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The Role Of Endoscopic Treatment In Lithiasic Cholangitis

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Abstract
Acute lithiasic cholangitis is a bacterial infection of the biliary tract due to a lithiasic obstruction. It is a therapeutic emergency that can be life-threatening. The aim of our work is to evaluate the results of endoscopic drainage in cases of acute lithiasic cholangitis.
Materials and Methods
This is a descriptive and analytical retrospective study conducted in the Gastroenterology II department of the HMI Med V of RABAT between April 2002 and April 2022 including 207 patients who underwent ERCP for acute cholangitis. We analyzed the epidemiological data of the patients, the results of the ERCP, as well as the morbidity and mortality post-endoscopic sphincterotomy.
Results
The mean age of the patients was 58 years with extremes ranging from 21 to 80 years and a sex ratio of 0.66. Endoscopic biliary sphincterotomy was performed in 91.4% of cases. A nasobiliary drain was placed in 16.1% of cases. The overall success rate of stone extraction was 95.2%. The cure rate at 7 days after ERCP was 92.4%. The overall rate of early post-ERCP complications was 8.5%. The mortality rate was zero.
Conclusion
Endoscopic sphincterotomy has revolutionized the treatment of common bile duct lithiasis and lithiatic cholangitis. It allows good biliary drainage. Its results are satisfactory, with less morbidity and mortality compared to surgical treatment.
Keywords: *Endoscopic sphincterotomy, ERCP, acute cholangitis, Tokyo Guidelines 2018*

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I. Introduction

Acute cholangitis is an inflammation of the bile ducts and bile. It is generally due to an infection of the bile by bacteria from the digestive tract following a sudden obstruction of the bile ducts. This obstruction is most often due (90%) to the presence of one or more stones in the bile ducts and is then referred to as lithiasic cholangitis.

The infection is due to aerobic (E.coli, streptococcus faecalis) or anaerobic digestive germs. Its frequency increases with age and the duration of the biliary disease.

The classic symptoms are represented by the Charcot triad (pain, fever, jaundice) and are only present in 50% of cases, the symptoms being most often dissociated. The diagnosis of cholangitis must be made precisely and quickly in order to be able to start appropriate treatment urgently [1].

Imaging, particularly cholangio-MRI (bili MRI) [2-4], is a key support for etiological diagnosis and therapeutic strategy.

Lithiatic cholangitis is a therapeutic emergency due to the possible progression to potentially fatal septic shock. This severe form of cholangitis is observed in 10 to 15% of patients. Endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic biliary sphincterotomy (ES) [2] constitute a therapeutic option of choice for acute lithiatic cholangitis, especially in patients who have already undergone cholecystectomy and in cases of severe cholangitis [5].

The aim of our study was to evaluate the results of emergency endoscopic drainage of lithiatic cholangitis in terms of stone extraction and improvement of morbidity and mortality.

II. Materials And Methods

A. Method

1. Type of study:

This is a descriptive and analytical retrospective study conducted in the Hepato-Gastro-Enterology II department of the Mohammed V Military Teaching Hospital in Rabat over a period of 20 years between April 2002 and April 2022.

2. Intervention:

ERCP is an interventional endoscopy technique of choice for the management of pathologies of the biliary-pancreatic intersection. It is a technique that combines an endoscopic and radiological time. It is the reference examination in the management of biliary lithiasis complicated by acute cholangitis, especially in elderly patients and/or those at high surgical risk. However, it remains not without short- and long-term complications, which requires a careful and precise choice of indications, and sufficient hindsight to assess long-term complications.

3. Instruments:

The endoscopes and instruments that were used were as follows: A side-viewing duodenoscope; a triple-lumen sphincterotome armed with a hydrophilic or totally hydrophilic tip guidewire, a biliary or esophageal dilatation balloon, a biliary extraction balloon, a Dormia basket, a nasobiliary drain, a lithotriptor and covered plastic or metal prostheses (See Appendix).

4. Ercp Procedure

The procedure involves several stages:

• The first stage is endoscopic: the first step is to perform a duodenoscopy, which allows us to reach the 2nd duodenum and thus locate the papillary orifice.

• Once well positioned in front of the papilla, selective catheterization of the CBD is performed using a sphincterotome armed with a guidewire under scopic control. • Opacification of the CBD by injection of a contrast agent, allowing to evaluate the size of the CBD, and to highlight the stones

• Endoscopic biliary sphincterotomy (EBS) is done using a sphincterotome and using a monopolar section-coagulation current (endocut).

