

Full Length Research Paper

Visualization rate of contrast-enhanced ultrasound and conventional ultrasound for pseudocapsule of renal cell carcinoma

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Accepted 22 June, 2010

In this present study, we analyzed and compared the visualization rate of contrast-enhanced ultrasound (CEUS) and conventional ultrasound for pseudocapsules of renal cell carcinoma. Totally 103 patients with renal cell carcinoma confirmed by operation and pathology were examined with CEUS and conventional ultrasound, and the visualization rate of CEUS and conventional ultrasound for pseudocapsule of renal cell carcinoma was compared. Among these 103 cases of renal cell carcinoma (RCC), there were 97 cases of clear cell RCC and 6 cases of papillary renal cell carcinoma. Under conventional ultrasound, the presence of pseudocapsule was detected in only 27 RCCs (26.2%), while CEUS revealed the presence of pseudocapsule in 78 RCCs (75.7%), indicating statistically significant difference ($p < 0.01$). The pseudocapsule was not visible either under conventional ultrasound or CEUS in 25 cases. Visualization rate of CEUS for RCC pseudocapsule is much higher than that of conventional ultrasound, indicating that CEUS is useful for diagnosis of RCC.

Key words: Ultrasonography, contrast-enhanced ultrasound, contrast agent, renal cell carcinoma.

INTRODUCTION

Two-dimensional ultrasound and color Doppler ultrasound are preferred imaging measures for diagnosis of renal tumors. Application of contrast-enhanced ultrasound (CEUS) visualizing renal tumors has been realized due to the fast development of CEUS techniques. However, the visualization results of renal tumors varied greatly because of the specific blood supply in kidneys. Renal cell carcinoma is rich in blood supply, and chromophobe cell carcinoma is offered with radial blood supply, while benign renal tumors are mostly lack of blood supply. Presence of pseudocapsule is the pathological feature of early renal cell carcinoma (Di Cristofano et al., 2009). The primary objective of this study was to compare the capacities of CEUS and conventional ultrasonography to visualize the pseudocapsule of renal cell carcinomas (RCC).

PATIENTS AND METHODS

Between December 2005 and June 2006, 103 patients aged 11 - 78 years (mean 53 ± 6.5 years) with RCC were admitted in our hospital. Of these patients, renal tumors were diagnosed in the right kidney in 62 cases, and left in 41 cases. The diameter range of these tumors was 1.1 - 6.4 cm (mean 3.4 ± 1.3 cm). Surgical treatments were performed in all cases with pathological results obtained. Among these patients, 97 were diagnosed as clear cell RCC, and 6 were papillary RCC. All patients gave written informed consent, and sample collection was approved by the ethics committee of Jinling Hospital.

GE LOGIQ-9 and SIEMENS SEQUIOA-512 color Doppler ultrasound diagnosis instrument with a 3-5 MHz multi-frequency probe were selected. Power pulse inversion (PPI) and contrast pulse sequence (CPS) imaging modes were applied, with the mechanic index range of 0.08 - 0.1. Ultrasound contrast medium SonoVue (Bracco, Milan, Italy) was chosen, into which 5 ml of normal saline was injected before administration. The mixture was completely shaken till opalescent liquid appeared, then 0.4 - 1.2 ml liquid was aspirated to perform superficial bolus injection or gradual intravenous injection via the ulnar vein, and 5 ml of normal saline was aspirated to flush the syringe and then injected. The volume of ultrasound contrast medium applied was determined by the visualization mode and mass size (CPS mode was selected with

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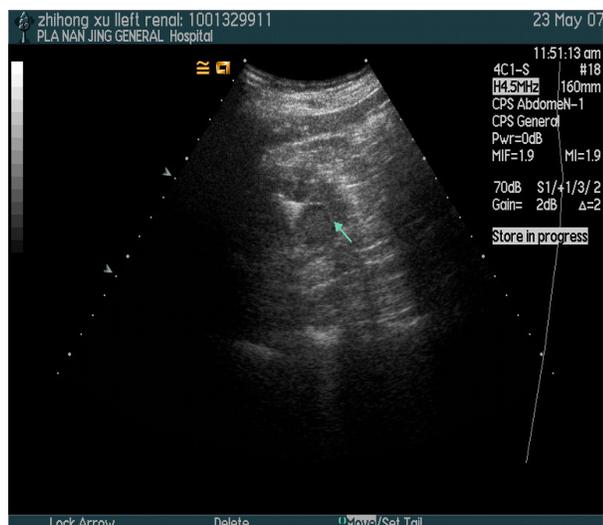


Figure 1. Peritumoral hyperechoic zone of RCC shown by conventional ultrasound (arrow).



