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Serum value of procalcitonin as a marker of intestinal damages: type, extension, and prognosis

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Abstract
Background Ischemic and necrotic damages are complications of digestive diseases and require emergency management. Nevertheless, the decision to surgically manage could be delayed because of no sufficiently preoperative accurate marker of ischemia diagnosis, extension, and prognosis.
Methods The aim of this study was to assess the predictive value of serum procalcitonin (PCT) levels for diagnosing intestinal necrotic damages, their extension, and their prognosis in patients with ischemic disease including ischemic colitis and mesenteric infarction by a gray zone approach. Between January 2007 to June 2014, 128 patients with ischemic colitis and mesenteric infarction (codes K55.0 and K51.9) were operated, for whom data on PCT were available. We perform a retrospective, multicenter review of their medical records. Patients were divided into subgroups: ischemia (ID group) versus necrosis (ND group); the extension [focal (FD) vs. extended (ED)] and the vital status [deceased (D) vs. alive (A)].
Results PCT levels were higher in the ND ($n = 94$; $p = 0.009$); ED ($n = 100$; $p = 0.02$); and D ($n = 70$; $p = 0.0003$) groups. With a gray zone approach, the predictive thresholds were (i) for necrosis 2.473 ng/mL, (ii) for extension 3.884 ng/mL, and (iii) for mortality 7.87 ng/mL.
Conclusion In our population, PCT could be used as a marker of necrosis; especially in case of extended damages and reflects the patient's prognosis.

Keywords Procalcitonin · Tissue damages · Ischemia · Gray zone approach

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Abbreviations

SB	Small bowel
PCT	Procalcitonin
CM	Conservative management
SM	Surgical management
Se	Sensitivity
Sp	Specificity
PPV	Positive predictive value
NPV	Negative predictive value
AUC	Area under the curve
ROC	Receiver operating curve
SD	Standard deviation

Intestinal ischemia is a major health problem that accounts for 1–2 % of intestinal diseases [1]. It corresponds to a lack of intestinal viability because of a decrease of mesenteric blood flow and is associated with a high mortality rate [2, 3]. The importance of this phenomenon is increasing considering the population aging [4].

The treatment of intestinal ischemia consists usually in an exploratory laparotomy to evaluate the severity of bowel damages and a resection of bowel segments prior (if necessary) to a second-look surgery 2 days later [5, 6]. The timing of this surgical management is very important especially for the recovery of intestinal viability [7].

Nevertheless in some cases tissue ischemia and/or necrosis are so extended that the surgical procedure is too late for expect a curative management. To adapt the patient's management, preoperative markers of ischemic and/or necrotic damages including their diagnosis, extension, and prognosis are required.

Procalcitonin (PCT) is a 116-amino-acid precursor of calcitonin [8] that was first described in 1993 by Assicot et al. [9]. A number of clinical studies have shown that PCT is a marker for sepsis and inflammation [10], for colonic ischemia after aortic surgery [11], and for bowel ischemia after bowel obstruction [12].

Our team previously proposed to use PCT as a marker of intestinal ischemia in patients with postoperative small bowel obstruction developed on abdominal adhesions [13]. In this condition, the ROC curve for PCT was 0.91 and the predictive values were above 80 %. We showed too that PCT was useful to guide the patient's management if measured at admission, 18 and 24 h. At admission for a PCT value $\leq$0.165 ng/mL, the surgical management was unnecessary for 93 % of patients; at 18 h after admission the surgery was useless for a PCT value $\leq$0.27 ng/mL and at 24 h after admission the surgery is pointless for 95 % of patients for a PCT value $\leq$0.255 ng/mL [14].

The aim of this study was to assess the predictive value of serum PCT levels for diagnosing the presence of intestinal necrotic damages, their extension, and their prognosis in patients with ischemic diseases including ischemic colitis and mesenteric infarction using the gray zone approach.

Patients and methods

Population

From January 2007 to June 2014, 128 patients with ischemic diseases (ischemic colitis and mesenteric infarction) were admitted at the emergency departments of Amiens University Hospital and Beauvais Hospital and had serum assessment of PCT before any management. No patient was below 18 years old, presented a mixt form of ischemic disease (defined as the presence on the pathological report of ischemic colonics damages and small bowel injuries) or presented acute abdominal pain and collapse without available serum PCT levels. All of these patients were surgically managed with bowel resection, 70 % after a cardiac surgical procedure and had available pathologist report.

