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# Polypoid Lesions of the Gallbladder: Diagnosis and Followup

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- BACKGROUND:** Polypoid lesions of the gallbladder (PLG) are commonly seen on ultrasonography (US), but optimal management of this problem is ill-defined. The aims of this study were to assess the natural history and the histologic characteristics of US-detected PLG.
- STUDY DESIGN:** Patients with PLG detected by abdominal US were identified retrospectively. Patients with infiltrative masses suspicious for gallbladder cancer were not included. Histologic findings were analyzed in patients who underwent cholecystectomy, and change in polyp size was determined in patients who underwent serial US imaging.
- RESULTS:** From 1996 through 2007, 417 patients with PLG detected on US were identified. Two hundred twenty-nine patients (55%) were women, and median age was 59 years (range 20 to 94 years). Two hundred sixty-five patients (64%) were found to have PLG on US during the workup of other unrelated disease; 94 patients (23%) had abdominal symptoms. Ninety-four percent of patients had PLG  $\leq$  10 mm, and 7% had PLG  $>$  10 mm; 59% of patients had a single polyp and 12% had gallstones. Among 143 patients who had repeat US followup, growth was observed in only 8 patients (6%). Cholecystectomy (n = 80) revealed that most patients had either pseudopolyps (58%) or no polyp (32%). Neoplastic polyps (adenoma) were found in 10% of patients. In situ cancer was seen in one patient with a 14-mm lesion.
- CONCLUSIONS:** Small PLG ( $\leq$ 10 mm in diameter) detected by US are infrequently associated with symptoms and can be safely observed. The risk of invasive cancer is very low, and was not seen in any patient in this study. (J Am Coll Surg 2009;208:570–575. © 2009 by the American College of Surgeons)
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Polypoid lesions of the gallbladder (PLGs), defined as elevated mucosal lesions, are seen in approximately 4% to 7% of the adult population undergoing abdominal ultrasonography (US).<sup>1,2</sup> The term *polypoid lesions of the gallbladder* represents a wide spectrum of findings and includes true polypoid neoplasms such as benign adenomas or adenocarcinomas and non-neoplastic polyps such as cholesterol polyps, inflammatory polyps, or adenomyomatous hyperplasia<sup>3</sup> (Fig. 1). Most PLGs incidentally found are benign

lesions, but rarely, some can be malignant or premalignant neoplasms.<sup>4-6</sup>

Although the real trend in prevalence of PLG is unclear, detection of small PLG has been increasing along with recent more frequent use of abdominal US and advances in imaging technology.<sup>7</sup> Currently, cholecystectomy is widely accepted as the treatment of choice for patients with symptoms or PLG  $>$  10 mm, based on earlier reports that most malignant polyps are  $>$  1 cm.<sup>4,8,9</sup> Other US findings, such as presence of concomitant stones, polypoid shape, or number are unreliable for distinguishing malignant neoplasms from benign neoplastic polyps or pseudopolyps,<sup>4-6,9</sup> making the decision of cholecystectomy for patients with asymptomatic small PLG  $\leq$  10 mm complex. Although followup with repeat US has been recommended, the data associated with the longterm natural history of PLG are limited and the optimal management of small PLG is not yet defined. The aims of this study were to assess the natural history and the histologic characteristics of US-detected PLG.

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### Abbreviations and Acronyms

PLG = polypoid lesions of the gallbladder  
 PPV = positive predictive value  
 US = ultrasonography

## METHODS

This study was approved by the Memorial Sloan-Kettering Cancer Center Institutional Review Board. Patients with PLG detected by US were retrospectively identified from a Department of Radiology database from 1996 through 2007. Ultrasonography studies were performed with 6-2 MHz curvilinear or 4-1 MHz vector transducers and Siemens Acuson or HDI 5000 Philips units. The patients were scanned in the supine and left lateral decubitus positions after fasting. Standard sonographic criteria were used to diagnose PLG: the lesion had to be immobile, nonshadowing, hyperechoic compared with the surrounding bile, and attached to the gallbladder wall.<sup>8</sup> Patients with infiltrative masses or asymmetric gallbladder wall thickening considered suspicious for gallbladder cancer were not included.

Radiology reports were retrospectively reviewed to determine polyp size, number of polyps, and presence or absence of gallstones. When two or more polyps were detected, the size of the largest lesion was recorded. Change in polyp size and number were determined in patients who underwent serial US imaging. Change in size was defined when an increase or decrease of  $\geq 3$  mm was recorded, as in previous studies.<sup>5,10,11</sup> Changes in size and number, if any, were documented throughout the followup period.

