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ORIGINAL ARTICLE

# Role of serum procalcitonin in predicting the surgical outcomes of acute calculous cholecystitis

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## Abstract

**Background** Acute calculous cholecystitis (AC) is a syndrome of right upper quadrant pain, fever, and leukocytosis associated with gallbladder inflammation. In the preoperative planning, the severity of AC should be considered as well as time of onset of symptoms and patient comorbidities. The aim of the present study was to investigate the role of an early PCT assessment in the emergency department in predicting the outcomes of laparoscopic surgery for AC.

**Study design** Retrospective, mono-centric study conducted in a teaching urban hospital. We evaluated all patients admitted to our ED from January 1st, 2015, to December 31st, 2019, underwent laparoscopic cholecystectomy for AC having a preoperative PCT determination in ED.

**Results** A total of 2285 patients in our ED were admitted for AC. Among them 822 patients were treated surgically, 174 had a PCT determination in ED. Median age was 63 [50–74]. Overall, 33 patients (19.0%) had major complications (MC): 32 needed an open surgery conversion, and 3 among them deceased. Multivariate analysis demonstrated that PCT, WBC, BUN, and CCI were significantly associated to MC in our cohort. When we calculated the area under the ROC curve with regard to MC, a procalcitonin value > 0.09 at admission had sensitivity = 84.8% [68.1–94.9] and specificity = 51.8% [43.2–60.3] for the occurrence of MC.

**Conclusion** Our results, suggest that a PCT > 0.09 ng/mL at ED admission, could be associated to a poor surgical outcome in patients treated by laparoscopic surgery for AC.

**Keywords** Acute cholecystitis · Procalcitonin · Surgical outcomes

## Introduction

Acute calculous cholecystitis (AC) refers to a syndrome of right upper quadrant pain, fever, and leukocytosis associated with gallbladder inflammation due to cystic duct blockage caused by a stone [1]. AC is the most common complication of gallstone disease and typically develops in patients with a history of symptomatic gallstones, and it is one of the most important causes of abdominal pain on presentation to the emergency department (ED) [2]. In the preoperative planning, the severity of AC should be considered as well as time of onset of symptoms and patient comorbidities [3, 4]. According to the Tokyo guidelines, the severity of AC could be predicted by assessing leukocytosis and C-reactive protein (CRP) levels [5]. Procalcitonin (PCT) has been suggested as adjunctive biomarker in working up patient infection status; however, the efficacy of PCT to predicting the severity of AC still needs to be investigated [6–9]. Procalcitonin (PCT) has been suggested to help emergency department physicians both in the assessment of patient infection status and for the antibiotic management decisions. However, the efficacy of PCT-guided antibiotic therapy in suspected or confirmed infection and sepsis has proved controversial over recent decades for the ED setting [10–12].

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As far as we know, in the literature, we found no studies that show a relationship between PCT and major complications after surgical treated AC. On the light of this, the aim of the present study was to investigate the role of an early PCT assessment in the emergency department in predicting the outcomes of laparoscopic surgery for acute cholecystitis.

## Material and methods

### Study design

This is a retrospective, mono-centric study conducted in a teaching urban hospital with an annual attendance at the ED of about 75,000 patients (more than 87% adults). We evaluated consecutive patients admitted to our ED from January 2015 to December 31st, 2019.

### Inclusion and exclusion criteria

We included in our analysis all adult patients, admitted from the ED, underwent laparoscopic cholecystectomy for acute calculous cholecystitis and having a preoperative PCT determination in ED.

Acute calculous cholecystitis diagnosis was established upon clinical condition (acute-onset clinical symptoms suggestive of AC such us positive Murphy and Blumberg signs), laboratories findings (elevated WBC and PCR, abnormality in bilirubin and y-gt value), and imaging (abdominal ultrasound (US) and contrasted enhanced CT (CECT)) according to the Tokyo guidelines 18 [5].

Patients with age < 18 years old, patients treated by immunosuppressive drugs for transplant, and patients with acute leukemia, lymphoma, and HIV + were excluded from this study. We also excluded all patients not fulfilling criteria for acute cholecystitis and patients that did not underwent any surgical procedure or treated only by endoscopic or percutaneous drainages.

