Uterine Artery Embolization: State of the Art

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ABSTRACT

Since the first report in 1995, there has been rapid expansion of uterine artery embolization as a therapy for symptomatic uterine fibroids. The published literature and clinical experience show that this procedure is safe and effective. This article discusses the history of the procedure, current issues in procedure technique, and the state of the literature regarding outcomes of embolization. Current and future research topics also are discussed.

KEYWORDS: Myoma, fibroid uterus, embolization

Objectives: Upon completion of this article, the reader will be able to (1) discuss the technique of uterine artery embolization, including the rationale for embolic agent choice and embolization endpoint, and (2) be familiar with the currently published or presented data concerning outcomes of uterine artery embolization for fibroid disease.

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Embolization of the uterine arteries has been the standard of care for management of acute bleeding after childbirth or after gynecologic surgeries since the late 1970s.[1,2] Symptomatic fibroids are a major health concern for women. An estimated 177,000 to 366,000 hysterectomies and ~35,000 myomectomies are performed each year in the United States for this problem.[3] In addition, many women receive medical treatment for fibroids and many others suffer symptoms but never undergo treatment. Through the 1980s, apparently nobody in either the interventional radiology or gynecologic communities had thought of treating uterine fibroids by embolization.

In the late 1980s, Jacques Ravina, a French gynecologist, became interested in the possible utility of embolization as a pre-emptive measure before gynecologic surgeries such as myomectomy. He was familiar with the utility of embolization for postoperative bleeding and decided to investigate preoperative embolization, hoping that this would decrease intraoperative bleeding as well as decrease the risk for postoperative hemorrhage. Preoperative embolization of the uterine arteries did indeed prove to be useful to decrease perioperative bleeding complications.[4]

In some cases, there was a delay between the embolization and the planned surgery of at least a few days and in some cases a few weeks. Many of these patients experienced relief of their fibroid-related symptoms from the embolization alone and refused to go on with the planned surgery. Ravina et al[5] published their initial experience in 1995, and have since continued their studies of uterine artery embolization (UAE) as a primary treatment for fibroids.[6,7]

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UAE for fibroids was first reported in the United States by McLucas and Goodwin[8] from University of California Los Angeles (UCLA) Medical Center in 1996. Since then, there has been rapid spread of the procedure across the United States, Europe, and worldwide, with steadily increasing numbers of publications in both the radiologic and the gynecologic literature. At the time of writing, the author estimates that the worldwide experience with UAE is ~35,000 cases, of which between one third and one half have been performed in the United States.

TECHNICAL CONSIDERATIONS

Although the procedure for UAE has been well documented in the literature,[9–11] there have been significant changes in the details of the technique over time.

Catheter Tip Position

There are two important branches of the uterine artery in addition to the vessels into the uterus itself. One of these is the cervicovaginal branch, which arises from either the mid to distal portion of the transverse segment or the proximal portion of the ascending segment. These branches collateralize with ascending branches of the vaginal artery. There is concern that because this vessel supplies nerve fibers and other structures in the cervix, its preservation may be important for sexual response and experience.[12] There has been significant debate in recent years over the importance of excluding this vessel from the embolization field. Although studies presented at recent Society of Cardiovascular and Interventional Radiology meetings[13,14] indicate that negative effects on sexual function are rare, embolization should be performed with the catheter tip beyond the origin of the cervicovaginal branch if technically feasible, excluding it from embolization. However, in many cases this will not be possible because of vessel tortuosity and/or the location of the branch origin. Including the cervicovaginal branch in the embolization field is not considered a technical fault.

Collateral Vessels

Collateral flow to the uterus can arise from several sources. The ovarian artery is the most likely source of collateral flow to the fibroid uterus. This collateral flow, if not addressed, can cause clinical failure of the UAE.[15,16] Ovarian flow can take one of two forms. In ~1% of cases anatomic variants occur with the absence of part or all of the uterine artery. In these instances the flow to the uterus is usually from the ovarian artery. In a small number of cases there is normal uterine artery anatomy but there is sufficient vascular demand by the uterus that there is significant flow into the uterus through the utero-ovarian collateral. This is visible in ~5% of cases.

When the ovarian artery provides supplemental flow to the uterus, it is important to ensure that sufficient embolic material gets to the portions of the uterine fundus beyond the point of ovarian artery inflow. Careful monitoring of the injection pressure during embolization will ensure that there is minimal reflux across the anastomosis and that embolic material does get beyond the anastomosis. Allowing a small amount of reflux (no more than a centimeter or so) and then having the refluxed material wash back into the uterus can ensure that the ovarian artery inflow helps to carry embolic material into the fundus, without embolizing the ovary itself, which is found several centimeters proximal to the utero-ovarian anastomosis.

