# Diagnostic value and clinical significance of ultrasound combined with CT in cystic renal cell carcinoma

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**Abstract.** This study investigated the value and clinical significance of ultrasound combined with CT in the diagnosis of cystic renal cell carcinoma. A total of 85 patients with cystic renal cell carcinoma, who were admitted to the Oncology Department of Yantai Yuhuangding Hospital Affiliated to Qingdao University from December 2015 to April 2017, were selected as the study group, and 70 patients with benign renal cyst, who were examined in Yantai Yuhuangding Hospital Affiliated to Qingdao University, were selected as the benign group. The patients in the two groups were examined by ultrasound and CT. The diagnostic value of ultrasound, CT, and ultrasound combined with CT in cystic renal cell carcinoma was analyzed. The sensitivity of ultrasound combined with CT was significantly higher than that of CT and ultrasound ($P<0.05$). The specificity and diagnostic coincidence rate of ultrasound combined with CT were significantly higher than those of CT ($P<0.05$). For unicapsular kidney cancer, there was no significant difference among ultrasound, CT and ultrasound combined with CT in the diagnosis of septum and wall nodule ($P>0.05$). For polycystic kidney cancer, there was no significant difference among ultrasound, CT and ultrasound combined with CT in the diagnosis of the presence or absence of septum ($P>0.05$). Ultrasound was significantly better than CT in cyst wall confounding ($P<0.05$). Ultrasound combined with CT was significantly better than ultrasound in calcification and blood supply of tumors ($P<0.05$). In conclusion, the accuracy of ultrasound combined with CT is higher than that of ultrasound or that of CT in the diagnosis of cystic renal cell carcinoma, which can be beneficial in accurately carrying out clinical diagnosis, reduce the incidence of missed diagnosis and misdiagnosis caused by a single diagnosis and treatment. Ultrasound combined with CT is good for clinical screening and can guide clinical symptomatic treatment, which is worthy of generalizing in clinic.

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## Introduction

Cystic renal cell carcinoma accounts for ~10% of renal cancer, and it refers to the renal cancer confirmed by pathology with mixed cystic-solid changes or cystic changes in imageology (1). This disease appears in people of any age, but is more common in elderly people and males. If the tumor grading of cystic renal cell carcinoma is low, the prognosis of patients can be improved by timely detection and effective treatment (2). In clinic, cystic renal cell carcinoma is rare, and patients with this disease have no obvious clinical symptoms. It is often found by physical examination. However, as cystic renal cell carcinoma is insufficiently acquainted, it may be misdiagnosed as benign cystic lesion of kidney (3). At present, pathological diagnosis is the optimal standard for cystic renal cell carcinoma, which is diagnosed by imageology in clinic (4).

With the improvement of the diagnostic level and imaging equipment, increased attention has been paid from clinicians and radiologists on the diagnostic methods of cystic renal cell carcinoma. Typical cystic renal cell carcinoma is easily diagnosed by ultrasound sonograms, but a small number of atypical cystic renal cell carcinomas with thin and regular cystic wall are easily misdiagnosed as benign renal cysts (2). The CT manifestation of cystic renal cell carcinoma has high density resolution. Thus, the characteristics of cystic renal cell carcinoma can be analyzed by imaging, which helps to accurately diagnose cystic renal cell carcinoma (5). However, the CT manifestation of cystic renal cell carcinoma is similar to that of other benign cystic lesion. Therefore, cystic renal cell carcinoma is easily misdiagnosed in clinic (6). Ultrasound is the preferred imaging diagnostic method of cystic renal cell carcinoma. As a small amount of new vessels appear in parenchymal part and septum of cystic renal cell carcinoma, a little blood flow signal can be sometimes seen in ultrasound, which is helpful for the diagnosis of cystic renal cell carcinoma. However, the sensitivity and specificity of ultrasound are poor in showing new microvascular vessels

of tumors (4). Studies have reported that the combined diagnosis of imageology has a high diagnostic value in Kawasaki disease (7), breast cancer lesion (8) and early cervical cancer (9). Baldari *et al* (10) found that ultrasound combined with CT has a high diagnostic value in complex congenital heart diseases. At present, the main diagnostic methods of cystic renal cell carcinoma are ultrasound and CT. There are few reports on the combined diagnosis of the two in cystic renal cell carcinoma.