Histologic findings were analyzed in patients who underwent cholecystectomy, in most cases, performed as a laparoscopic procedure. Some patients underwent cholecystectomy as part of another unrelated operation.

Continuous variables were expressed as median (range). Categorical variables were compared using a chi-square-test. A  $p$  value  $< 0.05$  was considered statistically significant.

## RESULTS

Four hundred seventeen patients with PLG detected on US were identified. Two hundred twenty-nine patients (55%) were women, and the median age was 59 years (range 20 to 94 years). Two hundred sixty-five patients (64%) were found to have PLG on US during workup of unrelated disease; 94 patients (23%) had abdominal symptoms, 55 patients (13%) had abnormal liver function tests, and 3 patients (1%) had fever. The majority of patients (94%) had PLG  $\leq 10$  mm. Fifty-nine percent of patients had a single polyp and 12% had associated gallstones (Table 1). Nineteen percent of patients with PLG  $< 6$  mm had ab-

dominal symptoms, compared with 32% of those with PLG  $\geq 6$  mm ( $p = 0.003$ ).

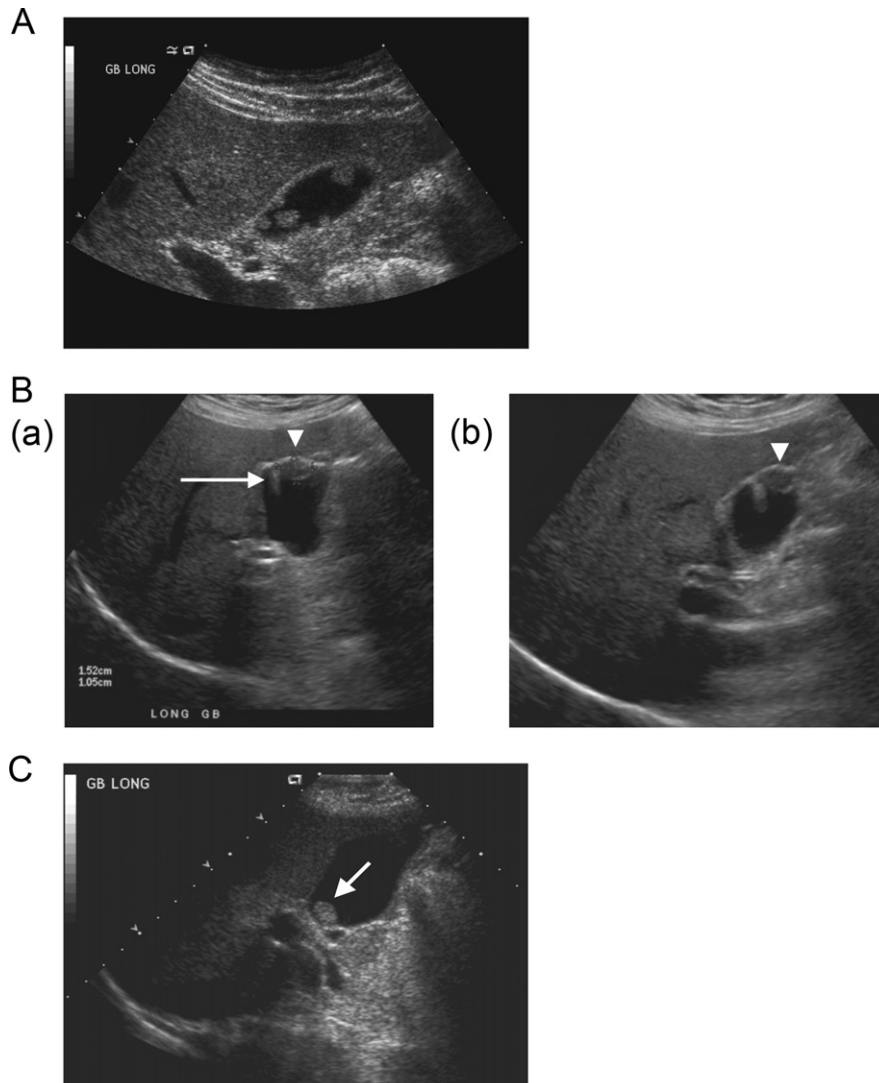
One hundred forty-three patients were followed with repeat US examinations (Fig. 2). The median interval between the initial US and most recent followup US was 17 months (range 1 to 81 months). Among those who had serial US examinations, growth was observed in 8 patients (6%), there was no change in 123 patients (86%), and regression was seen in 12 patients (9%). The median change in size among the polyps that grew was 3.5 mm (range 3 to 6 mm). In terms of number, 17 patients, including 13 with a single polyp and 4 with multiple polyps on initial US, had more polyps seen on the most recent followup study. The median change in number among those polyps was 1 (range 1 to  $> 3$ ). Detailed changes in size and number of PLG are summarized in Table 2.