### Patient's characteristics

We collected all clinical and demographic data from the computerized hospital records. We reviewed the records to assess demographic and clinical characteristics regarding ED presentation and visit and the outcome at discharge from the hospital. For all patients included in the analysis, we evaluated the following:

1) Procalcitonin determination in ED. The PCT was obtained in ED based on the clinical judgment of emergency physician at admission visit. Cut-off value of PCT serum level predictive of sepsis was set at 1 ng/ml, and a PCT interval between 0.5 and 1 ng/ml was considered as uncertain area. Procalcitonin determination was available 24 h a day in our ED.
2) Demographic characteristics, including age and gender.
3) Associate comorbidities according to the Charlson's comorbidity score index (CCI) [13].
4) Presence of Sepsis-3 criteria at admission or its development during the hospital stay. Sepsis was defined based on clinically suspicion of infection and a quick Sequential Organ Failure Assessment (qSOFA) score ≥ 2 [14].
5) Need for ventilation, defined as necessity of mechanical ventilation (MV) (including non-invasive ventilation and use of high-flow oxygen therapy) in any phase of in-hospital stay as clinical sign of incipient organ dysfunction.
6) Need for conversion to open surgery.

Patient whose developed complication were divided in two group: no/minor complication group and major complication group. Major complication were defined as death, need of mechanical ventilation, and conversion to open surgery.

Length of hospital stays (LOS) was calculated from ED admission to hospital discharge or death. Occurrence of death was considered combined for all patients deceased in the ED or in the later ward admission. Morbidity and mortality have been considered as the conventional 30-day outcome. We considered all causes of in-hospital death. We correlated these study endpoints with early PCT determination value in the ED.

### Study outcomes

The main endpoint of the study was occurrence of major complications. Secondary endpoints were sepsis rate, intrahospital mortality rate, and length of hospital stay.

### Statistical analysis

Dichotomous data and counts were presented in frequencies, whereas continuous data were presented as median [25–75 interquartile range (IQR)]. Continuous variables were statistically compared Mann–Whitney U test. Categorical variables were compared by Chi-square test (with Yates correction or Fisher's exact test if needed). Receiver operating characteristic (ROC) curve analysis was performed to test the specificity and sensitivity of the PCT predicting surgical outcomes. ROC Youden's index J was used to determine the best cut-off values for PCT with respect to defined outcomes. The c-statistic evaluates PCT discrimination and represents the area under the ROC curve (AUC). A value of 0.5 is equivalent to chance; a value of 1.0 indicates a perfect discrimination.

Significant parameters at univariate analysis were entered into a multivariate logistic regression model in order to identify independent predictors of poor outcome. In order to improve model fitting, prior to be entered into the logistic model, continuous variables were dichotomized into low/high values according to ROC analysis Youden index J. To avoid analysis redundancy or model overfitting, the single comorbidities already included in the Charlson Comorbidity Index were excluded from the analysis. A two-sided p value < 0.05 was considered as significant.

Statistical analysis was carried out using SPSS for Windows, V25®(SPSS, IBM, Armonk, NY, USA).

### Sample size analysis

Since six factors were entered into the logistic regression model with respect to cumulative major complications, a 60 events would have been needed for an optimal parameters estimation. Thus, our sample size is slightly underpowered for the multivariate estimation.

## Results

### Study cohort

During the study period, 2285 patients in our ED were admitted for AC (median age 62 [52–80]). Among them, 1411 were treated conservatively or underwent only percutaneous or endoscopic drainage. Further 52 patients were excluded due to our exclusion criteria, and among the remaining 822 patients treated surgically, 174 had a PCT determination in ED and were included in the study cohort. The overall median age was 63 [50–74] with an equal gender distribution (51.1% were males). The most common symptoms at ED presentation were abdominal pain (74.7%), followed by fever (44.8%). We observed 3 cases (1.7%) of septic shock, 6 cases (3.4%) of diffuse peritonitis, and 11 cases (6.3%) of abdominal collection (Table 1). The laboratory values for PCT, CRP, WBC, hemoglobin, creatinine, and BUN are listed in Table 1. The overall mean PCT value was 0.11 (0.05–0.56). The overall mean CRP value was 25 (11–40). The overall median CCI was 2 [1–4], while diabetes (10.9%) and peripheral vascular disease (7.5%) were the most common associated comorbidities.

Conversion to open surgery was needed in 18.4% of cases (32 patients). Ten patients (5.7%) developed a septic status. Three patients deceased, with an overall mortality rate of 1.7%. Cumulative major complication rate was of 19.0% (33 patients).

