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Contrast enhanced ultrasound role in renal tumors

Abstract

Conventional ultrasound scanning has a limited ability to accurately outline renal pathology and cannot be accurately differentiating between malignant and benign lesions. Contrast-enhanced ultrasound has many values: being safe, does not require the utilization of ionizing radiation, and is quick and costly reasonable. Moreover, it is our experience that contrast-enhanced ultrasound is an easy and simple procedure to master for the experienced ultrasound practitioner. In this article, we discuss the technique, indications and value of contrast-enhanced ultrasound in renal tumor imaging.

Keywords: contrast-enhanced, renal, tumor, ultrasound

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Introduction

US was the primary imaging modality used in the renal diseases evaluation. Although, there was a greater improvement in Doppler imaging and B-mode, there was some limitations regarding US in assessing renal parenchyma tissue caused by absence of contrast difference between lesions and the renal tissue either in cortex and medulla. On the other hands, US also has limitations in the assessment of the renal microvascular circulation, focal masses, and complex cysts. Contrast-enhanced US (CEUS) is widely used in the detection of liver lesions, while its application in the renal tract, however, still to increased and expanded over the last years.[1]

Ultrasound contrast medium has potential advantages superior to CT and MRI contrast agents, as CEUS agents remain intravascular without diffusing into the interstitial space, allow better visualization of microvasculature, more resolution of ultrasound than of CT or MRI, without known risk of nephrotoxicity in patients with renal dysfunction.[2]

Contrast agents structure

Contrast medium is a substance used to increase the contrast of structures or organ tissue within the body in medical imaging.[3] Microbubbles are used as contrast agents for ultrasound examination. These microbubbles are composed of agitated saline solution, mostly larger to be filtrated through the lung capillaries. The drop-in density on the interface between the gas in the bubble and the surrounding liquid leads to scatters and reflects the ultrasound waves back to the probe giving the liquid with these bubbles a high signal, allow them to be seen in the resulting image.[4] The lifetime of air bubbles is short. Metabolism mediated by uptake of these microbubbles by Kupffer in the liver and by macrophages in reticuloendothelial system. Makes CEUS a suitable in patients with renal impairment, without the need for renal function test before contrast agent application. [5] Their metabolism depends on its shell composition, microbubble size, and surface characters and cannot be predicted.[6]

Indications for renal CEUS

The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)[7] have explored the guidelines concerned on indications of US contrast agents for the kidneys imaging at 2011.[8]

Differentiation between benign and malignant renal tumors

The contrast agent microspheres utilized in CEUS allowed in-time imaging of renal masses with improved outlines of renal vessels, vascularity of solid tumor, and detection of either septa or wall vascularity of complex renal masses.[9] CEUS cannot considered a reliable tool to differentiated between malignant and benign mass based on their enhancement characteristics as not all solid lesions with enchasing characters are malignant, and based on this fact, it was not recommended in the EFSUMB guidelines.[7] The differentiation between renal cell carcinoma (RCC) and other benign mass is difficult. Angiomyolipomas for example, usually show a hyper echogenic signal due to the higher content of fat can, however, in some cases it may be low in fat, making the differentiation very difficult. Also, the tumor diagnostics for RCC are difficult as there are mixed forms (for example; hypovascular malignant renal lesions as papillary RCCs and lipid-poor AMLs). This difficulty is mainly caused by “overlapping features”.[10] In this situation, the application of perfusion analysis was proper tool for differentiating between benign and malignant masses clearly. [11] If AMLs was suspected, MRI or non-contrast CT was essential to confirm the diagnosis based on detection of macroscopic fat.[12] The classic patterns of malignant lesions contrast enhancement were including either exaggerated enhancement or early washout in complex cysts, more delayed enhancement and nodularity appearance of enhancing appearance. And the diagnostic features of RCC including an enhancing pseudo-capsule which resulted from ischemic compressed and necrotic renal tissue encircling the lesion.[13]

