CONTRAST ENHANCED ULTRASOUND IN DIFFERENTIAL DIAGNOSIS OF RENAL CYSTIC TUMOURS

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Abstract

The aim of the study was the study of diagnostic capabilities of Contrast enhanced Ultrasound (CEUS) and computed tomography in renal cystic mass.

Materials and methods: CEUS and CT with contrast data in evaluation of vasculature in the cystic walls and septa with Fusion accompanied the CEUS study were compared in 17 patients (8 men and 9 women). US and CT data analysis were reformed by 2 radiologists independently. Benign cyst classified as BOSNIAK I-IIF, malignant as BOSNIAK III-IV.

Results: High informativity of CEUS in evaluation of microvasculature in cystic lesions, which allows adequately classify the character of the cystic lesion under BOSNIAK classification was proved. Some examples of comparison of possibilities of both methods were demonstrated. The consistency of CEUS with CT was higher than US without contrast and CT in evaluation of BOSNIAK category of the cystic lesions.

Safe and informative method of diagnosing cystic lesions with Fusion without iodine containing contrasts was proposed.

Key words: ultrasound, CEUS, real-time CEUS/CT Fusion, discusses

Introduction

21,660 new cases of kidney cancer were diagnosed in Russia in 2017. At present 25–40% of the cases are detected by chance during check-up examinations [1]. Cystic

renal cell carcinoma (CRCC) is believed to account for 10–15% of all tumors of this type [2], with most cases of CRCC possessing symptoms similar to multilocular cyst. BOSNIAK classification is considered a gold standard in treatment planning for such tumors but there are drawbacks associated with evaluating cysts of II and III categories [3]. The main goal of the diagnostic methods is to detect cysts with a potentially high risk of malignancy (Bosniak III and IV cysts) requiring surgical treatment, differentiate such cysts from benign cysts of categories I and II that require surveillance only. Despite significant advances in imaging methods, the differential diagnosis of cystic RCC remains a difficult problem. Cystic form of RCC occurs with increased frequency among all types of kidney cancer prompting an increased interest in the capabilities of one of the most common screening methods – ultrasound examination. This method is known to reliably detect even small cysts in the kidneys, while using Doppler technology helps determine the nature of cysts by identifying presence or absence of the blood flow. However, quite often it is technically impossible to identify weak blood flow in the cyst wall with the use of dopplerography for effective BOSNIAK classification.

Kidney examination using contrast enhanced ultrasound provides great prospects for detecting weak blood flow in tiny vessels not only in the wall of the cystic formation, but also in thin intracystic septations, allowing to obtain a contrast enhancement analogous to CT and MRI contrast enhancement techniques [4]. A distinctive feature of the ultrasound contrast agents is their intravascular circulation which provides contrasting of the smallest blood vessels to the level of precapillaries. The absence of interstitial proliferation effect and subsequent smearing of contrasting at small tissue blood flow level gives this technology certain advantages over CT and MRI kidneys contrasting.

The aim of this work is to evaluate the contrast ultrasound diagnostic capabilities for kidney cystic lesions and compare the results with data from contrast computed tomography.

Materials and Methods

17 patients (8 males and 9 females) were selected for the study. The patients underwent ultrasound and CT kidney scans in which cysts of different BOSNIAK categories were detected. All enrolled were patients of the urology department at the Clinical Hospital from 2012 to 2019.

Initially a CT scan of the kidneys was performed using standard contrasting method. In order to clarify the topography of cystic formations, their nature, and for surgical procedure planning, an ultrasound contrast examination of kidneys was further carried out taking into account the previously obtained CT data.

Ultrasonography devices equipped with convex probes with the main operating frequency of 3.5 MHz and special software for working with echo contrast agents were used for ultrasound examinations of kidneys. During the ultrasound examination, data from CT and contrast ultrasound was synchronized on the ultrasound scanner screen. Using special navigation system that relies on a magnetic field to determine the physical position of the ultrasonic probe, CT images identical to ultrasound scans were selected. We were able to compare data for the CT and ultrasound with the use of contrast agents with the help of Fusion technology, utilised earlier for solid kidney tumor examinations [5]. Previously obtained CT data were transferred to the ultrasound scanner computer and used to synchronise CT and ultrasound images of the kidney examined. In the dual screen mode, a zone of interest was identified - the cyst zone. The examination was performed by contrast ultrasound medical experts. Before echo contrast agent was administered, each patient provided informed consent in accordance with the approved protocol. Echocontrasting of the cyst was then performed under the control of one of the screens. The second screen holding the contrast CT scan cyst image served as a reference object. Following echo contrasting using different phases of kidney contrasting, the vascular pattern was examined, the exact localisation of the cyst, presence of internal cystic septations, intracystic growths, vascularity of the cystic walls and septations were determined, and regions of necrosis were identified. During the examination video clips at various

time intervals of kidney contrasting were recorded for retrospective analysis and comparison with CT data in all phases of contrasting [Fig. 1].