Eligible patients in this multicenter, retrospective, for diagnostic purposes study were identified from a local database extracted thanks to Business Object Software (Washington state, USA) and after request to the medical information department of the two institutions (codes K55.0 and K51.9). Each list was reviewed to identify patients with ischemic disease and preoperative serum PCT assessment. Patients were retrospectively informed with an information letter.

The histological grading of intestinal damages was obtained according to the Park's classifications [15] and performed by one pathologist. To identify patients with tissue necrotic damages, the overall population was divided into subgroups: patients with tissue ischemic damages (ID group, $n = 34$) and those with necrotic damages (ND group, $n = 94$).

To identify the extension of tissue damages, the overall population was divided into subgroups: patients with focal damages (FD group, $n = 28$) and those with extended damages (ED group, $n = 100$).

To identify patients at high risk of death, the overall population was divided into subgroups: the deceased patients (D group, $n = 70$) and those alive 90 days after the management (A group, $n = 58$).

Surgery

The open surgical procedure consisted in an exploratory laparotomy with bowel resection. A stomy was created, as required. In each case, the presence of macroscopic bowel

ischemia and/or necrosis, the extension, and the location of the lesions were noted.

Study design

The study' main objective was to assess the predictive value of serum PCT levels for diagnosing intestinal necrotic damages in patients with ischemic diseases. Secondary objectives were the predictive value of PCT for predicting the degree of extension of these damages and the vital status of these patients.

The following items of patient's medical records were retrospectively collected in an excel file: demographic information, laboratory blood test results (white blood cell count, C reactive protein, lactate, ions, and PCT), comorbidities (diabetes, hypertension, cardiopathy, neurological disorder, chronic obstructive pulmonary disease, and peripheral arterial disease), and the vital status. Data related to pathologist report's analysis included ischemic and/or necrotic damages and extension of these damages.

The procalcitonin assay

For each patient, PCT had been measured prior to the surgical procedure. The Kryptor® T.R.A.C.E® assay (THERMOFISHER, Clichy, France) was used on-site in each biochemical laboratory. The reference value is 0.5 ng/mL.

Statistical analysis

Quantitative data are expressed as mean ± standard deviation (SD) or median (minimum–maximum), qualitative data as effective (percentage). Univariable analyses were performed with the χ^2 test or a fisher test for qualitative variables and the t test for quantitative variables.

The threshold for statistical significance was set to $p \leq 0.05$ and presented as bold number in the several tables. To determine the predictive values of PCT for predicting (i) intestinal necrotic damages, (ii) extended damages, and (iii) the postoperative mortality, we generated receiver operating characteristic (ROC) curves and calculated the area under the ROC curve (AUROCC). These curves were obtained by averaging 1,000 populations bootstrapped (sampling with replacement) from the original study population. This method limits the impact of outliers and allows the provision of more robust representations. Box plots were used to depict the confidence interval of the average ROC curves [16]. The predictive values were then presented with the sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), the threshold, and the positive and negative likelihood ratios (LR+ and LR−). Statistical analysis was performed with SAS 9.2 (SAS Institute Inc., Cary, NC, USA) and PASW 18 (SPSS Inc., Chicago, IL, USA).

Gray zone calculation

A gray zone was calculated to determine the conditions in which PCT would be not informative-enough with the R software with the ROCR package. The technique we used was described by Canesson et al. in their article "To determine this range of values, we first assessed the "optimal" threshold using Youden's index (J) defined as (Sp + Se − 1). Maximizing J corresponds to maximizing the overall correct classification rates. It minimizes misclassification rates. Youden's index determination was then conducted for each bootstrapped population, resulting in a set of 1,000 "optimal" values. The mean value of these optimal values and its 95 % CI were then estimated. Thus, the gray zone was defined as well as its 95 % CI. This first approach was completed by an alternative approach, aiming at defining three classes of response: negative, inconclusive, positive" [16].

The study was performed according to the STARD criteria.

Results

The value of procalcitonin for diagnosing the presence of intestinal necrotic damages

Demographic and clinical data for the ID and ND groups are summarized in Table 1. These groups are similar in term of demographic data, comorbidities, and biology but there is an imbalance for PCT (2.34 vs. 25.09 ng/mL, respectively; $p < 0.009$).

The AUROCC for PCT and tissue necrotic damages was 0.92 [95 % CI 0.86–0.98] (Fig. 1). The gray zone is comprised between 1.761 and 3.884 ng/mL. The more pertinent threshold is ≥2.473 ng/mL for predicting tissue necrosis and yielded a sensitivity of 94.6 %, a specificity of 68 %, a PPV of 89.8 %, a NPV of 80.9 % (Fig. 1), a LR+ of 2.96, and a LR− of 0.08.

