Small Polypoid Lesions of the Gallbladder

Differential Diagnosis and Surgical Indications by Helical Computed Tomography

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Objectives: To demonstrate the helical computed tomographic (CT) features of small polypoid lesions of the gallbladder and to establish a clinical strategy based on CT findings for the treatment of such lesions.

Design: Validation cohort study.

Setting: Tertiary care public hospital.

Patients: Thirty-one patients with polypoid lesions of the gallbladder (≤3 cm) underwent CT followed by resection.

Main Outcome Measure: The detectability of the lesions on both unenhanced and enhanced CT and the configuration of the lesions on enhanced CT were prospectively evaluated in comparison with the histopathological findings.

Results: Unenhanced CT detected 14 (45%) of the 31 lesions, whereas enhanced CT detected all of the lesions. The detection rates of the neoplastic lesions (adenoma, adenocarcinoma, and metastatic tumor) and cholesterol polyps were 81% (13/16) and 7% (1/15), respectively (P<.001). Among the 20 lesions demonstrated as pedunculated, 6 (30%) were neoplastic, whereas 10 (91%) of the 11 lesions demonstrated as sessile were neoplastic (P<.001). When a lesion was demonstrated on unenhanced CT or its shape was sessile on enhanced CT, the case was diagnosed as a neoplastic lesion. The sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of the CT diagnosis of the neoplastic lesions were 88% (14/16), 87% (13/15), 88% (14/16), 87% (13/15), and 87% (27/31), respectively.

Conclusion: Computed tomography can differentiate neoplastic and nonneoplastic small polypoid lesions of the gallbladder and reliably identify the presence of neoplastic lesions that should be resected.

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Recent advances in ultrasound techniques have made it possible to detect small polypoid lesions of the gallbladder, including early-stage gallbladder cancer. One epidemiological study in Japan found that the prevalence of polypoid lesions in healthy subjects as determined by ultrasonography (US) was 3.5% in men and 6.3% in women. In a study in Denmark, the prevalence was 4.6% and 4.3% in men and women, respectively. Among polypoid lesions of the gallbladder, the incidence of carcinoma is not high; cholesterol polyps are the most common form of polypoid lesions.

The most typical US appearance of a cholesterol polyp is a small, round, echogenic mass without acoustic shadowing. Relatively large cholesterol polyps have an irregular surface that gives a mulberrylike appearance. However, some cholesterol polyps appear partially or completely echopenic on US, which often makes them difficult to distinguish from adenocarcinoma. Therefore, US alone is not sufficient to differentiate these polypoid lesions.

Although advanced gallbladder cancers are still associated with a poor prognosis, the prognosis of patients with early-stage cancers has been favorable. Early-stage gallbladder cancers are defined as those confined to the mucosa or muscular layers, and the lesions may have several different macroscopic shapes, such as pedunculated, sessile, superficial raised,

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PATIENTS AND METHODS

PATIENTS

In this study, polypoid lesions of the gallbladder were defined as lesions 3 cm or less in maximum diameter visualized by means of US as protruding into the gallbladder lumen. In patients with multiple polyps, the size of the largest polyp was measured. Patients with gallbladder polyps that were small (<5 mm), hyperechoic masses thought to be undoubtedly cholesterol polyps were excluded from this study. Thirty-one consecutive patients who underwent resection for polypoid lesions of the gallbladder between September 1, 1993, and February 28, 1997, were included in this study. The patients were 10 men and 21 women with a mean age of 61.4 years (age range, 37-77 years). The average diameter of the lesions was 13.1 mm (range, 5-29 mm). Six patients had symptoms that included vague pain and discomfort in the upper part of the abdomen. In the remaining 25 asymptomatic patients, the polypoid lesions were found incidentally by means of US at a regular health checkup or a preoperative screening for other abdominal diseases. Six of the 31 patients had gallstones. Twenty-six (84%) of the 31 lesions were larger than 10 mm, and only 5 (16%) were 10 mm or smaller (Table 1).

