

Differentiation between hepatic cystic echinococcosis types 1 and simple hepatic cysts

A retrospective analysis

Bo Ran, PhD, Tuerganaili Aji, PhD, Tieming Jiang, MM, Ruiqing Zhang, PhD, Qiang Guo, MM, Abuduaini Abulizi, MM, Yusfu Yimiti, MM, Hao Wen, PhD, Yingmei Shao, PhD*

Abstract

This study aims to evaluate the clinic value of ultrasound, computed tomography (CT) and serological testing in the differentiation between hepatic Cystic Echinococcosis (CE) types 1 and simple hepatic cysts.

Totally 50 patients with CE Types 1 and 50 patients with simple hepatic cysts were included. All patients examined by ultrasound, CT and serological testing respectively. The receiver operating characteristic (ROC) curve of diagnosis methods was drawn and their sensitivity, specificity, Youden index, positive likelihood ratio, negative likelihood ratio, positive predictive value and negative predictive value were compared. Pathology result was used as golden standard.

The area under ROC curve of ultrasound was 0.97 and of CT and serological testing was 0.79 and 0.71 respectively. The sensitivity of ultrasound in the diagnosis of CE Types 1 was 96.00%, specificity was 98.00%, the positive likelihood ratio was 48.00, and negative likelihood ratio was 0.04. Disease prevalence was 50%, positive predictive value was 97.96%, and negative predictive value was 96.08%. The sensitivity of CT was 80.00%, specificity was 62.00%, positive likelihood ratio was 2.11, and negative likelihood ratio was 0.32. Disease prevalence was 50%, positive predictive value was 67.80%, and negative predictive value was 75.61%. The sensitivity of immunological test was 86.00%, specificity was 72.00%, positive likelihood ratio was 3.07, and negative likelihood ratio was 0.19. Disease prevalence was 50%, positive predictive value was 75.44%, and negative predictive value was 83.72%. Combined ultrasound and immunological test, the sensitivity and the specificity was 82% and 100% respectively. Combined CT and immunological test, the sensitivity the specificity was 70% and 82% respectively.

In the differentiate diagnosis of CE Types 1 and simple hepatic cyst, ultrasound is better than CT with high sensitivity and specificity, therefore recommended. Immunological examination is an important complement to the imaging examination.

Abbreviations: CE = cystic echinococcosis, CT = computed tomography, ROC = receiver operating characteristic curve.

Keywords: differentiation, hepatic cystic echinococcosis, simple hepatic cysts

1. Introduction

Cystic hydatid disease is an important parasitic zoonosis caused by the larval cyst stage of the dog tapeworm *Echinococcus granulosus* which impacts on both population health and animal production in hyper endemic areas in Central Asia, the Mediterranean countries and South America.^[1] Surgery has

been considered as the only definitive and curative method.^[2] Simple hepatic cyst is also known as congenital hepatic cyst, a condition that may be related to congenital biliary developmental aberrations.^[3] Simple hepatic cysts grow slowly and usually require no specific treatment except in cases of complications, such as intracystic hemorrhage, infection, cyst rupture, jaundice, or portal hypertension.^[4] The clinical manifestations and laboratory and imaging findings are similar and are particularly difficult to differentiate between Hepatic Cystic Echinococcosis (CE) Type 1 and simple hepatic cysts.^[5-7] However, wrong diagnosis may lead to severe clinical outcome.^[8,9] For example, if CE Types 1 misdiagnosed as simple hepatic cysts, surgery will be performed, leading to cyst fluid overflow spread in abdominal cavity or even anaphylactic shock; therefore, a clear diagnosis is very important. Ultrasound, CT and serological testing are important methods for disease differentiation.^[10] Therefore, a retrospective analysis was conducted and the diagnostic value of each combined detection method was evaluated.

