

## Acute alithiasic cholecystitis in patients in intensive care: an integrative review

### *Colecistite alitiásica aguda em pacientes na terapia intensiva: uma revisão integrativa*

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**ABSTRACT:** *Introduction:* Acute allitiasis cholecystitis (AAC) is an inflammation of the gallbladder without the presence of gallstones. It is predominant in post-operative conditions, in trauma patients, or in those admitted to intensive care units (ICU) because of a serious illness. The pathophysiology of AAC, despite being associated with some known factors, is not well elucidated, which hinders the development of preventive, diagnostic, and therapeutic actions, thus leading to an increase in the number of cases of death. *Objective:* To review and synthesize available knowledge on acute allitiasis cholecystitis in intensive care patients. *Methods:* This is an integrative review of literature in PubMed, VHL and Web of Science databases using the descriptors: “acalculous cholecystitis”, “Intensive Care”, “Intensive Care”, “Gallbladder Inflammation” and “Diagnosis”. Initially, 60 articles were selected, without time limitation, in Portuguese and/or English, complete and free. After analysis, 10 articles met the proposed objective. *Results:* From the studies a prevalence of acute acalculous cholecystitis was demonstrated in male patients and aged 45 - 73 years. The most common reason for admission to intensive care was pneumonia, infections and trauma, having a median interval of 11 days for diagnosis of acute acalculous cholecystitis after admission to intensive care and a median length of stay of 26.5 days. It was observed that the influence of the duration of use of total parenteral nutrition, analgesics, mechanical ventilation, vasoactive drugs, and shock time were factors that contributed to the development of the disease. *Conclusion:* For the treatment of cholecystitis althiasis, laparoscopic cholecystectomy was indicated in patients with adequate clinical conditions and percutaneous cholecystostomy in those with worse clinical conditions because it is less aggressive than open or laparoscopic cholecystectomy.

**KEYWORDS:** Acalculous cholecystitis; Cholecystitis; Critical care; Diagnosis.

**RESUMO:** *Introdução:* A colecistite alitiásica aguda (CAA) consiste em uma inflamação da vesícula biliar sem a presença de cálculos biliares. É predominante em quadros pós-operatórios, em pacientes traumatizados ou nos internados em unidades de terapia intensiva (UTI) em razão de uma doença grave. A fisiopatologia da CAA apesar de ser associada a alguns fatores conhecidos, não é bem elucidada o que prejudica o desenvolvimento de ações preventivas, diagnósticas e terapêuticas levando assim, o aumento dos casos de óbito. *Objetivo:* Analisar e sintetizar os conhecimentos disponíveis sobre a CAA em pacientes em terapia intensiva. *Métodos:* Trata-se de uma revisão integrativa da literatura na base de dados PubMed, BVS e Web Of Science usando os descritores: “Colecistite acalculosa”, “Colecistite”, “Cuidados críticos” e “Diagnóstico”. Inicialmente, foram selecionados 60 artigos, sem limitação de lapso temporal, em português e/ou inglês, completo e gratuito. Após análise, 10 artigos corresponderam ao objetivo proposto. *Resultados:* A partir dos estudos foi demonstrado uma prevalência da CAA em pacientes do sexo masculino e com idade entre 45 - 73 anos. O motivo mais comum de internação na terapia intensiva foi pneumonia, infecções e traumas, tendo um intervalo mediano de 11 dias para o diagnóstico da CAA após a admissão na terapia intensiva e um tempo médio de internação de 26,5 dias. Foi observado que a influência da duração do uso da nutrição parenteral total, analgésicos, ventilação mecânica, drogas vasoativas e a duração do estado de choque foram fatores que contribuíram para o desenvolvimento da doença. *Conclusão:* Para o tratamento da colecistite alitiásica foi indicada a colecistectomia laparoscópica em pacientes com condições clínicas adequadas e a colecistostomia percutânea naqueles em piores condições clínicas por ser menos agressiva que a colecistectomia aberta ou laparoscópica.

