Contrast-enhanced ultrasound (CEUS) assessment of superselective uterine fibroid embolization (SUFE): Preliminary experience[☆]

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KEYWORDS

Fibroids;
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Abstract *Purpose:* The use of superselective uterine fibroid embolization (SUFE) requires imaging techniques that can be used to verify the success of the procedure. The purpose of our study was to analyze the potential value of pre- and post-treatment contrast-enhanced ultrasonography (CEUS) for assessing the outcome of SUFE and for posttreatment follow-up.

Materials and methods: We studied twelve women undergoing SUFE for uterine fibroids. In those with multiple fibroids, only the three largest were considered in this study. A total of 21 lesions (size range 3.5–9.0 cm, mean 5.2 cm) were examined. Each myoma was examined immediately before and after SUFE (while the patient was still in the angiography room) with transabdominal CEUS performed after intravenous administration of a single bolus of contrast agent. The follow-up protocol included CEUS evaluation one month after treatment and CEUS plus dynamic magnetic resonance (MR) studies six months after treatment.

Results: In 20/21 cases, postembolization CEUS revealed total fibroid devascularization. The remaining lesion (in a woman with multiple lesions) showed persistent vascularization after SUFE. These findings were all consistent with angiographic data. No recurrences were observed during the six-month follow-up. One patient reported the reappearance of symptoms 18 months after SUFE, and CEUS showed the persistence of intralesional vascularization.

Conclusions: CEUS is effective for assessing the completeness of vascular occlusion following SUFE for uterine fibroids. CEUS findings correlate with clinical results observed one and six months after treatment. Compared with dynamic MR, CEUS is reliable and cost-effective.

Sommario *Obiettivi:* L'introduzione della embolizzazione superselettiva dei miomi uterini (SUFE) in radiologia interventistica ha reso necessario lo studio di metodiche di imaging che consentano di definire correttamente il risultato terapeutico. Lo scopo di questo lavoro è di

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descrivere i reperti ottenuti tramite CEUS prima e dopo SUFE e di stabilire se la CEUS può giocare un ruolo nella valutazione dei risultati e nel follow up di questa procedura.

Materiali e metodi: Abbiamo valutato tramite CEUS 21 miomi in 12 pazienti immediatamente prima e dopo la SUFE direttamente in sala angiografica. A causa della dimensione dei miomi (range 3.7–9.0 cm, media 5.2 cm), tutte le valutazioni sono state effettuate per via trans-addominale. In caso di miomatosi multipla, abbiamo valutato solo i tre miomi più grandi. In tutti i pazienti, è stato iniettato un singolo bolo di mezzo di contrasto. Il protocollo di follow up ha previsto una valutazione CEUS dopo un mese e una valutazione con CEUS e risonanza magnetica (RM) dopo sei mesi.

Risultati: In 20/21 casi, la CEUS ha dimostrato una devascularizzazione totale delle lesioni immediatamente dopo l'embolizzazione. In un caso di lesioni multiple, un fibroma ha mantenuto la propria vascolarizzazione. Questi risultati sono coerenti con i reperti angiografici. Non è stata osservata alcuna recidiva di malattia durante il follow up. Una paziente ha riferito la ricomparsa dei sintomi dopo 18 mesi dall'esecuzione della procedura; in questo caso, la CEUS ha dimostrato nuovamente la presenza di vascolarizzazione intralesionale.

Conclusioni: La CEUS è efficace nel dimostrare il grado di devascularizzazione al termine delle procedure di SUFE. I risultati della CEUS sono concordi con i risultati clinici dopo uno e sei mesi. La CEUS è affidabile ed economica se confrontata con la RM.

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Introduction

The introduction of interventional radiological techniques like superselective uterine fibroid embolization (SUFE) has created the need for diagnostic imaging methods that can be used to monitor each phase of treatment, to determine whether the purposes of embolization have been achieved, and to define the probability of success [1,2]. In fact, evidence of persistent lesional vascularization – even minimal – is indicative of treatment failure [3,4]. Current approaches provide for progressive, selective embolization of the uterine fibroids (also known as myomas). Use of appropriate-sized embospheres allows to embolize only those vessels that supply the myoma (and not those of the rest of the uterus) until the typical pruned-tree appearance is seen on angiography [5]. One month after the procedure, dynamic magnetic resonance (MR) imaging is performed to assess vascularization of the myoma, including both the macro- and micro-circulation. MR imaging is currently the standard of reference for assessing the success of embolotherapy [6]. However, the microcirculation of the tumor can also be examined with contrast-enhanced ultrasonography (CEUS). CEUS has been demonstrated to be a highly sensitive technique capable of detecting minimal levels of blood flow. Its use during SUFE was described by Marret et al. in a case report published in 2004 and by Dorenberg et al. in their 2007 report of a pilot study [1,2].

