

Gallbladder polyps

To treat or not to treat?

SARAH Z. WENNMACKER MD

THOMAS J. HUGH MD, FRACS

Gallbladder polyps do not usually cause symptoms and they are often identified incidentally during ultrasound investigation of the abdomen for other reasons. Most are harmless 'pseudo' polyps. Large polyps suggest the possibility of malignancy, indicating the need for additional diagnostic imaging and likely cholecystectomy.

KEY POINTS

- Small gallbladder polyps do not cause symptoms.
- Biliary symptoms may occur, but these are caused by gallstones, microcalculi or a functional gallbladder disorder rather than the polyps.
- Most gallbladder polyps are not true adenomatous polyps and therefore there is no malignant risk.
- Indications for laparoscopic cholecystectomy include gallbladder polyps of 10mm or larger in size, or when there is an increase in the size or number of polyps during surveillance.

The management of patients with gallbladder (GB) polyps can be challenging. These polyps are elevated lesions of the inner GB wall projecting into the lumen and are often picked up incidentally on ultrasound during investigation for other reasons. They are relatively uncommon and are found in less than 5% of patients undergoing biliary tree imaging.^{1,2} The incidence of GB polyps increases with age, with a median age at diagnosis of 46 years.³ Men are slightly more likely to experience GB polyps than women (ratio, 1.15:1).⁴

Aetiology

Risk factors for GB polyps are not well defined but include age over 60 years, the presence of gallstones, primary sclerosing cholangitis and inflammatory bowel

disease. GB polyps can be subdivided into 'true' polyps and 'pseudo' polyps. About 90% are pseudo polyps, which are harmless nonneoplastic lesions consisting of cholesterol aggregations (cholesterol polyps), inflammatory hyperplasia (inflammatory polyps) or adenomyomatosis.⁵ In the absence of gallstones or a functional GB disorder, pseudo polyps do not cause symptoms, and cholecystectomy is indicated only if these lesions cannot be differentiated from more sinister lesions.

True GB polyps are rare and can be divided into benign and malignant lesions. Benign adenomas (Figure 1) are uncommon and account for only 5% of all GB polyps.^{5,6} These have malignant potential and can give rise to adenocarcinomas, similar to the adenoma–carcinoma sequence of colonic polyps. Malignant polyps are mostly



MedicineToday 2018; 19(4): 30-34

Dr Wennmacker is a surgical trainee in the Upper Gastrointestinal Surgical Unit, Royal North Shore Hospital, Sydney. Professor Hugh is the Chair of Surgery at the Northern Clinical School, The University of Sydney; and Head of the Upper Gastrointestinal Surgical Unit, Royal North Shore Hospital and North Shore Private Hospital, Sydney, NSW.

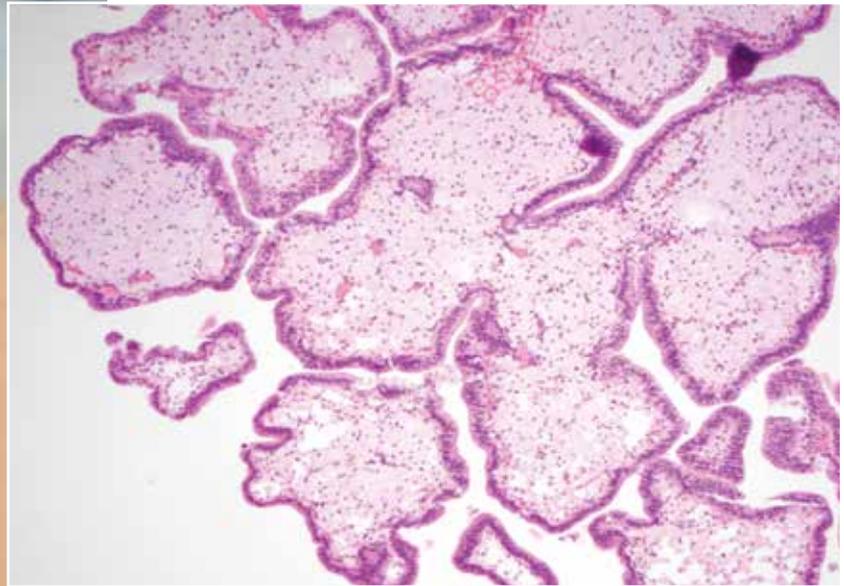


Figure 1. Histological view of a 'true' benign adenomatous gallbladder polyp.

