Clinical aspects of uterine artery embolization
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UTERINE FIBROIDS:
TARGETED EMBOLIZATION,
AN UPDATE ON TECHNIQUE

Chapter 2
Abstract

Uterine Fibroid Embolization has become an attractive alternative therapy for symptomatic uterine fibroids. Since the introduction the applied embolization technique underwent several refinements. First complete blockage of both uterine arteries was the goal to obtain complete fibroid devascularization. Lately more sophisticated targeted embolization of the fibroid itself (preserving cervical branches, vaginal branches and ovarian anastomosis) has been carried out by more and more interventionalists. Meanwhile the utilization of calibrated embolic agents has become more and more popular. In this article we will provide the reader an update on the modern uterine fibroid targeted embolization technique, including a summary of catheterization related problems, flaws and tricks.
Introduction

Embolization therapy has been routinely carried out by many radiologists since the last 30 years for the treatment of various diseases and conditions such as bleedings, arterio-venous malformations or fistulae, aneurysms and benign as well as malign tumours.

Uterine fibroid embolization (UFE) however is a relatively new topic, since the first publication on UFE concerning a group of patients treated at Lariboisière Hospital in Paris was published in 1995 (1-2). Different technical approaches of UFE have been extensively described in literature (3-8). The main issue is superselective bilateral catheterization of the uterine arteries and flow-directed injection of embolic agents into the uterine arteries to obtain blockage of fibroid vasculature. The goal is to obtain complete fibroid devascularization in one session with minimal complications and side effects as well as a successful clinical outcome. There still exist many differences in applied embolization technique between centers. Many authors used to advocate catheterization of the uterine arteries directly with 5-French catheters while others are used to manage the uterine arteries mainly with microcatheters and advocate an ipsilateral or bilateral femoral approach (2-8). The utilization of calibrated spheres is becoming more and more popular but the ideal type and size of embolization material is still subject to further evaluation and discussions (9,25).

Technical aspects of UFE in terms of catheterization and embolization procedure

The right common femoral artery is usually punctured after local anaesthesia and a 4 or 5-French introducer sheath is placed. A 0.035 inch angled hydrophilic guidewire (Terumo Europe, Leuven, Belgium) together with a braided 4-French hydrophilic-coated Cobra-shaped (C2) selective catheter (Cordis Europe, Roden, the Netherlands) is manoeuvred over the top into the contralateral iliac system (3,4,8,10). In case of a steep aortic bifurcation and/or elongated aorta-iliac vasculature utilization of a 5-French hook catheter (Cordis Europe, Roden, the Netherlands) may be useful. The contralateral internal iliac artery is catheterized under fluoro or roadmap guidance. In case of a non-conclusive roadmap digital subtraction angiography (DSA) is performed in order to identify the origin of the uterine artery. It is extremely important to refrain from DSA series as much as possible and stick to proper collimated roadmap-guided
manipulations in order to avoid extensive ovarian radiation exposure. The 4-French catheter is advanced over the wire into the anterior division of the internal iliac artery and, using road-mapping technique, the uterine artery is carefully selected. The tip of the catheter is next advanced into the horizontal part of the uterine artery, ideally distal to the origin of cervico-vaginal branches. DSA is performed prior to the embolization procedure itself in order to achieve image data of the pre-embolization vasculature including the presence of any uterine-ovarian anastomoses (11). In many cases we appreciate more or less hampered flow after selective catheter placement. In almost all patients we immediately switch over to coaxial microcatheter technique simply because of the fact that appropriate embolization results can only be achieved by real free flow-directed embolization. The only way to achieve guaranteed fibroid devascularization is injecting embolization material under strict free flow circumstances.

Since the goal is to preserve the uterine, cervico-vaginal and ovarian branches one must consider the fact that the in-fibroid centripetal vessels (<500 micron) are endarteries. The size of the peri-fibroid plexus arteries ranges between 500-1000 micron and the size of the cervico-vaginal and ovarian branches is <500 microns. These differences in artery size provide the rationale for the concept of fibroid-targeted embolization with calibrated embolization material. Spheres larger than 500 micron will trespass vessels of 500 micron in diameter. In other words one is able to preserve cervico-vaginal branches and ovarian anastomoses avoiding post-procedural vaginal dryness and permanent amenorrhea. We utilize coloured calibrated microspheres pre-packed in sterile syringes (Embogold, Biosphere Medical, Roissy-en-France, France). We add 5 cc saline and 10 cc Omnipaque 320 (Amersham Cygne, Eindhoven, the Netherlands) and mix over a three-way stopcock to achieve a stable mixture. Omnipaque is used instead of Visipaque for microcatheter applications because of viscosity aspects. Connection of the stopcock assembly to the hub of the microcatheter provides the possibility to work with a closed system without spill of embolization material. After sufficient embolization of the contralateral uterine artery the same braided C2 catheter is used to select the ipsilateral internal iliac artery after performing the Waltman loop manoeuvre in the aorta (12). A non-braided type catheter will absolutely kink in the distal aorta and can only be used for bilateral procedures. The right uterine artery is managed by pulling back the catheter with the use of a selectively placed guidewire. In almost all cases again a microcatheter is placed in the horizontal
part of the right uterine artery avoiding selective catheterization of cervico-vaginal branches by checking its position with contrast medium injections. Control injections should not be too forceful because malposition in tiny branches might blow-up these vessels. Proper catheter tip position will be followed by the embolization procedure itself. We do not routinely perform an aortic flush angiogram to define the ovarian arteries; only when suspicion of parasitic flow to fibroid tissue arises prior to or during the procedure. During the work-up MR imaging we routinely perform MR angiography providing us with clues concerning parasitic vessels and deviation of normal uterine artery anatomy (5). At the end of the procedure an abdominal view is taken to determine the renal status such as hydrenephrosis.

