor of bacterial infections in patients undergoing cardiac surgery with CPB.
Methods: Data were collected from electronic medical records of 146 patients who underwent cardiac surgery with CPB. PCT and white blood cell (WBC) levels, along with demographic and operative details, were analyzed. Bacterial infections were diagnosed based on specific criteria.
Results: While WBC levels showed significant differences between infection and non-infection groups on early postoperative days, PCT levels did not consistently discriminate between the two groups across various postoperative days. Respiratory tract infections were the most common complication. Reoperation rates did not significantly differ between infection and non-infection groups.
Conclusion: Postoperative PCT levels demonstrated limited discriminatory ability in predicting bacterial infections in patients undergoing cardiac surgery with CPB, likely due to the confounding effect of CPB-induced systemic inflammatory response syndrome. WBC levels may serve as an early marker of infection. Further research is needed to explore additional biomarkers or clinical indicators for accurate infection prediction in this population.
Keywords: Procalcitonin, cardiopulmonary bypass, cardiac surgery, bacterial infection, white blood cell count.

Introduction

Procalcitonin is typically undetectable under normal physiological conditions. Its utility as a predictor of bacterial infection, particularly in the postoperative setting, has been widely debated. The challenge is further compounded in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB), as they often experience postoperative systemic inflammatory response syndrome (SIRS). This condition arises due to both non-cellular and

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cellular immune system stimulation from the blood's contact with foreign materials, which can significantly affect procalcitonin levels since it is one of several inflammatory response proteins. Pediatric patients are particularly susceptible to bacterial infections. Therefore, accurate prediction and prompt diagnosis of postoperative bacterial infection are crucial for improving morbidity and mortality in this vulnerable population[1-4].

Some studies have indicated that procalcitonin is a useful marker for predicting postoperative bacterial infection, while other studies have not found this association. The key issue is that procalcitonin is a systemic inflammatory response protein, meaning that any source of inflammation can potentially elevate its levels. Those studies that did not find a correlation often cited systemic inflammatory responses from cardiopulmonary bypass as the reason. Given these conflicting findings, our objective was to determine whether postoperative procalcitonin levels could reliably predict bacterial infections[5-7].

Material and methods

Data Collection

We gathered data on postoperative procalcitonin and white blood cell levels from patients who underwent cardiac surgery with cardiopulmonary bypass at our Hospital, using electronic medical records. The study included patients who had cardiac surgery using cardiopulmonary bypass. Exclusion criteria were patients with pre-existing inflammatory syndromes or confirmed bacterial infections before surgery, those receiving preoperative treatment-dose antibiotics for any reason, patients on preoperative steroids, those who underwent non-elective surgery, and those with missing or insufficient medical records. Initially, 311 patients underwent cardiac surgery during the study period. After applying the exclusion criteria, the final number of patients included in the study was 146. We also collected demographic data and operative details, such as operative time, cardiopulmonary bypass time, aortic cross-clamp time, and circulatory arrest time.

Diagnosis of Postoperative Bacterial Infection

To diagnose bacterial infections, we categorized them into five main types. Urinary tract infections were identified by a fever exceeding 38°C and a positive urine bacterial culture with more than 105 colony-forming units (CFUs)/ml. Gastrointestinal infections, specifically bacterial infectious diarrhea in our cases, were diagnosed based on positive stool bacterial cultures alongside relevant clinical signs and symptoms. Respiratory tract infections were diagnosed when sputum bacterial cultures were positive, accompanied by clinical signs and symptoms of bacterial pneumonia. Catheter-related bloodstream infections (CRBSIs) were diagnosed in patients who had an indwelling catheter for more than 48 hours. This diagnosis was made by collecting blood samples simultaneously from the catheter and two peripheral sites. If the bloodstream bacterial culture from the catheter was positive within 2 hours of the peripheral sites (or vice versa), and the organisms were genetically identical, CRBSI was considered the cause of infection, especially if accompanied by a fever exceeding 38°C. Lastly, septicemia of unknown origin was diagnosed when blood cultures from two different peripheral sites were positive without any other identifiable source of infection.