adenocarcinomas (GB cancer), although other rarer types include squamous cell carcinoma, lymphoma and metastases.^{5,6}

Symptoms

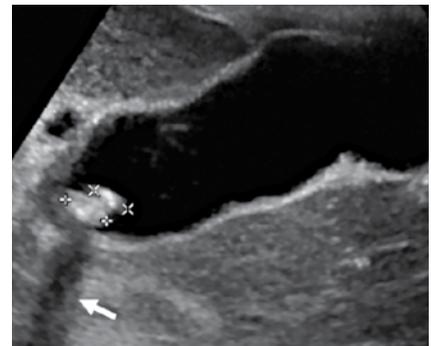
Most patients with GB polyps are asymptomatic, although nausea, vomiting and right-sided abdominal pain, similar to the symptoms of biliary colic, can occur. These symptoms may be caused by obstruction of the cystic duct by small fragments that become detached from the polyp, or by large polyps near the neck of the GB. However, most often they are caused by concomitant gallstones.⁷

Diagnosis

Ultrasound is the diagnostic modality of choice as it is cheap, noninvasive and readily available in Australia. Although the diagnostic accuracy of ultrasound for detecting GB polyps is reported as being only moderate (sensitivity, 50 to 73%; specificity, 98%), it is still superior to CT or MRI.⁸⁻¹⁰ Most GB polyps are found incidentally when screening the abdomen for other reasons.

The classic ultrasound appearance of a

polyp is a lesion fixed to the GB wall, projecting into the lumen and with no displacement during patient repositioning. GB polyps can have either a pedunculated or sessile shape but, unlike gallstones, they do not have an acoustic shadow (Figure 2).¹¹ When a polyp is found on ultrasound, the size, number and shape of all polyps should be evaluated, as these characteristics influence the decision to intervene. Multiple small cholesterol polyps are not uncommon, whereas adenomas or carcinomas are mostly solitary (Figure 3).



Figures 2a and b. Ultrasound image of a 6 mm gallbladder polyp (a, left) compared with a 6 mm gallstone (b, right), showing characteristic posterior echogenic shadowing from the gallstone only (arrow).

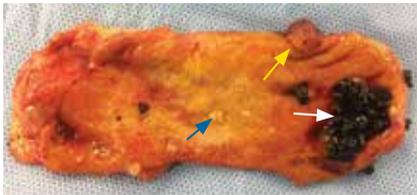


Figure 3. Opened gallbladder showing a cholesterol polyp (blue arrow), multiple pigmented gallstones (white arrow) and an adenomyoma (yellow arrow).



Figures 4a and b. Ultrasound image (a, left) and the surgical specimen (b, above) of a 20 mm benign adenomyoma of the gallbladder (arrow) mimicking a gallbladder cancer.

A large GB mass should always raise concerns about a malignant process. However, a well-defined lesion in a patient with typical biliary symptoms may turn out to be a benign ‘sludge ball’ of inspissated bile (Figure 5). In contrast, poorly defined infiltrating lesions or sessile polyps are more suspicious for

cancer (Figures 6 and 7).¹²

If a malignancy is suspected, additional diagnostic imaging is required. This may include a CT, MRI or positron emission tomography (PET) scan to further characterise the lesion and to exclude local or distant dissemination. As there is no Medicare rebate in Australia for an MRI or PET scan for either the diagnosis or work-up of a GB cancer, patients having these investigations will incur an out-of-pocket expense. If available, endoscopic ultrasound may also be helpful to characterise a suspicious lesion and has the added advantage of enabling a fine-needle biopsy to be done. However, it is important for patients to be assessed by a multidisciplinary hepatobiliary cancer unit before a biopsy is arranged, as this has the potential to increase local recurrence rates, thereby decreasing the chance of long-term cure.

differentiating a benign from a malignant process, especially for small GB polyps.¹²

Management

The presence of a GB polyp often causes clinical concern, particularly in asymptomatic patients, as surgical intervention is usually only indicated for neoplastic polyps. However, distinguishing between true and pseudo GB polyps based on imaging alone is not always easy or possible.