A bilateral femoral approach, with simultaneous embolization of both uterine arteries in order to decrease the amount of radiation exposure, can be used. We have to consider the fact that radiation exposure to the patient is directly associated with technical factors implemented by the interventionalist. Although each patient is unique from an anatomical and consequently angiographic point of view, several variables may cause increased patient dose. One should avoid, if possible, excessive image acquisition, unnecessary image magnification, avoid oblique views, large field of views with inadequate collimation and a large air gap between patient and image intensifier (7,13). Catheterization from the contralateral side using a crossover technique is usually easier to perform and requires less fluoroscopy time in particular with less-experienced radiologists. When both catheters are in place two operators can simultaneously inject contrast medium for imaging and together embolize both uterine arteries. Simultaneous embolization of both uterine arteries is consequently associated with a significant decrease in fluoroscopic time. One has to stress the fact that fluoroscopy accounts for the majority of the absorbed ovarian dose during the procedure (14). In our practice, we are using this two-catheter technique only in young women seeking to conceive.

Flow-limiting spasm is a frequent and serious problem during UFE procedures. Spasm slows down the procedure or may even prevent an adequate targeted embolization. The principle of UFE is based on a preferential free flow of embolic agents towards all fibroids, which means that it is crucial to avoid spasm. Spasm is almost always very well noticed distal to the tip of the catheter. Spasm may also develop, and not be directly appreciated, more proximal in the uterine artery around the catheter shaft only
detectable on fluoroscopy by hampering of the contrast medium flow. When encountering one-sided spasm, it might be wise to switch over to the other side or to leave the catheter in place for several minutes and have a coffee break (8,13). The use of vasodilators such as nitro-glycerine 300 microgram intra-arterially may be helpful for a short period of time but is associated with inconsistent results (8). Catheterization using coaxial technique with selective placement of a microcatheter and pulling back the primary catheter out of the uterine artery is in our opinion the best option. In case of small and/or tortuous uterine arteries it is advised to use a microcatheter leaving the guiding C2 catheter positioned in the anterior division of the internal iliac artery or at the level of the uterine artery origin.

When it is difficult to catheterize the ipsilateral uterine artery or when kinking of the catheter is observed during the Waltman loop manoeuvre technique, a second puncture of the contralateral femoral artery may be wise (13). When the uterine artery originates with an acute angle from the anterior division of the internal iliac artery, we always advised to use coaxial approach to deal with this problem. An alternative is a different shaped catheter tip such as a mamarian configuration providing the possibility to manage an acute angled uterine artery origin. Left and/or right anterior oblique views maybe very helpful to determine the in most cases antero-medial oriented origin of the uterine arteries. Pelage stressed the importance and angiographic consequences of the variant uterine artery anatomy. In 45% of cases the uterine artery is the second branch from the anterior division, in 45% there is a trifurcation with anterior and posterior division, in 8% the uterine artery arises from the obturator artery and 8% from the posterior division (11). In case of a unilateral absence of the uterine artery even a replacement by an enlarged round ligament artery has been described (11,26). We have to consider the extreme importance of instructions concerning medication prior to UFE. Patients should refrain from GnRH analogues for at least 6 weeks prior to the procedure in order to prevent overall arterial and uterine artery spasm during catheterization.

