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Gallbladder Polyps: Benign Bystanders or Malignant Precursors? Defining the Path from Detection to Treatment

ABSTRACT

Gallbladder polyps (GP) are defined as elevations of the gallbladder wall that project into the lumen. They are commonly detected incidentally during abdominal ultrasonography and are predominantly asymptomatic. Based on their malignant potential, gallbladder polyps are broadly classified into neoplastic and non-neoplastic types. Although most cases remain clinically silent, some patients may present with right upper quadrant pain, localized tenderness, and, in certain instances, a palpable mass in the upper abdomen. Abdominal ultrasound (US) remains the primary modality for both diagnosis and surveillance of GP. In general, a polyp size of ≥ 10 mm serves as a key threshold for considering cholecystectomy.

Keywords: *gallbladder, cholecystectomy, neoplastic, polyps, ultrasound (US)*

ABSTRAK

Polip kantung empedu (GP) adalah elevasi dinding kantung empedu yang mengalami protusi ke dalam lumen kantung empedu, sering ditemukan secara tidak sengaja pada saat pemeriksaan ultrasound abdomen, dan kebanyakan bersifat asimtomatik. Polip kantung empedu dibagi menjadi neoplastik dan non neoplastik berdasarkan kemampuannya untuk menjadi suatu lesi keganasan. Walaupun kebanyakan tidak bergejala, beberapa pasien bisa merasakan nyeri perut kanan atas, nyeri tekan, hingga pada kasus tertentu dapat teraba massa di bagian kanan atas abdomen. Pemeriksaan ultrasound (US) abdomen adalah pilihan utama untuk mendiagnosis dan follow up GP. Secara garis besar ukuran polip ≥ 10 mm menjadi acuan untuk dilakukan tindakan kolesistektomi.

Katakunci : *kantung empedu, kolesistektomi, neoplastik, polip, ultrasound (US)*

INTRODUCTION

Gallbladder polyps (GP) are defined as elevations of the gallbladder wall that project into the gallbladder lumen. These lesions may present as either sessile or pedunculated forms and are characterized by their immobility and absence of acoustic shadowing, features that help distinguish them from gallstones.^{1,2} Gallbladder polyps are frequently detected incidentally during abdominal

ultrasonography, with a reported prevalence of approximately 4–7%, and are most often asymptomatic.²

Gallbladder polyps can be classified into neoplastic and non-neoplastic types based on their histopathological characteristics. Neoplastic polyps include malignant lesions, such as adenocarcinomas, as well as premalignant conditions like adenomas. In contrast, non-neoplastic polyps comprise entities such as cholesterol polyps, adenomyomatosis, and inflammatory polyps.³

Several risk factors have been associated with gallbladder polyps, including obesity, dyslipidemia, and metabolic syndrome. Male sex, low high-density lipoprotein (HDL) levels, and age ≥ 60 years are linked to an increased likelihood of polyps measuring greater than 5 mm.⁴ This review aims to enhance clinical awareness and inform appropriate management strategies for patients with gallbladder polyps.

PREVALENCE AND RISK FACTOR

Most GP are incidentally detected during abdominal ultrasonography. In the United States, the reported prevalence ranges from approximately 4% to 5.6%. One study identified 734 cases of GP diagnosed by ultrasound among 15,835 cholecystectomy specimens collected between 2007 and 2020.⁵ In Qatar, the prevalence of GP was reported at 7.4%, comprising 4.2% solitary and 3.2% multiple polyps, with a comparable distribution between males (7.7%) and females (7%).⁶

A population-based study in Korea reported a prevalence of 6.3% between 2002 and 2012, with a notable increase from 2.9% in 2002 to 8.5% in 2012.⁷ A meta-analysis further identified several risk factors associated with GP in East Asian populations, including male sex, high body mass index (≥ 25 kg/m²), increased waist circumference, higher diastolic blood pressure, elevated low-density lipoprotein (LDL) levels, low HDL levels (< 50 mg/dL in women and < 40 mg/dL in men), and positive hepatitis B surface antigen (HBsAg).⁸