**PALAVRAS-CHAVE:** Colecistite acalculosa; Colecistite; Cuidados críticos; Diagnóstico.

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## INTRODUCTION

Acute acalculous cholecystitis (AAC) involves inflammation of the gallbladder without the presence of gallbladder stones causing this acute abdominal condition. It is responsible for around 6% to 10% of cases of acute cholecystitis and occurs mainly in postoperative patients who have experienced trauma or been admitted to an intensive care unit (ICU) on account of a serious disease. In such cases, the incidence of AAC may be as high as 4% among patients undergoing total parenteral nutrition<sup>1</sup>. Gallbladder ischemia, which leads to hypoperfusion and biliary stasis, plays a fundamental role in the evolution of AAC. This is because hypoperfusion may be exacerbated by hypotension, dehydration, or the administration of vasoactive drugs. Biliary stasis is induced by the use of analgesics, fasting with total parenteral nutrition, and mechanical ventilation with positive final expiratory pressure. Furthermore, diseases such as diabetes mellitus, shock, sepsis, and congestive heart failure may also be associated with the development of AAC<sup>2</sup>, with these factors frequently being found in patients undergoing intensive care.

AAC has been found to develop in 10.6% of patients with trauma who have needed intensive care for more than four days<sup>3</sup>. Critically ill patients who develop AC are also more susceptible to more severe complications. The incidence of gallbladder gangrene in ICU patients with AAC is higher than 50% and the incidence of perforation is over 10%<sup>4</sup>. If AAC is not treated early, mortality may therefore be as high as 65%, owing to the rapid development of complications, such as perforation, biliary peritonitis, or gangrenous cholecystitis. Diagnosis is difficult, however, especially in patients undergoing intensive care, because such patients have usually undergone some kind of surgery and it is therefore difficult to interpret pain and the results of abdominal palpation, artificial ventilation making it impossible for patients to communicate symptoms. Diagnosis is also made difficult under such circumstances, because of the effects of analgesics, which eliminate one possible parietal defense, vulnerability to frequent hospital infections with no initial signs, and the fact that parenteral nutrition may disrupt the hepatic balance<sup>1</sup>.

In view of the complicated physiopathology of CAA, there are therefore no specific diagnostic criteria, and diagnosis is based on a combination of clinical signs and symptoms, laboratory tests, and imaging technologies such as ultrasound and computerized tomography (CT), which may not be reliable in the case of patients in intensive care<sup>5</sup>. Magnetic resonance is not indicated in such cases. Cholescintigraphy, carried out using a hepatobiliary iminodiacetic acid (HIDA) scan, can be used for early diagnosis of AAC in critically ill patients, in whom ultrasound alone does not provide sufficient information for choosing a suitable surgical procedure<sup>1</sup>. In addition to

the use of laparoscopic diagnosis in patients in intensive care, this technique has also been reported in the literature as having great potential value and high precision<sup>6</sup>.

Another important negative impact of the lack of detailed physiopathology is the treatment of AAC in patients in intensive care. Studies have thus reported the use of laparoscopic cholecystectomy (LC), open cholecystectomy (OC) and percutaneous cholecystostomy (PC), a comparison of these techniques having been carried out with a view to providing evidence of the benefits and disadvantages of each.

The aim of the present study was thus to examine the available body of knowledge on AAC in patients in intensive care with a view to providing an overview of the findings available in relation to this disease and identifying gaps, as a way of justifying the need for further studies of this condition.

## METHODS

An integrative review of the literature was carried out in the following stages: 1) identification of the subject matter and development of the research question; 2) establishing criteria for the inclusion and exclusion of studies; 3) determining the information to be extracted from selected studies; 4) critical analysis of included studies based on levels of evidence; 5) discussion of results; and 6) presentation of the integrative review<sup>7</sup>.

To this end, the guiding question was drawn up using the PICO strategy (Patient (Person/Problem), Intervention, Comparison, and Outcomes). The following research question was thus developed: What knowledge is available regarding the development of acute acalculous cholecystitis in patients in intensive care?

