Factors Associated with Mortality in Severe Acute Cholangitis in a Moroccan Intensive Care Unit: A Retrospective Analysis of 140 Cases

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1. Introduction

Acute cholangitis is a bacterial infection of the biliary tract following cholestasis mainly caused by lithiasic or tumoral biliary obstruction. The classic pain-fever-jaundice symptoms, representing the Charcot triad, were first described in 1877 [1]. The severity of cholangitis is due to infection dissemination with risk of septic shock and organ failure. “The Reynolds pentad,” described in 1958 as Charcot triad-shock-confusion, was associated with high mortality in the absence of adequate treatment [2]. Early diagnosis and recognition of severe presentations are therefore a challenging task for every clinician in order to initiate an early and appropriate therapeutic management. This management is continuously progressing in terms of resuscitation, antibiotics, surgical techniques, and less invasive techniques such as interventional endoscopy and radiology. It therefore requires multidisciplinarity (anesthetists, intensivists, hepatobiliary endoscopists, surgeons, radiologists, and microbiologists) and the implementation of standardized protocols. The recommendations of “the Tokyo Guidelines Working Group” are regularly updated from 2007 to 2018 [1, 3–5]. Resuscitation, antibiotics, and biliary drainage as an early intervention approach are absolutely essential for survival in severe acute cholangitis. Mortality has certainly decreased from 50% to 10-30% over the past 30 years, but it remains high, and...
several questions still unanswered regarding the application of these recommendations on a local level. Furthermore, other factors may influence the prognosis. Recent studies consider admission to intensive care as a predictor of mortality [6]. Our aim in this study was to identify the factors associated to mortality in severe acute cholangitis in our context.

2. Materials and Methods

2.1. Study Design and Setting. In this retrospective observational monocentric study, we evaluated patients of age ≥ 16 years with severe acute cholangitis admitted to our Intensive Care Unit (ICU) between January 2009 and December 2018. The diagnosis of acute cholangitis was based on clinical-biological and radiological criteria according to the Tokyo guidelines. The severity was assessed by the presence of at least one organ failure and/or an unbalanced comorbidity. The criteria for diagnosis and severity are presented in Tables 1 and 2. Patients with incomplete and/or nonexploitable records were excluded from the analysis. The study setting was a 14-bed medico-surgical ICU in a tertiary university hospital in Morocco (ICU A4–Hassan II University Hospital of Fez). The study was approved by the institutional review board (Comité d’Ethique Hospitalo-Universitaire de Fès) with a waiver of informed consent.

2.2. Data Collection. Study data were collected retrospectively from both paper charts and electronic medical records of patients using HOSIX electronic data capture tools hosted at Hassan II University Hospital of Fez. Variables collected included demographic information, diagnostic parameters, the Sequential Organ Failure Assessment (SOFA) and quick-SOFA scores, and TOKYO grading upon ICU admission, patient comorbidities, therapeutics, and evolution.

2.3. Statistical Analysis. The statistical analysis of the parameters was performed using the SPSS 20 software in the epidemiology laboratory of the Faculty of Medicine and Pharmacy of Fez. Factors associated with mortality were analyzed using univariate and multivariate analysis. Descriptive statistics were used to summarize baseline patient characteristics. The results were expressed in numbers and percentages for the qualitative variables and in means ± standard deviations (SD) for the quantitative variables. Comparison of the quantitative and qualitative variables was based, respectively, on the Student’s t-test and the chi-2 test (χ²) through univariate analysis. Both p values and odds ratio (OR) with corresponding 95% confidence interval (CI) were reported for qualitative (categorical) variables while only p values were presented for quantitative (continuous) variables. Multivariable logistic regression was used to identify variables associated with ICU mortality as the outcome variable of interest. Multiple logistic regression models were fitted by regressing mortality status on multiple clinical variables. Considering the large number of clinical variables included in the study, we chose a stepwise regression approach using backward elimination. Order of elimination was based on clinical relevance and statistical strength. The statistical significance threshold was determined at p = 0.05. Results of the multivariate analysis were shown as odds ratio (OR) and corresponding 95% confidence interval (CI). Most of the significant variables at the univariate analysis were entered in the multivariate analysis: antithrombotic therapy, time to hospital consultation, tumor origin, quick-SOFA ≥ 2 on admission, SOFA on admission, TOKYO Grade III on admission, time to biliary decompression, mechanical ventilation, use of catecholamines, septic shock during stay, persistence of hematological failure after decompression, and persistence of renal failure after decompression.

