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Comparison of MRI and Symptom Outcomes of Uterine Artery Embolization for Uterine Leiomyomata Using Tris-Acryl Gelatin Microspheres, Poly-Vinyl Alcohol Spheres and Poly-Vinyl Alcohol Particles.

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Abstract

Purpose: To compare the recurrence rate of symptoms and MRI enhancement of uterine fibroids in patients treated with uterine artery embolization (UAE) among three embolic agents: polyvinyl alcohol (PVA) particles, spherical polyvinyl alcohol (SPVA) particles and tris-acryl gelatin microspheres (GM).

Materials & Methods: Women treated with UAE for fibroids with PVA, SPVA or GM were contacted by telephone/ mail to complete a modified Uterine Fibroid Symptom Quality of Life (UFS-QOL) survey. Baseline and post-UAE gadolinium-enhanced magnetic resonance imaging (MRI) studies were evaluated for residual or persistent enhancement of any uterine fibroids after UAE. Data was analyzed using 2-tail fisher's exact test to correlate symptoms and enhancement and determine the liklihood of recurrence of enhancement and symptoms following UAE among three embolic agents.

Results: A total of 101 women underwent UAE with one of the three embolic agents and had complete pre- and post-embolization MRI follow-up. In this group, a total of 24 of 59 (41%) women in the PVA group, 18 of 24 (75%) women in the SPVA group, and 4 of 18 (22%) women in the GM group showed residual enhancement in some or all fibroids. Statistically significant differences in recurrence of residual enhancement on follow-up MR imaging were found between SPVA and PVA ($p=0.0072$), as well as SPVA and GM ($p=0.0015$), but not between PVA and GM ($p=0.1756$). No statistically significant correlation between residual enhancement and symptom recurrence was found based on the survey responses.

Conclusion: Patients embolized with SPVA have a higher risk of having residual enhancement on follow-up MR imaging than those embolized with PVA or GM.

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Introduction

Uterine fibroids are the most common benign tumor of the female reproductive tract, affecting 20-77% of the population (1). These benign tumors take a significant toll on the US health care system, accounting for over 1 billion dollars of US health care expenditures per year, as well as approximately 900,000 hospital days per year (2). Roughly thirty-five to fifty percent of women with fibroids suffer from a constellation of symptoms including menorrhagia, dyspareunia, dysmenorrhagia, reproductive difficulties such as infertility or miscarriage, as well as pressure-related symptoms such as urinary frequency or urgency, bloating, and constipation (3). The tumors typically arise during perimenopausal years and regress during menopause. The diagnosis of uterine fibroids is typically made by history and physical examination and can be confirmed with either pelvic ultrasound or magnetic resonance imaging with or without gadolinium contrast.

Treatment Options

There are several options available for management of fibroid-related symptoms including hysterectomy and myomectomy, though more recently techniques such as transvaginal resection of fibroids (4), laparoscopic-directed thermal coagulation (5), endometrial ablation (6), laser coagulation (7), cryotherapy (8) and MR-guided focused ultrasound surgery (9). Hysterectomy is the most commonly prescribed surgical option for women with symptomatic fibroids, with an estimated 177-366,000 women undergoing hysterectomies annually for this indication (2). Myomectomy is the second most common treatment, with an estimated 37-45,000 women undergoing myomectomies each year (2).

Typically, women often seek non-surgical alternatives for treatment of fibroid-related symptoms. Medical therapies include GnRH analogs (10), gestrinone, (11) and low-dose mifepristone (12). However, these alternatives are not successful in all candidates, and quite often women experience recurrence of symptoms upon discontinuation of the medication (13). As a result, therapies such as Uterine Artery Embolization (UAE), which was first described by Ravina et al. in 1995 (14) but used previously for treatment of intractable post-partum hemorrhage (15), have been growing in popularity.

The rates of clinical success of these procedures – defined as complete resolution of fibroid-related symptoms requiring no additional treatment – are comparable. UAE is typically quoted at approximately 90%, myomectomy at 80% and hysterectomy at 100% (2). Hysterectomy is a major surgical procedure, involving several days of hospitalization followed by four to six weeks of recovery resulting in permanent loss of uterus. While myomectomy preserves the uterus, it is still a major operation with similar recovery times as hysterectomy. In contrast, UAE requires a relatively short hospital stay, typically one day or less, and 1-2 weeks of recovery (16). According to the American College of Obstetricians and Gynecologists' (ACOG), the overall morbidity for UAE is reported to be 5%, as opposed to that of myomectomy at 38.6% and hysterectomy at 40.1% (17). Although UAE preserves the uterus while providing relief of fibroid related symptoms, the ACOG regards it as an investigational or relatively contraindicated procedure in women wishing to retain fertility (18). However, Ornan et al (19) studied the long-term sequelae of uterine artery embolization for intractable post-partum hemorrhage and found that all patients who desired to get pregnant were able to

do so, and experienced uncomplicated deliveries years after the embolization. Nevertheless, gynecologists are increasingly recommending UAE to their patients as a treatment alternative for symptomatic fibroids (20).

Recurrence rates after UAE are estimated around 10% after 2 years (21). While some studies have shown that some patients may require further invasive treatment 3-5 years after the procedure, the satisfaction level with the procedure remains high among the women who choose to undergo UAE (22). In a large multicenter trial comparing 100 patients undergoing UAE with 50 patients undergoing hysterectomy for symptom improvement after 12 months showed that both procedures had comparable results with an advantage for hysterectomy on pelvic pain, yet complications were infrequent in both procedures (23).

Embolic Agents used in Uterine Artery Embolization for Uterine Leiomyomata

Despite the large number of studies evaluating the procedure (24-29) and the individual embolic agents commercially available (28, 30-35), there have been few studies comparing the MRI enhancement and clinical outcomes among different embolic agents (36, 37). Among the first agents used for UAE to treat fibroids were poly-vinyl alcohol particles (PVA) and gelfoam (38). Gelfoam was traditionally used when embolizing the female reproductive organs because it caused only a temporary occlusion of the targeted vasculature (38). Before UAE for fibroids, PVA was not routinely used for pelvic embolization procedures in women (38).

The introduction of tris-acryl gelatin microspheres (GM; Embosphere Microspheres; Biosphere Medical, Rockland, MA) provided the first spherical embolic

agent for UAE. As this new agent was introduced to practice, a modified technique for UAE was developed which consisted of a limited embolization endpoint with similar results as the previous agents being used (32). The introduction of spherical PVA (SPVA) particles (Contour SE; Boston Scientific) provided yet another spherical embolic agent, which received approval from the Food and Drug Administration for the specific indication of treatment of uterine fibroid tumors in 2004. This embolic agent was available in the same size categories as the GM, and was considered to have similar performance characteristics as GM.

There is little evidence in the literature comparing clinical outcomes among different embolic agents. A randomized prospective trial compared the original PVA with GM which demonstrated that both embolic agents had similar efficacy as measured by short-term clinical outcome and imaging follow-up (36). Recently, a prospective randomized trial comparing GM and SPVA was conducted to evaluate clinical outcome and MR imaging outcome at 3 months after the UAE (37). This study was terminated before patient enrollment was completed because SPVA was found to have worse symptom outcome as measured with the Uterine Fibroid Symptom – Quality of Life questionnaire (UFS-QOL) and more likely to have incomplete infarction of uterine leiomyomata as seen on contrast-enhanced MR imaging (37).

Diagnostic Imaging Follow-Up

There are two general modalities for imaging of the female pelvis which allow visualization of uterine fibroids: pelvic or transvaginal ultrasound and magnetic resonance imaging (MRI). While both transvaginal ultrasonography and MRI are

accurate at detecting uterine fibroids (39), ultrasound is limited because it does not allow for assessment of fibroid perfusion, and does not permit the large field of views obtainable with MRI for accurate volume assessment (40). Contrast-enhanced MR imaging allows for visualization of perfused areas of myometrium and fibroid tissue, which can be used to monitor response to UAE treatment (41, 42). The goal of UAE is to cause complete infarction of all fibroids while maintaining perfusion of the myometrium (43). Residual enhancement of uterine fibroids has been associated with an increased risk for recurrence of fibroid-related symptoms within the first two years after UAE (42). As such, it is necessary to employ imaging modalities that can distinguish fully infarcted fibroids from incompletely infarcted ones to be used when designing studies that evaluate clinical outcomes of uterine artery embolization (37).

Therefore, the aim of this research is to retrospectively compare the enhancement of fibroids at 6-month gadolinium-enhanced MRI studies with prospective recurrence of symptoms and in patients treated with UAE with the three aforementioned embolic agents; poly-vinyl alcohol particles (PVA), poly-vinyl alcohol spheres (SPVA) and tris-acryl gelatin microspheres (GM).

Statement of Purpose

The purpose of this study was to compare the clinical outcomes among three commercially available embolic agents used for uterine artery embolization for uterine leiomyomas. Our hypothesis is that there are differences in the clinical outcomes, as measured by enhancement of fibroids on gadolinium-enhanced MRI and survey responses on modified UFS-QOL survey, among the three embolic agents: PVA, SPVA and GM. This study is clinically relevant because there are few studies in the literature comparing clinical outcomes among embolic agents. The practical benefit is that physicians will use this information when deciding on which embolic agent to use for uterine artery embolization to treat symptomatic uterine leiomyomata.

Materials and Methods

We began our study after obtaining approval from the human investigation committee and ensuring adherence to Health Information Portability and Accountability Act (HIPAA) compliance. A total of 247 women who underwent UAE at our institution were contacted by mail to complete a post-UAE survey. These patients underwent embolization at a single institution from January 1999 to November 2004. Inclusion criteria consisted of pre-menopausal women ages 30-55 years of age with symptomatic leiomyomas, with or without adenomyosis; completion of the survey, either by telephone or mail; treatment with UAE at our institution with a single embolic agent (PVA, SPVA, or GM), baseline gadolinium-enhanced magnetic resonance (MR) imaging examination as well as post-UAE gadolinium-enhanced MRI at our institution approximately 6 months after the UAE. Patients with diagnosis or suspicion of diagnosis of leiomyosarcoma were excluded from the study.