A systematic bibliographical search was carried out in the following databases: PubMed, Web of Science and Biblioteca Virtual em Saúde (BVS) [Virtual Health Library], with the last of these yielding only scientific articles also referenced in Medline. The following DeCS/MeSH-validated descriptors were used: "acalculous cholecystitis", "cholecystitis", "critical care" and "diagnosis". The search terms were combined using the Boolean operator "AND" and no time limit was set. The search terms were in English because the databases use English terms and because most articles indexed are available in English, such that a search using Portuguese terms would limit the results to those that contain both a Portuguese and an English version.

The functioning of each database has a number of peculiar features for reason of the different kinds of software used and this results in different ways of searching for scientific articles. In PubMed and Web of Science, the searches covered all fields, yielding 28 and 2 articles, respectively. In the BVS, the same search terms were used but the search was restricted to titles, abstract, and subject

matter of the articles, yielding 30 articles in all. The total number of articles identified was 60.

Articles included were required to be full articles available free of charge written in Portuguese or English. The review was also required to include studies that described the factors contributing to the development of AAC in patients in intensive care, the possible diagnostic tools used and the available forms of treatment. Methodological rigor, as an indicator of high quality, was also used as an inclusion criterion, and this was evaluated using levels of scientific evidence<sup>7</sup>.

Studies were excluded if they did not answer the research question, were incomplete, or were written in languages other than English or Portuguese. Studies were also excluded if they did not address the development, diagnosis, and treatment of AAC in patients receiving intensive care.

The sixty articles found were assessed independently. Systematic selection of articles was ensured by using the RAYYAN - Intelligent Systematic Review tool, using the PRISMA Statement 2020 search strategy, as illustrated in Figure 1. This process identified 26 duplicate articles, which were removed, giving a total of 34 articles for analysis of title and abstract. This second phase resulted in the exclusion of nine articles in which the title and the abstract were not aligned with the aims of the present review, thereby leaving 25 articles for assessment of the full text. Careful examination of the full text of each article led to exclusion of a further 15 studies that did not fit the research proposal, leaving 10 articles in the final integrative review. At the end of this process, the methodological quality of these 10 articles was categorized as Level III scientific evidence, which refers to retrospective cohort studies. The results are outlined in Table 1.

