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Serum procalcitonin correlates with colonoscopy findings and can guide therapeutic decisions in postoperative ischemic colitis☆

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ABSTRACT

Background: Postoperative ischaemic colitis (POIC) is a life-threatening vascular gastrointestinal condition. Serum procalcitonin (PCT) levels be of value in the detection of necrosis.
Aims: To evaluate the correlation between serum PCT levels and the colonoscopic assessment of the severity of POIC.
Methods: Between January 2007 and November 2014, 150 patients with POIC and PCT data were included in the study. The main outcome measure was the correlation between serum PCT and the colonoscopy-based assessment of the severity of POIC (according to Favier's classification: stage 1/2 without multi-organ failure vs. stage 2/3 with multi-organ failure).
Results: Eighty-five percent of the stage 1 cases (n = 22) had a serum PCT level ≤2 μg/L; 63% (n = 19) of the stage 2 cases with multi-organ failure had a PCT level between 4 and 8 μg/L, and 70% (n = 52) of the stage 3 cases had a PCT level ≥8 μg/L. The PCT level was strongly correlated with the Favier stage (Spearman's rho: 0.701; p < 0.0001). PCT levels were similar in stage 2 cases with multi-organ failure and in stage 3 cases (16.06 μg/L vs. 7.79 μg/L, respectively; p = 0.35).
Conclusion and relevance: Serum PCT is correlated with stage 2/3 POIC requiring surgery. If PCT ≥5 μg/L, surgery should be considered.
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1. Introduction

Ischaemic colitis (IC) is a life-threatening gastrointestinal (GI) vascular condition that constitutes a medical emergency and may therefore require prompt, aggressive treatment [1]. It accounts for 50–60% of vascular GI emergencies and 3–10% of episodes of lower GI bleeding. Thankfully, IC is a relatively rare condition [2] that is caused by variations in blood flow to the colon and thus results in ischaemic and necrotic phenomena [3,4]. The condition may occur postoperatively (i.e. postoperative ischaemic colitis, POIC, especially after cardiovascular surgery) or spontaneously (in which case it is usually treated outside hospital).

Importantly, the mortality rate associated with POIC may be as high as 57% in cases with resection and 96% in the absence of treatment [5]. To improve the prognosis for POIC, surgical treatment must be performed in a timely manner. However, the key issue is deciding when to operate and on which patients.

The selection of candidates for surgery is currently based on the presence of multi-organ failure and the colonoscopic aspect of the bowel. Colonoscopy is thus mandatory for the management of patients with POIC because it provides information on the extent and severity of bowel damage (staged according to the Favier classification) [6]. In stages 1 and 2 IC, only regular colonoscopic monitoring is required—particularly 6 weeks after the episode (to check for colonic stricture) and in patients who fail to show a clinical improvement. In stage 3 IC or in stage 2 IC with the failure of at

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least one organ (the liver, lung, kidney or hemodynamic system), surgery is the standard treatment [7,8]. However, colonoscopy is sometimes prevented by pain or a technical problem. Furthermore, the endoscopist may sometimes be unable to reliably distinguish between stages 2 and 3 damage.

To guide the surgeon's decision, it has been suggested that levels of serum biomarkers (such as procalcitonin (PCT), the 116-amino-acid precursor of calcitonin [9]) may be of value in predicting the severity of IC—especially since there are no IC-specific clinical symptoms per se. A relationship between PCT and sepsis was first described in 1993 by Assicot et al. [10]. PCT has been defined as a marker of bacterial infection [11] and, more recently, bowel ischaemia and necrosis [12–14]. Furthermore, our group identified PCT as a useful marker of the type, extent and prognosis of intestinal damage [15]. However, little is known about the correlation between serum PCT levels and colonoscopy findings in the context of POIC.

The objective of the present study was thus to evaluate the correlation between serum PCT and the severity of POIC in a colonoscopic assessment (i.e. staged according to the Favier classification).

2. Patients and methods

2.1. Population

Between January 2007 and November 2015, patients with POIC (other than the extension of mesenteric infarction to the colon) diagnosed during the postoperative course in the digestive surgery or the intensive care departments at Amiens University Hospital (Amiens, France) or Beauvais General Hospital (Beauvais, France) were screened for inclusion in this two-center, retrospective study (n = 211). Eligible patients (queried ICD-10-CM codes: K55.0 and K51.9) were identified in a local database (managed using Business Objects software (Business Objects, Levallois-Perret, France)) by the hospitals' respective medical informatics departments.