The value of procalcitonin for predicting the degree of extension of tissue damages

Demographic and clinical data for the FD and ED groups are summarized in Table 2. These groups are similar in

Table 1 Characteristics of the study groups (ID and ND groups)

Variable	Tissue ischemic damages ($n = 34$)	Tissue necrotic damages ($n = 94$)	p value
Mean age, years (min–max)	69 (53–87)	69 (19–92)	0.94
Male sex, *n* (%)	15 (44)	61 (65)	0.07
Diabetes, *n* (%)	10 (29)	28 (30)	0.73
Cancer, *n* (%)	13 (38)	22 (23)	0.09
Hypertension, *n* (%)	16 (47)	59 (63)	0.76
Previous history of neurological disorders, *n* (%)	5 (15)	25 (27)	0.57
Peripheral vascular disease, *n* (%)	10 (29)	24 (26)	0.77
Cardiopathy, *n* (%)	22 (65)	68 (72)	0.47
Smoker, *n* (%)	12 (36)	39 (42)	0.69
Chronic obstructive pulmonary disease, *n* (%)	11 (32)	26 (28)	0.63
Leukocytes, $\times 10^3/mm^3 \pm$ SD	17.3 ± 12.7	15.1 ± 8.2	0.42
C reactive protein (mg/L) ± SD	131 ± 95	156 ± 107	0.27
Lactates (mmol/L) ± SD	3.8 ± 3.1	3.8 ± 3.8	0.97
Sodium (mmol/L) ± SD	139 ± 6	140 ± 5	0.55
Chloride (mmol/L) ± SD	104 ± 8	106 ± 7	0.28
Phosphorus (mmol/L) ± SD	1.25 ± 0.5	1.23 ± 0.4	0.85
Procalcitonin (ng/mL) (min–max)	2.34 (0.16–11.83)	25.09 (0.22–621.20)	**0.009**

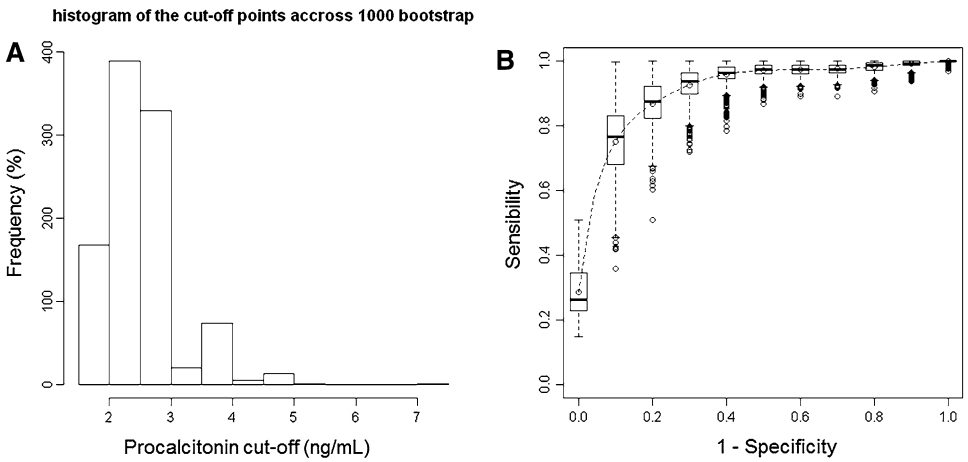

Fig. 1 Gray zone approach for predicting the presence of tissue necrotic damages including the histogram for the threshold (**A**) and the ROC curve (**B**)

term of demographic data but there is an imbalance for previous history of neurological disorders (5 vs. 29 %, respectively; $p = 0.03$); CRP (111 vs. 160 mg/L, respectively; $p = 0.03$); and PCT (3.8 vs. 23.04 ng/mL, respectively; $p < 0.02$).

The AUROCC for PCT and extended tissue damages was 0.82 [95 % CI 0.71–0.92] (Fig. 2). The gray zone is comprised between 2.473 and 4.91 ng/mL. The more pertinent threshold is ≥3.884 ng/mL for predicting the damage's extension and yielded a sensitivity of 76.3 %, a specificity of 84.2 %, a PPV of 95.3 %, a NPV of 45.7 % (Fig. 3), a LR+ of 4.83, and a LR− of 0.28.