3. Results

3.1. Study Population Characteristics. A total of 140 patients were included in the study. There were 88 female and 52 male patients. Median age was 61 years ± 17.88 (range 16–93 years), and 26% of patients were older than 75 years of age. Mean time between onset of symptoms and admission was 10 days ± 5.28 (range 1–21 days). The most common comorbidities in our population were history of biliary procedure (42%), cardiovascular disease (24%), diabetes (16%), hypertension (16%), stroke (6%), and antithrombotic treatment (11%). Acute cholangitis was lithiasic in most cases (69%), tumoral (15%), hydatic (13%), inflammatory (oddities), and iatrogenic (postcholecystectomy) in the other cases. Underlying causes for tumoral cholangitis were cholangiocarcinoma (7 patients), pancreas cancer (6 patients), vater ampullaoma (4 patients), and gallbladder cancer (4 patients). All patients had ultrasound examination. Hepatobiliary ultrasound showed a biliary dilatation in 98.6% of the cases and evidence of etiology in 74% of the cases. Abdominal computed tomography (CT), bili MRI, and echoendoscopy were needed.

Table 1: TG18/TG13 diagnostic criteria for acute cholangitis. Adapted from Kiriyama et al. [24].

| (A) Systemic inflammation |
|--------------------------|
| (A-1) Fever (temperature > 38°C) and/or shaking chills |
| (A-2) Evidence of Inflammatory Response: White blood cells (WBC) count < 4000 or >10000/mm³, C-reactive protein ≥ 10 mg/l |

| (B) Cholestasis |
|-----------------|
| (B-1) jaundice. Total bilirubin ≥ 20 mg/l |
| (B-2) Abnormal Liver Function Tests. AST, ALT, ALP, r-GTP (>1.5 × STD) |

| (C) Imaging |
|-------------|
| (C-1) Biliary dilatation |
| (C-2) Evidence of etiology on imaging (stricture, stone, stent, etc.) |

Suspected diagnosis: one item in A + one item in either B or C.
Definite diagnosis: One item in A + one item in B + one item in C.

Other factors may be helpful in diagnosis of acute cholangitis: right upper quadrant or upper abdominal pain, a history of biliary disease (gallstones, previous biliary procedures, biliary stent). In acute hepatitis, marked systematic inflammatory response is observed infrequently. Virological and serological tests are required when differential diagnosis is difficult.

ALP: alkaline phosphatase; r-GTP (GGT): r-glutamyltransferase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; STD: upper limit of normal value.
respectively, in 25, 12, and 1 patients. Eighteen patients had cholangitis etiology diagnosed during endoscopic retrograde cholangiopancrectomy (ERCP). Upon admission, 70% of patients presented with a systemic inflammatory response syndrome, and 41.4% of patients had a quick-SOFA score $\geq 2$. Grades III, II, and I of TOKYO Grading severity were present, respectively, in 81%, 15%, and 4% of the cases. Mean SOFA score was $8\pm 3$, range 0-16. Mechanical ventilation was required in 32 patients (23%) with mean duration of $3.42\pm 2.99$ days (range 1–15 days). Catecholamines and renal replacement therapy were needed in, respectively, 31.4% and 6.42% of patients. Ceftriaxone + metronidazole were used as initial empirical antibiotherapy in 87%. Antibio-