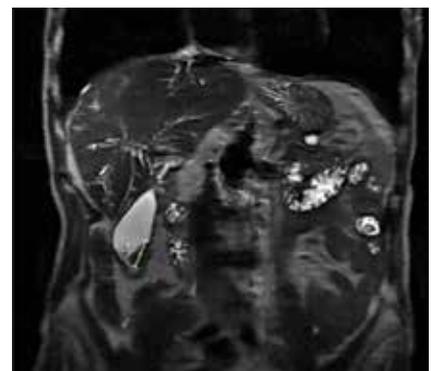
Patients with polyps of 10 mm or more in diameter should undergo cholecystectomy irrespective of whether they have symptoms. This is not because large polyps have a greater potential to become malignant than smaller polyps but because most benign polyps never exceed 10 mm in diameter. In contrast, once a polyp becomes larger than 10 mm in maximal diameter, it is much more likely to be malignant, even if there are no sinister radiological features.¹³⁻¹⁸ A GB polyp



Figure 5. Ultrasound image of a 22 mm benign ‘sludge ball’ with well-defined borders and posterior acoustic shadowing.



Figure 6. Ultrasound image of a 25 mm polypoid gallbladder cancer showing indistinct and infiltrative borders.



Figures 7a and b. Ultrasound image from May 2013 (a, left) and an MRI scan from March 2016 (b, right) showing slow growth of a 25 mm sessile polypoid gallbladder cancer (arrow) over 33 months.

RISK FACTORS WARRANTING CHOLECYSTECTOMY FOR GALLBLADDER POLYPS OF 5 TO 9 MM

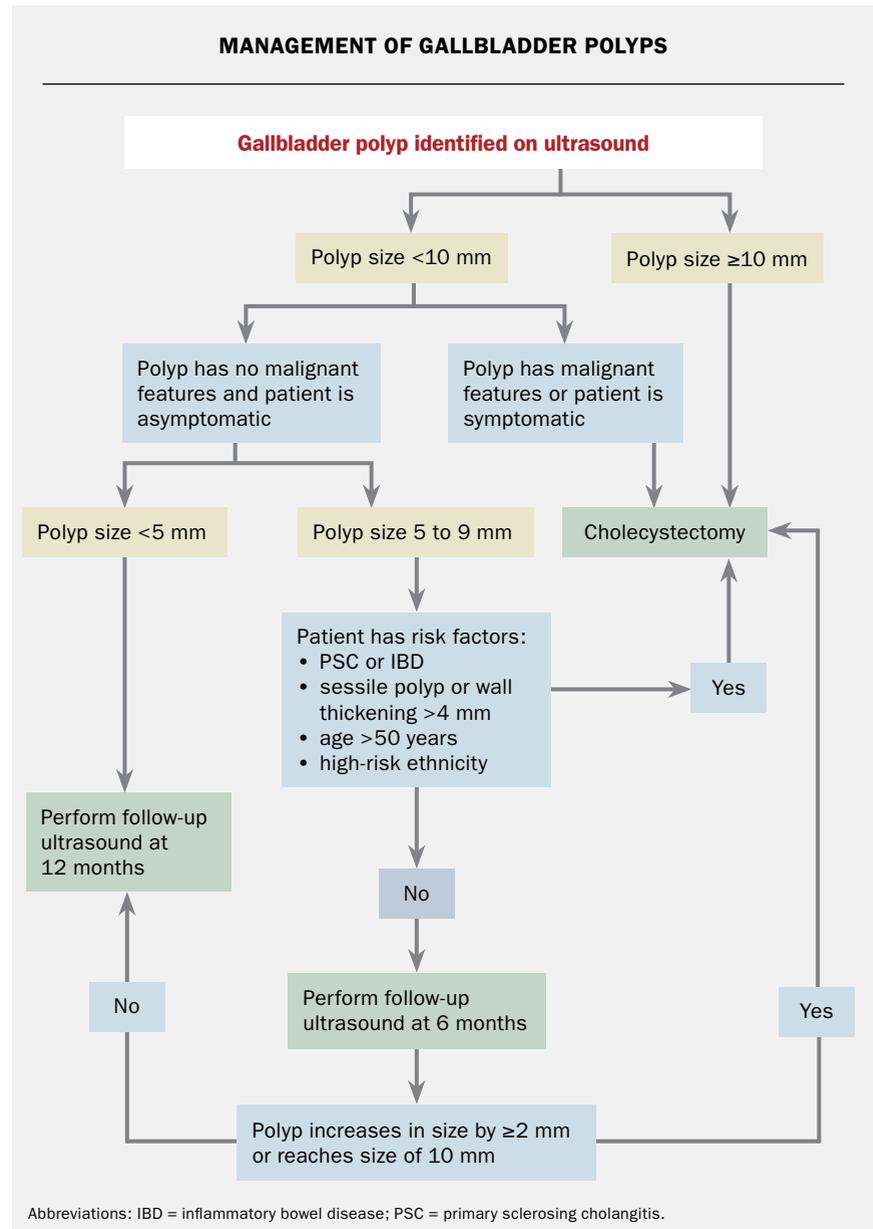
- Primary sclerosing cholangitis
- Inflammatory bowel disease
- Sessile polyp shape
- Imaging evidence of asymmetrical gallbladder wall thickening greater than 4 mm
- Age older than 50 years
- High-risk ethnicity (e.g. Northern Indian, Polish, Pima Native American, Chilean Mapuche Indian)

