Pre-operative predictive factors for gallbladder cholesterol polyps using conventional diagnostic imaging

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AIM: To determine the clinical data that might be useful for differentiating benign from malignant gallbladder (GB) polyps by comparing radiological methods, including abdominal ultrasonography (US) and computed tomography (CT) scanning, with postoperative pathology findings.

METHODS: Fifty-nine patients underwent laparoscopic cholecystectomy for a GB polyp of around 10 mm. They were divided into two groups, one with cholesterol polyps and the other with non-cholesterol polyps. Clinical features such as gender, age, symptoms, size and number of polyps, the presence of a GB stone, the radiologically measured maximum diameter of the polyp by US and CT scanning, and the measurements of diameter from postoperative pathology were recorded for comparative analysis.

RESULTS: Fifteen of the 41 cases with cholesterol polyps (36.6%) were detected with US but not CT scanning, whereas all 18 non-cholesterol polyps were observed using both methods. In the cholesterol polyp group, the maximum measured diameter of the polyp was smaller by CT scan than by US. Consequently, the discrepancy between those two scanning measurements was greater than for the non-cholesterol polyp group.

CONCLUSION: The clinical signs indicative of a cholesterol polyp include: (1) a polyp observed by US but not observable by CT scanning, (2) a smaller diameter on the CT scan compared to US, and (3) a discrepancy in its maximum diameter between US and CT measurements. In addition, US and the CT scan had low accuracy in predicting the polyp diameter compared to that determined by postoperative pathology.

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Key words: Cholesterol; Polyps; Gallbladder; Computed tomography; Ultrasonography

INTRODUCTION

The development of radiological diagnostic tools such as ultrasonography (US) and computed tomography (CT) scanning has led to an increased frequency of the diagnosis of gallbladder (GB) lesions, such as GB polyps[1-3]. Because of the poor prognosis of GB malignancies, it is very important to distinguish between benign and malignant GB polyps so that malignant disease can be treated as soon as possible. Currently, clinical data such as the size and number of GB polyps and the age of the patient are used to help distinguish benign from malignant disease. Improved diagnostic methods are needed to differentiate between benign and malignant disease, and to determine which GB polyps
require surgical intervention\[4-6\].

Therefore, we evaluated clinical data to determine which factors would help distinguish benign from malignant GB polyps. We retrospectively analyzed the preoperative US and CT findings in patients with GB polyps and compared the results with their postoperative gross and microscopic findings.

MATERIALS AND METHODS

Fifty-nine patients who underwent laparoscopic cholecystectomy for a GB polyp of around 10 mm between January 2006 and August 2007 were enrolled in this study. We divided these patients into two groups, a cholesterol polyp group and a non-cholesterol polyp group. Data were collected for clinical features such as gender, age, symptoms, size and number of polyps, presence of a GB stone, radiological data from the preoperative US and CT scanning, and postoperative pathology data.

We compared the radiologically measured maximum diameters of the GB polyps obtained by one radiologist with the postoperatively obtained pathologic measurements of maximum diameters obtained by one pathologist. Results are reported as the mean ± standard deviation. For statistical analysis, a Chi-square, t-test and Fisher’s Exact Test were used (SPSS version 15.0 software). A P-value < 0.05 was considered statistically significant.

RESULTS

Pathologic findings of the GB polyps

Of the 59 cases, 46 (78%) were pseudo-polyps such as a cholesterol polyp, inflammatory or hyperplastic polyp. Of these 46 pseudo-polyps, 41 (69.5%) were cholesterol polyps. True polyps were observed in 13 cases. Among the true polyps, 10 cases (17%) were adenomatous polyps and three cases (5.0%) were malignant.

Clinical findings of the GB polyps

Of the 59 patients, 37 patients were male and 22 were female. No difference was observed in gender ratios for the cholesterol polyp group (M:F = 25:16) and the non-cholesterol polyp group (M:F = 12:6 P > 0.05). The mean ages for each group were 40.98 ± 9.41 and 48.39 ± 16.87 respectively. The mean values for all these measurements of maximum diameters obtained by one pathologist. Results are reported as the mean ± standard deviation. For statistical analysis, a Chi-square, t-test and Fisher’s Exact Test were used (SPSS version 15.0 software). A P-value < 0.05 was considered statistically significant.