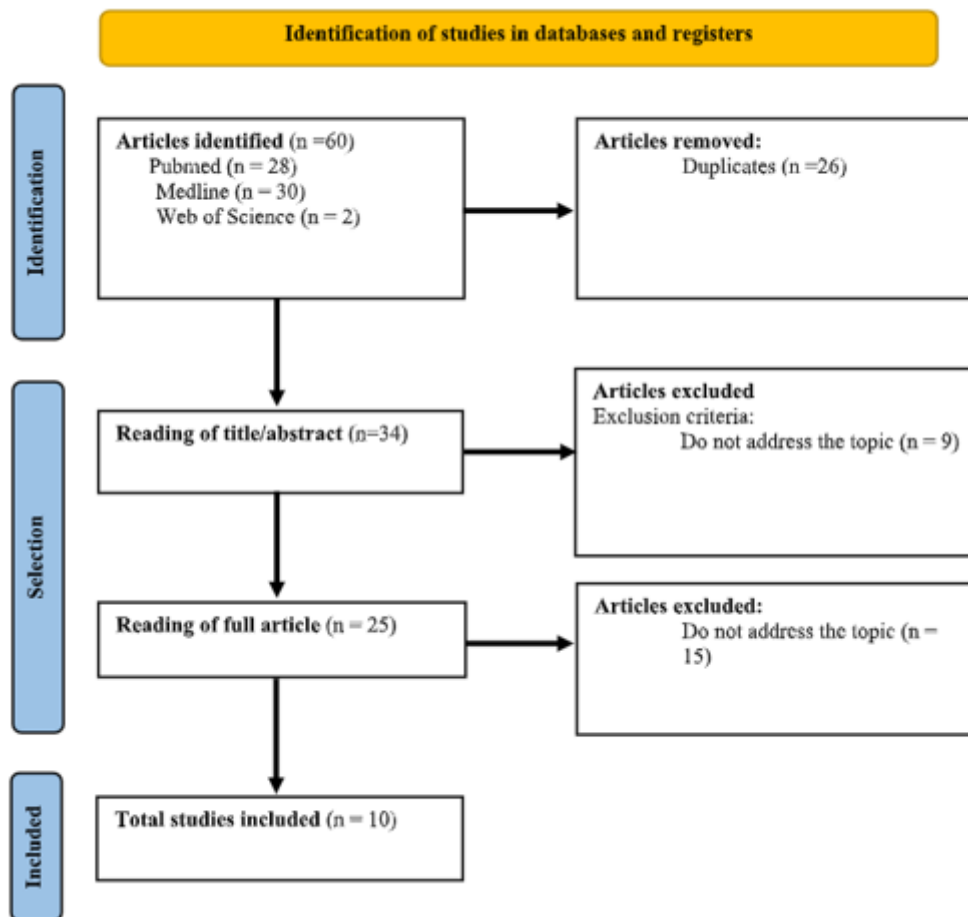


Figure 1 - Flowchart illustrating selection of articles for integrative review (PRISMA).

## RESULTS

Most of the articles were retrospective cohort type studies, as can be seen in Table 1, which lists the selected

articles and provides a brief description of each.

Analysis of the studies shows that AAC occurred predominantly among male patients aged between 45 and 73 years, except in the case of patients with AAC and

bacteremia, who tended to be younger.

The most common reasons for admission to ICU were pneumonia, sepsis and trauma, and the median length of time spent in AAC prior to diagnosis was 11 days, with a mean duration of intensive care of 26.5 days<sup>8</sup>. The duration of use of total parenteral nutrition, mechanical ventilation, and vasoactive drugs and the duration of shock were all found to have contributed to the development of AAC and these factors were found to be substantially more frequent in the group with AAC than in the group with acute calculous cholecystitis (ACC)<sup>9</sup> <sup>10</sup>. The incidence of bacteremia was found to have been significantly greater in patients with AAC and these were frequently younger patients who spent longer in ICU<sup>10</sup>.

The most commonly used methods for diagnosis, along with clinical detection of signs and symptoms, were ultrasound, CT, laparotomy, exploratory laparoscopy, and HIDA cholescintigraphy, the last of which has a sensitivity of 79% and a specificity of 100%, which corresponds to the percentage of positive results among patients with AAC and the likelihood of this test being negative in individuals without the disease, respectively. It was reported that imaging and laboratory examinations alone are not reliable means of diagnosis and cholescintigraphy was thus considered to be a valuable complement to ultrasound,

with sensitivity of 93% and low specificity of 17%. This occurs when at least two of the three main signs are seen to be present, these being biliary sludge, a thickened wall, and distension of the gallbladder. In cases of low sensitivity (36%) and high specificity (89%) the presence of all three can be observed<sup>1</sup>. The use of laparoscopy was reported to be a more precise method of diagnosis, in addition to not producing false-positive or false-negative results and having zero morbidity associated with the procedure. Comparison of multiple clinical, laboratory and radiological findings showed that only laparoscopy succeeded in distinguishing with a high degree of precision patients with AAC from those with ACC<sup>11</sup>.

In relation to treatment, it was found that patients undergoing PC presented lower morbidity of 8.7% in comparison with patients who underwent OC, with 47% morbidity after the procedure, and fewer admissions to hospital and a shorter length of time spent in intensive care (7 days with PC, compared to 8 for OC). The mortality rate was similar for the two procedures, with 13% after PC and 16% after OC<sup>12,13</sup>. In comparison to OC, LC was found to be associated with lower mortality and morbidity, a shorter stay in ICU, (7 days for LC and 8 days for OC), similar rates of readmission within 30 days, and a conversion rate of 26% for an open procedure<sup>13, 14</sup>.

