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Review Article

### SURGICAL APPROACHES TO GALLBLADDER DISEASES; A SYSTEMATIC REVIEW OF RECENT LITERATURE

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#### Abstract:

**Introduction:** One of the major, most common health issues in the United States, Europe, and around the world is gallbladder disease. About 6.3 million and 14.2 million, men and women, respectively, suffer from a gallbladder disease in the United States alone. Most patients who have gallstones stay asymptomatic for a long time. However, it is still important to address their disease, and prevent it from turning into a symptomatic disease.

**Aim of work:** We will discuss the most recent approaches to gallstone disease treatment, and we will focus on surgical approaches to symptomatic and complicated gallstone disease.

**Methodology:** We conducted a systematic comprehensive search in literature review using Medline, Pubmed, and Embase. We used the terms gallbladder disease, gallbladder stones, gallstones, surgical approaches, laparoscopy, and cholecystectomy as search items.

**Conclusions:** About three quarter of gallstone cases are classified as cholesterol gallstones. Risk factors for developing cholesterol gallstone disease include older age, female sex, pregnancy state, insulin resistance, obesity, decreased physical activity, use of oral contraception, and diabetes mellitus type 2. The definitive treatment for gallstones disease is surgical cholecystectomy. Laparoscopic cholecystectomy was primarily introduced in the year 1985 and led to significant advance in the management of gallstone disease. Since then, it has replaced open cholecystectomy and became the standard surgical approach in the treatment of gallstone disease, due to its safety and cost-effectiveness. Open cholecystectomy could be used in patients who cannot undergo laparoscopic cholecystectomy, or who have severe gallbladder disease. Other options include percutaneous cholecystectomy, and endoscopic drainage.

**Keywords:** gallbladder, gallstones, cholecystectomy, laparoscopy.

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**INTRODUCTION:**

One of the major, most common health issues in the United States, Europe, and around the world is gallbladder disease. Of gallbladder diseases, the most common one is gallstone disease which has a prevalence that could reach 15% of the general population [1]. In the United States alone, and based on the National Health and Nutrition Examination survey, about 6.3 million and 14.2 million, men and women, respectively, suffer from a gallbladder disease [2]. In addition to high prevalence, gallbladder diseases have significantly high costs, especially when complications occur requiring surgery [3]. Moreover, gallstones [especially cholesterol type] have strong association with metabolic syndrome, hyperinsulinemia, dyslipidemia, and diabetes mellitus type 2 [1]. Therefore, it is essential to continuously conduct clinical research and trials in order to improve treatment and management of gallbladder disease and decrease its incidence and prevalence.

Most patients who have gallstones stay asymptomatic for a long time, or even never suffer from symptoms. However, it is still important to address their disease, and prevent it from turning into a symptomatic disease. For individuals who have risk factors of gallbladder disease, primary prevention is crucial and has been found to significantly decrease the incidence and severity of a symptomatic gallstone disease. Primary prevention measures of the disease are somewhat similar to those of metabolic syndrome. In addition to primary prevention, proper management and treatment of gallstones disease will lead to significant reduction of severe complications, and thus significant reduction in treatment costs [3]. In this review, we will discuss the most recent approaches to gallstone disease treatment, and we will focus on surgical approaches to symptomatic and complicated gallstone disease.

**METHODOLOGY:**

We did a systematic search for gallbladder disease and surgical approaches using PubMed search engine [<http://www.ncbi.nlm.nih.gov/>]. EMBSE and Google Scholar search engine [<https://scholar.google.com/>] from January 1997 to March 2018. All relevant studies were retrieved and discussed. We only included full articles. The following search terms were used: gallbladder disease, gallbladder stones, gallstones, surgical approaches, laparoscopy, and cholecystectomy.

The study was approved by the ethical board of King Abdulaziz University.

**Classification of gallstones:**

About three quarter of gallstone cases are classified as cholesterol gallstones. These include pure cholesterol stones and mixed cholesterol stones. Pigment gallstones, on the other hand, contain calcium bilirubinate, and can be black [about 20% of gallstone cases] or brown [about 4.5 of gallstone cases] [1].

Risk factors for developing cholesterol gallstone disease include older age, female sex, pregnancy state, insulin resistance, obesity, decreased physical activity, metabolic syndrome, diet that has high concentrations of cholesterol, exogenous estrogen, use of oral contraception, dyslipidemia, and diabetes mellitus type 2 [4]. Most of these risk factors are in fact risk factors of metabolic syndrome and insulin insensitivity. A proposed mechanism for this is that the role of insulin insensitivity in altering cholesterol homeostasis and the motility of gallbladder [5].

