Original Article

Early Kinetics of Procalcitonin in Predicting Surgical Outcomes in Type A Aortic Dissection Patients

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Abstract

Background: In cardiac surgery, elevation of procalcitonin (PCT) could be observed postoperatively in the absence of any evidence of infection and also seems to be a prognostic marker. PCT levels measured in patients undergoing Type A aortic dissection (TAAD) were used to determine prognostic values for complications and surgical outcomes.

Methods: Measurements of PCT, C-reactive protein (CRP), and leukocyte count were observed in TAAD surgery patients ($n = 251$; average age: 49.02 ± 12.83 years; 78.5% male) at presurgery (T0) and 24 h (T1), 48 h (T2), and 7 days (T3) postsurgery. PCT clearance (PCTc) on days 2 and 7 was calculated: $(PCT_{day1} - PCT_{day2/day7})/PCT_{day1} \times 100\%$. Endotracheal intubation duration, length of stay (LOS) in the Intensive Care Unit (ICU)/hospital, and complications were recorded.

Results: PCT peaked 24 h postsurgery (median 2.73 ng/ml) before decreasing. Correlation existed between PCT levels at T1 and duration of cardiopulmonary bypass ($P = 0.001$, $r = 0.278$). Serum PCT concentrations were significantly higher in nonsurvivor and multiple organ dysfunction syndrome groups on all postoperative days. PCT levels at T1 correlated with length of time of ventilation support and ICU/hospital LOS. Comparing PCT values of survivors versus nonsurvivors, a PCT cutoff level of 5.86 ng/ml at T2 had high sensitivity (70.6%) and specificity (74.3%) in predicting in-hospital death. PCTc-day 2 and 7 were significantly higher in survivor compared with nonsurvivor patients (38% vs. 8%, $P = 0.012$, 83% vs. −39%, $P < 0.001$). A PCTc-day 7 cutoff point of 48.7% predicted survival with high sensitivity (77.8%) and specificity (81.8%).

Conclusions: PCT level and PCTc after TAAD surgery might serve as early prognostic markers to predict postoperative outcome. PCT measurement may help identify high-risk patients.

Key words: Perioperative Period; Procalcitonin; Sensitivity; Specificity; Type A Aortic Dissection

Introduction

In the clinical setting, morbidity and mortality associated with the Stanford Type A aortic dissection (TAAD) remain higher than for other cardiac operations, such as valvular surgery and coronary artery surgery. The most recent International Registry of Acute Aortic Dissection report showed an 18% operative mortality.[1] Although improved surgical experience and perioperative management have contributed to enhanced operative outcome of this lethal aortic disease, severe postoperative complications continue to arise. Intimal tear and crossing of blood into the artery wall leads to the formation of a false lumen and subsequent systemic inflammatory responses.[2] Aortic surgery, along with greater surgical trauma, longer cardiopulmonary bypass (CPB) time, deep hypothermic circulatory arrest (DHCA), and massive transfusion aggravates this response. Presentations of TAAD, such as tamponade and malperfusion, have a major impact on clinical outcome,[3] but prolonged or severe systemic inflammatory responses also negatively affect postoperative recovery and surgical outcome. Typical markers, such as

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white blood cells (WBCs) and C-reactive protein (CRP), may reflect this response but nonspecifically. Procalcitonin (PCT) is the calcitonin precursor protein comprising 116 amino acids. It originates from the liver upon stimulation by tumor necrosis factor or interleukin-6 arising from bacterial infection.[4] PCT is usually undetectable in healthy humans and is considered a specific marker of infection.[5] Studies have shown that PCT is a promising diagnostic and prognostic biomarker of severe sepsis and septic shock.[6,7] However, it is now known that PCT is elevated in several noninfectious conditions such as myocardial infarction, malaria, severe trauma, surgery, cardiogenic shock, and burns.[8-10] In cardiac surgery, elevation of PCT has been observed postoperatively in the absence of any evidence of infection and also appears to be a good prognostic marker.[11] A single postoperative PCT measurement predicts delayed complications in patients undergoing elective cardiac surgery.[12] To our knowledge, only a few studies of small sample size have examined perioperative PCT levels in TAAD patients.[13,14] The objective of our study was to investigate the perioperative changes in PCT levels and their value in reflecting postoperative complications and mortality in TAAD patients.

Methods

Ethical approval

This study was approved by the Ethics Committee of this hospital. And all patients provided informed consents.

