PROCALCITONIN

Assessment of the Accuracy of Procalcitonin to Diagnose Postoperative Infection after Cardiac Surgery

Mohamed Adel Jebali, M.D.,* Pierre Hausfater, M.D.,† Zoubeir Abbes, M.D.,* Zied Aouni, Pharm.D., Bruno Riou, M.D., Ph.D.,* Mustapha Ferjani, M

Background:

The authors studied the accuracy of procalcitonin to diagnose postoperative infection after cardiac surgery and compared it with those of CRP, WBC, and IL 6 and 8.

Procalcitonin is a propeptide of calcitonin produced by the thyroid gland and is usually undetectable in the blood of healthy humans.

Indeed, either minor or moderate elevation of procalcitonin has been observed postoperatively depending on surgical stress in the absence of any evidence of infection.
Aim of study

- determine the accuracy of procalcitonin to diagnose postoperative infection
- after conventional CPB surgery, and to compare it with those of C-reactive protein (CRP), white blood cell count (WBC), interleukin 6 (IL-6), and interleukin 8 (IL-8).

Materials and Methods

- single-center prospective
- elective open heart surgery with CPB were included.
- Exclusion criteria were age less than 16 yr, clinically detectable preoperative infection, systemic disease, and corticoids within the last 7 days before surgery

Antibiotic prophylaxis

- 2 g cefazolin after induction
- 1 g every 4 h during surgery
- maintained during 24 h postoperatively.

Biologic Measurement

- after induction of anesthesia (baseline)
- at the end of CPB,
- and daily until the seventh postoperative day.
- In a subgroup of patients, IL-6 (n 52) and IL-8 (n 54) were measured only twice, before surgery and on the third postoperative day.
- Normal values of plasma IL-6 and IL-8 levels were 1; 11.3 and 4; 27 pg/ml

Results

- One hundred patients were included in the study, 65(65%) men and 35 (35%) women, with a mean age of 58±12 yr
- Baseline procalcitonin (0.21[0.14; 0.27] vs. 0.16 [0.12; 0.31] ng/ml; not significant
- CRP (8 [7; 9] vs. 8 [5; 9] mg/l; NS), WBC (8,800[7,800 9,600] vs. 7,850 [6,400 10,500] mm3; NS), IL-6(8.0 [3.9 11.0] vs. 4.6 [22.9] pg/ml; NS), and IL-8(11.5 [8.0 18.0] vs. 21.4 [8; 49] pg/ml; NS) were not significantly different between the control and infection groups.
- All preoperative procalcitonin measurements were less than 0.5 ng/ml.
In the control group, 20 patients (24%) developed a postoperative SIRS, and 38 patients (45%) developed cardiac events.

In the infection group, patients had pneumonia (n = 9, 56%), mediastinitis (n = 3, 19%), bacteremia (n = 3, 19%). In the remaining patient (n = 1, 6%), the infection site was not precisely identified.

After CPB, procalcitonin was not significantly different between the control and infection groups (0.25 [0.17; 0.40] vs. 0.25 [0.10; 1.00] ng/ml; NS).

In the control group, procalcitonin increased progressively from the end of CPB, peaked on the first postoperative day (1.01 [0.54; 1.33] ng/ml), and began to decrease from the second postoperative day.

In the infection group, patients had pneumonia (n = 9, 56%), mediastinitis (n = 3, 19%), bacteremia (n = 3, 19%). In the remaining patient (n = 1, 6%), the infection site was not precisely identified.

After CPB, procalcitonin was not significantly different between the control and infection groups (0.25 [0.17; 0.40] vs. 0.25 [0.10; 1.00] ng/ml; NS).

In the control group, the maximum value of procalcitonin was significantly higher in patients with cardiogenic shock (13.8 [0.4; 15.4] vs. 1.01 [0.7; 1.4] ng/ml; P = 0.035).
WBC peaked on the 3rd postoperative day, but there were no significant differences between the two groups.

CRP peaked also on the third postoperative day and remained elevated in the two groups.