### Patient's distribution according to elevated PCT value

Overall 37 (21.3%) patients had a PCT value at admission ≥ 1 ng/mL. Patients with elevated PCT were older and had more fever and peritonitis at presentation. Laboratory values associated to high PCT were elevated creatinine, BUN, and fibrinogen. Interestingly WBC was similar in PCT ≥ 1 ng/mL and PCT < 1 ng/mL group, while CRP value were higher in the PCT ≥ 1 ng/mL patients (32 [18–52] p = 0.013) (Table 1).

### Factors associated to progression to sepsis

The ten (5.7%) patients that progressed to sepsis had higher rate of obstructive jaundice at presentation (80.0% vs 26.2%, p < 0.001) and a higher PCT values at admission (0.21 [0.17–3.75] vs 0.10 [0.05–0.53], p = 0.014). However, at multivariate analysis, only obstructive jaundice was independently associated to sepsis. Moreover, nether CRP values were not associated to progression to sepsis (p = 0.410) (Table 2).

### Factors associated to major complications, including need for open surgery conversion

Overall, 33 patients (19.0%) had major complications (MC) in our cohort: 32 needed an open surgery conversion, and 3 among them deceased. One further patient needed MV after laparoscopic surgery and was discharged alive. Table 3 shows the factors associated to major complications. As expected, patient in the MC group had a longer LOS (13.2 [7.9–23.3] vs 7.4 [5.4–11.5], p < 0.001). At the univariate analysis, patients with MC were more frequently male and had higher CCI and higher WBC, BUN, and PCT values (Table 3). Multivariate analysis demonstrated that PCT, WBC, BUN, and CCI were significantly associated to MC in our cohort (Table 3).

### PCT values sensitivity and specificity for MC

When we calculated the area under the ROC curve (AUC) with regard to MC, a procalcitonin value > 0.09 at admission had sensitivity = 84.8% [68.1–94.9] and specificity = 51.8% [43.2–60.3] for the occurrence of MC (Fig. 1).

## Discussion

We evaluated the PCT performance in ED in a large series of patients underwent laparoscopic cholecystectomy for acute calculous cholecystitis, investigating if the assessment of PCT could yield a relevant impact on patient-related

**Table 1** Population demographics and clinical characteristics in patients admitted in the emergency department for acute cholecystitis and subsequently treated by surgical cholecystectomy. Comparison between patients with low and high PCT values (according to laboratory reference value)