The value of procalcitonin for predicting the mortality

Demographic and clinical data for the D and A groups are summarized in Table 3. These groups are similar in term of demographic data but there is an imbalance for PCT (32.1 vs. 6.3 ng/mL, respectively; $p = 0.04$).

The AUROCC for PCT and prognosis was 0.82 [95 % CI 0.736–0.901] (Fig. 3). The gray zone is comprised between 2.56 and 10.82 ng/mL. The more pertinent threshold is ≥7.87 ng/mL for predicting the mortality and yielded a sensitivity of 72 %, a specificity of 79.6 %, a PPV of 78.3 %, a NPV of 73.6 % (Fig. 3), a LR+ of 3.53, and a LR− of 0.35.

Table 2 characteristics of the study groups (FD and ED groups)

Variable	Focal damages ($n = 28$)	Extended damages ($n = 100$)	p value
Mean age, years (min–max)	70 (52–85)	70 (19–92)	0.95
Male sex, n (%)	16 (58)	60 (60)	0.87
Diabetes, n (%)	10 (37)	28 (28)	0.42
Cancer, n (%)	6 (21)	29 (29)	0.50
Hypertension, n (%)	15 (53)	60 (60)	0.56
Previous history of neurological disorders, n (%)	1 (5)	29 (29)	**0.03**
Peripheral vascular disease, n (%)	9 (32)	25 (25)	0.56
Cardiopathy, n (%)	22 (79)	68 (68)	0.33
Smoker, n (%)	13 (47)	38 (38)	0.43
Chronic obstructive pulmonary disease, n (%)	9 (32)	28 (28)	0.72
Leukocytes, $\times 10^3/mm^3 \pm$ SD	15.8 ± 9.7	15.6 ± 9.5	0.95
C reactive protein (mg/L) ± SD	111 ± 73	160 ± 109	**0.03**
Lactates (mmol/L) (min–max)	4.6 (1–23)	3.6 (1–14)	0.45
Sodium (mmol/L) ± SD	139 ± 5	140 ± 6	0.91
Chloride (mmol/L) ± SD	106 ± 7	105 ± 7	0.90
Phosphorus (mmol/L) ± SD	1.19 ± 0.5	1.25 ± 0.4	0.63
Procalcitonin (ng/mL) (min–max)	3.81 (0.21–27.2)	23.04 (0.16–621.2)	**0.02**

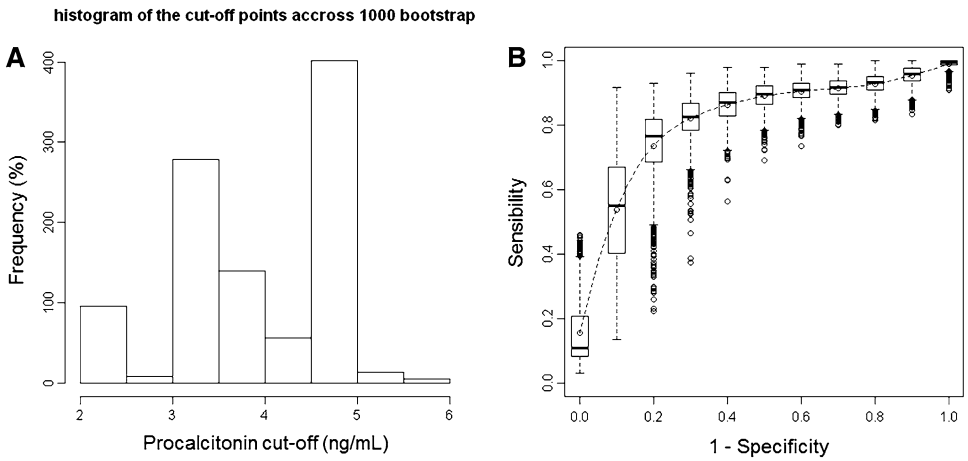

Fig. 2 Gray zone approach for predicting the presence of extended damages including the histogram for the threshold (**A**) and the ROC curve (**B**)

All the predictive characteristics are depicted in Table 4.

Discussion

This retrospective, multicenter study was tailored to evaluate the predictive value of PCT as a marker of (i) tissue necrotic damages, (ii) extended damages, and (iii) the poor prognosis in patients with ischemic diseases especially ischemic colitis and mesenteric infarction. This study shows that PCT could be used as a marker for these four conditions with at least a 5-times threshold.