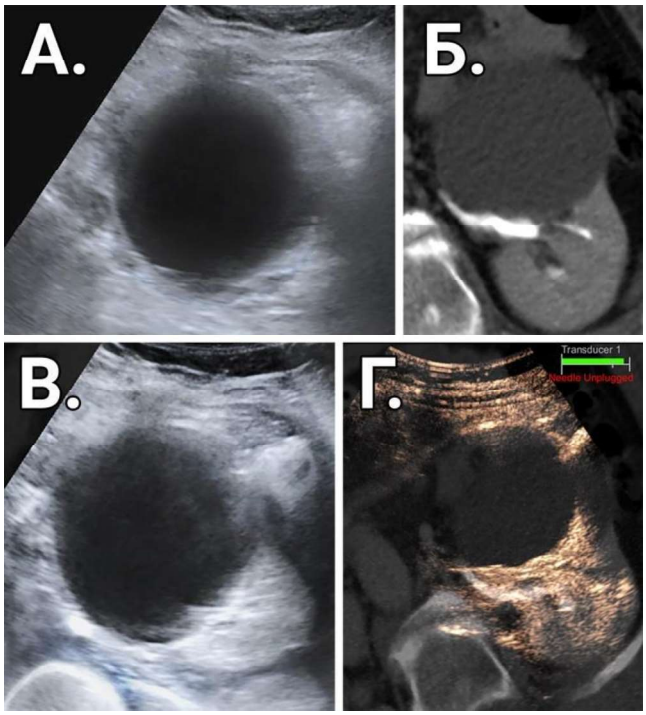

Figure 1

Figure 1. Targeted CT and ultrasound scans of simple kidney cyst (BOSNIAK I). A - Ultrasound image of a cyst in B-mode. B - Computed tomography with contrast. The absence of intracystic septations. C - Synchronisation of images of ultrasound and CT using Fusion technology. D - Synchronized images after echo contrasting. Absence of intracystic septationsons.

Repeated administration of additional dose of echo contrast agent was performed were necessary.

It is important to note that during ultrasound contrast examination rapid microbubble destruction was prevented by using low mechanical index values(MI <0.1). After intravenous administration of 2–4 ml of echo contrast agent (SonoVue) satisfactory contrast enhancement is expected to last for 2–5 minutes, with the concentration of the contrast agent gradually decreasing and almost disappearing within 5–9 minutes. All cysts are normally clearly visible against the background of a contrasting renal parenchyma.

Echogram and CT tomogram analysis was carried out by two independent radiation diagnostics experts with experience of contrast enhanced ultrasound and CT. Benign cysts were classified as BOSNIAK I-IIF, malignant - BOSNIAK III-IV. A higher BOSNIAK category indicated by one of the experts was taken as true result.

Renal malignancies were suspected in 6 patients (according to ultrasound and MDCT), pyelonephritis in 2, simple renal cyst in 9 according to MDCT and in 10 according to ultrasound, and suspicious kidney lesions in the rest of the patients.

11 patients were operated, 4 patients with benign cystic formations were under supervision from 2 to 5 years during which time the BOSNIAK category was not upgraded.

For the statistical analysis inter-expert agreement, Cohen kappa coefficient and informativity of the echo contrast ultrasound were calculated.

Results

In the group of 17 patients with cystic kidney lesions several types of echo contrast were identified. Since the ultrasound BOSNIAK (I-IV) cyst classification corresponded to that of X-ray, comparing CT and ultrasound data allowed differential diagnostics of benign and malignant renal cysts based on the identified echo contrast types. Presence of early contrasting of the formation or individual structures in the formation was an important diagnostic indicator for malignancy. Adverse reactions to the administration of echo contrast drug were not observed in any of the patients examined.

Of the 17 renal cystic formations, 4 (23%) were upgraded in BOSNIAK category after echo contrast. From 4 cases of BOSNIAK category II cysts, 3 cases were upgraded to category IIF after contrast ultrasound, and 1 to category III. In 1 case the IIF category was upgraded to BOSNIAK III following contrast ultrasound.