| Variable | All patients n 174 | ED PCT < 1 ng/ml n 137 | ED PCT ≥ 1 ng/ml n 37 | *p* value |
|---|---|---|---|---|
| Age[§] | 63 [50–74] | 60 [47–71] | 74 [64–81] | *< 0.001* |
| Sex (Male) | 89 (51.1%) | 66 (48.2%) | 23 (62.2%) | 0.131 |
| *Symptoms* | | | | |
| Fever | 78 (44.8%) | 51 (37.2%) | 27 (73.0%) | *< 0.001* |
| Abdominal pain | 130 (74.7%) | 106 (77.4%) | 24 (64.9%) | 0.120 |
| Jaundice | 51 (29.3%) | 37 (27.0%) | 14 (37.8%) | 0.199 |
| Vomit | 47 (27.0%) | 36 (26.3%) | 11 (29.7%) | 0.675 |
| Constipation | 11 (6.3%) | 9 (6.6%) | 2 (5.4%) | 1.000 |
| Diarrhea | 6 (3.4%) | 4 (2.9%) | 2 (5.4%) | 0.609 |
| *Clinical presentation* | | | | |
| Shock | 3 (1.7%) | 2 (1.5%) | 1 (2.7%) | 0.514 |
| Diffuse peritonitis | 6 (3.4%) | 2 (1.5%) | 4 (10.8%) | *0.019* |
| Abdominal collection | 11 (6.3%) | 7 (5.1%) | 4 (10.8%) | 0.250 |
| *Laboratory Values* | | | | |
| Hemoglobin (g/dL) | 12.9 [11.7–14.2] | 12.9 [12.1–14.2] | 12.1 [10.9–14.6] | 0.223 |
| WBC | 10.8 [8.3–14.9] | 10.7 [8.1–14.9] | 11.0 [9.4–15.4] | 0.433 |
| Blood glucose | 120 [102–153] | 120 [101–146] | 123 [103–161] | 0.319 |
| Creatinine | 0.95 [0.73–1.22] | 0.91 [0.69–1.15] | 1.12 [0.87–1.55] | *0.015* |
| BUN (mg/dL) | 18 [13–28] | 17 [13–25] | 25 [17–37] | *< 0.001* |
| Fibrinogen (mg/dL | 550 [430–747] | 516 [414–726] | 691 [513–824] | *0.002* |
| CRP (mg/dL) | 25 [11–40] | 23 [10–37] | 32 [18–52] | *0.013* |
| Procalcitonin (ng/mL) | 0.11 [0.05–0.56] | 0.07 [0.05–0.18] | 3.24 [1.53–9.91] | *< 0.001* |
| PCT > 0.09 ng/mL | 96 (55.2%) | 59 (43.1%) | 37 (100%) | *< 0.001* |
| *Comorbidities* | | | | |
| Charlson Index[§] | 2 [1–4] | 2 [0–3] | 3 [2–4] | *0.003* |
| Ischemic heart disease | 11 (6.3%) | 9 (6.6%) | 2 (5.4%) | 1.000 |
| Congestive heart failure | 7 (4.0%) | 7 (5.1%) | 0 | 0.348 |
| Peripheral vascular disease | 13 (7.5%) | 0 (7.3%) | 3 (8.1%) | 1.000 |
| Diabetes | 19 (10.9%) | 12 (8.8%) | 7 (18.9%) | 0.079 |
| Chronic kidney disease | 5 (2.9%) | 4 (2.9%) | 1 (2.7%) | 1.000 |
| *Outcomes* | | | | |
| Death | 3 (1.7%) | 1 (0.7%) | 2 (5.4%) | 0.115 |
| Mechanical ventilation | 8 (4.6%) | 6 (4.4%) | 2 (5.4%) | 0.678 |
| Progression to sepsis | 10 (5.7%) | 6 (4.4%) | 4 (10.8%) | 0.136 |
| Conversion to open surgery | 32 (18.4%) | 20 (14.6%) | 12 (32.4%) | *0.013* |
| Cumulative major complications[@] | 33 (19.0%) | 21 (15.3%) | 12 (32.4%) | *0.019* |
| Length of hospital stay[§] | 8.3 [5.6 – 13.5] | 7.6 [5.6 – 13.1] | 10.4 [6.1 – 18.0] | 0.126 |

[#Hypotension]/shock was defined as systolic blood pressure < 100 mmHg at emergency department admission; §values are expressed as median [interquartile range]; [@]cumulative major complications include: death, admission to ICU/ventilation, and conversion to open surgery (only for major surgery)

endpoints. The major finding of present study is that a PCT values > 0.09 ng/mL was an independent predictor of major complications, including the need for conversion to open surgery. Clinical evaluation is the starting point of the management of AC, and prompt and timely diagnosis should lead to early treatment and lower mortality and morbidity [15]. Specific diagnostic criteria are necessary to accurately diagnose typical, as well as atypical cases and the latest guidelines, and will refer to the Tokyo International Consensus Meeting in 2018, where almost unanimous agreement was achieved on the criteria [5]. Moreover, patients with AC may present with a spectrum of disease stages ranging from a mild, self-limited illness to a fulminant, potentially life-threatening disease [16]. The progression of acute cholecystitis from

