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Original Article

The diagnostic value of high-frequency ultrasound combined with color Doppler ultrasound versus surgical pathology in gallbladder polyps

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Abstract: Objective: This study aimed to analyze the value of high-frequency ultrasound combined with color Doppler ultrasound in the diagnosis of gallbladder polyps. Methods: A retrospective analysis was performed on 108 patients with gallbladder polyps, all of whom were examined by high-frequency ultrasound and color Doppler ultrasound with surgical or pathological findings as the gold standard. Results: Taking surgical pathology findings as the gold standard, the diagnostic accuracy, sensitivity and specificity of high-frequency ultrasound for gallbladder polyps were 63.89%, 63.27%, and 70.00%, respectively. The diagnostic accuracy, sensitivity and specificity of color Doppler ultrasound were 74.07%, 73.47%, and 80.00%, respectively. The diagnostic accuracy, sensitivity and specificity of high-frequency ultrasound combined with color Doppler ultrasound were 91.67%, 90.82%, and 100.00%, respectively. The proportion of mulberry-like or papillary projections was 56.18% in 89 benign lesions diagnosed by high-frequency ultrasound combined with color Doppler ultrasound, the proportion of hyperechoic lesion was 47.19%, and the proportion of single lesion was 59.55%. The incidence rate of blood flow signal was 26.97% in 89 benign lesions, including 10 cases of punctiform blood flow signal, 9 cases of band-like blood flow signal and 5 cases of multiple stones in the lumen of the gallbladder. Conclusion: High-frequency ultrasound combined with color Doppler ultrasound has high accuracy in the diagnosis of gallbladder polyps, and can yield better diagnostic results than either method, which can be used as an optional method for the diagnosis of gallbladder polyps.

Keywords: High-frequency ultrasound, color Doppler ultrasound, gallbladder polyps, diagnosis, surgery, pathology

Introduction

Gallbladder polyps, or gallbladder polyp-like lesions, generally refer to a polyp-like confined projection of the gallbladder wall into the gallbladder interior, and are clinically included into several types, including benign non-cholesterol polyps, cholesterol polyps, and early gallbladder cancer, among which cholesterol polyps have the highest incidence [1]. Surgery is the main choice for the treatment of gallbladder polyps, and accurate preoperative diagnosis can guide the establishment of treatment plans and ensure that patients receive appropriate treatment.

Ultrasound is the preferred method for the clinical diagnosis of gallbladder polyps. Abdominal ultrasound is usually performed due to operational convenience with a 3.5 MHz low-frequency probe for routine scanning. However, the distance between the anterior wall, base of the gallbladder is very close to abdominal wall in most patients with gallbladder polyps, and a low-frequency probe is likely to be interfered by the near-field effects, leading to misdiagnosis and missed diagnosis [2]. With the continuous progress of diagnosis technology, high-frequency ultrasound has been gradually applied in clinical practice, which can eliminate the influence of near-field effect to the greatest extent and can clearly display the bottom of the gallbladder, effectively compensating for the deficiencies of low-frequency ultrasound [3]. Color Doppler ultrasound, on the other hand, can clearly display the blood flow signal at the lesion location, and can more accurately identify the nature of the diseased tissues [4]. However, the

diagnosis of gallbladder polyps in previous studies has mostly been performed with either high-frequency ultrasound [5] or color Doppler ultrasound [6], or high-frequency ultrasound in comparison with conventional low-frequency ultrasound [7], and few studies have explored the value of combined method in the diagnosis of gallbladder polyps.

In this study, 108 patients with gallbladder polyps were retrospectively analyzed, and the value of high-frequency ultrasound combined with color Doppler ultrasound in the diagnosis was specifically analyzed to explore more alternative and useful methods for the clinical diagnosis of gallbladder polyps.