Differentiation between RCCs and another renal neoplastic lesion

Neoplastic lesions can be divided into primary originated from the renal parenchyma or the renal pelvis, and secondary as metastases of another site adjacent or near to the renal parenchyma as adrenal gland lesions, urothelial cell carcinoma, transitional cell carcinoma, and retroperitoneal tumor, lymphoma, plasmocytoma and leukemia.[14] The characteristic morphological features of RCC were including intratumoral necrosis, hemorrhagic spots, and intratumoral calcifications. In B mode of ultrasound, the small size tumors are usually has hyperechoic appearance due to rich blood flow in their thin-walled blood vessels which is similar to angiomyolipoma.[15] On CEUS, RCC showed the following vascular appearance: early hyperenhancement than normal parenchyma, delayed phase, perilesional enhancement, wash-out on, rim-like structure from its pseudocapsule and a heterogeneous enhancement which corresponding to large size lesion.[16] Imaging features of either lymphoma or other renal metastases were including lack of spherical appearance, bi-laterality, multiplicity, infiltrative growth and lack of encapsulated appearance or area of calcifications.[17] There are a few published studies concerned with CEUS characteristics of renal lymphoma metastasis. However throughout renal perfusion, Gulatiet al., observed a case with a renal allograft in which lymphoma was appeared more hypovascular.[16] Ignee et al.[16] showed that, metastases in CEUS are usually hypovascular in more than 80% of patients. [18] As RCCs may be has an identical pattern, CEUS cannot be done to differentiate RCCs and different renal malignancy.[16,18,19]

Characterization of indeterminate renal lesions

Usually CT or MRI are diagnostic modalities of choice in characterization of indeterminate renal masses, but sometimes they can be inconclusive. In those case and in patients with contradiction for the use of iodine contrast agents, CEUS play as a perfect alternative to evaluate those renal masses. Also, can replace contrast enhanced CT (CECT) or contrast enhanced MRI (CEMRI) if the patient with limited renal function, hypersensitivity these agent, or fear of radiation exposure.[20] CEUS was a helpful tool for the diagnosis of indeterminate renal mass based on its ability to detect slow and low flow within renal lesions which was a characteristic appearance of solid mass. In addition to any particular enhancement pattern, the key characterization of renal lesions was depends generally show enhancement characteristics of malignant lesion which different than that of renal cortex in at least one phase.[12] Based on this, the diagnosis of pseudotumor can be finally and accurately made if enhancement characteristics was similarly matched to that of the cortex in all phases.[2] Although CEUS was an accurate diagnostic technique in either indeterminate or complex cystic renal lesions, the majority of hospitals still in need to develop an organized approach for its use. It has been suggested that, in all complex cystic lesions, patients should be at first examined using CEUS.[20] Although this may be applicable within some hospitals, other hospitals cant applied this protocol due to a limited number of trained practitioners with a short available time to perform these studies in every case.[21]

Differentiate between malignant tumors and pseudotumor

Pseudo-tumors are congenital masses as columns of Bertin, dromedary hump and fetal lobation with no characteristic pathological changes. US can easily diagnose this condition based on its similar echogenicity to the normal renal parenchyma with smooth renal contour without posterior enhancement. Moreover, by Doppler US, arterial and venous flow can be detected in septa of Bertin which identical to that in normal renal parenchyma. Also, normal cortical tissue between renal medullary pyramids can be easy confirmed by CEUS.[22]

Monitoring of intervention in renal tumor

Locally acting treatment modalities (i.e, microwave ablation (MWA). radiofrequency ablation (RFA) and cryoablation) was minimally invasive that allow quick recovery. RFA was preferred methods in the treatment of small renal tumors when the lesion can't be surgically resected. Traditionally, the CT was used to guide to placed RFA probes as CT provides perfect visibility of the probe, but it need experience for proper image capture and probe placement because it does not allow a real in-time image.[23] Wink et al.[23] developed a CEUS score system for monitoring different therapeutic interventions in which 0 score equal to no enhancement, one mean a rim enhancement, two for diffuse enhancement, three for localized enhancement, and four mean no defect in enhancement.[24] Percutaneous ablation was used effectively for the management of patients with kidney tumors. The advantages of CEUS including its ability to show the ablation zone in real-time, and to visualize the surrounding the renal vessels and the renal parenchyma that may more important than detecting local tumor progression. The optimal time of CEUS to evaluate the therapeutic effects of thermal ablation is another important factor to improve its diagnostic ability. The accurate detection of the residual tumor in proper time is a necessary step for planning the ideal treatment to improve the tumor-free survival rate. Some researchers reported an one week to one month interval after the ablation were an ideal time.[8]

