Can contrast-enhanced ultrasonography r substitute CT scan in postoperative renal tumor imaging?

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Abstract

Introduction/Purpose: Among its many applications, contrast-enhanced ultrasonography (CEUS) is used with very good results in oncology imaging to evaluate the effect of several therapeutic interventional radiology techniques. The aim of this study is to evaluate the efficacy of CEUS in postoperative renal tumor imaging.

Material and Method: The study group consisted of 17 consecutive patients (11 males and 6 females, aged between 71 and 87) who underwent palliative embolization or chemoembolization of renal tumors between January 2008 and December 2017. All patients underwent preoperative imaging with CEUS and CT scan and they were followed postoperatively with CEUS and CT scan for up to 24 months after initial intervention. The ultrasound and CT operators were blind to each other’s findings.

Results: CEUS proved to be an effective means of monitoring both arterial embolism and RFA of renal tumors with comparable findings with CT and could be an alternative technique to CT and MRI.

Introduction

Arterial embolization (AE) aims to discontinue blood supply to an organ or to a specific area by introducing an angiography catheter into a blood vessel and the subsequent use of occlusion materials (spiralls, beads, hemostatic sponges, cyanoacrylate adhesives and alcohols). Stopping blood flow leads to acute necrosis of tissues, generating an acute phase reaction and eventually causing tumor shrinkage. Embolization of renal artery was intro-
duced into clinical practice in the 1970s as an invasive sequencing of arteriography that at that time was the basic diagnostic method for the identification of renal tumors. It contributes primarily for the treatment of serious symptoms such as bleeding and pain, however evidence shows that it can also contribute to prolonging survival. Nowadays, renal artery embolization (RAE) is still used for the palliative treatment of unsuitable for surgical treatment bleeding benign and malignant tumors however it has a particular role to play as neoadjuvant treatment of large malignant tumors. Published studies and current experience suggest that AE may not always cause significant shrinkage of some tumors (e.g. large and fatty angiomyolipomas), and can therefore be followed by RFA (Thermo-Failure Radiofrequency). RFA is currently used as an initial therapeutic option in patients who are bad candidates for surgery. Of note, the ischemic effect of AE may increase the safety of subsequent RFA during the needle removal process, limiting the risk for iatrogenic bleeding while RFA is more effective when applied to reabsorbed tissue as blood circulation caused by blood circulation limits the thermal effect of RFA.

CEUS is a relatively new application that extends the potential of traditional ultrasonography. It is based on enhancers containing sulfur hexafluoride gas microbubbles that have a high degree of echogenicity and are heavily reflexive to surrounding tissues due to different physical properties and behavior. The intravenous administration of enhancers causes significant reflection of the ultrasound beam while the simultaneous software restriction of reflections from the rest of the tissues enhances the reflection difference of the ultrasound waves. The combination of the above produces an ultrasound imagewith increased contrast able to dynamically assess the vascularization of the target lesion. Based on the original image, the test may be repeated after the therapeutic intervention in order to evaluate the result. This article focuses on effectiveness of CEUS in postoperative renal tumor imaging.

Material and Method

The study group consisted of 17 consecutive patients (11 men and 6 women aged 71-87 years) who underwent palliative renal tumor embolization between January 2008 and December 2017. Seven patients were presented with heavy macroscopic haematuria, 5 patients with insisted back pain, one with anaemia, while the rest were asymptomatic.

In 9 out of 17 cases the tumor had malignant features. One of those nine cases involved secondary renal metastasis while the remaining were primary kidney carcinomas. In one case, the disease was bilateral and in 4 cases there were more than one tumor in the affected kidney. Six patients had practically untreatable or progressed disease (two IVa, M , one IVa stage, M-, two IVB, M+ and one Ila, M+), while the other 3 patients had a potentially operable disease (localized masses of 2 and 4 cm in one and two respectively), however, were unsuitable for surgical treatment. Of the 8 cases with benign characteristics one was oncocytoma and the remaining 7 large angiomyolipomas (diameter> 5cm).

All patients followed the same procedure: Local anesthesia (xylocaine 1%) was injected on the catheter insertion side, followed by femoral artery catheterization under ultrasound guidance. The vascular catheter was then advanced to the abdominal aorta (Seldinger method), and selective renal artery catheterization was performed via a 5-Fr Cobra I hydrophilic catheter under continuous infusion of contrast agent. Following selective catheterisation of the tumor vessels, embolization with irinotecan loaded microparticles (IAIRIM) (DC-Beads, Biocompatible diameter 300-500 μm, dosing: 50mg / ml) and hydrogel microspheres of 100 -700μm (Embozene, Boston Scientific, MA, USA) was performed. The procedure was completed with a spiral deposition, until complete elimination of tumor outline. In the case of multiple vascularization of the tumor, the same procedure is repeated separately for each vessel. The whole procedure lasted for 30-60 minutes and its effect (lack of blood flow in the embolized area) was confirmed by angiography after reinfusion of the contrast medium. A 24-hour post-embolization CT-scan and contrast medium ultrasound (SonoVue, Bracco) were performed in order to evaluate the early post-embolization results.

