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Early Detection of Infectious Complications After Laparotomy for Acute Digestive Abdomen Using C-Reactive Protein and Procalcitonin: A Prospective Multicentre Analysis in Yaoundé

Early detection of infectious complications after laparotomy for acute digestive abdomen using c-reactive protein and procalcitonin: a prospective multicentre analysis in Yaounde

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Mots-clés : Complications infectieuses postopératoires, abdomen aigu, protéine C-réactive, procalcitonine, Valeurs seuils.

ABSTRACT

Introduction. Early detection of postoperative infections remains a challenge worldwide. The use of C-reactive protein (CRP) and procalcitonin (PCT) as predictive factors of the occurrence of these infections have not yet been studied in our context. **Methods.** This was a multicentre cross-sectional study conducted in Yaoundé. Prospectively, we collected all adult's patients operated for an acute digestive abdomen through a laparotomy approach. CRP and PCT levels were measured preoperatively and in postoperative day 3. Patients were followed until postoperative day 14; the occurrence of a postoperative infectious complication (PIC) was the main outcome investigated. The Youden index, the receiver operating characteristic (ROC) and areas under the curve were used to determine the cut-off values of CRP and PCT with their sensibility and specificity. **Results.** We collected a total of 54 patients. PIC were the commonest morbidity, encountered in 38 cases (70.4%); they were diagnosed within an average of 5.65±1.8 days after the surgery. The postoperative (day 3) threshold value was of 68.8mg/ml (predictive positive value of 96.9%) and 5ng/ml (predictive positive value of 100%), respectively for CRP and PCT. The specificity of these cut-off values were of 90.7% and 100%, respectively for CRP and PCT. The sensibility of the cut off value was of 81.6% for CRP and 78;9% for PCT. The area under the ROC curve was of 0.956 (95% CI = [0.862- 0.993] for PCT and 0.894 (95% CI = [0.780-0.961]) for CRP. **Conclusion.** CRP and PCT values at postoperative day 3 can be used for the early diagnosis of PIC.

RÉSUMÉ

Introduction. La détection précoce des infections postopératoires reste un défi pour les praticiens. L'utilisation de la protéine C-réactive (CRP) et de la procalcitonine (PCT) comme facteurs prédictifs de la survenue de ces infections n'a pas encore été étudiée dans notre contexte. **Methodes** Il s'agissait d'une étude transversale multicentrique menée à Yaoundé. Prospectivement, nous avons colligé tous les patients adultes opérés par voie ouverte d'un abdomen aigu d'origine digestive. Les taux de CRP et de PCT ont été mesurés en préopératoire et au 3ème jour postopératoire. Les patients ont été suivis jusqu'au 14ème jour postopératoire ; la survenue d'une complication infectieuse postopératoire était le principal résultat étudié. L'indice de Youden, les courbes ROC et les aires sous la courbe ont été utilisés pour déterminer les valeurs seuil de CRP et PCT avec leur sensibilité et spécificité. **Resultats.** Nous avons recueilli un total de 54 patients. Les complications infectieuses étaient la morbidité la plus fréquente, rencontrées dans 38 cas (70,4 %) ; elles ont été diagnostiquées dans un délai moyen de 5,65 ± 1,8 jours après la chirurgie. La valeur seuil postopératoire (3ème jour) était de 68,8 mg/ml (valeur prédictive positive de 96,9 %) et de 5 ng/ml (valeur prédictive positive de 100 %), respectivement pour la CRP et la PCT. La spécificité de ces valeurs seuils était de 90,7 % et 100 %, respectivement pour la CRP et la PCT. La sensibilité de la valeur seuil était de 81,6 % pour la CRP et de 78,9 % pour la PCT. L'aire sous la courbe ROC était de 0,956 (IC à 95 % = [0,862- 0,993] pour la PCT et de 0,894 (IC à 95 % = [0,780-0,961]) pour la CRP. **Conclusion.** Les valeurs de CRP et PCT au jour 3ème jour postopératoire peuvent être utilisées pour le diagnostic précoce de complications infectieuses.

