Role of contrast enhanced ultrasound in the study of complex renal cystic lesions and tumors.

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Authors: I. López-Vidaur¹, F. Cordido², L. I. Armendariz Blanco², I. Rozas Gómez², E. agrela², T. M. Garcia², J. Carrero Álvaro³, ¹Madrid/ES, ²Alcorcón/ES, ³Segovia/ES
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Learning objectives

- To review complex renal cysts according to the Bosniak classification using Contrast enhanced ultrasound (CEUS).

- To show the normal sonographic findings of these entities and their correlation with other imaging techniques.

- To show the advantages of CEUS as the technique of choice in the initial study of patients presenting with complex cystic renal lesions incidentally.
Background

Introduction

A considerable percentage of renal cell carcinomas appear as complex cystic lesions in the imaging techniques.

Ultrasound (US) is the method of choice for initial evaluation of the kidney.

Although precisely differentiating mixed renal cysts and solid tumors is sometimes difficult using only conventional US or Doppler, so it has traditionally done with computed tomography (CT) and magnetic resonance (MR) with contrast. But nowadays CEUS revealed promising perspectives in the diagnosis of these renal lesions.

Technique

We perform our studies using ultrasound Toshiba Aplio 500 with a volumetric abdominal convex transducer (6.0 MHz). After intravenous bolus injection of 2.4 ml of contrast agent, images are acquired with the specific software and photos and videos were made during a period of approximately 3-5 minutes.

The monitor is divided into two screens, left image contrast and right the same image in grayscale.

The ultrasound agent we use is SonoVue (Bracco, the most used in Europe) composed of sulfur hexafluoride and stabilized with phospholipid.

Pharmacokinetic properties of the contrast agent

The ultrasound contrast agents are composed of gas microbubbles stabilized by different substances (sugars or surfactants).
Findings and procedure details

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Each bubble has a mean diameter of about 2.5 µm. The interface between the sulfur hexafluoride bubble and the aqueous medium acts as a reflector of the ultrasonic wave, improving, thus the blood echogenicity and increasing the contrast between the blood and the surrounding tissues.

Sulfur hexafluoride is an inert gas, poorly soluble in aqueous solutions and innocuous. Is dissolved in the blood and is exhaled through the lungs subsequently, therefore there is no renal excretion.

The main contraindications are acute myocardial infarction (<7 days), class III / IV heart failure, right-to-left shunts, severe pulmonary hypertension, pregnancy and lactation.

Physiology of ultrasound contrast in the kidney

The kidneys have a blood supply in a single step, allowing a quick contrast enhancement and the evaluation after the administration thereof.
Enhances normal kidney follows:

a) Early arterial phase: The renal arteries are demonstrated good.

b) Late arterial phase or cortical phase: Intense and uniform enhancement of the renal cortex.

C) Medullary phase: The pyramids enhance gradually until they become isoechogenic with the parenchyma.

**Bosniak classification of complex renal cystic lesions**

The complex renal cysts represent 10% of renal cell carcinomas, hence its diagnostic significance. Its malignancy vary depending on the number and thickness of the septa and the presence of mural nodules or peripheral calcifications.

It is not rare that a homogeneous cystic/watery lesion in the TAC have after a solid complex internal structure when evaluating it with ultrasound (Fig. 2 on page 10).

The complex renal cysts are divided based on the Bosniak classification initially used for the TAC, but that is ample evidence that can be extrapolated to CEUS.

**BOSNIAK I**

Simple renal cysts with a thin wall without septa, calcifications, or solid components. They have an attenuation as water on CT, an anechoic content on ultrasound and do not enhance after contrast administration. No follow-up required.

**BOSNIAK II**

Benign renal cysts which may contain a few thin septa (<1mm thick) or thin or linear calcifications on its walls or septa.

- Minimal enhancement (perceived but not measurable) on CT septa or cyst wall, because these structures contain fine capillaries.
- In CEUS can be visualized few microbubbles passing through the septa.

- No follow-up required, although the clinical context helps us to determine whether you should or not.

Hyperdense renal cysts (> 20UH) with all the features of cysts of category I (except for the homogeneous signal hyperdense on CT without contrast) less than 3 cm in diameter and at least a quarter of its wall extending beyond the kidney.

- Most contain blood, degradation products, proteins or colloids, which can be anechoic / hypoechoic.

- The anechogenic cysts would be classified as Bosniak I by ultrasound.