PATHOPHYSIOLOGY AND CLASSIFICATION

The term *true neoplastic polyps* refers to lesions with malignant potential, encompassing both adenomas and adenocarcinomas. In contrast, the majority of GP are non-neoplastic pseudopolyps, which lack malignant potential and include cholesterol polyps, inflammatory polyps, hyperplastic polyps, and focal adenomyomatosis.⁴

Cholesterol (pseudo) polyps account for approximately 60–90% of cases and are thought to arise from the deposition of cholesterol or bile salts within the gallbladder wall, often in association with chronic cholecystitis. Inflammatory polyps represent around 5–10% of cases and are linked to inflammation involving the gallbladder mucosa and wall. Both cholesterol and inflammatory polyps are typically smaller than 1 cm and are frequently multiple. True adenomatous polyps are neoplastic, relatively uncommon, and are often associated with gallstones. Adenomyomatosis, although more commonly encountered, is also considered a true lesion with potential premalignant features.⁹

Several studies have demonstrated that a polyp size ≥ 1 cm is associated with an increased risk of adenoma, and this threshold is commonly used as an indication for cholecystectomy.¹⁰ The distinguishing features between neoplastic and non-neoplastic polyps are summarized in Table 1 and Table 2.

Table 1. Nonneoplastic Gallbladder Polyps¹¹

Nonneoplastic polyp	Mean size (mm)	Radiologic finding	Pathologic finding	Number (single/multiple, %)	Frequency (%)
Cholesterol polyp	< 10	US: hyperechoic polyp, typically round shape with "ball on the wall" sign	Grossly, yellow appearance, microscopically, distinctive cauliflower configuration and cholesterol-laden macrophages	Single (36.4) Multiple (63.6)	60–90
Inflammatory polyp	< 10	US: variable echogenicity (iso-, hypo-, or hyper-)	Pseudopapillary fronds with reactive mucosal changes, inflammation, and increased vascularity	Usually multiple	10
Adenomyoma	NA	US: wall thickening with "comet tail" MRI: "pearl necklace" sign of by fluid containing diverticula	Trabeculated appearance cystic dilation of glandular spaces (Rokitansky-Aschoff sinuses) and smooth muscle hypertrophy	Usually single	25–40
Fibromyoglandular polyp	4.3 (2–13)	NA	Broad-based polyps Lobular units of small glands Fibroblastic and/or muscular stroma	Single (56) Multiple (44)	48
Hamartoma	NA	NA	NA	NA	Very rare

US, ultrasonography; MRI, magnetic resonance imaging; NA, not available.

Table 2. Neoplastic Gallbladder Polyps¹¹

Neoplastic polyp	Mean size (mm)	Radiologic finding	Pathologic finding	Number (single/multiple, %)	Frequency (%)
Benign tumor					
Epithelial tumor					
Adenoma	7 (5–20)	US: isoechoic sessile or pedunculated	Sessile or pedunculated benign glandular structures	Mainly single	4–8.9
ICPN with low- and high-grade intraepithelial neoplasia	> 20	NA	A distinct polypoid mass, intraluminal papillary growth, with low- and high-grade dysplasia	Single (82) Multiple (18)	0.5–0.8
Mesenchymal tumor					
Leiomyoma/lipoma	NA	NA	NA	NA	NA
Malignant tumor					
Epithelial tumor					
Adenocarcinoma	> 10	US: a wide polyp base, thickening of wall (> 3 mm), a polypoid mass projecting intraluminally	Mainly papillary form; densely cellular papillary fronds protruding into the lumen, with infiltrative growth	Mainly single	0.6–1.7 (80% of gallbladder malignancy)
ICPN with associated invasive carcinoma	> 20		Intraluminal growth; mainly papillary growth pattern and stromal invasion	Single (78) Multiple (22)	0.5–0.8
Mesenchymal tumor					
Leiomyosarcoma	NA	NA	NA	NA	< 0.1 (1%–2% of gallbladder malignancy)

US, ultrasonography; ICPN, intracholecystic papillary neoplasm; NA, not available.