INTRODUCTION

Surgical acute abdomen remains one of the commonly encountered emergency worldwide; however, access and outcomes of surgical care varies widely. Thus, only 6% of the surgical procedures recorded each year are performed in developing countries and less than one-third of the world's population has access to safe, timely and affordable surgery [1]. Mortality and morbidity of surgical acute abdomen in low-income countries (LMICs) are three to seven times higher than in middle and high-income ones [2-4]. Postoperative morbidity rate of acute abdomen in LMICs varies from 16.6 to 50.6% of cases, septic complications being the commonest [5-7]. These septic complications are also the main cause of postoperative deaths [6,8]; Abdominal infections-related mortality rates range between 5 to 24.5% [9-12] in sub-Saharan Africa. Early diagnosis of postoperative infections is undoubtedly necessary to further improve patient outcomes in developing countries in general and in Africa in particular.

Among several markers of inflammation and sepsis, serum procalcitonin (PCT) and C-reactive protein (CRP) concentrations are well-established ones, utilized for the early diagnosis of postoperative infections after abdominal surgeries in developed countries [13-19]. To the best of our knowledge, there is no study to date on this subject in sub-Saharan Africa. This study aimed to determine the predictive values of CRP and PCT in the occurrence of postoperative infections after digestive emergency surgeries in Yaounde, a sub-Saharan low income setting.

METHODS

Study setting

This was a multicentre study, conducted in three tertiary hospitals of Yaoundé, the capital city of Cameroon (central African region): Yaoundé university teaching hospital, Yaoundé central hospital and Yaoundé emergency centre. These three hospitals have the biggest activity on digestive surgery in Yaoundé.

Study design, inclusion criteria, procedure, ethics consideration

We conducted an analytical cross-sectional study with prospective data collection. We included all adults' patients operated for an acute digestive abdomen through a laparotomy approach, from December 1st,2020 to June 30th, 2021. CRP and PCT levels were measured in peripheral venous blood on admission before the surgery and on postoperative day 3, with immune-detection by the rapid quantitative test FinecareTM. Patients were followed until postoperative day 14 for the occurrence of septic complications. Septic complications were diagnosing on clinical (fever, pain, tenderness, presence of pus through the surgical wound or a drain, requiring specific wound care) radiological (intra-abdominal collections) and biological (positive pus or urinary culture). Patients with acute abdomen of non-digestive origin, those operated through laparoscopic approach and those lost to follow-up before the postoperative day 14 were not included. Malaria wasn't considered as a postoperative infectious complication. Information on patients' age and sex, diagnosis, operative time, postoperative 14-day morbidity and mortality, were recorded. The study was conducted after the approval of our institutional research and ethical committee. The consent of each patient was obtained before any inclusion in the study.

Statistical analysis

Data analysis was conducted using IBM SPSS software for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA). Means ± standard deviations were calculated for continuous variables and categorical variables were reported using absolute values and percentages. The Youden index was used to determine the cut-off values of CRP and PCT (with 95% of confidence interval), their sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The correlation between CRP, PCT and postoperative infections was analysed firstly with the receiver operating characteristic (ROC); predictive values of theses parameters were evaluated by their respective areas under the curve (AUC). Then we calculate the spearman's correlation between the cut-off value of CRP and PCT on postoperative day 3 and the occurrence of infectious complications. The association between these parameters was considered as strong if the spearman correlation coefficient, r, was closer to 1. The differences were considered as significate for a p-value less than 0.05.

RESULTS

We collected a total of 54 patients among whom 33 males (61.1%) with a sex ratio of 1.6. Their mean age was 39.1 ± 16.3years. The mean delay from symptom onset to consultation and from admission to surgery were 3.5±2.5 days and 48.8±12.4 hours, respectively. The main aetiology of acute abdomen (Table 1) was peritonitis due to peptic ulcer perforation (n= 15, 27.8%). The mean operative time was 2.37±0.6 hours.

Table 1: Aetiologies of acute surgical abdomen

Aetiology	Number	Percentage
Non complicated appendicitis	3	5.6
Peritonitis		
▪ Perforated peptic ulcer	15	27.8
▪ Appendicular	5	9.2
▪ Ileal perforation	5	9.2
▪ Colic perforation	5	9.2
▪ Jejunal perforation	2	3.7
Bowel obstruction		
▪ Band	3	5.6
▪ strangulated hernia	5	9.2
▪ Sigmoid colon volvulus	1	1.9
▪ Colic tumour	10	18.6

Postoperative complications (table 2) were found in 41 patients (75.9%) and were infectious in 38 (70.4%) of them. Surgical site infection (SSI) was the main postoperative complication with 22 cases (57.9%). The mean occurrence delay of infectious complications was 5.65±1.8 days. Among the 54 patients, five deaths (9.2%) were recorded; sepsis was the death cause in all of these cases.