• Extraction of gallstones is done either by using standard maneuvers or sometimes if necessary by additional maneuvers that we will see below.

• A control cholangiography is performed at the end to check the emptiness of the CBD.

• The procedure is completed by washing the CBD with isotonic saline

In case of failure to extract the stones, by the standard technique (use of an extraction balloon or Dormia basket after SBE) additional maneuvers can be used such as: mechanical lithotripsy, sphincteroplasty, extracorporeal lithotripsy. A nasobiliary drain is placed in case of incomplete vacuity of the CBD.

A second extraction attempt is made within 3 to 7 days in patients with a nasobiliary drain. In case of further failure, patients will be referred for surgical treatment.

In elderly patients or those with a contraindication to surgery, a covered plastic or metal prosthesis is placed after failure of the first extraction attempt, it reduces the size of the stones and facilitates their endoscopic extractions thereafter. The initial success rate is defined by the clearance of the CBD at the end of the first catheterization attempt. The overall success rate is defined after the patient has been taken back to work and/or additional maneuvers have been performed.

After ERCP, hospital monitoring was recommended for all patients, in order to detect early complications. It was based on 24-hour clinical monitoring (onset of abdominal pain, particularly epigastric), as well as hemodynamic status (heart rate, blood pressure, and temperature).

The patient was declared discharged in the absence of complications.

A one-month consultation is systematic, including a complete liver assessment and an abdominal ultrasound, in order to detect late complications, particularly residual lithiasis of the main bile duct.

B. Patients:

207 patients were collected for acute lithiasic cholangitis between April 2002 and April 2022.

The positive diagnosis was established according to the diagnostic criteria of Tokyo Guidelines 2018 for acute cholangitis:

Signs of systemic inflammation

1: Fever > 38 °C and / or chills

2: Evidence of an inflammatory response:

* GB > 10,000 or < 4,000 / mm3 or
* CRP > 10 mg / l
Cholestasis
1: Jaundice or Total Bilirubin > 20 mg / l or
2: Abnormal liver function tests:
PAL (IU) > 1.5 * N
GGT (IU) > 1.5 * N
ASAT (IU) > 1.5 * N
ALAT (IU) > 1.5 * N
Imaging
1: Dilation of the airways biliary
2: Evidence of etiology: lithiasis, stenosis, stent, etc.

Tokyo guidelines 2018 (TG18) criteria
• Suspected diagnosis: one item of A + one item of B or C
• Confirmed diagnosis: one item of A + one item of B and one item of C

Patients received intravenous antibiotic therapy (biliary elimination antibiotics, combined with metronidazole or adapted to the results of the antibiogram) and hydro-electrolytic rebalancing in case of ionic disorder.

All patients included in the study received a pre-anesthetic consultation, and they were all hospitalized. They underwent a complete clinical examination and a biological assessment, mainly the hemostasis assessment.

Patients were informed about the course of the examination as well as about possible complications, and all gave their consent for the intervention. The latter was performed in fasting patients, under general anesthesia with intubation in the supine position.

All patients underwent therapeutic endoscopic retrograde cholangiopancreatography (ERCP) with stone extraction either after the first attempt or after the use of additional maneuvers or after the patient had resumed.

1. Inclusion criteria:
-Patients aged > 18 years
-With confirmed acute lithiasic cholangitis.

2. Exclusion criteria:
-Patients with non-lithiasic biliary pathology (tumor or malignant stenosis)
-Patients with a contraindication to endoscopic biliary sphincterotomy (e.g. hemostasis disorder)

C. Data collection:

Data collection was done on the patients' medical records, however the technical part relating to the endoscopic procedure was completed by the operator explaining the different stages of the endoscopic procedure.

The data that were used are: (see appendix for the operating sheet)
1. Demographic data:
-Age
-Sex
-Surgical history (cholecystectomy, CBD surgery, gastroduodenal surgery, history of endoscopic biliary sphincterotomy).
2. Endoscopic data, including the presence or absence of a periampullary diverticulum.
3. Cholangiography data: The size, location, number of stones and CBD diameter were obtained on cholangiography after injection of the contrast agent. The size (long transverse axis) of the stones and the caliber of the CBD were measured using the diameter of the duodenoscope as a reference. It also makes it possible to identify whether or not there is a stenosis or disparity in the caliber of the CBD. The cholangiography data form the basis for the rest of the endoscopic procedure.
4. Primary emptiness of the CBD after use of standard techniques.
5. Secondary emptiness of the CBD after use of additional maneuvers.
6. Presence of early complications: hemorrhage, perforation, acute pancreatitis after ERCP, infection, impaction of the Dormia.