### Table 2: Severity assessment of acute cholangitis.

| Variables/score | 0   | 1   | 2   | 3   | 4   |
|-----------------|-----|-----|-----|-----|-----|
| PaO$_2$/FiO$_2$ (mmHg) | > 400 | ≤ 400 | ≤ 300 | ≤ 200 | ≤ 100 |
| Platelets ($\times 10^9$/mm$^3$) | > 150 | ≤ 150 | ≤ 100 | ≤ 50 | ≤ 20 |
| Bilirubin (mg/l) | < 12 | 12-19 | 20-59 | 60-119 | > 120 |
| Cardiovascular ($\mu$g/kg/min) | No hypotension | MAP $\leq$ 70 mmHg | Dopa $\leq$ 5 or Dobu (any dose) | Dopa $> 5$ or norepi $\leq 0.1$ | Dopa $> 15$ or norepi $> 0.1$ |
| Glasgow coma scale | 15 | 13-14 | 10-12 | 6-9 | < 6 |
| Creatinine (mg/l) or urine output | < 12 | 12-19 | 20-34 | 35–49 or $< 500$ ml/day | $> 50$ or $< 200$ ml/day |

MAP: mean arterial pressure; Dopa: dopamine; Dobu: dobutamine; Norepi: norepinephrine.

### Quick-SOFA [26]

| Variables | Score | Point |
|-----------|-------|-------|
| Systolic blood pressure $\leq$ 100 mmHg | 1 point |
| Respiratory rate $\geq$ 22 breaths/min | 1 point |
| Glasgow coma scale $\leq$ 14 | 1 point |

gram based antibiotherapy was performed secondary in 13 patients. 92% of patients underwent biliary drainage. Mean time to biliary drainage was $1.58\pm 0.89$ days (range 0–5 days). Endoscopic unblocking was the technique used in 76% of cases (106 patients), with sphincterotomy in most cases (94 patients). Surgical and percutaneous techniques were performed in, respectively, 22 and 3 patients. Mean duration of ICU stay was $6\pm 3.96$ days (range 1-23 days). Overall, ICU mortality rate was 28%. 90% of these patients died due to cholangiosepsis.

3.2. Univariate and Multivariate Analysis of Risk Factors for Mortality in Severe Acute Cholangitis. Univariate analysis
Table 3: Univariate analysis of risk factors for mortality in severe acute cholangitis.