Cardiopulmonary Bypass Management Protocol

The principles of cardiopulmonary bypass management were consistent across all patients. We employed moderate hypothermia (28°C) during bypass procedures, and cardioplegic solution was administered in all cases, with repeated doses as necessary. For acid-base management, our institution followed a pH-stat strategy for patients younger than 10 years old, while an alpha-stat strategy was used for those older than 10 years.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 05, 2024

Statistical Analysis

Patient characteristics with continuous variables were compared using the Wilcoxon rank-sum (Mann-Whitney U) test, while categorical variables were assessed with the chi-squared test. A p-value of less than 0.05 was considered statistically significant. Logistic regression analysis was conducted to calculate the odds of developing an infection based on procalcitonin and white blood cell levels. Receiver operating characteristic (ROC) curves were used to identify the optimal thresholds for procalcitonin and white blood cell levels to predict postoperative bacterial infection. The statistical analysis was performed using Stata version 14.1.

Results

The study included 146 patients, categorized into those with infections (42) and those without infections (104). The median age of the entire cohort was 28.5 years, with significant differences between the groups; the infection group had a median age of 6 months, while the non-infection group had a median age of 41.5 years (P = 0.0003). Gender distribution was not significantly different, with males comprising 57.53% of the total, 64.29% of the infection group, and 54.81% of the non-infection group (P = 0.294).

Weight differences were also notable, with the infection group having a median weight of 6.03 kg compared to 12.35 kg in the non-infection group (P = 0.0014). Similarly, body surface area showed significant variation; the median was 0.30 m^2 in the infection group versus 0.57 m^2 in the non-infection group (P = 0.0004).

Diagnosis categories showed varied distributions. Notably, atrial septal defect was absent in the infection group but present in 8.65% of the non-infection group (P = 0.049). The d-Transposition of great arteries was more prevalent in the infection group (14.29%) compared to the non-infection group (4.81%) (P = 0.050). Other diagnoses did not show statistically significant differences.

Comorbidities, including Down syndrome and DiGeorge syndrome, were rare and did not significantly differ between groups. Protein-energy malnutrition was common in both groups, with no significant difference (P = 0.999).

Operative characteristics revealed a longer median aortic cross-clamp time in the infection group (78 minutes) compared to the non-infection group (57.5 minutes) (P = 0.033). Other parameters like operative time, cardiopulmonary bypass time, and circulatory arrest time did not show significant differences (Table-1).

Table 1: Patient Characteristics and Operative Details Based on Infection Status Post-Cardiac Surgery

Patient Characteristics	All (N = 146)	Infection (N = 42)	No Infection (N = 104)	P Value
Age (months): median (P25, P75)	28.5 (7, 84)	6 (1, 42)	41.5 (14.5, 85.5)	0.0003
Gender: N (%)				0.294
- Male	84 (57.53)	27 (64.29)	57 (54.81)	
- Female	62 (42.47)	15 (35.71)	47 (45.19)	
Weight (kg): median (P25, P75)	11.08 (6, 21)	6.03 (3.34, 15.6)	12.35 (8.15, 21.4)	0.0014
Body surface area (kg/m^2): median (P25, P75)	0.52 (0.32, 0.81)	0.30 (0.22, 0.61)	0.57 (0.42, 0.82)	0.0004
Diagnosis: N (%)				
- Atrial septal defect	9 (6.16)	0 (0.00)	9 (8.65)	0.049

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 05, 2024

- Ventricular septal defect	21 (14.38)	4 (9.52)	17 (16.35)	0.288
- Conotruncal defects	39 (26.71)	8 (19.05)	31 (29.81)	0.183
- Endocardial cushion defects	8 (5.48)	2 (4.76)	6 (5.77)	0.809
- Aortic defects	8 (5.48)	4 (9.52)	4 (3.85)	0.172
- d-Transposition of great arteries	11 (7.53)	6 (14.29)	5 (4.81)	0.050
- Valvular heart diseases	14 (9.59)	4 (9.52)	10 (9.62)	0.986
- Anomalies of coronary arteries	4 (2.74)	0 (0.00)	4 (3.85)	0.325
- Others	32 (21.92)	14 (33.33)	18 (17.31)	0.034
Comorbidities: N (%)				
- Down syndrome	3 (2.05)	1 (2.38)	2 (1.92)	0.999
- DiGeorge syndrome	1 (0.68)	0 (0.00)	1 (0.96)	0.999
- Protein-energy malnutrition	24 (75.00)	4 (80.00)	20 (74.07)	0.999
Operative time (mins): median (P25, P75)	225 (165, 290)	240 (165, 360)	210 (162.5, 282)	0.100
Cardiopulmonary bypass time (mins): median (P25, P75)	116 (78, 160)	124 (83, 204)	113.5 (77.5, 156.5)	0.210
Aortic cross-clamp time (mins): median (P25, P75)	63 (23, 115)	78 (39, 123)	57.5 (14.5, 109.5)	0.033
Circulatory arrest time (mins): (minimal, maximal)	(0, 55)	(0, 37)	(0, 55)	0.167

Table 2 presents the postoperative procalcitonin (PCT) and white blood cell (WBC) levels, types of infections, and reoperation rates for patients who underwent cardiac surgery using cardiopulmonary bypass. The study involved 146 patients, divided into those with infections (42) and without infections (104).