Pathomorphology revealed clear cell carcinoma (5), papillary carcinoma (2), renal medullary carcinoma (1) and cases of chronic inflammation.

Table 1

Patient cystic formations characteristics per Bosniak classification type.

BOSNIAK Category	Non-contrast Ultrasound	Contrast Ecography	Contrast CT	Surgery/observation > 2yrs, but < 5 yrs.	Pathomorphology (cancer)
B I	2	2	2	1/1	0
B II	8	4	6	1/3	0
B IIF	1	3	3	3	0
B III	2	4	2	4	4
B IV	4	4	4	4	4
Total	17	17	17	11/4	8

In 8 cases with cystic form of kidney cancer (BOSNIAK III and IV), heightened contrasting of the cystic wall and internal cystic septations were observed, allowing to upgrade the cystic formation BOSNIAK category from II to III in 2 cases and refer patients for surgery. Based on the identified criteria cystic kidney cancer (Bosniak III-IV) was correctly diagnosed in 2 cases and later confirmed during surgery.

In 15 cases the results of CT and echo contrast ultrasound were in full agreement with regard to the BOSNIAK category. In 2 cases there were disparities with the CT data. The echo contrast ultrasound data in these cases of BOSNIAK II and IIF cystic formations were more informative. Contrast enhanced ultrasound in the early arterial phase revealed vessels in septations, which made it possible to upgrade the category to BOSNIAK III and identify cancer.

Contrast echography with FUSION technology made it possible to diagnose cancer in 2 cases in addition to CT contrast data. CT and contrast ultrasound data consistency is higher than non-contrast ultrasound in clarifying the cystic kidney formation BOSNIAK category.

Discussion

Renal cysts are much more common in adult patients amounting to 50% in persons 50 years and older [6]. While simple single or even multiple cysts without the presence of internal cystic septations and solid intracystic lesion do not necessarily present diagnostic problems, complex cysts do. The surgeon would often require to have clear information regarding the nature of a complex cyst in order to determine the type of treatment or to consider monitoring tactics. The Bosniak classification, that has greatly facilitated treatment planning, unfortunately does not provide clear differential criteria between cysts categories II and III. According to this classification, developed in 1986 [3], all cystic formations of the kidneys could be divided into categories based on CT data. As per Bosniak, category I and II have a probable benign nature, category III is potentially malignant and IV is mostly malignant.

Category IIF (B II F) was introduced into the classification for those cysts that are difficult to classify as category II or III and are subject to monitoring. Since 1993, when this category was added by M.A. Bosniak, only a small number of papers were published on this category of cysts, with only three articles where the number of patients with B IIF cysts exceeded 10 cases [7–13].

Organ-preserving surgery could be advised in most cases of such tumors. The probability of malignancy of category II cysts - 24.2% reflects the situation more appropriately. But according to the Bosniak classification, these are not subject to surgical treatment [14]. Modern visualization methods provide urologists with the opportunity to choose from a wider range of tactics. In this regard, new ultrasound techniques that allow differential diagnosis between benign and malignant cystic formations can be considered as a method of choice. Microbubble suspensions are used as contrast agent in echo contrasting of the kidneys that are administered intravenously as special gas-forming substance and do not cause any negative effects in patients. The size of these microbubbles does not exceed the size of an erythrocyte and they are completely harmless to the patient due to the lack of nephrotoxicity, that is present in iodine containing agents. Also, in contrast to CT, ultrasound examination

does not cause patient irradiation. As a result, contrast enhanced ultrasound is considered rival to contrast CT in kidney examination by many researchers. And the ability to synchronize CT and ultrasound data allows, in some cases, to replace the nephrotoxic drug with one that is almost harmless.

In this paper we attempted to determine the diagnostic capabilities of echo contrast in the diagnosis of various categories of kidney cysts using our own clinical material. Analysis of the results showed a high prognostic value of echo contrast for differentiation of kidney cystic formations using BOSNIAK, high consistency between CT and contrast ultrasound data in categorisation of cysts and certain advantages of contrast ultrasound in characterising cysts of II and IIF category. This is explained by better visualization of the microcirculation in the early arterial phase of contrasting due to the intravascular circulation of the ultrasound contrast agent [Fig.2].

