Radiology

REVIEWS AND COMMENTARY • STATEMENTS AND GUIDELINES

Management of Incidentally Detected Gallbladder Polyps: Society of Radiologists in Ultrasound Consensus Conference Recommendations

Aya Kamaya, MD • Christopher Fung, MD • Jean-Luc Szpakowski, MD, FAASLD • David T. Fetzer, MD • Andrew J. Walsh, MD, PhD • Yewande Alimi, MD • David B. Bingham, MD • Michael T. Corwin, MD • Nirvikar Dahiya, MD • Helena Gabriel, MD • Walter G. Park, MD • Matthew R. Porembka, MD • Shuchi K. Rodgers, MD • Mitchell E. Tublin, MD • Xin Yuan, RDMS, RVT, RMSK, MS • Yang Zhang, MD • William D. Middleton, MD

From the Departments of Radiology (A.K.), Pathology (D.B.B.), Medicine (W.G.P.), and Ultrasound (X.Y.), Stanford University School of Medicine, Stanford Hospital and Clinics, 300 Pasteur Dr, H1307, Stanford, CA 94305; Department of Radiology, University of Alberta Hospital, Edmonton, Alberta, Canada (C.F., A.J.W.); Department of Gastroenterology, Kaiser Permanente Northern California, Oakland, Calif (J.L.S.); Departments of Radiology (D.T.F.) and Surgical Oncology (M.R.P.), University of Texas Southwestern Medical Center, Dallas, Tex; Department of Surgery, MedStar Georgetown University Hospital, Washington, DC (Y.A.); Department of Radiology, University of California Davis Medical Center, Sacramento, Calif (M.T.C.); Department of Radiology, Mayo Clinic Scottsdale, Phoenix, Ariz (N.D.); Department of Radiology, Northwestern University Feinberg School of Medicine, Chicago, Ill (H.G.); Department of Radiology, Sidney Kimmel Medical College, Thomas Jefferson University, Cherry Hill, NJ (S.K.R.); Department of Radiology, University of Pittsburgh School of Medicine, Pittsburgh, Pa (M.E.T.); Joint Pathology Center, Silver Spring, Md (Y.Z.); and Mallinckrodt Institute of Radiology, Washington University School of Medicine, St Louis, Mo (W.D.M.). Received December 4, 2021; revision requested January 4, 2022; revision received March 6; accepted March 14. **Address correspondence to** A.K. (email: *kamaya@stanford.edu*).

Conflicts of interest are listed at the end of this article.

See also the editorial by Sidhu and Rafailidis in this issue.

Radiology 2022; 000:1–12 • https://doi.org/10.1148/radiol.213079 • Content codes: GI US

Gallbladder polyps (also known as polypoid lesions of the gallbladder) are a common incidental finding. The vast majority of gallbladder polyps smaller than 10 mm are not true neoplastic polyps but are benign cholesterol polyps with no inherent risk of malignancy. In addition, recent studies have shown that the overall risk of gallbladder cancer is not increased in patients with small gallbladder polyps, calling into question the rationale for frequent and prolonged follow-up of these common lesions. In 2021, a Society of Radiologists in Ultrasound, or SRU, consensus conference was convened to provide recommendations for the management of incidentally detected gallbladder polyps at US.

Incidental gallbladder polyps (also known as polypoid lesions of the gallbladder) are a common sonographic finding, occurring in approximately 3%–6% of the general population (1,2). Although most are benign cholesterol polyps (also known as cholesterol pseudopolyps) or inflammatory polyps, a small percentage of them are true neoplastic polyps, which have an unknown though small malignant potential. Differentiating nonneoplastic from neoplastic polyps at imaging is challenging. In addition, only 6% of gallbladder cancers (GBCs) may arise from a polypoid precursor lesion, with the vast majority of GBCs developing from flat dysplastic epithelium (3). Even in gallbladder polyps larger than 10 mm, some studies suggest only 0.4% are malignant, with most malignant polyps typically measuring greater than 20 mm (4,5). With increasing evidence showing that the overwhelming majority of resected gallbladder polyps are benign, current management guidelines are being questioned (4–7). Aggressive management of small gallbladder polyps may lead to patient harm, including unnecessary surgical resection, frequent and prolonged follow-up imaging of questionable benefit, and patient anxiety and inconvenience.

Recently, a large population study (6) found the same rate of GBC in patients with gallbladder polyps at US (0.053% [19 of 35 856 patients]) as those without gallbladder polyps (0.054% [316 of 586 357 patients]). In addition, those with GBC had a similar incidence of coexisting gallbladder polyps (6.0% [22 of 365 patients]) compared with those without GBC (5.8% [35 856 of 622 227 patients]). Thus, the relative risk of GBC in those with asymptomatic gallbladder polyps does not appear to be increased (6). A further recent study of 156 patients with histopathologically proven gallbladder polyps in four Dutch hospitals concluded that polyp size was often overestimated at US and that the 10-mm threshold for surgical resection led to overtreatment of nonneoplastic polyps (4). Another recent study of 434 patients with gallbladder polyps at serial US showed that growth of 2 mm or more is common over time and concluded that a 2-mm increase in polyp size (as suggested by the European multisociety guidelines [8]) may be too low of a threshold to warrant cholecystectomy (9).

The Society of Radiologists in Ultrasound (SRU) consensus conference committee was created to review the literature on the association of gallbladder polyps and GBC, the natural history of gallbladder polyps and, if appropriate, revise recommendations for the management of incidental gallbladder polyps at US. It is expected that as evidence and technologies advance, these recommendations may evolve.

Materials and Methods

Experts in gallbladder disease in the fields of radiology, surgery, gastroenterology, pathology, and sonography were

Abbreviations

CEUS = contrast-enhanced US, EUS = endoscopic US, GBC = gallbladder cancer, ICPN = intracholecystic papillary neoplasm, PSC = primary sclerosing cholangitis, SRU = Society of Radiologists in Ultrasound

Summary

The Society of Radiologists in Ultrasound, or SRU, consensus conference provides management recommendations for extremely low risk, low risk, and indeterminate risk gallbladder polyps incidentally detected at US.

Essentials

- The Society of Radiologists in Ultrasound, or SRU, consensus conference guideline for gallbladder polyps provides evidence-based and expert consensus–based risk-stratified management recommendations for incidentally detected gallbladder polyps at US.
- On the basis of their morphologic features, gallbladder polyps are stratified into three categories: extremely low risk, low risk, and indeterminate risk.
- Extremely low risk polyps are pedunculated with a "ball-on-the-wall" configuration or thin stalk; low risk polyps are pedunculated with a thick or wide stalk or sessile configuration; indeterminate risk polyps have focal wall thickening adjacent to the polyp.

invited by the consensus conference chair (A.K.) to participate in the SRU gallbladder polyp consensus conference. Each member was assigned a topic to present after performing a comprehensive literature review. Risk categories and recommendations were created and refined during a series of conference calls between July and September 2021. Proposed guidelines were derived based on the existing literature, expert opinion, and panel consensus.

SRU Consensus Conference Algorithm

For a patient with an incidental sonographically detected gallbladder polyp, the applicability of the SRU algorithm can be determined after applying crosschecks and exclusions as listed in Figure 1.

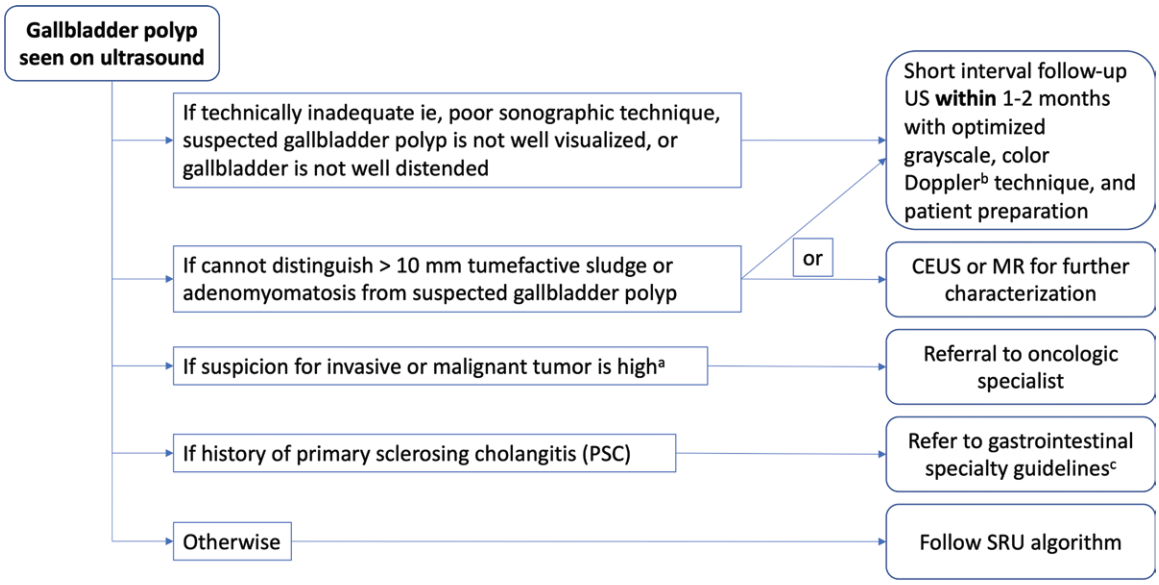
To stratify management, the SRU consensus conference committee divided gallbladder polyps into extremely low risk, low risk, and indeterminate risk lesions (Fig 2). Categorical examples are also provided in Figure 2. Follow-up recommendations for each category are based on the premise that most malignant polyps are larger and will grow faster over time than most nonmalignant polyps. Definitions are provided in the Table. SRU consensus conference recommendations for management according to size threshold, growth rates, and risk categories are outlined in Figure 2 and its footnotes.

Gallbladder Polyp Pathologic Characteristics

Gallbladder polyps may be broadly grouped into nonneoplastic polyps and neoplastic polyps. The majority of sonographically identified gallbladder polyps are nonneoplastic, most commonly benign cholesterol polyps or inflammatory-type polyps. Nonneoplastic polyps are usually smaller than 10 mm in diameter with negligible, if any, risk of developing dysplasia or malignancy.