Patient selection

Patients who underwent TAAD surgery from April 2013 to November 2015 were included in the study. All procedures involved a median sternotomy and total CPB. CPB was instituted using right axillary artery or femoral artery perfusion and right atrial venous drainage. Core cooling was carried out to an esophageal temperature of 20–25°C. Antegrade selective cerebral perfusion was applied during circulatory arrest.

Definitions and experimental protocol

Blood samples were obtained preoperatively (T0) and at 24 h (T1), 48 h (T2), and 7 days (T3) postoperation. Serum concentrations of CRP, leukocyte counts, and PCT were measured. PCT clearance (PCTc) on days 2 and 7 was calculated using the following formula: $PCTc_{day2/day7}$ (%) = $(PCT_{day1} - PCT_{day2/day7})/PCT_{day1} \times 100\%$. Body temperature measurements, microbiologic culture, and radiologic examinations were performed postoperation. Duration of endotracheal intubation, duration of stay in the Intensive Care Unit (ICU) and hospital, and complications were recorded.

Asides from clinical examination, infection was diagnosed by chest radiography, leukocyte count, blood culture, sputum culture, and drainage culture. The final diagnosis of infection was determined by two independent experts in regard to the complete medical chart. Mortality was defined as death occurring within 30 days of operation during the initial hospital stay. Organ dysfunctions included respiratory dysfunction (PaO_2/FiO_2 <200 or the need for ventilator support for >72 h), cardiac dysfunction (low cardiac output syndrome or continuous infusion of inotropic agents or vasopressor in absence of hypovolemia), renal dysfunction (an increase in serum creatinine of 44 μmol/L over baseline value or the need for hemodialysis), and nervous system complications (including persistent paraparesis or paraplegia due to impairment of blood supply to the spinal cord and brain or signs of central neurological damage after cerebral hypoperfusion). Multiple organ dysfunction syndrome (MODS) was defined when two or more organ dysfunctions were present.

Statistical analysis

Quantitative variables were expressed numerically as the mean ± standard deviation or medians (25–75%), depending on the nature of the distribution. Qualitative variables were expressed as frequencies. Student's *t*-test or the Mann–Whitney *U*-test was used to evaluate differences between groups. Categorical variables were analyzed by the Pearson's Chi-square test. To explore the relationship between serum PCT concentration and duration of CPB and aortic clamping, linear regression analysis was performed. To identify factors affecting 30-day mortality, we performed binary logistic regression analysis using death as a dependent variable. Differences were considered statistically significant when the $P < 0.05$. The optimum cutoff points were determined with a receiver operating characteristics (ROC) curve. Statistical analysis was performed using SPSS Statistics 17.0 (SPSS Inc., Chicago, USA).

Results

Demographics of patients

Two patients were excluded from the study due to death on the 1st postoperative day. A total of 251 patients were included in the study, of which 197 patients (78.5%) were male and 54 were female. The average age was 49.02 ± 12.83 years. Two hundred and twenty-five patients (89.6%) were admitted with acute aortic dissection (chest pain or other related symptoms which presented less than 14 days before the operation). The preoperative characteristics and comorbidities of the patients are shown in Table 1, and there was no difference between survivor and nonsurvivor groups. Mean pump time, cross-clamp time, and DHCA time were 165.54 ± 37.80 min, 101.23 ± 28.69 min, and 29.11 ± 9.50 min, respectively. The surgical procedures are shown in Table 1. Concomitant procedures included coronary artery bypass grafting (CABG) in 13 patients, aortic-femoral artery bypass in nine patients, mitral valve replacement in one patient, and atrial septal defect repair in two patients.

Of the 251 patients, 56 (22.3%) developed cardiac dysfunction, 69 (27.5%) developed severe renal dysfunction requiring dialysis therapy, 98 (39%) developed respiratory dysfunction, 50 (19.9%) developed infections, and 47 (18.7%) developed nervous complications. Twenty-seven patients (10.8%) died within 30 days of operation and 79 patients (31.5%) developed MODS.