The value of ultrasound combined with CT in the diagnosis of cystic renal cell carcinoma was investigated in the present study in order to provide an effective, sensitive and accurate detection method for the diagnosis of cystic renal cell carcinoma and improve the efficacy of the follow-up treatment and prognosis of patients.

## Patients and methods

*General data*. A total of 85 patients with cystic renal cell carcinoma, who were admitted to the Oncology Department in Yantai Yuhuangding Hospital Affiliated to Qingdao University (Yantai, China) from December 2015 to April 2017, were selected as the study group, with an average age of 47.89±5.12 years, including 68 males and 17 females. The tumor diameter of patients was 50.13±11.76 mm, and there were 49 cases with cystic renal cell carcinoma in left kidney, 36 cases in right kidney, 47 cases with upper abdominal discomfort, 23 cases with pain and discomfort in the waist, and 15 cases without obvious symptoms. A total of 70 patients with benign renal cyst examined in Yantai Yuhuangding Hospital Affiliated to Qingdao University during the same period were selected as the benign group, with an average age of 46.21±4.85 years.

Inclusion criteria: i) patients >18 years of age; ii) patients who actively cooperated with the research; and iii) patients who had not received antitumor treatment before examination.

Exclusion criteria: i) patients with mental illness or a family history of mental illness in the past; ii) patients with incomplete clinical data; iii) patients with severe diseases in heart, liver and kidney; iv) patients who had contraindications for ultrasound and CT; v) patients in gestation or lactation period; and vi) patients with cystic renal cell carcinoma, severe fungal infection, bacterial infection and virus infection.

The study was approved by the Ethics Committee of Yantai Yuhuangding Hospital Affiliated to Qingdao University. Patients who participated in this study had complete clinical data. Signed informed consents were obtained from the patients or their guardians.

*Detection methods*. All patients in both groups were examined by ultrasound and CT, with an interval of <3 days. ATL HDI-5000 energy Doppler (Soma Technology, Inc.) and GE-LOGIQ9 color Doppler (GE Healthcare) ultrasound diagnostic instruments were used. The probe frequency was from 2.0 to 5.0 MHz. All patients fasted and did not drink water for >8 h before ultrasound examination, and in the next morning the patients with an empty stomach were examined. A routine renal examination was carried out for the patients, the echographic characteristics of the cystic lesions of the kidneys were observed, and the size of the tumors was measured. Energy Doppler and color Doppler ultrasound diagnostic instruments were used to observe internal and peripheral blood flow of the lesion part. The presence of swollen lymph nodes in renal hilus and tumor thrombus in renal vein and postcava was checked, as well as whether there was contralateral kidney and normal renal tissue around the tumors.

Light speed 64-tier spiral CT instrument, produced by GE Healthcare, was used to examine the patients. Plain scanning and 3-phase dynamic enhanced scanning were carried out. The patients were restricted from eating 8 h before the examination and kept fasting. Before scanning, the patients were instructed to drink purified water, and then the parameter of plain scanning was set and the patients were scanned in supine position. The scanning parameters were: tube current, 150-250 mA; tube voltage, 90-120 kV; time product, 200 mAs; layer thickness, 5-10 mm; screw pitch, 1.0. The vein mass in the anterior elbow of the patients was injected with contrast agent by high-pressure automatic injectors. According to the condition of the patients, the dosage of iohexol was adjusted between 1.5 and 2.0 ml/kg (SFDA approval no. H19980218; Beijing BeiLu Pharmaceutical Co., Ltd.) and the injection rate of contrast agent was 2-3 ml/sec. The enhanced scanning was carried out in renal cortex phase (delayed 25-30 sec), parenchymal phase (delayed 60-90 sec), and renal pelvis phase (delayed 3-5 min).

The results were analyzed by the double-blind method (at least four radiologists), and the final results were determined after the radiologists came to an agreement.

*Observation indicators*. The scanning results of all patients were recorded and graded. Bosniak grading (11): Grade II: septum thickness was <1.0 mm. There was calcification with the shape of filament and no enhancement of enhanced scanning. Grade IIF: there were more complex features in Grade IIF compared with Grade II. The calcification may be nodular, the septum wall thickened, and there was no enhanced scanning or there was little enhancement. Grade III: intracapsular signal was uneven, irregular strip calcification could be seen, and cyst was characterized by high density. Grade IV: intracapsular septum was distributed irregularly, and substantial nodule could be seen. Clinical observation indicators: the diagnostic results of surgery and needle biopsy were used as reference. The sensitivity, specificity, diagnostic coincidence rate, missed diagnosis rate and misdiagnosis rate of ultrasound, CT and ultrasound combined with CT in diagnosis of cystic renal cell carcinoma were calculated.