Approximately 0.4% of patients undergoing cholecystectomy are found to have neoplastic polyps (3). These neoplastic polyps were previously referred to as various types of adenomatous polyps; however, in the past decade, the terminology was updated to the more specific pyloric gland adenoma or intracholecystic papillary neoplasm (ICPN) depending on histologic findings (3).

According to the 2019 *WHO Classification of Tumours*, fifth edition, Digestive System Tumours (10), ICPNs are defined as mass-forming, noninvasive epithelial neoplasms of 10 mm or more arising in the mucosa and projecting into the lumen of the gallbladder. There are four morphologic patterns (biliary, gastric, intestinal, and oncocytic), and they may be classified as having low-grade or high-grade epithelial dysplasia. Only 6% of all gallbladder



[a] Findings that may indicate invasive tumor include the following: wall invasion, concurrent liver masses, malignant biliary obstruction, or pathologic lymph node enlargement at the porta hepatis or para-aortic chain
[b] Higher sensitivity Doppler techniques such as power Doppler, B-Flow, and microvascular Doppler may help differentiate a polyp from tumefactive sludge
[c] American Gastroenterology Association https://www.cghjournal.org/article/S1542-3565(19)30744-X/pdf

Figure 1: Flowchart for determination of applicability of the Society of Radiologists in Ultrasound (SRU) algorithm. CEUS = contrast-enhanced US.

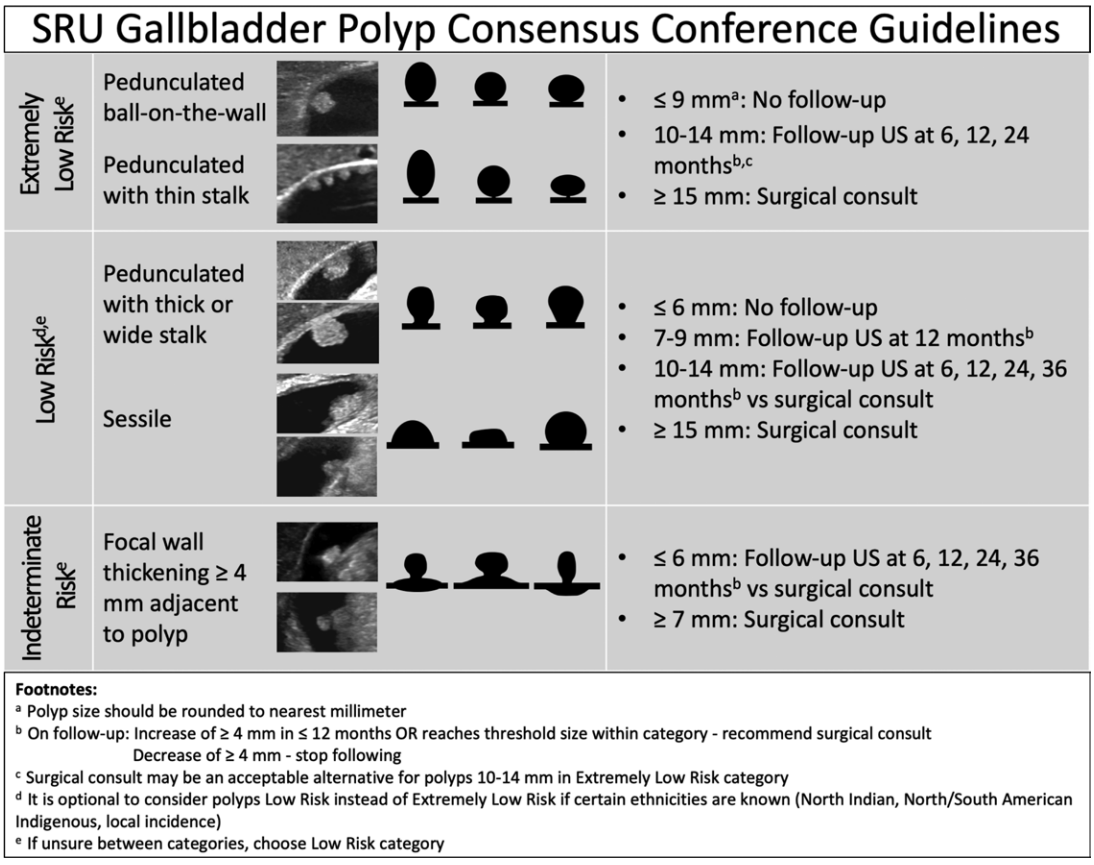


Figure 2: Diagram shows Society of Radiologists in Ultrasound (SRU) gallbladder polyp consensus conference guidelines.

Definitions

Term	Definition
Gallbladder polyp	Solid nonmobile, nonshadowing protrusion arising from gallbladder mucosa that is not attributable to gallstones, inspissated bile (ie, sludge), a mucosal fold, or diffuse or focal wall thickening; may be pedunculated or sessile in configuration
Pedunculated	Point of attachment to the wall is via a stalk or pedicle
Sessile	Flat or dome-shaped mass that extends out from the mucosal layer and does not have a stalk; point of attachment to wall is broad-based
Focal wall thickening adjacent to polyp	Localized wall thickening ≥4 mm in thickness adjacent to gallbladder polyp that cannot be attributable to edema, adenomyomatosis, mucosal fold, or gallbladder underdistention
"Ball-on-the-wall" appearance	Pedunculated polyp, typically rounded or ovoid though barely attached to the wall simulating a ball resting on a flat surface
Sludge	Inspissated bile that has precipitated out of solution, often echogenic, nonshadowing, mobile, and layering dependently
Tumefactive sludge	Biliary precipitate that has coalesced into a more solid appearance ("sludge ball"), which can mimic a mass or polyp
Adenomyomatosis	Mural hyperplasia that may be diffuse, focal, or segmental with comet-tail artifact (at gray-scale imaging) or twinkling artifact (at color Doppler imaging) due to intramural cholesterol crystals; Rokitansky-Aschoff sinuses may appear as intramural cysts
Gallstone	Solid shadowing hyperechoic nonvascular structure within the gallbladder lumen that is generally mobile

carcinomas are thought to arise in association with an ICPN, with favorable survival rates for ICPN-associated gallbladder carcinoma (60%–90% 3-year survival) compared with carcinomas without a precursor polypoid lesion (27% 3-year survival) (3,10).

Pyloric gland adenomas are smooth-surfaced polypoid lesions composed of tightly packed glands with pyloric-type low cuboidal epithelium. Pyloric gland adenomas occur in 0.2%–0.5% of cholecystectomy specimens (11) and may be associated with familial adenomatous polyposis or Peutz-Jeghers syndrome (10).

On average, neoplastic polyps are larger (mean size, 18–21 mm) than nonneoplastic polyps (mean size, 4–7.5 mm) (5,12). It is unclear what percentage of neoplastic polyps are expected to undergo malignant transformation; however, if this does occur, the rate of transformation is estimated to be

extremely low, given the limited association with gallbladder carcinoma in the literature.

While most prior studies have attempted to differentiate neoplastic (ICPN or pyloric gland adenoma) polyps from nonneoplastic (cholesterol or inflammatory) polyps, it may be more relevant to attempt to differentiate only malignant polyps from both benign neoplastic and nonneoplastic polyps. That is, the main concern when a gallbladder polyp is identified is the potential risk of the polyp being an early cancer.

GBC Incidence

GBC is rare, but lethal. In 2020, an estimated 116 000 cases were diagnosed worldwide (5200 in the United States), resulting in 84 695 deaths (13).

The literature regarding the malignancy risk of polyps is largely based on surgically resected specimens, with the majority of studied polyps measuring over 10 mm. Histopathologic studies are therefore subject to selection bias and exaggerate the proportion of gallbladder polyp–associated malignant neoplasms. Conversely, the majority of sonographically identified gallbladder polyps are under 10 mm and are not resected. Thus, results from surgical cohorts cannot be extrapolated to the majority of sonographically visualized gallbladder polyps. Most studies divide polyps into neoplastic versus nonneoplastic categories (4,5,7,14–17), while very few studies have assessed malignant versus nonmalignant polyps (6).

Patient and polyp factors may influence the risk of GBC. The patient factors studied typically relate to the absolute increased risk of overall GBC incidence; however, it is unclear if these directly extrapolate to the risk of a gallbladder polyp being an early cancer or progressing into cancer, given that most GBCs will not manifest as a gallbladder polyp.

Patient Factors

Genetic and Geographic Risk

Geographic and ethnic variations in incidence suggest underlying environmental and genetic influences. The highest incidences of GBC (up to 7.5 cases per 100 000 for men and 23 cases per 100 000 for women) are seen in North and South American Indigenous populations and North Indian populations, with rates of up to five cases per 100 000 also recorded in the Japanese population and Hispanic American population (18). Potential genetic loci have been identified in North Indian (19) and Japanese populations (20). Familial GBC (standardized incidence ratio, 5.21) may be associated with maternal transmission (21), although the familial risk of GBC was shown to be largely mediated through a family history of gallstones in a Chinese population (22). It is not clear that an increased risk of GBC is secondary to an increased incidence of gallbladder polyps.

The SRU consensus conference committee agreed that, if known, geographic and genetic patient factors may increase polyp risk stratification up to the low risk category.

Primary Sclerosing Cholangitis

Primary sclerosing cholangitis (PSC) is associated with the development of gastrointestinal cancers, cholangiocarcinoma, gallbladder polyps, and GBC secondary to a biliary epithelium field defect (23). Many factors influence the management of patients with PSC and gallbladder polyps. In patients with PSC, gallbladder lesions—including polyps—at cholecystectomy have been shown to have a higher association with GBC (18%–50%) and premalignant lesions (25%–35%), although studies may be affected by surgical referral bias. The lesion size to recommend surgery versus observation in patients with PSC remains controversial (23–30).

The SRU consensus conference committee agreed that the SRU consensus guidelines should not be applied to patients with PSC. We recommend that radiologists be aware of the increased risk of malignancy in patients with PSC and refer to specialty guidelines (American Gastroenterology Association and American College of Gastroenterology) for specific management recommendations and thresholds for surgical consideration in patients with PSC.

Age

The literature regarding age and risk of GBC is varied. A brief 1997 Lancet review (31) of strategies for managing gallbladder polyps suggested age older than 50 years as a risk factor. However, no evidence or rationale to support this statement was provided. Szpakowski and Tucker (6) found that age greater than 65 years was not a risk factor for polyp growth and the average age of patients with GBC was 71 years. Aldouri et al (2) found that age older than 60 years was independently associated with higher odds of developing GBC with or without gallbladder polyps. Other investigators have suggested variable age thresholds. In many studies, whether cancers arose from a preexisting gallbladder polyp or elsewhere in the gallbladder is often unstated and loosely inferred (16,32–35).