Uterine Artery Embolization Procedure

Bilateral UAE was performed by an experienced interventional radiologist in each case. Arterial access was obtained at the right femoral artery. In order to minimize technical failures due to collateral blood supply to fibroids, pelvic aortography using an Omniflush Catheter (AngioDynamics, Queensbury, NY) from the level of renal arteries was performed to evaluate for the presence of collateral blood supply to the fibroids (44). Selective catheterization of each of the uterine arteries was then performed with a 5-F catheter (Cook Medical Inc., Bloomington, IN), followed by insertion of a 3-F

microcatheter (Renegade Hi-Flow; Target Therapeutics/Boston Scientific, Natick, MA) for selective embolization of the uterine arteries.

Preparation of embolic materials varied according to product specifications. PVA particles and SPVA particles were mixed with 6-7 mL of normal saline and 6-7 mL of IV Contrast (various manufacturers). GM spheres were mixed with 10 mL of IV contrast to obtain a 50% concentration of contrast in the syringe. The end point of embolization varied among the three embolic agents according to the standard at the time of embolization. Slow flow with near stasis in the ascending uterine artery was the end point for the GM. Complete stasis was the end point for the PVA and SPVA. Embolic sizes used were 500-700 and 700-900 Microns for both GM and Contour SE, while we used particles 300-500 Microns for PVA. The choice of embolic agent used was left to the discretion of the interventional radiologist performing the procedure.

Following embolization of both uterine arteries, pelvic aortography was repeated from the level of the renal arteries for evaluation of perfusion of the uterine arteries as well as evaluation for any new collateral blood supply to the uterus. In some cases, ovarian artery collateral flow was observed, and the ovarian arteries were embolized during the procedure.

During the procedure, patients received intravenous fentanyl and midazolam for analgesia and sedation while a nurse monitored the patient. Ciprofloxacin was given prior to the procedure. Patients also received IV ketorolac prior to the completion of the procedure for additional analgesia.

Post-Procedure Care

Immediately following the procedure, patients began using a patient-controlled analgesia (PCA) pump, which provided morphine in the majority of patients. Seldomly, patients would require alternate medication, such as Dilaudid (Abbott Laboratories, Abbot Park, Illinois). These alternatives were implemented when the patient had a known allergic reaction to morphine, or a patient had inadequate pain control with morphine. Antiemetic drugs were used routinely during patient stay. Patients were discharged the next morning, and were provided with oral ketorolac, oxycodone/ acetaminophen, and antiemetic medications. Patients were followed in the interventional radiology clinic 1, 3 and 6 months after the procedure.

MRI Protocol

Patients underwent gadolinium-enhanced MR imaging before and approximately 6-months after UAE for evaluation of fibroids. Imaging was performed using a 1.5 T Signa scanner (GE Signa, Milwaukee, WI). Sequences obtained were a localizer, fat-suppressed sagittal fast spin-echo scans (TR 6200/TE 104), coronal fast spin-echo scans (TR 3900/TE 103), axial T1 weighted gradient echo scans (TR 180/TE 2.3, 4.8), and coronal 3D gradient echo (TR 5.9/1.2/40) pre and post IV gadolinium administration (0.1mmol/kg). A timing bolus was used to obtain the arterial phase. Three post contrast-enhanced scans were obtained during the arterial phase, then at 60, and 120 seconds after gadolinium administration. Subtraction images of the pre and post gadolinium scans were subsequently performed. The field of view varied from 20 to 28cm and the matrix was 256x256.

Images were evaluated for uterine volume and myoma enhancement, readily discerned on the subtraction images. The volume of the uterus was determined by the attending radiologist dictating the case using the formula for the volume of a prolate ellipse (transverse x axial x cranio-caudal x 0.5233) (45). On the post-UAE MRI scans, an enhancement score (0%, 25%, 50%, 75%, or 100%) was assigned based on visual estimate of percentage volume of all fibroids showing residual enhancement in each patient. Baseline MRI was evaluated before the post-UAE MRI when determining enhancement percentages in the event that there were fibroids that were already partially infracted before UAE, and/or to identify fibroids that may have disappeared post-UAE because they were sloughed (e.g. submucosal fibroids). A score of 0% meant complete infarction of all fibroids, and 100% meant complete enhancement of all fibroids. Both baseline and post-UAE MRI were assigned enhancement scores. MRI studies were reviewed by Jorge Gálvez, with assistance from Shirley M. McCarthy MD, PhD, and Jeffrey Weinreb MD for assignment of enhancement scores. The studies were read using a Synapse (PACS) workstation (FUJIFILM Medical Systems USA, Stamford, CT).

Survey Design

Clinical follow-up consisted of completion of a modified UFS-QOL survey which inquired about change of symptoms, symptom recurrence, additional interventions or treatments, and satisfaction with outcome (46, 47). Scaling of symptoms consisted of 9 options (never had this symptom; new symptom since UAE; much worse; slightly worse; unchanged; slightly better; much better; completely resolved; initially improved but then worsened). The survey was modified by Jorge Gálvez in consultation with Michael G

Tal, MD, and Elizabeth Kagan Arleo, MD, to inquire about symptom recurrence, as well as any therapies for fibroid-related symptoms the patient may have undergone before or after the UAE.

Each patient's survey was evaluated individually to assess whether a given symptom had improved, remained the same, or worsened since the UAE. Patients were sorted into 4 categories: improvement of symptoms, no change, deterioration of symptoms, and initial improvement followed by deterioration of symptoms. The survey was mailed to patients on November 2004. Patients who did not respond within 2 months were contacted by telephone by Jorge Gálvez to complete the survey.

Data Collection

Survey, MRI and UAE data was compiled in a database created by Jorge Gálvez with Microsoft Access 2003 (Microsoft Corporation, Redmond, WA). Data confidentiality was maintained according to HIPAA standards, using anonymous patient ID numbers, with the identification key stored separate from the database. Initial UAE and MRI data was obtained through chart-review conducted by Jorge Gálvez using IDXrad (IDX Systems, Burlington, VT).

Baseline Data

The demographic characteristics, as well as treatments for fibroid-related symptoms before or after undergoing UAE are outlined in Table 1. A total of 54 women completed the survey, and the mean patient age was 45 years for the SPVA and GM groups, and 49 years for the PVA group. The majority of the women treated were

Caucasian, and approximately 50% had not sought therapies for fibroid related symptoms prior to the UAE. A total of seven (29%) of the women embolized with PVA sought additional therapy, two (8%) sought hysterectomy, one (5%) sought a myomectomy and two (8%) sought a repeat UAE. Of the women embolized with SPVA, a total of six (32%) sought additional therapy, five of which chose a repeat UAE. Lastly, of the women embolized with GM, a total of six (55%) sought additional therapy following UAE, including three (27%) who sought dilatation and curettage while one (9%) sought a hysterectomy.

The fibroid-related symptoms that the women reported on the surveys occurred at similar rates across the three embolic agents. The mean use of sanitary napkins during the heaviest day of bleeding ranged from 6-11 sanitary napkins on the heaviest day of flow, while the number of tampons ranged from 7-10 per day among the three embolic agents. About half of the women in both the PVA (54%) and SPVA (44%) groups reported that bleeding lasted more than 7 days during their menstrual cycle, in contrast to 100% of the women in the GM group.

Statistical Analysis

Data was analyzed with the use of SAS for Windows 9.1 (SAS Institute Inc, Cary, NC) with assistance from Daniel Zelterman, PhD. Analysis was limited to comparison of the two groups in terms of baseline and follow-up imaging outcomes, and symptoms at time of completion of the survey. All *P* values reflect the result of 2-tailed fisher's exact tests ($a = 0.05$).

Results

MRI Analysis

A total of 101 women underwent UAE with one of the three embolic agents and had complete pre- and post-embolization MR imaging follow-up. In this group, the mean uterine volume for patients embolized with PVA was 656 cc (± 440 cc), for SPVA it was 802 cc (± 663 cc) and for GM it was 757 cc (± 680 cc) as measured on the pre-UAE MRI study (Table 2). A total of 24 of 59 (41%) women in the PVA group, 18 of 24 (75%) women in the SPVA group, and 4 of 18 (22%) women in the GM group showed residual enhancement in some or all fibroids. The PVA group had 35 (59%) women with 0% enhancement, 21 (36%) women with partial enhancement (25-75%), and three (5%) women with 100% enhancement of fibroids (Figure 1). The SPVA group had six (25%) women with 0% enhancement, 16 (67%) women with partial enhancement (25-75%), and two (8%) women with 100% enhancement (Figure 2). The GM group had 14 (78%) women with 0% enhancement, four (22%) women with partial enhancement (25-75%), and no (0%) women with 100% enhancement (Figure 3). When comparing embolic agent in pairs using 2-tail Fisher's exact test, the GM-PVA group resulted with $p=0.1756$, the PVA-SPVA group resulted with $p=0.0072$ and the SPVA-GM group resulted with $p=0.0015$ (Figure 4).

A total of four (3.9%) women underwent unilateral UAE due to absence of an angiographically visible right or left uterine artery. Three of these women (17% of GM patients) underwent UAE with GM, and one with PVA (1.7% of PVA patients). Only one patient embolized with GM showed residual enhancement on post-UAE MRI. A total of two (2%) women underwent unilateral ovarian artery embolization at the time of

the UAE for an observed enlarged ovarian artery. Both of these women were embolized with SPVA (8% of PVA patients), and one of them showed residual enhancement on post-UAE MRI.

Survey Results

A total of 54 patients completed the survey by telephone or mail. Of these, 24 (44%) had been embolized with PVA, 19 (35%) with SPVA, and 11 (20%) with GM, Seventeen (31%) patients were categorized with recurrent or persistent symptoms following the UAE according to the survey data. Of these 17 patients, seven (29%) were embolized with PVA, seven (37%) with SPVA, and three (27%) with GM.