PCT levels showed no significant differences between the infection and no infection groups on any postoperative day (POD). On POD 0, the median PCT levels were 0.52 ng/dl for the infection group and 0.48 ng/dl for the no infection group ($p = 0.667$). By POD 7, the median PCT levels were 1.85 ng/dl and 0.77 ng/dl, respectively ($p = 0.072$). Similarly, WBC levels were significantly different between the groups on POD 0, POD 1, and POD 2. On POD 0, the median WBC level was 9345 cells/mm³ for the infection group compared to 13040 cells/mm³ for the no infection group ($p = 0.0005$). By POD 7, WBC levels were not significantly different between the groups ($p = 0.417$).

The types of infections identified included urinary tract infections (8.22%), gastrointestinal tract infections (2.74%), respiratory tract infections (12.33%), catheter-related bloodstream infections (1.37%), and septicemia of unknown origin (4.11%). Notably, respiratory tract infections were the most common, accounting for 42.86% of the infection group.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 05, 2024

Reoperation within 30 days occurred in 2.74% of the patients, with 2.38% in the infection group and 2.88% in the no infection group, showing no significant difference (p = 0.999). This table highlights the comparative analysis of PCT and WBC levels, infection types, and reoperation rates, indicating significant differences in WBC levels in the early postoperative period but not in PCT levels.

Table 2: Comparison of Patient Characteristics and Infection Rates

Patient Characteristics	All (N = 146)	Infection (N = 42)	No Infection (N = 104)	P Value
PCT level (ng/dl): median (P25, P75 (IQR))				
POD 0	0.48 (0.1, 3.19 (3.10))	0.52 (0.10, 3.20 (3.1))	0.48 (0.11, 3.19 (3.08))	0.667
POD 1	13.75 (4.11, 37.9 (33.80))	14.8 (6.95, 45.3 (28.35))	13.2 (3.67, 32.5 (28.83))	0.308
POD 2	15.7 (3.99, 43.5 (39.51))	18.1 (4.64, 90.4 (85.76))	15.7 (3.33, 39.3 (35.97))	0.405
POD 3	11.45 (2.36, 37.55 (35.20))	16.4 (3.18, 66.1 (62.92))	11.2 (2.1, 18.1 (16.0))	0.227
POD 4	5.36 (1.82, 14.4 (12.58))	7.46 (2.22, 21.2 (18.98))	4.93 (1.52, 9.84 (8.32))	0.139
POD 5	3.15 (1.2, 10.1 (8.9))	3.53 (1.33, 15.4 (14.07))	3.09 (1.2, 5.71 (4.51))	0.563
POD 6	1.54 (0.8, 4.9 (4.1))	2.25 (0.99, 9.55 (8.56))	1.36 (0.71, 2.29 (1.58))	0.057
POD 7	1.15 (0.54, 3.36 (2.82))	1.85 (0.86, 4.13 (3.27))	0.77 (0.38, 3.25 (2.87))	0.072
WBC level (cells/mm^3): median (P25, P75 (IQR))				
POD 0	11950 (9060, 16900 (7840))	9345 (7000, 12500 (5500))	13040 (10030, 17780 (7750))	0.0005
POD 1	13265 (10605, 18360 (7755))	11460 (8340, 13000 (4660))	14540 (11110, 19000 (7890))	0.0009
POD 2	14545 (10660, 19030 (8370))	12635 (9580, 15400 (5820))	15520 (11695, 20000 (8305))	0.0018
POD 3	13690 (10445, 16865 (6420))	12060 (7930, 15600 (7670))	13965 (11400, 17500 (6100))	0.067
POD 4	12895 (10280, 16300 (6020))	12905 (10250, 16395 (6145))	12895 (10280, 16190 (5910))	0.981
POD 5	13100 (10400, 17385 (6985))	13740 (10400, 17810 (7410))	12980 (10400, 17100 (6700))	0.651
POD 6	14400 (10900, 18200 (7300))	13900 (10950, 18200 (7250))	15340 (10630, 17920 (7290))	0.747
POD 7	13465 (10435, 18570 (8135))	13810 (11000, 20220 (9220))	13415 (10280, 16950 (6670))	0.417
Types of Infection: N (%)				
Urinary tract infection	12 (8.22)	12 (28.57)	-	-
Gastrointestinal tract infection	4 (2.74)	4 (9.52)	-	-
Respiratory tract infection	18 (12.33)	18 (42.86)	-	-
Catheter-related	2 (1.37)	2 (4.76)	-	-