Ultrasound was performed preoperatively in all patients with a real-time gray-scale device with a 3.5-MHz transducer (HUB-450 or 555; Hitachi Medical, Tokyo, Japan) or a 3.75-MHz transducer (SSA-270A; Toshiba Medical, Tokyo). Since the possibility of carcinoma of the gallbladder could not be excluded by US, all 31 lesions were resected.

CT EXAMINATION

The helical CT examinations were performed with 1 of 2 scanners (Toshiba X-Vigor or 900S, Toshiba Medical) in all 31 patients. After a scout view, unenhanced table incremental CT (UCT) was performed with 120-kilovolt peak (kV[p]), 250-mA, 5-mm slice thickness, 0-cm interscan gap, and a 9- to 12-cm scan length including the whole gallbladder to define the longitudinal length of the gallbladder. After UCT, enhanced helical CT (EHCT) was performed with 120-kV(p), 250-mA, 5-mm collimation, and 5-mm per second table movement (scan time per section, 1 second; scan collimation, 5 mm; scan pitch, 1) with a mechanical injection of 100 to 150 mL of ioversol (Optiray 320, Yamanouchi Pharmaceutical, Tokyo) into the antecubital vein at a rate of 2 to 3 mL per second. The CT scanning commenced 40 to 60 seconds after the start of the injection of the contrast medium. Transaxial images from the helical CT scan were reconstructed with 2- to 5-mm overlapping intervals. In some cases, the CT images were magnified (×1.5-2) and a multiplanar display was reconstructed by an accessory software program of the CT scanner to optimize the visualization of the lesion to evaluate its shape. Most patients underwent surgical procedures within 2 weeks after the CT examination.

INTERPRETATION OF CT SCAN

The CT examinations of all 31 patients were evaluated prospectively by 2 radiologists without knowledge of the findings of US or histopathological examination. They examined the visualization of the polypoid lesions on UCT and EHCT, and the configuration of the lesions depicted on EHCT, since these findings were found to be useful for differential diagnosis in a preliminary retrospective study.8 The configuration of the polypoid lesions on EHCT was classified into 2 types according to Ishikawa and coworkers’ classification of resected specimens: (1) pedunculated type, defined as a pedunculated or floating lesion with or without a narrow base in the lumen of the gallbladder, and (2) sessile type, defined as a protruding lesion with a broad base. Discrepancies were resolved by consensus. Results were analyzed by means of Fisher exact test. Differences were considered significant at P<0.05.

HISTOPATHOLOGICAL EXAMINATION

The surgically resected specimens were examined according to the General Rules for Surgical and Pathological Studies on Cancer of the Biliary Tract by the Japanese Society of Biliary Surgery.9 Resected specimens were immediately fixed in 10% buffered formalin, cut serially to 5-mm-thick sections, and processed routinely and embedded in paraffin. Paraffin sections were stained with hematoxylin-eosin. The histopathological findings of the benign lesions were divided on the basis of the criteria proposed by Christensen and Ishak11 (Table 1).

| Table 1. Histological Findings and Size of Polypoid Lesions of the Gallbladder |
|--------------------------|-----------------|------------------|---------------------|----------------|-------------------|
| Tumor Size, mm | Cholesterol Polyp | Adenoma | Adenocarcinoma | Metastatic | Total |
| 1-10 | 5 | 0 | 0 | 0 | 5 |
| 11-20 | 10 | 2 | 10 | 1 | 23 |
| 21-30 | 0 | 0 | 3 | 0 | 3 |
| Total | 15 | 2 | 13 | 1 | 31 |

*Metastatic renal cell carcinoma of the gallbladder.

and flat.7 Although the former 2 shapes can be detected more easily by US than the others, occasionally it is difficult to differentiate them from benign polyoid lesions.

If a polypoid lesion of the gallbladder is diagnosed as a cholesterol polyp and the patient is asymptomatic, surgical treatment is not necessary. In contrast, surgical resection is needed when the lesion is suspected to be neoplastic. Therefore, it is important to establish criteria for selecting which lesions should be resected and which surgical procedure is appropriate.