**Table 1** - Overview of studies included in the systematic review.

Author	Periodical/Year	Aim	Type of study	Results	Level of Evidence
Kim, S.J. et al. <sup>8</sup>	Official journal of the Australian College of Critical Care Nurses Ltd/2018	To investigate the clinical characteristics of acute cholecystitis (AC) when it occurs in critical patients after admission to an intensive care unit.	Retrospective cohort study	Prolonged fasting, total parenteral nutrition, the use of analgesics, vasoactive drugs, or mechanical ventilation are associated with acute acalculous cholecystitis, after abdominal pain, unexplained fever, or hemodynamic instability.	III
Zhang, Y. et al. <sup>9</sup>	Comput Math Methods Med/2022	To examine the correlation between patients with AAC during treatment in intensive care and the duration of use of a ventilator and total parenteral nutrition.	Retrospective cohort study	Quantity of norepinephrine used, duration of use of ventilator, white blood cell count, and quantity of C-reactive protein (CRP) were correlated with the occurrence of AAC.	III
Simorov, A. et al. <sup>15</sup>	The American Journal of Surgery/2013	To compare the results of patients with critical disease treated using percutaneous cholecystostomy (PC), with those treated using laparoscopic cholecystectomy (LC) and those treated using open cholecystectomy (OC).	Retrospective cohort study	Extremely sick patients with AAC presented more satisfactory results with PC than with OC. For those patients in whom the risk of conversion is low and where medical conditions permit, LC should be conducted.	III
Melloul, E. et al. <sup>14</sup>	World Journal of Surgery/2011	To compare PC in the gallbladder with PC in a group of patients with AAC- and ACC-related sepsis.	Retrospective cohort study	In severely ill patients, PC and emergency cholecystectomy are both efficient ways of resolving sepsis caused by AC. However, emergency cholecystectomy is associated with greater risk of complications and the laparoscopic approach is not always possible.	III

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Author	Periodical/Year	Aim	Type of study	Results	Level of Evidence
Rincon, J. et al. <sup>11</sup>	Surgical Infections/2020	To examine the hypothesis that patients with AAC have higher levels of bacteremia and less satisfactory outcomes than patients with ACC.	Retrospective cohort study	The incidence of bacteremia in patients with AAC was five times higher than in patients with ACC. The AAC patients spend eight more days in ICU compared to those with ACC and bacteremia.	III
Laurila, J. et al. <sup>10</sup>	Acta Anaesthesiologica Scandinavica/2004	To identify all the patients with surgically confirmed AAC during the two-year study and to shed light on the clinical profile of this disease and its possible association with multiple organ failure in critically ill patients.	Retrospective cohort study	AAC was associated with infection, a long stay in ICU of 19 days on average, serious disease, and multiple organ failure. Mortality was associated with the degree of organ failure.	III
Orlando, R. et al. <sup>16</sup>	The American Journal of Surgery/2004	To identify the clinical characteristics of AAC in a surgical ICU.	Retrospective cohort study	Ultrasound was found to be the most effective diagnostic tool; PC and cholecystectomy were used. Cholecystostomy resolved inflammation in all patients undergoing this procedure, while cholecystectomy was indicated for those patients with extensive gallbladder necrosis. Hypotension was related to the development of AAC, since heightened intraluminal pressure in the gallbladder caused by edema and increased biliary viscosity may cause hypotension to lead to ischemia and necrosis of the mucous with subsequent bacterial colonization.	III
Prévôt, N. et al. <sup>1</sup>	European Journal of Nuclear Medicine/1999	To assess the contribution of cholescintigraphy to early diagnosis of AAC in ICU patients and in establishing better diagnostic criteria that enable more appropriate surgical decisions to be taken.	Retrospective cohort study	The advantages of morphine-stimulated cholescintigraphy in diagnosis of AAC were demonstrated. With sensitivity of 79% and specificity of 100%, this examination can be used to complement ultrasound. There is no relation between the presence of AAC and delayed visualization of the gallbladder after administration of morphine. In contrast to what is commonly reported in the literature, AAC does not exclude the possibility of using cholescintigraphy as a diagnostic tool.	III
Boland, G. et al. <sup>13</sup>	American Journal of Roentgenology/1994	To assess the effectiveness of PC as a tool for diagnosis and treatment in ICU patients presenting with persistent unexplained sepsis.	Retrospective cohort study	An attempt to perform PC in a critically ill patient with persistent unexplained sepsis has beneficial clinical effects. Almost 60% of patients exhibited a marked clinical response to PC and, in the others, the gallbladder was removed as a source of sepsis. The absence of a non-invasive test for diagnosis of AC in critically ill patients led to the use of PC as a tool for diagnosis and treatment. The fact that it is possible to carry out PC at the bedside and the low incidence of complications makes this procedure ideal for severely ill patients.	III

