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The role of ultrasonography in the diagnosis of gallbladder cancer



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The role of ultrasonography in the diagnosis of gallbladder cancer

OBJECTIVE: To investigate the value of ultrasonography in the diagnosis of gallbladder cancer in a community. METHODS: A total of 24 cases of gallbladder carcinoma confirmed by operation and pathology were retrospectively analyzed.

RESULTS: There were 14 cases (14/24) of gallbladder cancer preoperatively diagnosed by normal scale ultrasound and 10 cases (10/24) of accidental gallbladder cancer diagnosed. The diagnostic sensitivity was 58.33%.

Irregular thickening of gallbladder wall was found in the 14 cases of preoperative diagnosis of gallbladder carcinoma. There were 22 cases of gallbladder cancer complicated with gallstones (22/24) and 2 cases without gallstones (2/24), among which 18 were multiple gallstones and 4 cases (4/24) were single gallstone. Signal of blood flow can be detected in the lesion of gallbladder wall in 7 cases (7/14).

CONCLUSION: The evaluation of the gallbladder in patients with high risk factors should be emphasized in community ultrasound examinations.

KEY WORDS: Conventional ultrasound mode, Gallbladder carcinoma incidental gallbladder carcinoma, Gallstone, Thickening of the gallbladder wall

Introduction

Gallbladder carcinoma (GBC) is a carcinoma of the biliary tract that has the shortest survival time (median survival time <1 year)¹. Unsuspected GBC refers to the discovery of unsuspected GBC during or after cholecystectomy for a benign disease of the gallbladder, and its incidence accounts for approximately 30% of total GBC cases. Since GBC specific symptoms are few, early detection remains difficult, and it is often detected in the advanced stage, leading to poor prognosis ^{2,3}.

GBC is not a common cancer ⁴. However, it is presently recognized as one of the most aggressive tumors ⁵. There is a lack of specific symptoms at the early stage of GBC, it is only identified in the middle and late stages for treatment, and its complications, such as liver infiltration, postoperative implantation, metastasis and recurrence, are common ^{6,7}. Hence, the overall treatment effect remains poor, and the five-year survival rate of more than 90% of patients remains less than 5% 8-11. With the development of laparoscopic surgery, an increasing number of GBC cases have been accidentally found. The World Health Organization (WHO) and the International Agency for Cancer Research have estimated that in 2012, there would be approximately 178,000 new cases of GBC worldwide and 143,000 deaths, accounting for 1.3% and 1.7% of all tumors, respectively ¹². In recent years, this incidence has continuously increased year by year ¹³.

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There are various diagnostic methods of GBC. But as mentioned above, early detection remains difficult ³. Thus, in the current study, we retrospectively analyzed the ultrasonography characteristics of 24 cases of GBC confirmed by surgery under conventional ultrasound examination mode. The diagnosis, omission and misdiagnosis are reported, as follows. We hope to find out and summarize the characteristics of the patients that were diagnosed with GBC, thus providing some useful guidance for the early detection of GBC by ultrasonography.

Materials and Methods

SUBJECTS

A total of 2,345 patients underwent cholecystectomy in our hospital from January 2010 to December 2018, and all patients had available pathological results. Among these patients, 882 patients were male and 1,463 patients were female, and the male-to-female ratio was approximately 1.00:1.66. The average age of these patients was 60.85 ± 13.91 years old. There are 983 people who are 65 years old or older, and 1,362 people who are less than 65 years old.

INSTRUMENTS AND EQUIPMENT

The instruments used for the examination were as follows: a GE Logiq-E9 color ultrasound machine with a C1-5 frequency conversion probe, an Esaote Mylab Twice color ultrasound machine with a CA5-11 frequency conversion probe, and a PHILIPS-HD11 color ultrasound machine with a C5-2 frequency conversion probe. The detection was performed in abdominal conditions.

The patient shonspection methoduld have an empty stomach for more than eight hours. The supine position, left supine position, and right anterior oblique position were routinely taken, and these positions were changed according to the requirements of the examination, in order to obtain the best diagnostic images. The long-axis and short-axis sections of the gallbladder were observed.

Statistical Methods

A statistical table was established in Excel (Microsoft) sheet for all data, and the SPSS 19.0 statistical software was used for the statistical processing of related data. Mean \pm standard deviation (X \pm D) refers to the calculation of the mean and standard deviation of measurement data. Independent samples *t*-test was used to analyze the differences of the measurement data. *P*<0.05 was considered statistically significant.