Helical (spiral) computed tomography (CT) has made it possible to obtain volumetric acquisitions during a single breath-holding period with little inaccessiveness. This technique allows scanning during the phase of maximal vascular enhancement and the acquisition of multiple thin sections through the area of interest. The advantages of this CT technique may be helpful for evaluating small polyoid lesions of the gallbladder; however, this has not been fully investigated.
The purpose of this study was to evaluate the accuracy of preoperative CT examinations and to establish a clinical strategy based on CT findings for small polyloid lesions of the gallbladder.

**RESULTS**

**VISUALIZATION OF POLYPOID LESIONS ON UCT AND EHCT**

Polypoid lesions of the gallbladder were detected in 14 (45%) of the 31 lesions on UCT, whereas all 31 lesions were demonstrated on EHCT (Table 2). Only 1 of the 15 cholesterol polyps was detected by UCT (Figure 1). The single cholesterol polyp detected on UCT was covered by well-developed epithelium with hyperplastic change. In contrast, 10 (77%) of the 13 adenocarcinomas were disclosed on UCT (Figure 2 and Figure 3). All 5 of the adenocarcinomas observed to be pedunculated lesions were confined to the mucosa or the muscular layer. Among the 8 adenocarcinomas that were sessile lesions, 2 were limited to the mucosa and 6 invaded into the subserosa. Two of the 6 patients whose cancer invaded to the subserosa had lymph node metastasis. Both of the 2 adenocarcinomas containing cholesterolosis in the polyp were limited to the mucosa. One adenoma was found to be pedunculated and another was observed to be a sessile lesion. One metastatic renal cell carcinoma was shown as a sessile lesion. Of the 20 lesions detected as the pedunculated type, 6 (30%) were neoplastic.

**CONFIGURATIONS OF POLYPOID LESIONS ON EHCT IN RELATION TO HISTOLOGICAL FINDINGS**

Since the detectability of polypoid lesions with EHCT was superior to that with UCT, the configurations of the lesions were evaluated on EHCT. Fourteen (93%) of the 15 cholesterol polyps were found to be pedunculated lesions (Table 2, Figure 1), whereas 5 (38%) of the 13 adenocarcinomas were pedunculated lesions (Figure 2), and the remaining 8 (62%) were sessile lesions (Figures 3 and 4). All 5 of the adenocarcinomas observed to be pedunculated lesions were confined to the mucosa or the muscular layer. Among the 8 adenocarcinomas that were sessile lesions, 2 were limited to the mucosa and 6 invaded into the subserosa. Two of the 6 patients whose cancer invaded to the subserosa had lymph node metastasis. Both of the 2 adenocarcinomas containing cholesterolosis in the polyp were limited to the mucosa. One adenoma was found to be pedunculated and another was observed to be a sessile lesion. One metastatic renal cell carcinoma was shown as a sessile lesion. Of the 20 lesions detected as the pedunculated type, 6 (30%) were neoplastic.

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**Table 2. Detectability of Polypoid Lesions of the Gallbladder on Computed Tomography (CT)**

<table>
<thead>
<tr>
<th>Histological Finding</th>
<th>No. of Lesions</th>
<th>No. (%) of Lesions Detected by Unenhanced CT</th>
<th>Enhanced CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol polyp</td>
<td>15</td>
<td>1 (7)</td>
<td>15 (100)</td>
</tr>
<tr>
<td>Adenoma</td>
<td>2</td>
<td>2 (100)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>13</td>
<td>10 (77)</td>
<td>13 (100)</td>
</tr>
<tr>
<td>Metastatic*</td>
<td>1</td>
<td>1 (100)</td>
<td>1 (100)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>31</strong></td>
<td><strong>14 (45)</strong></td>
<td><strong>31 (100)</strong></td>
</tr>
</tbody>
</table>

*Metastatic renal cell carcinoma of the gallbladder.
neoplastic, whereas 10 (91%) of the 11 lesions demonstrated as the sessile type were neoplastic. The difference in the configurations of the nonneoplastic and neoplastic lesions on EHCT was significant ($P < .001$).