2. Materials and methods

2.1. Patients

A total of 50 patients with CE type 1 and 50 patients with simple hepatic cysts were enrolled, and they were diagnosed by pathology. All patients underwent ultrasound, CT and serological testing before surgery. This study was approved by the Ethical

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Xinjiang Key Laboratory of Echinococcosis, The First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, China.

* Correspondence: Yingmei Shao, Xinjiang Key Laboratory of Echinococcosis, The First Affiliated Hospital of Xinjiang Medical University, No. 1, Liyushan Road, Xinshi District, Xinjiang 830011, China (e-mails: syingmei3000@163.com, Shaoyingmei1000@sina.com).

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2.2. Ultrasound

Ultrasound was performed using the Siemens G60 color Doppler ultrasound imaging instrument and convex array probe with the frequency of 3.5 to 5.0 MHz. Patients were in supine or lateral position. Parenchymal echo and lesions, cyst size, number and its relationship with the surrounding blood vessels were recorded.

2.3. CT detection

The scanning parameters include layer thickness of 5 mm, layer space of 5 mm, tube voltage of 120 KV, tube current of 300 mA and automatic milliampomy. The ROI was selected according to the contour of the lesion. The CT value (mean and standard deviation (SD)) of the ROI was recorded.

2.4. Immunological tests

The dot immunogold filtration assay was used to detect the antibodies of EgCF, EgP, EgB, and Em2. All patients underwent immunological tests before surgery.

2.5. Statistical analysis

All data were analyzed using SPSS version 22.0. Comparison between the 2 groups was performed by the Student's *t* test for continuous variables and the Chi-squared test for categorical variables. *P* value less than .05 was considered as statistically significant.

3. Results

3.1. Patient characteristics

The clinical data of patients were shown in Table 1. Among 50 patients with CE type 1, 32 cases were male, and 18 cases were female. Patients aged 2 to 14 years old and the median age was 7. A total of 32 cases had multiple cysts, and 18 cases had single cyst. The cysts were located in the right lobe in 24 patients, in the left lobe in 12 patients, and in both lobes in 14 patients. The mean cyst size was 8.40 ± 2.58 cm (range 5–14 cm) in diameter. Among 50 patients with simple hepatic cysts, 19 were males and 31 females. Patients aged 29 to 71 years with the median age of 61 years. A total of 36 cases had multiple cysts, and 14 cases had single cyst. The cysts were located in the right lobe in 29 patients, in the left lobe in 10 patients, and in both lobes in 11 patients. The mean cyst size was 9.81 ± 3.57 cm (range 7–13 cm) in diameter. One patient in CE group developed hydrothorax at 5 days post-operation and was treated by thoracocentesis. Other patients recovered well after surgery. Patients were followed up for 1 to 3 years without recurrence.

3.2. Ultrasound

Diagnosis of CE types 1 was considered positive, and simple hepatic cystic was considered negative. All diagnoses were based on pathological diagnosis. Ultrasound was performed for detection of diagnostic value. The comparison value was shown in Figure 1. The sensitivity of the ultrasound is 96.00%, specificity was 98.00%, positive likelihood ratio was 48.00, negative likelihood ratio was 0.04, disease prevalence was 50%,

Table 1

The characteristics of patients.

	Patients with CE type 1 (N=50)	Patients with simple hepatic cysts (N=50)	Total	$\chi^2/Z/t$	<i>P</i>
Sex					
Male	32	19	51	6.763	.009
Female	18	31	49		
Average age (yr) (range)	7 (2–14)	61 (29–71)		4.564	.000
Number of cysts					
Multiple cysts	32	36	68	0.735	.391
Single cyst	18	14	32		
Cyst size	8.40 ± 2.58 cm	9.81 ± 3.57 cm		2.264	.026
Cyst distribution					
Right lobe	24	29	53	1.014	.602
Left lobe	12	10	22		
Both lobes	14	11	25		

The comparison of cyst size was performed by *t* test. The factors of gender and number and distribution of cyst were analyzed by chi-square test. The comparison in age was performed by rank sum test.

positive predictive value was 97.96%, and negative predictive value was 96.08%.