Although the literature indicates that patients with GBC tend to be older, there is no evidence to suggest that advancing age is a sufficient risk factor to alter management, and there is no clear age threshold at which more aggressive management of gallbladder polyps is shown to improve survival.

Importantly, the increased risks of surgery with advancing age must be counterbalanced by the relative benefit of surgical resection of a benign or low-malignant-potential lesion. Patient selection for surgery is multifactorial, requiring shared decision-making and consideration of patient health status as well as the risk implied by imaging findings. With increasing patient age and frailty, risks of postoperative morbidity and mortality also increase, which must be carefully considered (36).

The SRU consensus conference committee agreed that, due to lack of evidence, patient age should not influence risk stratification.

Coexisting Gallstones

Although one study reported a higher incidence of malignancy in polyps with coexisting stones or sludge (37), other studies have not found a strong correlation of gallstones with either malignancy or benignity (14,17,38).

Given the ubiquity of gallstones, the SRU consensus conference committee agreed that coexisting gallstones should not influence risk stratification of gallbladder polyps.

Other Patient Risk Factors

Other patient factors that have been associated with the development of GBC include smoking (relative risk, 1.25), diabetes mellitus (relative risk, 1.97) (39), and obesity (relative risk, 1.31), with premenopausal women having shown the greatest risk associated with obesity (40). GBC may have a two to six times greater incidence in women than men (18). Because the absolute number of cancers is low at baseline, the slight increase in relative risk does not substantially alter absolute risk.

The SRU consensus conference committee agreed that these other patient factors do not increase the absolute risk of malignancy sufficiently to influence risk stratification.

Risk of Gallbladder Polyp Harboring a Malignant Neoplasm or Transforming into a Cancer

Size

In a 2014 meta-analysis of 10 studies (41), no GBCs were seen in polyps of 5 mm or less. A systematic review from 2015 by Babu et al (42) showed 0% malignancy in polyps smaller than 5 mm, and a separate systematic review from 2016 by Bhatt et al (43) showed that 4-mm polyps had a 0% rate of malignancy. Many single-institution studies found no GBCs in polyps measuring less than 10 mm (44–52). In a 2020 study by Rafaelsen et al (53), 154 patients with polyps smaller than 6 mm underwent follow-up US 12 years after initial polyp discovery; none had GBC. The authors proposed no follow-up of gallbladder polyps smaller than 6 mm. Furthermore, some investigators have found that 61%–69% of polyps seen at US are not identified at subsequent cholecystectomy, only some of which are accounted for by adherent stones. For apparent polyps of 5 mm or smaller, no polyp is found at subsequent cholecystectomy in up to 83% of patients (50,54).

In a recent 20-year population study (6), the incidence of GBC in 2055 patients with gallbladder polyps larger than 10 mm was estimated at only 0.4%. In this study, the overall rate of cancer in 35 856 patients with gallbladder polyps was found to increase with the size of the polyps, with rates of 1.3, 8.7, and 128 per 100 000 patients for those with polyps smaller than 6 mm, at least 6 mm but smaller than 10 mm, and 10 mm or larger, respectively. An increasing risk of malignancy with increasing polyp size was similarly seen in many other studies, with variation in the absolute risk dependent on the selected study population (37,44,55).

A 2019 study by Wennmacker et al (5) of 2085 polyps or focal wall thickening (>5 mm) with histopathologic confirmation found that neoplastic polyps were larger compared with nonneoplastic polyps (18.1 mm vs 7.5 mm). Furthermore, neoplastic lesions and cancers were more likely to manifest as focal wall thickening (29.1% and 37.9%, respectively) rather than lumen-protruding polyps (15.6% and 15.9%, respectively) ($P < .001$ for both).

A 2021 study by Liu et al (7) found that neoplastic polyps were significantly larger than nonneoplastic polyps (18.5 mm ± 4.7 vs 12.6 mm ± 3.6) and that size larger than 15 mm was an independent risk factor to discriminate neoplastic polypoid gallbladder lesions. Similarly, studies by Kim et al in 2016 (16) and Cha et al in 2011 (32) showed that size of 15 mm or greater was a significant predictor of neoplastic polyp at univariable analysis.

A survey performed in 2021 that focused on the practice patterns, preferences, and experience of SRU fellows indicated that polyp size was universally used to determine management recommendations. The estimated combined number of gallbladder sonograms interpreted by the responders was approximately 3 million. Despite this substantial experience, there were no documented cases of a polyp smaller than 10 mm that was proven to be malignant at the time of initial US detection or during subsequent follow-up (56).

The SRU consensus conference committee agreed that polyp size may be associated with risk of neoplasia and recommends surgical consultation for polyps of 15 mm or greater. For polyps measuring 10–14 mm, the decision for surgical consultation may be made depending on patient factors or evidence of growth at follow-up imaging.

Growth

The correlation between growth and development of malignancy is unclear. The majority of growth studies evaluate the proportion of polyps that increase or decrease in size, generally defined as change of 2 mm or greater over an unspecified length of time, rather than growth rate.

Although the majority of polyps are stable in size over 3–10 years, the longer polyps are followed—as may be expected—the more growth is appreciable (49–51,57). In the study by Szpakowski and Tucker (6), at 10-year follow-up, two-thirds of polyps smaller than 6 mm and over half of polyps measuring 6–10 mm had growth of 2 mm or more. Thus, growth of small polyps can be expected as part of their natural history and does not necessarily increase the risk of malignancy. Conversely, a decrease in the size or resolution of polyps has been noted in up to 34% of cases (58).

In a study by Walsh et al (9) of patients with serial hepatocellular carcinoma screening sonograms, gallbladder polyps appeared to be dynamic, with almost half increasing (2.6 mm ± 1.2) or decreasing (−3 mm ± 1.5) in size, or both, suggesting that fluctuation in size of gallbladder polyps by 2–3 mm is part of the expected natural history.

Several studies have either calculated or extrapolated nonneoplastic polyp growth rates ranging from 0.16 mm/year to 2.76 mm/year (59–62), while one study showed no growth (63). Only one study initially found that a polyp growth rate of 0.6 mm/month was a predictor of malignancy; however, this no longer held true at subsequent multivariable analysis (59). Thus, despite documentation of growth, no clear relationship with malignancy has been established (51,58,59,64).

In addition, growth to a threshold of 10 mm is not necessarily associated with increased risk of GBC (6). In the study by Szpakowski and Tucker (6), 507 polyps that were initially smaller than 10 mm (8% of 6359 polyps with follow-up) grew to 10 mm or larger. None were associated with malignancy in 1549 person-years of follow-up.

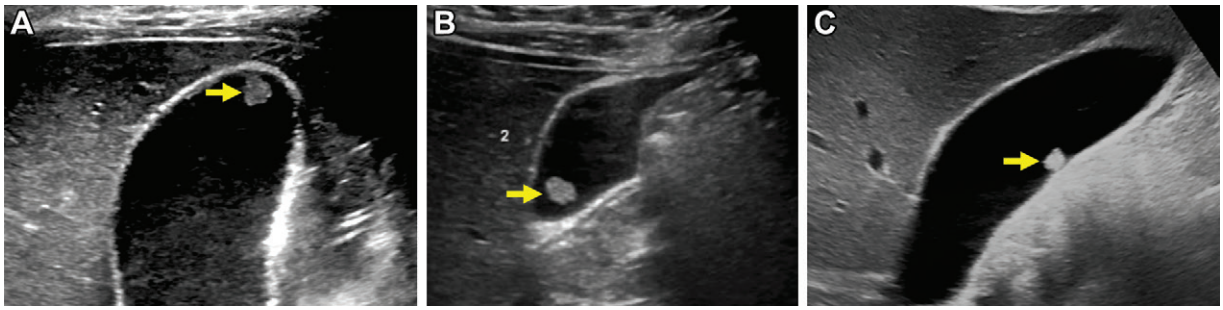


Figure 3: **(A–C)** US images show three examples of pedunculated "ball-on-the-wall" gallbladder polyps. Pedunculated ball-on-the-wall gallbladder polyps (arrow) resemble a ball resting on a flat surface and would be categorized as extremely low risk polyps. In the extremely low risk category, no follow-up is recommended for polyps of 9 mm or smaller; follow-up US at 6, 12, and 24 months is recommended for polyps measuring 10–14 mm; and surgical consultation is recommended for polyps of 15 mm or larger. If, at follow-up, a polyp has increased in size by 4 mm or more within a 12-month period or reaches 15 mm, surgical consultation is recommended.

Rapid sustained growth is conceptually concerning, although specific criteria for an objective size increase and time interval that constitute concerning growth are not well established. There are, however, some anecdotal reports in the literature of rapid polyp growth leading to malignancy, such as in a study by Patel et al (65), where a single GBC was identified in a cohort of 168 patients who underwent US surveillance. This patient had a gallbladder polyp that grew from 7 to 16 mm over 6 months. Additionally, in a study of 453 patients with PSC and gallbladder polyps, van Erp et al (25) found three cancers, one of which grew from 2 to 18 mm over 2 years; of the other malignant polyps, one measured 17 mm when first detected, and the other was described as a suspicious mass.

The SRU consensus conference committee agreed that growth of up to 3 mm may be part of the natural history of nonmalignant gallbladder polyps. The SRU consensus conference committee agreed that growth of 4 mm or more within 1 year constitutes rapid growth.

Length of Follow-up

In the longitudinal study by Szpakowski and Tucker (6), the majority of GBCs (53% [10 of 19]) were diagnosed within the first 6 months after initial polyp detection, and 68% (13 of 19) were detected within 1 year, presumably reflecting the inherent cancer prevalence. Nine of the 13 polyps that were diagnosed as malignant within 1 year after detection were either 15 mm or larger or described as "large." After 1 year, the overall rate of GBC per 100 000 person-years decreased to 0 (polyp size, <6 mm), 4.5 (at least 6 mm but less than 10 mm), and 33.4 (≥10 mm). After 4 years, only one cancer was found in 137 633 person-years of follow-up, in a patient with a polyp initially measuring between 6 and 10 mm (rate, 5.8). After the 4th year, no cancer was found in polyps initially measuring 10 mm or larger. This study demonstrated that 4 years of follow-up is low-yield and that a shorter follow-up length may be sufficient to identify gallbladder polyp–associated malignancies.