| Factors                                           | Survivors (N = 101) | Nonsurvivors (N = 39) | p value | Brut OR (95% CI)  |
|---------------------------------------------------|---------------------|-----------------------|---------|-------------------|
| Age, mean ± SD                                    | 59.49 ± 18.96       | 64.36 ± 14.37         | 0.150   |                   |
| Age ≥ 75 years, n (%)                             | 27 (26.7%)          | 10 (25.6%)            | 0.896   | 0.94 (0.40-2.19)  |
| Female gender, n (%)                              | 67 (66.3%)          | 21 (53.8%)            | 0.170   |                   |
| Comorbidities, n (%)                              |                     |                       |         |                   |
| Diabetes                                          | 15 (14.85%)         | 7 (17.94%)            | 0.414   |                   |
| Cancer                                            | 3 (2.97%)           | 1 (2.56%)             | 0.690   |                   |
| Heart disease                                     | 22 (21.78%)         | 11 (28.2%)            | 0.277   |                   |
| Stroke                                            | 6 (5.9%)            | 2 (5.1%)              | 0.853   | 0.85 (0.16-4.43)  |
| Antithrombotic therapy                            | 5 (5%)              | 10 (25.6%)            | ≤0.001  | 6.62 (2.09-20.93) |
| History of complicated lithiasic disease          | 9 (8.9%)            | 2 (5.1%)              | 0.456   | 0.55 (0.11-2.68)  |
| History of biliary procedure                      | 41 (40.6%)          | 14 (35.9%)            | 0.610   | 0.82 (0.38-1.76)  |
| Time to hospital consultation (days), mean ± SD   | 9.07 ± 5.011        | 12.03 ± 5.426         | 0.003   |                   |
| Type of admission, n (%)                          |                     |                       |         |                   |
| Emergency                                         | 85 (84.2%)          | 27 (69.2%)            | 0.048   | 0.42 (0.17-1.00)  |
| Surgical ward                                     | 15 (14.9%)          | 7 (17.9%)             | 0.652   | 1.25 (0.46-3.35)  |
| Medical ward                                       | 1 (1%)              | 5 (12.82%)            | 0.002   | 14.70 (1.65-130.3)|
| Charcot triad, n (%)                              | 94 (96.03%)         | 36 (92.3%)            | 0.563   |                   |
| Etiology, n (%)                                    |                     |                       |         |                   |
| Lithiasic                                         | 75 (74.3%)          | 22 (56.4%)            | 0.040   | 0.44 (0.20-0.97)  |
| Tumor                                             | 10 (9.9%)           | 11 (28.2%)            | 0.007   |                   |
| Hydatic                                           | 12 (11.9%)          | 6 (15.4%)             | 0.579   | 1.34 (0.46-3.88)  |
| Severity assessment upon admission                |                     |                       |         |                   |
| Septic shock, n (%)                               | 7 (6.9%)            | 25 (64.1%)            | ≤0.001  |                   |
| Respiratory failure, n (%)                        | 11 (10.89%)         | 15 (38.5%)            | ≤0.001  |                   |
| GCS, mean ± SD                                    | 14.52               | 13.07                 | ≤0.001  |                   |
| GCS< 15, n (%)                                    | 22 (21.8%)          | 25 (64.21%)           | ≤0.001  | 6.41 (2.86-14.37) |
| Quick-SOFA ≥ 2, n (%)                             | 24 (23.76%)         | 27 (69.2%)            | ≤0.001  |                   |
| SOFA, mean ± SD                                   | 6.5 ± 2.95          | 11.27 ± 3.066         | ≤0.001  |                   |
| TOKYO Grade III, n (%)                            | 76 (75.2%)          | 38 (97.4%)            | 0.002   |                   |
| Laboratory finding upon admission, mean ± SD      |                     |                       |         |                   |
| Creatinine, mg/l                                  | 23.20               | 37.18                 | 0.001   |                   |
| White blood cell count, /mm³                       | 19718.4             | 23888.5               | 0.257   |                   |
| C-reactive protein, mg/l                          | 197.5               | 209.84                | 0.496   |                   |
| Aspartate amino transferase, IU/l                 | 166.91              | 208.25                | 0.185   |                   |
| Alanine aminotransferase, IU/l                    | 141.81              | 202.58                | 0.139   |                   |
| Alkaline phosphatase, IU/l                        | 364.92              | 478                   | 0.052   |                   |
| Total bilirubin, mg/l                             | 106.5               | 174.76                | 0.002   |                   |
| Prothrombin time < 50%, n (%)                     | 33 (32.7%)          | 16 (41.02%)           | 0.353   |                   |
| Organ support therapies                           |                     |                       |         |                   |
| Catecholamines, n (%)                             | 21 (20.8%)          | 32 (82.1%)            | ≤0.001  | 17.41 (6.74-44.96) |
| Mechanical ventilation, n (%)                     | 6 (5.9%)            | 26 (66.7%)            | ≤0.001  | 31.66 (10.96-91.41)|
| Dialysis, n (%)                                   | 2 (2%)              | 7 (17.9%)             | 0.001   | 10.82 (2.14-54.78) |
| Initial empiric antibiotherapy, n (%)              |                     |                       |         |                   |
| Amoxicillin + clavulanic acid                     | 13 (12.9%)          | 4 (10.3%)             | 0.671   | 0.77 (2.36-2.53)  |
| Ceftriaxone + metronidazole                       | 87 (86.1%)          | 35 (89.7%)            | 0.568   | 1.40 (0.43-4.57)  |
| Time to biliary decompression (days), mean ± SD   | 1.39 ± 0.840        | 1.41 ± 1.186          | 0.910   |                   |
identified 19 variables that were significantly (p < 0.05) associated with mortality in severe acute cholangitis in our population (Table 3). The variables entered into the logistic regression model were antithrombotic therapy, time to hospital consultation (days), tumor origin, severity assessment upon admission (quick-SOFA ≥ 2, SOFA, TOKYO Grade III), organ support therapies during ICU stay (use of catecholamines, mechanical ventilation), persistence of renal failure after decompression, persistence of hematological failure after decompression, and septic shock during ICU stay. Variables considered but not retained in the final model were creatinine, total bilirubin, GCS, respiratory failure as they are included in the severity assessment scores upon admission, dialysis as it is highly correlated to persistence of renal failure after decompression, and admission from medical ward as we considered it is not clinically relevant. Multivariate analysis showed that mortality in our ICU population was significantly associated with the history of taking antithrombotic treatment (OR = 10.146), the time to hospital consultation (OR = 1.137), and the use of catecholamines (OR = 5.819) and mechanical ventilation (OR = 13.649) during ICU stay (Table 4).