*Statistical analysis*. Experimental data were statistically analyzed by SPSS 17.0 statistical software (SPSS, Inc.). Enumeration data were expressed in the form of n (%) and Chi-square test was used for the comparison between groups. Measurement data were expressed as mean ± standard deviation and paired t-test was used for the comparison between two groups. ANOVA, with LSD post hoc test, was used for comparison between multiple groups. $P<0.05$ was considered to indicate a statistically significant difference.

## Results

*Comparison of the general data between the two groups*. There were no significant differences in age, sex, body mass index, smoking, drinking, history of diabetes, history of hypertension, white blood cells, red blood cells, and platelet

Table I. Comparison of general data between the two groups [n (%), mean ± standard deviation].

| Variables | Study group (n=85) | Benign group (n=70) | $\chi^2$/t | P-value |
|---|---|---|---|---|
| Age (years) | 47.89±5.12 | 46.21±4.85 | 0.842 | 0.401 |
| Sex | | | 0.048 | 0.827 |
| Male | 68 (80.0) | 55 (78.6) | | |
| Female | 17 (20.0) | 15 (21.4) | | |
| Body mass index (kg/m$^2$) | 26.12±3.09 | 25.97±2.99 | 0.305 | 0.761 |
| Smoking | | | | |
| Yes | 43 (50.6) | 36 (51.4) | 0.011 | 0.917 |
| No | 42 (49.4) | 34 (48.6) | | |
| Drinking | | | 0.876 | 0.350 |
| Yes | 56 (65.9) | 41 (58.6) | | |
| No | 29 (34.1) | 29 (41.4) | | |
| History of diabetes | | | 0.308 | 0.579 |
| Yes | 24 (28.2) | 17 (24.3) | | |
| No | 61 (71.8) | 53 (75.7) | | |
| History of hypertension | | | 0.034 | 0.854 |
| Yes | 16 (18.8) | 14 (20.0) | | |
| No | 69 (81.2) | 56 (80.0) | | |
| White blood cells (x10$^9$/l) | 6.24±3.67 | 6.37±3.77 | 0.829 | 0.217 |
| Platelets (x10$^9$/l) | 173.23±21.09 | 169.26±23.87 | 1.099 | 0.274 |
| Red blood cells (x10$^{12}$/l) | 4.65±0.65 | 4.77±0.71 | 1.097 | 0.274 |

Table II. Comparison of diagnostic results.

| Detection results | Pathological results + | Pathological results - | Summation |
|---|---|---|---|
| CT + | 65 | 27 | 92 |
| CT - | 20 | 43 | 63 |
| Summation | 85 | 70 | 155 |
| Ultrasound + | 74 | 14 | 88 |
| Ultrasound - | 11 | 56 | 67 |
| Summation | 85 | 70 | 155 |
| Ultrasound combined with CT + | 84 | 15 | 99 |
| Ultrasound combined with CT - | 1 | 55 | 56 |
| Summation | 85 | 70 | 155 |

count between the groups (P>0.05). The groups were comparable (Table I).

*Comparison of diagnostic results*. As shown in Table II, 85 cases were diagnosed with cystic renal cell carcinoma by pathology; 92 cases were diagnosed by CT, among which 65 cases were true-positive; 88 cases were diagnosed by ultrasound, among which 74 cases were true-positive; and 99 cases were diagnosed by ultrasound combined with CT, among which 84 cases were true-positive.

As shown in Table III, the accuracy of the different methods was compared. The sensitivity of ultrasound combined

Table III. Comparison of the accuracy of different methods.

| Variables | Sensitivity | Specificity |
|---|---|---|
| CT | 76.5% | 61.4% |
| Ultrasound | 87.1% | 80.0%[a] |
| Ultrasound combined with CT | 98.8%[a,b] | 78.6%[a] |
| $\chi^2$ | 22.44 | 11.69 |
| P-value | <0.001 | 0.003 |

[a]P<0.05, compared with CT; [b]P<0.05, compared with ultrasound.