Results

CLINICAL INFORMATION

There were 24 cases of GBC, and the average age of these cases as 67.52 ± 11.37 years old. 17 cases were older than or equal to 65 years old, accounting for 1.72% (17/983), and 7 cases were younger than 65 years old, accounting for 0.51% (7/1362). There were 19 cases of cancer in females, so the prevalence rate was 1.29% (19/1463), and 5 cases in males, the prevalence rate was 0.56% (5/882). The difference in age and gender was statistically significant (*P*<0.05, Table I).

SURGICAL AND PATHOLOGICAL RESULTS

Among the 24 cases, 23 cases had adenocarcinoma, while one case had adenocarcinoma complicated with mucinous adenocarcinoma. The gross pathology of GBC was mainly localized lesions, accounting for 70.83% (Table II).

Sonographic Analysis of Conventional Ultrasound Examination Modal GBC

The conventional ultrasonographic manifestations of gallbladder cancer in this group mainly included thickening of the wall of the gallbladder, detecting blood flow signals on the thickening wall of the gallbladder and associated gallstones. In GBC group, 14 patients had gallbladder wall thickening, 18 patients had multiple gallbladder stones and 4 had single gallbladder stone, while 2 did not have gallbladder stones. Biliary wall thickening was non-uniform and irregular with an average thickness of 14.23mm, and the average thickness of non-cancerous thickening biliary wall in this group was 8.47mm; the difference between the two was statistically significant (P < 0.05). High resistance blood flow signal was detected on the thickened biliary wall in 7 cases, RI > 0.7 (Table III).

TABLE I - Gallbladder cancer in relation to age and sex.

	Age		Gender	
Number of casesPrevalence	65	< 65	male	female
	171.72	70.51%	50.56%	191.29%

TABLE II - Gross pathological results of 24 cases of gallbladder carcinoma surgery.

	Diffuse	Lesions Limitations	Mucosal surface			
Number of cases	4	17	3			
Accounted for	16.67%	70.83%	12.50%			

TABLE III - Ultrasonographic features in gallbladder carcinoma with conventional ultrasonography.

Gallbladder stones							
	Gallbladder wall thickening	Multiple	Single	No stone	Blood flow of gallbladder wall		
Gallbladder carcinoma	14	18	4	2	7		

TABLE IV - Causes of missed diagnosis of gallbladder cancer by conventional ultrasonography.

	UGC				
	Gallbladder wall flat	allbladder Stone Gas wall flat block interferend		Mirizzi sydrome	
Case number	6	2	1	1	

Ability Analysis of Ultrasonography in Diagnosis of Gallbladder Cancer with Normal Scale

Preoperative diagnosis of gallbladder carcinoma by conventional ultrasonography was performed in 14 cases with sensitivity of 58.33%. There were 10 cases of undiagnosed unsuspected gallbladder cancer, with a missed diagnosis rate of 41.67%. The main reasons for missed diagnosis were the absence of obvious thickening of the biliary wall, obstruction of gallstones, interference of gas in the gastrointestinal tract around the gallbladder and other details, and another case of Miruizzi syndrome was missed (Table IV).

TUMOR MARKERS

Tumor markers were detected in 17 of 24 cases, but no specific tumor markers of GBC were found (Table V).

Discussion

The cause of GBC remains unknown ¹⁴. There have been reports that gallbladder polyps larger than 1 cm, a history of gallstones of 10-15 years, an age of over 70 years

old, irregular thickening of the gallbladder wall, and factors such as Mirizzi syndrome are risk factors for increased incidence of GBC ¹⁵⁻¹⁸. Furthermore, chronic stimulation of the gallbladder stones may be a major risk factor for GBC ¹⁹.

In the present group of GBC cases, the incidence of gallstones reached as high as 91.67%. Due to the need for long-term stimulation, the incidence of GBC was mainly found in the elderly. Hence, older age is also a feature of the incidence of GBC. Among the 24 cases of cancer in this group, 17 were elderly and 19 were female. The difference in the prevalence of gallbladder cancer in age and gender was statistically significant (P < 0.05). Therefore, attention should be given to patients with high-risk factors.

It has been reported that the detection of high resistance blood flow signals in gallbladder tumors is also an important diagnostic index, and its diagnostic coincidence rate can reach 86.3% ²⁰. It has also been reported that CDFI is not highly sensitive for the diagnosis of early GBC ²¹. In the present group of cases, merely seven GBC cases were associated with high resistance blood flow, accounting for 29.17%. The investigators consider that determining whether there is high resistance blood flow in the lesion area under a normal size state is not an important basis for the diagnosis of GBC. In the present group of patients, the sensitivity of the constantsize ultrasound in the diagnosis of GBC was 58.33% and the missed diagnosis rate was 41.67%. These were consistent with the diagnostic coincidence rate of 42.9-83.4% reported in a literature ²². In the present group of cases, there was no change from gallbladder polyp to GBC.