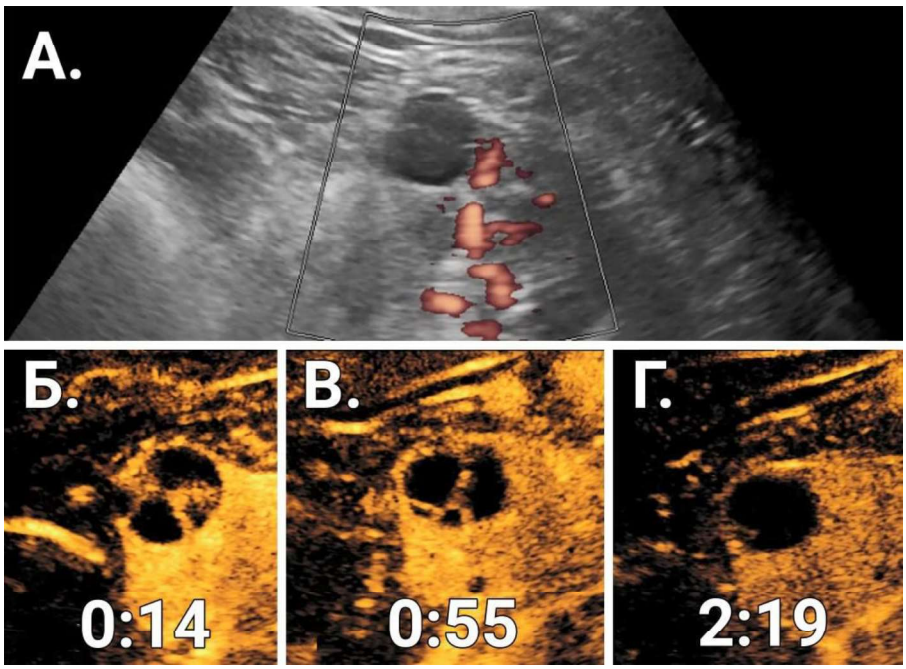

Figure 2. Echo contrast examination of the left kidney. A - Doppler ultrasound shows the absence of internal cystic septations. B - early arterial phase of echo contrast. The presence of internal cystic septations and papillary component in the cyst. B - parenchymal phase of echo contrast. Only internal cystic septations visualised. G -

late parenchymal phase echo contrast. The lack of visualisation of internal cystic septations and papillary component.

With the presence of microcirculation in the cyst wall confirmed, the presence of thickened intracystic septations suggests the tumorous nature of the cystic formation, being consistent with findings of similar papers [8,15-19]. As a result, there is an upgrade in the category of cystic formation to Bosniak III and the formation, previously classified with CT or MRI as not requiring a surgical procedure, becomes a formation requiring surgical intervention according to contrast enhanced ultrasound data [Fig.3].

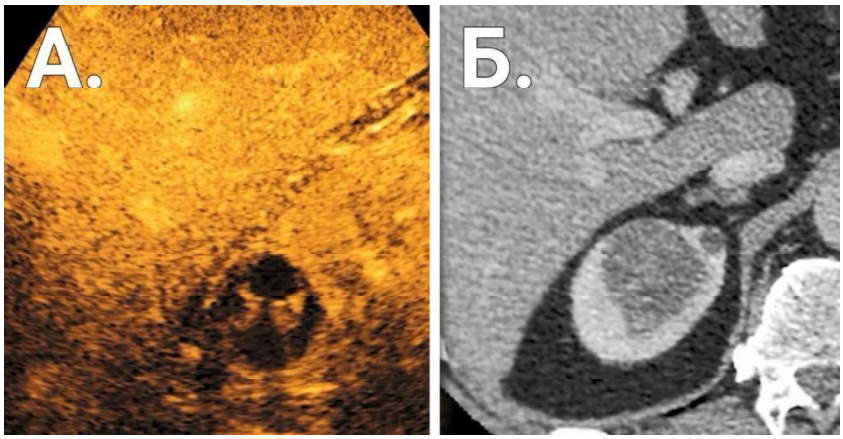

Figure 3. Large cyst in the upper pole of the right kidney with computed tomography with contrast and echo contrast ultrasound. A -during echo contrasting, the internal cystic septations are well differentiated. B - with computed tomography there is no visualization of internal cystic septations.

Numerous publications have shown similar results for the upgraded category of cystic formations following contrast ultrasound [16-20].

Conclusion

The informativity of contrast kidney echography is not inferior to contrast CT and, in some cases, for example with complex cystic formations, surpasses that of contrast CT. Echo contrasting in renal cysts needs to be included in the diagnostic algorithm of patient examinations at the first stage of instrumental diagnostics. The advantages

of the method such as absence of radiation exposure, absence of nephrotoxicity in the echo contrast agent, as well as its high informativity allow it to be considered a method of choice.

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No conflict of interest stated.