### 4. Discussion

This is a single center retrospective study analyzing the factors related to mortality in patients with severe acute cholangitis in ICU. Four variables, including the history of taking antithrombotic treatment, the time to hospital consultation, and the use of catecholamines and mechanical ventilation during ICU stay, were associated with the mortality of ICU patients with severe acute cholangitis.

Since the first surgical biliary decompression attempt was only described in 1903, mortality associated with acute cholangitis treated without biliary drainage was close to 100%. Despite surgical advances and the introduction of antibiotics over the following decades, mortality remained at 50%. But it has decreased to 10-30% since 1980, with the development of endoscopic biliary drainage techniques and the various associated therapeutic modalities [1, 7, 8]. Current mortality rates vary between 9.6% and 37% [6, 9–11], and death is most often due to a multiorgan failure related to a refractory septic shock [1]. This is consistent with our results which showed a mortality rate of 28% and refractory septic shock as the leading cause of death.

| Factors                                           | Survivors (N = 101) | Nonsurvivors (N = 39) | p value | Brut OR (95% CI) |
|---------------------------------------------------|---------------------|-----------------------|---------|-----------------|
| Decompression technique, n (%)                    |                     |                       |         |                 |
| Endoscopic                                        | 82 (81.2%)          | 29 (74.4%)            | 0.371   | 0.67 (0.28-1.61) |
| Surgical                                          | 16 (15.8%)          | 6 (15.4%)             | 0.947   | 0.96 (0.34-2.68) |
| Percutaneous                                      | 2 (2%)              | 1 (2.6%)              | 0.831   | 1.30 (0.11-14.78) |
| Persistence of renal failure after decompression, n (%) | 3 (3%)              | 10 (25.6%)            | ≤0.001  | 11.26 (2.90-43.67) |
| Persistence of hematological failure after decompression, n (%) | 5 (5%)              | 35 (89.7%)            | ≤0.001  | 168 (42.66-661.50) |
| ICU stay (days), mean ± SD                        | 5.60 ± 3.65         | 5.62 ± 4.67           | 0.988   |                 |
| Septic shock during ICU stay, n (%)               | 0 (0%)              | 35 (89.7%)            | ≤0.001  |                 |

There are few studies on the prognostic factors for severe acute cholangitis. Although the TG18/TG13 severity criteria are currently widespread and very precise for the diagnosis and assessing the severity, they are based on expert opinions and therefore requiring additional validation in clinical practice [12]. In Morocco, to our knowledge, there has been no study to investigate prognostic factors in critically ill patients with severe acute cholangitis. In this study, multivariate analysis identified four independent risk factors for mortality: history of taking antithrombotic treatment, time to hospital consultation, and the use of catecholamines and mechanical ventilation during ICU stay. Table 5 summarizes the different prognostic factors found in different studies compared to those in our study.

Severity assessment scores such as TOKYO grading as well as the classic quick-SOFA and SOFA did not stand out as prognostic factors in our study. There are two possible reasons: (1) the inclusion of patients in the study was based on these scores and (2) admission to ICU is considered in itself as a prognostic factor [6]. On the other hand, use of catecholamines and mechanical ventilation (both reflect of hemodynamic and respiratory failures) did stand out as prognostic factors. Both criteria are included in the SOFA and the TOKYO grading. Furthermore, mechanical ventilation is also associated with its own complications. Organ failure is therefore the main prognostic factor and the detection of patients at risk of progression to organ failure by scores such as quick-SOFA, SOFA, or TOKYO would improve the prognosis. In a recent study [13], quick-SOFA was associated with high specificity but decreased sensitivity to predict severity (97% vs. 43%) and admission to intensive care (96% vs. 60%). However, it is an easily reproducible clinical tool in

| Factors                                           | p value | Adjusted odds ratio (95% confidence interval) |
|---------------------------------------------------|---------|-----------------------------------------------|
| History of antithrombotic therapy                 | 0.004   | 10.146 (2.125; 48.44)                         |
| Use of catecholamines                              | 0.005   | 5.819 (1.71; 19.80)                           |
| Mechanical ventilation                            | ≤0.001  | 13.649 (3.715; 50.148)                        |
| Time to hospital consultation                     | 0.019   | 1.137 (1.023; 1.264)                          |