Parasitic fibroid blood supply from ovarian arteries has been reported as the potential cause of failure of UFE (15). Identification of a significant flow from the ovarian artery is possible by pre or post-embolization pelvic flush aortography and/or pre-embolization MR angiography (16). Subsequently superselective catheterization of the ovarian artery
can be successfully performed using a 4-French Cobra-shaped catheter in combination with a microcatheter. A reversed curve of the 4-French catheter after forming a Waltman loop allows easy catheterization of the ovarian artery origin (11). Free flow embolization of the fibroids with larger particles can be performed successfully with the tip of the catheter positioned 3-4 cm distal to the origin of the ovarian artery. In case of ovarian artery supply we however refrain from prompt ovarian artery embolization during the first session. In our experience, in almost all circumstances the primary embolization results are satisfactory and no secondary ovarian artery embolization is needed (16).

Angiographic end-point
The standard technique (embolization to stasis) consisted of embolizing until the flow has ceased in the main uterine artery (2-6,8). Injection of embolic agent is stopped when no more proximal arterial flow and/or reflux of contrast material is noticed. Pathology data from pre- and postoperative fibroid embolization cases reveal that the peri-fibroid plexus with artery diameters ranging between 500 to 900 µm is the wanted target for embolization (24,25). Consequently the embolization procedure should come to an end when a so-called “pruned-tree” appearance of the ascending segment of the uterine artery with complete disappearance of the fibroid feeding vessels is observed. During embolization changes in vascular flow can be appreciated such as opening of vessels to the contralateral vasculature and sudden visualization of ovarian anastomoses. We use calibrated spheres sized 500-700 micron in cases without ovarian anastomoses. For women presenting with ovarian branches and women seeking to conceive 700-900 micron sized particles are employed. Our goal is to preserve cervico-vaginal branches, ovarian anastomoses and as many normal uterine vessels as possible. This targeted embolization concept handling this angiographic end-point reveals appropriate clinical success rates preserving ovarian and endometrial function (21,25).

Embolic agents
There are currently three embolic agents widely used for UFE: gelatin sponge, non-spherical PVA particles and tris-acryl gelatin microspheres such as Embospheres and Embogold (9).
Gelfoam has been extensively used for 30 years to perform haemostatic embolization. Pledgets manually cut into strips and then rolled and loaded into the nozzle of a 2 cc syringe are particularly suitable for pelvic embolization. This embolic agent is inexpensive and often used for UFE in less prosperous countries (18). Short-term results are encouraging but it may be hypothesized that a higher rate of clinical failures, recurrences and post-embolization sequelae may be expected (18,19).

Non-spherical PVA has been successfully used as an embolic agent in various territories for more than 20 years and for uterine purposes since 1989 (2-9). Non-spherical PVA has certain disadvantages in clinical practice. The material has to be delivered in an adequate suspension but still occlusion of delivery catheters may occur, especially when microcatheters are used (17). After the initial experience of UFE using small PVA particles, most groups have been using 355-500 and 500-700 micron PVA particles (3,4,7).

Until now, a single spherical embolic agent is widely available on the market. These tris-acryl gelatin microspheres have been used in Europe since 1995 in various territories (20,25). In our facility we started to use these calibrated microspheres in 1999 for UFE in order to achieve targeted devascularization of the perifibroid plexus preserving uterine and ovarian vasculature. Microspheres have certainly advantages over non-spherical agents because they neither create proximal aggregation in vessels nor occlude the microcatheters that easy (21). This material can even be delivered through a catheter smaller than their nominal diameter because they are compressible. We currently utilize the Renegade Hi-Flo microcatheter with an inner lumen of 0.027 inch (Boston Scientific international, La Garenne Colombe, Cedex, France) providing the possibility for an easy injection of 700-900 micron spheres and even the 900-1200 sizes will pass with some effort (22).

Alternatively spherical PVA particles are already available on the market (Contour SE, Boston Scientific International, Watertown, Ma, USA) or will be very soon. There are however not many clinical evidence-based data available yet to prove that either one of these three types of embolization agents is more effective than others in terms of UFE clinical outcome (25). In initial reports of UFE, the injection of PVA particles was followed by the placement of coils or injection of gelatin sponge pledgets to ensure durable occlusion of the uterine artery (2,5,8). Most groups are not currently using any
type of secondary embolization agent. However, in problems during UFE, sometimes alternative embolization material is needed.

**Conclusion**

In conclusion we have to accept the fact that there are still many questions to be answered, not only considering UFE in general but also from a technical point of view. Although there are not yet many evidence-based data widely available concerning the choice of the most effective and safest embolic agent, we strongly advocate the targeted embolization concept with calibrated spheres. Smaller particles will probably cause more fibroid shrinkage, but may also be associated with an increased risk of complications. Complete occlusion of both uterine arteries may cause unnecessary myometrial, endometrial and ovarian ischemia.

A limited devascularization by targeted embolization of the perifibroid plexus is consequently an attractive and rational approach. Liberal use of microcatheters to guarantee free flow embolization will provide a better devascularization of uterine fibroids than with the larger 4-French catheters because of a reduced incidence of flow-limiting conditions.
References