Table 2: Postoperative complications		
Item	**Number**	**(%)**
Infectious complications		
Surgical site infection	22	53.6
Postoperative peritonitis	6	14.6
Anastomotic fistulae	6	14.6
Septic shock	4	9.7
Pneumonia	6	14.6
Non-infectious complications		
Wound haemorrhage	1	2.4
Hypovolemic shock	4	9.7
Hematoma	4	9.7
Evisceration	1	2.4
Thrombophlebitis	1	2.4
Malaria	10	24.3
Cardiac arrhythmia	5	12.1
Dehydration	5	12.1
Prolonged ileus	7	17.1
Denutrition	3	7.3

When CRP and PCT were elevated (Table 3) on postoperative day 3, 82.2% of patients developed an infection (p<0.001). The AUCs of PCT and CRP (Figure 1) levels on preoperative period were 0.624 (95% of IC: 0.482-0.752) and 0.557 (95% of IC: 0.415-0.692), respectively. The AUCs of PCT and CRP levels on postoperative day 3 (Figure 2) were 0.956 (95% of IC: 0.862-0.993) and 0.894 (95% of IC: 0.780-0.961), respectively.

Table 3: Relation between CRP and PCT value and occurrence of infectious postoperative complications				
Résultats CRP/PCT	Complications infectieuses postopératoires		OR (IC à 95%)	Valeur p
	Oui	**Non**		
Valeurs préopératoires				
CRP (+) PCT (+)	7 (43.8)	24 (63.2)	0.5 (0.1 – 1.5)	0.235
CRP (+) PCT (-)	8 (50)	12 (31.6)	2.2 (0.7 – 7.2)	0.230
CRP (-) PCT (+)	0 (0)	1 (2.6)	-	1.000
CRP (-) PCT (-)	1 (6.3)	1 (2.6)	2.5 (0.1 – 42.1)	0.509
Valeurs postopératoires				
CRP (+) PCT (+)	8 (50)	37 (97.4)	0.03 (0.003 – 0.2)	< 0.001
CRP (+) PCT (-)	4 (25)	0 (0)	-	0.006
CRP (-) PCT (+)	1 (6.3)	1 (2.6)	2.5 (0.1 – 42.1)	0.509
CRP (-) PCT (-)	3 (18.8)	0 (0)	-	0.023
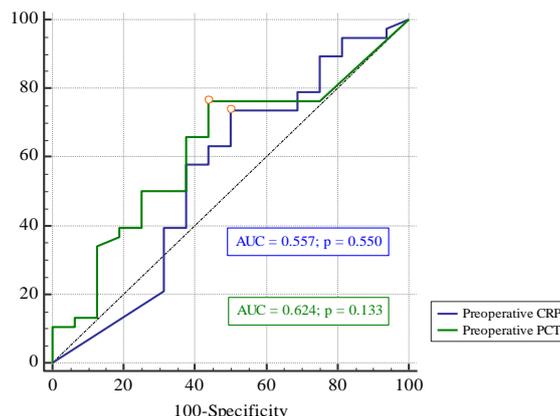
**Figure 1**: Preoperative areas under the curve (AUC) of CRP and PCT

AUC = 0.557; p = 0.550
AUC = 0.624; p = 0.133
— Preoperative CRP
— Preoperative PCT
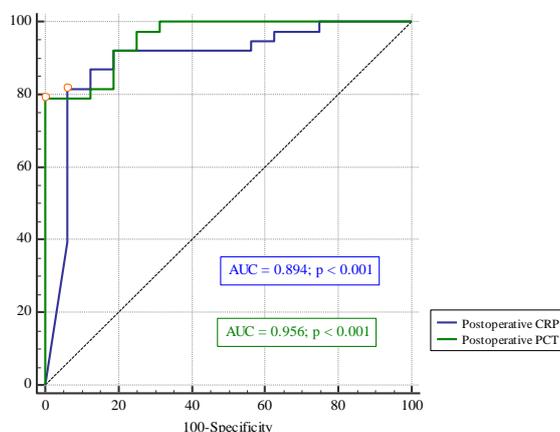
Figure 2: Postoperative day 3 areas under the curve (AUC) of CRP and PCT.