The severity of bleeding symptoms, characterized by women reporting bleeding during the menstrual cycle lasting more than 7 days decreased from 44%-100% before therapy with UAE to 4-13% following UAE according to our surveys. Additionally, the number of sanitary napkins or tampons used decreased by approximately 50% (Table 3).

There were only two patients with coexisting adenomyosis who reported recurrence of symptoms after UAE. The symptoms listed as worsening were vaginal bleeding and pelvic pain for one patient, and abdominal distension for the other. Both of these patients underwent UAE with PVA. (We did not receive surveys from a total of 17 women with coexisting adenomyosis who underwent UAE. Of these, 1 underwent UAE with GM, 4 with SPVA, and 12 with PVA. See Table 4).

Of the four patients that underwent unilateral UAE (three were embolized with GM and one with PVA), none of them reported worsening or recurrent fibroid-related

symptoms on the surveys. Two women underwent ovarian artery embolization at the time of the UAE for a single enlarged ovarian artery (both embolized with SPVA). One of the patients reported initial improvement of abdominal distension followed by worsening of this symptom while the other remains symptom-free (Table 5). While more than half of the women in each group sought no additional therapy following UAE, there was a number of women who sought further therapies, ranging from medical (e.g. anti-inflammatory medications) to more invasive alternatives (e.g. repeat UAE, hysterectomy), at some point after the UAE procedure.

The length of time from post-UAE MRI to completion of survey by patients, whether by telephone or mail, varied among the three embolic agents. Patients embolized with PVA had the longest intervals between MRI and survey completion at 34.2 months (SD ± 16.3 months), while the interval for SPVA was 3.0 months (± 4.0 months) and GM was 10.7 months (± 9.5) months (Table G).

Nearly all patients (84%) reported being satisfied with the procedure, with a total of 57% being greatly satisfied among all embolic groups. Over 90% of patients would recommend the procedure to a friend, and more than 80% would be willing to undergo a repeat UAE if the fibroid-related symptoms recurred (Figure 5).

Correlation of MR imaging with clinical follow-up

Within the group of 54 patients with MR and survey data, the PVA group had seven (29%) women with recurrent symptoms and 13 (54%) with residual enhancement, of which five (21%) coincided with both recurrent symptoms and enhancement on follow-up MR imaging. The SPVA group had seven (37%) women with recurrent

symptoms and 12 (63%) with residual enhancement, of which seven (37%) coincided with both recurrent symptoms and enhancement on follow-up MR imaging. The GM group had three (27%) women with recurrent symptoms and three (27%) with residual enhancement, of which two (18%) coincided with both recurrent symptoms and enhancement on follow-up MR imaging (Table 7).

"Even in instances in which uterine volume decreases and the dominant fibroid shrinks, recurrence can be predicted when infarction of substantial fibroids is not achieved."

James B. Spies (43)

Discussion

We designed our study as a retrospective review of patients treated with UAE for symptomatic fibroids. We prospectively reviewed the pre-UAE and post-UAE MRI images for residual enhancement, and prospectively conducted a survey of patients to assess improvement of fibroid-related symptoms. We were interested in evaluating the symptomatic and imaging outcomes among three embolic agents routinely used at our institution between 1999 and 2005. In a previous study, Pelages et al showed that incompletely infarcted fibroids are likely to continue to grow after embolization, and thus are more likely to cause recurrent symptoms in the future (42). Similarly, we used gadolinium-enhanced MR imaging to classify the degree of perfusion of the fibroids because we believe that contrast enhanced MR imaging is the best way to adequately evaluate fibroid perfusion after fibroid ablative therapy such as UAE. Other techniques such as ultrasound or non-contrast MRI would not detect the perfusion of the fibroids, thus are not adequate for the purposes of this study.

In our study, statistically significant differences in recurrence of residual enhancement on follow-up MR imaging of 101 patients were found between SPVA and PVA, as well as SPVA and GM, but not between PVA and GM. Patients embolized with SPVA have a higher risk of having residual enhancement on follow-up MR imaging than

those embolized with PVA or GM. This is particularly important because of the associated risk of developing recurrent fibroid-related symptoms with incomplete infarction of fibroids after UAE as detected by gadolinium enhanced MR imaging (41, 42). It is likely, that if follow up of the SPVA patients were longer, recurrence of symptoms would have occurred in larger number of patients. Embolic agents available for UAE have different properties, which show statistically significant differences in recurrence of enhancement on follow-up MR imaging.

It is conceivable that the differences in residual enhancement on patients embolized with SPVA could be due to a systematic error in our study. However, the endpoint used was the same endpoint that had been established for PVA, and all interventional radiologists performing the UAE had experience with this endpoint using all three embolic agents. We also attempted to minimize false angiographic endpoints by performing post-UAE aortography to evaluate perfusion of fibroids by uterine arteries or by collateral ovarian arteries. The size of the embolic agents used was 500-700 Microns for SPVA and GM, with increase to 700-900 Microns in some patients, and 355-500 Microns for PVA with increase to 500-755 Microns in some patients. Only a small number of patients were embolized with two different sizes of a single embolic agent.

The MRI findings prior to the procedure of patients across the three embolic agent groups were comparable, although the uterine volume was somewhat larger for patients embolized with SPVA and GM than it was with PVA, yet this difference was not statistically significant. Patients with larger fibroid burden became eligible for the procedure as new embolic agents became available and the procedure was more widely accepted by patients and clinicians.

We used gadolinium-enhanced MR imaging to obtain qualitative estimates of the percent of enhancement of all fibroids. This is different than previous studies, which measure the enhancement of the dominant leiomyoma (41, 42, 48, 49). Recent studies have taken into consideration the enhancement properties of all fibroids as a means of assessing clinical outcomes for UAE (33, 37). We felt that it was important to consider the perfusion of all fibroids, rather than only the dominant fibroid, to thoroughly determine whether fibroids are at higher risk of recurring after UAE. We agree with Spies et al. (37) that had we used ultrasonography or non-contrast MR imaging, we would not have detected a difference among the three embolic agents. Our method may be responsible for the relative high frequency of incomplete infarction across all embolic agents considered in our study.

In our study, we took the necessary steps to reduce the technical causes of failure to a minimum (43). Microcatheters were used to reduce spasm of the uterine arteries, and thus preventing a false angiographic endpoint. Embolization endpoints used were the standard of care at the time of the UAE. Although we included four women who underwent unilateral UAE due to the absence of angiographically visible bilateral uterine arteries, none of these women were embolized with SPVA.

The embolization techniques used varied according to the standards for each embolic agent. The endpoint for patients undergoing UAE with spherical or nonspherical PVA was near-stasis. Alternatively, the endpoint for patients undergoing UAE with GM was sluggish-flow, according to the technique described by Spies et al (34).

We performed abdominal aortography before and after UAE to evaluate for enlarged ovarian arteries, which are a known source of collateral flow to the fibroids (44).

We feel that it is important to minimize the cause of technical failures for this procedure, particularly when evaluating the effectiveness of different embolic agents. The question of aortography use in routine practice is beyond the scope of this study.

One of the limitations of our study was that the selection of embolic agent for each embolization procedure was non-randomized. There were a small number of patients that met the inclusion criteria, which may have affected the results of other outcome measures. We also did not have complete baseline information to compare the fibroid-related symptoms before and after the treatment, thus resulting in potential for recall bias.

Another limitation was that the completion of the survey took place at a separate time from the post-UAE. We, therefore, have no imaging data to exactly correlate with the symptomatic status of the patients as portrayed by their survey answers. The most recent patients included in the study underwent embolization with SPVA and GM, accounting for a shorter follow-up interval for these patients compared to the interval for the PVA patients. Lastly, the patients were embolized by one of three experienced interventional radiologists, who may have variations in technique.

The correlation between symptom recurrence and MR enhancement recurrence after UAE does not show statistically significant differences between the three embolic agents with the current sample of 54 patients. Patients with residual enhancement on post-UAE MRI may not have developed symptoms at the time the survey was completed. On the other hand, the patients whose survey responses show worsening or recurrence of symptoms while the MRI showed no residual enhancement can be explained by the time

between acquisition of the MRI sequences and the completion of the survey. In some cases, the patients returned the survey up to 4 years after the UAE.

We individually evaluated every survey for signs of symptom recurrence. We did not have baseline, pre-UAE surveys to compare, thus we relied on patient's ability to remember their symptoms before the embolization and compare them to their present state. Furthermore, it was challenging to compare the surveys across the three groups because the time lapsed between UAE and completion of survey varied highly among the three groups. Interestingly, regardless of whether the patient had a successful embolization or eventually developed recurrent symptoms and underwent further therapy (from hysterectomy to repeat UAE), the majority of the women treated were glad to have chosen UAE, and would opt to repeat the procedure rather than undergo a hysterectomy if the need arose.

The failure of SPVA in our study, in accordance with the previous study by Spies et al. (37), raises the question about the quality of evidence that we consider for products that are introduced into practice. It is clear that both the composition of embolic agents, as well as their size and shape are important factors that affect the way they behave once deployed. It is important for future studies to use adequate imaging protocols to measure the outcomes when evaluating new embolic agents prior to their use in clinical practice.

The reason for the higher incidence of residual enhancement following UAE with SPVA can only be speculated. Indirect evidence suggests that SPVA migrates more distally than other embolics (50). Perhaps it is compressed as it passes through the microcatheters, and thus temporarily assumes a different shape, allowing it to travel through smaller vessels. It is also possible that the material clumps after it is compressed

in the microcatheter, and thus causes occlusion of a proximal vessel, resulting in a false angiographic endpoint. At some point after the procedure is completed, the clump can break down and migrate distally to incompletely occlude all of the fibroid vessels.

When used as described in our methods, SPVA has a substantially lower likelihood of achieving complete infarction of uterine fibroids in comparison to GM and PVA. However, there are currently no studies evaluating the effectiveness of different embolization techniques with SPVA, which could produce a higher infarction rate. In conclusion, nonetheless, it is our opinion that spherical poly-vinyl alcohol (SPVA) does not qualify as an effective embolic agent for Uterine Artery Embolization for symptomatic fibroids.

