Acute cholecystitis: diagnosis, complications and therapy: an integrative literature review

Colecistite aguda: diagnóstico, complicações e terapêutica: uma revisão integrativa de literatura

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Abstract

Acute cholecystitis is an inflammatory pathological process of the gallbladder resulting from acute obstruction of the cystic duct. Although it is more frequent in females, the number of male patients increases with advancing age, reaching 30% of cases over 65 years of age. It presents as a surgical emergency and usually requires hospitalization for treatment. It is associated with significant morbidity and mortality, especially in elderly patients. The most frequent cause is lithiasis, responsible for 90% of cases. In the differential diagnosis of acute cholecystitis, inflammatory or non-inflammatory diseases with expression located in the upper right hemiabdomen must be considered. They are: right-based pneumonia, hepatitis, pyelonephritis, and even myocardial ischemia or infarction. Other diseases of the digestive tract should be kept in mind, such as acute appendicitis of subhepatic location, complicated peptic ulcer and acute pancreatitis. Imaging of the gallbladder and bile ducts has changed dramatically in the last 20 years. The
replacement of transparietal cholangiography and oral cholecystography by modern, non-invasive techniques has brought great advances in the diagnosis of diseases of the bile ducts. Currently, the diagnosis and imaging follow-up of biliary diseases is based on ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI) and scintigraphy. US remains the test of choice in the initial evaluation of acute biliary diseases, due to its ease of performance, wide availability and high accuracy in the diagnosis of acute cholecystitis.

**Keywords:** Cholecystectomy; Cholecystitis; Gallbladder; General surgery.

### 1. Introduction

Acute cholecystitis can be defined as chemical and/or bacterial inflammation of the gallbladder, most often triggered by cystic duct obstruction. As cholelithiasis is the main cause of this disease, the obstruction results from the impaction of a stone in the infundibulum-colocystic region, with consequent hypertension, stasis, vascular and inflammatory phenomena and bacterial proliferation. The process thus unleashed can involute, abort, as a result of the mobilization of the calculus. It can also progress to vesicular hydrops, empyema, necrosis, blocked perforation or free peritoneum (choleperitoneum). Less frequently, acute cholecystitis can occur in the absence of cystic duct obstruction, when it is called alithiatic with little known pathophysiology. It can be associated with autoimmune processes, circulating toxins or vasoconstrictor substances, affecting
chronic hospitalized patients, in intensive care units, polytraumatized, septic, postoperative and elderly patients (Maya et al., 2020).

Acute cholecystitis preferentially affects females, young adults and the elderly, being, in most cases, the first manifestation of lithiasic disease. Pain is the main manifestation of acute cholecystitis, often triggered by the ingestion of cholecystokinetic foods. Initially, it assumes the character of colic, a clinical expression of the obstructive phenomenon, and then it becomes continuous, as a result of vascular and inflammatory phenomena. The initial location in the right hypochondrium is followed by irradiation to the epigastrium, back and diffuse to the abdomen in the presence of complications. Nausea and vomiting are often seen. The general condition depends on the intensity of the inflammatory process and mainly infectious (Sankarankutty et al., 2013).

It is usually preserved, without major hemodynamic changes and rarely presents a fever above 38°C. In approximately 20% of patients it is possible to observe mild jaundice. Inspection of the abdomen reveals antalgic position or mild distention. Palpation of the abdomen is, without a doubt, the most valuable propaedeutic resource, and may reveal hypersensitivity in the right hypochondrium, voluntary defense or not even painful plastron. In 25% of patients, it is possible to observe a palpable and painful vesicle. Murphy's sign (interruption of deep inspiration due to pain on palpation of the vesicular region) is perhaps the greatest expression of abdominal workup in acute cholecystitis. Abdominal percussion reveals pain at the level of the right hypochondrium, resulting from irritation of the visceral peritoneum, the same occurring with the hydro-air sounds that are reduced or even normal. It is important to emphasize that such propaedeutic exuberance may be masked in elderly or immunocompromised patients (Teixeira et al., 2014).