**Table 2** Factors associated to progression to sepsis in the 174 patients treated by surgical cholecystectomy

| Variable | None or minor complications n 164 | Evolution to sepsis n 10 | Univariate *p* value | Hazard ratio [95% confidence interval] | Multivariate *p* value |
|---|---|---|---|---|---|
| Age[§] | 63 [49–74] | 63 [56–79] | 0.512 | | |
| Sex (Male) | 82 (50.0%) | 7 (70.0%) | 0.219 | | |
| *Symptoms* | | | | | |
| Fever | 73 (44.5%) | 5 (50.0%) | 0.755 | | |
| Abdominal pain | 123 (75.0%) | 7 (70.0%) | 0.724 | | |
| Jaundice | 43 (26.2%) | 8 (80.0%) | *< 0.001* | 5.46 [1.10–26.9] | **0.038** |
| Vomit | 45 (27.4%) | 2 (20.0%) | 1.000 | | |
| Constipation | 10 (6.1%) | 1 (10.0%) | 0.489 | | |
| Diarrhea | 6 (3.7%) | 0 | 1.000 | | |
| *Clinical presentation* | | | | | |
| Shock | 3 (1.8%) | 0 | 1.000 | | |
| Diffuse peritonitis | 5 (3.0%) | 1 (10.0%) | 0.303 | | |
| Abdominal collection | 10 (6.1%) | 1 (10.0%) | 0.489 | | |
| *Laboratory Values* | | | | | |
| Hemoglobin (g/dL) | 12.9 [11.7–14.2] | 12.3 [10.8–13.9] | 0.367 | | |
| WBC | 10.9 [8.4–14.9] | 8.6 [5.7–12.3] | 0.077 | | |
| Blood glucose | 120 [102–154] | 107 [92–150] | 0.367 | | |
| Creatinine | 0.94 [0.73–1.22] | 0.97 [0.62–1.30] | 0.844 | | |
| BUN | 18 [13–28] | 17 [15–24] | 0.941 | | |
| Fibrinogen | 552 [433–755] | 490 [373–710] | 0.372 | | |
| CRP | 24 [11–40] | 29 [20–42] | 0.410 | | |
| Procalcitonin | 0.10 [0.05–0.53] | 0.21 [0.17–3.75] | *0.014* | 0.79 [0.19–3.31] | 0.791 |
| *Comorbidities* | | | | | |
| Charlson Comorbidity Index[§] | 2 [1–4] | 3 [1–6] | 0.213 | | |
| Ischemic heart disease | 8 (4.9%) | 3 (30.0%) | *0.018* | 4.04 [0.12–133.5] | 0.434 |
| Congestive heart failure | 6 (3.7%) | 1 (10.0%) | 0.344 | | |
| Peripheral vascular disease | 10 (6.1%) | 3 (30.0%) | *0.029* | 0.90 [0.28–29.4] | 0.957 |
| Diabetes | 19 (11.6%) | 0 | 0.604 | | |
| Chronic kidney disease | 5 (3.0%) | 0 | 1.000 | | |
| *Outcomes* | | | | | |
| Conversion to open surgery | 29 (17.7%) | 3 (30.0%) | 0.329 | | |
| Mechanical ventilation | 6 (3.7%) | 2 (20.0%) | *0.017* | | |
| Length of hospital stay[§] | 7.6 [5.5–12.4] | 14.8 [13.3–20.3] | *0.001* | | |

[#]Shock was defined as systolic blood pressure < 100 mmHg at emergency department admission; §values are expressed as median [interquartile range]; *WBC* white cell blood count; *BUN* blood urea nitrogen

For multivariate analysis, continuous variables were categorized into dichotomous variable according to ROC Youden index J. Selected values were WBC > 15.25; BUN > 20; procalcitonin > 0.09; Charlson index > 5

the mild/moderate to the severe form includes the development of sepsis which could led to multiple organ dysfunction syndrome (MODS) and failure (MOF) [17, 18]. The optimization of the management and the risk stratification of AC patients could have an important impact on outcomes [19–21]. In patients with AC, early warning scores associated with abdominal signs and symptoms such as abdominal pain and tenderness can screen for patients needing prompt surgical procedures [22]. Early warning scores employ physiological, easy-to measure parameters, assessing variables such as systolic blood pressure, pulse rate, ventilatory rate, temperature, oxygen saturations, and level of consciousness [23–25]. However, physiological parameters are often not sufficient for risk stratification, as the AC involves a wide range of patients of different ages, with different morbidities and therefore different functional reserves. On the light of this, conceding the clinical importance of AC, considerable research is directed at identifying biomarkers suitable in predicting the severity of acute cholecystitis [19, 20]. Several authors report that the higher is the severity AC, the higher is the PCT levels of the patients at the admission [26–30]. Yuzbasioglu et al. in their study suggest that PCT level may

**Table 3** Cumulative major complications (including conversion to open surgery, need for mechanical ventilation, and death) in the 174 patients treated by major surgical procedures