Conclusions

In summary, we designed a retrospective study comparing symptom and imaging outcomes among three embolic agents available for uterine artery embolization.

We hypothesized that there are differences in clinical outcome among the three embolic agents: PVA, SPVA and GM. We found that there is a higher incidence of incomplete infarction for patients who underwent UAE with SPVA as measured by gadolinium-enhanced MRI when compared to both PVA and GM, but there is no difference in infarction rates of fibroids between PVA and GM. We found no statistically significant differences among clinical outcomes when grouping residual MR enhancement and recurrent symptoms based on the questionnaire responses. However, this could be due to the small sample of patients who completed the survey.

In conclusion, poly-vinyl alcohol spheres, when used as described in the methods section, is not an effective embolic agent for use in uterine artery embolization for treatment of symptomatic fibroids.

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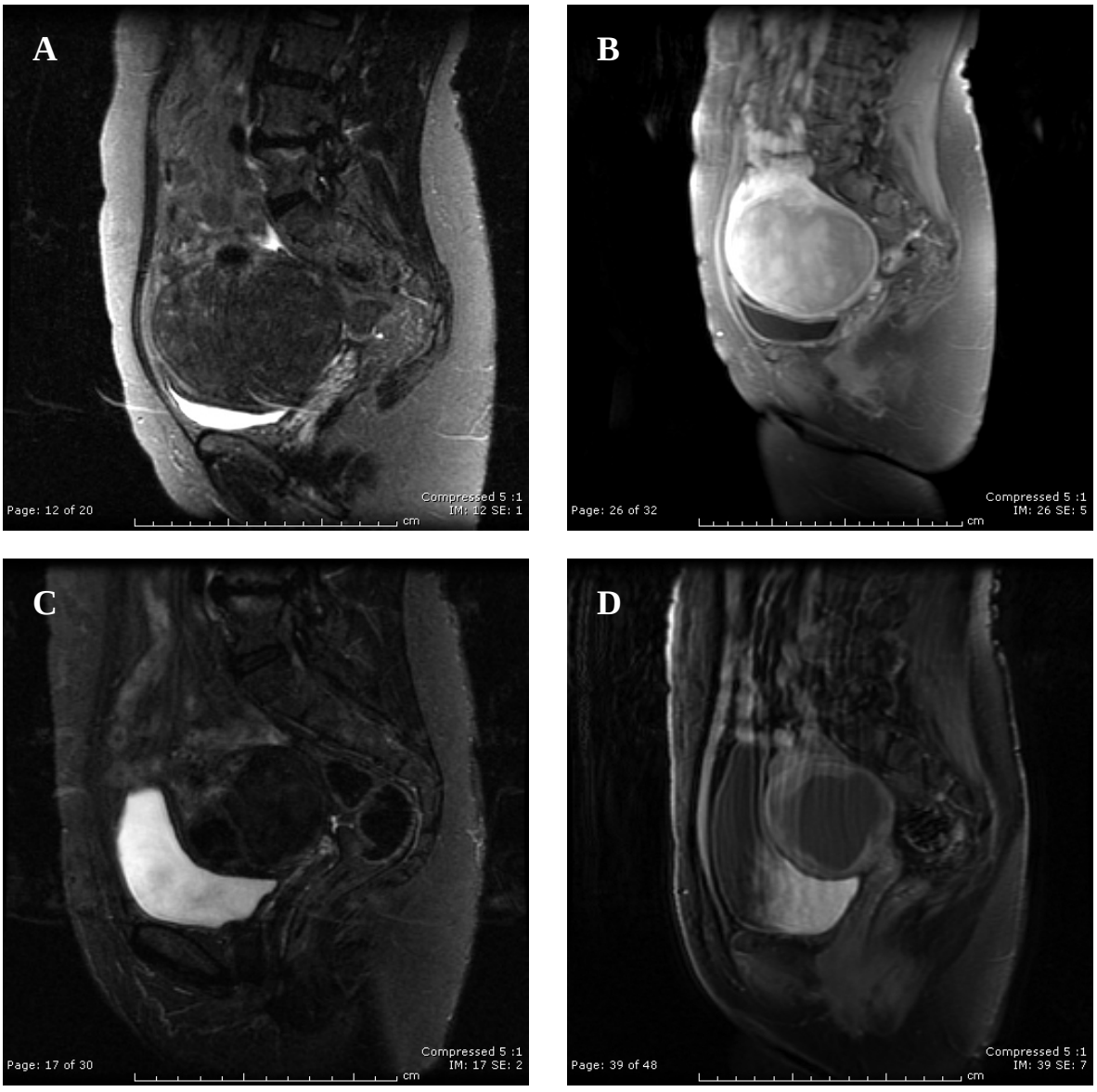
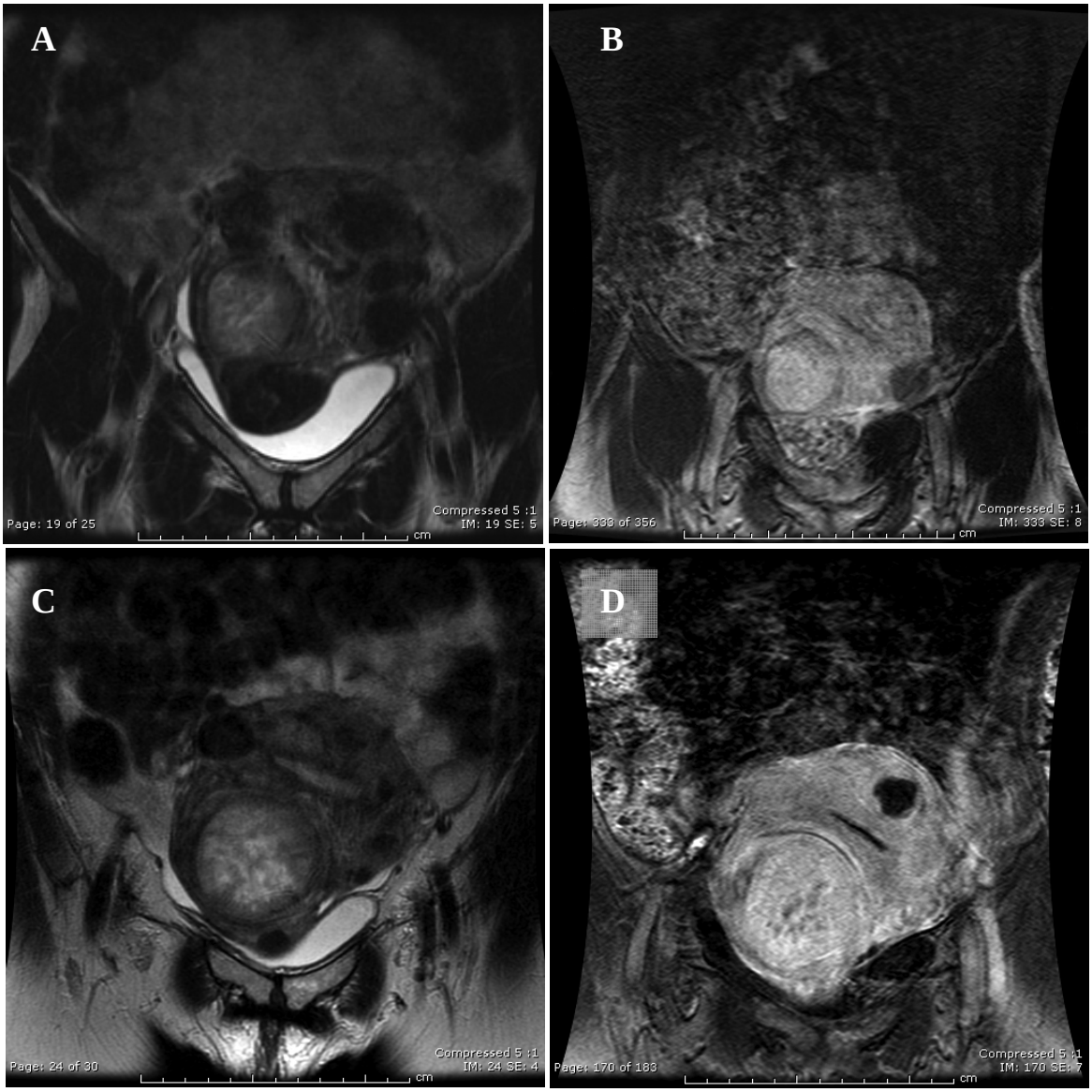
Appendix A - Figures

Figure 1 – MRI studies before and after UAE with PVA particles.(PVA)