On the other hand, pigment gallstones are a result bilirubin dysregulation that could be caused by cirrhotic liver, hemolysis of RBCs, cystic fibrosis, inflammatory bowel diseases, resection of the ileum, infections of the biliary tract, folic acid or vitamin B12 deficiency, along with other causes that lead to any dysfunction in the metabolic mechanisms of bile and bilirubin [6].

**Diagnosis and surgical approaches to gallbladder disease:**

Gallbladder disease can remain asymptomatic in most cases. These asymptomatic cases are most likely to remain undiscovered or to be incidentally discovered. Mild symptomatic cases will lead to some colic pain. Otherwise, gallbladder disease is detected when complications occur [1]. Patients who have an asymptomatic disease, have a 1% chance of developing symptoms per year, and a 10% chance of developing symptoms within five years. However, as soon as the symptoms start to appear, the patient will likely suffer from a chronic recurrent symptomatic disease. Risk of complications remains to be relatively low. Therefore, asymptomatic low-risk patients are usually expectantly managed.

Techniques that are generally used in the detection and diagnosis of gallstones include ultrasound, CT imaging, MRCP imaging, and cholescintigraphy. Plain films are of limited value, and are only useful when there is calcification. Following the visualization of the stone, ERCP is usually indicated to drain the bile ducts [7]. Prophylactic cholecystectomy could be indicated to asymptomatic patients who have high risk of developing

complications, cancer, or pancreatitis [8]. Examples of these patients include patients who develop asymptomatic gallstone disease secondary to sickle cell disease [8].

Symptomatic patients will usually suffer from colic pain along with dyspepsia, vomiting, flatulence, nausea, heartburn, bloating, belching, and regurgitation. However, most of these symptoms are not specific to gallstone disease [9]. Therefore, imaging techniques must be used to confirm or exclude the diagnosis. The first step when dealing with a suspected gallbladder disease is to perform an abdominal ultrasound [7].

Mild cases can be treated symptomatically using non-narcotic analgesics [10]. The definitive treatment for symptomatic disease is elective cholecystectomy [11]. Open cholecystectomy is considered less safe and less cost-effective when compared with laparoscopic cholecystectomy, making the later the preferred choice [12].

However, laparoscopic cholecystectomy is sometimes associated with fatal complications. These occur when there is hard dissection within the Callot's triangle. In these cases, laparoscopy must be immediately converted to open cholecystectomy [13]. Performing cholecystectomy within a day of diagnosis has been found to be associated with significant decrease in later comorbidities. Similarly, it is recommended to perform cholecystectomy within 2-3 days following acute cholecystitis and 2 days following acute pancreatitis [14]. Laparoscopy is always recommended as the first surgery choice unless there is a contraindication [severe cirrhosis, coagulopathy, gallbladder malignancy, pregnancy...], where open cholecystectomy become the preferred safer choice to perform [14].

Despite its major role in decreasing the complications and morbidities associated with gallbladder disease, cholecystectomy is also associated with some risk of developing long-term metabolic symptoms. A recent large Korean study that included more than 17,000 patients concluded that cholecystectomy [regardless of the cause] significantly increases the risk and predisposes to the development of non-alcoholic fatty liver disease [15].

#### **Laparoscopic Surgical Approaches to Cholecystectomy:**

Laparoscopic cholecystectomy was primarily introduced in the year 1985, when it led to significant advance in the management of gallstone disease. Since then, it has replaced open cholecystectomy and

became the standard surgical approach in the treatment of gallstone disease, due to its safety and cost-effectiveness [16]. Moreover, it became the standard treatment for asymptomatic and non-complicated gallbladder disease. In fact, most recent guidelines recommend performing laparoscopic cholecystectomy as soon as a diagnosis of gallbladder disease is made, as this is associated with significantly better outcomes than medical and pharmacological therapy [17].

Recently, a large clinical trial was conducted on patients with acute cholecystitis, and found that performing laparoscopic cholecystectomy early following the diagnosis was associated with a significant decline in morbidities rates, duration of hospitalization, and costs of treatment [18]. In addition, laparoscopic cholecystectomy was found to be associated with a relatively safe profile with very few adverse events. However, risk of injury to bile-duct remains higher in laparoscopic cholecystectomy when compared to open cholecystectomy [17].