- No follow-up required (Fig. 3 on page 11)

BOSNIAK IIF

Renal cysts which may contain multiple thin septa or have a minimum wall thickening or septa with +/- thick nodular calcifications.

Hyperdense completely intrarenal renal cysts that do not enhance with contrast or are # 3cm in size.

- Minimal enhancement (perceived but not measurable) on CT septa or cyst wall.

- In CEUS can be visualized few microbubbles passing through the septa.

- F = "follow-up" # The risk of malignancy is approx. 5%. Follow-up until observe stability over time.
  
  - 1-2 years of follow if more resembles a Bosniak II.
  - 3-5 years of follow if more resembles a Bosniak III. (Fig. 3 on page 11)

BOSNIAK III
Renal cysts with thickened irregular walls or walls / thin septa which clearly capture contrast (CT attenuation change> 10 HU).

- Malignancy range: 25-100%. The decision to close monitoring or surgery should be individualized in each case.

-This category includes hemorrhagic cysts, renal cell carcinoma, multilocular cystic nephromas, unilateral / focal cystic diseases, and renal abscess (Fig. 4 on page 12, Fig. 6 on page 14, Fig. 7 on page 15).

**BOSNIAK IV**

Clearly malignant cystic masses that have similar characteristics Bosniak III but also contain separate solid components of its walls, or septa that capture contrast (Fig. 4 on page 12, Fig. 5 on page 13, Fig. 8 on page 16)

Must be taken into mind that even with fine cuts the average volume of CT can mask the enhancement of fine septa.

The evaluation with CEUS provides real time step of the microbubbles through the septa, resulting in an enhancement thereof, while sometimes in the CT the same lesions have a negative or indeterminate enhancement of their septa.

And the degree of contrast enhancement of the wall and mural nodules is a key factor to determine the clinical, surgical or conservative course.

**Renal tumors and indeterminate solid masses**

CEUS is not valid for evaluating large solid masses because it does not provides more information than conventional ultrasound, CT and the MRI regarding the evaluation or staging.

Small tumors visualized with conventional ultrasound are best assessed after administration of contrast. Many renal masses are too small to be adequately characterized with MRI or CT.
• In particular hypoechoic masses, most require a preoperative CT study to see if there is involvement of the renal vein, the status of the contralateral kidney and staging.

• The, particularly small, hyperechoic mass (fat) have to be assessed principally to differentiate them between clear cell carcinoma or angiomyolipoma. Cystic hemorrhagic or inflammatory hyperechoic mass can also be differentiated from renal tumors based on the absence of contrast enhancement, while a cystic renal cell carcinoma can be diagnosed by evidence of vascularization within the irregular walls, septa and mural nodules itself (Fig. 9 on page 17).

Furthermore it has been shown that ultrasound contrast is useful for demonstrating the characteristic pseudocapsule of clear cell carcinoma.

The presence of pseudocapsule is a major criterion for partial nephrectomy.

With CEUS tumor usually enhances more than the adjacent parenchyma, reaching a maximum enhancement in the arterial phase (Fig. 9 on page 17).

Has also been described a slight uptake in the late phase (Fig. 10 on page 18 Fig. 11 on page 19 Fig. 10 on page 18

CEUS also increases the sensitivity for detecting acute or focal pyelonephritis. Typically in conventional mode ultrasound and Doppler mode shows a hypoechoic and hypoperfusion area with a morphology inverted triangle at the level of cortical. (Fig. 12 on page 20)

It is also proven diagnostic use in renal infarcts, radiofrequency ablation, characterization of pseudotumors and perirenal tumors.

**Advantages and disadvantages of ultrasound contrast compared to the CT in the study of complex cystic lesions and tumor kidney**

**Advantages**

- Principally that it is possible to obtain real-time information on the microcirculation of the septa and solid poles.
- Are described less hypersensitivity reactions.

- As it excretion is not renal, is not nephrotoxic and can be used in patients with renal failure.

- It can also be supplied in patients allergic to iodine.

- Does not emits ionizing radiation.

- It is better for the assessment of small tumors.

- Better assessment of solid components in cystic tumors.

- Good differentiating between angiomyolipoma and renal cell carcinoma.

- It is the "Gold Standard" technique in the study of complex renal cystic lesions.

- It has few contraindications and adverse effects.

**Disadvantages**

- Morbid obesity as limitation of the technique.

- Does not possibility to study simultaneously both kidneys. Need double dose of contrast.