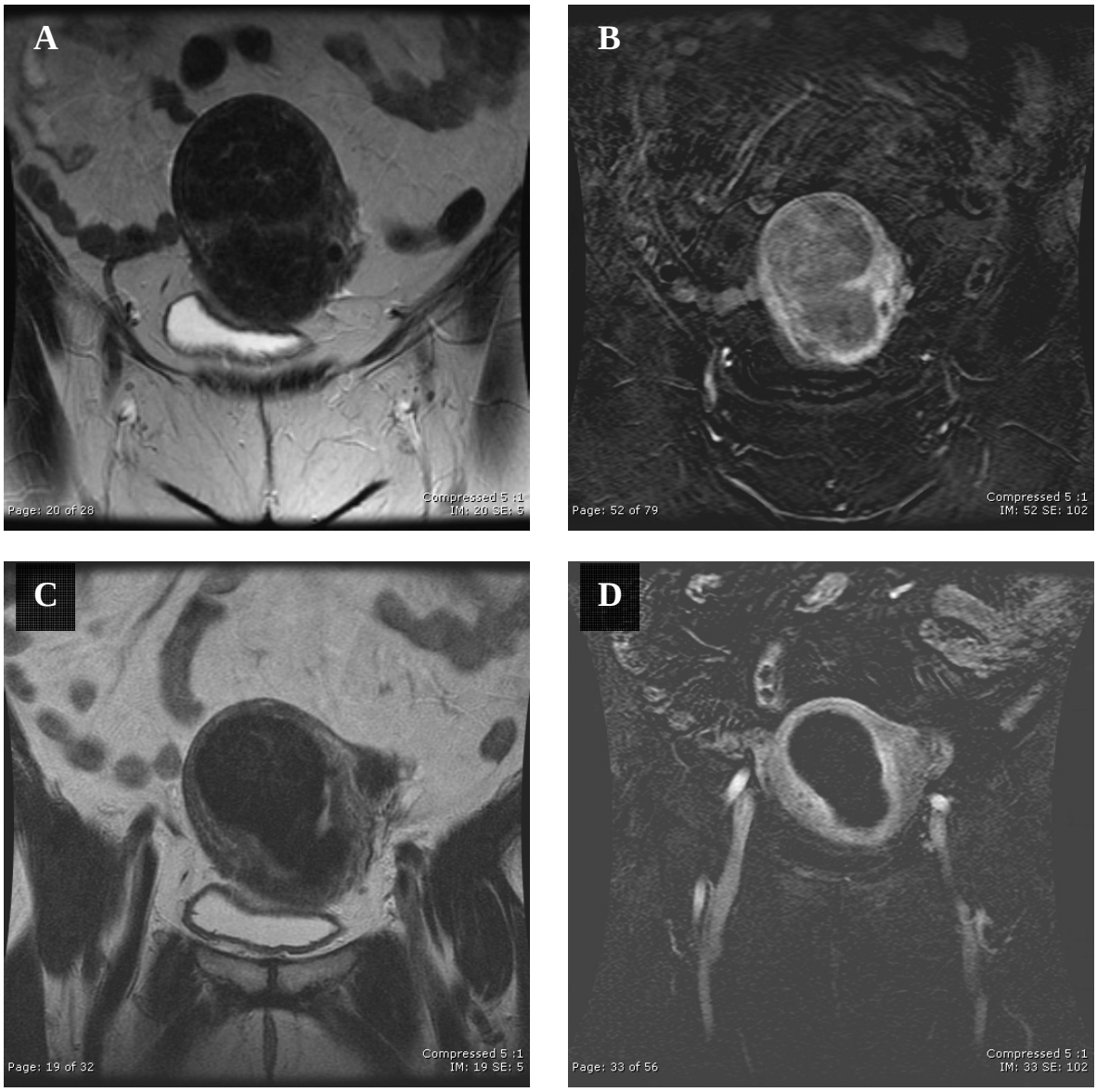
Pre-UAE imaging shown in (A): T2-weighted sagittal image demonstrating large fibroid, which (B) completely enhances on sagittal gadolinium SPGR sequence (B). Follow-up imaging approximately 10 months after UAE shows the fibroid have diminished in size on (C) T2 sagittal-weighted image, and (D) are no longer enhancing post-gadolinium administration.

Figure 2 - MRI studies before and after UAE with poly-vinyl alcohol spheres (SPVA) particles.



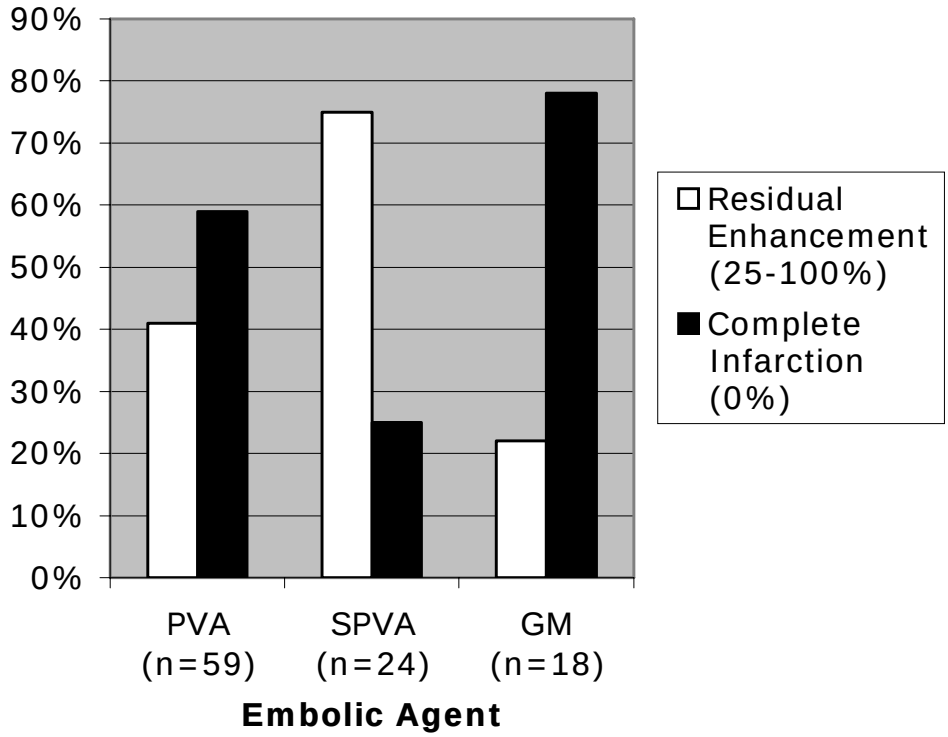
Pre-UAE MRI scans shown (A and B); Multiple large fibroids visible on coronal T2-weighted image (A) which completely enhance with gadolinium administration (B). Follow-up imaging at 7 months after UAE shows several fibroids on T2-weighted coronal image (C) that continue to demonstrate complete enhancement following gadolinium administration (D).

Figure 3 - MRI studies before and after UAE with tris-acryl gelatin (GM) particles.



Pre-UAE imaging shows two large fibroids on T2-weighted coronal image (A) which completely enhance post-gadolinium administration (B). Follow-up at 5 months after UAE show some decrease in the size of fibroids on T2-weighted coronal image (C) with no residual enhancement post-gadolinium administration (D).

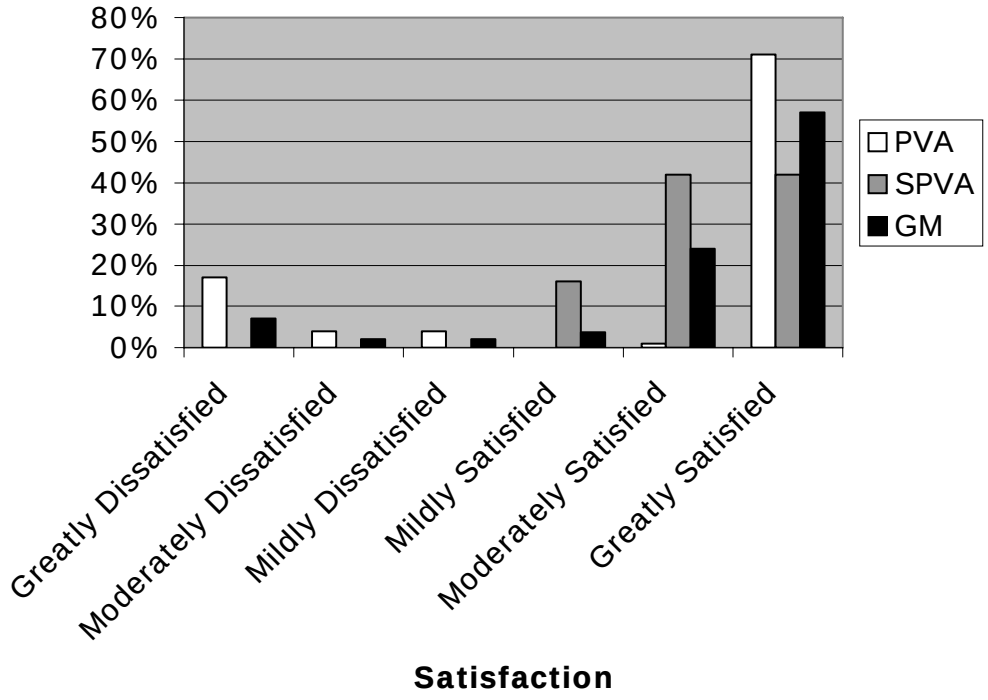
Figure 4 - Correlation of embolic agents with post-UAE gadolinium-enhanced MRI residual enhancement



Statistical analysis with 2-tail Fisher's exact test, PVA-SPVA (24, 35, 18, 6) p=0.0072; SPVA-GM (18, 6, 4, 14) p=0.0015); PVA-GM (24, 35, 4, 14) p=0.1756.

	Residual Enhancement (25-100%)	No Residual Enhancement (0%)
PVA	24 (41%)	35 (59%)
SPVA	18 (75%)	6 (25%)
GM	4 (22%)	14 (78%)

Figure 5 - Patient satisfaction results from survey data



Summary of patient satisfaction items from survey data.

	PVA n=24	SPVA n=19	GM n=11	Overall
Willingness to undergo repeat UAE for recurrent symptoms	21 (88%)	15 (79%)	11 (100%)	47 (87%)
Willing to recommend UAE for treatment of fibroid-symptoms to friends	23 (96%)	19 (100%)	11 (100%)	51 (94%)

Appendix B – Tables

Table 1 – Baseline characteristics of women undergoing UAE (based on survey's returned)

	PVA	SPVA	GM
Number of patients (n=51)	n=24	n=16	n=11
Age (years)	49 (+/- 5.9)	45 (+/- 4.0)	45 (+/- 9.1)
Ethnicity			
African American	5 (21%)	7 (44%)	2 (18%)
Caucasian	17 (71%)	8 (50%)	6 (55%)
Asian	1 (4%)	0	1 (9%)
Hispanic	1 (4%)	0	0
Other	0	0	2 (18%)
Omitted	0	1 (6%)	0
Pre-UAE Therapies^			
No therapy	15 (63%)	8 (50%)	5 (45%)
Medical therapy	7 (29%)	6 (38%)	5 (45%)
Dilatation & Curettage	2 (18%)	2 (12.5%)	6 (54%)
Myomectomy	1 (4%)	3 (19%)	0
Endometrial Ablation	0	0	1 (9%)
Post-UAE Therapies^			
No additional therapy	18 (75%)	11 (69%)	7 (64%)
Medical Therapy	2 (8%)	1 (6%)	2 (18%)
Dilatation & Curettage	0	0	3 (27%)
Myomectomy	1 (4%)	0	0
Hysterectomy	2* (8%)	0	1** (9%)
Uterine Artery Embolization	1 (4%)	2 (13%)	0
Coexisting Adenomyosis[«]	16 (27%)	7 (29%)	3 (17%)

* One hysterectomy done to treat cervical cancer, and the other to treat fibroid-related symptoms.