Eighty patients underwent cholecystectomy during the study period. Among them, 17 patients (21%) underwent cholecystectomy for large PLG ( $> 10$  mm), and 18 patients (23%) for abdominal symptoms. Eleven patients (14%) with small PLG ( $< 10$  mm) elected surgery rather than imaging followup, and 34 patients (43%) underwent cholecystectomy along with an unrelated abdominal operation (25 liver resections, 4 pancreatectomies, 3 bile duct resections, 1 colectomy, 1 debulking of metastatic ovarian cancer). Histologic diagnoses of these patients are summarized in Table 3. Twenty-six patients (32%) had no polypoid lesions identified (normal gallbladder [ $n = 9$ ], chronic cholecystitis [ $n = 8$ ], and cholelithiasis [ $n = 9$ ]); 46 patients (58%) had pseudopolyps (cholesterol polyps or cholesterosis [ $n = 33$ ], inflammatory polyps [ $n = 3$ ], and adenomyomatous hyperplasia [ $n = 10$ ]). Eight patients (10%) had adenomas; one 14-mm polyp contained high grade dysplasia (carcinoma in situ). None had adenocarcinoma.

The positive predictive value (PPV) for detecting either neoplastic or pseudopolyps was 68%: 61% for PLG  $< 6$  mm and 75% for PLG  $\geq 6$  mm ( $p = 0.20$ ). Among patients with PLG  $< 6$  mm on US, none was found to be neoplastic.

## DISCUSSION

PLG are frequent incidental findings on US, and the incidence has been reported as 5% to 7% in a healthy population.<sup>1,2,12</sup> Because of the increasing use of US and advanced imaging technology, small lesions are being detected with greater frequency,<sup>7</sup> and surgeons often encounter a clinical dilemma concerning management of such lesions. Although the option of cholecystectomy for patients with polyps  $> 10$  mm or any associated symptoms is currently accepted widely,<sup>8</sup> the significance of small, asymptomatic



**Figure 1.** Representative ultrasonographic findings of non-neoplastic and neoplastic polyps of the gallbladder. (A) Cholesterol polyp: multiple smooth echogenic polyps are seen throughout the gallbladder. (B) Adenomyomatous hyperplasia: longitudinal (a) and transverse (b) images of the gallbladder show a broad-based fundal polyp (arrowhead) with a thin echogenic rim. An adjacent area of “ring-down” artifact (arrow in a) caused by cholesterol crystals in Rokitansky-Aschoff sinuses is a classic ultrasonographic finding of adenomyomatosis. (C) Adenoma: longitudinal image of the gallbladder shows a nonshadowing smooth polyp in the neck of the gallbladder (arrow).

US-detected PLG is unclear. Currently, management of patients with these findings is driven by concern about development of gallbladder cancer, although it is not clear that such concern is justified.

Small PLG are easily detected by US, but accuracy in diagnosis of PLG based solely on US is controversial. In our series, 33% of the patients with PLG on US who underwent cholecystectomy did not have polyps by histologic examination (PPV, 68%). There are conflicting reports in the literature about the accuracy of US in diagnosis of PLG.

In two different series of cholecystectomy specimens reported by Ozdemir and colleagues<sup>13</sup> and Damore and associates,<sup>14</sup> the PPVs of US for PLG were as poor as 57% and 46%, respectively. Conversely, false positive results were seen in only 6% of patients in the series reported by Yang and coworkers.<sup>9</sup> This discrepancy in the accuracy of US to detect PLG may be explained partially by the size of polyps in each series. In the reports from Ozdemir and associates<sup>13</sup> and Damore and colleagues,<sup>14</sup> patients had relatively smaller polyps and there were no patients with pol-