greater than 18 mm in size has a high likelihood of being an advanced cancer and should be removed with open cholecystectomy and en-bloc liver resection and lymphadenectomy. Resection is also warranted irrespective of polyp size where there are characteristic malignant features, such as rapid growth or typical malignant radiological findings.

Laparoscopic cholecystectomy is warranted for symptomatic patients with GB polyps smaller than 10 mm where no alternative cause for the symptoms can be found. Typical biliary symptoms may be caused by either microcalculi or an underlying functional GB abnormality that cannot be detected on ultrasound.¹⁷

The management of asymptomatic patients with GB polyps smaller than 10 mm is more difficult and remains controversial. For polyps of 5 to 9 mm in size, cholecystectomy is recommended in the presence of other risk factors for malignancy (Box).¹⁷⁻¹⁹

It has also been suggested that the presence of concomitant gallstones increases the risk of a GB polyp being malignant, although this is contentious.^{20,21} Overall, the consensus is that patients with uncomplicated GB polyps (i.e. no associated risk factors and no malignant features on imaging) measuring 5 to 9 mm should only be offered cholecystectomy if they are symptomatic.¹⁷ Regardless, the resected specimen of any patient with GB polyps should be opened and inspected, then



sent for histopathological analysis to establish the polyp subtype and to exclude a malignancy.

Management of GB polyps is summarised in the Flowchart.

Follow up

GB polyps that are not resected should be followed up with serial ultrasound examinations, although there are no clear guidelines on the exact screening intervals.

For polyps measuring 5 to 9 mm but without other risk factors for malignancy, follow-up ultrasound is recommended six months after the initial diagnosis. For uncomplicated polyps smaller than 5 mm, follow up at 12 months is more reasonable.¹⁸ If, during the follow-up period, the polyp increases in size by 2 mm or more since the previous examination, cholecystectomy should be considered, as rapid growth may be a feature of malignancy. For polyps that reach the threshold of



Figure 8. Ultrasound image showing a 6 mm gallbladder polyp that has remained unchanged in size or shape over three years.

10 mm during follow up, cholecystectomy is also advisable.^{17,19} Annual ultrasound examinations are often recommended until a maximum of five years after the initial diagnosis, although there is little evidence to support this approach. If the polyp disappears during the follow-up period, further surveillance is unnecessary. The question of whether cholecystectomy is indicated if more polyps develop during the follow-up period is also controversial because ultrasound imaging is user-dependent and minor changes in the size or number of polyps are subject to interpretation. A pragmatic approach is to offer cholecystectomy whenever there is a significant change in the imaging characteristics during the follow-up period.

An alternative to this rigid surveillance program is to offer more flexible and tailored surveillance. As pseudo polyps do not grow over time, it could be argued that further imaging surveillance is unnecessary if there is no change in the size or characteristics of an otherwise uncomplicated polyp smaller than 10 mm during the follow-up period (Figure 8). Also, some patients do not want the inconvenience of regular ultrasound screening or prefer to avoid the anxiety about the potential for malignant change. In these situations, upfront laparoscopic

cholecystectomy may be the best option. This approach must be individualised, and the pros and cons should be discussed in detail with the patient.

Conclusions

Most patients with GB polyps are asymptomatic, and the lesions are often picked up incidentally during imaging for other reasons. Biliary symptoms are usually caused by concomitant gallstones, although undetectable microcalculi or a functional GB disorder may be the cause. Most patients can be reassured that their GB polyps are not cancerous and that there is no risk of malignant change, especially for small polyps. Laparoscopic cholecystectomy is indicated for GB polyps of 10 mm or larger in size, or when there is an increase in the size or number of polyps during surveillance. Surveillance of small GB polyps is best done using abdominal ultrasound but the exact frequency and duration of surveillance have not been well established.

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COMPETING INTERESTS: None.