Table 1: Baseline characteristics and in-hospital outcome

Characteristics	All patients (n = 251)	Survivor (n = 224)	Nonsurvivor (n = 27)	P
Medical history				
Age (years)	49.02 ± 12.83	48.94 ± 12.85	49.67 ± 12.87	0.781
Male, n (%)	197 (78.5)	174 (77.7)	23 (85.2)	0.266
Hypertension, n (%)	163 (64.9)	145 (64.7)	18 (66.7)	0.513
Diabetes, n (%)	10 (4)	9 (4.0)	1 (3.7)	0.707
Renal dysfunction, n (%)	10 (4)	10 (4.5)	0	0.313
Cardiac/vascular surgery, n (%)	28 (11.2)	24 (10.7)	4 (14.8)	0.354
Marfan syndrome, n (%)	31 (12.4)	28 (12.5)	3 (11.1)	0.505
Aortic valvular insufficiency (mild-severe), n (%)	143 (57.0)	129 (57.6)	14 (51.9)	0.681
Pericardial effusion, n (%)	74 (29.5)	69 (30.8)	5 (18.5)	0.264
Malperfusion, n (%)	9 (3.6)	9 (4)	0	0.353
Acute aortic dissection, n (%)	225 (89.6)	200 (89.3)	25 (92.6)	0.450
Intraoperative characteristics				
Mean pump time (min)	165.54 ± 37.80	161.11 ± 35.87	195.29 ± 37.76	<0.001
Cross-clamp time (min)	101.23 ± 28.69	100.07 ± 29.35	109.05 ± 22.80	0.182
DHCA time (min)	29.11 ± 9.50	32.00 ± 10.23	28.67 ± 9.35	0.155
Operation				0.350
Ascending aorta + arch replacement + stent implantation, n (%)	137 (54.6)	121 (54.0)	16 (59.3)	
Bentall/Wheats + arch replacement + stent, n (%)	28 (11.2)	28 (12.5)	0	
David + arch replacement + stent, n (%)	32 (12.7)	27 (12.1)	5 (18.5)	
Sinus plasty + arch replacement + stent, n (%)	19 (7.6)	16 (7.1)	3 (11.1)	
Ascending aorta + arch replacement, n (%)	23 (9.2)	21 (9.4)	2 (7.4)	
Ascending aorta replacement/Bentall/David, n (%)	8 (3.2)	8 (3.6)	0	
Arch replacement + stent, n (%)	4 (1.6)	3 (1.3)	1 (3.7)	
Outcome				
Cardiac dysfunction, n (%)	56 (22.3)	39 (17.4)	17 (63.0)	<0.001
Respiratory dysfunction, n (%)	98 (39.0)	81 (36.2)	17 (63.0)	0.011
Renal dysfunction requiring dialysis therapy, n (%)	69 (27.5)	51 (22.8)	18 (66.7)	<0.011
Infection, n (%)	50 (19.9)	36 (16.1)	14 (51.9)	<0.001
Nervous complications, n (%)	47 (18.7)	35 (15.6)	12 (44.4)	0.001
MODS, n (%)	79 (31.5)	57 (25.4)	22 (81.5)	<0.001

Data are presented as mean ± SD or percentage of patients per group, respectively. DHCA: Deep hypothermic circulatory arrest; MODS: Multiple organ dysfunction syndrome; SD: Standard deviation.

Perioperative level of procalcitonin and other inflammatory markers

Table 2 shows the postoperative course of the inflammatory markers in different groups. The concentrations of PCT, CRP, and WBC increased significantly compared to the basal value from T1 to T3 ($P < 0.01$). The peak level of PCT was reached at T1 (2.73 ng/ml). Peak serum CRP concentrations and leukocyte counts occurred at T2, and decreased slowly thereafter, but had not returned to normal by T3.

Correlation existed between PCT levels at T1 and duration of CPB ($P = 0.001$, $r = 0.278$), but no significant correlation was found between PCT levels and time of aortic clamping ($P = 0.687$) or DHCA time ($P = 0.692$) [Table 3].

Serum procalcitonin level and surgical outcomes

As shown in Table 2, the serum PCT concentrations were significantly higher in the nonsurvivor group than in the survivor group on all postoperative days, with a peak value of 19.11 pg/ml at T2. Furthermore, serum PCT concentration increased significantly in MODS compared with non-MODS patients from T1 to T3.

Correlation existed between serum PCT concentration at T1 and the duration of endotracheal intubation ($P < 0.001$, $r = 0.390$), duration of stay in the ICU ($P < 0.001$, $r = 0.371$), and duration of stay in the hospital ($P = 0.008$, $r = 0.182$) [Table 3].

Table 4 shows intragroup analysis of survivors and nonsurvivors within the infected and noninfected groups. We found significantly higher serum PCT levels at T2 and T3 in the nonsurvivors.