**Table 1.** Characteristics of Polypoid Lesions of Gallbladder on Ultrasonography

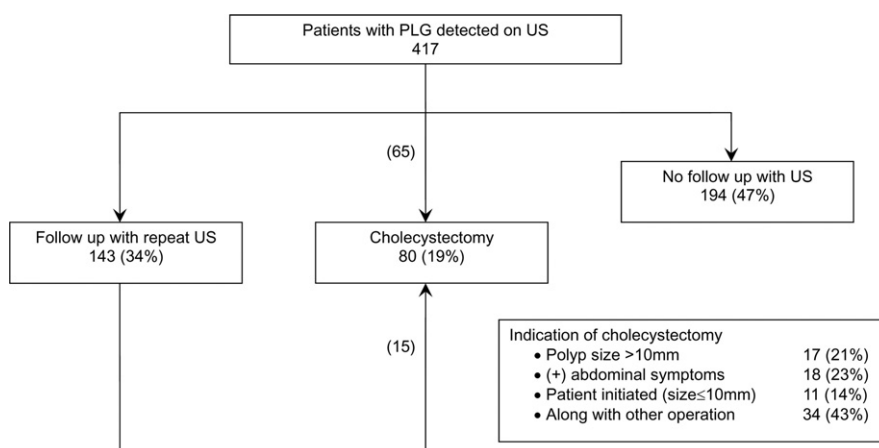
Characteristic	n	%
Size, mm		
1–5	302	73
6–10	88	21
≥11	26	6
Number		
Single	244	59
Multiple	173	42
Presence of gallstones		
Yes	48	12
No	369	89

yps > 10 mm; in Yang and coauthors's series,<sup>9</sup> 20% of polyps were > 10 mm. In fact, Akyurek and coworkers<sup>15</sup> compared the accuracy of US for polyps ≤ 10 mm and polyps > 10 mm in their prospective series of 56 patients; they concluded that the PPV for polyps ≤ 10 mm was poorer (5%) than that for polyps > 10 mm (57%). In our series, the PPV to detect small polyps < 6 mm was only 61%, and the PPV for polyps > 10 mm was 75%. Although there were data suggesting additional endoscopic US improved accuracy in diagnosis of PLG to 97% from 76% with abdominal US alone,<sup>5,11</sup> we do not believe that routine use of such a resource is financially practical, and the indications for this study should be discussed in the context of balancing its cost and benefit.

Distinguishing between a benign non-neoplastic polyp and a potentially premalignant or malignant neoplastic polyp based on US features is challenging and clinically far more relevant than distinguishing from among the various pseudopolyps.<sup>5,11</sup> Several discriminating features between benign and malignant polyps have been reported, and only

size appears to be a consistent feature throughout the literature. Yang and colleagues<sup>9</sup> reported that malignant lesions were seen in 8% of postcholecystectomy specimens with PLG, and all of them were > 10 mm and solitary. Kubota and associates<sup>4</sup> reported similar findings, that malignant lesions were seen in 11% of cholecystectomy specimens with PLG, 88% of which were > 10 mm and 56% of which were sessile in shape. These observations resulted in the current practice of performing cholecystectomy for PLG > 10 mm. Of note, in these two series, most of the patients with gallbladder cancer had a diagnosis of cancer before operation and underwent an appropriate radical procedure. We must emphasize that PLG with features suspicious for cancer, which were usually large and sessile, reported by a radiologist as “gallbladder mass” were not included in our study. Seventeen (of 26) patients with PLG > 10 mm underwent cholecystectomy, but none was found to have invasive cancer, except for one patient with an adenoma who had carcinoma in situ identified. Four patients had been followed with repeat US and five patients had no intervention because of the presence of malignant disease unrelated to the gallbladder. This study showed some relationship between size and the presence of adenomatous polyps, but the very low rate of malignancy, combined with sample size and followup limitations, does not allow any conclusions about the safety of observing larger PLG.

Although sonographic followup for patients with polyps < 10 mm has been recommended for presumed risk of gallbladder cancer developing, it is unclear whether gallbladder adenomas progress to cancer in a manner similar to colonic adenomas, and if so, how often it happens and how long it takes remain open questions. The theory of adenoma-carcinoma sequence is supported by histologic observation by Kozuka and colleagues,<sup>16</sup> who reviewed

**Figure 2.** The final disposition of all patients with ultrasonography-detected polypoid lesions of the gallbladder. The reasons for cholecystectomy are indicated.