Establishing the nature of pyelocaliceal masses, renal infections (pyelonephritis or renal abscess) and Pseudotumor

10-15% of all urinary tract tumors are primary tumors of the renal pelvis and ureter.[25] CEUS diagnostic value in cases with uncomplicated pyelonephritis are still matter of debate, with no clear indications. By CEUS, focal pyelonephritis appears as areas of reduced enhancement secondary to edema after contrast injection. If a localized abscess was formed, it was appeared as a non-enhancing area with peripheral uptake. In the pelvicalyceal system, echogenic pus can be differentiated from neoplastic tissues by CEUS as they show no uptake.[26]

Optimization of percutaneous renal biopsy

CEUS can be helpful in identifying tissue considered as target that was poorly visualized or not visualized with B-mode of US. With CEUS, the viability of tumor tissue, influenced by the presence of vascularity, can be reliably identified and evaluated and it improved targeting of vascularized regions of the tumor.[27] Any post-biopsy complications such as pseudoaneurysm formation can be detected by CEUS without the need for contrast-enhanced CT and avoid the potential nephrotoxic hazards associated with iodinated contrast agents.[28]

Assessment of inferior vena cava (IVC) and renal vein thrombosis

Renal veins and inferior vena cava thrombus from RCC is generally reported in 21-35% and 4-10% of cases respectively. [29] It is necessary in preoperative imaging to detect the type and the extension of the renal thrombus which influence the choice of surgical technique. The US sensitivity of detecting inferior vena cava thrombosis depends on the site of the thrombus. It has lower sensitivity (68%) for infra-hepatic (level I) and (100%) for intra-hepatic (level II) thrombi.[30] CEUS has an accuracy like CECT in diagnosis of malignant renal

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vein invasion or thrombi as enhancing thrombus is diagnostic features of neoplastic invasion, while bland thrombus has no contrast uptake.[7] In the staging of vein invasion, CEUS had identically similar results to CECT but appear to be superior in the differentiation of bland from the tumoral renal vein involvement.[18]

Safety

While the overall safety of microbubble contrast agents is now more accepted, with a really low rate of hypersensitivity reaction (1 to 7000 patients).[31,32] However, as in all medication, precautions for certain patient groups must be kept in mind. A "black box" warning by Food and Drug Administration (FDA) regarding contraindications contrast agent uses was including acute myocardial infarction, decompensated heart failure, arrhythmias, or patients with high risk for respiratory failure, emphysema, and pulmonary hypertension. In the United States, due to an old warning by FDA at 2007, which was recently modified, these agents were not allowed for clinical uses except in echocardiography.[33] The gaze part (sulfur hexafluoride) of the contrast agent, is an inert, nontoxic gase, with biocompatible membranes and easily removed by respiration. These agents are not excreted by the kidneys or interfered with renal function. So, they can be safely used in the patients with renal impairment or failure, and doesn't require pre-injection assessment of kidney function. This is very useful when CT or MR studies that with contrast injection were contraindicated.

Side effect

CEUS has a very rare side effects raised from the mechanical or chemical interaction of ultrasound with contrast agent microbubbles. Mechanical interaction an associated with bubble expansion and capillary rupture. And chemical interaction leads to transient hyperthermia during bubbles recovering after expansion which associated with free radicals generation. [34]

Limitations

At first, there was no international standard for evaluating renal microvascular perfusion; so, well-designed clinical trials are required to establish the parameters which considered as ideal for clinical evaluation and the normal range in different patient's groups. Second, additional time is necessary for placing an intravenous catheter and for quantitative analysis, third; the cost of agents should also be considered especially in low income countries. Fourth, patients with serious cardiopulmonary disease cannot be candidate to CEUS. Finally, contrast agents used in CEUS are not excreted into the renal collecting apparatus. So, this part cannot be adequately imaged. Despite these limitations, CEUS was still a safe and promising method for evaluation of renal microvascular.[33]

Conclusion

CEUS could be a safe, accurate alternative capable of improving the diagnostic possibility of B mode US. In spite of the limitations, it provides a new diagnostic imaging tool to analyze patients once CT/MRI imaging were either contraindicated or yielding similar finding.

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Conflicts of interest

The author declares there is no conflict of interest.

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