AUC = 0.894; p < 0.001
AUC = 0.956; p < 0.001
— Postoperative CRP
— Postoperative PCT

According to the Youden index, The optimal cut-off values of CRP, PCT, their sensibility, specificity and their PPV and NPV are presented in table 4. Preoperetively, the optimal cut-off value of CRP and PCT were of 73mg/l and 0.2ng/ml, respectively. On postoperative day 3, these values were of 68.8mg/ml and 5ng/ml, respectively for CRP and PCT.

Table 4: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and Youden Index of the CRP and PCT cut-off values in the occurrence of postoperative infectious complications.				
	Preoperative CRP	**CRP on POD3**	**Preoperative PCT**	**PCT on day 3**
Sensitivity	73.68	81.6	76.3	78.9
Specificity	50	93.7	56.2	100
PPV	77.8	96.9	80.6	100
NPV	44.4	68.2	50	66.7
Youden Index	0.237	0.753	0.326	0.790

For the early detection of PIC, we found a strong positive and highly significant correlation between their occurrence and the optimal cut-off levels of CRP and PCT on postoperative day 3 and the occurrence of PIC, compared with preoperative CRP/PCT (Figure 3).
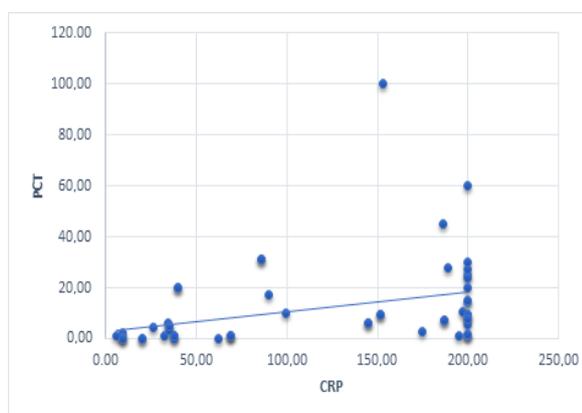

Figure 3: Correlation between CRP and PCT at postoperative day 3. SPEARMAN : r= 0.578 P = <0.001

DISCUSSION

This study confirms that postoperative morbidity of acute abdomen is high in a LMIC setting and infectious complications are the commonest type encountered [2-7]. In our report 70.4% of the patients presented an infectious complication. The mortality-related rate of septic complication is high in the present report with 9.2% of postoperative deaths, all of them related to an infectious concern. The delayed consultation (3.5 days) and delayed surgical management (48.8 hours after the admission) highlighted in this study have probably a significant impact on the occurrence of such complications. These two factors may be all the more pejorative, when we know that infectious causes were the main etiologies of acute abdomen in our study as in several other African studies [5,7,20,21]. These complications appeared in our patients within an average of 5.65 days following the surgery as previously reported in our setting [12]. Early diagnosis, before the postoperative day 5, of infectious complications is therefore important.

This study demonstrates that, a PCT value higher than 5ng/ml on POD3 have a PPV of 100% in the occurrence of a PIC with 100% of specificity. Moreover, A CRP value higher than 68.8mg/ml on POD3 have a PPV of 96.9% and a specificity of 93.7% on the occurrence of a PIC. The NPV of these cut-off value was high, 68.2% for CRP and 66.7% for PCT. We therefore emphasize the surgeons to perform routinely the dosage of CRP and PCT on POD3 to identify early patients who may develop PIC later.

The cut-off value of PCT in our series was higher than that reported in the literature, ranging from 0.25 to 0.264ng/ml [22,23]. In the same way, the cut-off value of CRP in this report is also higher than that reported in the literature [22-24] which varies from. We didn't find an explanation to this fact and further studies are required to confirm or not our cut-off values. We think that the POD3 is the best moment to perform the dosage of CRP and PCT, after surgery-related inflammation which is important during the first two days and before the average time to onset of infectious complications (5 days). Routinely dosage of PCT is related with reduced infection-associated adverse events, 28-day mortality, and cost of hospitalization [25]. Survival Sepsis Guidelines 2016 suggests the use of PCT as a marker for diagnosing sepsis as well as a marker for de-escalation of antibiotics [26].

The limitations of this study are related to its small sample which does not allow large conclusion. Nevertheless, this is the first report on this subject in our setting to the best of our knowledge and our recruitment was multicentre. Further studies may assess if some infectious complications are more related with a particular cut-off value of CRP or PCT.

CONCLUSION

On postoperative day 3, CRP and PCT values higher than 68.8mg/ml and 5ng/ml, respectively are predictive of the occurrence of septic complications with good sensibility and specificity. We emphasize surgeons to use these markers in the early detection of such complications in our setting.

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