### Table 3: Continued.

| Factors                                           | Survivors (N = 101) | Nonsurvivors (N = 39) | p value | Brut OR (95% CI) |
|---------------------------------------------------|---------------------|-----------------------|---------|-----------------|
| History of antithrombotic therapy                 | 0.004   | 10.146 (2.125; 48.44) |
| Use of catecholamines                              | 0.005   | 5.819 (1.71; 19.80)   |
| Mechanical ventilation                            | ≤0.001  | 13.649 (3.715; 50.148) |
| Time to hospital consultation                     | 0.019   | 1.137 (1.023; 1.264)  |
the emergency room. Particular attention is to be addressed to the elderly and the immune suppressed patients. Often these patients do not have clear and definite clinical symptoms to guide the diagnosis and are also more likely to deteriorate rapidly due to their limited physiological reserve.

In this study, mean time to hospital consultation was of 10 days. This delay in consultation, and therefore the delay in the administration of antibiotics and biliary drainage, will make infection control more difficult with poor treatment results, especially in patients with comorbidities [6, 14]. The use of traditional therapies (fire points, etc.) and difficult access to care in remote areas is still a real problem to be taken into account in local and national policies to raise awareness and provide care.

Early antibiotic therapy is as important as appropriate antibiotic therapy. Several studies have also reported inappropriate probabilistic antibiotic therapy as a prognostic factor [15], which underlines the importance of bile samples and blood cultures for secondary adaptation as well as knowledge of local ecology. Moreover, other study [10] has reported that the presence of ESBL organism was significantly associated with organ failure in bacteria cholangitis. The initial empiric antibiotherapy dose did not show significant association with mortality in this study, but further analysis based on bile sample results is needed. We did not study this etiological factor since the bile sample results were missing in some cases.

No other study, to our knowledge, has reported taking antithrombotics as a prognostic factor. A history of antithrombotic therapy may reflect the severity of the underlying comorbidity, can worsen or precipitate hematological failure, and may delay or complicate biliary drainage. This factor is included as prognosis factor in some ICU scores such as for trauma patients. Further studies are needed, but we should pay particular attention to these patients.

Emergency biliary decompression is the primary treatment for severe acute cholangitis. Increasing bile pressure promotes biliary sepsis dissemination and prevents biliary penetration of antibiotics. Antibiotic therapy, which main purpose is to limit the infection spread while waiting for biliary decompression, remains essential but is alone insufficient. Biliary drainage is then recommended in acute cholangitis regardless of severity, with the exception of a few nonserious cases progressing spontaneously under antibiotic therapy and initial resuscitation measures [16]. 92% of our patients underwent biliary decompression. Three patients died before, and nine patients formed in 2% of cases, is a technique recently introduced to our center. Early biliary drainage is associated with less inhospital mortality, 30-day mortality, and hospital costs,