Figure 2. Enhanced echo surrounding the mass shown by contrast-enhanced ultrasound of RCC

0.4 ml of medium injected; medium volume for PPI mode should be more than 1.0 ml).

Conventional fundamental imaging and color Doppler imaging were performed before CEUS to primarily observe the presence of pseudocapsule, echoes and blood flow, and simultaneously record the corresponding tumor location, size, morphology, boundaries and peripheral lymph nodes, etc. The study only discussed the detection ability of two kinds of ultrasonic detection methods on pseudocapsule, while other ultrasound features of renal cell carcinoma were not analyzed. The probe was fixed to orient the renal mass, and then PPI and CPS modes were initiated to inject intravenous bolus dose or gradual intravenous dose at superficial ulnar vein. Peritumoral pseudocapsule, influent and effluent times of contrast agent (compare to renal cortex) as well as the distributions of contrast agent in the masses and adjacent areas were observed in real time. The tota procedure of CEUS was

recorded. All CEUS procedures were conducted by the author alone to minimize the errors produced during observations.

Statistical analysis

Case number and percentage values were obtained by qualitative examinations. Data of paired fourfold table were analyzed by using McNemar's test. $p < 0.05$ was considered statistically significant.

RESULTS

Conventional ultrasound and CEUS were performed on 103 patients with RCC. Conventional ultrasound (fundamental wave) detected 27 cases of pseudocapsule (27/103, 26%, Figure 1), while CEUS detected 78 cases of pseudocapsule (78/103, 75.7%, Figure 2). The visualization rate of pseudocapsule by CEUS was obviously higher than that of conventional ultrasound ($p < 0.01$, Table 1). There were 25 patients in whom the pseudocapsule was neither detected by CEUS nor by conventional ultrasound. The RCC pseudocapsule under conventional ultrasound was represented as two kinds of echoes: (1) A thicker peritumoral hypoanechoic halo (> 1.0 mm), which could not be easily displayed; (2) A thinner rim of perilesional enhancement (< 1.0 mm) which could be easily shown. It was confirmed that there were more pressed normal kidney tissues and less fibrous tissues in the thick pseudocapsule while there was mainly fibrous tissue in thin pseudocapsule. Pseudocapsule features displayed by CEUS: The enhancement order of kidney and tumors after contrast agent injection: renal arteries and segmental arteries \rightarrow pseudocapsule \rightarrow mass and renal cortex \rightarrow renal medulla; elimination order of contrast medium: renal arteries and segmental arteries \rightarrow mass inside (only RCC with abundant blood supply) \rightarrow renal cortex \rightarrow renal medulla \rightarrow pseudocapsule. The above orders indicated that the pseudocapsule had longer and obvious enhancement. Of 103 patients with RCC, 83 patients with pseudocapsule were confirmed by pathological evidences (83/103, 80.5%, Figure 3). The pseudocapsule structure of another 20 patients was not identified because their tumors were larger than 4.0 cm.

DISCUSSION

CEUS of renal tumors is seldom reported because of the specific blood supply in kidneys. The blood supply in kidneys is abundant, but without communicating branches between the intrarenal arteries. Renal tumors are different from hepatic tumors, as hepatic tumors are supplied by hepatic artery and portal vein. No definite vein phase is available in kidneys during the classification of phases. If renal visualization is divided at the times when renal contrast agent flows in and out of renal cortex, cortex phase and tardive phases is defined. When renal visualization is divided this way, the times when contrast

Table 1. Visualization rates of pseudocapsule in 103 patients with RCC by conventional ultrasound and CEUS.