When comparing PCT values of survivors versus nonsurvivors, the area under the ROC curve was 0.646 ($P = 0.131$) at T0, 0.727 ($P = 0.003$) at T1, and 0.782 ($P < 0.001$) at T2 [Figure 1]. For a cutoff of 5.86 ng/ml measured at T2, PCT had a sensitivity of 70.6% and a specificity of 74.3% in predicting in-hospital death.

PCTc was associated with survival prediction. Both PCTc-day 2 and PCTc-day 7 were significantly higher in survivors versus nonsurvivors ($P = 0.012$, $P < 0.001$). The area under ROC curve of PCTc-day 7 for survival prediction was 0.870 ($P < 0.001$). A cutoff point of 48.7%

Table 2: Perioperative course of inflammatory markers

Markers	All patients (n = 251)	Survivor group (n = 224)	Nonsurvivor group (n = 27)	P	Non-MODS group (n = 172)	MODS group (n = 79)	P
PCT (ng/ml)							
T0	0.11 (0.05–0.33)	0.11 (0.52–0.32)	0.29 (0.08–0.45)	0.131	0.11 (0.05–0.27)	0.22 (0.06–0.36)	0.237
T1	2.73 (0.96–9.55)	2.46 (0.94–8.45)	12.38 (2.47–37.38)	0.001	1.77 (0.82–4.92)	8.33 (2.73–23.29)	<0.001
T2	1.88 (0.67–8.05)	1.68 (0.60–6.27)	19.11 (2.63–75.31)	<0.001	1.19 (0.48–2.41)	6.60 (2.33–26.32)	<0.001
T3	0.72 (0.27–3.59)	0.57 (0.21–1.94)	8.33 (3.75–59.88)	<0.001	0.37 (0.16–0.96)	2.7 (0.77–8.12)	<0.001
PCTc (%)							
Day 2	34.49 (9.58–53.22)	37.72 (14.68–53.71)	7.66 (–65.46–45.92)	0.012	44.23 (26.39–58.18)	17.10 (–26.47–43.98)	0.002
Day 7	81.62 (35.71–91.75)	83.09 (60.00–93.30)	–38.83 (–194.97–47.77)	<0.001	87.23 (68.32–93.32)	49.63 (3.90–88.41)	<0.001
WBC (× 10^9/L)							
T0	11.10 ± 4.17	10.82 ± 3.81	13.44 ± 6.05	0.040	10.57 ± 3.77	12.26 ± 4.75	0.007
T1	13.00 ± 4.43	12.78 ± 4.35	14.77 ± 4.72	0.027	13.13 ± 4.43	12.72 ± 4.43	0.501
T2	15.38 ± 5.29	15.06 ± 5.14	17.97 ± 5.84	0.010	15.04 ± 5.11	16.06 ± 5.61	0.177
T3	15.25 ± 5.37	14.66 ± 5.10	20.96 ± 4.71	<0.010	14.49 ± 4.94	16.90 ± 5.92	0.003
CRP (mg/L)							
T0	58.13 ± 64.68	57.91 ± 65.14	60.48 ± 61.53	0.872	62.45 ± 66.00	48.08 ± 60.86	0.147
T1	142.14 ± 75.80	138.78 ± 68.52	173.33 ± 123.91	0.305	137.76 ± 68.85	153.10 ± 90.84	0.258
T2	160.92 ± 60.89	158.17 ± 60.53	185.70 ± 60.83	0.122	160.45 ± 61.65	161.71 ± 60.23	0.909
T3	94.90 ± 65.24	92.82 ± 57.29	128.10 ± 156.80	0.684	83.92 ± 49.57	113.78 ± 83.65	0.113

Data are presented as mean ± SD or median (25–75%), respectively. T0: Presurgery; T1: 24 h postsurgery; T2: 48 h postsurgery; T3: 7 days postsurgery; PCT: Procalcitonin; PCTc: Procalcitonin clearance; WBC: White blood cells; CRP: C-reactive protein; MODS: Multiple organ dysfunction syndrome; SD: Standard deviation.

Table 3: Correlation analysis between PCT at T1 and operation factors or outcomes

Items	r	P
CPB time	0.278	0.001
Aortic clamping time	−0.034	0.687
DHCA time	0.036	0.692
Endotracheal intubation time	0.390	<0.001
Duration of stay in the ICU	0.371	<0.001
Duration of stay in the hospital	0.182	0.008

CPB: Cardiopulmonary bypass; ICU: Intensive Care Unit; DHCA: Deep hypothermic circulatory arrest; PCT: Procalcitonin; T1: 24 h postsurgery.