In cases where there is significant inflammation in the gallbladder, dissection could become more challenging, leading to increased risk of laparoscopy-related ducts injury. Therefore, surgeons should always be open to converting into open cholecystectomy when there is difficult dissection and high risk of injuring the bile ducts. Moreover, they should avoid dissection in cases where the anatomy is significantly disrupted [17].

Based on the previously mentioned information, laparoscopic cholecystectomy remains the first choice of surgery, that could be, in selected cases, converted to open cholecystectomy.

Recent efforts have been attempting to further decrease risks associated with laparoscopic cholecystectomy. These efforts include minimizing surgical trauma that is done to the abdominal wall by using a smaller number of smaller ports for the laparoscopes. One of the techniques is to perform a laparoscopic cholecystectomy with a single-incision, where only a single big surgical instrument is used through the umbilicus. This surgical approach has been found to only leave a periumbilical scar, which is considered better than the four-incision approach. Moreover, some authors claim that the single-incision approach is associated with better cosmesis, less postoperative pain, shorter recovery time, and less rates of wound infections. However, these later advantages are yet to be proven [19]. Risk of developing hernias postoperatively remains to be significantly higher following laparoscopic

cholecystectomy when compared to open cholecystectomy [17].

To further decrease risk of adverse events following laparoscopic cholecystectomy, the mini-laparoscopic surgical approach was introduced. This approach uses instruments through very small ports [less than 5 mm] leading to improved cosmesis. However, other advantages of this approach are not proven yet [20]. Both mini-laparoscopic cholecystectomy and single-incision laparoscopic cholecystectomy have been found to significantly improve outcomes and reduce the risk of adverse events. However, they are still not considered preferred to ordinary laparoscopic cholecystectomy. The reason behind this is the hard, advanced techniques which make these procedures hard to be learnt and performed by surgeons. Moreover, both approaches have higher costs and require longer time of operation, making it necessary to perform studies on their cost-effectiveness [20]. The same reasons are also why robotic-assisted approaches in performing laparoscopic cholecystectomy have not become the standard surgical approaches for cholecystectomy. In fact, robotic-assisted approaches lack sufficient evidence to prove being superior to ordinary standard laparoscopic cholecystectomy, and have significantly higher costs [20].

#### **NOTES Cholecystectomy:**

The NOTES technique is a surgical approach where cholecystectomy is done through a natural orifice, thus preventing the development of a post-operative scar. NOTES cholecystectomy was introduced in the year 2007 [21]. NOTES is usually performed through vaginal or gastric access using endoscopes [could be either rigid or flexible]. Endoscopes could be used alone or together with laparoscopic techniques, which is called hybrid NOTES [22].

The main difference between NOTES cholecystectomy and laparoscopic cholecystectomy is the avoidance of creating an abdominal wall incision. This can dramatically reduce the risk of pain and wound infections post-operatively. Being a relatively new and advanced approach, NOTES cholecystectomy have only been performed on a few thousands of patients, most likely through the vagina, and with the absence of acute cholecystitis [22]. Studies on NOTES cholecystectomy have concluded that NOTES approach could lead to significantly less duration for recovery, decreased pain, and better outcomes, when compared to standard laparoscopic cholecystectomy [23]. There has been some concerns on the possible effects of transvaginal NOTES on later sexual functions of the patient. However, studies

have concluded that transvaginal NOTES did not negatively impact sexual functions [24]. In addition, transvaginal NOTES cholecystectomy was not associated with development of fistulas.

Despite all these advantages and improved safety, the use of NOTES cholecystectomy has not become the standard treatment for performing cholecystectomy due to its high costs, limited availability, requirement of advanced techniques, and needing high experience [22].

#### **Percutaneous Cholecystostomy:**

It was in the year 1980 when percutaneous cholecystostomy surgical approach was first introduced. Percutaneous cholecystostomy technique uses punctures to the gallbladder with guidance with ultrasound or CT imaging. This will then be followed with a pigtail catheter placement [25]. Reports suggest that percutaneous cholecystostomy could resolve symptoms of acute cholecystitis in up to ninety percent of patients. The main indication of percutaneous cholecystostomy is acute cholecystitis that require cholecystostomy in patients who cannot undergo laparoscopic cholecystostomy. Reasons for this could be anesthesia intolerance, complicated cholecystitis, late presentation after more than three days of symptoms onset, or poor response to medical treatment [25].