3.3. CT performance

CT scan was performed for detection of diagnostic value. The comparison value was shown in Figure 1. The sensitivity of CT was 80.00%, specificity was 62.00%, positive likelihood ratio was 2.11, negative likelihood ratio was 0.32, disease prevalence was 50%, positive predictive value was 67.80%, and negative predictive value was 75.61%.

3.4. Serological testing

Serological testing was performed for detection of diagnostic value. The comparison value was shown in Figure 1. The sensitivity of the immunological test was 86%, specificity was 72.00%, positive likelihood ratio was 3.07, negative likelihood ratio was 0.19, disease prevalence was 50%, positive predictive value was 75.44%, and negative predictive value was 83.72%.

3.5. Analysis ROC curve area

ROC was drawn to compare the diagnostic value of the ultrasound, CT and serological testing (Fig. 2). The larger the area under the ROC curve, the greater the value of differential diagnosis. The comparison value was shown in Table 2. The area under ROC curve of ultrasound was 0.97, CT and serological testing was 0.79 and 0.71 respectively. It showed that ultrasound is a preferred differential diagnosis tool.

3.6. Combined analysis of ultrasound with serological testing

Combined diagnostic value of ultrasound with serological testing was evaluated. The combination was considered positive if both techniques were positive, and negative if both negative. The comparison value was shown in Table 3. The diagnostic sensitivity of this combination was 82%, and the specificity was 100%. Then we integrated the serological testing results and ultrasound into a diagnostic model, and performed logistic