At day 3, IL-6 (25.0 [19.6–36.9] vs. 28.0 [9.9–28.0] pg/ml; NS) and IL-8 (24.2 [17.3–45.3] vs. 31.0 [5.7–27.2] pg/ml; NS) were not significantly different.

Discussion

Procalcitonin permitted an early diagnosis. After CPB, activation of inflammatory cascades may occur, and this reaction shows strong similarities to those observed in sepsis. Conventional clinical and biologic signs may be misleading. Procalcitonin has been reported to rise earlier than CRP after the onset of sepsis and to decrease earlier during the course of controlled sepsis.

In our study, procalcitonin was more accurate than other biologic markers to predict postoperative infection. Procalcitonin has already been postulated to be superior to commonly used laboratory tests, such as CRP or WBC. Diagnostic properties of procalcitonin could not be observed during the first 2 postoperative days.
Procalcitonin seems to correlate with the severity of sepsis and may be also useful in predicting the prognosis.

In our study, higher procalcitonin values were observed in nonsurviving patients.

In conclusion, procalcitonin is an early and specific biologic marker of infection in patients undergoing cardiac surgery, a value greater than 1.5 ng/ml beyond the second postoperative day being strongly predictive of an infectious complication.

Usefulness of procalcitonin for diagnosis of infection in cardiac surgical patients.

Table 5. Comparison of the Maximum Value of Procalcitonin, CRP, WBC, IL-6, and IL-8 between the Surviving Patients and Those Who Died

<table>
<thead>
<tr>
<th></th>
<th>Patients Who Died (n = 19)</th>
<th>Patients Who Survived (n = 86)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procalcitonin, ng/ml</td>
<td>27.5 [1.65–40.5]</td>
<td>1.2 [0.7–1.5]</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CRP, mg/l</td>
<td>232 [140–398]</td>
<td>202 [187–221]</td>
<td>NS</td>
</tr>
<tr>
<td>WBC, 10^3/mm³</td>
<td>16.3 [14.3–22.8]</td>
<td>13.5 [12.6–14.3]</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IL-8, pg/ml</td>
<td>12 [12–12]</td>
<td>26 [20–45]</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are expressed as median [95% confidence interval].
CRP = C-reactive protein; IL = interleukin; NS = not significant; WBC = white blood cell count.


Service d’Anesthèse-Reanimation and EA 1896 (Université Claude Bernard Lyon I), Hopital Cardiovasculaire et Pneumologique L. Pradel, France. abdellah.aouifi@vnumail.com
Phase 1

- To determine the normal perioperative kinetics of PCT, 20 consecutive patients undergoing elective cardiac surgery with cardiopulmonary bypass were included.
- Serum PCT concentration was 0.17 +/- 0.08 ng/mL (mean +/- SD).
- Serum PCT increased after cardiac surgery with a peak on POD 1 (1.08 +/- 1.36).
- Serum PCT returned to normal range on POD 3 and remained stable thereafter.

Phase 2

- In noninfected patients, serum PCT concentration was 0.41 +/- 0.36 ng/mL (range, 0.08-1.67 ng/mL).
- Serum PCT concentration was markedly higher in patients with septic shock (96.98 +/- 119.61 ng/mL).
- Moderate increase in serum PCT concentration occurred during pneumonia (4.85 +/- 3.31 ng/mL).
- Serum PCT concentration remained low during mediastinitis (0.80 +/- 0.58 ng/mL).
- Five patients with mediastinitis, two patients with bacteremia, and one patient with pneumonia had serum PCT concentrations of <1 ng/mL (during A/B tx).

For prediction of infection by PCT, the best cutoff value was 1 ng/mL, with sensitivity 85%, specificity 95%, positive predictive value 96%, and negative predictive value 84%.

Phase 3

- Serum PCT concentration was significantly higher in patients with septic shock than in those with cardiogenic shock (96.98 +/- 119.61 ng/mL vs. 11.30 +/- 12.3 ng/mL).
- For discrimination between septic and cardiogenic shock, the best cutoff value was 10 ng/mL, with sensitivity of 100% and specificity of 62%.