**DIAGNOSTIC ACCURACY OF CT FOR DIFFERENTIAL DIAGNOSIS OF POLYPOID LESIONS**

According to the above results, we differentiated the polyloid lesions on the basis of the CT findings and the following criteria: When a lesion was not demonstrated on UCT and its shape on EHCT was pedunculated, the case was diagnosed as a cholesterol polyp. When a lesion was demonstrated on UCT or its shape was sessile, the case was diagnosed as a neoplastic lesion. The sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of CT of neoplastic lesions with these criteria were 88% (14/16), 87% (13/15), 88% (14/16), 87% (13/15), and 87% (27/31), respectively.

**COMMENT**

Several indicators have been investigated for recognizing benign polyps without overlooking carcinoma. Koga et al$^{12}$ indicated that lesions larger than 1 cm in diameter should be considered malignant, because in their study, 30 (94%) of the 32 benign lesions were smaller than 1 cm and 7 (88%) of the 8 malignant lesions were larger than 1 cm. In the present study, the prevalence of carcinoma including metastasis was 0% among the 1- to 10-mm lesions; 48% (11/23) of the 11- to 20-mm lesions; and 100% of the 21- to 30-mm lesions (Table 1). Thus, even lesions larger than 10 mm in diameter may not always be malignant. The measurement of lesion size by conventional US alone is inadequate for differentiating them.

Cholesterol polyps of the gallbladder can readily be detected by abdominal US. They are composed of foamy histiocytes that contain cholesterol, are covered by a single layer of columnar cells similar to those lining the adjacent mucosa, and are considered benign.$^{11}$ Their cause is still unclear. Salmenkivi$^{13}$ hypothesized that this lesion is derived from the direct deposition of cholesterol from the blood similar to the plaque formation in atherosclerosis. However, Tilvis et al$^{14}$ investigated subjects with and without cholesterolosis and concluded that free sterols can be transferred from the bile to the gallbladder mucosa, and that the development of cholesterolosis might be associated with an altered hepatic cholesterol synthesis. Feldman and Feldman$^{15}$ suggested that venous and lymphatic stasis is an etiologic factor that causes a disturbance of the absorptive or secretory mechanism of the gallbladder. We also believe that the cholesterol is derived chiefly from the bile, which is absorbed by the mucous membrane of the gallbladder. In our study, 93% (14/15) of the cholesterol polyps were not detected on the UCT. Although the UCT was performed by the table incremental mode, the slice thickness was 5 mm; the smallest lesion was 5 mm. Thus, neither the scanning mode nor the lesion size was a major reason that almost all of the cholesterol polyps were not detected on UCT. We believe that the cholesterol polyps were not visualized because a cholesterol polyp and the surrounding bile have the same x-ray permeability, since the main component of a cholesterol polyp is derived from the surrounding bile. In contrast, 81% (13/16) of the neoplastic lesions were detected on UCT, because these lesions are composed of neoplastic epithelium and dense connective tissue, and the x-ray permeabilities of neoplastic lesions and bile are different. Therefore, the lesions’ appearance on UCT reflected the tissue characteristics of polyloid lesions of the gallbladder. After the bolus injection of contrast medium,

![Figure 4. Adenocarcinoma (Ad) combined with cholesterolosis (Ch). A. No lesion is seen in the gallbladder on unenhanced computed tomography. B. On enhanced computed tomography, a sessile mass (arrow) is demonstrated. C. Histologically this polyp was composed of areas of Ad and Ch (hematoxylin-eosin, original magnification $\times$ 200).](https://jamanetwork.com/)