D. Statistical study:

We performed a descriptive statistical analysis including the different demographic, clinical, endoscopic and radiological variables:

a. Qualitative: in number and percentage
*Sex
*History of surgery
*Presence or absence of associated acute pancreatitis.
*Presence or absence of periampullary diverticulum
*Presence or absence of stenosis of the CBD
*Presence or absence of a stone and/or large choledochal stones.
*Initial emptiness of the CBD
*Use of additional maneuvers
*Resumption of patients
*Overall emptiness of the CBD.
*Early complications
b. Quantitative:
*Age (Gaussian distribution: Mean ±standard deviation)
*Diameter of the CBD (Gaussian distribution: Mean ±standard deviation)

Statistical analysis was performed using SPSS software version 24.0

III. Results

I. General Characteristics Of The Population:

A. Frequency:

In our study, the total number of ERCPs performed for gallstones was 1080. The indication for ERCP was acute lithiasic cholangitis in 207 patients, which represents 19.16% of all ERCPs performed.

B. Age distribution:
The mean age was 62.77 ± 13.74 years, with extremes ranging from 21 to 96 years.

C. Sex distribution:

Among the 207 cases of acute lithiasic cholangitis, there were 106 women with a percentage of 51.2% and 101 men for a percentage of 48.8%.
The sex ratio M/F was 0.95.

D. History:

Among the patients included in the study, 19.5% were cholecystometrists, 7.3% had undergone endoscopic biliary sphincterotomy, and 1% had a history of gastroduodenal surgery.

E. Endoscopic data:
Periampullary diverticulum was observed in 19 patients (9.2%)

F. Cholangiography data:
The mean diameter of the CBD was 14.98mm ± 4.5.
A stenosis of the CBD was objectified in 7.7%

96 (46.4%) patients had a simple lithiasis, 64 (30.9%) had a choledochal stone, 26 (12.6%) had a large obstructing stone measuring more than 15mm, and 21 (10.1%) had a choledochal stone associated with a large stone.

II. Therapeutic Procedures Performed And Success Rate:

A. Initial emptiness rate:

The initial emptiness rate of the CBD after using standard maneuvers, namely the biliary dilatation balloon and the Dormia basket is 90.5%
A recovery of the patient was noted in 9.5% of cases.

B. Additional maneuvers:

Additional maneuvers were performed in 32.8% of cases, namely: a nasobiliary drain in 19.3%, a sphincteroplasty in 4.8% of cases. Mechanical lithotripsy was used in 2.9% of cases, the biliary prosthesis was placed in 5.8%.

C. Overall success rate:

The overall success rate after resuming the patient and/or performing the additional maneuvers described above was 97.6%.

III. Early complications:

Early complications post-ERCP during our study were noted in 15 patients (7.3%):

• Eleven patients (5.3%) presented acute pancreatitis post-ERCP.

• Two patients (1%) presented minimal hemorrhage by bleeding from the edges of the sphincterotomy, hemostasis was obtained by endoscopic treatment (pneumatic compression by extraction balloon).

• One patient presented a post-ERCP infection

• One patient presented an impaction of the Dormia basket

IV. Discussion

Angiocholitis is a bacterial infection of the main bile duct or intrahepatic bile ducts causing general signs [19]. This infection almost always complicates an obstruction to the flow of bile. In more than 90% of cases, this obstruction is of lithiatic origin. The infection of the bile is accompanied by an inflammatory thickening of the walls of the extra- or intrahepatic bile ducts. This is an acute inflammation of the walls, reactive to the infection.

Angiocholitis manifests itself in its typical form by the Charcot triad associating: pain like hepatic colic, a high fever of sudden onset, and delayed cholestatic jaundice. This triad is present in its entirety in less than 50% of cases [20]. In the elderly, severe forms are frequent from the outset and result in a picture of septicemia, associating shock and acute renal failure [21], confusional syndrome and disorders of consciousness are frequent in this context and sometimes complicate the diagnosis. Generally speaking, the severe form is observed in 10 to 15% of patients [22].