The data related on the serum PCT levels were higher of those proposed as a positive diagnosis threshold (0.2–0.5 ng/mL) whatever the condition [17]. This report could be explained by the pathologic situation in which the patients are. Indeed, the patients were recruited because of the confirmed presence of ischemic or necrotic damages. Whereas this study was performed in two centers, the observed PCT levels were homogenous into each group. The absence of intra-group variation could be due to the analyser performance of the Kryptor T.R.A.C.E® assay (limit of detection of 0.06 ng/mL; the intra-assay and inter-assay coefficients of variation below 5 % and below 10 %, respectively) and the reproducibility of the assessment described in a five-center study [18].

The dilemma for the surgeon to operate the patient is laid on the difficulty to identify the good candidate but his decision should be as quick as possible to avoid alternating

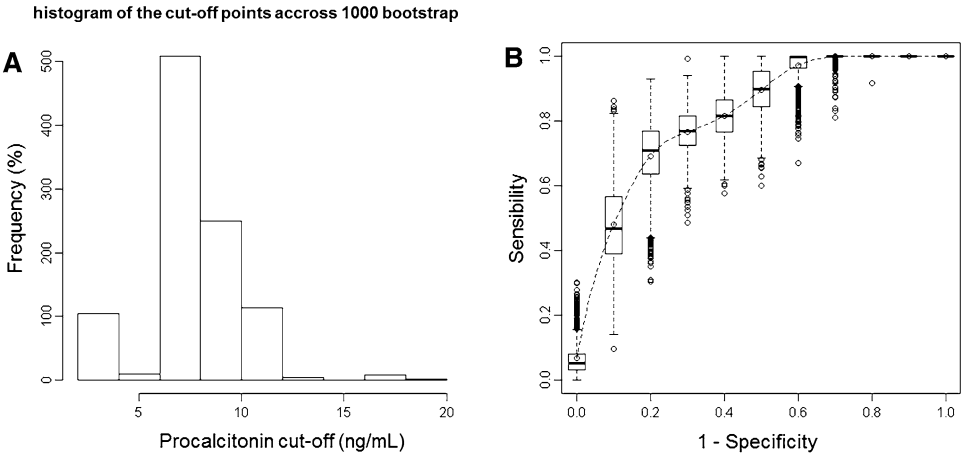

Fig. 3 Gray zone approach for predicting the prognosis including the histogram for the threshold (**A**) and the ROC curve (**B**)

Table 3 characteristics of the study groups (D and A groups)

Variable	Deceased patients ($n = 70$)	Alive patients ($n = 58$)	p value
Mean age, years (min–max)	69 (19–92)	71 (50–89)	0.49
Male sex, *n* (%)	41 (58)	35 (61)	0.74
Diabetes, *n* (%)	22 (32)	16 (27)	0.55
Cancer, *n* (%)	15 (22)	20 (33)	0.23
Hypertension, *n* (%)	41 (58)	34 (59)	0.90
Previous history of neurological disorders, *n* (%)	20 (28)	10 (17)	0.38
Peripheral vascular disease, *n* (%)	20 (28)	14 (24)	0.69
Cardiopathy, *n* (%)	50 (72)	40 (69)	0.61
Smoker, *n* (%)	24 (34)	27 (47)	0.27
Chronic obstructive pulmonary disease, *n* (%)	15 (22)	22 (38)	0.16
Leukocytes, $\times 10^3/mm^3 \pm$ SD	14.6 ± 7.9	16.7 ± 10.9	0.26
C reactive protein (mg/L) ± SD	162.5 ± 109	135.7 ± 99	0.21
Lactates (mmol/L) ± SD	3.9 ± 4	3.6 ± 3.1	0.64
Sodium (mmol/L) ± SD	141 ± 6	138 ± 5	0.55
Chloride (mmol/L) ± SD	106 ± 7	104 ± 7	0.18
Phosphorus (mmol/L) ± SD	1.2 ± 0.35	1.3 ± 0.47	0.45
Procalcitonin (ng/mL) (min–max)	32.1 (0.21–621.2)	6.3 (0.16–27.2)	**0.04**

Table 4 Predictive characteristics of procalcitonin

Damages	Cut off	Gray zone	Se	Sp	PPV	NPV	LR+	LR-	AUC	CI AUC
Necrosis	2.47	1.76–3.88	94.6	68	89.8	80.9	2.96	0.08	0.92	0.86–0.98
Extension	3.88	2.47–4.91	76.3	84.2	95.3	45.7	4.83	0.28	0.82	0.71–0.92
Mortality	7.87	2.56–10.82	72	79.6	78.3	73.6	3.53	0.35	0.82	0.74–0.90