An important aspect in the diagnosis is that most patients have no previous history, around 60% of cases acute cholecystitis is the first manifestation of the presence of stones. Another aspect is that atypical cases occur in the most serious cases in which there can be no delay in establishing a course of action. These cases include the elderly, diabetics, immunosuppressed by corticosteroids and leukemia, etc. The clinical picture of acute cholecystitis is variable and can be confused with other causes of acute abdomen and even with biliary colic. About 30% of patients with an acute abdomen of various causes also have gallstones; therefore, a careful analysis of the data is necessary to establish or rule out acute cholecystitis as responsible for the acute abdominal condition. Laboratory tests contribute indirectly because they are not specific. The blood count usually shows leukocytosis, which may be mild in more severely ill patients. Direct bilirubin may or may not be increased, the marked and progressive increase suggests the presence of choledocholithiasis, without, however, ruling out the diagnosis of acute cholecystitis. Amylase may be elevated, reaching levels of up to 500 IU; higher elevations suggest the diagnosis of acute pancreatitis (Sankarankutty et al., 2013).

Elevated alkaline phosphatase may be an indicator of acute cholecystitis in critically ill patients on parenteral nutrition. In AIDS patients, transaminases may be elevated, and in this group leukocytosis is also rarely observed. Elevation of C-reactive protein (CRP) has a greater discriminative value than leukocyte count and represents an important marker in the diagnosis of acute cholecystitis. ducts. The guideline is that the following are sufficient for clinical diagnosis: one of the findings of abdominal examination (Murphy sign or pain or plastron in the right hypochondrium) plus a systemic sign of inflammation (fever or leukocytosis or elevated CRP) and confirmed by an imaging test (Teixeira et al., 2014).

Plain radiography, as an initial exploration, can rule out other causes of acute abdomen such as hollow viscer perforation, mesenteric thrombosis, and intestinal obstruction. Eventually, it may demonstrate emphysema in the gallbladder, resulting from gangrene of the organ. The exam specifically indicated in the diagnosis of acute cholecystitis, among us, is ultrasound. This examination may demonstrate the presence of an impacted stone in the neck of the gallbladder or in the cystic duct. The diagnosis can be confirmed by thickening or separation of the layers of the gallbladder wall, biliary sludge or debris, as well as perivesicular fluid collections and marked distention of the gallbladder. the vesicle is visualized. This sign, added to
the presence of stones, has a 90% diagnostic positivity. Gallbladder wall thickening greater than 4 mm plus the presence of stones also has a 90% positive predictive value. Layer separation is much more frequent in acute cholecystitis, but appears in other conditions that alter the thickness of the gallbladder, such as portal hypertension, heart failure edema, renal failure, hypoalbuminemia, hepatitis, and multiple myeloma (Shindler et al., 2021).

Gallbladder gangrene detaches the mucosa, which can be seen on ultrasound as a line parallel to the serosa. In acute alithiatic cholecystitis, ultrasound can detect gangrene and perforation. In these patients, positivity is lower, around 67%. Computed tomography of the abdomen and magnetic resonance imaging, although not the first indication, contribute to the diagnosis, demonstrating a dilated vesicle (above 8 × 4 cm), thickening diffuse and foci of attenuation in the gallbladder wall, corresponding to parietal liquefaction. They demonstrate the presence of perivesicular fluid and areas of perivesicular fat densification. Calculations may not be detected. The main indications for these tests are in obese patients, in cases of protracted evolution, when there is suspicion of liver or cavity abscesses, and especially in the suspicion of alithiatic cholecystitis in patients with AIDS. In this eventuality, parietal thickening due to edema may be revealed, translated into decreased wall attenuation or gangrene with the presence of air in the lumen or in the gallbladder wall. MRI and CT have equivalent results (Sankarankutty et al., 2013).

In specific situations, it may be necessary to exclude acute cholecystitis as a cause of acute abdomen and, for this, the indicated test is cholecintigraphy. Iminodiacetic acid derivatives (IDA) labeled with TC-99 are used, with DISIDA being the most used. The injected marker is taken up from the blood stream by the liver and excreted in the bile, and the counter takes serial images of the liver, bile duct, gallbladder and duodenum. In fasting condition, visualization of the gallbladder, bile duct and duodenum within one hour after injection rules out the hypothesis of acute cholecystitis. On the other hand, if the gallbladder is not filled, it is assumed that the cyst is obstructed, confirming the presence of acute cholecystitis. The best indication for this test is to exclude or confirm acute cholecystitis in patients with sepsis or abdominal pain of undetermined origin who are at high surgical risk, since 30% of the elderly have gallstones, which may not be the origin of the clinical condition of organic dysfunction. Imaging depends on hepatic excretion, and thus the data obtained can be falsified in severe liver failure (Teixeira et al., 2014). From this perspective, the objective of this study sought to highlight, through empirical and current analyses, the main imaging findings present in acute cholecystitis, as well as its complications and treatment.