The SRU consensus conference committee agreed that extended follow-up of gallbladder polyps is not productive. If a polyp is followed, a maximum of 3 years is sufficient to identify the vast majority of polyp-associated malignancies.

Morphologic Features of Polyps

In addition to polyp size, morphologic features that can be assessed sonographically include shape, echogenicity, vascularity, focal wall thickening, and multiplicity. Most studies determine these morphologic features by inspection of surgical specimens rather than US findings, and almost all only include patients who underwent cholecystectomy and are thus limited by a substantial selection bias. Histologic analysis is limited, and many studies are divided into neoplastic (primarily ICPN and cancer) versus nonneoplastic (primarily cholesterol, inflammatory, and adenomyomatosis) lesions (4,7,12,15–17,32,33,43,59,66–71), rather than comparing malignant versus benign polyps (14,38,57,72). Additionally, many studies provide only univariable analysis of the morphologic features. Given these multiple limitations, it is difficult to draw strong conclusions regarding the influence of morphologic features of polyps on the likelihood of malignancy.

Sessile versus Pedunculated

Pedunculated polyps have a point of attachment to the wall via a stalk or pedicle. The stalk itself is rarely perceptible sonographically, and the polyp simulates a "ball on the wall" (73) (Fig 3). In some cases, the thin stalk is implied by a single small vessel exiting the polyp at the base (Fig 4). Rarely, the polyp can be seen wiggling in place, and this also implies a thin stalk. Sessile polyps are flat or dome-shaped masses that extend out from the mucosal layer with a broad-based attachment with no stalk or pedicle (Fig 5). Almost all studies show a higher percentage of malignant or neoplastic polyps with a sessile appearance rather than pedunculated (14–16,37,43,72). Only one study showed that shape was an independent risk factor for carcinoma versus adenoma in multivariable analysis, though review of the US images was not performed (68). The group acknowledged that further studies regarding polyp shape are needed and will likely influence future iterations of SRU recommendations.

The SRU consensus conference committee agreed that polyps with a "ball-on-the wall" or pedunculated thin stalk configuration should be placed in the extremely low risk category (Figs 3, 4) and do not require follow-up if 9 mm or smaller, while those that are sessile or pedunculated with a thick or wide stalk should be placed in the low risk category and do

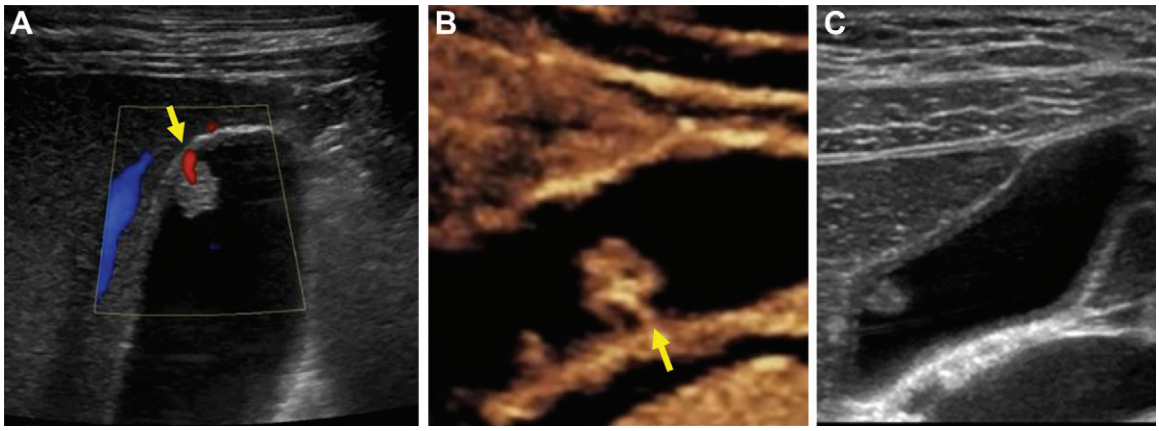


Figure 4: **(A)** Color Doppler, **(B)** contrast-enhanced, and **(C)** gray-scale US images show three examples of pedunculated polyps with a thin stalk. A thin stalk may be nearly invisible at gray-scale imaging but inferred to be present or visualized with color or power Doppler (arrow in **A**), other flow-sensitive techniques, or contrast-enhanced US (arrow in **B**). A polyp occasionally can be seen wiggling in place, which implies a thin stalk (**C**). A pedunculated polyp with thin stalk should be categorized as an extremely low risk polyp. In the extremely low risk category, no follow-up is recommended for polyps of 9 mm or smaller; follow-up US at 6, 12, and 24 months is recommended for polyps measuring 10–14 mm; and surgical consultation is recommended for polyps of 15 mm or larger. If at follow-up, a polyp has increased in size by 4 mm or more within a 12-month period or reaches 15 mm, surgical consultation is recommended.

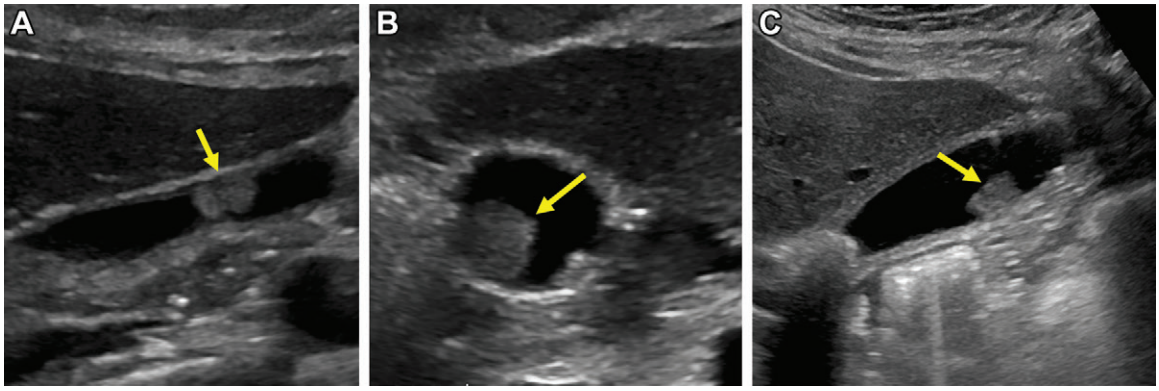


Figure 5: **(A–C)** US images show three different examples of sessile polyps. A sessile polyp is defined as a flat or dome-shaped mass (arrow) that extends from the mucosal layer and does not have a stalk. The point of attachment to the wall is broad-based. Sessile polyps are categorized as low risk polyps. In the low risk category, no follow-up is recommended for polyps of 6 mm or smaller; follow-up US at 12 months is recommended for polyps measuring 7–9 mm; follow-up US at 6, 12, 24, and 36 months is recommended for polyps measuring 10–14 mm; and surgical consultation is recommended for polyps of 15 mm or larger. If, at follow-up, a polyp has increased in size by 4 mm or more within a 12-month period or reaches 15 mm, surgical consultation is recommended.

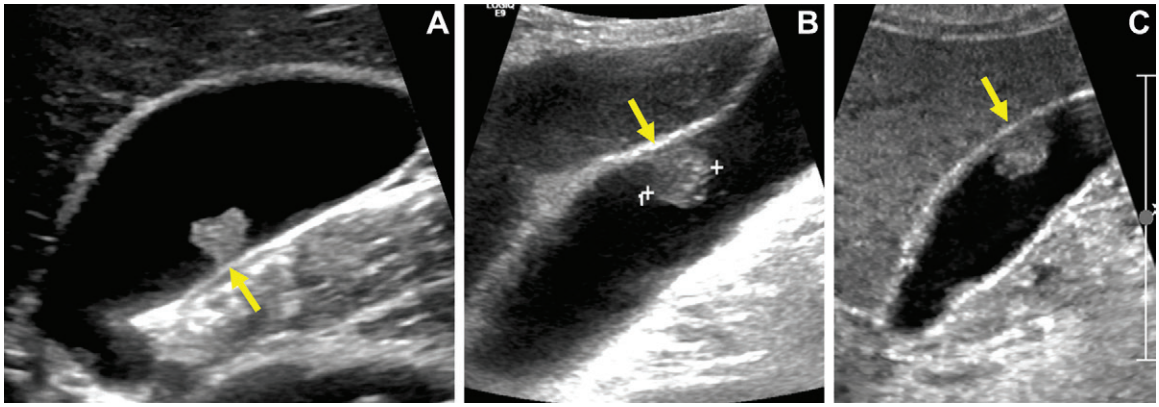


Figure 6: **(A–C)** US images show three different examples of pedunculated polyp with thick or broad-based stalk. The plus signs in **B** demarcate a polyp. With thicker or broad-based stalks (arrow), these gallbladder polyps would be categorized as low risk polyps. In the low risk category, no follow-up is recommended for polyps of 6 mm or smaller; follow-up US at 12 months is recommended for polyps measuring 7–9 mm; follow-up US at 6, 12, 24, and 36 months is recommended for polyps measuring 10–14 mm; and surgical consultation is recommended for polyps of 15 mm or larger. If, at follow-up, a polyp has increased in size by 4 mm or more within a 12-month period or reaches 15 mm, surgical consultation is recommended.

not require follow-up if 6 mm or smaller (Figs 5, 6). If there is uncertainty regarding the shape of the polyp, the SRU consensus conference committee agreed that the low risk category may be used.

Polyp Vascularity

Few studies have analyzed polyp vascularity, and the number of cases is low. While all available studies indicated that detectable vascularity, typically at the polyp base, is more often seen with neoplastic polyps, none showed that vascularity was an independent risk factor for malignancy (16,17,68). Expert experience shows that larger cholesterol polyps indeed may have demonstrable internal vascularity at color Doppler imaging. Further, substantial improvements in sonographic sensitivity, including microvascular Doppler techniques, increasingly allow detection of subtle vascularity in polyps previously below the detection threshold. To improve the depiction of slow blood flow with use of the Doppler technique, several novel modified power Doppler–based techniques that operate at very low velocity scales using advanced clutter suppression have been developed, including Superb Microvascular Imaging (or SMI, Canon Medical Systems), MicroFlow Imaging (or MFI, Philips Healthcare), and microvascular flow imaging (MV-Flow, Samsung Medison). These techniques can separate slow or small-vessel flow signals from clutter artifacts that arise from voluntary and involuntary motion by using a vendor-specific adaptive filter and can display flow information at a high spatial resolution and frame rate (74).