Table IV. Comparison of the accuracy of different methods in the diagnosis of unicapsular and polycystic kidney cancer [n (%)].

| Methods | Cases | Ultrasound | CT | Ultrasound combined with CT | $\chi^2$ | P-value |
|---|---|---|---|---|---|---|
| Unicapsular kidney cancer (n=39) | | | | | | |
| Absence of septum | 10 | 10 (100.0) | 9 (90.0) | 10 (100.0) | 2.069 | 0.355 |
| Presence of septum | 29 | 28 (96.6) | 26 (89.7) | 29 (100.0) | 3.669 | 0.160 |
| Absence of wall nodule | 12 | 12 (100.0) | 11 (91.7) | 12 (100.0) | 2.057 | 0.358 |
| Presence of wall nodule | 27 | 27 (100.0) | 25 (92.6) | 27 (100.0) | 4.101 | 0.129 |
| Polycystic kidney cancer (n=46) | | | | | | |
| Absence of septum | 13 | 12 (92.3) | 11 (84.6) | 13 (100.0) | 2.167 | 0.338 |
| Presence of septum | 33 | 33 (100.0) | 31 (94.0) | 33 (100.0) | 4.082 | 0.130 |
| Absence of wall nodule | 30 | 16 (53.3) | 28 (93.3)[a] | 30 (100.0)[a] | 26.150 | <0.001 |
| Presence of wall nodule | 16 | 9 (56.3) | 14 (87.5)[a] | 15 (93.8)[a] | 7.832 | 0.020 |

[a]P<0.05, compared with ultrasound.

Table V. Display rate of different symptoms [n (%)].

| Symptoms | Cases | Ultrasound | CT | Ultrasound combined with CT | $\chi^2$ | P-value |
|---|---|---|---|---|---|---|
| Cyst wall slightly irregular or completely irregular | 66 | 64 (97.0) | 66 (100.0) | 66 (100.0) | 4.041 | 0.133 |
| Septum | 62 | 61 (98.4) | 56 (90.3) | 62 (100.0)[b] | 9.20 | 0.010 |
| Calcification | 26 | 12 (46.2) | 24 (92.3)[a] | 26 (100.0)[a] | 27.05 | <0.001 |
| Wall nodule | 43 | 36 (83.7) | 39 (90.7) | 42 (97.7) | 4.962 | 0.084 |
| Cyst wall confounding | 68 | 68 (100.0) | 62 (91.2)[a] | 68 (100.0)[b] | 12.36 | 0.002 |
| Blood supply of tumor | 74 | 61 (82.4) | 73 (98.6)[a] | 74 (100.0)[a] | 23.94 | <0.001 |

[a]P<0.05, compared with ultrasound; [b]P<0.05, compared with CT.

with CT was significantly higher than that of CT and that of ultrasound (P<0.05). There was no significant difference between the sensitivity of CT and the sensitivity of ultrasound (P>0.05). The specificity of ultrasound combined with CT and ultrasound alone was significantly higher than that of CT (P<0.05). There was no significant difference between the specificity of ultrasound combined with CT and the specificity of ultrasound (P>0.05). It can be seen from Fig. 1 that the diagnostic coincidence rate of ultrasound was significantly higher than that of CT and the diagnostic coincidence rate of ultrasound combined with CT was significantly higher than that of CT (P<0.05).

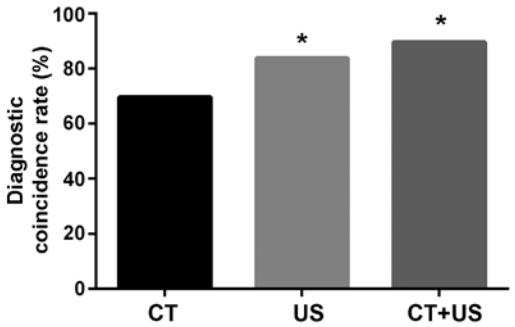


Figure 1. Comparison of the diagnostic coincidence rate of different methods. The diagnostic coincidence rates of CT, US, and CT+US were 69.7, 83.9, and 89.7%, respectively. The diagnostic coincidence rates of US and CT+US were significantly higher than that of CT (P<0.05). *P<0.05, compared with CT. US, ultrasound.