Conventional ultrasound	CEUS		Sum (%)
	Positive	Negative	
Positive	17	10	27
Negative	61	15	76
Sum(%)	78	25	103

McNemar test, $p < 0.01$.

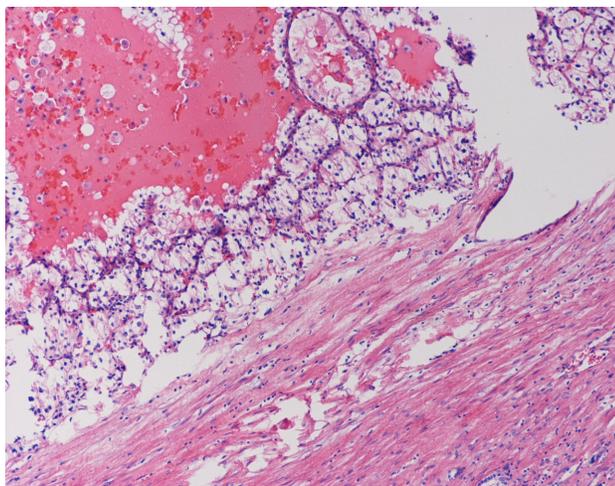


Figure 3. Plenty of reddish fibrous tissues at the right inferior corner of RCC, that is, pseudocapsule (HE staining, $\times 100$).

agent enter and exit renal tumor and cortex, can be observed conveniently. Moreover, the characteristics of blood supply in kidneys can fit better when renal cortex is selected as the reference (Yang et al., 2007; Fu et al., 2007).

This study compared the enhanced intensity, enhanced time and clearance time among renal cortex, tumor and pseudocapsule around the tumor. High enhancement was defined when the tumor and pseudocapsule intensity were higher than the renal cortex or equivalent to renal cortex, while low enhancement was defined when the tumor and pseudocapsule intensity were lower than the renal cortex. Fast-in was defined when tumor enhancement occurred earlier than renal cortex or synchronous with renal cortex, while slow-in was defined when tumor enhancement occurred later than kidney cortex. Fast-out was defined when intratumoral contrast agent clearance occurred earlier than renal cortex or synchronous with the renal cortex, and slow-out was defined when intratumoral contrast agent clearance occurred later than renal cortex (Jiang et al., 2010).

For RCC, renal clear cell carcinoma is the most commonly found in clinical practice, followed by multilocular cystic RCC, papillary RCC and chromophobe

RCC. Most of them are tumors with abundant blood supply and pseudocapsules. However, there are also a group of RCCs with insufficient blood supply. It is noticeable that most RCCs have shown a rim of enhancement surrounding the mass in a ring shape. It is identified in pathological results that the pseudocapsule is composed of plenty of fibrous tissues and peripheral normal renal tissues. The pseudocapsule of RCC exhibits an obvious difference compared to renal angiomyolipoma, and is also an important index to diagnose RCC. Yamashita et al. (1996) reported that the presence of pseudocapsule meant the early stage of carcinomas. As observed by CT or MRI, for RCCs not more than 4.0 cm, 66% (19/29) had a pseudocapsule as confirmed by pathological examinations, and the proportion decreased to 28% (7/25) for RCCs more than 4 cm, suggesting that RCCs with pseudocapsules are poorly differentiated (Yamashita et al., 1996). Ascenti et al. (2004) investigated pseudocapsules of RCCs by CEUS, and the results showed: For pseudocapsule visualization of RCCs, the sensitivity was 85.7% (12/14) for CEUS and 21% (3/14) for conventional ultrasound; 53.8% (14/26) pseudocapsules were confirmed by pathological evidences (Ascenti et al., 2004).

In the group of 103 patients with renal cell carcinoma, pseudocapsules (27/103, 26%) were found by conventional ultrasound in 27 cases, among which 25 cases had the tumor size less than 4.0 cm, while tumor size was larger than 4.0 cm in the other 2 cases. Pseudocapsule sign was found in 78 cases (78/103, 75.7%), and no pseudocapsule was detected in 20 cases whose tumor size was larger than 4.0 cm.