Table 4: Intragroup analysis of survivors and nonsurvivors within the infected group and noninfected group

PCT (ng/ml)	Survivor (n = 224)	Nonsurvivor (n = 27)	Z*	P
Infected group				
T0	0.08	0.29	−1.318	0.187
T1	8.34	16.07	−1.633	0.102
T2	4.46	41.48	−2.468	0.014
T3	1.89	12.24	−2.839	0.005
Noninfected group				
T0	0.11	0.25	−0.547	0.584
T1	2.27	6.05	−1.775	0.076
T2	1.62	7.70	−2.795	0.005
T3	0.4	5.69	−2.846	0.004

Data are presented as median. *Mann–Whitney U-test was performed. PCT: Procalcitonin; T0: Presurgery; T1: 24 h postsurgery; T2: 48 h postsurgery; T3: 7 days postsurgery.

had a sensitivity of 77.8% and a specificity of 81.8% [Figure 2].

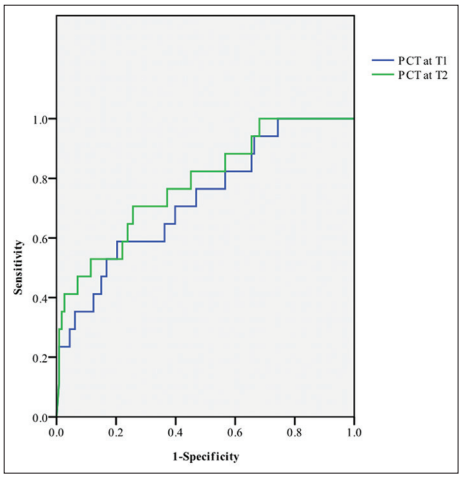

Figure 1: Receiver operating characteristics curve when comparing procalcitonin values of survivor versus nonsurvivor groups at 24 h postsurgery (T1) and 48 h postsurgery (T2).

To determine factors associated with 30-day mortality after surgery, binary logistic regression analysis was carried out using age, sex, PCT >6 ng/ml at T2, duration of CPB, respiratory dysfunction, renal dysfunction, and infection as independent variables. Serum PCT level >6 ng/ml at T2 (odds ratio [OR] = 7.473, 95% confidence interval [CI] = 1.061–32.885, P = 0.043) and infection (OR = 5.908, 95% CI = 1.684–33.168, P = 0.008) were associated with 30-day mortality [Table 5].

A cutoff point of 6 ng/ml at T2 was used to stratify patients into the PCT <6 ng/ml group and PCT ≥6 ng/ml group [Table 6]. Patients with elevated levels of PCT after aortic dissection surgery had a longer duration of endotracheal

intubation (296.54 ± 321.57 min vs. 140.28 ± 274.45 min, P = 0.01) and longer ICU stay (9.71 ± 12.77 min vs. 15.88 ± 13.90 min, P = 0.013) and a greater probability of cardiac dysfunction (P < 0.001), renal dysfunction (P < 0.001), nervous complication (P = 0.002), infection (P = 0.034), and death in hospital (P = 0.002).

Discussion

When measuring PCT in TAAD patients, we found that the early kinetics of PCT might show a better prognostic value compared to other classic markers. The finding of this study had verified the prior hypothesis. First, serum PCT concentrations and PCTc were significantly higher in the nonsurvivor group and MODS group. ROC analyses revealed that PCT levels and PCTc had a highly predictive accuracy to detect in-hospital death. Second, increased PCT levels were related to complications and poor outcomes after TAAD surgery.

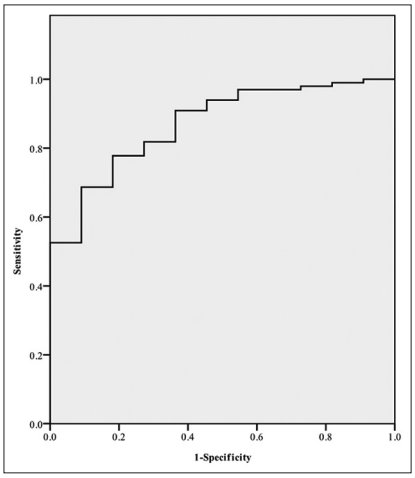

Figure 2: Receiver operating characteristics curve of procalcitonin clearance - day 7 for survival prediction.