A previous study revealed that after cholecystectomy, approximately 0.7% of cases of histopathological examination indicated cancer ²³. In Johns Hopkins University ⁵ and the Memorial Sloan Kettering Cancer Center ²⁴ in the United States, unsuspected GBC accounted for approximately half of the number of GBC cases, and in our current study, unsuspected GBC accounted for 41.67% of the cases, which is similar to the above reports. The reasons for the missed diagnosis of unsuspected GBC in the group of cases were analyzed, as follows: In six cases the lesions were located in the mucosa and muscle layer of the gallbladder wall, which did not cause changes in the anatomical structure, preventing the ultrasound diagnosis from being performed. Two cases of missed diagnosis were due to the decrease in bile and

TABLE V - Results of tumor markers in 17 cases of gallbladder carcinoma.

	AFP	CEA	CA125	CA153	CA199	CA724
Number of cases	0	4	3	2	5	3
Mean (normal value)	2.56 ± 1.55 (≤6.05 or IU/ml)	3.44 ± 1.95 (< 5.09 ng/ml)	37.04 ± 65.26 (0-35 U/ml)	17.05 ± 15.13 (0-25 U/ml)	34.98 ± 63.91 (0-39 U/ml)	6.52 ± 16.78 (0-6.9 U/ml)

multiple stones, and the increase in acoustic shadow range, which affected the evaluation of the gallbladder cavity and gallbladder wall. For the Mirizzi syndrome in one case, the missed diagnosis was caused by the inexperienced examination performed by the physician, who did not carefully observe the gallbladder neck tube to identify the cause of the Mirizzi syndrome. There was one case of missed diagnosis due to the interference of gas in the gastric antrum and poor quality of the gallbladder image. Hence, a constant scale ultrasound has no diagnostic ability for GBCs with a flat gallbladder wall and multiple filled gallstones. Therefore, the complexity of the gallbladder neck structure and interference of the gastric antrum gas could affect the observation of the gallbladder neck performed by physicians. In the present group of cases, 17 cases were tested for tumor-related markers, but no specific tumor marker for GBC were found. This may be correlated to the small sample size of the study.

From the above retrospective analysis of this group of cases, we summarized the following several factors that may be useful in diagnosing GBC: (1) strengthening attention to GBC; (2) attaching importance to the gallbladder evaluation of patients with high-risk factors; (3) for patients with multiple stones and turbidity of the bile, the body position should be changed to induce the stones and bile sludge to move, fully expose the gallbladder wall, reduce the interference of stone sound shadow and bile sludge, and avoid a missed diagnosis; (4) for patients with Mirizzi syndrome, efforts should be made to identify other causes, other than GBC. At the same time, attention should also be given to the differential diagnosis of benign lesions, such as gallbladder adenomyosis and xanthogranulomatous cholecystitis²⁵. Further examination and differential diagnosis of magnetic resonance imaging (MRI) and computed tomography (CT) should be carried out in time for unevaluated and suspicious cases. At present, there is no effective method for the early diagnosis of GBC, and community ultrasound remains as the first stop for gallbladder lesions ^{26,27}. Therefore, it is of practical clinical significance to improve the ability of community ultrasound doctors to diagnose GBC, and reduce and avoid missed diagnoses and misdiagnoses, which plays an important and decisive role in the success of the clinical treatment, as well as the prognosis of patients.

Riassunto

SCOPO DELLO STUDIO: indagare il valore dell'ecografia nella diagnosi del carcinoma della cistifellea in una comunità.

A tal fine sono stati analizzati retrospettivamente un totale di 24 casi di carcinoma della cistifellea confermati dall'operazione e dall'esame anatomo-patologico.

RISULTATI: Ci sono stati 14 casi (14/24) di diagnosi pre-

operatoria con ultrasuoni su scala normale e 10 casi (10/24) di carcinoma della cistifellea diagnosticato accidentalmente, con una sensibilità diagnostica del 58,33%. Nei 14 casi di diagnosi preoperatoria è stato riscontrato ispessimento irregolare della parete della cistifellea da carcinoma della colecisti. 22 casi di cancro alla cistifellea erano complicati con calcoli biliari (22/24) e 2 casi senza calcoli biliari (2/24): in 18 erano si trattava di calcoli biliari multipli e 4 casi (4/24) erano calcoli biliari singoli. Il segnale del flusso sanguigno può essere rilevato nella lesione della parete della cistifellea in 7 casi (7/14).

CONCLUSIONE: La valutazione della cistifellea nei pazienti con fattori ad alto rischio dovrebbe essere enfatizzata negli esami ecografici di comunità.

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