2. Methodology

This is a descriptive research of the integrative literature review type, which sought to highlight, through empirical and current analyses, the main imaging findings present in acute cholecystitis, as well as its complications and treatment. The research was carried out through online access to the National Library of Medicine (PubMed MEDLINE), Scientific Electronic Library Online (Scielo), Google Scholar, Virtual Health Library (BVS) and EBSCO Information Services databases, in August 2022. To search for the works, the keywords present in the descriptors in Health Sciences (DeCS) were used, in English: "acute cholecystitis", "imaging", "ultrasonography", "cholecystectomy" and in Portuguese: "acute cholecystitis", "image", "ultrasound", "cholecystectomy".

As inclusion criteria, original articles and books were considered, which addressed the researched topic and allowed full access to the study content, published between 2013 and 2022, in English and Portuguese. The exclusion criterion was imposed on those works that did not address inclusion criteria, as well as articles that did not undergo a peer review process. The article selection strategy followed the steps of searching the selected databases, reading the titles of all articles found and excluding those that did not address the subject, critically reading the abstracts of the articles and reading the articles selected in the previous steps in full. Thus, 16 materials were totaled for the review.
3. Results and Discussion

In the differential diagnosis of acute cholecystitis, inflammatory or non-inflammatory diseases with localized expression in the right upper hemiabdomen should be considered (Kolla et al., 2016). They are: right-based pneumonia, hepatitis, pyelonephritis, and even myocardial ischemia or infarction. Other diseases of the digestive tract should be kept in mind, such as acute appendicitis of subhepatic location, complicated peptic ulcer and acute pancreatitis (Schirmer et al., 2015).

Imaging of the gallbladder and bile ducts has changed dramatically over the past 20 years. The replacement of transparietal cholangiography and oral cholecystography by modern, non-invasive techniques has brought great advances in the diagnosis of bile duct diseases (Gurusamy et al., 2016). Currently, the diagnosis and imaging follow-up of biliary diseases is based on ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI) and scintigraphy. US remains the test of choice in the initial evaluation of acute biliary diseases, due to its ease of performance, wide availability and high accuracy in the diagnosis of acute cholecystitis (Barie et al., 2013).

3.1 Conventional Radiology

Of patients with acute cholecystis, 90-95% have stones, but only 10-20% contain enough calcium to be radiopaque (Melo, 2013). The stone obstructing the cystic duct or Hartmann's pouch interrupts the flow of bile, causing progressive production of mucus, with distention, edema and ischemia of the vesicle, which is filled with pus. In uncomplicated acute cholecystitis, the radiological signs are presence of calculus, paralytic ileus of the loops adjacent to the gallbladder, and distention of the gallbladder (Schirmer et al., 2015).

3.2 Computed tomography

It is a useful modality when ultrasound results are uncertain or when the clinical picture suggests involvement of adjacent organs (eg, pancreatitis or duodenitis). The low sensitivity of CT for cholelithiasis is well established, although CT almost always demonstrates gallbladder (BV) in fasting patients (Teoh et al., 2015). Unlike US, the description of the stone on CT is highly dependent on its size and composition. Calcified stones are easily seen as hyperattenuating images in BV, and cholesterol stones are seen as hypoattenuating filling faults of the surrounding bile. However, many stones are composed of a mixture of calcium, bile pigments and cholesterol and appear isoattenuating to the surrounding bile; therefore, such stones are not detected at CT, regardless of their size (Boland et al., 2013).

According to Vargas et al. (2016), the sensitivity and specificity of CT for the diagnosis of acute cholecystitis have not been determined in prospective studies, and CT signs should be interpreted with caution due to their low positive predictive value (Howard et al., 2015). CT is very useful when there is suspicion of ductal or BV cholangiocarcinoma, choledocholithiasis, as well as to evaluate the complications of cholecystitis; these situations of diagnostic limitation of the US. In choledocholithiasis, CT is more accurate than US in determining the location (accuracy: 97%) and cause (accuracy: 94%) of the obstruction, with a sensitivity of 87 to 90%. CT is particularly useful in the distal assessment of the common hepatic duct and ampulla of Vater, areas that are difficult to visualize at US; and can detect stones, even in the absence of bile duct dilatation.