Materials and methods

Clinical data

The clinical data of 108 patients with gallbladder polyps admitted to our hospital, including 65 males and 43 females, aged 35-76 years, with a mean age (56.38±12.19) years, gallbladder wall thickness of 2-6 mm, mean thickness (4.18±1.13) mm, lesion diameter of 5-11 mm, and mean lesion diameter (8.75±1.94) mm, were retrospectively analyzed. Of the 108 patients, 20 presented with varying degrees of subxiphoid pain and right upper abdominal pain, 6 presented with recurrent epigastric pain, and the remaining patients had no obvious clinical manifestations. Inclusion criteria: patients who met the diagnostic criteria for gallbladder polyps in the Consensus on the Management of Benign Gallbladder Diseases (2011 edition) [8]; all underwent cholecystectomy; all underwent pathological histological examination after surgery; all underwent high-frequency ultrasound and color Doppler ultrasound examination before surgery; and who had complete clinical data were included. All the patients voluntarily participated in this study and signed the study consent form. This study passed the ethical approval of Penglai Traditional Chinese Medicine Hospital. Exclusion criteria: patients combined with neoplastic disease, with coagulation disorders, with psychiatric disorders, with severe cardiac, hepatic and renal dysfunction, lack of clinical data, and the presence of contraindications to the examination were excluded.

Methods

All the patients underwent high-frequency ultrasonography and color Doppler ultrasonography before surgery. Patients were advised to discontinue drugs that might affect the contraction of the gallbladder, maintain a light diet and abstain from high-fat foods the day before examination. After fasting for 8 h before examination, patients received the examination in the early morning on a fasting stomach using high-frequency ultrasound instrument (Philips IU22, probe frequency 7-10 MHz) and the color Doppler ultrasound instrument (German Siemens SONOLINE Premier, probe frequency 2.5-5 MHz). During the examination, the patient was instructed to adopt a supine or left lateral decubitus position, or a sitting, standing, or thoracic-knee position. A high-frequency ultrasound examination was performed, followed by color Doppler ultrasound examination. Both examinations were performed in the same way, with the probe coated with coupling agent and placed in the patient's right intercostal space, under the fenestra, and under the costal margin, *etc*. A multisection scan was performed to explore the gallbladder and the adjacent condition, and further magnification was performed on the suspicious area. The location of the gallbladder lesion, its specific size, shape, borders, echogenicity, and blood flow signal were observed in detail and recorded carefully. The sample volume size was set at 1 mm*1 mm*1 mm, and the angle between blood flow and sound velocity was controlled to be below 60°, while the resistance index was measured and recorded in detail.

At the end of the examination, two highly qualified imaging physicians read the figures together, and the final results were determined after mutual discussion where there was disagreement.

Observation indicators

The surgical pathology findings, including specific types of benign lesions and malignant lesions were analyzed.

The efficacies of high-frequency ultrasound alone, color Doppler ultrasound alone, and the efficacy of both methods combined, including accuracy, sensitivity, and specificity, were analyzed with pathology findings as the gold standard. Sensitivity = true positive/(true positive + false negative), specificity = true negative/(true negative + false positive), and accuracy = (true positive + true negative)/(true positive + false negative + true negative + true negative + false positive).

Table 1. Diagnostic efficacy of high-frequency ultrasound for gallbladder polyps (cases)

High-frequency ultrasound	Surgical pathology		Total
	Benign	Malignant	
Benign	62	3	65
Malignant	36	7	43
Total	98	10	108

Table 2. Diagnostic efficacy of color Doppler ultrasound for gallbladder polyps (cases)

Color Doppler ultrasound	Surgical pathology		Total
	Benign	Malignant	
Benign	72	2	74
Malignant	26	8	34
Total	98	10	108

The image and blood flow signal characteristics of high frequency ultrasound combined with color Doppler ultrasound were analyzed.

Statistical analysis

Statistical analysis was performed with SPSS 23.0. Count data were expressed as [n (%)] and examined by X^2 test. ROC curves were produced using SPSS. GraphPad Prism 8 was used to draw the figures. $P < 0.05$ was considered statistically significant.

Results

Surgical pathology results

In 108 patients with gallbladder polyps, 98 cases of benign lesions and 10 cases of malignant lesions were diagnosed by surgery and pathological examination, including 58 cholesterol polyps, 32 inflammatory polyps, 6 adenomas and 2 adenomyosis. All 10 of the malignant lesions were adenocarcinomas.

Diagnostic results of high-frequency ultrasound, color Doppler ultrasound, and combined method

High-frequency ultrasound exhibited a diagnostic accuracy of 63.89% (69/108), a diagnostic sensitivity of 63.27% (62/98), and a diagnostic specificity of 70.00% (7/10) (**Table 1**).

Color Doppler ultrasound showed a diagnostic accuracy of 74.07% (80/108), a sensitivity of 73.47% (72/98), and a diagnostic specificity of 80.00% (8/10) (**Table 2**).