The present study was carried out to determine whether or not the use of CEUS with sonographic algorithms designed to reveal contrast medium provides diagnostic information that cannot be obtained with conventional ultrasound (US), i.e., the degree of myoma perfusion before treatment and the degree of devascularization after SUFE with microspheres.

Materials and methods

We studied twelve women with solitary or multiple fibroids who were considered candidates for SUFE based on clinical findings and

the results of previous imaging studies. The 21 myomas included in the study ranged in diameter from 3.5 to 9.0 cm (mean 5.2 cm). The patients underwent suprapubic CEUS before (Fig. 1) and after the myomas had been embolized with microspheres. In four cases, transvaginal US was also performed, but the results were not considered in the present study.

The CEUS protocol provided for the intravenous administration of 4.8 mL of second-generation US contrast agent SonoVue® (Bracco, Italy) followed by 5 mL of 0.9% saline solution.

The sonographic examination was performed with an iU22 system (Koninklijke Philips Electronics, Eindhoven, The Netherlands) equipped with algorithms for the elaboration of contrast in the pulse-inversion mode, and with experimental side-by-side software that provides simultaneous, same-screen viewing of normal B-mode images with corresponding contrast-enhanced images.

The aspects of SUFE that were evaluated with CEUS included the degree of myoma perfusion before treatment (greater vascularity is associated with increased growth and greater responsiveness to embolization); the degree of devascularization after treatment; and the presence of any areas of persistent vascularity, which are a cause of mid-to-long-term recurrence.

Fig. 1 Pre-SUFE CEUS image of a solitary uterine fibroid tumor in a 56-year-old woman. After intravenous administration of contrast agent the myoma (M) exhibits rich intralesional enhancement.

At the end of the embolization procedure, each patient underwent a second CEUS examination before leaving the angiography room. The examination was repeated one and six months after SUFE; at the six-month assessment, patients also underwent dynamic MR [5]. The methods used for all post-treatment CEUS examinations were identical to those described for the pretreatment examination.

To evaluate interoperator variability, the pretreatment CEUS study, the CEUS examinations performed one and six months after embolization, and the six-month MR were each repeated, 1 h later, by a second radiologist, who – like the first – had over ten years of experience in gynecologic imaging. The two CEUS assessments were performed independently, and the operators were unaware of their colleagues' findings. The CEUS examination carried out in the angiography room was performed by the same two radiologists, but in this case the result was based on consensus.

One of the patients was excluded from the study on the basis of the pretreatment CEUS findings, which revealed that the fibroid scheduled for embolization was already completely avascular.

The study was conducted in accordance with the principles of the Declaration of Helsinki, and all patients provided written informed consent prior the enrolment in our study.

Statistical analyses

Cohen's κ value was calculated to assess interobserver variability in the interpretation of CEUS and MRI findings. The κ values were classified as follows: 0–0.20 poor concordance; 0.21–0.40 modest concordance; 0.41–0.60 moderate concordance; 0.61–0.80 substantial concordance; ≥ 0.81 almost perfect concordance.

Results

The posttreatment CEUS examination performed in the angiography room revealed complete embolization (i.e., defined as the absence of intralesional enhancement) (Fig. 2) of all fibroids treated with SUFE. The absence of vascularization was confirmed in all cases at the one-month follow-up CEUS, which also revealed progressive decreases

in volume in 15/21 myomas. At six months, all lesions remained avascular and there were additional decreases in volume. In all cases, CEUS findings were similar to those that emerged from the dynamic-MR examination.

Interobserver concordance was excellent for all CEUS examinations (0.86 pretreatment, 0.84 at one month, 0.85 at six months) and for the six-month MRI examination (0.96).

Discussion

Uterine myomas are the most commonly diagnosed benign tumors of the myometrium. Their prevalence among women over 35 years of age ranges from 20% to 25%. They are the cause of 30% of all hysterectomies performed for non-neoplastic disease [7]. The vascular pattern of a myomas consists of peripheral macrocirculation with a "basket-like" pattern that can be easily recognized on color Doppler studies (Fig. 3) [8], but the tiny intramyomatous vessels that constitute the microcirculation can be visualized only with computed tomography (rarely used today), MR, or CEUS [9–12].