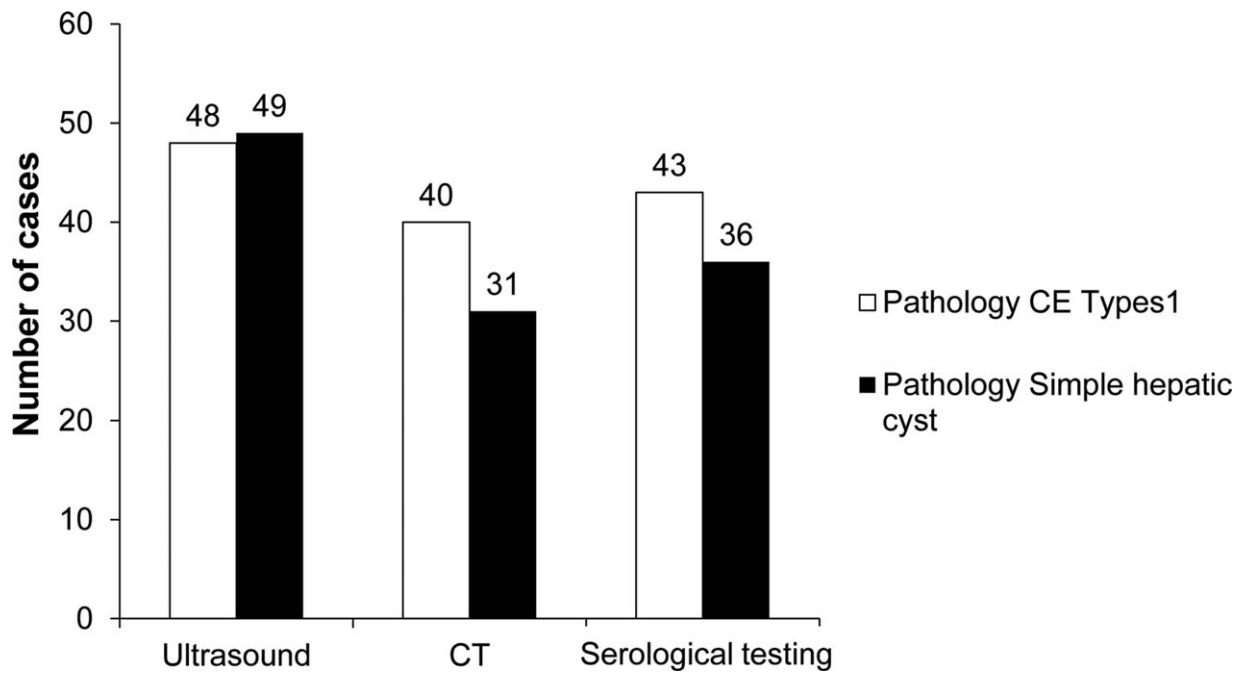


Figure 1. The diagnostic value of ultrasound, CT, and serological testing in liver cystic lesions. CT = computed tomography.

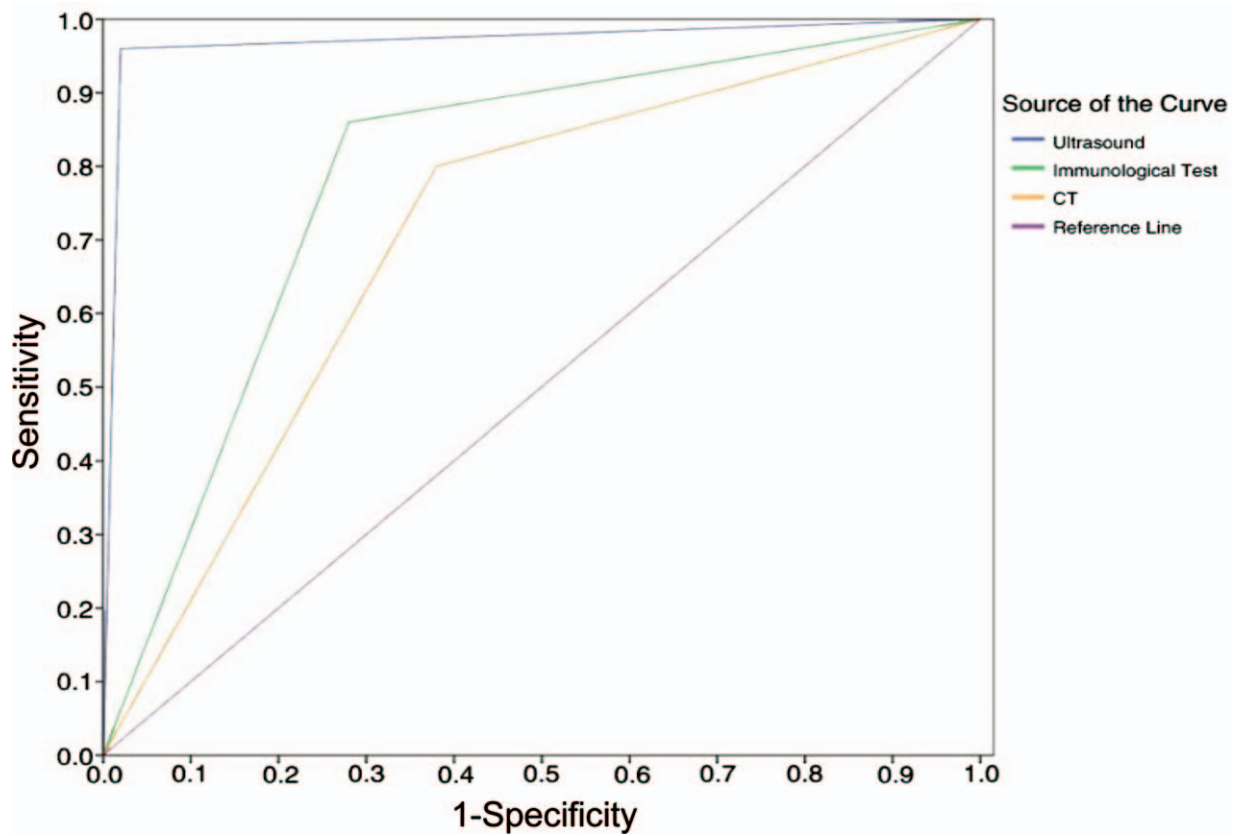


Figure 2. ROC analysis. ROC was used to compare the diagnostic value of the ultrasound, CT and serological testing. The area under ROC curve of ultrasound, CT and serological testing was 0.97, 0.79, and 0.71, respectively. CT = computed tomography, ROC = receiver operating characteristic.