When an anatomic variant of the uterine artery is observed, or if a portion of the uterus is not demonstrated during embolization of the uterine arteries, then selective injection of the ovarian artery on the relevant side might be useful. When the ovarian artery injection shows that there is flow to the uterus, embolization can be considered. Care should be taken to avoid an embolization scheme that risks embolization of the ovary itself. Proximal embolization of the ovarian artery with relatively large gelatin sponge pledgets can decrease the filling pressure into the uterus enough to ensure a good clinical result from the embolization without endangering the ovaries (R.L. Worthington-Kirsch, manuscript in preparation).[17] Embolization of the ovarian artery with relatively large particles (more than 500 to 600 μm) can also be considered because these particles are likely to be too large to enter the ovarian vascular bed and so will bypass the ovary and go into the uterine vascular bed.[18]

Some authors have advocated routine pre-embolization aortography to assess the ovarian arteries.[19] If this is done, it is important to do the aortogram after the uterine arteries have been embolized because embolization of the uterine arteries may well have already occluded any intrauterine branches that the ovarian artery was supplying. It is still unknown whether aortography should be performed routinely after embolization of the uterine arteries. The author only does so when there is a suspicion for a residual ovarian artery contribution after the uterine arteries have been embolized.

There is a recent report that the artery of the round ligament, a branch of the inferior epigastric artery, can also be a source of flow to the uterus.[20] This vessel can apparently be embolized with little fear of complication.

Embolic Agent Choice and Embolization End Point

When UAE was first introduced as a therapy for fibroids, the protocol was simple.[9] The uterine artery was selectively embolized with polyvinyl alcohol (PVA)

particles followed by capping with a plug of gelatin sponge. The end point for embolization was to have a static column of contrast in the uterine artery, with only a stump filling when the internal iliac artery was injected. The gelatin sponge cap was thought to both complete the occlusion of the uterine artery and to prevent PVA particles from being drawn out of the uterine artery by the Venturi effect, which would result in nontarget embolization.

The author has repeated arteriography in several patients who had been embolized in this fashion and were not entirely satisfied with the results of their UAE, usually due to what they perceived as inadequate uterine volume reduction. In 10 patients who had repeat arteriography between 4 months and 2 years after UAE, the author found that 19 of the 20 uterine arteries remained completely occluded. Razavi et al[21] have presented work that showed the main uterine arteries patent after embolization with PVA alone. UAE appears to destroy most (if not all) of the fibroids present at the time of the UAE,[22,23] but there is no evidence that UAE changes the underlying tendency of the uterus to form new fibroids. Therefore, it is important to preserve the main uterine artery segments after UAE, especially in younger women, if only to preserve access for a second UAE at some point in the future.

It appears that the inflammatory response incited by gelatin sponge is durable and sufficient to occlude the uterine artery. This is seemingly in contradiction to the standard teaching that gelatin sponge is a temporary agent, but there must be a tissue reaction that stimulates the body to remove the gelatin sponge material from the vessel. Given these observations, the author has abandoned the use of gelatin sponge in UAE.

With the introduction of calibrated microsphere embolic agents, embolization has become technically somewhat easier.[24] The chief advantage of calibrated microspheres is that they are more uniformly sized than standard PVA preparations. This results in a more predictable level of embolization and minimizes the clogging of both standard and microcatheters, which is a continuous problem with standard PVA preparations.

This difference is so significant that a simple dose equivalence between standard PVA and microspheres cannot be determined. The two different preparations behave in markedly different ways. It has quickly become apparent that UAE with calibrated microspheres does not have to be performed to the end point of complete occlusion of the uterine artery. In fact, this end point is difficult, if not impossible to achieve with calibrated microspheres. Comparison of embolization with PVA and microspheres in an animal model shows that PVA forms aggregates, which often occlude vessels much more proximally than would be expected from the particle size used. This apparently is what leads to cessation of flow in the main uterine arteries during UAE with standard PVA preparations.

It must be remembered that the aim of embolization is not to occlude the main uterine artery, but to occlude the vessels that supply the fibroid while sparing the vessels supplying normal uterine tissue as much as possible. Nobody has yet proposed a full explanation of the underlying physiology that allows UAE to result in infarction of the fibroids with preservation of normal uterine tissue. Part of the answer includes the fact that the vessels of the perifibroid plexus apparently have a lower resistance than vessels supplying normal tissue; in addition, fibroid tissues are much more sensitive to anoxia than normal myometrium.