** Hysterectomy done to treat fibroid-related symptoms.

^ Some patients underwent multiple therapies before and after UAE, thus numbers may not reflect sample size of 51.

[«] Percentage of patients with coexisting adenomyosis calculated from total patients with MRI studies (PVA n=59; CSE n=24; GM n=18)

Table 2 – Mean uterine volume measured before on pre-UAE MRI studies.

Embolic Agent	Mean Uterine volume
PVA	656 cc (± 440cc)
SPVA	802 cc (± 663 cc)
GM	757 cc (± 680 cc)

Measurements were obtained using the formula for volume of a prolate ellipse (transverse x craniocaudal x sagittal x 0.5233).

Table 3 – Baseline fibroid-related symptoms from survey

	PVA (n=24)		SPVA (n=16)		GM (n=11)	
Bleeding longer than 7 days during menstrual cycle						
Before UAE	13 (54%)		7 (44%)		11 (100%)	
After UAE	1 (4%)		2 (13%)		1 (9%)	
Mean number of sanitary towels used on heaviest day of bleeding during menstrual cycle						
	Mean (Std Dev)	*N*	Mean (Std Dev)	*n*	Mean (Std Dev)	*n*
Before UAE	6 (± 3)	17	9 (± 6)	13	11 (± 10)	11
After UAE	1 (± 2)	20	6 (± 6)	12	4 (± 5)	10
Mean number of tampons used on heaviest day of bleeding during menstrual cycle						
	Mean (Std Dev)	*n*	Mean (Std Dev)	*n*	Mean (Std Dev)	*n*
Before UAE	9 (± 6)	13	10 (± 7)	11	7 (± 3)	6
After UAE	2 (± 3)	19	5 (± 3)	8	1 (± 2)	11

Table 4 - Patients with coexisting adenomyosis showing either complete infarction of all fibroids on post-UAE MRI, or partial enhancement of some or all fibroids on post UAE MRI.

	PVA (n=54)	SPVA (n=24)	GM (n=18)
Incomplete Infarction	3 (6%)	3 (13%)	0 (0%)
Complete Infarction	12 (22%)	4 (17%)	3 (17%)

Table 5 - Summary of symptom outcomes from survey data.

		PVA n=24	SPVA n=19	GM n=11
Abdominal Distension				
	Deteriorating	0	1	0
	Initially improved then worsened	1	4	1
	No change	1	3	2
	Improve	18	10	7
	Never had Symptom	2	2	1
Urinary Frequency				
	Deteriorating	0	1	0
	Initially improved then worsened	0	1	2
	No change	2	3	0
	Improve	15	10	7
	Never had Symptom	5	4	2
Heavy Vaginal Bleeding				
	Deteriorating	0	0	0
	Initially improved then worsened	1	1	1
	No change	1	2	1
	Improve	16	16	10
	Never had Symptom	4	0	0
Pelvic Pressure or Pain				
	Deteriorating	0	1	0
	Initially improved then worsened	0	1	0
	No change	0	3	1
	Improve	15	11	10
	Never had Symptom	5	3	0
Dyspareunia				
	Deteriorating	n/a	1	1
	Initially improved then worsened	n/a	1	0
	No change	2	1	1
	Improve	5	5	4
	Never had Symptom	15	11	5
Hot Flashes				
	Deteriorating	2	0	1
	Initially improved then worsened	0	0	2
	No change	3	1	1
	Improve	4	0	1
	Never had Symptom	13	17	5

Note that discrepancies on survey answer totals are due to patients omitting answers to some of the questions on the survey.

Table 6 – Time between post-UAE MRI and completion of survey

	Months
SPVA	3.0 (± 4.0)
PVA	34.2 (± 16.3)
GM	10.7 (± 9.5)

Mean time (months) elapsing between post-UAE MRI study and completion of symptom questionnaire. The mean time difference between follow-up MR imaging and completion of survey was 34.2 months (+/- 16.3 months) for PVA, 3 months (+/- 4 months) for SPVA, and 10.7 months (+/- 9.5 months) for GM.

Table 7 – Correlation of follow-up MRI residual enhancement and recurrent symptoms

Agent	Residual Enhancement (25%-100%)		No Residual Enhancement (0%)	
	Recurrent Symptoms	Symptom-Free	Recurrent Symptoms	Symptom-Free
PVA (n=25)	5 (20%)	7* (28%)	2** (8%)	11 (44%)
SPVA (n=16)	7 (44%)	5* (31%)	0**	4 (25%)
GM (n=10)	2 (20%)	1* (10%)	1*** (10%)	6 (60%)

* Patients may not have developed recurrent symptoms yet despite having residual enhancement on post-UAE MRI.
** These patients were embolized with PVA, and follow-up MRI was done at six and 10 months after UAE, while surveys were returned at 5.4 and 2.3 years after UAE respectively. *** This patient was embolized with GM, who had the follow-up MRI at 2.2 months after UAE and returned the questionnaire at 8.5 months after UAE.
, * None of these patients had evidence of adenomyosis, enlarged ovarian arteries, or spasm during embolization procedure.

Instructions:

These questions ask about symptoms experienced by women who have uterine fibroids, as well as about treatments for fibroids, pregnancy, and sexual function. Please answer them as honestly as possible. There are no right or wrong answers. Your responses will be kept completely confidential.

UAE = Uterine Artery Embolization (Also known as Uterine Fibroid Embolization)

1. Last Name	First Name	Date of Birth

2. Ethnicity (circle one)

a. Caucasian b. African American c. Asian d. Other (specify):

3. Today's Date	4. Date of your uterine artery embolization (UAE) procedure?

5. What therapies did you have to treat fibroids **before your UAE?** (circle all that apply)
   a. I did not have any therapies to treat fibroids before UAE
   b. Medical therapy with (circle all that apply):
      i. Birth control pills
      ii. Anti-Inflammatory (such as Motrin, Alleve, Advil, Aspirin, Ibuprofen)
      iii. Lupron (also known as Leuprolide)
      iv. Other (circle one): Danazol / Gestrione / Raloxifene / Mifepristone (RU-486)
   c. Myomectomy (surgical removal of fibroids without hysterectomy)
   d. Endometrial ablation (removing the uterine lining using laser or electrosurgery)
   e. D&C (scraping and removing the uterine lining using a curette inserted through the vagina)
   f. Other (specify): _____

6. What therapies have you had *after* your UAE for recurrent or continuing fibroid-related symptoms, or due to a complication of UAE? (circle all that apply and specify the reason why)
   a. I have not had any additional therapies after UAE
   b. Repeat UAE: reason why - _____
   c. Hysterectomy (surgical removal of uterus) – reason _____
   d. Myomectomy - _____
   e. Medical therapy with (circle all that apply) reason _____
      a. Birth control pills
      b. Anti-inflammatory (such as Motrin, Alleve, Advil, Aspirin, Ibuprofen)
      c. Lupron (also known as Leuprolide)
      d. Other (circle one) Danazol / Gestrione/ Raloxifene / Mifepristone RU-486
   f. endometrial ablation – reason: _____
   g. D&C – reason: _____
   h. Other (specify reason): _____

II. Fibroid-related symptoms

1. Before UAE, did your menstrual periods last longer than 7 days? YES NO

2. Before uterine artery embolization (UAE), approximately how many pads and/or tampons did you use on the heaviest day of bleeding during your menstrual period? (fill in the blanks)
Number of pads = Number of tampons =

3. When did your menstrual periods resume after UAE (circle one)
e. My menstrual periods have not resumed after UAE
f. Within 1 month after UAE
g. Within 3 months after UAE
h. Within 6 months after UAE
e. Within 9 months after UAE
f. Within 12 months after UAE
g. Other: Within ____ months after UAE.

4. If your menstrual periods have resumed after UAE, is your menstrual cycle regular? YES NO

5. Now (during the past 3 months), do your menstrual periods last longer than 7 days?
a. YES: this began approximately ____ months after UAE
b. NO

6. Now (during the past 3 months), approximately how many pads and/or tampons do you use on the heaviest day of bleeding during your menstrual period? (circle one)
a. Number of pads = _____ Number of tampons = _____
b. I have not had menstrual periods during the past three months

7. At any time after UAE, have you had a recurrence of any fibroid-related symptoms?
a. YES : the following symptoms have recurred: _____ b. NO

8. How would you rate the following fibroid-related symptoms **now** (during the past 3 months) in comparison to before you underwent UAE? (for each symptom, check one box)

	Never had this symptom	New symptom since UAE	Much worse	Slightly worse	No change	Slightly improved	Much improved	Completely resolved	Initially improved but then got worse
Abdominal distension/ bulk									
Urinary frequency/urgency									
Heavy vaginal bleeding									
Pelvic pressure / pain									
Painful sexual intercourse									
Hot flashes									

9. If your fibroid-related symptom(s) improved after UAE, how long did it take for them to improve (for each symptom, check one box).