DIAGNOSIS

Most cases of GP are asymptomatic. However, some patients may present with right upper quadrant abdominal pain, food intolerance, bloating, nausea, a positive Murphy's sign, and tenderness on palpation of the right upper abdomen. The intensity of right upper quadrant pain may increase with larger adenomatous lesions, and in certain cases, a palpable mass may be detected.⁹

Ultrasound (US)

Abdominal US is the primary modality for both diagnosis and follow-up of gallbladder polyps.¹ The examination is typically performed in the supine position, with or without additional decubitus positioning. Characteristic findings include a hyperechoic lesion projecting into the gallbladder lumen, without posterior acoustic shadowing, and remaining fixed despite changes in patient position.¹¹ Differentiating benign from malignant polyps using US alone can be challenging, and lesions are generally detectable when they exceed 5 mm in size.¹² Small gallstones or biliary sludge (<5 mm) may occasionally mimic polyps on imaging.¹¹

Additional imaging modalities, such as contrast-enhanced ultrasound and endoscopic ultrasound (EUS), may be utilized in specialized centers for challenging cases but are not routinely recommended.¹ Endoscopic ultrasound has a reported sensitivity of 91.7% and specificity of 87.7% for diagnosing carcinoma.¹¹ Furthermore, contrast-enhanced harmonic EUS (CEH-EUS) can aid in distinguishing adenomas from cholesterol polyps, with a sensitivity of 75% and specificity of 66.6%.^{13,14} The presence of an irregular vascular pattern further improves diagnostic performance, increasing sensitivity and specificity to 90.3% and 96.6%, respectively.¹⁴

Other Modalities

Other imaging modalities, including computed tomography (CT), fluorine-18 fluorodeoxyglucose (¹⁸F-FDG) PET-CT, and magnetic resonance imaging (MRI), are generally employed to improve diagnostic accuracy in cases suspected of gallbladder malignancy or for cancer staging. Computed tomography has relatively low sensitivity for detecting small polyps and is more commonly used in the preoperative evaluation of suspected gallbladder cancer.¹¹

Computed tomography is not reliable for distinguishing between true and pseudopolyps, is not suitable for long-term surveillance, and does not offer superiority over US.¹⁵ The literature on gallbladder polyp detection using CT or MRI remains limited. Polyps are more likely to be identified on non-contrast CT when they exceed 15 mm in size, exhibit a sessile morphology, and raise suspicion for malignancy. Only about 45% of polyps larger than 5 mm are detected on non-contrast CT; however, detection rates may approach 100% with the use of contrast enhancement.¹⁶

TREATMENT

A systematic review has reported that polyps measuring <10 mm may still harbor malignant potential; however, the available data are limited, and a definitive association between small polyp size and malignancy cannot be established. Most malignant cases are observed in polyps >10 mm.¹⁷ An observational study further suggested that a 10 mm threshold alone may not be sufficient as an indication for cholecystectomy, as only approximately 56.4% of such cases were found to be neoplastic.³

Although several studies have proposed higher thresholds (12–15 mm), these have not demonstrated stronger evidence; therefore, a 10 mm cutoff remains the standard for considering cholecystectomy.¹ Surgical removal of the gallbladder is recommended for patients with polyps

≥ 1 cm, with or without gallstones, provided the patient is fit for surgery and consents to the procedure.^{1,10} Cholecystectomy should also be considered in symptomatic patients when no alternative cause for the symptoms is identified, assuming the patient is suitable for surgery.¹

In patients with primary sclerosing cholangitis (PSC), there is a higher incidence of malignant lesions and intraepithelial neoplasia; therefore, cholecystectomy is recommended even for polyps < 1 cm.¹⁰ Additionally, cholecystectomy is advised for patients with polyps measuring 6–9 mm who possess one or more risk factors for malignancy, including age > 60 years, a history of PSC, Asian ethnicity, and sessile morphology (including gallbladder wall thickening > 4 mm). For patients with polyps measuring 6–9 mm without risk factors, or ≤ 5 mm with risk factors, follow-up with ultrasonography is recommended at 6 months, 1 year, and 2 years. Surveillance may be discontinued if no growth is observed after 2 years. In cases of polyps ≤ 5 mm without risk factors, no follow-up is required.¹

During follow-up, if the polyp increases in size to 10 mm, cholecystectomy is recommended. If growth of ≥ 2 mm is observed within the 2-year surveillance period, management should be reassessed based on the current size and the patient's malignancy risk factors to determine the need for surgery. If the polyp disappears during follow-up, surveillance can be discontinued.¹ The management pathway for gallbladder polyps is summarized in Figure 1.