**Table 2.** Change in Size and Number of Polypoid Lesions of Gallbladder During Followup

Characteristic	Followup period, mo									
	<11		12-23		24-47		≥48		Total	
	n	%	n	%	n	%	n	%	n	%
Patients	47	33	44	31	29	20	23	16	143	100
Size										
No change	40	85	36	82	27	93	20	87	123	86
Enlarged	2	4	2	5	1	3	3	13	8	6
Reduced	2	4	2	5	0	0	0	0	4	3
Disappeared	3	6	4	9	1	3	0	0	8	6
Number										
No change	42	89	36	82	25	86	15	65	118	83
Increased	2	4	4	9	3	10	8	35	17	12
Disappeared	3	6	4	9	1	3	0	0	8	6

1,605 cholecystectomy specimens and found 18 adenomas and 79 adenocarcinomas with evidence of transformation from adenoma to invasive cancer traceable histologically (in situ carcinoma in adenoma, and adenomatous remnant in adenocarcinoma), and it is the theoretic rationale of the current recommendation. But others believe that gallbladder carcinoma arises in situ from flat and dysplastic epithelium,<sup>17</sup> and the actual risk of a benign adenoma progressing to carcinoma is uncertain. In our study, 141 patients were followed by repeat US, and 94% of the lesions did not grow and no cancer developed. Similarly, Eelkema and associates<sup>18</sup> reported that gallbladder cancer did not develop in any patients with cholecystography-detected PLG during followup of 15 years. In addition, in recent prospective studies in which patients with US-detected PLG were followed up to 12 years, gallbladder cancer did not develop in any.<sup>10,19,20</sup> Aldouri and coworkers<sup>21</sup> analyzed multiinstitutional radiology and

cancer registries, including more than 70,000 patients who underwent US examination, and found that the prevalence of gallbladder cancer in Caucasian patients with PLG was as low as 0.08%. This finding makes the role of longterm routine surveillance for all patients with PLG questionable. On the other hand, Kubota and associates<sup>4</sup> reported that among the patients who had repeat US before cholecystectomy, all patients with cancer had rapid growth of lesions (1.4- to 4-fold within 4 to 12 months); benign lesions showed no growth during followup. So short-term US followup may be reasonable to detect small cancerous lesions missed on the initial test.

Limitations of this study include the retrospective design and sample size considerations. We as a tertiary referral cancer center specializing in cancer, often see patients with multiple diagnoses. In many cases, patients require prolonged and intensive therapy for these conditions, making followup for PLG a lower priority. But this fact should not detract from the results, which describe one of the largest series assessing the accuracy of US examination in cholecystectomy specimens and followup data with US. To date, prospective data concerning natural history of PLG are very limited and given the rarity of true neoplastic polyps in the gallbladder, multiinstitutional prospective data collection may be warranted to address this issue.

In conclusion, small PLG ( $\leq 10$  mm in diameter) detected by US can be safely observed, and PLG  $< 6$  mm on US will rarely represent true neoplastic polyps. Cholecystectomy appears to be warranted for lesions  $> 10$  mm for potential malignancy, although it appears to be very rare.

**Table 3.** Pathologic Diagnosis of Polypoid Lesions of Gallbladder after Cholecystectomy, Stratified by Size on Ultrasonography

Histology	Largest diameter of PLG on US, mm			Total
	<6	6-10	≥11	
Normal gallbladder, n	8	1	0	9 (11%)
Cholecystitis (no polyp), n	3	3	2	8 (10%)
Cholelithiasis, n	6	1	2	9 (11%)
Cholesterol polyp, cholesterosis, n	22	8	3	33 (41%)
Inflammatory polyp, n	0	0	3	3 (4%)
Adenomyomatous hyperplasia, n	5	2	3	10 (13%)
Adenoma, n	0	4	4*	8 (10%)
Total, n	44 (55%)	19 (24%)	17 (21%)	80 (100%)

\*Includes one adenoma with high grade dysplasia (carcinoma in situ). PLG, polypoid lesions of the gallbladder; US, ultrasonography.

#### Author Contributions

Study conception and design: Ito, Hann, D'Angelica, Allen, Fong, Klimstra, Blumgart, Jarnagin  
Acquisition of data: Ito, Hann, Jarnagin

Analysis and interpretation of data: Ito, Hann, D'Angelica, Allen, Fong, Klimstra, Blumgart, Jarnagin  
 Drafting of manuscript: Ito, Hann, Jarnagin  
 Critical revision: Ito, Hann, D'Angelica, Allen, Fong, Klimstra, Blumgart, Jarnagin

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