Transcatheter embolization of the uterine artery for treatment of symptomatic fibroids was first described by Ravina et al. in 1995 [1]. A study conducted by the Society of Interventional Radiology found that from 13 to 14 thousand uterine–artery embolization procedures are performed each year in the United States.

Several studies (retrospective and prospective) have demonstrated the efficacy and the safety of this approach for the control of bleeding, bulk-related symptoms, and pain: morbidity and mortality are minimal, and short-to-mid-term success rates are 85% [13,14].

The procedures commonly used in clinical practice to identify patients who are candidates for embolization include conventional US (suprapubic and transvaginal) and dynamic MR with T1-weighted sequences before and after the administration of gadolinium. Both methods provide morphovolumetric data on the myoma, and MR with gadolinium also provides functional information on its perfusion.

Fig. 2 Post-SUFE CEUS image of the myoma shown in Fig. 1. After embolization, administration of the contrast agent reveals a completely avascular myoma (M). The hyperechoic spots within the avascular area (arrows) represent the micro-spheres used for the embolization procedure.

Fig. 3 Normal appearance of a uterine myoma on the color Doppler examination with the characteristic circular (basket-like) pattern representing different vessels of the peripheral macrocirculation of the myoma (M).

Conventional US cannot reveal structural alterations in the myoma caused by ischemia: it simply furnishes an indicator of the effectiveness of therapy based on reductions in lesion volume. Color Doppler is not suitable for verifying fibroid devascularization because its sensitivity to changes in the microcirculation is low. Dynamic MR with gadolinium provides good quality information on morphology, size, changes induced by ischemia, and perfusion. However, this type of examination is quite expensive. In addition, it is not available in all centers [9–12].

As noted earlier, current guidelines provide for progressive embolization until the so-called pruned-tree appearance is observed and dynamic MR follow-up one month after treatment. In fact, false negatives can emerge during the simple angiographic assessment carried out immediately after embolization. These are caused by the activation of small, low-flow vascular circuits that are not detected at the time of treatment. The microcirculation of the myoma can be evaluated only with MR angiography and the use of contrast agents, techniques which are often very expensive and not always readily available [10].

CEUS is the only low-cost method available for accurate monitoring of the microcirculation and the changes provoked by embolization with microspheres. Because it can also be carried out during the embolization procedure, CEUS findings can also have prognostic value [1,2].

We excluded one patient from our study whose lesion had exhibited signs of growth during pregnancy. The CEUS examination, which was done 6 months after delivery, revealed that the myoma was completely avascular. In all probability, the decreased vasodilatation caused by the postpartum drop in plasma estrogen levels provoked a marked reduction in blood flow to the myoma with diffuse thrombosis of the intralesional vessels.

Transvaginal ultrasound proved to be more sensitive for the study of small myomas (which are of little or no clinical significance), but it was much less sensitive in the detection of intralesional contrast enhancement. This is due primarily to the well-known fact that the harmonics produced by contrast medium are very difficult to evaluate with high-frequency transducers. For this reason, the results of this study are limited to those obtained with a suprapubic approach.

Conclusions

The results of this study demonstrate that for microcirculatory studies, CEUS is characterized by sensitivity that is as high or higher than that of dynamic MR. These findings are consistent with the conclusions that have emerged from previous studies conducted mainly in the liver. Post-embolization imaging assessment of uterine fibromas focuses on lesion size and interruption of the fibroid's blood supply. CEUS provides equally good visualization of both these aspects at a cost that is considerably lower, and this makes it a valid alternative to MR. In addition, it can also be carried out in the angiography room while the catheter is still in the artery supplying the fibroid. It provides a highly sensitive method for evaluating the intralesional microcirculation of myomas, which is not based on indirect evidence

such as the pruned-tree appearance on angiography, which is currently considered as the most sensitive parameter of devascularization. If our findings are confirmed in studies of larger series of patients, the use of CEUS might reduce the amount of embolic material needed and shorten radiation exposure times associated with SUFE. CEUS itself does not expose the patient to any ionizing radiation whatsoever, so it can be repeated as needed during the SUFE procedure until the fibroid has been completely devascularized. Finally, all of these characteristics help reduce the overall costs of therapeutic embolization.

Conflict of interest

The authors have no conflict of interest.

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