The cut off and the gray zone values are expressed in ng/mL; Se, Sp, PPV, NPV, LR+, and LR− are expressed as %. CI AUC corresponds to 95 % CI

the prognosis. Some elements are available to help the clinician especially biological (lactates, leukocytes) and CT scan signs but these elements are quite informative because none of them was found in our study. The importance of PCT in diagnosing the necrotic damages (with a PCT level lower than 2.5 ng/mL) could orientate the surgeon to an emergency surgery in which the damages are still reversible before a multivisceral dysfunction occurs. With a PCT higher than 3.9 ng/mL, an extensive gesture with a segmentary bowel resection is required. In case of high PCT levels (higher than 7.9 ng/mL), the situation is life-threatening and the performance of the surgery should

be discussed with the patient and his family because it foretells difficulties during the postoperative curse. These data feed the trend that PCT is a marker of mortality, which has been already reported during the two last decades in many fields (sepsis; mesenteric infarction) [19–25].

The increase of serum PCT could be explained by its secretion. During the necrotic phenomenon, the inflammatory state is enhanced because of the reperfusion mechanism that release reactive oxygen species (ROS). These ROS promote the secretion of proinflammatory cytokines (TNFα and IL-6). This secretion associated with an alteration of the immunological role of the mucosae layer and a bacterial translocation [26] engenders a release of bacterial endotoxins inducing PCT excretion [10, 27–29]. The reperfusion mechanism plays an important part considering the splanchnic vascularization of the colon that predisposes it to more frequent ischemic and necrotic damages especially after cardiovascular surgery. The origin of production of PCT involves many sources. One of them is the peripheral mononuclear blood cells (PMBC) especially under the effects of bacterial lipopolysaccharides (LPS) and the endothelial cells [30, 31]. A second one could involve the colonic bacterial content. The high serum PCT value in the group with extended tissue damages could be explained by the feedback engendered by PCT. Indeed, at low dose PCT maintains this phenomenon engendering a systemic inflammatory response syndrome (SIRS) reliable as shown by Al Nawas et al., Carboni et al., and Becker et al. to PCT, LPS, and TNFα [27, 32, 33] whereas at high dose it is deleterious for the tissue viability spreading the ischemic and necrotic phenomenon along the tissue [34]. These data were divergent with those of Rau et al. that shows no correlation between necrosis' extension and PCT but these works were performed in pancreas in which the bacterial load is not sufficient-enough to promote PCT release [35]. The values we obtained do not reflect the presence of an infection that could be a bias for the explanation. Indeed, our thresholds were below 10 ng/mL suggesting the absence of septic shock [36]; the temperatures were normal and no evidence of an infection was found in the pathologist' reports. During the ischemic or necrotic phenomenon, PCT is not involved in the blood flow decrease in the vessel as shown by Kettelhack et al. (no correlation with the arterial blood pressure or the systemic vascular resistance) but rather with the NO synthesis in the cells [37]. Indeed, it seems that PCT inhibits the effects of iNO-induced of proinflammatory cytokines as a part of the physiological mechanism protecting against a massive excretion of NO [38].

The collected data in this study are consistent with those of Markogiannakis et al., Nagata et al. on humans [11, 12], and those of Karabulut et al. in rabbits [39]. All of these studies could propose PCT as a marker of ischemia and necrosis even if there are some bias such as the retrospective design, the number of center, the effective, and the possible infection distant from the intestine (lung, urinary system) that could increase the PCT levels. In our study, the use of a gray zone approach, a specific statistical method, permits to obtain more robust results.

Conclusion

In our population, PCT could be used as a marker of necrosis; especially in case of extended damages and reflects the patient's prognosis.

Disclosures Cosse C, Sabbagh C, Browet F, Mauvais F, Rebibo L, Zogheib E, Chatelain D, Kamel S, and Regimbeau JM have no conflicts of interest or financial ties to disclose.

