Serum Procalcitonin (PCT) as a Negative Screening Test for Colonic Ischemia after Open Abdominal Aortic Surgery

J. Nagata,* M. Kobayashi, N. Nishikimi and K. Komori

Division of Vascular Surgery, Department of Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Shouwa-ku, Nagoya, Aichi, #466-8550, Japan

Background and aim. We assessed serum procalcitonin (PCT) as a screening test for early detection of ischemic colitis.

Patients and methods. Ninety-three patients (81 men and 12 women) undergoing elective aortic surgery were enrolled in this study. Their mean age was 70.3 ± 8.1 years old. Serum procalcitonin was measured postoperatively.

Results. Four patients suffered from colon ischemia. Based on a cut off value of serum PCT ≥ 2.0 ng/ml, fourteen patients had a false positive but none had a false negative result. Sensitivity was 100%, and specificity was 83.9% in detecting ischemic colitis. Negative predictive vale was 100%.

Conclusion. Serum PCT is a non-invasive test that has a high negative predictive vale in ruling out colon ischemia after aortic surgery.

Introduction

The incidence of ischemic colitis after aortic reconstruction has been variably reported as between 0.2 and 10%.1–3 When routine colonoscopy is used the incidence is approximately 6% after all aortic procedures and 12% after abdominal aortic aneurysm repair (7.4% in elective cases, 60% in ruptured cases).1,4 Ischemia is related to both the macro- and micro-circulation of the bowel. The macro-circulation can deteriorate after ligation of the inferior mesenteric artery and/or internal iliac arteries, if there is insufficient collateral flow. Even when the macro-circulation is not interrupted, perioperative hypotension and/or administration of catecholamine can cause micro-circulatory insufficiency.

The clinical manifestation vary in relation to the degree of bowel ischemia from the a subclinical form to bowel gangrene with perforation.5,6 It is reported that 60% of symptomatic cases had transmural bowel damage, and their mortality is as high as 90%.5–10 The severity of intestinal damage is difficult to evaluate with clinical findings and routine blood examination, since the patients are in a postoperative inflammatory condition. Colonoscopy is a reliable modality to evaluate ischemia of the intestine, but it is not cost nor risk effective as a screening test.

Serum procalcitonin (PCT) has been used as a reliable marker of bacterial infection. It is possible to differentiate bacterial infection from non-bacterial related inflammation by measuring serum PCT levels.11–13 Distinguishing between these two conditions is usually difficult simply by routine blood examination, because high white blood cell count and CRP level are observed in both of these conditions.

It is reported that serum PCT level is elevated by endotoxin.14 In the case of bowel ischemia, endotoxemia might occur due to a breakdown of the mucosal barrier function, which can be detected by looking for an increase in PCT levels.

The purpose of this study was to evaluate serum PCT levels as a screening test of intestinal ischemia after open aortic surgery.

Patients and Methods

Patients

From October 2000 to September 2004, 93 patients in which elective open aortic surgery was performed at
Nagoya University Hospital were enrolled in this study. Eighty one were male and twelve were females. Their mean age was 70.3 ± 8.1 (range 51–86) years of age. All patients enrolled in this study were informed of the purpose of the study and agreed to have a post-operative blood sample for PCT measurement. This study includes only elective open aortic surgery, in which PCT levels were measured post operatively. The total number of patients meeting these criteria was 93. During this period, there were a total of 180 aortic surgical treatments. Emergency cases, thoracic aortic surgery and abdominal aortic aneurysms treated by stents were excluded. We had planned to measure PCT levels in all of the elective cases, but in 66 cases PCT was not measured because the examination room was not available. We did not have any intentional exclusion criteria.

Of the patients entered 69 had an abdominal aortic aneurysm (AAA), 6 had an iliac aneurysm (IAA), 14 had aortoiliac occlusive disease, and 4 had both AAA and arterial occlusive disease. Seventy-eight underwent aortic graft replacement, and 15 underwent bypass grafting (Table 1).

**Serum PCT measurement**

The level of serum PCT on the 1st, 2nd and, 7th post-operative days (POD) was measured. Blood was collected from the ante-cubital vein on the relevant morning. We used the immunochromatographic test to measure PCT (B R A H M S Diagnostica GmbH: PCT-Q). This semi-quantitative test has an advantage over conventional quantitative tests in terms of the amount of time required for measurement. The results can be obtained within 30 minutes.

**Evaluation of serum PCT level**

According to the description of the test, a PCT < 0.5 ng/ml is normal, 0.5–2.0 suggests systemic inflammatory response, and >2.0 sepsis is suspected.

The initial 23 consecutive patients are summarized in Table 2, categorized by PCT and post operative periods. In this series, patients that showed a PCT level <0.5 ng/ml on the 2nd and 7th POD had no complications. Although some of these patients showed higher PCT levels on the 1st POD, they went down to less than 0.5 ng/ml on 2nd POD. We decided therefore to evaluate the PCT level on 2nd POD, setting the cut off level of normal at ≤2.0 ng/ml.

**Definite diagnosis**

Patients whose PCT level was >2.0 ng/ml on the 2nd POD, were evaluated by colonoscopy to examine for possible colon ischemia, when their condition permitted such an examination. Chest X-rays, urine exams, computed tomography, blood cultures, endotoxin and β-D gulcan were evaluated to rule out infectious complications.

**Results**

The data for the presence of colon ischemia and PCT levels on the 2nd POD are summarized in Table 3. Four patients had ischemic intestinal complications. PCT concentrations were >2.0 ng/ml in all these cases. Three patients suffered from ischemic colitis, 1 had massive necrosis of the small and large intestine.