*Comparison of the accuracy of the different methods in the diagnosis of unicapsular and polycystic kidney cancer.* There were 39 cases diagnosed with unicapsular kidney cancer and 46 cases diagnosed with polycystic kidney cancer. The accuracy of the different methods in the diagnosis of unicapsular and polycystic kidney cancer was compared. As seen in Table IV, in terms of unicapsular kidney cancer, there was no significant difference among ultrasound, CT and ultrasound combined with CT in the diagnosis of septum and wall nodule (P>0.05). In terms of polycystic kidney cancer, there was no significant difference among ultrasound, CT and ultrasound combined with CT in the diagnosis of the presence or absence of septum (P>0.05), but the accuracy of ultrasound combined with CT and that of CT alone was significantly higher than the accuracy of ultrasound in the diagnosis of the presence or absence of wall nodule (P<0.05).

*Display rate of different symptoms*. In terms of the display of nidus and blood supply, CT was significantly better

Table VI. Comparison of the results of Bosniak grading diagnosis [n (%)].

| Bosniak grading | No. | Ultrasound | CT | Ultrasound combined with CT | $\chi^2$ | P-value |
|---|---|---|---|---|---|---|
| II | 37 | 36 (97.3) | 34 (92.0) | 37 (100.0) | 3.63 | 0.163 |
| IIF | 22 | 18 (81.8) | 14 (63.6) | 22 (100.0)[a,b] | 9.78 | 0.008 |
| III | 15 | 11 (73.3) | 8 (53.3) | 14 (93.3)[b] | 6.14 | 0.047 |
| IV | 11 | 9 (81.8) | 9 (81.8) | 11 (100.0) | 2.28 | 0.320 |

[a]P<0.05, compared with ultrasound; [b]P<0.05, compared with CT.

than ultrasound in calcification and blood supply of tumor (P<0.05). Ultrasound was significantly better than CT in cyst wall confounding (P<0.05). Ultrasound combined with CT was significantly better than ultrasound in calcification and blood supply of tumor (P<0.05). Ultrasound combined with CT was significantly better than CT in septum and cyst wall confounding (P<0.05; Table V).

*Comparison of the results of Bosniak grading diagnosis.* Comparison of the results of Bosniak grading diagnosis showed no significant difference between ultrasound and CT (P<0.05). Ultrasound combined with CT was significantly better than CT in the diagnosis of grades IIF and III (P<0.05). Ultrasound combined with CT was significantly better than ultrasound in the diagnosis of grade IIF (P<0.05; Table VI).

## Discussion

Cystic renal cell carcinoma is a general term for cystic space-occupying lesions of the kidney, which is separated into four subtypes, i.e., the monolocular, multilocular, cystic necrosis, and cyst epithelial-derived type (12). However, some scholars only separate it into polycystic and unicapsular kidney cancers (13). Among the four pathological types, polycystic kidney cancer accounts for ~33% of renal cystic tumors (14). The main pathological feature of cystic renal cell carcinoma is that there are multiple cysts with different size in cancer tissue. The cyst wall is lined with transparent cancer cells, there are agminated transparent cancer cells in septum of the cyst. Cystic renal cell carcinoma is a renal gland cancer, and a cyst is caused by cystic expansion of the glandular cavity of adenocarcinoma (15). In the last 30 years, with the popularization of B-ultrasound and CT, the detection rate of cystic renal cell carcinoma has improved, which helps to accumulate experience for preoperative diagnosis (16).

Accurate diagnosis is sometimes difficult because there are similar imaging features among cystic renal cell carcinoma, conventional renal cell carcinoma with cystic changes and benign renal cystic diseases (17). Cystic small renal carcinoma is generally graded and screened by ultrasound or CT. Bosniak grading is mainly based on examination results of CT. It is divided into four grades. Grades I and II represent benign nidus, grades III and IV represent malignant nidus. Grade IIF is between grades II and III. There are more lesions in grade IIF in clinic, so the diagnosis is relatively difficult (18). Studies have shown that ultrasound combined with Bosniak criteria can improve the diagnostic rate of benign and malignant renal cystic lesions (19). Therefore, the accuracy of different diagnostic methods in Bosniak grading diagnosis of cystic renal cell carcinoma was compared in this study.