- Specific signs: distended gallbladder, with wall thickening greater than 3 mm and parietal enhancement by contrast medium.
- Secondary signs: transient focal hyperattenuation of the liver, in the region adjacent to the gallbladder, in the arterial phase of contrast medium injection, due to increased flow in the cystic vein.
• Non-specific signs: perivesicular fluid, blurring or heterogeneity of perivesicular fat, hyperattenuation of vesicular bile and perivesicular abscess. From this perspective, below are typical computed tomography (CT) images of gangrenous cholecystitis (Figure 1).

**Figure 1** - CT with dynamic contrast (a. simple; b. initial phase; c. equilibrium phase). Gallbladder enlargement, gallbladder wall thickening, and edematous lesions below the gallbladder serosa are evident on plain CT (arrows). On contrast-enhanced CT (b, c), irregularity of the gallbladder wall and partial lack of contrast enhancement can be seen (arrows) as the characteristic appearance of gangrenous cholecystitis. Transient early-phase staining of the liver parenchyma (b) and edematous changes in the hepatoduodenal ligament (c. arrowhead) are also apparent, suggesting widespread inflammation.

Source: Boland et al. (2013)

### 3.3 Ultrasonography (US)

In patients with suspected acute cholecystitis, US has proved to be the best screening test, as it has greater sensitivity and positive and negative predictive values than CT for the same specificity. In choledocholithiasis, US has high sensitivity (99%) and accuracy (93%) in demonstrating ductal dilatation, but is less reliable in determining the location (60 to 92%) and cause of obstruction (39 to 71%). due to the difficulty in visualizing the distal common bile duct (Rodríguez et al., 2018). The limitation of US in choledocholithiasis is related to several factors, including stones located in undilated bile ducts or in the distal common hepatic duct, absence of bile around the stones, and stones that do not produce a posterior acoustic shadow. CT should not be used as an initial examination, nor for the follow-up of acute cholecystitis in cases where US has provided a positive diagnosis. However, CT should be reserved for cases with nonspecific signs and symptoms when other diagnoses are considered, in the presence of a prior history of biliary disease or to study the complications of acute cholecystitis (Arnot, 2020). Among the signs present in the US, the following stand out:

• Presence of calculation(s). It occurs in 95% of patients. The specificity of the signal is much higher when it is possible to identify an image of a stone fixed to the infundibulum of the gallbladder, immobile when changing decubitus. Stones present as hyperechoic images producing posterior acoustic shadow (Figure 2).

• Ultrasonographic Murphy's sign. It consists of painful compression on the vesicle by the ultrasound transducer. May not be present in cases of gangrenous cholecystitis.

• Gallbladder wall thickening (≥ 3mm). It may be associated with delamination of the wall layers (Figures 2).

• Free perivesicular fluid.

• Increase in the dimensions of the vesicle (longitudinal ≥ 10cm, transversal ≥ 4cm). Little specific. The combination of ultrasonographic signs has the following diagnostic performance: Ultrasonographic Murphy's sign and presence of
gallstones: positive predictive value of 92% and negative predictive value of 95%; gallbladder wall thickening and presence of gallstones: positive predictive value of 95% and negative predictive value of 97%.

Furthermore, the Image demonstrates a rounded hyperechoic image (calculus), producing posterior acoustic shadow, fixed to the gallbladder infundibulum (arrow). Wall thickening (arrowheads) and increased dimensions of the gallbladder (BV) are also observed.

Figure 2 - Acute cholecystitis on US.

Source: Vargas et al. (2016).

3.4 Magnetic resonance cholangiopancreatography

Vesicular calculi, characterized as signal failure, are detected with a sensitivity between 90 and 95%. Small amounts of perivesicular fluid, characterized as a hyperintense signal on T2-weighted images, are seen in 91% of cases of acute cholecystitis, with an accuracy of 89%. Stones in the common hepatic duct or hepatocholedochal duct are detectable with much higher sensitivity than ultrasound and even computed tomography (Arnot, 2020).

3.5 Complications

Among the complications of acute cholecystitis, emphysematous cholecystitis, frequent in diabetic patients, is highlighted, resulting from the colonization of the gallbladder by microorganisms that produce gas, which collects in the lumen and in the gallbladder wall, in addition to hemorrhagic cholecystitis, characterized by hemorrhage. intraluminal, which presents as multiple echogenic images in the vesicle lumen, which do not produce posterior acoustic shadowing. Also, gangrenous or necrotizing cholecystitis, a severe and advanced form of acute cholecystitis, as well as perivesicular abscess, which results from perforation of the gallbladder wall and is seen as a fluid collection with echoes inside, close to the bottom of the gallbladder. In addition, liver abscesses can also occur (González et al., 2019).