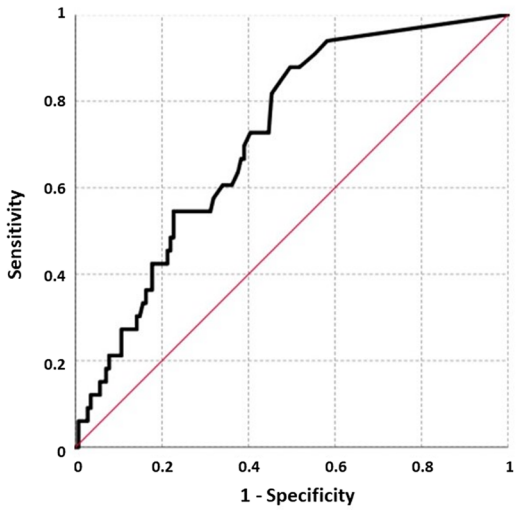
| Variable | None or minor complications n 141 | Cumulative major complications n 33 | Univariate p value | Cumulative major complications n 33 | Multivariate p value |
|---|---|---|---|---|---|
| Age[§] | 62 [48–73] | 69 [55–76] | 0.053 | | |
| Sex (Male) | 67 (47.5%) | 22 (66.7%) | 0.048 | 1.13 [0.44–2.92] | 0.796 |
| *Symptoms* | | | | | |
| Fever | 62 (44.0%) | 16 (48.5%) | 0.639 | | |
| Abdominal pain | 109 (77.3%) | 21 (63.6%) | 0.104 | | |
| Jaundice | 38 (27.0%) | 13 (39.4%) | 0.157 | | |
| Vomit | 41 (29.1%) | 6 (18.2%) | 0.204 | | |
| Constipation | 6 (4.3%) | 5 (15.2%) | 0.036 | 2.06 [0.45–9.41] | 0.351 |
| Diarrhea | 5 (3.5%) | 1 (3.0%) | 1.000 | | |
| *Clinical presentation* | | | | | |
| Shock | 1 (0.7%) | 2 (6.1%) | 0.093 | | |
| Diffuse peritonitis | 4 (2.8%) | 2 (6.1%) | 0.319 | | |
| Abdominal collection | 5 (3.5%) | 6 (18.2%) | 0.002 | | |
| *Laboratory values* | | | | | |
| Hemoglobin (g/dL) | 12.9 [11.7–14.2] | 12.7 [11.1–14.6] | 0.720 | | |
| WBC | 10.7 [8.2–14.2] | 13.9 [8.6–18.5] | *0.017* | 3.27 [1.31–8.17] | *0.011* |
| Blood glucose | 121 [102–152] | 119 [100–156] | 0.781 | | |
| Creatinine | 0.94 [0.69–1.22] | 0.97 [0.84–1.22] | 0.333 | | |
| BUN | 17 [13–26] | 24 [14–33] | *0.041* | 2.61 [1.05–6.53] | *0.040* |
| Fibrinogen | 541 [428–742] | 589 [418–802] | 0.463 | | |
| CRP | 26 [12–38] | 23 [11–40] | 0.910 | | |
| Procalcitonin | 0.08 [0.05–0.36] | 0.45 [0.11–2.08] | *< 0.001* | 4.38 [1.44–13.29] | *0.009* |
| *Comorbidities* | | | | | |
| Charlson Comorbidity Index[§] | 5 [3–7] | 5 [5–7] | *0.018* | 3.88 [1.09–13.82] | *0.036* |
| Ischemic heart disease | 10 (7.1%) | 1 (3.0%) | 0.692 | | |
| Congestive heart failure | 4 (2.8%) | 3 (9.1%) | 0.127 | | |
| Peripheral vascular disease | 11 (7.8%) | 2 (6.1%) | 1.000 | | |
| Diabetes | 14 (9.9%) | 5 (15.2%) | 0.365 | | |
| Chronic kidney disease | 2 (1.4%) | 3 (9.1%) | *0.048* | | |
| *Outcomes* | | | | | |
| Bloodstream infection | 7 (5.0%) | 3 (9.1%) | 0.403 | | |
| Length of hospital stay[§] | 7.4 [5.4–11.5] | 13.2 [7.9–23.3] | *< 0.001* | | |

[#]Shock was defined as systolic blood pressure < 100 mmHg at emergency department admission; §values are expressed as median [interquartile range]; *WBC* white cell blood count; *BUN* blood urea nitrogen

For multivariate analysis, continuous variable were categorized into dichotomous variable according to ROC Youden index J. Selected values were WBC > 15.25; BUN > 20; procalcitonin > 0.09; Charlson index > 5

be considered to be a parameter that could be added to the assessment of the severity of acute cholecystitis in the Tokyo guidelines, although further studies are needed to support this finding [26]. Moreover Wu t et al. in a study involving 115 patients who underwent emergency cholecystectomy tested PCT value to predict difficult laparoscopic cholecystectomy (DLC) before operation. As results, they conclude that PCT is superior to CRP in diagnosing DLC. The cut-off value for PCT of > 1.50 ng/ml has a high predictive value for DLC in AC patients. Monitoring PCT trends may be used as a preoperative risk assessment in AC patients (27).