<p>| Table 3. Configuration of Lesions on Computed Tomography in Relation to Histological Findings |
|-----------------------------------------------|-----------------------------------------------|</p>
<table>
<thead>
<tr>
<th>Histological Finding</th>
<th>No. of Patients</th>
<th>Configuration of Lesions, No. (%)$^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol polyp</td>
<td>15</td>
<td>14 (93)</td>
</tr>
<tr>
<td>Adenoma</td>
<td>2</td>
<td>1 (50)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>13</td>
<td>5 (38)</td>
</tr>
<tr>
<td>Metastatic†</td>
<td>1</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>20 (65)</td>
</tr>
</tbody>
</table>

$^*$Evaluated by enhanced computed tomography.
†Metastatic renal cell carcinoma of the gallbladder.
all lesions were enhanced by the contrast medium, since polypoid lesions, including cholesterol polyps, have a blood supply. Thus, the density between the lesions and bile was contrasted, and all lesions became detectable.

The configurations of the lesions are also important for differential diagnosis. Ishikawa et al reported that, according to their histopathological examination, the patients with sessile polyps had a higher prevalence of malignancy than did the patients with pedunculated polyps, and that the sessile carcinomas were at a more advanced stage than the pedunculated carcinomas. The use of EHCT enables the acquisition of multiple thin sections or multi-planar reconstructions through the lesion, which is advantageous for evaluating the lesion’s shape. Thus, also in this series, the sessile polyps were more likely to be malignant and of advanced stage than the pedunculated polyps. More than 90% of the sessile lesions were neoplastic, and only 30% of the pedunculated lesions were neoplastic. It is important to determine whether the base is constricted or broad or has a stalk.

These CT findings led us to establish the above-mentioned criteria for differentiating polypoid lesions of the gallbladder, ie, a lesion not demonstrated on UCT and pedunculated in shape on EHCT was diagnosed as a cholesterol polyp, and the other lesions were neoplastic. The overall accuracy of this guideline was up to 90%. Adenomas have been reported to carry a risk of developing into cancer or to have focal cancer within them. Therefore, these neoplastic lesions diagnosed by CT should be resected.

All of the present pedunculated carcinomas were limited to the mucosa or muscular layer. These superficial carcinomas have been cured only by cholecystectomy, even by the laparoscopic approach. In contrast, since sessile carcinomas have the possibility of subserosal invasion and lymph node metastasis, these should be resected by the radical approach. Computed tomography can help determine the strategy for treating small polypoid lesions of the gallbladder, including operative approaches.

It has been thought that cholesterol polyps have no malignant potential. However, we have seen 3 cases of carcinoma associated with cholesterolosis, including a previously reported case. Since cholesterol polyps often have hyperplastic epithelium, it is possible that the epithelium of a cholesterol polyp has a neoplastic potential similar to that of the surrounding flat mucosa. All cancers in the cholesterol polyps observed in the present study were limited to the mucosa, and the patients were cured only by cholecystectomy, although these polyps are difficult to diagnose preoperatively as malignant.

There are a few reports of the radiological differential diagnosis of polypoid lesions of the gallbladder. Sugiyama et al reported that the aggregation of echogenic spots was a US feature characteristic of cholesterol polyps, and that endoscopic US has high enough resolution to demonstrate such structural details. We confirmed that CT was also useful for the differential diagnosis and selection of therapeutic approaches with less invasiveness and without interference by gallstones.

According to the CT findings, we recommend the following strategy for treating polypoid lesions of the gallbladder: When a lesion is demonstrated on UCT or its shape is sessile, it may be cancerous and invade the subserosa or beyond with an associated risk of lymph node metastasis. For such patients, radical cholecystectomy (ie, cholecystectomy with wedge resection of the gallbladder bed of the liver and dissection of lymph nodes in the hepatoduodenal ligament) or a more extended procedure may be necessary, according to the extent of the presumed disease. When a lesion is demonstrated on UCT and its shape is pedunculated, it may be carcinoma limited to the mucosa or adenoma. For these patients, a simple cholecystectomy by the laparoscopic approach is adequate for cure. When a lesion is not demonstrated on UCT, it is highly suggestive of cholesterol polyp, and resection is usually unnecessary. However, the possibility of cancer associated with cholesterolosis cannot be excluded, and the patient should be carefully followed up.

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