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Author	Periodical/Year	Aim	Type of study	Results	Level of Evidence
Brandt, C. et al. <sup>12</sup>	Surg Endosc/1994	To review experiences of laparoscopy in trauma patients in ICU with suspected AAC and to ascertain whether this procedure might be capable of providing an earlier and more definitive diagnosis of AAC.	Retrospective cohort study	Diagnostic laparoscopy is a safe and definitive procedure in trauma patients in ICU with suspected AAC and should be the examination of choice when this diagnosis is considered based on clinical evidence and auxiliary examinations. Laparoscopy should be carried out before proceeding to exploration for suspected AAC, as a way of minimizing non-therapeutic laparotomy in patients who are already severely ill.	III

**Key:** AC – Acute cholecystitis; ICU – Intensive care unit; AAC – Acute acalculous cholecystitis; ACC – Acute calculous cholecystitis; CRP – C-reactive protein; PC – Percutaneous cholecystostomy; LC – Laparoscopic cholecystectomy; OC – Open cholecystectomy

Examination of these articles showed that there are still considerable gaps in knowledge concerning the physiopathology of AAC in patients in intensive care, despite the fact that the development of this condition is associated with trauma and serious diseases, which clearly hinders the development of a standard for diagnosis and treatment.

**DISCUSSION**

**The development of acute acalculous cholecystitis in patients in intensive care**

As reported in the studies, AC developed within approximately 10 days in severely ill patients subsequent to admission to ICU. Most of these patients had pneumonia or some other type of infection, in addition to fasting and prolonged total parenteral nutrition, prior use of analgesics or vasoactive drugs, and mechanical ventilation. Surgically confirmed AAC was found to be associated with the severity of the disease, infection, a prolonged stay in ICU, and multiple organ failure, with infection being the most common diagnosis leading to admission to ICU<sup>15</sup>. In patients with pneumonia, liver biopsies revealed irregular necrosis and dilation of the biliary canaliculi, leading to the release of inflammatory mediators, since the systemic inflammatory response induced an inflammatory process in the gallbladder. Cholestasis, gallbladder ischemia, and systemic inflammation resulting from pneumonia or sepsis may thus contribute to the development of AAC in patients undergoing intensive care<sup>8</sup>.

Different from ACC, the onset of AAC is unexpected, with atypical symptoms and rapid progression of the disease, normally accompanied by severe complications, such as gangrene, perforation of the gallbladder or peritonitis. Most ICU patients are critically ill with multiple organ failure and are thus prone to develop AAC. These patients are

incapable of communicating their symptoms themselves and this, in combination with the effect of medication, the limitations of examinations and other factors, may lead to late diagnosis and a delay in treatment, leading to a high clinical mortality rate for patients with AAC.

The duration of the state of shock and the prevalence of use of a ventilator and sedatives were all significantly greater in the AAC patients than in the ones with ACC. It has been confirmed that patients in shock are more prone to develop AAC, since vasodilation and improved blood flow result in reperfusion of blood with many inflammatory mediators, causing damage to the gallbladder and increasing inflammation.

Furthermore, high doses of norepinephrine, used to treat shock, maintain arterial pressure, and guarantee the supply of blood to organs in patients in intensive care, and may increase peripheral vascular resistance. As a result, blood vessels leading to the gallbladder contract, generating blood supply problems, mucosal ischemia, and increased gallbladder inflammation.

Although sedation and analgesia are beneficial in ICU patients in so far as they aid early recovery, these medications have side-effects that include diminished gastrointestinal motility. This is caused by diminished levels of gastrin, which may result in insufficient secretion of cholecystokinin, absence of normal gallbladder contraction, absorption of biliary water by the epithelial cells of the gallbladder and retention and increased viscosity of bile, hindering excretion. Some studies, however, reported no correlation between the use of sedatives and AAC.