Polyp number

| Histologic finding | Cholesterol polyp | Non-cholesterol polyp | P-value |
|--------------------|------------------|-----------------------|---------|
| Age (yr)           | 40.98 ± 9.41     | 48.39 ± 16.87         | < 0.05  |
| Sex (male/female)  | 25/16            | 12/6                  | 0.677   |
| Height (m)         | 1.70 ± 0.09      | 1.65 ± 0.07           | 0.595   |
| Weight (kg)        | 69.39 ± 13.26    | 64.85 ± 10.73         | 0.207   |
| Cholesterol (mg/dL)| 3.00 ± 2.65      | 2.80 ± 2.33           | 0.245   |
| Fasting glucose (mg/dL) | 97.05 ± 21.76  | 96.94 ± 15.0          | 0.985   |
| Insulin (µU/mL)    | 10.54 ± 3.63    | 9.47 ± 2.71           | 0.412   |
| BMI (kg/m²)        | 1.49 ± 1.85      | 1.26 ± 1.35           | 0.64    |
| HbA1c (%)          | 5.58 ± 0.74      | 5.41 ± 0.23           | 0.593   |
| US size (mm)       | 22.67 ± 2.65     | 19.78 ± 5.19          | 0.01    |
| CT size (mm)       | 0.64             | 0.05                  |         |
| Pathology size (mm)| 4.83 ± 2.97      | 11.06 ± 5.11          | < 0.01  |

Table 2 The number of polyps in cases with cholesterol and non-cholesterol polyps n(%)

| Ultrasonographic findings | Cholesterol polyp | Non-cholesterol polyp | Total                   |
|---------------------------|-------------------|-----------------------|-------------------------|
| Polyp number              | 19 (46.3)         | 6 (84.2)              | 25 (42.4)               |
| Multiple                  | 22 (53.7)         | 3 (15.8)              | 25 (42.4)               |
| Total                     | 41 (69.5)         | 9 (15.3)              | 50 (84.7)               |

The discrepancy in maximum diameter between US and CT scanning

The preoperative mean maximum diameters measured by US in the cholesterol polyp group and the non-cholesterol polyp group were 9.95 ± 2.31 mm and 11.94 ± 4.02 mm, respectively, whereas for the CT scan they were 6.77 ± 2.65 mm and 9.78 ± 5.19 mm, respectively. The mean values for CT scanning tended to be smaller than for US.

The discrepancies in maximum diameters between US and CT scanning were 5.66 ± 3.87 mm in the
cholesterol polyp group and $2.17 \pm 2.12$ mm in the non-cholesterol polyp group and this difference was statistically significant ($P < 0.01$). In 40 out of 41 cholesterol polyps (97.6%) and 12 out of 18 non-cholesterol polyps (66.6%) the diameters were smaller with CT scanning than with US ($P < 0.01$).

All 18 cases in the non-cholesterol polyp group were detected both by US and CT whereas 15 cases in the cholesterol polyp group among 41 (36.6%) were detected by US but not by CT scanning ($P < 0.01$, Table 3).

**Table 3** The difference in the maximum polyp size between cholesterol and non-cholesterol polyps (mean ± SD)

| Polyp Type          | US-CT size difference (mm) | US size > CT size | CT undetectable rate (%) | US-pathologic size (mm) | P-value |
|---------------------|----------------------------|-------------------|--------------------------|-------------------------|---------|
| Cholesterol polyp   | 5.66 ± 3.87                | 2.17 ± 2.12       | 12/18 (0.002)            | 5.12 ± 3.42             | 0       |
| Non-cholesterol polyp | 40/41                      | 0/18 (0.001)      | 0/18 (0)                 | 0.89 ± 3.69             | 0.001   |

1Indicates number of patients having a larger size with US than CT.