High-frequency ultrasound combined with color Doppler ultrasound had a diagnostic accuracy of 91.67% (99/108), a diagnostic sensitivity of 90.82% (89/98), and a diagnostic specificity of 100.00% (10/10) for gallbladder polyps (**Table 3**; **Figure 1**).

Image features and blood flow characteristics

Based on the predominance of benign lesions in the gallbladder polyps in this study, the analyses for image features and blood flow characteristics were performed on basis of benign lesions. The 56.18% of the 89 benign lesions was in the shape of masses, papillae, and mulberry, and hyperechoic lesion accounted for 47.19%, and the proportion of single polyp was 59.55% (**Table 4**).

Twenty-four of the 89 benign lesions demonstrated blood flow signal within the lesion. Ten of these cases showed a punctiform blood flow signal (41.67%), without a detectable spectrum. Nine cases showed a band-like blood flow signal (37.50%), with a resistance index between 0.46 and 0.75. There were 5 cases (20.83%) combined with multiple stones in the gallbladder lumen (**Figures 2**, **3**).

Discussion

The incidence of biliary tract disease is increasing due to marked changes in lifestyle and dietary habits. Gallbladder polyps are a type of gallbladder disease with high clinical incidence, mainly appearing in the wall cavity of the gallbladder, which will slowly grow into the cavity without timely treatment in the early stage, and can be clinically divided into pseudopolyps and true polyps, with the former showing higher incidence, including inflammatory pseudopolyps, cholesterol pseudopolyps, and focal adenomyosis, which basically do not have the risk of malignant transformation [9]. True polyps, however, may be benign or malignant, with the benign being mainly adenomas and the malignant being adenocarcinomas [10]. The 10 malignant lesions revealed by surgical pathology in this study were all adenocarcinomas.

Benign gallbladder polyps such as inflammatory polyps, cholesterol polyps, and gallbladder

Table 3. Diagnostic efficacy of high-frequency ultrasound combined with color Doppler ultrasound for gallbladder polyps (cases)

High-frequency ultrasound + color Doppler ultrasound	Surgical pathology		Total
	Benign	Malignant	
Benign	89	0	89
Malignant	9	10	19
Total	98	10	108

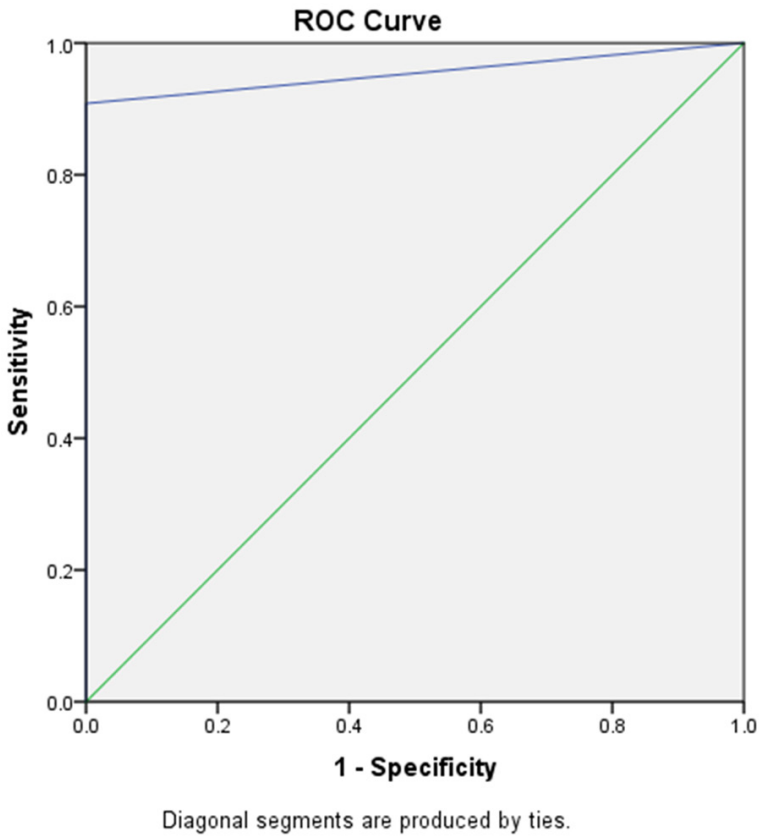

Figure 1. ROC curve for high-frequency ultrasound combined with color Doppler ultrasound. Area under the curve (AUC) = 0.954.