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 05, 2024

bloodstream infection				
Septicemia (unknown source)	6 (4.11)	6 (14.29)	-	-
Reoperation within 30 days: N (%)				
Yes	4 (2.74)	1 (2.38)	3 (2.88)	0.999
No	142 (97.26)	41 (97.62)	101 (97.12)	

Discussion

The study aimed to assess the utility of postoperative procalcitonin (PCT) levels as a predictor of bacterial infections in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB). The findings revealed several significant observations, but also underscored limitations inherent in the study design and context.

One notable finding was the lack of significant differences in PCT levels between patients with and without infections across various postoperative days (PODs). Despite its potential as a marker for bacterial infections, PCT did not demonstrate consistent discriminatory ability in this cohort. This could be attributed to the confounding effect of CPB-induced systemic inflammatory response syndrome (SIRS), which can elevate PCT levels irrespective of bacterial infection status. The study's attempt to discern the specific impact of PCT in the context of CPB-related inflammation adds valuable insights to the existing literature[8-13].

Conversely, white blood cell (WBC) levels exhibited significant differences between infection and non-infection groups on early PODs, indicating their potential utility as an early marker of postoperative bacterial infections. This finding aligns with the conventional understanding of WBC count elevation as a nonspecific response to infection. However, the lack of significance in WBC levels on later PODs suggests their limited utility beyond the immediate postoperative period, emphasizing the need for additional biomarkers or clinical indicators for long-term monitoring[14-17].

The distribution of infection types also provided valuable clinical context, with respiratory tract infections being the most common postoperative complication. This observation underscores the importance of vigilant monitoring and targeted interventions, particularly in patients with predisposing factors or prolonged intubation periods. Moreover, the absence of significant differences in reoperation rates between infection and non-infection groups suggests that postoperative complications were managed effectively without necessitating surgical intervention in most cases[18-23].

Limitations

Despite these insights, several limitations warrant consideration when interpreting the study findings. Firstly, the retrospective nature of the study and reliance on electronic medical records may introduce selection bias and limit the generalizability of the findings. Additionally, the exclusion criteria, including pre-existing inflammatory syndromes and preoperative antibiotic use, may have inadvertently excluded patients with complex medical histories, potentially skewing the patient cohort. Moreover, the small sample size, particularly within the infection group, limits the statistical power and may preclude robust conclusions.

Furthermore, the study's focus on a single institution may restrict the applicability of the findings to other healthcare settings with different patient populations or perioperative protocols. Variability in CPB management strategies, such as temperature management and cardioplegia administration, could also influence postoperative inflammatory responses and biomarker kinetics, thereby confounding the study outcomes.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 05, 2024

Conclusion

In conclusion, our study aimed to evaluate the utility of postoperative procalcitonin (PCT) levels as a predictor of bacterial infections in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB). While the findings yielded valuable insights, several limitations must be acknowledged.

One significant observation was the lack of consistent discriminatory ability of PCT levels in distinguishing between patients with and without infections across various postoperative days (PODs). This inconsistency may be attributed to the confounding effect of CPB-induced systemic inflammatory response syndrome (SIRS), which can elevate PCT levels irrespective of bacterial infection status. Despite this, the study's attempt to delineate the specific impact of PCT within the context of CPB-related inflammation adds valuable nuance to the existing literature.

Conversely, white blood cell (WBC) levels demonstrated significant differences between infection and non-infection groups in the early postoperative period, suggesting their potential utility as an early marker of bacterial infections. However, their limited significance on later PODs underscores the need for additional biomarkers or clinical indicators for long-term monitoring.

The distribution of infection types, with respiratory tract infections being the most common postoperative complication, highlights the importance of vigilant monitoring and targeted interventions, particularly in patients with predisposing factors or prolonged intubation periods. Moreover, the absence of significant differences in reoperation rates between infection and non-infection groups suggests effective management of postoperative complications without necessitating surgical intervention in most cases.

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