Table 2**The area under ROC curve of ultrasonography, CT and laboratory tests.**

	Area	Std. Error	Asymptotic Sig	95% CI	
				Lower level	Upper level
Ultrasound	0.970	0.020	0.000	0.000	1.000
Serological testing	0.790	0.047	0.000	0.697	0.883
CT	0.710	0.053	0.000	0.607	0.813

CT = computed tomography, ROC = receiver operating characteristic.

analysis (Table 4). The result showed that both ultrasound and serological testing were positive, which can increase 5.39 units in logistic P. And, the accuracy of positive results was 218-fold higher than that of negative ones. This result confirmed the validity of the model. And we evaluated the diagnostic value of the model through the misjudgment matrix of this model. It showed that in 50 patients with simple hepatic cysts, 49 patients were predicted correctly and the accuracy rate was 98%. And, in 50 patients with hepatic cystic echinococcosis types 1, 41 patients were predicted correctly with accuracy rate of 82%. The overall prediction rate of the model was 89.9% (Table 5). It showed that ultrasound combined with serological testing were the most reliable method for differential diagnosis of CE type1 and simple hepatic cyst.

3.7. Combined analysis of CT with immunological test

Combined diagnostic value of CT with serological testing was evaluated. The combination was considered positive if both techniques were positive, and negative if both negative. The diagnostic sensitivity of this combination was 70%, and the specificity was 82%, as shown in Table 6.

4. Discussion

Echinococcosis is a zoonosis caused by the larval (metacystode) stages of cestodes (flat worms) belonging to the genus *Echinococcus* and the family Taeniidae.^[11] The most common location for the development of hydatid cysts is the liver (50–70%).^[12] According WHO-*Informal Working Group Classification on Echinococcus* (IWGE), Liver hydatid cyst were categorized into 5 types^[13] and CE type 1 was an early stage. It showed unilocular cystic lesion with anechoic content, similar as the simple liver cysts. However, due to the significantly different treatments for these 2 diseases, a new diagnosis model is warranted to distinguish CE type1 and simple hepatic cyst preoperatively.

Ultrasound has become a widely used diagnostic technique for CE detection. The diagnostic criteria of ultrasound for CE are thick walled cystic lesions with 2 lines along the wall. These cysts

Table 3**The diagnostic value of combined test in liver cystic lesions.**

Ultrasound	Serological testing	CE Types1	Simple hepatic cyst
+	+	41	0
+	–	7	1
–	+	2	14
–	–	0	35
Total		50	50

usually have fine internal echoes.^[14] In this study, the sensitivity and the specificity of ultrasound was 96% and 98% respectively, and it has higher value when compared with CT and serological testing. However, the results are dependent on user's technique and experience. For example, when patients are overweight or have intestinal gas accumulation, ultrasound may miss some of the lesions. In this study, only 2 patients with CE type 1 were misdiagnosed as simple hepatic cyst, and only 1 patient with simple hepatic cyst was misdiagnosed as CE type 1. If ultrasound combined with serological testing, the specificity can reach 100%. Based on our study, ultrasound is considered as a feasible, simple, fast, and cheap method for differential diagnosis of CE type1 and simple hepatic cyst.