Table 5: Variables for multiple logistic regression analysis to predict mortality

Items	*OR*	95% *CI*	*P*
Sex	2.321	0.302–17.819	0.418
Age	1.011	0.950–1.076	0.729
Duration of CPB	1.015	0.995–1.036	0.140
Respiratory dysfunction	0.946	0.179–4.990	0.947
Renal dysfunction	1.928	0.253–14.681	0.525
Infection	7.473	1.684–33.168	0.008
PCT >6 ng/ml at T2	5.908	1.061–32.885	0.043

CPB: Cardiopulmonary bypass; PCT: Procalcitonin; *OR*: Odds ratio; *CI*: Confidence interval; T2: 48 h postsurgery.

The normal range of serum PCT concentration after cardiac surgery is undefined. Serum PCT levels peak within 24 h postoperatively and return to normal values in the days following an uncomplicated cardiac surgery. Peak values of PCT range from 0.5 to 7.0 ng/ml.[15] Specific surgical techniques may influence the evolution of serum PCT concentration after cardiac surgery in the absence of postoperative complications. Patients are reported to have higher PCT levels after CABG than after off-pump coronary artery bypass[16] and higher PCT levels after valvular and thoracic aortic surgeries than after CABG.[17] Other investigators have not found a difference in PCT levels between different types of operations.[18,19] Intraoperative factors such as aortic cross-clamping time, duration of CPB, and duration of surgery influence serum PCT levels.[20,21] Our research shows that median PCT levels peaked (2.73 ng/ml) at 24 h postoperation. Patients may have higher PCT levels after aortic surgery than after CABG or valve surgery because they have a longer duration of operation and CPB.

PCT levels are higher in patients with a poor outcome and are increased in patients who develop later postoperative complications. Several studies have reported higher PCT levels in nonsurvivors compared with survivors after cardiac surgery. Dörge *et al*.[22] found that PCT levels >10 ng/ml 24 h after operation could discriminate nonsurvivors in a high-risk group of patients with a sensitivity of 72% and a specificity of 51%. They also reported higher PCT levels in patients who developed postoperative organ failure than in those who did not. Adamik *et al*. reported that PCT concentrations were significantly elevated in patients with complications.[23] Loebe *et al*. investigated 722 patients after routine cardiac operations and found that an elevated PCT level of >5 ng/ml 24 h after CPB was predictive of outcome.[17] CRP does not represent a useful prognostic marker likely because of its prolonged elevation after an uncomplicated course. On

Table 6: Surgical outcome compared between <6 and ≥6 ng/ml PCT group at 48 h postsurgery

Items	PCT at T2 <6 ng/ml (n = 107)	PCT at T2 ≥6 ng/ml (n = 46)	Statistical value	*P*
Endotracheal intubation time (h)	140.28 ± 274.45	296.54 ± 321.57	−2.678*	0.01
LOS in ICU (days)	9.71 ± 12.77	15.88 ± 13.90	−2.514*	0.013
LOS in hospital (days)	20.71 ± 12.86	22.42 ± 13.99	−0.730*	0.467
Cardiac dysfunction, n (%)	13 (12.1)	24 (52.2)	28.108†	<0.001
Renal dysfunction, n (%)	18 (16.8)	27 (58.7)	27.169†	<0.001
Respiratory dysfunction, n (%)	46 (43.0)	20 (43.5)	0.003†	0.547
Nervous complication, n (%)	18 (16.8)	19 (30.1)	10.516†	0.002
Infection, n (%)	18 (16.8)	15 (32.6)	4.739†	0.034
Death in hospital, n (%)	7 (6.5)	12 (26.1)	11.299†	0.002

Data are presented as mean ± SD or percentage of patients per group, respectively. *Student's t-test was performed; †Pearson Chi-square test was performed. ICU: Intensive Care Unit; LOS: Length of stay; PCT: Procalcitonin; SD: Standard deviation; T2: 48 h postsurgery.

the other hand, PCT yields an elevated negative predictive value of complications after cardiac surgery. A study by Kerbaul *et al*. suggests that PCT concentrations of <5 ng/ml are not associated with any postoperative complication.[24] Our results showed that serum PCT concentrations were significantly higher in the nonsurvivor group on all postoperative days than in the survivor group. For a cutoff of 5.86 ng/ml at T2, PCT had a sensitivity of 70.6% and specificity of 74.3% in predicting in-hospital death. Patients with PCT ≥6 ng/ml 48 h after aortic dissection surgery had a longer duration of endotracheal intubation, a longer stay in the ICU, and greater probability of cardiac dysfunction, renal dysfunction, nervous complication, infection, and death in hospital. Correlation existed between serum concentration of PCT at 24 h postoperation and the duration of endotracheal intubation and duration of stay in the ICU/hospital. This finding supports the prognostic value of PCT.