In present study we found a relationship with PCT values and worst outcomes in terms of MC, including the need for conversion from laparoscopic to open surgery. As expected, we also found that higher comorbidities, WBC, and BUN at admission were associated to a worse outcome. However, even after adjusting for these factors, a PCT value > 0.09 at ED admission had a sensitivity of 84.8% [68.1–94.9] and a specificity of 51.8% [43.2–60.3] for the occurrence of a major complication, having also a superior predictive value if compared to WBC, BUN, and CCI. Moreover, CRP was not associated with sepsis




| Reference PCT criterion | Sensitivity [95% CI] | Specificity [95% CI] | Positive predictive value | Negative predictive value |
|---|---|---|---|---|
| PCT > 0.09 ng/mL | 87.9 [71.8 – 96.6] | 50.3 [33.6 – 50.4] | 29.3 [25.2 – 33.8] | 94.7 [87.5 – 97.8] |
| PCT > 0.50 ng/mL | 45.5 [28.1 – 63.6] | 78.0 [70.3 – 84.5] | 32.6 [22.9 – 44.0] | 85.9 [81.6 – 89.4] |
| PCT > 1.00 ng/mL | 36.4 [20.4 – 54.9] | 82.3 [74.9 – 88.2] | 32.4 [21.3 – 46.0] | 84.7 [80.8 – 87.8] |

**Fig. 1** Receiver operating characteristics (ROC) analysis of procalcitonin (PCT) value in emergency department and surgical outcome of patients treated by urgent laparoscopic surgery for acute cholecystitis. Values of 1 ng/mL and 0.5 ng/ml are the current cut off values for, respectively, elevated and uncertain area serum PCT in our institution. A value of PCT > 0.09 ng/mL was identified by Youden index J as the best predictor for major complications (including conversion to open surgery) in our cohort

progression or need of conversion, may be because it is less specific and it has a slowly raise of the mean values if compared to PCT. To the best of our knowledge, the present study is the first focusing on the correlation of early assessment of PCT in the ED and outcomes after emergency cholecystectomy finding that a higher value of PCT could be a useful tool to stratify patient surgical outcome.

### Study limitations

As for any retrospective study, some limitations are worth considering. First, PCT assessment in ED was requested at discretion of treating physician, thus introducing a selection bias that cannot be avoided. Moreover, the sample size is reduced and evaluated post-hoc, both limiting the power of our analysis and the multivariate parameter estimations. Finally, criteria for conversion to open surgery were leaved to the operating surgeon. However, being this a single institution study, these latter criteria were uniform and consistent in the study period.

## Conclusions

Our results, although in a limited sample, suggest that a PCT > 0.09 ng/mL at ED admission, could be associated to a poor surgical outcome in patients admitted for AC and treated by laparoscopic surgery. Obstructive jaundice represented the main clinical finding associated to sepsis progression in our cohort. Further, and prospective studies are needed to evaluate the role of PCT in stratifying AC patients to surgery.

**Authors' contributions** PF, MC: study conception and design, literature search, acquisition, interpretation and analysis of data, drafting and critically revising the article for important intellectual content; and final approval of the version to be published. VC, FR: drafting and critically revising the article for important intellectual content and final approval of the version to be published. ALG, GQ, CP: acquisition of data and critically revising the article for important intellectual content. FF,SA, GS: drafting and critically revising the article for important intellectual content and final approval of the version to be published.

**Data availability** Not applicable. Our manuscript does not contain data from any individual person, so this section is not applicable to our submission.

**Code availability** Not applicable.

## Declarations

**Ethics approval and consent to participate** Not applicable. Our manuscript does not report on or involve the use of any animal or human data or tissue and does not contain data from any individual person, so this section is not applicable to our submission.

**Conflict of interest** The authors declare no competing interests.

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