Given these observations, what should be the arteriographic end point? One should look for evidence that the flow dynamics of the uterus have significantly changed, that the blood flow to the perifibroid plexus has been interrupted. The angiographic signs of this include the following:

1. The appearance of new collaterals that were not present on initial injection of the uterine artery. This may be the sudden appearance of filling across the utero-ovarian anastomosis, or the appearance of vessels cross-filling to the opposite uterine artery.
2. An increase in resistance of the uterine body vessels to further injection of contrast. This can be manifested by the beginning of reflux in the uterine artery proximal to the catheter tip, dilation of the uterine artery when pressure is exerted on the injection syringe, or cessation of flow in the ascending ramus of the uterine artery with contrast staining of the lower uterine segment.
3. Occlusion of the main uterine artery. It appears that one can achieve the more subtle of these end points more easily with calibrated microspheres than with standard PVA preparations. However, it also should be noted that there has been little or no observed difference in the safety or clinical efficacy of UAE with any of the embolic agents used for the procedure. This may be demonstrated by controlled studies comparing different embolic preparations in significant numbers of patients.

UAE OUTCOMES

The initial reports about UAE were short- and mid-term case series.[5–7,9–11,25–31] These reported high technical and clinical success rates with low complication rates. Typically, UAE is technically successful in 95 to 99% of cases. It is successful in controlling menorrhagia in 85 to 95% of patients, and in controlling bulk symptoms in 80 to 90% of patients. Volume reduction is the easiest outcome to measure. At 3 to 6 months post UAE, overall uterine volume reduction is typically

reported to average 40 to 60%, and dominant fibroid volume reduction is typically reported at 50 to 75%. Unfortunately, volume reduction appears to be the least important outcome measure. Many women with relatively small volume reductions still report significant improvement in fibroid-related symptoms of menorrhagia and pressure.

Several case reports of complications from UAE have been published.[12,32–40] However, those recent series that have examined complication rates in large series of UAE cases have shown rates of significant complications in the range of 1 to 3%.[31,41,42] The most common issues that arise after UAE are management issues rather than complications. These include post-UAE pain, postembolization syndrome, and vaginal discharge. Transcervical sloughing of a necrosed fibroid occurs in ~5% of UAE patients overall,[43–45] and may occur in as many as 20 to 25% of patients who have dominant submucosal fibroids.[46] This is usually easily managed and resolves with spontaneous passage of the tissue, but some patients may require surgical evacuation of the uterus.

Studies comparing UAE to surgical therapies (either myomectomy or hysterectomy) have begun to be reported.[47–49] These all have shown similar results. In all three studies reported to date, the clinical outcomes of UAE are similar to or better than the outcomes of surgery for control of symptoms. Complication rates are comparable between UAE and surgery, with UAE having fewer serious complications. UAE consistently outperforms surgery in terms of duration of hospitalization, time to return to work, and time to return to normal activity levels. Other comparative studies in progress have not yet been reported. In addition, the FIBROID Registry, sponsored by Cardiovascular and Interventional Radiology Research and Education Foundation, promises to provide a wealth of longitudinal data about UAE outcomes, complications, and patient satisfaction.

FERTILITY

Fertility after UAE remains a major issue. There are many women who have become pregnant after UAE. In the author's experience, most have had normal pregnancies with uncomplicated delivery of healthy infants. However, there is not yet enough information available to predict fertility rates after UAE. This issue is complicated by the fact that the literature on fertility after myomectomy is in general of relatively poor quality. Evaluation of data from three recent reports[31,46,50] suggests that fertility after UAE is probably similar to fertility after myomectomy, at least for women with multiple fibroids. Clearly, there is a tremendous need for a well-designed longitudinal study of fertility after uterine-sparing fibroid therapies.

The author does not consider a desire to retain fertility to be a contraindication for UAE. However, the decision about whether to recommend UAE in these women is very complex, depending on the severity of symptoms, size, number, and distribution of fibroids, and other issues (both medical and social) that affect the patient's chances of becoming pregnant. In women for whom fertility is the only concern, the author does not offer UAE unless the referring gynecologist feels that there is a high risk of complication if myomectomy were attempted. Treatment recommendations for women who wish to retain fertility should be made in cooperation with the referring gynecologist, with consultation to a fertility specialist in many cases.

CONCLUSION

UAE has emerged as a valuable treatment for fibroid disease. Although there are many questions that remain to be answered, it is clear that UAE will be a part of the range of therapies for fibroids for the foreseeable future. Ongoing research as well as further refinements in technique and patient management will establish the boundaries of the procedure's place in medical practice.

ABBREVIATIONS

UAE	uterine artery embolization
UFE	uterine fibroid embolization
PVA	polyvinyl alcohol
CIRREF	Cardiovascular and Interventional Radiology Research and Education Foundation

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