The SRU consensus conference committee agreed that detection of polyp vascularity should not influence risk stratification.

Polyp Echogenicity

Similarly, few studies have analyzed polyp echogenicity. Most cholesterol polyps are hyperechoic in appearance; however, echogenicity may be impacted by posterior acoustic shadowing, enhancement, or machine parameters, and assessment is prone to subjectivity. While all studies noted that polyps that were isoechoic or hypoechoic compared with either the liver or echogenic gallbladder wall were more likely to be neoplastic than hyperechoic polyps, none showed that echogenicity was an independent risk factor for neoplasia at multivariable analysis (68,72).

The SRU consensus conference committee agreed that polyp echogenicity should not influence risk stratification.

Focal Wall Thickening Adjacent to the Polyp

Although gallbladder wall thickening has not been sufficiently studied to be histologically predictive, Kim et al (16) found that focal gallbladder wall thickening adjacent to a gallbladder polyp was a significant predictor for a neoplastic polyp. Wennmacker et al (5) found that focal mural thickening, rather than a lumen-protruding polyp, was associated with neoplastic polyps and increased risk of malignancy.

The SRU consensus conference committee agreed that focal wall thickening of 4 mm or greater adjacent to a gallbladder polyp that cannot be attributed to wall edema, mucosal fold or folds, adenomyomatosis, or gallbladder underdistention is a concerning finding that warrants risk stratification into the indeterminate risk category (Fig 7).

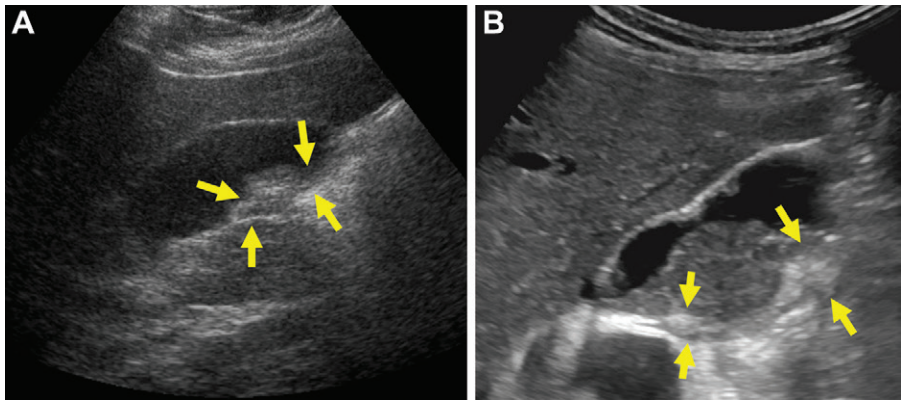


Figure 7: **(A, B)** US images show indeterminate risk polyps. Two different patients had gallbladder polyps with adjacent focal wall thickening of 4 mm or greater (between arrows) adjacent to the polyp, which meet criteria for indeterminate risk. For patients with indeterminate risk polyps that measure 6 mm or less, follow-up at 6, 12, 24, and 36 months is recommended. If, at follow-up, a polyp has increased in size by 4 mm or more within a 12-month period or reaches 7 mm, surgical consultation is recommended. For polyps measuring 7 mm or larger, surgical consultation is recommended. In both examples, polyps measured at least 7 mm, and the patients were referred for surgical resection. Both examples were adenocarcinomas at pathologic examination.

Single versus Multiple

Although many studies have shown that malignant or neoplastic polyps were more likely to be single than multiple (4,5,7,14–17,37,43,72,75), many benign polyps are also single (4,5,35). Notably, most studies evaluating single versus multiple polyps compared their results with pathologic findings, which significantly skews the study population. Only two studies showed that a single polyp was an independent risk factor for malignancy at multivariable analysis (43,68). This may reflect the fact that most single polyps are still benign and/or nonneoplastic due to their considerably greater prevalence.

The SRU consensus conference committee agreed that the number of polyps should not influence risk stratification.

Alternative Imaging Evaluation

Contrast-enhanced US

Compared with CT and MRI, several studies have shown the advantages of microbubble contrast-enhanced US (CEUS) in the characterization of gallbladder polyps due to its high spatial and temporal resolution (76). CEUS can help distinguish a vascular lesion from sludge (77,78). CEUS may also improve visualization of polyp morphologic features and detection of mural or hepatic invasion (78) (Fig 8) or adenomyomatosis as a focal area of tiny cysts in the gallbladder wall compared with CT or MRI (77).

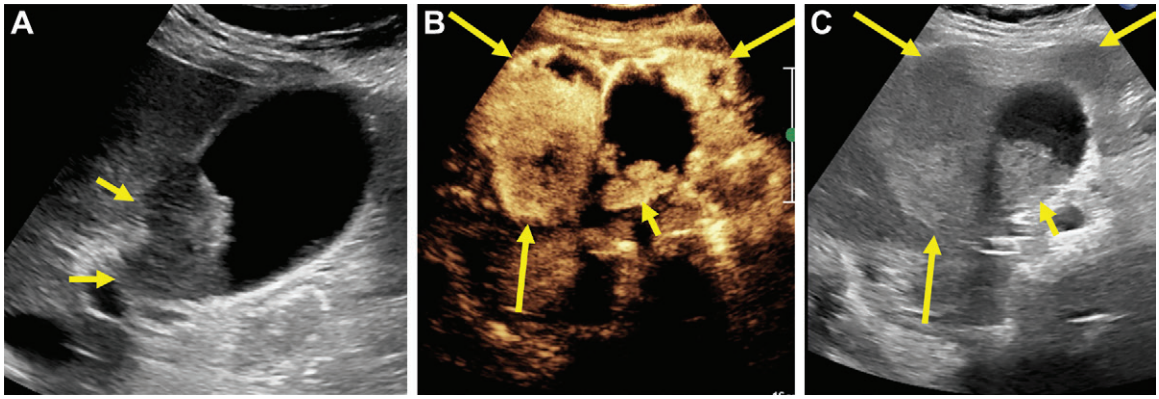


Figure 8: Frank liver invasion and liver metastases. **(A)** Gray-scale US image shows a 23-mm hypoechoic mass with frank direct liver invasion (arrows). Given findings of suspected malignant invasion, the Society of Radiologists in Ultrasound algorithm should not be used, and referral to an oncologic specialist would be recommended. **(B)** Contrast-enhanced and **(C)** corresponding gray-scale US images obtained 6 months later, as patient was lost to follow-up, show an enlarging polypoid mass (now 33 mm) (short arrow). Microbubble contrast (**B**) demonstrates heterogeneous enhancement and ulceration and outlines multiple liver metastases (long arrows in **B** and **C**).

Furthermore, the degree of enhancement relative to the gallbladder wall or liver, as well as dynamic temporal change, may be predictive in differentiating nonneoplastic from neoplastic polyps and identifying malignant lesions (69,79,80). Nonneoplastic lesions show late microbubble enhancement that is hypoenhancing compared with the liver, whereas neoplastic lesions show marked early enhancement (69,80). Eccentric hyperenhancement and sustained homogeneous enhancement are more commonly seen in adenomatous polyps, while washout is often seen in malignant polyps (81).

Intralesional microvasculature patterns can also be delineated with CEUS (69,80). Stalk-like central enhancement may indicate a cholesterol polyp (81). Intralesional straight vessels are associated with adenomatous polyps (82), whereas intralesional branching vessels correlate with malignant neoplasms and may indicate internal perfusion defects (69,80,83).

CT and MRI

The literature regarding CT and MRI for gallbladder polypoid lesions is scarce and confounded by low numbers and selection bias of polyps over 10 mm (66,84). Significant findings suggesting malignancy at multivariable analysis include size larger than 15 mm, sessile shape, and identification at unenhanced CT (66). In a 1998 study by Furukawa et al (84), only 45% of polypoid lesions larger than 5 mm seen sonographically were detected at unenhanced CT, although 100% were detected at enhanced CT. The majority of undetected lesions were cholesterol polyps, leading the authors to conclude that an undetectable polyp at unenhanced CT, if pedunculated and seen at enhanced CT, represents a benign cholesterol polyp with 90% accuracy. Dual-energy CT may also be helpful in differentiating nonneoplastic from neoplastic polyps larger than 10 mm (85), but further studies are needed.

The sensitivity of MRI in gallbladder polyp detection relative to that of US is unknown. Studies evaluating pathologic features of the gallbladder at MRI typically combine polypoid lesions with focal wall thickening. High T1-weighted signal may indicate cholesterol polyps or pigment stones, while restricted diffusion on diffusion-weighted images may be suggestive of malignancy (70,86–88). Benign polyps tend to have low T2-weighted signal intensity; however, intermediate to high T2 signal intensity may be a more suspicious finding. In one study, malignant neoplasms tended to show early peripheral and sustained enhancement, whereas benign lesions tended to show washout (89).

Additionally, MRI may be useful to exclude adenomyomatosis or tumefactive sludge. Adenomyomatosis can be definitively diagnosed by the demonstration of cystic-like Rokitansky-Aschoff sinuses of the gallbladder wall, while inspissated bile or tumefactive sludge will not enhance with postgadolinium sequences, as opposed to typically vascular GBC (90).

The SRU consensus conference committee agreed that short-interval follow-up US within 1–2 months with optimized technique and patient preparation may be helpful in the evaluation of gallbladder lesions larger than 10 mm in which differentiation of tumefactive sludge from a gallbladder mass, polyp, or adenomyomatosis is challenging. Alternatively, CEUS may be used for further characterization. If CEUS is not readily available, MRI may be considered (Fig 9).

The SRU consensus conference committee agreed that while CT may be helpful in distinguishing the aforementioned entities, the diagnostic accuracy of CT is inferior to that of CEUS or MRI for this purpose.