Multiple liver abscesses are a serious complication occurring in cases of cholangitis that are treated insufficiently or delayed. These data underline the importance of early diagnosis and emergency treatment of acute cholangitis. Early decompression of the biliary tract is considered the priority objective in the management of AAL. The frequency of cholangitis is linked to that of biliary pathology because it constitutes the major complication of choledocholithiasis. It varies from 30 to 40% in CBD stones [23, 24] and represents 6 to 13% of all biliary procedures [23]. In our series, the indication for ERCP was acute lithiasic cholangitis in 6.3% of cases.

Lithiatic cholangitis can occur at any age but more frequently between 50 and 80 years, exceptionally before 20 years [25-34].

The distribution of our patients according to age shows a mean age of 58 years, with extreme ages of 21 and 95 years, which is close to thes reported by most authors. The frequency of cholangitis in relatively younger people in Maghreb series (MOUMEN, ABARRAH, FARIH) can be explained by the diet, in particular a diet rich in lipids and low in fiber.

In the series reported in the literature, there is a female predominance of acute lithiasic cholangitis. This most likely follows that of gallstones.

It is probably linked to the influence of hormonal disturbances in genital life, particularly pregnancies [37]. MOUMEN and colleagues reported in their series 82% women and 18% men. In the study by LAURU et al [38] there were 86% women and 14% men.

In our series, the patients are divided into 63 women (60%) and 42 men (40%), with a sex ratio of 0.66.

The frequency of biliary history in patients with cholangitis is described in the literature. The incidence of cholangitis increases in patients who have undergone biliary surgery, endoscopy procedures, or known carriers of gallstones [39]. Surgical history mainly cholecystectomy was found in 43.3% of our patients. On the other hand, only 16.2% of patients had a gallstone gallbladder.

The diagnosis of AAL is based on clinical, biological and morphological arguments. The role of imaging in the diagnosis and management of patients suspected of cholangitis is essential [1]. Ultrasound remains the first-line examination in patients suspected of cholangitis of lithiasic origin. Unfortunately, dilation of the bile ducts is not always present in the acute phase and the performance of ultrasound to detect stones in the main bile duct is poor.

Non-enhanced CT scans, with thin-slice acquisitions, are more sensitive than ultrasound for detecting lower bile duct stones. However, they are less effective than MRI cholangiography, which, along with endoscopic echography, is the most sensitive technique for detecting lower bile duct stones [40]. MRI cholangiography uses specific sequences that produce a clear hyperintensity of all stationary fluids. No injection of contrast agent is necessary to visualize the bile ducts. The images provided by MRI cholangiography are very similar to those obtained by direct cholangiography, but obtained in a completely non-invasive manner. On thick slices, bile duct stones are visualized as a more or less hypointense area within the bile. The main limitation of cholangio-MRI lies in the diagnosis of mini-lithiasis (less than 3 mm) and that of stones enclosed at the level of the ampulla of Vater. Echo-endoscopy is a semi-invasive technique that has demonstrated its effectiveness in the diagnosis of

lesions of the head of the pancreas and the exploration of extra-hepatic biliary obstacles. Echo-endoscopy offers a spatial resolution significantly lower than a millimeter. It is thanks to this exceptional spatial resolution that echo-endoscopy will be able to detect mini stones invisible to other imaging techniques with a sensitivity varying between 95 and 100% and a specificity close to 100% [41].

In terms of therapy, all patients with ALA regardless of the severity of the cholangitis, should receive antibiotic therapy. Empiric antibiotic therapy should include broad-spectrum antibiotics with high biliary excretion and will be adapted according to the results of blood cultures and biliary samples.

The biliary concentration of antibiotics decreases sharply (up to 20% of the serum concentration) in the presence of biliary obstruction and the reason why some patients do not respond to medical treatment without urgent biliary decompression.

Endoscopic biliary drainage is the procedure of choice for biliary decompression in case of ALA. ERCP is associated with significantly lower morbidity and mortality than surgical decompression. In a randomized controlled trial comparing surgical decompression vs. endoscopic decompression in patients with LAA, the morbidity and mortality rate was significantly higher in the surgically treated group [42].

In our series, the initial success rate of endoscopic treatment of LAA in terms of CBD clearance was 90.5% and the overall rate after the use of complementary maneuvers or patient recovery was 95.2%. This success rate varies in the literature from 81.4% to 100% [43].

In our series, the rate of healing of LAA within 7 days following endoscopic treatment was 92.4%. In the literature, this rate varies from 92 to 94% [44].