None of 73 patients whose PCT level was <2.0 ng/ml, suffered from intestinal ischemia or post-operative infections. Two had ileus, and one had

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**Table 2. Results of the initial 23 cases**

<table>
<thead>
<tr>
<th>PCT level</th>
<th>1POD</th>
<th>2POD</th>
<th>7POD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.5</td>
<td>15</td>
<td>17</td>
<td>22</td>
</tr>
<tr>
<td>0.5–&lt;2.0</td>
<td>8</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>&lt;2.0</td>
<td>20</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>≥2.0</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

POD: post operative date.
No patients had infectious complications in these cases.

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**Table 3. PCT levels and ischemic intestinal complications**

<table>
<thead>
<tr>
<th>PCT levels at 2POD</th>
<th>Numbers in each level</th>
<th>No ischemic complications</th>
<th>Ischemic complication (+)</th>
<th>Remarkable situation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.5</td>
<td>n=56</td>
<td>56</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0.5–&lt;2.0</td>
<td>n=17</td>
<td>17</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2.0–&lt;10</td>
<td>n=16</td>
<td>11</td>
<td>3</td>
<td>2: death (Unknown cause)</td>
</tr>
<tr>
<td>10–</td>
<td>n=4</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

All four cases with ischemic intestinal complication showed PCT levels over 2.0 ng/ml.
sustained a fever that was thought to be an allergic reaction against the graft coating. In the other 70 cases, the postoperative course was uneventful.

Significant complications occurred in five out of 16 patients whose PCT level ranged from 2.0 to 10 ng/ml. Two of them had ischemic colitis confirmed by colonoscopy and subsequently were treated conservatively. One patient, in whom intestinal ischemia was suspected during the operation, underwent a second operation on the 3rd POD to examine the patient's bowel. Large and small bowel necrosis was confirmed in this patient. One diagnosed to have pseudomembrane colitis on 10POD. Two early deaths occurred, but autopsies were not carried out. The postoperative course of the remaining 11 patients was uneventful and colonoscopy and clinical evaluation did not reveal any cause of high PCT levels.

One out of the four patients, whose PCT level was >10 ng/ml had ischemic colitis. The remaining three had no evidence of colon ischemia or other complications.

We retrospectively evaluated PCT value as a screening test for bowel ischemia after open abdominal aortic surgery, using 2.0 ng/ml as normal. Applying this range, sensitivity is 100%, specificity is 83.9%, false negative rate is 0%, and false positive rate is 16.1%. Setting the pretest probability rate to be 6%, positive predictive value of PCT is 27%, and negative predictive value is 100%. There were 11 false positive cases. Possible causes of raised PCT in these cases include renal dysfunction, intraoperative autotransfusion, colon polyps and advanced age (Table 4).

Discussion

Operative mortality of elective abdominal aortic reconstructive surgery is about 3%,15–19 and the incidence of ischemic colitis after aortic reconstruction is approximately between 0.2 and 10%.1 Overall mortality of colon ischemia is 50% and when the ischemia is transmural, it rises to 90%.1,5–10 Early diagnosis and evaluation of the severity of intestinal ischemic damage is required for adequate treatment of this complication. Colonoscopy is a reliable modality to evaluate ischemia of the intestine, but it is somewhat invasive for patients and not cost effective as a screening test.

When PCT was used as a screening test of ischemic colitis we found a 100% sensitivity for detecting this complication. False positive cases were seen in patients with renal failure, autotransfusion, older age and incidental colon polyps. Since PCT is excreted into the urine, poor clearance results in increased serum PCT levels in patients with deteriorated renal function. As endotoxemia is reported to elevate serum PCT levels,14 remaining endotoxin in the circuit of an intra-operative auto-transfusion system might cause an elevation of PCT. In elderly patients, turnover rate of intestine mucosa is decreased, and in patients with colon polyps, normal mucosa integrity might be broken. In these particular patients, manual compression of the colon during surgery could cause deterioration of the mucosal function of the colon and result in increased bacterial translocation, and endotoxin may be released into the portal vein. In this study, endotoxin levels in the same blood samples of PCT were within a normal range. Portal endotoxemia may cause elevation of PCT but endotoxin itself is cleared by the liver and endotoxin in serum obtained from ante-cubital vein was not elevated.

We postulated that elevation of endotoxin in the portal system occurred because the ischemic colon could act as a barrier to bacterial translocation. Possibly systemic serum endotoxin, filtered by the liver, was not elevated to a level high enough to be diagnosed. When PCT was used as a screening test of intestinal ischemia, it had a false positive rate of 16.1%, with no false negative cases. We conclude that PCT test may be a possible screening test of colon ischemia. When PCT level is >2.0 ng/ml on the second postoperative day of aortic surgery, colonoscopy is recommended for early diagnosis of ischemic complications in the colon.

Conclusion

A semi-quantitative PCT test is possible screening test to rule out colon ischemia in patients after open aortic surgery. It is simple and easy to measure. When PCT level is low after open aortic surgery, colon ischemia is unlikely. When PCT level is high after open aortic surgery, further investigation for postoperative complications should be carried out.

Table 4. Special notes of false positive patients

<table>
<thead>
<tr>
<th>Notes</th>
<th>Older than 80 years</th>
<th>Renal failure</th>
<th>Used ATS</th>
<th>Colon polyps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>3</td>
<td>1</td>
<td>8</td>
<td>3</td>
</tr>
</tbody>
</table>

ATS: intraoperative auto-transfusion system.

References

5 Brucks RO. Acute and delayed colon ischemia after aorta aneurysm surgery. Arch Intern Med 1966;122:249.
13 Assicot M. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 1993;341:515–518.

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