Table 4. Image characteristics of benign lesions diagnosed by high-frequency ultrasound combined with color Doppler ultrasound (cases, %)

Image characteristics		Number of detected cases	Proportion
Lesion morphology	Mass, papillate, mulberry	50	56.18
	Wide base	29	32.58
	tipped, basal stenosis	10	11.24
Echo	hyperechoic	42	47.19
	Slightly hyperechoic	15	16.85
	Isoechoic	8	8.99
	Strong echo	24	26.97
Number of polyps	Single	53	59.55
	Multiple	36	40.45

adenomas, are usually small in diameter, mostly no more than 10 mm, making clinical diagnosis more difficult [11]. Most gallbladder polyps have no typical manifestations in the early stages, sometimes presenting with a feeling of fullness in the epigastrium and chronic pain in the right upper abdomen, and some patients are even asymptomatic, which increases the difficulty of early diagnosis [12]. Benign gallbladder polyps, if not diagnosed in time, may lead to a delay in the best time for treatment, and a few patients may even develop into life-threatening malignancy, [13]. Therefore, the early diagnosis of gallbladder polyps must be made and the differentiation between benign and malignant is the key to guide the clinical treatment and ensure the best prognosis for patients. Low-frequency ultrasound has its limitations while high-frequency ultrasound combined with color Doppler ultrasound was more preferred [14]. High-frequency ultrasound has been shown to be of good value in the diagnosis of breast cancer [15], microscopic thyroid nodules [16], and nodules on chest wall. Compared to low-frequency ultrasound, high-frequency ultrasound not only shows the lesion outline, but also the internal structure of the thickened cystic wall [17]. However, a study also found

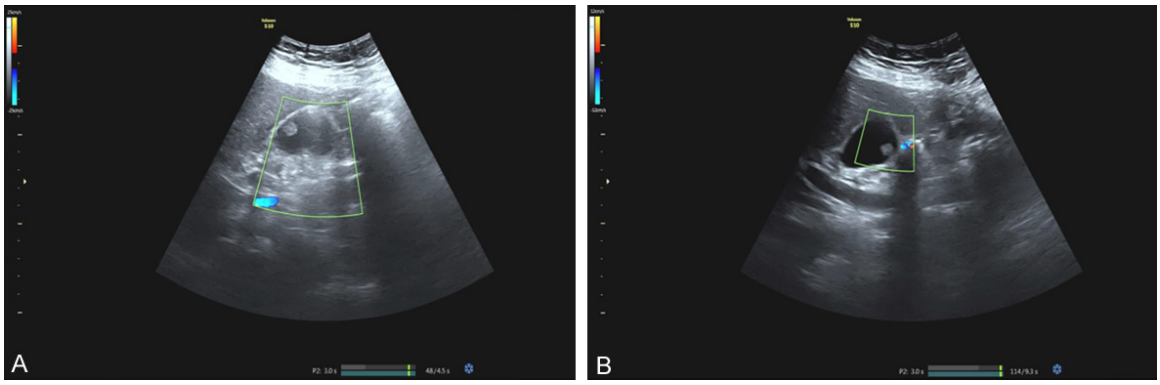

Figure 2. Blood flow characteristics of cholesterol polyps diagnosed by ultrasound. Hyperechoic mass with clear outline and no blood flow signal in the posterior wall of the gallbladder (A). Hyperechoic lesion with mulberry-like attachment to the posterior wall of the gallbladder and inconspicuous blood flow signal (B).