Several studies have studied the interest of SBE in the early treatment of AAL, two well-documented and randomized series are particularly interesting:

In the study of Lai [45] which included 111 patients, 50 patients benefited from SBE while 61 patients did not receive any endoscopic treatment, there was a significant difference in the duration of fever between the "SBE" group and the "control" group "mean duration: 3.2 vs 4.3 days", the duration of hospitalization was shorter in the "endoscopic treatment" group "mean duration 8.1 (3.0) vs 9.1 (3.2) days).

In the study of Leese et al [46] which included 71 patients and which compared the mortality rate of surgical decompression vs endoscopic biliary sphincterotomy. Surgical treatment was associated with a significant increase in mortality (6/28) compared to that linked to SBE (2/43). In our series, endoscopic sphincterotomy was performed in 91.4% of cases . This frequency varies in the literature from 86% to 100% [47-52].

The analysis of the results of the different trials allows us to conclude that early EBS has a real benefit in reducing the duration of acute cholangitis, the duration of hospitalization, but also the incidence of cholangitis recurrences, with a mortality rate lower than that of surgery. The aim of endoscopic sphincterotomy is to allow the extraction of stones and decompression of the biliary tract. In favorable cases and especially in the case of small stones or biliary sludge, the evacuation of stones occurs spontaneously under the effect of bile flow (58.5% for Safrany et al [53]). But most often, the use of extractors, in particular the basket catheter (Dormia catheter) or balloon catheter is necessary (32% for the same author).

In the case of severe cholangitis with hemostasis disorders, simple temporary endoscopic biliary drainage without EBS is recommended [54]. This biliary drainage can be performed by placing a DNB or a plastic biliary prosthesis. Both drainage methods have similar technical and clinical success rates [44].

In the study by Zhang et al [55], nasobiliary drainage allowed a reduction in mortality rates from 30% to 10%. Generally speaking, nasobiliary drainage is indicated, in addition to cases of hemostasis disorders, whenever the emptiness of the biliary tract is uncertain or there is a risk of superinfection of the bile. It allows the control of the decompression of the biliary tract and the repetition of cholangiographic examinations if necessary [56]. In our series, DNB was set up in 16.1% of cases.

Endoscopic retrograde cholangiopancreatography (ERCP) has changed the management of pathologies of the biliary-pancreatic junction in recent years. However, this examination is not trivial and carries a significant operative risk, hence the importance of evaluating early complications in order to prevent them [57,58]. Early complications of ERCP are those occurring within 30 days of the procedure.

The criteria for defining early complications of ERCP have long been problematic. However, the classification established by Cotton [59,60] in 1994 is currently considered the reference for definition.

Many prospective multicenter studies have evaluated the risk of endoscopic sphincterotomy [61,62]. While other studies have been devoted mainly to the prevention of the main complication of ERCP, which is acute pancreatitis (AP) [63,64].

The results of ES depend above all on the experience of the operator [65].

A multicenter survey of 3853 procedures showed a rate of 7% of immediate complications and 6.4% of distant complications.

For Freeman, the complication rate was 9.75% [61]. In our series, the overall complication rate was 8.5%. Some of these complications are not specific to the technique, but related to the terrain. They are observed in 4% of cases, and lead to the death of the patient in ¾ of cases, or 3% of patients [65].

They are closely related to age: from less than 1% before 60 years, to 6.5% beyond 80 years [65], excluding non-specific complications.

The main complications of biliary catheterization with SBE are represented in order of frequency by: AP, hemorrhage, biliary infection and perforation [70].

The landmark study by Freeman et al [61] involving 2347 patients showed that post-sphincterotomy bleeding is significantly higher in patients with acute cholangitis even in the absence of coagulopathy.

In our series, among the 6 concomitant bleedings at SBE, or 5.7%, none corresponded to a true hemorrhage according to Cotton's definition. It was a minimal bleeding of the banks that was controlled by pneumatic compression.

V. Conclusion

Acute lithiasic cholangitis is an infection of the bile following an obstruction of the main bile duct. It is a therapeutic emergency due to the possible progression to a potentially fatal septic shock, and therefore requires rapid intervention and management combining:

-Appropriate medical treatment and

-Effective biliary unblocking

Endoscopic biliary drainage is currently the treatment of choice for AAL, allowing both rapid decompression of the biliary tract, optimization of antibiotic therapy and removal of the lithiasic obstruction. In our series, endoscopic treatment of AAL led to clearance of the CBD in 97.6% with an overall complication rate that remains acceptable and far lower than that of surgical decompression.

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