Another factor associated with the development of AAC is mechanical ventilation, which may cause increased intra-abdominal pressure. This continuous hypertension may compromise the supply of blood to the intestine, resulting in ischemia, hypoxia, necrosis, or damage to the intestinal mucus barrier. It may also facilitate the passage of bacteria through the blood or lymphatic system into the

bile ducts, contributing to bacterial infection of bile.

The white blood cell count is also an indication of AAC, since patients with this condition frequently present with necrosis and perforation of the gallbladder wall, with inflammation spreading rapidly into the abdominal cavity, resulting in localized or diffuse peritonitis.

Another condition is C-reactive protein (CRP), which is a systemic inflammation indicator that helps to monitor cholecystitis. This occurs by way of bacterial infection or aseptic inflammatory stimuli, which cause CRP to bind to lipoproteins, activating the immunological system and producing inflammatory mediators and free oxygen radicals, causing damage to vessels, increasing vascular permeability, and exacerbating the systemic inflammatory response.

Total parenteral nutrition and fasting lead to a reduction in use of the gastrointestinal tract and affect peristalsis. This may consequently cause damage to the discharge of bile, causing congestion and edema of the gallbladder mucous and a series of acute inflammatory reactions. In combination with the use of sedative medication, this may hinder the opening of the duodenal papilla and the emptying of the gallbladder, thereby increasing the risk of AAC.

It should be noted that the physical pathogenesis of AAC is not clearly described in the literature, and this hinders the development of specific preventive measures for patients in intensive care at high risk of AAC. Currently available published works on AAC concentrate mainly on diagnosis and treatment of disease, and there are still few studies of the risk factors and factors correlated with the incidence of AAC in patients in intensive care.

### **Diagnosis of acute acalculous cholecystitis in patients in intensive care**

Diagnosis of AAC in critically ill patients is difficult. Clinical, biochemical, and imaging findings are generally non-specific, owing to the poor health conditions of the patients in intensive care. These patients are normally on mechanical ventilation and receiving opiates, making it difficult to evaluate abdominal pain. Liver function exams frequently furnish high values as a result of various factors, including medication, sepsis, and multiple organ failure. Ultrasound results indicative of cholecystitis may be seen in a variety of other conditions. HIDA cholescintigraphy produces a high rate of false positives in patients who are severely ill or are receiving total parenteral nutrition, even with increased morphine and cholecystocine<sup>16</sup>. Gram coloration and percutaneously aspirated bile culture are not sensitive in patients who are already receiving antibiotics<sup>10</sup>.

Some studies have shown that a high proportion of intensive care patients present ultrasound abnormalities similar to cholecystitis even though they do not have AAC, while some who do not present such findings on ultrasound,

are diagnosed with AAC on surgery. CT has been shown to have shortcomings as a diagnostic tool, in view of the fact that, in one study, three of twelve patients in whom this technique found no indication of AAC were later found to present with a necrotic gallbladder. In this same study, liver enzyme tests were carried out and presented alterations in only 59-79% of patients. The white blood cell count was abnormal in only 54% of patients and CRP alterations varied, indicating that such techniques are unreliable in cases of AAC. Only a small proportion of bile cultures tested positive for enteric organisms and this may be associated with antibiotic treatment prior to cholecystectomy or to the fact that AAC is sterile<sup>15</sup>. One study, however, reported higher rates of positive hemocultures in patients with AAC, with the incidence of bacteremia being five times higher than in the group with ACC<sup>10</sup>.