- It is not useful for the study of the urinary tract.

- Not useful for staging.

- It is not accepted intravenous use in pediatric patients (mainly because there are no published studies).

- The few contraindications.
Fig. 1: SonoVue. Injection preparation.

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Fig. 2: Axial and coronal CT images after administration of intravenous contrast in venous phase. Cystic, cortical lesion with peripheral calcifications in the interpolar region of the left kidney displayed in the CT, presents a complex solid structure on CEUS (pictured above right), which enhances in the early and late arterial phase (images below). The lesion was classified as a Bosniak III and proved to be a papillary renal carcinoma according to histology.

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**Fig. 3:** Bosniak classification examples.

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Fig. 4: Bosniak III Same as displayed in Figure 2. It turned out to be a papillary carcinoma. Bosniak IV- Cystic, multiseptate lesion located in the interpolar cortical region of the kidney. Studied by CEUS (image below left), CT (coronal section with intravenous contrast portal phase, image below right) and MRI. It proved to be a renal cell carcinoma (Fuhrman grade 1) in the piece of tumorectomy.

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Fig. 5: Same lesion as figure 4. Axial and coronal T2 MRI sequences (left) and fat-suppressed T1 gadolinium (right), showing a significant enhancement of the septa thickened as it was with CEUS and with the CT. The lesion was already classified as Bosniak IV, recommending lumpectomy in the initial examination with CEUS. It proved to be a renal cell carcinoma (Fuhrman grade I).

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Fig. 6: Bosniak III lesion in a Horseshoe kidney.

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Fig. 7: Same lesion as in figure 6, correlation with CT.

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Fig. 8: CT (picture left above, axial cut with intravenous contrast venous phase): Shows an exophytic cystic lesion in the right kidney cortex. Strikingly had grown compared to previous CT of 5 years before, so I was requested a CEUS to complete the study. CEUS (image left above): several thick septa were targeted in its interior, which enhanced avidly following administration of contrast, however no Doppler flow was demonstrated, so it was suggested that it was a tumor lesion not aggressive with cystic degeneration. Macroscopic piece (pictured right below) was Eventually a multilocular cystic nephroma.

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**Fig. 9:** Conventional ultrasound (images above): Initially the lesion was classified as a cyst in the right kidney cortex, with thickened septa, showing Doppler blood flow in some of them. CEUS (images below): Lump, solid cystic, having thick septa and solid thickening of the posterior wall. The solid component of this lesion shows intense uptake of ultrasound contrast. In arterial phase, you can see further enhancing than the healthy renal adjacent parenchyma, remains hyperintense equal to the renal parenchyma in venous phase and in late phase uptake loses like the adjacent renal parenchyma is appreciated. Piece of partial nephrectomy renal clear cell carcinoma with hemorrhagic cystic cavities

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Fig. 10: Conventional and CEUS: The nodule in the posterior cortex of the upper pole of the left kidney is well defined, has an ovoid morphology, is hypoechoic with a slightly more echogenic central zone (picture left above). In the study with ultrasound contrast (picture right) demonstrates its solid nature, since there is a tenuous captation of the node lower in all phases as the normal adjacent renal parenchyma uptake. CT (axial, with IVC arterial phase): the left node described in previous scans and other nodule in the right kidney in interpolate region, both isodense with the renal parenchyma showed in the baseline study and enhancement are observed in the upper pole of the kidney after administration of CIV.

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Fig. 11: RM of lesions described in Figure 10. In the study the presence of two solid focal lesions located one on each kidney is confirmed. Both lesions show a similar behavior in different sequences. They are relatively isointense with the renal parenchyma on T1-hypointense on T2. Do not have decreased signal in the sequence obtained out of phase with respect to that performed in phase, have a slightly restricted diffusion and during the dynamic study presented faint enhancement after contrast that begins in arterial phase to remain hypointense relative to the renal parenchyma in the later stages. It proved to be a bilateral papillary carcinoma in the pathology study.

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**Fig. 12:** Conventional and dynamic contrast curves quantification, where a clear zone of hypoperfusion is seen in the upper pole of the kidney ultrasound.

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Conclusion

Ultrasound contrast allows to predict the risk of malignancy of renal cystic lesions and classify them according to their degree of complexity.

The advantages over other diagnostic modalities and its accessibility, stand it as the technique of choice in the evaluation of these lesions incidentally visualized.
References