	Did not have symptom before UAE	Improved within 1 month	Improved within 6 months	Improved within 12 months	Improved within 24 months	Initially improved but then got worse	Did not improve at all
Abdominal Distension/bulk							
Urinary frequency/urgency							
Heavy vaginal bleeding							
Pelvic Pressure/pain							
Painful sexual intercourse							
Hot flashes							

1. Before UAE, did you think you might want to try to get pregnant after UAE? Yes No

2. Before UAE, how many times had you been pregnant, including miscarriages and abortions/surgical terminations of pregnancy (fill in the blanks with a number)

a. Number of pregnancies before UAE = _____
b. Number of miscarriages before UAE = _____
c. Number of abortions/surgical terminations before UAE = ____

3. After UAE, have you tried to get pregnant? (circle one) Yes No

4. After UAE, have you engaged in heterosexual intercourse without contraceptive use? (circle one)
Yes No

5. After UAE, how many times have you been pregnant, including miscarriages and abortions/surgical terminations of pregnancy? (fill in the blanks with a number)

a. Number of pregnancies after UAE = ___
b. Number of miscarriages after UAE = ___
(i) how far along in the pregnancy were you when the miscarriage occurred? ___
(ii) how many months after UAE did the miscarriage occur? ___
c. Number of abortions/surgical terminations after UAE? ___

6. If you have been pregnant after UAE, please answer the following questions about each baby you have delivered. If you have not been pregnant after UAE, please skip this question.

a. What was your delivery date? (m/d/y)? _____
b. What was the original due date of your pregnancy? (m/d/y) _____
c. How much did your baby weigh? (lbs and ozs) _____
d. How was your baby delivered? (circle one)
(i) Vaginal (including forceps or vacuum)
(ii) Planned C-section
(iii) C-section after labor started
e. Baby's position right before delivery: (circle one)
(i) head first
(ii) feet first
(iii) sideways
(iv) I don't know
f. Did you have any complications? (circle as many as apply)
(i) no complications
(ii) uterine rupture
(iii) retained placenta
g. Other (please specify) _____

7. Were you ever diagnosed with any of the following conditions? (circle all that apply and specify appropriate date of diagnosis)

a. Adenomyosis, diagnosed _____
b. Endometriosis, diagnosed _____
c. Pelvic inflammatory disease, diagnosed _____
d. Infertility (specify) _____; diagnosed _____
e. I have not been diagnosed with any of the above conditions.

IV. Sexual Function Questions

1. How would you rate the following aspects of your sexual function now (during the past three months) in comparison to before UAE? (for each aspect of sexual function, check one box).

In answering this section, the following definitions apply:

- Sexual desire or interest: wanting to have a sexual experience, feeling receptive to a partner's sexual initiation, and thinking or fantasizing about having sex
- Sexual arousal: a feeling that includes both mental as well as physical aspects of sexual excitement, including feelings of warmth or tingling in the genitals, lubrication/wetness, or muscle contractions

	Much worse	Slightly worse	Unchanged	Slightly improved	Much improved	Initially improved but then got worse
Sexual desire or interest						
Sexual arousal						
Orgasm/climax (frequency/intensity)						
Discomfort or pain during sexual intercourse						
Overall satisfaction with sexual function						

V. Treatment of Satisfaction Questions

1. Would you be willing to undergo another UAE if necessary to treat recurrent or continuing fibroid-related symptoms? (circle one) YES NO

2. Would you recommend UAE to other women for treatment of symptomatic fibroids (circle one) YES NO

3. Overall satisfaction rating with UAE (circle one)
   a. Greatly Dissatisfied
   b. Moderately Dissatisfied
   c. Mildly Dissatisfied
   d. Midlly satisfied
   e. Moderately Satisfied
   f. Greatly Sastisfied

Thank you for completing this questionnaire! Please return it in the pre-addressed, pre-stamped envelope. If the envelope has been misplaced, please return the questionnaire to the physician(s) who performed your uterine artery embolization (UAE)

Michael Tal MD, Jeffrey Pollak MD, or Robert White MD
Yale-New Haven Hospital
Department of Diagnostic Radiology
20 York St 2-213 SP
New Haven, CT. 06520-8042

Appendix D – Presentations

Galvez J, McCarthy S, Tal M, et al. **Comparison of MRI and symptom outcomes of uterine artery embolization for uterine leiomyoma using tris-acryl gelatin microspheres, poly-vinyl alcohol spheres and poly-vinyl alcohol particles.** Radiology Society of North America 2005.

Galvez J, Pollak J, Tal M. **Repeat uterine artery embolization after recurrence of symptoms.** Radiology Society of North America 2005.

Galvez J, McCarthy S, Pollak J, Tal M. **MRI Determined Tissue Perfusion Of Ovaries, Myometrium And Fibroids Before And 6 Months After UAE.** Society of Interventional Radiology, March 2005.

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JVIR SUPPLEMENT (S1-S132)
Journal of Vascular and Interventional Radiology
February 2005 ◆ Volume 16 ◆ Number 2 ◆ Part 2

Outpatient vs Inpatient UFE

	Inpatient UFE (n=82)	Outpatient UFE (n=19)	p
Technical success	97%	95%	0.53
Mean hospital stay (h)	21.3	8	N/A
% of patients reporting return visit to MD for related problems	45%	26%	0.20
% of patients reporting readmission for related problems	8%	0%	0.58
Mean length of readmission (d)	0.21	0	N/A
Median patient satisfaction with management of post-UFE pain	9.75	10	0.85
Median overall patient satisfaction with UFE procedure/process	10	9.5	0.54

Abstract No. 222

Initial Experience with Use of PVA Microspheres for UFE: Results of a Prospective Two Center Registry.

T.J. Kroencke, Charité Campus Mitte, Berlin, Germany · L.E.H. Lampmann · F. Boekkooi · C. Scheurig · B. Hamm · P.N.M. Lohle

PURPOSE: To evaluate the safety, technical efficacy and clinical effectiveness of a new polyvinyl alcohol (PVA) microsphere for uterine fibroid embolization (UFE).

MATERIALS AND METHODS: Bilateral UFE using 500-1200 µm PVA microspheres (BeadBlock®) was performed in 42 patients (pts.), median age 43 years (range 34-54 years), with symptomatic uterine fibroids. Primary objective was the clinical efficacy as measured by the uterine fibroid symptom severity & quality of life questionnaire (UFS-QOL®) and patient satisfaction using a 10 point visual analogue scale translated into 5 descriptive categories (very satisfied, satisfied, mixed results, unsatisfied, very unsatisfied). Secondary objectives included a comparison of baseline and follow-up contrast-enhanced magnetic resonance (MR) imaging data at 3 and 6 months after UFE with respect to fibroid perfusion and dominant fibroid volume.

RESULTS: Bilateral UFE was technically successful in 42/42 pts (100%). Minor complications occured in 2 pts. No major complication or emergency hysterectomy was observed. At 3 months follow-up 14/30 pts. (46.7%) were very satisfied, 9/30 pts. (30%) satisfied, 5/30 pts. (16.7%) reported mixed results and 2/30 pts. (6.7%) were unsatisfied with the clinical results. Dominant fibroid volume decreased in 28/30 pts (93.3%) from a median volume of 280 cc (range: 7-1072 cc) to 98 cc (range: 0-614 cc). On contrast-enhanced MR imaging 100% devascularization of all previously detected fibroids was seen in 14/30 pts. (46.7%), 90-99% in 11/30 pts (36.7%), 20-50% in 3 pts. (10%; one of them with ovarian artery supply). 2 pts. (6.7%) had 0% infarction of targeted fibroids and were re-embolized. Final data compilation of 3 and 6 months follow-up including UFS-QOL scores to be collected by March 2005 and presented at the meeting.

CONCLUSION: BeadBlock® PVA microspheres are a safe embolic agent for UFE. More than two thirds of patients treated were satisfied regarding alleviation of symptoms at short term follow-up. Devascularization of targeted fibroids is lower than expected and possible explanations will be presented.

Abstract No. 223

MRI Determined Tissue Perfusion of Ovaries, Myometrium and Fibroids before and 6 Months after UAE.

J.A. Galvez, Yale University School of Medicine, New Haven, CT, USA · S.M. McCarthy · J. Pollak · M. Tal

PURPOSE: To evaluate the tissue perfusion of myometrium, fibroid, and ovarian stroma with MRI before and 6-months after uterine artery embolization (UAE) with two different embolic materials.

MATERIALS AND METHODS: This ongoing study comprised of 12 women (ages 31 to 55) with uterine fibroids who underwent UAE with Contour SE spherical Poly-Vinyl Alcohol (SPVA) particles (n=6) or Embosphere Microspheres (MS) (n=6) in 2003-04. MRI studies were obtained before and six months after UAE. Regions of interest on 3DSPGR gadolinium enhanced sequences were measured for myometrium, ovarian stroma, and largest enhancing fibroid, if one enhanced, as a means of comparing perfusion of tissues before and after embolization. Statistical analysis was performed using paired student t-test.

RESULTS: Preliminary analysis of twelve UAEs demonstrated no significant difference in perfusion before and after UAE of the myometrium, ovarian stroma and dominant fibroid between the two groups. In this initial data set, the trend shows improved perfusion of myometrium with SPVA compared to MS, and no change in perfusion of ovarian stroma after UAE. As anticipated, there was reduced perfusion to the dominant fibroid. The data are presented in the table below.

Mean Enhancement for Largest Enhancing Fibroid, Myometrium and Ovarian Stroma

		Contour SE Poly-Vinyl Alcohol (n=6)	Embosphere Microspheres (n=6)
Fibroid	Pre	68.33 (+/- 34.41)	43.17 (+/- 22.65)
Fibroid	Post	50.00 (+/- 24.45)	19.00 (+/- 5.94)
Myometrium	Pre	62.83 (+/- 19.59)	50.33 (+/- 23.43)
Myometrium	Post	50.00 (+/- 16.58)	49.67 (+/- 20.80)
Right Ovary	Pre	30.50 (+/- 15.41)	17.00 (+/- 4.06)
Right Ovary	Post	16.80 (+/- 4.15)	20.67 (+/- 7.00)
Left Ovary	Pre	19.17 (+/- 5.81)	20.60 (+/- 4.45)
Left OvaryPost UAE	Post	18.00 (+/- 7.48)	29.40 (+/- 11.57)

CONCLUSION: Preliminary data show there was no significant difference in myometrial or ovarian perfusion before and at six months post-embolization. In addition, no significant difference in perfusion between the two UAE embolic materials was seen. In those that exhibited residual enhancement, there was no significant difference compared to the pre-UAE MRI.