It should also be pointed out that abdominal ultrasound is the most commonly requested initial examination, due to the fact that it is a simple easily repeated bedside method of diagnosis. The diagnostic signs indicative of AAC normally found, such as distension and thickening of the gallbladder wall, may be ambiguous in intensive care patients. This is because fasting and analgesics may be responsible for distension of the gallbladder and the presence of ascites may produce false ultrasound images of thickening of the gallbladder wall. As demonstrating the presence of biliary calculi is one of the most important criteria for ultrasound diagnosis of AC and these are not present in AAC, the sensitivity of ultrasound has been reported as low, at around 67% for this subgroup of patients<sup>16</sup>. One study, however, reported a sensitivity of 92% and specificity of 96% for ultrasound based on the presence of at least two major ultrasound criteria or one major criterion and two minor ones. The major criteria for AAC included thickness of the gallbladder wall of 4mm or greater, pericholecystic liquid or subserosal edema without ascites, calculi, intramural gas, damaged mucosal membrane or lack of response to cholecystokinin<sup>17</sup>. It was thus reported that CT does not provide additional information compared to ultrasound and provides less precise visualization of the distension and thickness of the gallbladder wall. Cholescintigraphy can be used for diagnosis of AAC using markers that are captured by the liver. The tracer then follows the metabolic pathway of bilirubin and is excreted through the bile ducts, accompanying the flow of bile and entering the gallbladder through the cystic duct and the duodenum through the common bile duct. Obstruction of the cystic duct by edema of the wall caused by AAC thus makes it impossible to visualize the gallbladder and this is indicative of AAC<sup>16</sup>.

Diagnostic laparoscopy was also used in intensive care patients with acute abdominal pain. One study involving nine trauma patients in intensive care with suspected AAC underwent laparoscopy and were diagnosed

with AAC, with no false positives or false negatives. This was subsequently confirmed by laparotomy, the clinical progression of the patient, or autopsy. The advantages of laparoscopy in these situations include direct visualization of the gallbladder, the possibility of performing the procedure under local anesthesia at the bedside in ICU and avoiding non-therapeutic laparotomy<sup>11</sup>.

### Treatment of acute acalculous cholecystitis in patients in intensive care

Although some studies describe early LC for AAC as being safer, in critically ill patients with AAC in ICU, the use of cholecystectomy has been associated with mortality rates of up to 50%<sup>18</sup>. However, the greatest concern regarding adoption of LC in severely ill patients is viability, in view of issues relating to the suitability of the patient for surgery and the high rate of 11% to 28% for conversion to an open procedure<sup>19,20</sup>. Severely ill patients who have developed AAC and undergone OC spend a longer period, of around 19 days, in ICU and have a higher rate of mortality<sup>15</sup>. The procedure should be carried out in the earliest stages of the disease in candidates who are likely to tolerate LC. On the other hand, men, patients with severe cholecystitis, multiple comorbidities, such as obesity, those who are not good candidates for surgery, and those who have a high risk of conversion to an open procedure will all benefit from PC<sup>13</sup>. Involving placement of a tube to decompress the inflamed gallbladder, PC was developed as an alternative to surgical cholecystectomy in high-risk patients with AAC-related sepsis, can be performed at the bedside, and has a low incidence of complications. This

makes the procedure ideal for patients in intensive care. PC can be employed not only for treatment, but also to rule out AC in critical patients. It may however be considered too aggressive and invasive for this purpose. The literature suggests that PC should be carried out in infirm patients with persistent inexplicable sepsis, on account of its clinical benefits<sup>14, 15</sup>.

### CONCLUDING REMARKS

AAC in intensive care patients has been associated with severe illness, infection, a long stay in ICU, and high mortality. It normally develops after the first week of critical illness, as multiple organ failure progresses. This may reflect the severity of the condition and the need for early and immediate diagnosis, in addition to active treatment to avoid a fatal outcome. Clinical and laboratory findings are of limited value and radiological imaging examinations, such as ultrasound and CT are not totally reliable for diagnosis of AAC when used in isolation. Cholescintigraphy is a useful tool for early diagnosis of AAC in patients in intensive care, in whom ultrasound alone does not provide sufficient information regarding the recommended treatment. The lack of a precise non-invasive examination for diagnosis of AAC in critical patients means that PC is used for both diagnosis and treatment. In relation to treatment, it has been shown that LC can be used in patients with a low risk of conversion and suitable medical conditions. Treatment using PC has been shown to be a safe strategy primarily in severely ill patients with AAC and has resulted in better outcomes than OC.

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