The inclusion criteria were as follows: (i) age 18 or over; (ii) a morphologically-confirmed diagnosis of POIC (other than the extension of mesenteric infarction to the colon); and (iii) the availability of preoperative data (colonoscopy and a PCT assay).

In line with the French legislation on retrospective studies, approval by an independent ethics committee was neither required nor sought. However, patients were retrospectively provided with an information sheet. The study protocol complied with the ethical tenets of the 1975 Declaration of Helsinki (6th revision, 2008).

The colonoscopy findings had been graded by the endoscopist according to Favier's classification and recorded in the patient's medical records [2]:

- Stage 1: Ischaemia limited to the mucosa with petechiae and small ulcerations, with separate areas of healthy mucosa.
- Stage 2: Ischemia extending to the muscularis mucosa, with large areas of ulceration.
- Stage 3: Transmural ischemia, with necrosis of the muscularis and possible perforation.

2.2. Surgery

Surgery was performed on all stage 3 patients and in stages 1 and 2 patients with multi-organ failure. The latter was defined as the development of potentially reversible, life-threatening physiological dysfunction affecting two or more organ systems not involved in the ischemic colitis (i.e. liver, kidney, lung or heart failure). The decision to operate on stage 1 or 2 patients with organ failure (kidney or liver failure, etc.) was taken when the symptoms occurred. As described previously, the open surgical procedure consisted in an exploratory laparotomy with colonic bowel resection (subtotal colectomy or left colectomy) and stomy [15].

2.3. Study design

The study's primary objective was to evaluate the correlation between the serum PCT level and the severity of POIC (according to the Favier stage in a colonoscopic assessment). The secondary objectives were to determine (i) the optimal serum PCT value for predicting the Favier stage, (ii) the post-therapeutic morbidity/mortality and (iii) the correlation between serum PCT levels and intraoperative findings.

The following items were retrospectively extracted from the patients' medical records into a Microsoft Excel® file: demographic information, laboratory blood test results (the white blood cell count and serum levels of electrolytes, C-reactive protein, lactate and PCT), comorbidities (diabetes, hypertension, cardiopathy, neurological disorders, chronic obstructive pulmonary disease and peripheral vascular disease) and vital status (the American Society of Anesthesiologists score). The only item of information extracted from the colonoscopy report was the Favier stage.

2.4. The PCT assay

In all cases, serum PCT had been assayed within 4 days of surgery. The Kryptor® T.R.A.C.E® assay (THERMOFISHER, Clichy, France) was used on-site in each hospital's biochemical laboratory. The laboratories' normal reference value was <0.5 μg/L.

2.5. Sample size calculation

To obtain a correlation of at least 0.25 (a mild correlation) between the serum PCT level and the Favier stage while applying an alpha risk of 5% and a power of 80%, the minimum effective sample size was 123 patients.

2.6. Statistical analysis

Quantitative variables were expressed as the mean ± standard deviation (SD) or the median (range). Qualitative variables were expressed as the number (percentage). Univariate analyses were based on the *t* test (for quantitative variables) and the chi-squared test (for qualitative variables).

The correlation between the serum PCT level and the Favier stage was quantified using Spearman's rho. The threshold for statistical significance was set to $p \leq 0.05$. To determine the value of serum PCT for predicting the Favier stage, we generated a receiver operating characteristic (ROC) curve and calculated the area under the ROC curve (AUROCC).

The predictive power was characterized by the sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), threshold, positive and negative likelihood ratios (LR+ and LR−), Youden index (I, calculated as $I = Se + Sp - 1$) and the diagnostic odds ratio (DOR, calculated as follows: $DOR = (Se*Sp)/(1 - Se)*(1 - Sp)$). To ensure the robustness of our data, the calculations were based on 1000 populations bootstrapped (sampling with replacement) from the original population.

Statistical analysis was performed with SAS software (version 9.2, SAS Institute Inc., Cary, NC, USA) and PASW software (version 22, SPSS Inc., Chicago, IL, USA).

The study's results were reported in accordance with the STROBE statement.

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