Endoscopic US

Endoscopic US (EUS) is often performed in patients with abdominal pain and suspected pancreaticobiliary disease. Given the proximity of the gallbladder to the EUS probe and the use of higher-frequency transducers, conceptually, EUS may be used to better identify and discriminate malignant gallbladder polyps; however, data are conflicting. In one study by Sugiyama et al (91), EUS helped better identify gallbladder polyp types than transabdominal US did (97% vs 71%), with tiny echogenic foci or an aggregation of echogenic foci seen in the vast majority of cholesterol polyps. Adenomyomatosis showed multiple microcysts or comet-tail artifacts at EUS, unlike adenomas and adenocarcinomas. Sadamoto et al (92) found three variables predictive of neoplastic polyps at

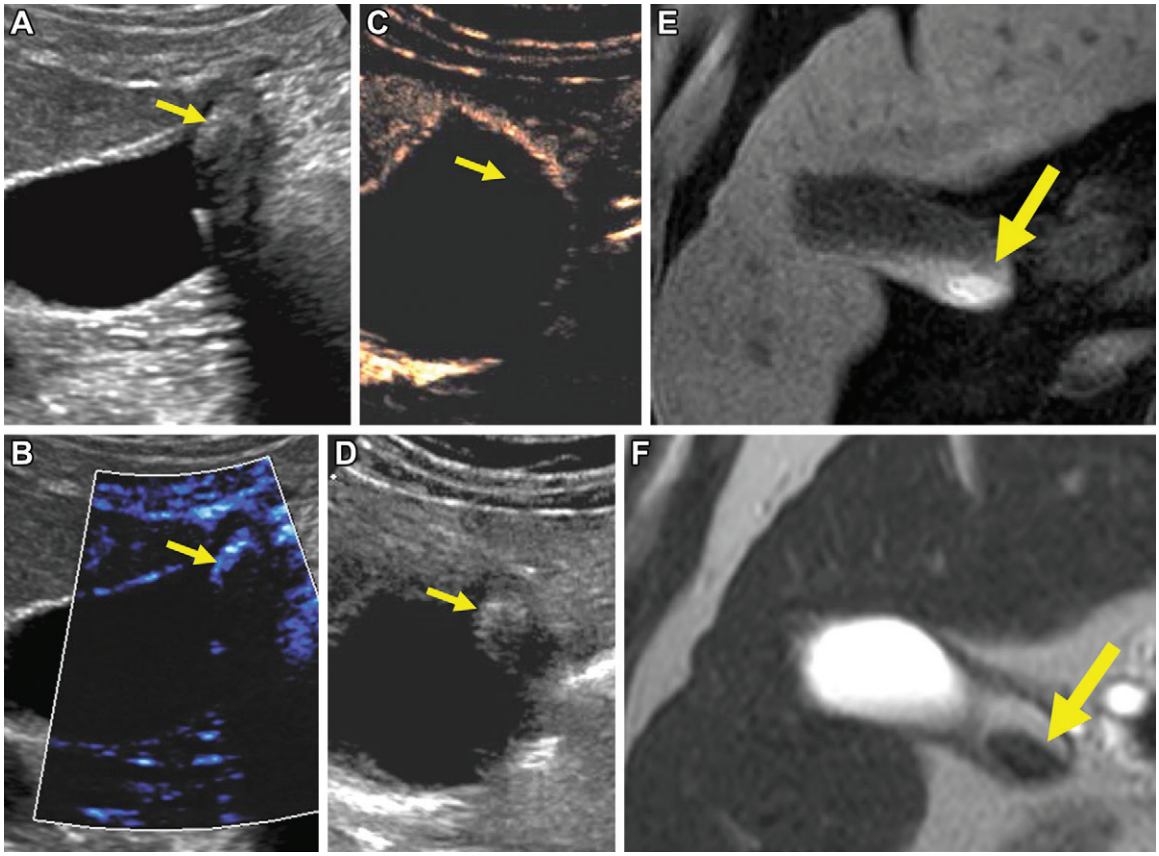


Figure 9: Tumefactive sludge proven to be avascular at contrast-enhanced US (CEUS). **(A)** Gray-scale US image of the gallbladder shows a polypoid mass (arrow) at the fundus of the gallbladder. **(B)** Flow-sensitive Doppler technique image shows peripheral artifact (arrow) but no definite internal vascularity. **(C)** CEUS and **(D)** gray-scale US images in the transverse oblique plane show no internal enhancement (arrows), consistent with tumefactive sludge. **(E)** T1- and **(F)** T2-weighted MRI scans obtained 6 months later show intrinsic high T1 signal intensity and low T2 signal intensity (arrows). MRI findings are concordant with CEUS findings of tumefactive sludge and interval formation of a gallstone.

EUS: maximum diameter of 11 mm or more, heterogeneous internal echoes, and absence of hyperechoic foci. Other studies, however, have not shown a diagnostic difference between transabdominal US and EUS (71).

The SRU consensus conference committee agreed that due to the invasive nature of EUS, it should not be considered part of the typical evaluation of gallbladder polyps.

Surgical Considerations

Historically, cholecystectomy has been recommended for polyps greater than 10 mm, with a subsequent increase in cholecystectomy rates due to increased polyp detection (47). Given that most surgically resected polyps are nonmalignant, the possibility of malignancy of the identified lesion must be weighed against the risks of cholecystectomy (6).

In general, surgical risk related to cholecystectomy is minimal and most closely associated with the surgical indication and underlying comorbidities (36). Cholecystectomy performed in acute illness, such as cholecystitis, is the greatest predictor of increased morbidity when compared with elective surgery for biliary colic or asymptomatic polyps. In studies examining cholecystectomies for all indications, the risk of morbidity was 2%–8%, including the devastating risk of bile duct injury (three to six of 1000 patients) (93,94). Mortality ranged between two and seven of 1000 patients and was related to operative complexity and medical comorbidities (95–97). As rates of cirrhosis and concomitant sonographic hepatocellular carcinoma screening increase, the decision to intervene must be carefully weighed against the increased surgical risk in this population (ie, patients with cirrhosis who undergo screening and have an incidental gallbladder polyp identified) (98). In all cases, the individual surgical risk of the patient must be balanced with the indication for surgery (36).

The SRU consensus conference committee agreed that patient selection for surgery is multifactorial, requiring shared decision-making, and must take into account patient health status as well as risk profiles of imaging findings.

Cost-effectiveness

Very few studies have evaluated the cost-effectiveness of surveillance US or other management strategies for patients with gallbladder polyps. In 2012, Cairns et al (99) concluded that surveillance of polyps between 5 and 10 mm and cholecystectomy for polyps of 10 mm or larger is cost-effective, presuming that all neoplastic polyps would become malignant and that all malignant neoplasms resected would result in complete treatment. Notably, as described earlier, the assumption that all neoplastic polyps become malignant is not supported by the literature. Cairns et al compared the cost of £150 ($235) per US

examination biannually over 20 years to the treatment of GBC at a cost of £60 000 ($94 069). In their study of 986 patients, 467 underwent follow-up, with only one invasive cancer identified (99). A second study, published by Patel et al (65) in 2019, used the same assumptions regarding neoplastic polyp progression and successful management, assessing 5 years of gallbladder polyp surveillance with the European guidelines in 558 patients. Of the 89 patients who underwent cholecystectomy, only three had dysplastic adenomatous polyps (all >10 mm), with only one polyp (16 mm) having a focus of adenocarcinoma. Despite the low malignancy rate in their study, the authors concluded that the 2017 European guidelines were cost-effective.

The SRU consensus conference committee agreed that there is a paucity of high-quality evidence to support cost-effectiveness of specific thresholds for polyp surgical resection versus surveillance strategy, and future cost-effectiveness studies are encouraged.

Summary

Substantial knowledge gains over the past several years have shown that aggressive follow-up and treatment of incidentally identified small gallbladder polyps may be unwarranted. The Society of Radiologists in Ultrasound consensus conference guidelines have taken into consideration the peer-reviewed literature and imaging features of gallbladder polyps to help stratify follow-up recommendations. Revisions to these recommendations are expected to occur as further evidence accumulates.

Acknowledgments: We acknowledge James Seow, MBBS, for his invaluable comments and Aarti Sekhar, MD, for her input.

Author contributions: Guarantors of integrity of entire study, **A.K., C.F., Y.A., N.D., Y.Z.**; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, all authors; clinical studies, **A.K., J.L.S., N.D., M.E.T., X.Y., Y.Z., W.D.M.**; and manuscript editing, all authors

Disclosures of conflicts of interest: **A.K.** Textbook royalties from Elsevier; research support from Canon Medical Systems. **C.F.** Honoraria from the College of Physicians and Surgeons of Alberta as an elected council member for Provincial College; shareholder in Mikata Health; partner radiologist at Medical Imaging Consultants. **J.L.S.** No relevant relationships. **DT.F.** Research support to institution from GE Healthcare, Philips Healthcare, and Siemens Healthineers; member of expert medical advisory board for Philips Healthcare; research equipment loan from GE Healthcare, Philips Healthcare, and Siemens Healthineers. **A.J.W.** No relevant relationships. **Y.A.** No relevant relationships. **D.B.B.** No relevant relationships. **M.T.C.** No relevant relationships. **N.D.** No relevant relationships. **H.G.** No relevant relationships. **W.G.P.** No relevant relationships. **M.R.P.** No relevant relationships. **S.K.R.** Textbook royalties from Elsevier. **M.E.T.** Textbook royalties from Amirsys and Elsevier; honoraria from the University of Pennsylvania Department of Radiology Grand Rounds, Mass General-Brigham Executive Leadership Group; Marshak Award for international travel for lectures; 2020 RSNA program committee lead in genitourinary radiology. **X.Y.** No relevant relationships. **Y.Z.** No relevant relationships. **W.D.M.** Textbook royalties from Elsevier; honoraria from World Class CME for lectures at the 2021 National Diagnostic Imaging Symposium.