Furthermore, acute cholecystitis associated with obstruction by gallbladder cancer, observed in 4% of our cases, has an incidence of 1 to 16% in other series, which increases progressively according to age groups.3 Other factors besides of gallstones can determine acute cholecystitis in specific situations. Acute cholecystitis can occur in both adults and children,
during prolonged parenteral nutrition and/or critical conditions, such as the postoperative period of major operations, multiple trauma and other complications that cause prolonged hospitalization in intensive care. Alithiasic cholecystitis has been attributed to numerous factors that can act synergistically: poor tissue perfusion caused by hypovolemia, sepsis, adrenergic stimulation, atherosclerosis, increased bilirubin concentration in bile caused by hematoma reabsorption, polytransfusion, and dehydration (Sekimoto et al., 2016).

3.6 Treatment

Acute cholecystitis has the removal of the gallbladder as its specific and definitive treatment. Although there are authors who advocate the clinical treatment mentioned above, to proceed with elective cholecystectomy 30 to 60 days later, we are of the opinion that early cholecystectomy is the best procedure, as it not only removes the cause of the process, but also avoids complications almost always. quite serious. The higher incidence of iatrogenic injury at the time of cholecystectomy performed in the acute phase can be avoided with surgical prudence, intraoperative cholangiography and, if necessary, cholecystostomy. For a hundred years, conventional cholecystectomy was the ideal method for the treatment of acute cholecystitis, with excellent results, with the main complications being abdominal wall infection and incisional hernia. Videolaparoscopy has made a great contribution and is now the first option for performing cholecystectomy, with conversion rates below 5%. However, one should not avoid converting to conventional surgery, given the anatomical difficulties, bleeding or exuberant inflammatory process (Yi et al., 2016).

Furthermore, antibiotics with a spectrum for Gram-negatives should be started during preparation for the operation and, depending on the surgical findings and intercurrences, they may be discontinued after the operation or maintained and suitable for cultures of the vesicular contents or the vesicle wall. Randomized studies of antibiotic therapy in acute cholecystitis suggest that antibiotics should be stopped early after cholecystectomy. Currently, morbidity and mortality from the surgical treatment of acute cholecystitis are very low, and are mainly related to the severity of the acute condition and the presence of portal hypertension and systemic complications of advanced age. Other complications also related to the severity of the condition, such as peritoneal infection, pancreatitis and organ failure, are infrequent in both procedures, when analyzing large series, and again reach incidences of up to 40% in series restricted to the elderly. Iatrogenic bile duct injuries in acute cholecystitis occur in approximately 0.1% of cases operated on by laparotomy (Ibrahim et al., 2016).

The incidence of injury with a laparoscopic procedure is similar; on the other hand, the recommendation of all consensuses is not to hesitate to convert the procedure if there is difficulty in identifying structures. Postoperative mortality in the treatment of acute cholecystitis is an infrequent event. The series that refer to deaths are those that analyze specific cases: cirrhotic patients, with portal hypertension, AIDS, alithiasic cholecystitis in critically ill and elderly patients. In short, success in the treatment of acute cholecystitis depends on rapid diagnosis and preoperative care and early indication of surgery. On the other hand, considering that in elective surgeries the mortality observed in several series is null, even when octogenarians are analyzed, and that it can reach up to 13% in octogenarians operated on in an emergency situation, it is recommended that elective cholecystectomy be indicated in elderly patients with of calculations (Silva et al., 2016).

4. Final Considerations

Acute cholecystitis remains a disease that the surgeon frequently encounters. It presents as a surgical emergency and usually requires hospitalization for treatment. It is associated with significant morbidity and mortality, especially in elderly patients. The most frequent cause is lithiasis, responsible for 90% of cases. In the differential diagnosis of acute cholecystitis, inflammatory or non-inflammatory diseases with expression located in the upper right hemiabdomen must be considered. They
are: right-based pneumonia, hepatitis, pyelonephritis, and even myocardial ischemia or infarction. Other diseases of the digestive tract should be kept in mind, such as acute appendicitis of subhepatic location, complicated peptic ulcer and acute pancreatitis.

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