References

1. Debus ES, Müller-Hülsbeck S, Kölbel T, Larena-Avellaneda A (2011) Intestinal ischemia. Int J Colorectal Dis 26:1087–1097
2. Park WM, Gloviczki P, Cherry KJ Jr, Bower TC, Panneton JM, Schleck C, Ilstrup D, Harmsen WS, Noel AA (2002) Contemporary management of acute mesenteric ischemia: factors associated with survival. J Vasc Surg 35:445–452
3. Kassahun WT, Schulz T, Richter O, Hauss J (2008) Unchanged high mortality rates from acute occlusive intestinal ischemia: six year review. Langenbecks Arch Surg 393:163–171
4. Menon NJ, Amin AM, Mohammed A, Hamilton G (2005) Acute mesenteric ischaemia. Acta Chir Belg 105:344–354
5. Denecke H, Stiegler H (1990) Indications and results of second-look operation in acute mesenteric vascular occlusion. Langenbecks Arch Chir Suppl II Verh Dtsch Ges Chir. 31:311–315
6. Renner P, Kienle K, Dahlke MH, Heiss P, Pfister K, Stroszczynski C, Piso P, Schlitt HJ (2011) Intestinal ischemia: current treatment concepts. Langenbecks Arch Surg 396:3–11
7. Wadman M, Syk I, Elmståhl S (2000) Survival after operations for ischaemic bowel disease. Eur J Surg 166:872–877
8. Maruna P, Nedelníková K, Gürlich R (2000) Physiology and genetics of procalcitonin. Physiol Res 49(Suppl 1):S57–S61
9. Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, Bohuon C (1993) High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 341:515–518
10. Baruti Gafurri Z, Pacarizi H, Zhubi B, Begolli L, Topciu V (2010) The importance of determining procalcitonin and C reactive protein in different stages of sepsis. Bosn J Basic Med Sci 10:60–64
11. Nagata J, Kobayashi M, Nishikimi N, Komori K (2008) Serum procalcitonin (PCT) as a negative screening test for colonic ischemia after open abdominal aortic surgery. Eur J Vasc Endovasc Surg 35:694–697
12. Markogiannakis H, Memos N, Messaris E, Dardamanis D, Larentzakis A, Papanikolaou D, Zografos GC, Manouras A (2011) Predictive value of procalcitonin for bowel ischemia and necrosis in bowel obstruction. Surgery 149:394–403
13. Cosse C, Regimbeau JM, Fuks D, Mauvais F, Scotte M (2013) Serum procalcitonin for predicting the failure of conservative management and the need for bowel resection in patients with small bowel obstruction. J Am Coll Surg 216:997–1004
14. Cosse C, Sabbagh C, Rebibo L, Grelpois G, Galmiche A, Regimbeau JM (2014) Kinetics of procalcitonin in the