References

1. Jørgensen T, Jensen KH. Polyps in the gallbladder. A prevalence study. Scand J Gastroenterol 1990;25(3):281–286.
2. Aldouri AQ, Malik HZ, Waytt J, et al. The risk of gallbladder cancer from polyps in a large multiethnic series. Eur J Surg Oncol 2009;35(1):48–51.
3. Adsay V, Jang KT, Roa JC, et al. Intracholecystic papillary-tubular neoplasms (ICPN) of the gallbladder (neoplastic polyps, adenomas, and papillary neoplasms that are ≥1.0 cm): clinicopathologic and immunohistochemical analysis of 123 cases. Am J Surg Pathol 2012;36(9):1279–1301.
4. Wennmacker SZ, de Savornin Lohman EAJ, Hasami NA, et al. Overtreatment of nonneoplastic gallbladder polyps due to inadequate routine ultrasound assessment. Dig Surg 2021;38(1):73–79.
5. Wennmacker SZ, van Dijk AH, Raessens JHJ, et al. Polyp size of 1 cm is insufficient to discriminate neoplastic and non-neoplastic gallbladder polyps. Surg Endosc 2019;33(5):1564–1571.
6. Szpakowski JL, Tucker LY. Outcomes of gallbladder polyps and their association with gallbladder cancer in a 20-year cohort. JAMA Netw Open 2020;3(5):e205143.
7. Liu K, Lin N, You Y, et al. Risk factors to discriminate neoplastic polypoid lesions of gallbladder: a large-scale case-series study. Asian J Surg 2021;44(12):1515–1519.
8. Wiles R, Thoeni RF, Barbu ST, et al. Management and follow-up of gallbladder polyps: joint guidelines between the European Society of Gastrointestinal and Abdominal Radiology (ESGAR), European Association for Endoscopic Surgery and other Interventional Techniques (EAES), International Society of Digestive Surgery-European Federation (EFISDS) and European Society of Gastrointestinal Endoscopy (ESGE). Eur Radiol 2017;27(9):3856–3866.
9. Walsh AJ, Bingham DB, Kamaya A. Longitudinal ultrasound assessment of changes in size and number of incidentally detected gallbladder polyps. AJR Am J Roentgenol 2022;218(3):472–483.
10. World Health Organization Classification of Tumours Editorial Board. Digestive System Tumours. 5th ed. Geneva, Switzerland: World Health Organization, 2019.
11. He C, Fukumura Y, Toriyama A, et al. Pyloric gland adenoma (PGA) of the gallbladder: a unique and distinct tumor from PGAs of the stomach, duodenum, and pancreas. Am J Surg Pathol 2018;42(9):1237–1245.
12. Taskin OC, Basturk O, Reid MD, et al. Gallbladder polyps: correlation of size and clinicopathologic characteristics based on updated definitions. PLoS One 2020;15(9):e0237979.
13. Sung H, Freedman RA, Siegel RL, et al. Risks of subsequent primary cancers among breast cancer survivors according to hormone receptor status. Cancer 2021;127(18):3310–3324. [Published correction appears in Cancer 2022 Feb 2. doi: 10.1002/cncr.34077.]
14. Kwon W, Jang JY, Lee SE, Hwang DW, Kim SW. Clinicopathologic features of polypoid lesions of the gallbladder and risk factors of gallbladder cancer. J Korean Med Sci 2009;24(3):481–487.
15. Kim JH, Lee JY, Baek JH, et al. High-resolution sonography for distinguishing neoplastic gallbladder polyps and staging gallbladder cancer. AJR Am J Roentgenol 2015;204(2):W150–W159.
16. Kim JS, Lee JK, Kim Y, Lee SM. US characteristics for the prediction of neoplasm in gallbladder polyps 10 mm or larger. Eur Radiol 2016;26(4):1134–1140.
17. Zielinski MD, Atwell TD, Davis PW, Kendrick ML, Que FG. Comparison of surgically resected polypoid lesions of the gallbladder to their pre-operative ultrasound characteristics. J Gastrointest Surg 2009;13(1):19–25.
18. Forman D, Bray F, Brewster DH, et al, eds. Cancer Incidence in Five Continents Vol X. IARC Scientific Publications No. 164. Lyon, France: International Agency for Research on Cancer, 2014.
19. Mhatre S, Wang Z, Nagrani R, et al. Common genetic variation and risk of gallbladder cancer in India: a case-control genome-wide association study. Lancet Oncol 2017;18(4):535–544.
20. Cha PC, Zembutsu H, Takahashi A, Kubo M, Kamatani N, Nakamura Y. A genome-wide association study identifies SNP in DCC is associated with gallbladder cancer in the Japanese population. J Hum Genet 2012;57(4):235–237.
21. Hemminki K, Li X. Familial liver and gall bladder cancer: a nationwide epidemiological study from Sweden. Gut 2003;52(4):592–596.
22. Hsing AW, Bai Y, Andreotti G, et al. Family history of gallstones and the risk of biliary tract cancer and gallstones: a population-based study in Shanghai, China. Int J Cancer 2007;121(4):832–838.
23. Buckles DC, Lindor KD, Larusso NF, Petrovic LM, Gores GJ. In primary sclerosing cholangitis, gallbladder polyps are frequently malignant. Am J Gastroenterol 2002;97(5):1138–1142.
24. Eaton JE, Thackeray EW, Lindor KD. Likelihood of malignancy in gallbladder polyps and outcomes following cholecystectomy in primary sclerosing cholangitis. Am J Gastroenterol 2012;107(3):431–439.
25. van Erp LW, Cunningham M, Narasimman M, et al. Risk of gallbladder cancer in patients with primary sclerosing cholangitis and radiographically detected gallbladder polyps. Liver Int 2020;40(2):382–392.
26. Chapman R, Fevery J, Kalloo A, et al. Diagnosis and management of primary sclerosing cholangitis. Hepatology 2010;51(2):660–678.
27. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. J Hepatol 2009;51(2):237–267.