Pseudocapsule visualization of RCCs has two clinical applications: (1) When a renal tumor, especially a smaller tumor (< 4.0 cm), has a pseudocapsule, the possibility of qualitative diagnosis of RCC will be increased; (2) If the RCC has a pseudocapsule, two operative methods can be selected: Radical nephrectomy and surgery. The pseudocapsule of RCC is composed of many fibrous tissues and compressed normal renal tissues, with significantly varied thicknesses. If the pseudocapsule is thick, the renal tissues will be compressed significantly to form an apparent halo, and the visualization rate is higher than even the conventional ultrasound can detect the pseudocapsule easily. The pseudocapsule displayed

on CEUS is surrounded in a ring shape, and the obvious and long lasting enhancement can be easily displayed and identified. This is because the fibrous tissues and compressed renal tissues contain abundant capillary networks, and the sulfur hexafluoride (SF₆) microbubble produced by contrast agent will reach quickly and stay for a long term in capillary networks of fibrous tissues and compressed renal tissues. Therefore, CEUS can realize real-time, continuous and long-term observation for pseudocapsules of RCCs, thus improving the capacity to qualitatively diagnose the presence of pseudocapsules.

CEUS can visualize the morphological features, vessel directions, blood supply, pseudocapsule, enhancement and subsidence, and make up the insufficiency of conventional ultrasound. The combination of conventional ultrasound and CEUS can improve the qualitative diagnosis of RCC (Tamai et al., 2005; Sabine et al., 2000; Ascenti et al., 2001; Shen et al., 2007).

In conclusion, CEUS has significantly more powerful capacity to detect or discriminate the presence of RCC pseudocapsules compared to conventional ultrasound, indicating that CEUS has important clinical values for diagnosis of RCC.

REFERENCES

- Ascenti G, Gaeta M, Magno C (2004). Contrast-enhanced second-harmonic sonography in the detection of pseudocapsule in renal cell carcinoma. *Am. J. Roentgenol.*, 182: 1525-1530.
- Ascenti G, Zimbaro G, Mazziotti S (2001). Usefulness of power Doppler and contrast-enhanced ultrasound in the differentiation of hyperechoic renal masses. *Abdom Imaging*, 26: 654-660.
- Di Cristofano C, Minervini A, Tuccio A, Della Rocca C, Minervini R, Carini M (2009). Pathological evaluation of peritumoral pseudocapsule status after nephron sparing surgery and its prognostic implication. *Arch. Ital. Urol. Androl.*, 81: 96-99.
- Fu NH, Yang B, Liu P (2007). Differential diagnosis between renal malignant and benign tumors with contrast-enhanced ultrasound. *Chin. J. Ultrasonography*, 16: 878-879.
- Jiang J, Chen Y, Zhou Y, Zhang H (2010). Clear cell renal cell carcinoma: contrast-enhanced ultrasound features relation to tumor size. *Eur. J. Radiol.* 73: 162-167.
- Sabine H, Robert S, Oliver S (2000). Contrast-enhanced power Doppler harmonic imaging influence on visualization of renal vasculature. *Ultrasound Med. Biol.*, 26: 1109-1115.
- Shen DJ, Yang B, Fu NH (2007). Contrast-enhanced ultrasonography of renal cell carcinomas: compared to contrast-enhanced CT. *Chin. J. Ultrasonography*, 16: 1061-1063.
- Tamai H, Takiguchi Y, Oka M (2005). Contrast-enhanced ultrasonography in the diagnosis of solid renal tumors. *J. Ultrasound Med.*, 24: 1635-1640.
- Yamashita Y, Honda S, Nishiharu T (1996). Detection of pseudocapsule of renal cell carcinoma with MR imaging and CT. *Am. J. Roentgenol.*, 166: 1151-1155.
- Yang B, Fu NH, Shen DJ (2007). Contrast-enhanced ultrasound in the characteristics of renal tumors. *Chin. J. Ultrasonogr.*, 16: 599-601.