Performing external drainage of the bile duct also gives time for the inflammation to resolve locally, leading to a significant reduction in the risk of needing open cholecystectomy [25].

Adverse reaction following percutaneous cholecystostomy can develop in about 25% of patients. Most commonly, the catheter can dislodge within weeks following the procedure, which could result in the development of peritonitis. Moreover, the use of cholecystostomy tubes has been linked to poor quality of life, and decreased satisfaction [26]. The catheter could be electively removed when the tract becomes mature [after about 3-6 weeks], and when the physician makes sure that the cholecystitis has resolved [25].

Recently, percutaneous cholecystostomy has been being used more recently than before. Up to 2.9% of procedures on patients with gallbladder disease in 2009 were percutaneous cholecystostomy [27]. However, up until now, no clinical trials have been conducted to compare the efficacy of percutaneous cholecystostomy in cases of cholecystitis.

**Peroral Endoscopic Gallbladder Drainage:**

There are several ways to establish gallbladder endoscopic drainage. These include the transpapillary route, and the transmural route. The transpapillary route passes through the Vater papilla using ERCP, whereas the transmural route uses endoscopic ultrasound to guide direct passage into the gastrointestinal tract [28]. Both these procedures can be considered similar to percutaneous cholecystostomy. However, there are still significant differences between the them, mainly regarding the diameter of the tube, the design of the tube, and the suction capacity. In patients where both laparoscopic cholecystostomy and percutaneous cholecystostomy are contraindicated, endoscopic draining procedures are indicated [29].

**Transpapillary Endoscopic Drainage:**

This procedure was primarily introduced more than 30 years ago. It can be simply summarized as cannulating the bile duct using ERCP techniques. This is achieved by passing a wire within the cystic duct to reach the bladder. According to previous reports, transpapillary endoscopic drainage can achieve complete resolution of acute cholecystitis in up to 90% of patients [30]. It is considered to provide definitive treatment of acute acalculous cholecystitis. However, it will still require performing another endoscopic operation for stent removal when the disease resolves. Another indication for transpapillary drainage is the facilitation of tube removal following a percutaneous cholecystostomy. It can also be performed in symptomatic cholelithiasis patients who have contraindications for a percutaneous procedure. Examples of these patients include patients with ascites, advanced cirrhosis, or untreated coagulopathy [30].

However, limitations of gallbladder transpapillary drainage including technical challenges that require strong experience, especially when the cystic duct is narrow, tortuous, long, and/or occluded with stones [31].

**Transmural Endoscopic Drainage:**

Transmural drainage of the gallbladder using endoscopic ultrasound guidance was produced in 2007 and is considered now the most advanced alternative to the use percutaneous cholecystostomy [32]. Anatomically, the gallbladder opposes the gastrointestinal organs closely. This approach depends on the use of Doppler imaging to avoid damaging vessels while passing to the gallbladder. Then, a wire is passed to enter the bladder and allow for catheters for drainage. This procedure has been found to achieve high efficacy in more than 95 of

patients with acute cholecystitis. However, no enough clinical trails have been conducted on it. Moreover, it is still controversial whether this technique could be used in patients who have chronic gallbladder disease, or patients who suffer from advanced cirrhosis [33].

**CONCLUSIONS:**

Gallbladder disease is considered to be one of the most common diseases that are encountered by physicians almost every day. It is associated with significant costs on the society making its prevention and proper treatment important to decrease these costs. Most patients with gallstones remain asymptomatic for long period of times before they are either diagnosed incidentally or develop symptomatic disease. Asymptomatic and mild disease can be treated medically and symptomatically. However, it is recommended to perform surgery as early as possibly following diagnosis. Cholecystectomy is the only definitive treatment of gallstones. Early cholecystectomy, even in asymptomatic disease, has been found to significantly improve outcomes, and decrease risks of complications and long-term morbidities. When considering cholecystectomy, laparoscopic cholecystectomy is considered to be the first choice that achieves the highest efficacy, with the best safety profile, and highest cost-effectiveness. Open cholecystectomy could be used in patients who cannot undergo laparoscopic cholecystectomy, or who have severe gallbladder disease. Other options include percutaneous cholecystectomy, and endoscopic drainage.

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