In two cases with concomitant cystic structures, directed injection of ethanol (PEI needle ++) was performed. In 8 cases (6 carcinomas and 2 large angiomyolipomas) RFA with a 17-gauge electrode (Jet-Tip, RF Medical Co., Seoul, Korea) was additionally performed. The day after RFA, CT-scan and CEUS are re-performed. Both imaging studies were repeated at 2, 6, 12 and 24 months after initial intervention.

Results

The mean hospital stay for all patients was 5.25 days. In all cases there has been technical success. At the time of analysis, 4 patients died, 9 were alive and the rest...
were lost to follow-up. Three of the patients with macroscopic haematuria were transfused until stabilization of the haemoglobin level before embolization. Recurrence of haematuria was observed in 2 of these patients. In the 5 patients who experienced pain, the symptoms improved to two and subsided to 3. The relapse rate (revascularization or tumor shrinkage failure) was 35.2% (6/17) with an average follow up time of 14.7 months (range 2.5-33). There was no differentiation in the local assessment of postoperative progression of renal tumors compared to CT (see attached picture).

**Discussion**

Imaging studies such as CT, MRI, and ultrasound are necessary not only for the diagnosis of renal masses but also for the determination of the treatment and the monitoring of outcome. Traditional ultrasound is an easily accessible, inexpensive, non-invasive method that provides real-time imaging. However, its diagnostic value may be limited due to the low precision in the imaging characterization of some renal masses, especially those with a small size (<3cm). In fact, about 30% of small kidney tumors appear to be benign renal masses as are largely similar in shape, margins and homogeneity. In addition, the distinction of mass through the development of perfusion with the use of doppler is limited. Given that CEUS has all the advantages of ultrasound plus the ability to detect microvessels has been successfully used in the detection and differential diagnosis of parenchymal lesions. The use of microbubbles proved to be harmless with minimal incidence adverse reactions. In addition to insignificant nephrotoxicity, CEUS is cost effective and comparable to CT and MRI in the evaluation of local disease. Moreover it is suitable for patients with metallic implants that cannot be subjected to MRI. Till now, its use in postoperative imaging of renal tumors has not been adequately evaluated. Although it exhibits comparable results with CT, current experience is small and there are several limitations from studies due to the small number and heterogeneity of the material. However, the following conclusions can be made:

1. Complete absence of CEUS amplification following AE of renal tumor is indicative of complete necrosis (full response) of the tumor.
2. Residual enhancing elements in the post-intervention CEUS are indicative of incomplete treatment and residual viable neoplastic tissue. An exception is the presence of thin peripheral support for a few weeks post-invasive, which is the result of reactive process.
3. CEUS can be performed during RFA or immediately after and so, if a residual enhanced element within the tumor is clearly displayed, an attempt to replace the electrode in the direction of the residual enhanced element should be tried in order to improve the therapeutic effect and increase the chance of complete tumor necrosis.
4. The post- post-intervention CEUS has many of the usual limitations of ultrasonography and so it cannot fully replace CT / MRI. Moreover, CEUS is affected by echogenic artifacts at the site of the lesion, which sometimes make difficult to assess the enhancement of the tumor.

In conclusion, CEUS is an effective means of monitoring both AE and RFA of renal tumors. It could be an alternative technique to CT scanning and MRI, with some advantages: low cost, short non-time-consuming process, no radiation exposure and extremely rare side effects. It should be stressed that knowledge of postoperative CEUS findings in renal tumors and familiarity with the method allows a more accurate assessment of the effect of intervention invasive renal tumor therapy and, if necessary, a targeted repetition to improve response could be tried. Familiarity with the indications, peculiarities and limitations of CEUS also ensures the most efficient use of the method and reduces the frequency of diagnostic errors.
Figure I. Small RCC (2cm): Complete necrosis following RFA

A: Pre interventional CEUS shows hyper echogenic, enhanced lesion (arrow).
B: Pre interventional CT scan.

C: CT scan during RFA.
D: CEUS image 2 months after RFA shows enhancement deficit (*) greater in diameter than the initial lesion and with no residual enhancing elements.
E: CEUS 4 months after RFA shows a minimal reduction of the size of the enhancement deficit (*), without evidence of recurrence. 
F: Corresponding CT scan image.

Figure II. Intracystic lesion in a patient with multicystic renal disease

A: Pre-interventional imaging (Left-side image: US, right side image: CEUS) reveals a nodule strengthened on the wall of one of the cysts (arrow). 
B: Corresponding CT scan (arrow).
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C: Ultrasound-guided FNA (positive for malignancy), and ethanol injection.

D: Control immediately after the intervention demonstrates preservation of nodule enhancement.

E: US & CEUS following a combination of RFA and complementary ethanol injection reveals elimination of nodule amplification.
Figure III. Medium-size renal cell carcinoma (4 cm), before and after combined interventional treatment

A: Pre-interventional CEUS demonstrates an over-exacerbated lesion with small cystic degeneration (arrow).
B, C: DSA before and after the embolization of the lesion (*).