The prognostic value based on the evolution of PCT levels may be more useful than the individual evaluation of initial PCT levels. When serum PCT levels were measured over several days, we observed that patients whose PCT levels remained elevated were at much greater risk of developing severe complications and death than those whose levels dropped in response to therapy. PCTc is an innovative concept that reflects PCT dynamics.[25] In our study, PCTc increased progressively in survivors but decreased in nonsurvivors with significant differences at PCTc-day 2 and 7. Reduction in PCT concentration above 48.7% between days 1 and 7 was considered a good predictor of survival. The dynamics of PCT level, better than the absolute values, could therefore be important in identifying patients who will survive.

The mechanism by which PCT levels are elevated after cardiac surgery is unclear. The use of CPB leads to varying degrees of tissue inflammation and cytokine liberation, triggering a systemic inflammatory response. On the other hand, during cross-clamp and DHCA in aortic dissection surgery, decreased blood flow affects the intestinal mucosa and enterocytes, reducing permeability of the intestinal wall. The endogenous bacteria proliferate and generate endotoxins that ultimately promote the release of PCT into the bloodstream.[26] A study by Klingele *et al*. hypothesized that increased mortality in patients with high PCT after cardiac surgery could, at least partially, be accounted for by undiagnosed nonocclusive mesenteric ischemia (NOMI).[27] However, identification of patients with NOMI remains clinically challenging due to its nonspecific symptoms, and its definitive diagnosis requires angiography which is both time- and cost-intensive.

Cardiac surgery is a sterile operation and the infection was ruled out before the operation. In a study by Chakravarthy *et al*., PCT elevation was not associated with bacterial load and was proposed to be due to one or more of the following factors encountered in cardiac surgery: stress of surgery, anesthesia, inotropic and/or vasoconstrictor agent use, hemorrhage, hemodynamic changes, and inflammatory mediator release due to CPB.[11] In a meta-analysis on PCT utility in surgical patients, Uzzan *et al*. suggested that elevated PCT alone should not be used as a criterion for diagnosing sepsis.[28] However, some studies have reported the diagnostic and predictive value of PCT levels for late infection. Aouifi *et al*. reported that PCT was superior to CRP in predicting an infection and that PCT had a sensitivity of 85% and specificity of 95% at a concentration of 1 ng/ml.[29] Comparably, Sharma *et al*. found that PCT >7 ng/ml had 95% sensitivity and 80% specificity to identify bacterial infection after cardiac surgery.[30] The early postoperative increase in serum PCT in the absence of infection after cardiac surgery shows that PCT is influenced by the postoperative inflammatory process related to CPB. Therefore, this increase may interfere with the diagnosis of infection during the immediate postoperative period. We focused on whether infection could influence the prognostic value of PCT in mortality. We compared survivors and nonsurvivors stratified into infected and noninfected groups and used multiple logistic regression analysis to predict mortality. This showed that PCT could predict mortality excluding the influence of infection.

Our study selected TAAD surgery patients as one single disease to evaluate PCT value in predicting surgical outcomes. It may provide new insights into this "infectious marker" and stimulate further investigations in the course of TAAD surgery. This study has several limitations. First, this is a single-center observational study, and a large sample size is needed to obtain more accurate prognostic information. Second, a series of PCT measurements during all hospitalization may be more valuable. Therefore, a prospective, large-scale multicenter study is required to confirm our results.

These results provide evidence that PCT and PCTc might serve as early prognostic markers in TAAD patients undergoing surgery. Measurement of PCT can be easily integrated into clinical practice, then help identify patients at high risk, and thereby improve prognosis of this population. In the future, we will try to elucidate the underlying mechanisms of PCT elevation and the relationship between PCT and other inflammatory markers such as cytokines in further study.

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Conflicts of interest

There are no conflicts of interest.

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