There were no significant differences in age, sex, body mass index, smoking, drinking, history of diabetes, history of hypertension, white blood cells, red blood cells, and platelet count of the patients between the two groups, and thus, the groups were comparable. Literature shows that generally CT and nuclear magnetic resonance are consistent in the diagnostic classification of cystic renal space-occupying lesions (20), but compared with CT, ultrasonic contrast can help to improve the diagnostic accuracy of cystic renal cell carcinoma (21). Furthermore, studies have shown that enhanced ultrasound is superior to unenhanced ultrasound and CT in the diagnosis of complex cystic renal tumors (22). This study showed that the sensitivity of ultrasound combined with CT was significantly higher than that of CT and that of ultrasound (P<0.05). The specificity and diagnostic coincidence rate of ultrasound combined with CT were significantly higher than that of CT (P<0.05). These results indicate that the combined diagnosis can also improve the sensitivity, and the accuracy of the combined diagnosis is high in the diagnosis of cystic renal cell carcinoma. The accuracy of different methods in the diagnosis of unicapsular and polycystic kidney cancer was also compared. For unicapsular kidney cancer, there was no significant difference among ultrasound, CT and ultrasound combined with CT in the diagnosis of septum and wall nodule. For polycystic kidney cancer, there was no significant difference among ultrasound, CT and ultrasound combined with CT in the diagnosis of the presence or absence of septum. The accuracy of CT and ultrasound combined with CT was significantly higher than that of ultrasound in the diagnosis of the presence or absence of wall nodule. The diagnosis of blood supply of the nidus is an important aspect in the diagnosis of cystic renal cell carcinoma and benign cystic renal diseases (23). The results of this study showed that CT was significantly better than ultrasound in wall nodule, calcification and blood supply of tumors. Ultrasound was significantly better than CT in cyst wall confounding. Ultrasound combined with CT was significantly better than ultrasound in calcification and blood supply of tumors. Ultrasound combined with CT was significantly better than CT in septum and cyst wall confounding (P<0.05). Previous studies have demonstrated that CT has a high display rate in showing wall nodule, calcification or tumor, but compared with CT, ultrasound has a good display rate in showing the number of septum, the enhancement of cystic tumors,

the thickness of septum or the thickness of the wall, and it can show the internal structure of cystic tumors (24,25), in agreement with the results of the present study. Ultrasound is a better choice in showing specific nidus response. At the same time, CT can effectively show the blood supply of the nidus in patients. Therefore, the combination of the two methods can significantly improve the diagnostic accuracy of cystic renal cell carcinoma and help patients to receive timely treatment in order to reduce the damage caused by cystic renal cell carcinoma (26,27). Katabathina *et al* (28) considered that the diagnosis of malignancy degree of renal cystic lesion is particularly important. In terms of the comparison of the results of Bosniak grading diagnosis, ultrasound combined with CT is significantly superior to CT from grade IIF to III, and ultrasound combined with CT is superior to ultrasound in grade IIF. This study showed that the accuracy of the combined diagnosis is higher than that of the other methods in the grading diagnosis. It has been proven (29) that the combination of imageology tests helps to improve space-occupying diagnostic coincidence rate of cystic kidney in complex cyst which is type II or above. Therefore, the combination of imageology tests has a high value in clinical diagnosis.

Single imaging and multiple imaging techniques were compared in the present study. The research presented is innovative, however, the number of cases in the groups is not sufficient, and the study is mainly retrospective, so there may exist deviations in the study results. Therefore, future studies confirming the above results are anticipated.

In summary, the accuracy of ultrasound combined with CT is higher than that of ultrasound and that of CT in the diagnosis of cystic renal cell carcinoma. Ultrasound combined with CT can help to accurately carry out clinical diagnosis, reduce the incidence of missed diagnosis and misdiagnosis caused by single diagnosis and treatment. Ultrasound combined with CT is good for clinical screening and can guide clinical symptomatic treatment, and therefore is worthy of generalizing in clinic.

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**Availability of data and materials**

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

**Authors' contributions**

MS interpreted the data and drafted the manuscript. CW conceived and designed the study. FJ and XF collected and analyzed the data. BG was responsible for the ultrasound and CT examination and revised the manuscript. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

The study was approved by the Ethics Committee of Yantai Yuhuangding Hospital Affiliated to Qingdao University (Yantai, China). Patients who participated in this study had complete clinical data. Signed informed consents were obtained from the patients or their guardians.

**Patient consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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