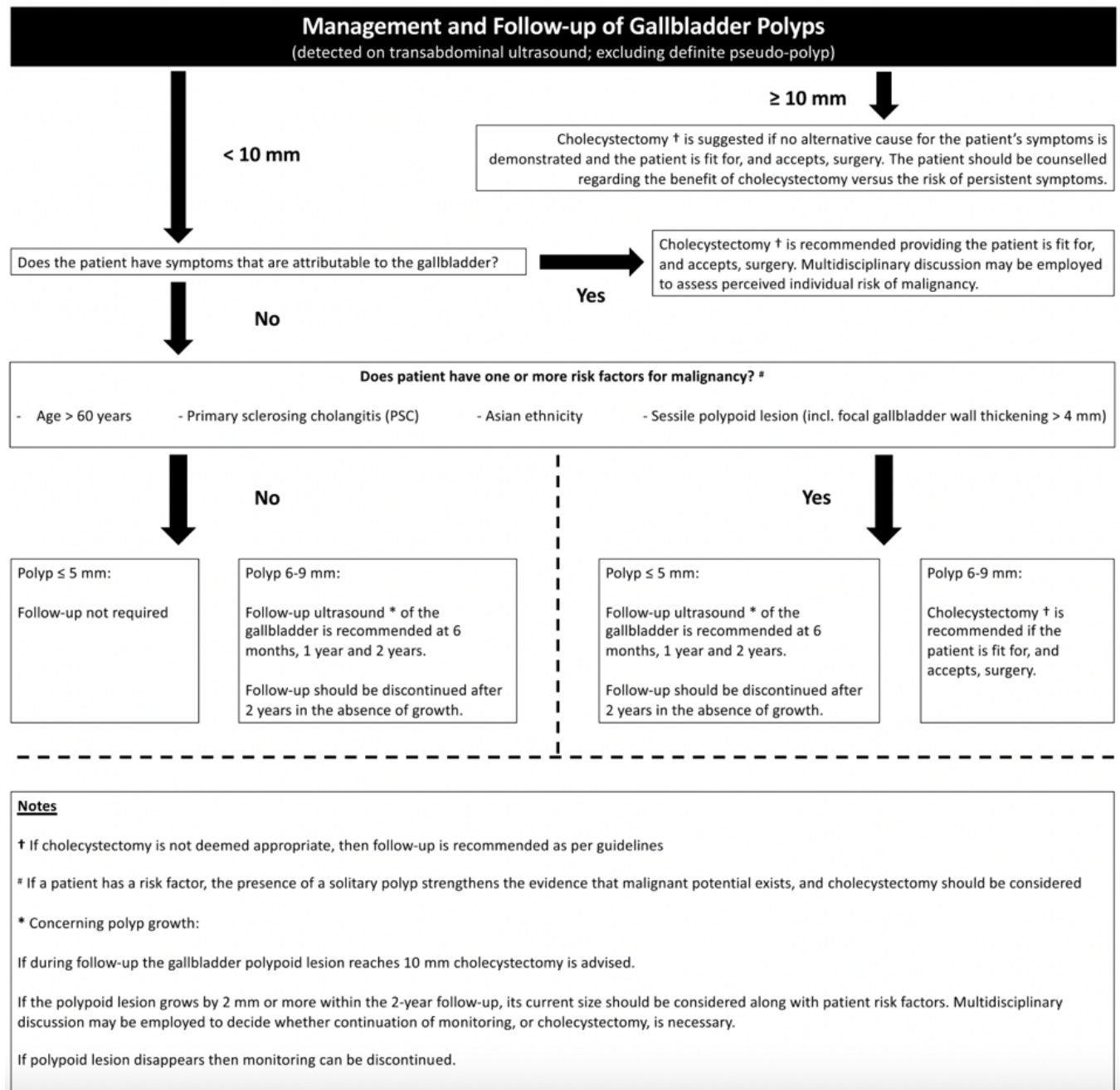


Figure 1. Management Pathway for Gallbladder Polyps¹

CONCLUSION

Gallbladder polyps are lesions that are frequently detected incidentally on ultrasonography. Their management may involve either surgical intervention or conservative observation, depending on polyp size, the presence of symptoms, and the patient's risk factors for malignancy.