The discrepancy between preoperatively and postoperatively measured maximum polyp diameters
The pathologically measured mean maximum diameters were $4.83 \pm 2.97$ mm in the cholesterol polyp group and $11.06 \pm 5.11$ mm in the non-cholesterol polyp group ($P < 0.01$). When we compared these values with the preoperatively US measurements the discrepancies between preoperative and postoperative measurements were $5.12 \pm 3.42$ mm in the cholesterol polyps and $0.89 \pm 3.69$ mm in the non-cholesterol polyps ($P < 0.01$, Table 3).

The correlation between radiologically measured and pathologically measured polyp diameters
The non-cholesterol polyps showed statistically significant linear correlations between the actual maximum diameter from the pathology examination and the preoperative US measured diameter (correlation coefficient 0.698) and the CT measured diameter (correlation coefficient 0.746, $P < 0.01$). The cholesterol polyps, however, did not show this correlation ($P > 0.05$, Table 4).

**Table 4** The correlation of size between cholesterol and non-cholesterol polyps

| Correlation coefficients | Pathologic size | US size | CT size |
|--------------------------|-----------------|---------|---------|
| Pathologic size          | Non-cholesterol polyp | 1 | 0.698* | 0.746* |
| Cholesterol polyp        | 1               | 0.181  | 0.324  |
| US size                  | Non-cholesterol polyp | 0.698* | 1     | 0.925* |
| Cholesterol polyp        | 0.181           | 1      | 0.427* |
| CT size                  | Non-cholesterol polyp | 0.746* | 0.925* | 1    |
| Cholesterol polyp        | 0.324           | 0.427* | 1      |

1$P < 0.01$ vs Pathologic size, 2$P < 0.05$ vs US size.

Although the patients with cholesterol polyps had higher levels of the BMI, HOMA-IR, and HbA1c, the differences did not reach statistical significance. The sample size might have been too small to detect any differences.

Regarding the number of polyps in the GB, it is also known that a single polyp is more likely to be a malignant polyp, which prompts the need for more aggressive interventions when a single polyp is identified compared to multiple polyps. We found a similar tendency among our study population. The patients with cholesterol polyps more frequently had multiple polyps than did the patients with non-cholesterol polyps. It is well known that the size of a GB polyp is related to malignancy. Many studies have reported that a GB polyp $\geq 10$ mm has a high risk of being a malignancy and this size is one of the criteria for surgical intervention. However, we also have observed that a benign polyp, such as a cholesterol polyp, can be as large as 10 mm. Therefore, size may not afford an accurate distinction between benign and malignant polyps.

In conclusion, the cholesterol polyp has a tendency to be observed more frequently in younger patients and has a higher multiplicity. The predictive signs for a cholesterol polyp, a benign tumor, include: a polyp observable by US but not CT scanning, a discrepancy $\geq 5$ mm in the maximum diameter of the polyp between the US and CT measurements, a smaller diameter of the polyp by CT compared to US, and a low correlation between the diameter of the polyp from postoperative pathology and radiological measurements.

**DISCUSSION**

The correct diagnosis of cholesterol polyps, which account for most of the pseudo-polyps of the GB, will help prevent unnecessary surgery and follow-up examinations. In this study, we attempted to characterize the features of the cholesterol polyp and determine accurate radiological predictive factors. Age is known to have a significant association with malignant polyps and is considered an independent risk factor. This study also found that patients with non-cholesterol polyps had a higher mean age than did the patients in the cholesterol polyp group. Metabolic syndrome is also known to have a close relationship with the development of cholesterol polyps.

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the preoperative radiological measurements.

We suggest that it would be more efficient to make a flexible and tailored follow up plan or treatment plan for GB polyps based on the above mentioned signs rather than fixed or inflexible guidelines. In addition, the preoperative radiological measurement of diameter is of predictive value for the postoperatively measured actual diameter only for non-cholesterol polyps. For cholesterol polyps, the preoperative radiological measurements are limited in their prediction of postoperative pathology diameter. Therefore, methods that are more accurate for the preoperative diagnosis of cholesterol polyps are needed.

COMMENTS

Background
The development of radiological diagnostic tools has led to an increased frequency of the diagnosis of gallbladder (GB) lesions, such as GB polyps.