28. Bowlus CL, Lim JK, Lindor KD. AGA clinical practice update on surveillance for hepatobiliary cancers in patients with primary sclerosing cholangitis: expert review. Clin Gastroenterol Hepatol 2019;17(12):2416–2422.
29. Lindor KD, Kowdley KV, Harrison ME; American College of Gastroenterology. ACG clinical guideline: primary sclerosing cholangitis. Am J Gastroenterol 2015;110(5):646–659; quiz 660.
30. Said K, Glaumann H, Bergquist A. Gallbladder disease in patients with primary sclerosing cholangitis. J Hepatol 2008;48(4):598–605.
31. Boulton RA, Adams DH. Gallbladder polyps: when to wait and when to act. Lancet 1997;349(9055):817.
32. Cha BH, Hwang JH, Lee SH, et al. Pre-operative factors that can predict neoplastic polypoid lesions of the gallbladder. World J Gastroenterol 2011;17(17):2216–2222.
33. Terzioğlu SG, Kılıç MO, Sapmaz A, Karaca AS. Predictive factors of neoplastic gallbladder polyps: outcomes of 278 patients. Turk J Gastroenterol 2017;28(3):202–206.
34. Lee H, Kim K, Park I, et al. Preoperative predictive factors for gallbladder cholesterol polyp diagnosed after laparoscopic cholecystectomy for polypoid lesions of gallbladder. Ann Hepatobiliary Pancreat Surg 2016;20(4):180–186.
35. Guo J, Wu G, Zhou Z. Polypoid lesions of the gallbladder: report of 160 cases with special reference to diagnosis and treatment in China. Int J Clin Exp Pathol 2015;8(9):11569–11578.
36. Fagenson AM, Powers BD, Zorbas KA, et al. Frailty predicts morbidity and mortality after laparoscopic cholecystectomy for acute cholecystitis: an ACS-NSQIP cohort analysis. J Gastrointest Surg 2021;25(4):932–940.
37. Park JY, Hong SP, Kim YJ, et al. Long-term follow up of gallbladder polyps. J Gastroenterol Hepatol 2009;24(2):219–222.
38. Park JK, Yoon YB, Kim YT, et al. Management strategies for gallbladder polyps: is it possible to predict malignant gallbladder polyps? Gut Liver 2008;2(2):88–94.
39. Lugo A, Peveri G, Gallus S. Should we consider gallbladder cancer a new smoking-related cancer? A comprehensive meta-analysis focused on dose-response relationships. Int J Cancer 2020;146(12):3304–3311.
40. Borena W, Edlinger M, Bjørge T, et al. A prospective study on metabolic risk factors and gallbladder cancer in the metabolic syndrome and cancer (Me-Can) collaborative study. PLoS One 2014;9(2):e89368. [Published correction appears in PLoS One 2014;9(7):e102291.]
41. Wiles R, Varadpande M, Muly S, Webb J. Growth rate and malignant potential of small gallbladder polyps—systematic review of evidence. Surgeon 2014;12(4):221–226.
42. Babu BI, Dennison AR, Garcea G. Management and diagnosis of gallbladder polyps: a systematic review. Langenbecks Arch Surg 2015;400(4):455–462.
43. Bhatt NR, Gillis A, Smoothey CO, Awan FN, Ridgway PF. Evidence based management of polyps of the gall bladder: a systematic review of the risk factors of malignancy. Surgeon 2016;14(5):278–286.
44. Kozuka S, Tsubone N, Yasui A, Hachisuka K. Relation of adenoma to carcinoma in the gallbladder. Cancer 1982;50(10):2226–2234.
45. Chattopadhyay D, Lochan R, Balupuri S, Gopinath BR, Wynne KS. Outcome of gall bladder polypoidal lesions detected by transabdominal ultrasound scanning: a nine year experience. World J Gastroenterol 2005;11(14):2171–2173.
46. Yang HL, Sun YG, Wang Z. Polypoid lesions of the gallbladder: diagnosis and indications for surgery. Br J Surg 1992;79(3):227–229.
47. Koga A, Watanabe K, Fukuyama T, Takiguchi S, Nakayama F. Diagnosis and operative indications for polypoid lesions of the gallbladder. Arch Surg 1988;123(1):26–29.
48. Mainprize KS, Gould SW, Gilbert JM. Surgical management of polypoid lesions of the gallbladder. Br J Surg 2000;87(4):414–417.
49. Colecchia A, Larocca A, Scaioli E, et al. Natural history of small gallbladder polyps is benign: evidence from a clinical and pathogenetic study. Am J Gastroenterol 2009;104(3):624–629.
50. Corwin MT, Siewert B, Sheiman RG, Kane RA. Incidentally detected gallbladder polyps: is follow-up necessary?—Long-term clinical and US analysis of 346 patients. Radiology 2011;258(1):277–282.
51. Csendes A, Burgos AM, Csendes P, Smok G, Rojas J. Late follow-up of polypoid lesions of the gallbladder smaller than 10 mm. Ann Surg 2001;234(5):657–660.
52. Pickering O, Pucher PH, Toale C, et al. Prevalence and sonographic detection of gallbladder polyps in a Western European population. J Surg Res 2020;250:226–231.
53. Rafaelsen SR, Otto PO, Pedersen MRV. Long-term ultrasound follow-up in patients with small gallbladder polyps. Dan Med J 2020;67(10):A06200414.
54. Konstantinidis IT, Bajpai S, Kambadakone AR, et al. Gallbladder lesions identified on ultrasound. Lessons from the last 10 years. J Gastrointest Surg 2012;16(3):549–553.
55. Elmasry M, Lindop D, Dunne DF, Malik H, Poston GJ, Fenwick SW. The risk of malignancy in ultrasound detected gallbladder polyps: a systematic review. Int J Surg 2016;33(Pt A):28–35.
56. Middleton WD, Fung C, Dahiya N, et al. Survey study on the experience, practice patterns, and preferences of the fellows of the Society of Radiologists in Ultrasound for evaluation and management of gallbladder polyps detected with ultrasound. Ultrasound Q 2022. 10.1097/RUQ.0000000000000597. Published online February 25, 2022.
57. Chou SC, Chen SC, Shyr YM, Wang SE. Polypoid lesions of the gallbladder: analysis of 1204 patients with long-term follow-up. Surg Endosc 2017;31(7):2776–2782.
58. Pedersen MR, Dam C, Rafaelsen SR. Ultrasound follow-up for gallbladder polyps less than 6 mm may not be necessary. Dan Med J 2012;59(10):A4503.
59. Shin SR, Lee JK, Lee KH, et al. Can the growth rate of a gallbladder polyp predict a neoplastic polyp? J Clin Gastroenterol 2009;43(9):865–868.
60. Choi SY, Kim TS, Kim HJ, et al. Is it necessary to perform prophylactic cholecystectomy for asymptomatic subjects with gallbladder polyps and gallstones? J Gastroenterol Hepatol 2010;25(6):1099–1104.
61. Ito H, Hann LE, D'Angelica M, et al. Polypoid lesions of the gallbladder: diagnosis and followup. J Am Coll Surg 2009;208(4):570–575.
62. Collett JA, Allan RB, Chisholm RJ, Wilson IR, Burt MJ, Chapman BA. Gallbladder polyps: prospective study. J Ultrasound Med 1998;17(4):207–211.
63. Kratzer W, Haenle MM, Voegtle A, et al. Ultrasonographically detected gallbladder polyps: a reason for concern? A seven-year follow-up study. BMC Gastroenterol 2008;8(1):41.
64. Ansari SM, Banu S, Awal MA, Siddique AB, Alam MM. Polypoid gall bladder lesions: is it necessary for immediate surgery? Bangladesh Med Res Counc Bull 2007;33(2):44–47.
65. Patel K, Dajani K, Vickramarajah S, Huguet E. Five year experience of gallbladder polyp surveillance and cost effective analysis against new European consensus guidelines. HPB (Oxford) 2019;21(5):636–642.
66. Park KW, Kim SH, Choi SH, Lee WJ. Differentiation of nonneoplastic and neoplastic gallbladder polyps 1 cm or bigger with multi-detector row computed tomography. J Comput Assist Tomogr 2010;34(1):135–139.
67. Bae JS, Kim SH, Kang HJ, et al. Quantitative contrast-enhanced US helps differentiating neoplastic vs non-neoplastic gallbladder polyps. Eur Radiol 2019;29(7):3772–3781.
68. Choi TW, Kim JH, Park SJ, Ahn SJ, Joo I, Han JK. Risk stratification of gallbladder polyps larger than 10 mm using high-resolution ultrasonography and texture analysis. Eur Radiol 2018;28(1):196–205.
69. Liu XS, Gu LH, Du J, et al. Differential diagnosis of polypoid lesions of the gallbladder using contrast-enhanced sonography. J Ultrasound Med 2015;34(6):1061–1069.
70. Wennmacker SZ, de Savornin Lohman EAJ, de Reuver PR, et al. Imaging based flowchart for gallbladder polyp evaluation. J Med Imaging Radiat Sci 2021;52(1):68–78.
71. Wennmacker SZ, Lamberts MP, Di Martino M, Drenth JP, Gurusamy KS, van Laarhoven CJ. Transabdominal ultrasound and endoscopic ultrasound for diagnosis of gallbladder polyps. Cochrane Database Syst Rev 2018;8(8):CD012233.
72. Kubota K, Bandai Y, Noie T, Ishizaki Y, Teruya M, Makuuchi M. How should polypoid lesions of the gallbladder be treated in the era of laparoscopic cholecystectomy? Surgery 1995;117(5):481–487.
73. Hertzberg B, Middleton W. The Gallbladder. In: Ultrasound Requisites. 3rd ed. Philadelphia, Pa: Elsevier, 2015; 32–50.
74. Kang HJ, Lee JM, Jeon SK, et al. Microvascular flow imaging of residual or recurrent hepatocellular carcinoma after transarterial chemoembolization: comparison with color/power Doppler imaging. Korean J Radiol 2019;20(7):1114–1123.
75. Terzi C, Sökmen S, Seçkin S, Albayrak L, Uğurlu M. Polypoid lesions of the gallbladder: report of 100 cases with special reference to operative indications. Surgery 2000;127(6):622–627.
76. Fei X, Li N, Zhu L, et al. Value of high frame rate contrast-enhanced ultrasound in distinguishing gallbladder adenoma from cholesterol polyp lesion. Eur Radiol 2021;31(9):6717–6725.
77. Zhang HP, Bai M, Gu JY, He YQ, Qiao XH, Du LF. Value of contrast-enhanced ultrasound in the differential diagnosis of gallbladder lesion. World J Gastroenterol 2018;24(6):744–751.
78. Tsuji S, Sofuni A, Moriyasu F, et al. Contrast-enhanced ultrasonography in the diagnosis of gallbladder disease. Hepatogastroenterology 2012;59(114):336–340.

79. Fei X, Lu WP, Luo YK, et al. Contrast-enhanced ultrasound may distinguish gallbladder adenoma from cholesterol polyps: a prospective case-control study. Abdom Imaging 2015;40(7):2355–2363.
80. Yuan Z, Liu X, Li Q, et al. Is contrast-enhanced ultrasound superior to computed tomography for differential diagnosis of gallbladder polyps? A cross-sectional study. Front Oncol 2021;11:657223.
81. Yuan HX, Cao JY, Kong WT, Xia HS, Wang X, Wang WP. Contrast-enhanced ultrasound in diagnosis of gallbladder adenoma. Hepatobiliary Pancreat Dis Int 2015;14(2):201–207.
82. Wang X, Zhu JA, Liu YJ, et al. Conventional ultrasound combined with contrast-enhanced ultrasound in differential diagnosis of gallbladder cholesterol and adenomatous polyps (1-2 cm). J Ultrasound Med 2022;41(3):617–626.
83. Choi JH, Seo DW, Choi JH, et al. Utility of contrast-enhanced harmonic EUS in the diagnosis of malignant gallbladder polyps (with videos). Gastrointest Endosc 2013;78(3):484–493.
84. Furukawa H, Kosuge T, Shimada K, et al. Small polypoid lesions of the gallbladder: differential diagnosis and surgical indications by helical computed tomography. Arch Surg 1998;133(7):735–739.
85. Yin SN, Chi J, Liu L, Ding N, Ji YD, Yuan JM. Dual-energy CT to differentiate gallbladder polyps: cholesterol versus adenomatous. Acta Radiol 2021;62(2):147–154.
86. Tsai HM, Lin XZ, Chen CY, Lin PW, Lin JC. MRI of gallstones with different compositions. AJR Am J Roentgenol 2004;182(6):1513–1519.
87. Irie H, Kamochi N, Nojiri J, Egashira Y, Sasaguri K, Kudo S. High b-value diffusion-weighted MRI in differentiation between benign and malignant polypoid gallbladder lesions. Acta Radiol 2011;52(3):236–240.
88. Lee NK, Kim S, Kim TU, Kim DU, Seo HI, Jeon TY. Diffusion-weighted MRI for differentiation of benign from malignant lesions in the gallbladder. Clin Radiol 2014;69(2):e78–e85.
89. Tseng JH, Wan YL, Hung CF, et al. Diagnosis and staging of gallbladder carcinoma. Evaluation with dynamic MR imaging. Clin Imaging 2002;26(3):177–182.
90. Haradome H, Ichikawa T, Sou H, et al. The pearl necklace sign: an imaging sign of adenomyomatosis of the gallbladder at MR cholangiopancreatography. Radiology 2003;227(1):80–88.
91. Sugiyama M, Xie XY, Atomi Y, Saito M. Differential diagnosis of small polypoid lesions of the gallbladder: the value of endoscopic ultrasonography. Ann Surg 1999;229(4):498–504.
92. Sadamoto Y, Oda S, Tanaka M, et al. A useful approach to the differential diagnosis of small polypoid lesions of the gallbladder, utilizing an endoscopic ultrasound scoring system. Endoscopy 2002;34(12):959–965.
93. Kumar A, Thombare MM, Sikora SS, Saxena R, Kapoor VK, Kaushik SP. Morbidity and mortality of laparoscopic cholecystectomy in an institutional setup. J Laparoendosc Surg 1996;6(6):393–397.
94. Sandblom G, Videhult P, Crona Guterstam Y, Svenner A, Sadr-Azodi O. Mortality after a cholecystectomy: a population-based study. HPB (Oxford) 2015;17(3):239–243.
95. Ismael HN, Cox S, Cooper A, Narula N, Aloia T. The morbidity and mortality of hepaticojejunostomies for complex bile duct injuries: a multi-institutional analysis of risk factors and outcomes using NSQIP. HPB (Oxford) 2017;19(4):352–358.
96. Fong ZV, Pitt HA, Strasberg SM, et al. Diminished survival in patients with bile leak and ductal injury: management strategy and outcomes. J Am Coll Surg 2018;226(4):568–576.e1.
97. Halbert C, Pagkratis S, Yang J, et al. Beyond the learning curve: incidence of bile duct injuries following laparoscopic cholecystectomy normalize to open in the modern era. Surg Endosc 2016;30(6):2239–2243.
98. Yeh CN, Chen MF, Jan YY. Laparoscopic cholecystectomy in 226 cirrhotic patients. Experience of a single center in Taiwan. Surg Endosc 2002;16(11):1583–1587.
99. Cairns V, Neal CP, Dennison AR, Garcea G. Risk and cost-effectiveness of surveillance followed by cholecystectomy for gallbladder polyps. Arch Surg 2012;147(12):1078–1083.