management of small bowel obstruction: a preliminary report. Surg Curr Res 4:184
15. Parks DA, Bulkley GB, Granger DN, Hamilton SR, McCord JM (1982) Ischemic injury in the cat small intestine: role of superoxide radicals. Gastroenterology 82:9–15
16. Cannesson M, Le Manach Y, Hofer CK, Goarin JP, Lehot JJ, Vallet B, Tavernier B (2011) Assessing the diagnostic accuracy of pulse pressure variations for the prediction of fluid responsiveness: a "gray zone" approach. Anesthesiology 115:231–241
17. Hausfater P (2007) Procalcitonin measurement in adult clinical practice. Rev Med Int 28:296–305
18. Steinbach G, Rau B, Debard AL, Javourez JF, Bienvenu J, Ponzio A, Bonfà A, Hubl W, Demant T, Külpmann WR, Buchholz J, Schumann G (2004) Multicenter evaluation of a new immunoassay for procalcitonin measurement on the Kryptor system. Clin Chem Lab Med 42:440–449
19. Whang KT, Steinwald PM, White JC, Nylen ES, Snider RH, Simon GL, Goldberg RL, Becker KL (1998) Serum calcitonin precursors in sepsis and systemic inflammation. J Clin Endocrinol Metab 83:3296–3301
20. Von Heimburg D, Stieghorst W, Khorram-Sefat R, Pallua N (1998) Procalcitonin—a sepsis parameter in severe burn injuries. Burns 24:745–750
21. Van Langevelde P, Joop K, van Loon J, Frölich M, Groeneveld PH, Westendorp RG, van Dissel JT (2000) Endotoxin, cytokines, and procalcitonin in febrile patients admitted to the hospital: identification of subjects at high risk of mortality. Clin Infect Dis 31:1343–1348
22. Merle C, Lepouse C, De Garine A, Frayssinet N, Leymarie F, Leon A, Jolly D (2004) Surgery for mesenteric infarction: prognostic factors associated with early death within 72 hours. J Cardiothorac Vasc Anesth 18:734–741
23. ten Boekel E, Vroonhof K, Huisman A, van Kampen C, de Kieviet W (2006) Clinical laboratory findings associated with in-hospital mortality. Clin Chim Acta 372:1–13
24. Viallon A, Guyomarc'h S, Marjollet O, Berger C, Carricajo A, Robert F, Laporte S, Lambert C, Page Y, Zéni F, Bertrand JC (2008) Can emergency physicians identify a high mortality subgroup of patients with sepsis: role of procalcitonin. Eur J Emerg Med 15:26–33
25. Cotoi OS, Manjer J, Hedblad B, Engström G, Melander O, Schiopu A (2013) Plasma procalcitonin is associated with all-cause and cancer mortality in apparently healthy men: a prospective population-based study. BMC Med 11:180
26. Ryan T, Mc Carthy JF, Rady MY, Serkey J, Gordon S, Starr NJ, Cosgrove DM (1997) Early bloodstream infection after cardiopulmonary bypass: frequency rate, risk factors, and implications. Crit Care Med 25:2009–2014
27. Carboni GL, Fahrner R, Gazdhar A, Printzen G, Schmid RA, Hoksch B (2008) Comparison of procalcitonin and CrP in the postoperative course after lung decortication. Eur J Cardiothorac Surg 33:777–780
28. Andona P, Nix D, Wilson MF, Aljada A, Love J, Assicot M, Bohuon C (1994) Procalcitonin increase after endotoxin injection in normal subjects. J Clin Endocrinol Metab 79:1605–1608
29. Carlstedt F, Lind L, Joachimsson PO, Rastad J, Wide L, Ljunghall S (1999) Circulating ionized calcium and parathyroid hormone levels following coronary artery by-pass surgery. Scand J Clin Lab Invest 59:47–53
30. Oberhoffer M, Stonans I, Russwurm S, Stonane E, Vogelsang H, Junker U, Jäger L, Reinhart K (1999) Procalcitonin expression in human peripheral blood mononuclear cells and its modulation by lipopolysaccharides and sepsis-related cytokines in vitro. J Lab Clin Med 134:49–55
31. Zannoni A, Giunti M, Bernardini C, Gentilini F, Zaniboni A, Bacci ML, Forni M (2012) Procalcitonin gene expression after LPS stimulation in the porcine animal model. Res Vet Sci 93:921–927
32. Al-Nawas B, Shah PM (1996) Procalcitonin in patients with and without immunosuppression and sepsis. Infection 24:434–436
33. Becker KL, Nylén ES, White JC, Müller B, Snider RH Jr (2004) Clinical review 167: procalcitonin and the calcitonin gene family of peptides in inflammation, infection, and sepsis: a journey from calcitonin back to its precursors. J Clin Endocrinol Metab 89:1512–1525
34. Hoffmann G, Czechowski M, Schloesser M, Schobersberger W (2002) Procalcitonin amplifies inducible nitric oxide synthase gene expression and nitric oxide production in vascular smooth muscle cells. Crit Care Med 30:2091–2095
35. Rau B, Steinbach G, Gansauge F, Mayer JM, Grünert A, Beger HG (1997) The potential role of procalcitonin and interleukin 8 in the prediction of infected necrosis in acute pancreatitis. Gut 41:832–840
36. de Werra I, Jaccard C, Corradin SB, Chioléro R, Yersin B, Gallati H, Assicot M, Bohuon C, Baumgartner JD, Glauser MP, Heumann D (1997) Cytokines, nitrite/nitrate, soluble tumor necrosis factor receptors, and procalcitonin concentrations: comparisons in patients with septic shock, cardiogenic shock, and bacterial pneumonia. Crit Care Med 25:607–613
37. Kettelhack C, Hohenberger P, Schulze G, Kilpert B, Schlag PM (2000) Induction of systemic serum procalcitonin and cardiocirculatory reactions after isolated limb perfusion with recombinant human tumor necrosis factor-alpha and melphalan. Crit Care Med 28:1040–1046
38. Hoffmann G, Totzke G, Seibel M, Smolny M, Wiedermann FJ, Schobersberger W (2001) In vitro modulation of inducible nitric oxide synthase gene expression and nitric oxide synthesis by procalcitonin. Crit Care Med 29:112–116
39. Karabulut K, Gül M, Dündar ZD, Cander B, Kurban S, Toy H (2011) Diagnostic and prognostic value of procalcitonin and phosphorus in acute mesenteric ischemia. Ulus Travma Acil Cerrahi Derg 17:193–198