Research frontiers
It is very important to distinguish between benign and malignant GB polyps because of the poor prognosis of GB malignancies. Improved diagnostic methods are needed to differentiate benign from malignant disease, and to determine which GB polyps require surgical intervention.

Innovation and breakthroughs
The predictive signs for a cholesterol polyp, the most common benign GB polyp, include: a polyp observable by ultrasonography (US) but not computed tomography (CT) scanning, a discrepancy ≥ 5 mm in the maximum diameter of the polyp between US and CT measurements, a smaller diameter of the polyp by CT than by US.

Applications
This study should help to distinguish a cholesterol polyp from a non-cholesterol polyp. It would be more efficient to make a flexible and tailored follow up plan or treatment plan for GB polyps.

Peer review
The concept of this study is useful.

REFERENCES
1 Chen CY, Lu CL, Chang FY, Lee SD. Risk factors for gallbladder polyps in the Chinese population. Am J Gastroenterol 1997; 92: 2066-2068
2 Segawa K, Arisawa T, Niwa Y, Suzuki T, Tsukamoto Y, Goto H, Hamajima E, Shimodaira M, Ohmiya N. Prevalence of gallbladder polyps among apparently healthy Japanese: ultrasonographic study. Am J Gastroenterol 1992; 87: 630-633
3 Onoyama H, Yamamoto M, Takada M, Urakawa T, Ajiki T, Yamada I, Fujita T, Saiteh Y. Diagnostic imaging of early gallbladder cancer: retrospective study of 53 cases. World J Surg 1999; 23: 708-712
4 Koga A, Watanabe K, Fukuyama T, Takiguchi S, Nakayama F. Diagnosis and operative indications for polypoid lesions of the gallbladder. Arch Surg 1988; 123: 26-29
5 Yeh CN, Jan YY, Chao TC, Chen MF. Laparoscopic cholecystectomy for polypoid lesions of the gallbladder: a clinicopathologic study. Surg Laparosc Endosc Percutan Tech 2001; 11: 176-181
6 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: 622-627
7 Jørgensen T, Jensen KH. Polyps in the gallbladder. A prevalence study. Scand J Gastroenterol 1990; 25: 281-286
8 Sahlin S, Granström L, Gustafsson U, Stählberg D, Backman L, Einarsson K. Hepatic esterification rate of cholesterol and biliary lipids in human obesity. J Lipid Res 1994; 35: 484-490
9 Sandri L, Colecchia A, Larocca A, Vestito A, Capodicasa S, Azzaroli F, Mazzella G, Mwangemi C, Roda E, Festi D. Gallbladder cholesterol polyps and cholesterolosis. Minerva Gastroenterol Dietol 2003; 49: 217-224
10 Doh YW, Lee JH, Lim HM, Chi KC, Park YG. Polypoid lesions of gallbladder: clinicopathological features and indication of operation. J Kor Surg Soc 2005; 69: 245-251
11 Akatsu T, Aiura K, Shimazu M, Ueda M, Wakabayashi G, Tanabe M, Kawachi S, Kitajima M. Can endoscopic ultrasonography differentiate nonneoplastic from neoplastic gallbladder polyps? Dig Dis Sci 2006; 51: 416-421
12 Mainprize KS, Gould SW, Gilbert JM. Surgical management of polypoid lesions of the gallbladder. Br J Surg 2000; 87: 414-417
13 Yang HL, Sun YG, Wang Z. Polypoid lesions of the gallbladder: diagnosis and indications for surgery. Br J Surg 1992; 79: 227-229
14 Pandey M, Sood BP, Shukla RC, Arya NC, Singh S, Shukla VK. Carcinoma of the gallbladder: role of sonography in diagnosis and staging. J Clin Ultrasound 2000; 28: 227-232
15 Levy AD, Murakata LA, Abbott RM, Rohrmann CA Jr. From the archives of the AFIP. Benign tumors and tumorlike lesions of the gallbladder and extrahepatic bile ducts: radiologic-pathologic correlation. Armed Forces Institute of Pathology. Radiographics 2002; 22: 387-413

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