D: Despite the apparent angiographic reduction of lesions' vasculature, CEUS, 20 days after embolization, shows no appreciable reduction of its enhancement.
E: Corresponding CT scan image.

F: Ultrasound-guided RFA on the lesion.
G: In CEUS immediately after RFA there are several artifacts at the site of the damage (*), which make difficult to estimate the amplification level.
H: CEUS 1 day after RFA reveals an amplification deficiency (*) throughout the lesion.
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**Figure IV.** Superficial RCC (4 cm) before and after RFA

A: Pre-interventional CEUS demonstrates a lesion that is ecographically similar to renal parenchyma.
B: Interventional CEUS after 1 cycle (12 h) of RFA demonstrates enough residual tumor (*) at the upper part of the lesion.
C: US-guided RFA, in the same session, targeting to the residual tissue.

D: CEUS 1 day after RFA, shows complete absence of amplification at the site of the lesion (*).
E: CT scan confirms the amplification deficiency at the tumor site.
Figure V. Renal angiomyolipoma before and after embolization

A: Pre-interventional DSA highlights the vascularity of the lesion.
B, C: Elongated and transversal images of pre-interventional CEUS highlighting part of the lesion.

D: DSA immediately after embolization showed elimination of vascularization of the lesion.
E, F: CEUS image 1 day after embolization indicate lack of outline for most of the lesion. In all the images, the dotted red line surrounds the fault position. CEUS images have been taken using the “Hybrid” technique, in which the signals (orange) from the microbubbles are displayed on the gray-scale image.
Figure VI. Ruptured renal angiomyolipoma before and after endoarterial embolization

A: Pre-interventional DSA highlights the vascularity of the lesion and shows active extravasation (arrow).
B, C: Pre-Interventional US and CEUS images indicative of active extravasation (arrow).
D: Triplex focused in the same point highlights arterial-type signals.
E: In DSA immediately after embolization, vascular damage and active extravasation are eliminated.
F: Post-interventional US imaging (Left side image: simple US, right side image: CEUS), which no longer sings of extravasation.
G: Similar findings in the post-invasive Triplex.
Figure VII. Renal oncocytoma in a patient with chronic renal failure. Partial necrosis after RFA

A: Pre-interventional CEUS shows an homogeneous enhancement of the lesion.
B: US-guided RFA electrode placement in the lesion. The procedure was not well tolerated and was interrupted.

C, D: Immediate post-interventional imaging indicates limited necrosis (*) and a small recurrent fluid collection (arrow).
E: Postoperative CT without contrast (frontal reconstruction), also highlights the perineal collection.
Μπορεί η υπερηχογραφία με ενισχυτή ηχογένειας να υποκαταστήσει την αξονική τομογραφία στην μετεπεμβατική απεικόνιση νεφρικών όγκων; ، σ. 23-34

**Περίληψη**

Εισαγωγή/Σκοπός: Μεταξύ των πολλών εφαρμογών της, η υπερηχογραφία με ενισχυτή ηχογένειας (Contrast-enhanced ultrasonography-CEUS) χρησιμοποιείται με πολύ ικανοποιητικά αποτελέσματα στην ογκολογική απεικόνιση, για την αξιολόγηση του αποτελέσματος θεραπευτικών τεχνικών επεμβατικής ακτινολογίας. Σκοπός της έκθεσης είναι η αξιολόγηση της αποτελεσματικότητας του CEUS στην μετεπεμβατική απεικόνιση νεφρικών όγκων σε σύγκριση με την αξονική τομογραφία (CT).

**Υλικό και Μέθοδος:** Η ομάδα μελέτης αποτελείτο από 17 διαδοχικούς ασθενείς (11 άνδρες και 6 γυναίκες, με εύρος ηλικίας 71-87 ετών), οι οποίοι υποβλήθηκαν σε παρηγορητικό εμβολισμό ή θερμοκαυτηρία διά ραδιοσυχνοτήτων νεφρικών όγκων μεταξύ Ιανουαρίου 2008 και Δεκεμβρίου 2017. Όλοι οι ασθενείς υποβλήθηκαν σε προεπεμβατική και μετεπεμβατική απεικόνιση με CEUS και αξονική τομογραφία μέχρι 24 μήνες από την αρχική παρέμβαση. Οι διαγνώστες του υπερήχου δεν γνώριζαν τα πορίσματα εκείνων του αξονικού και το αντίστροφο.

**Αποτελέσματα:** Το CEUS αποδείχθηκε ως αποτελεσματικό μέσο για την παρακολούθηση τόσο του ΑΕ όσο και της RFA των νεφρικών όγκων με συγκρίσιμα ευρήματα με την αξονική τομογραφία και θα μπορούσε να αποτελέσει μια εναλλακτική τεχνική αντί της αξονικής τομογραφίας και της μαγνητικής τομογραφίας.

**References**