The typical CT findings of hepatic cystic echinococcosis are water-like density of cystic lesions, calcification of the cyst wall, daughter cyst or collapsed inner cyst. Liver CE type 1 always showed a sharply defined homogeneous hypodense lesion with a CT value of 14 to 20 HU.^[15] Differential diagnosis of CE type 1 from simple hepatic cyst using CT is difficult. CT can diagnose or differentially diagnose them based on CT values.^[16] When compared the CT values of hepatic hydatid cyst and hepatic cysts, there was no significant difference. Therefore, CT staff can only identify the 2 diseases based on past experience; this objective determination brought great confusion and challenges to clinical work. In this study, among 50 patients with simple hepatic cyst, only 31 cases were successfully diagnosed by CT, and the rest 19 cases cannot be differentiated from the CE type 1. In the 50 cases of CE type 1, 40 cases were successfully diagnosed by CT, and the rest 10 cases cannot be differentiated from the hepatic cyst. Therefore, CT can only provide a reference for clarifying the size and position of cysts for the surgical approach, but cannot assist the future surgeries.

Serological testing are useful to confirm with imaging diagnosis and is an important tool in differential diagnosis.^[17] The sensitivity of serological testing is dependent on the echinococcal antigen levels and its cross-reactivity with antigens of other diseases.^[18,19] In this study, the dot immunogold filtration assay was used to detect antibody response to parasite. It showed among 50 patients with simple hepatic cyst, there were 14 cases positive and among 50 patients with CE type1, 43 cases were positive. The sensitivity and the specificity was 86.00% and 72.00% respectively, which was similar to Fu Yan large sample research (sensitivity of 92.61%).^[20] For uncertain cases, for

Table 4**The results of logistic analysis of combined tests.**

	B	S.E.	Wals	P	OR	95% CI of OR	
						Lower limits	Upper limits
Combined tests	5.39	1.08	25.10	.00	218.67	26.57	1799.31
Constants	–1.67	0.36	21.24	.00	0.19		

Table 5**The diagnostic value of the model.**

Observed	Predicted		Percentage correct
	Patients with CE group	Patients with simple hepatic cysts group	
Patients with CE group	49	1	98%
Patients with simple hepatic cysts group	9	41	82%
Overall percentage			89.9%

Table 6**The diagnostic value of combined test in liver cystic lesions.**

CT	Serological testing	CE Types ¹	Simple hepatic cyst
+	+	35	9
+	–	5	10
–	+	8	6
–	–	2	25
Total		50	50

CT = computed tomography.

example in patients whose hepatic cysts cannot be differentiated from simple liver cyst using ultrasound or CT, combination with serological testing can get higher diagnostic value. In our study, it showed the specificity of combination of serological testing and ultrasound can reach 100%.

Currently, clinical diagnosis of hepatic hydatid cyst is mainly based on medical history, clinical symptoms, imaging and serological testing.^[21] However, imaging examinations can be difficult to differentiate between CE cyst and hepatic cyst. Serological testing can help supplement imaging examinations to further diagnosis. Combination of imaging examinations and serological testing can provide a more reliable diagnosis.

This study has several limitations. First, this is a retrospective study from a single-institution experience. The number of patients enrolled may be not sufficient. Second, all the data were collected through the medical records and selection bias possibly exists. Therefore, randomized controlled researches with large sample size are expected in the future.

In conclusion, ultrasound is a considerably helpful technique for differentiating hydatid cyst from simple hepatic cyst. Serological test can be an important supplement to ultrasound.

Author contributions

Data curation: Tuerganaili Aji, Abuduaini Abulizi, Yusfu Yimiti, Hao Wen.

Formal analysis: Tuerganaili Aji, Tieming Jiang, Yusfu Yimiti.

Funding acquisition: Yingmei Shao.

Methodology: Bo Ran, Tieming Jiang, Ruiqing Zhang, Qiang Guo, Abuduaini Abulizi.

Resources: Ruiqing Zhang, Qiang Guo, Abuduaini Abulizi, Yusfu Yimiti.

Supervision: Yingmei Shao.

Validation: Yingmei Shao.

Visualization: Yingmei Shao.

Writing – original draft: Bo Ran, Ruiqing Zhang, Hao Wen.

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