### Table 5: Prognostic factors in acute cholangitis in different studies.

| Studies                        | Study design         | Prognostic factors                                                                 |
|-------------------------------|----------------------|-----------------------------------------------------------------------------------|
| Yildiz et al. [6]              | Retrospective        | (i) Total bilirubin ≥ 6.9 mg/dl                                                   |
| Turkey                        | Suppurative acute cholangitis | (ii) RDW1 ≥ 14.45%                                                                |
|                               | 104 ICU patients     | (iii) Admission to ICU                                                             |
|                               | 2010-2015            |                                                                                   |
| Valsangiacomo et al. [9]      | Retrospective        | (i) Age > 65 years                                                                |
| Uruguay                       | Suppurative acute cholangitis | (ii) Male                                                                            |
|                               | 81 patients          | (iii) Septic shock on admission                                                    |
|                               | 2002–2015            | (iv) Time to biliary decompression                                                 |
| Ban Seok Lee et al. [10]      | Retrospective        | (i) ESBL2                                                                         |
| South Korea                   | Acute cholangitis    | (ii) Total bilirubin                                                              |
|                               | 211 patients         | (iii) Blood urea nitrogen                                                          |
|                               | 2003-2011            | (iv) Biliary decompression                                                         |
| Mohammed Aboelsoud et al. [11]| Retrospective        | (i) Albumin                                                                      |
| USA                           | Severe acute cholangitis | (ii) Total bilirubin                                                              |
|                               | 177 patients         | (iii) SAPS-II                                                                     |
|                               | 2001–2012            | (iv) Age                                                                          |
| Gravito-Soares et al. [12]    | Retrospective        | (v) Time to biliary decompression                                                  |
| Portugal                      | Acute cholangitis    | (i) Systolic blood pressure < 90 mmHg                                              |
|                               | 183 patients         | (ii) Hypoalbuminemia                                                              |
|                               | 2017                 | (iii) Active neoplasia                                                            |
| Our study                     | Retrospective        | (iv) Tumor obstruction                                                             |
| Fez, Morocco                  | Severe acute cholangitis | (i) Time to hospital consultation                                                  |
|                               | 140 patients         | (ii) Catecholamines                                                                |
|                               | 2009–2018            | (iii) Mechanical ventilation                                                      |
|                               |                      | (iv) History of antithrombotic therapy                                             |

1RDW: red cell distribution width. 2ESBL: extended-spectrum beta-lactamase.
We also considered the scientific, traumatic, neurological, septic factors. As with any other observational study, even after centric recruitment, but this is the retrospective design of our study and by the monocentric patients is recently raised by several studies but needs to be validated by more studies.

The prognostic value of RDW in different acute or chronic inflammatory circumstances (cardiovascular, traumatic, neurological, septic…) and especially in critically patients is recently raised by several studies. RDW is associated to intensive care and bilirubin levels within a predictive mortality score but does not significantly affect mortality.

RDW (Red Cell Distribution Width) is traditionally high in cases of ineffective erythropoiesis or excessive destruction of erythrocytes. The prognostic value of RDW in different acute or chronic inflammatory circumstances (cardiovascular, traumatic, neurological, septic…) and especially in critically patients is recently raised by several studies. RDW is associated to intensive care and bilirubin levels within a predictive mortality score but needs to be validated by more studies.

Our results may not be generalized as they are limited by the retrospective design of our study and by the monocentric recruitment, but this is the first large study of ICU patients with severe cholangitis identifying local prognostic factors. As with any other observational study, even after adjusting for clinically and statistically significant prognostic factors, other unmeasured factors may have contributed to patient mortality. All retrospective series on this question are limited by significant confounding factors. The key to a successful logistic regression model is to choose the correct variables to enter into the model. While it is tempting to include as many input variables as possible, this can dilute true associations and lead to large standard errors with wide and imprecise confidence intervals, or, conversely, identify spurious associations. We first run the univariate analyses and then used only the variables meeting a preset cutoff for significance of \( p < 0.05 \) to run a multivariable model. We also considered the scientific plausibility and the clinical meaningfulness of the association while trying to avoid the use of highly correlated variables.

As multiple organ failure is often associated with mortality in severe acute cholangitis; predictive risk factors for organ failure should be further investigated. Finally, a local contextualized protocol emerged from this work and is being validated in practice. These procedures are provided in Supplementary Materials (available here).

5. Conclusions

History of taking antithrombotic treatment, the time to hospital consultation, and the use of catecholamines and mechanical ventilation during ICU stay were associated with the mortality of ICU patients with severe acute cholangitis in this study. Predictive risk factors for organ failure should be further investigated.

In addition, severe acute cholangitis management requires multidisciplinarity (anesthetists, intensivists, hepatobiliary endoscopists, surgeons, radiologists, and microbiologists) and implementation of standardized protocols.

Data Availability

All data and tables used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest with the contents of this article.

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Supplementary Materials

The file includes our local contextualized procedure for the management of severe acute cholangitis and is provided both in its original language (French) and in English. (Supplementary Materials)

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