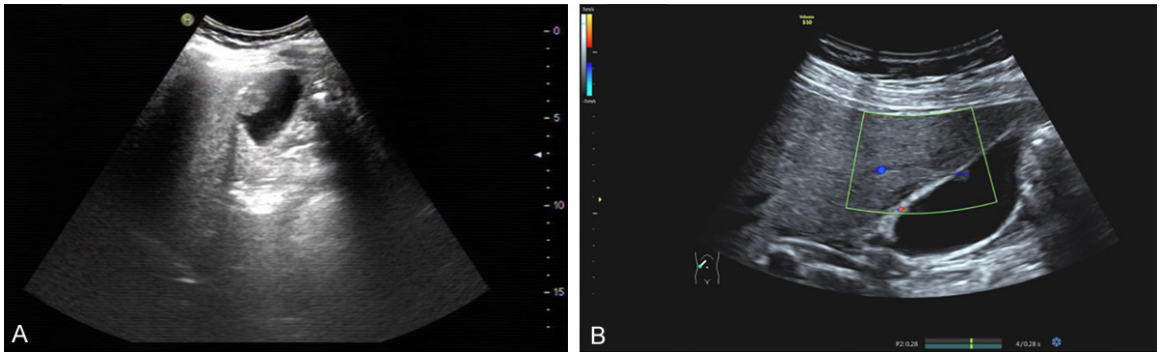

Figure 3. Blood flow features of the ultrasonically diagnosed adenoma. Hyperechoic mass in the anterior wall of the gallbladder body with irregular morphology and well-defined outline (A). High-frequency ultrasound showed hyperechoic, mass-like attachment at the anterior wall of the gallbladder, and a distinct basal wide blood flow signal at the base of the lesion (B).

that high-frequency ultrasound has shortcomings, as shown by the lack of clarity in the display of gallbladder polyps located in deeper locations, and the imaging is blurred, lowering the diagnostic accuracy [18]. The color Doppler ultrasound makes up for the shortcomings of high-frequency ultrasound, which can clearly display the specific location, shape, size, echo, outline, *etc*. of the lesions. It can also visualize the blood flow and improve the diagnostic efficacy [19, 20]. Evidence showed that intra-mass blood flow and resistance indices revealed by color Doppler ultrasound aid the identification of benign and malignant lesions [21]. However, some evidence has also found deficiencies in the application of color Doppler ultrasound in the diagnosis of similar lesions with poor specificity [22]. For example, color Doppler ultrasound exhibited a diagnostic specificity of less than 50% in differentiating gallbladder stones from gallbladder polyps [23]. A study [24] applied color Doppler ultrasound to diagnose gallbladder polyps and showed one case of submucosal nodule misdiagnosed as adenoma. While high-frequency ultrasound can show the state of microvascular circulation, so that the deficiencies existing in color Doppler ultrasound examination can be compensated, therefore, it is recommended to apply high-frequency ultrasound and color Doppler ultrasound jointly for diagnosis, thereby giving full play to the advantages of the application of both and compensate each other's deficiencies, so as to obtain higher diagnostic efficacy.

Taking surgical pathology findings as the gold standard, the accuracy of applying high-frequency ultrasound for the diagnosis of gallbladder polyps in this study was 63.89%, sensitivity was 63.27% and specificity was 70.00%.

The accuracy of applying color Doppler ultrasound for diagnosis was 74.07%, sensitivity was 73.47% and specificity was 80.00%. The combined application of high-frequency ultrasound and color Doppler ultrasound diagnosis had an accuracy of 91.67%, a sensitivity of 90.82%, and a specificity of 100.00%. It can be seen that when a single application of high-frequency ultrasound or color Doppler ultrasound is performed for diagnosis, the diagnostic efficiency of the latter is slightly higher than the former, but the diagnosis accuracy of both is less than 80%. The combined diagnostic results of the two methods are all above 90%, and the ROC curve was drawn to show the area under the curve (AUC) = 0.954, which confirmed that the combined method had a high efficiency in the diagnosis of gallbladder polyps. A study [25] showed an accuracy rate of 96.4% of combined methods in the diagnosis of gallbladder polyps, which was consistent with the present study. The lesion morphology of gallbladder polyps in this study were mass, papillary, and mulberry shaped with wide base, tipped, or narrow base, of which the highest proportion was in mass, papillary, and mulberry shape, 56.18%, and the echogenic features included several types of hyperechoic, slightly hyperechoic, isoechoic, and strongly echogenic, of which the highest proportion was in hyperechoic, 47.19%, and the proportion of singe polyp was higher, 59.55%. 26.97% of 89 benign lesions diagnosed by high-frequency ultrasound combined with color Doppler ultrasound showed blood flow signals. These blood flow signals helped confirm the diagnosis of gallbladder polyps and also assisted in the differentiation of benign and malignant, ensuring a higher diagnostic specificity.

In conclusion, the combined application of high-frequency ultrasound and color Doppler ultrasound for the diagnosis of gallbladder polyps can achieve better diagnostic results than either method, and has good application value for the diagnosis of gallbladder polyps as well as the differentiation of benign and malignant. However, this study included small sample size, the analysis was retrospective, and no in-depth study was conducted regarding the mechanism of action of high-frequency ultrasound combined with color Doppler ultrasound, which are shortcomings that need to be addressed in future studies.

Disclosure of conflict of interest

None.

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