Abstract No. 224

Treatment of Primary Post-Partum Hemorrhage with Uterine Artery Embolization.

J.M. Kirby, University Health Network, Toronto, ON, Canada · J.R. Kachura · D.K. Rajan · R.D. Lim · J.C. Kingdom · R.C. Windrim

PURPOSE: To evaluate the efficacy and safety of uterine artery embolization in the treatment of primary post-partum hemorrhage, and factors associated with clinical success.

MATERIALS AND METHODS: A retrospective analysis of all patients undergoing uterine artery embolization for primary post-partum hemorrhage from 1996 to 2004 at 2 hospitals was conducted. Imaging studies and patient records were reviewed. Adverse outcome was defined as need for repeat embolization, laparotomy, hysterectomy after embolization, or death.

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METHOD AND MATERIALS: 277 ultrasound studied breast lesions on which percutaneous or surgical biopsy was performed, were retrospectively evaluated by two experienced radiologists who are unaware of the diagnosis. Each lesion was classified according to BI-RADS descriptors and was categorized by the BI-RADS final assessment categories. The positive and negative predictive values (PPV and NPV) of ultrasound features and assessment categories was calculated.
RESULTS: Carcinoma was present in 174/277 lesions. 2 cases were assigned to class II (2 benign lesions), 37 to class III (2 malignant and 35 benign lesions), 102 to class IV (48 malignant and 54 benign lesions), and 136 to class V (124 malignant and 12 benign lesions). ACR BI-RADS US showed 0.75 accuracy, 0.99 sensitivity, 0.36 specificity, 0.72 PPV and 0.95 NPV. NPV for classes II and III were 100% and 94.6%. PPV for classes IV and V were 47% and 91.2%. Typical signs of malignancy was irregular shape, anti-parallel orientation, not-circumscribed margin, echogenic halo and decreased sound transmission. Typical signs of benignity was oval shape, circumscribed margin, and anechoic or hyperechoic echo pattern.
CONCLUSIONS: Placing ultrasound breast lesions into BI-RADS categories allows quantification of the likelihood of carcinoma. The results of our study confirm that US represent a valid diagnostic tool in differentiating benign from malignant breast masses.

Monday Morning · Room E253CD

ISP: Vascular/Interventional (Women's Intervention)

VI

PRESIDING: **Matthew A. Mauro, MD★**, Chapel Hill, NC
Computer Code: SSC02 • AMA PRA Category 1 Credit: 1.5 • ARRT Category A Credit: 1.5
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SSC02-01 • 10:30 AM
Vascular/Interventional Keynote Speaker
J.B. Spies, MD▲, Washington, DC

SSC02-02 • 10:40 AM
Post Uterine Artery Embolisation (UAE) Leiomyoma Enhancement on Follow-up MRI: Etiology and Clinical Significance
C.J. Johnston, MD★, Dublin, Ireland • D.J. Tuite, MBBCH, FFRRCSI★ • S.M. Ford, MBBCh★ • M.F. Ryan, MD★ • N. Mc Eniff, MBBCH★
PURPOSE: To determine the etiology and clinical significance of persistent enhancement on MRI in uterine leiomyomata post UFE
METHOD AND MATERIALS: 300 consecutive women were treated between May 1999 and February 2004. Indications for treatment were menorrhagia, menstrual pain, abdominal swelling or other pressure effects. Bilateral uterine artery embolization was performed using hydrophilic microspheres (500-700um). Nonselective abdominal aortography was performed pre-embolization to visualize and characterize any collateral ovarian supply. Post gadolinium MRI was performed pre-procedurally and at 6 months post UAE. Significant fibroid enhancement on post UAE MRI was correlated with patient symptoms and with retrospective review of initial flush aortogram for the presence of ovarian collaterals.
RESULTS: 28 (9.3%) patients had post UAE MRI pelvis that showed significant enhancement post contrast injection. 26/28 (92.9%) patients had recurrent symptoms versus 28/272 (10.3%) in the group with no enhancement on MRI post procedure ($p<0.05$). Aetiology of post UAE leiomyoma enhancement ranged from failure to cannulate both uterine arteries (unilateral embolization – 1 patient), to inadequate embolisation (17 patients). In 10 patients there was significant ovarian collateral supply to the fibroid uterus (bilateral in 6 patients, unilateral in 4 patients). The presence of ovarian collaterals correlated significantly with post UAE leiomyoma enhancement on MRI (10/28 patients (35.7%) in enhancement group vs. 41/272 (15.0%) patients with ovarian collaterals in non enhancement group, $p<0.05$).
CONCLUSIONS: Post UAE leiomyoma enhancement correlates significantly with patient symptoms. The presence of ovarian collateral supply is a major factor in post UAE leiomyoma enhancement.

SSC02-03 • 10:50 AM
Correlation of Incomplete Infarction on MRI and Long-term Symptom Recurrence among Three Different Embolic Agents for Uterine Artery Embolization
J. Galvez, BS★, New Haven, CT • S.M. McCarthy, MD, PhD★ • J.C. Weinreb, MD★ • J.S. Pollak, MD★ • R.I. White, MD★ • M.G. Tal, MD★ • et al (jorge.galvez@yale.edu)
PURPOSE: To compare the long-term recurrence of symptoms (6 months to 5 years) with 6-month MRI findings in women treated with UAE with Polyvinyl Alcohol Particles (pPVA) Polyvinyl Alcohol Spheres (Contour SE), or Gelatin microspheres(GM).
METHOD AND MATERIALS: 247 women treated with UAE from 1999-2004 were asked to complete a symptom survey. The survey was designed to evaluate fibroid-related symptom recurrence. Women reporting any symptom worsening after initial improvement, or development of any new symptoms were classified as symptomatic recurrence of fibroids. Post-embolization MRI was evaluated for any residual enhancement on any of the fibroids was considered incomplete infarction. Of the 46 women in this study, 23 women were treated with pPVA, 14 were treated with Contour SE, and 9 were treated with GM. UAE endpoint was near stasis in both uterine arteries.
RESULTS: Mean MRI follow-up was 6 months, and mean survey follow-up was 27 months. 46 women returned the symptom questionnaire (modified UFS-QOL). 6 (26%) and 2 (22%) patients treated with pPVA particles and GM, respectively, had recurrence of some symptoms and residual enhancement on MRI, compared to 6 (43%) of patients treated with Contour SE. 12 (52%) and 5 (56%) of women treated with pPVA particles and GM were symptom-free and had no residual enhancement on follow-up MRI compared to 3 (21%) of those treated with sPVA. 3 women (6.5%) had no residual enhancement on MRI but still had recurrence of some symptoms in the questionnaire. 9 patients (19.6%) had residual enhancement on MRI but no recurrent symptoms. The positive predictive value (PPV) of MRI to detect patients who will have recurrent symptoms is 65%. 89% of the women reported being satisfied with the procedure. 87% stated they would be willing to undergo a repeat UAE if symptoms recurred.
CONCLUSIONS: Preliminary data shows a correlation between incomplete infarction on MRI and recurrence of fibroid-related symptoms. Patients treated with Contour SE particles have a higher rate of incomplete infarction on MRI, and long-term symptom recurrence. The women in the study were satisfied with the procedure, and the majority would consider a second UAE to treat recurring fibroid-related symptoms.

SSC02-04 • 11:00 AM
Repeat Uterine Artery Embolization after Recurrence of Fibroid-related Symptoms
J. Galvez, BS★, New Haven, CT • J.S. Pollak, MD★ • M.G. Tal, MD★ (jorge.galvez@yale.edu)
PURPOSE: To evaluate the repeat uterine artery embolization (UAE) as a treatment option for patients with recurrent fibroid-related symptoms after initial UAE.
METHOD AND MATERIALS: Of 247 patients treated with UAE from 1999 until December 2004, 12 patients presented with recurrence of symptoms warranting further treatment. Of those, 5 opted to have a hysterectomy, 2 had myomectomy and 5 had a repeat UAE procedure. The time of recurrence, type of symptoms, MRI appearance of the uterus and fibroids before and after the first and second embolization were recorded. In addition, the technical aspects of the initial procedure and second embolization procedure, including type of embolic material used, amount of material used and other technical aspects of the procedures were recorded.
RESULTS: 12 of 247 (4.9%) patients had treatment for fibroid-related symptoms after initial improvement since treatment with UAE. No differences in recurrence rates were found among the different embolic agents used in our patient population. 5 of these patients underwent repeat UAE. When comparing the first and second embolization procedures, greater amount of embolic material was used in the second embolization. In addition, patients reported that post-procedure pain was markedly worse after the second embolization compared to the post procedural pain after the initial embolization. No complications have been documented, and all patients treated with repeat embolization reported symptomatic improvement at follow-up.
CONCLUSIONS: Small number of patients (4.9%) who undergo uterine artery embolization for uterine fibroids may develop recurrent fibroid-related symptoms after short interval of symptom improvement. Repeat UAE, which may require greater amount of embolic material, is an effective therapy for management of recurrent fibroid-related symptoms.

Appendix E: Press-Releases

November 2005

Fibroid treatment outcomes vary with embolic agent

By: Emily Hayes

The message of a Monday morning interventional session at the RSNA meeting was clear: When it comes to embolization of uterine fibroids, all embolic agents are not created equal.

The success of uterine artery embolization (UAE), a minimally invasive treatment for fibroids, can be related to the type of embolic agent used, according to research conducted at Yale University Medical Center. Some agents show better results than others, said presenter Jorge Galvez.

The finding has important implications for women. Uterine fibroids are the most common type of tumor in the female reproductive system. Treatment options include hysterectomy and myomectomy, which removes the fibroids while sparing the uterus. Interest is growing in alternatives such as UAE, however, provided that treatment proves to be effective in the long term.

The Yale researchers compared long-term results, including recurrence of fibroids and fibroid-related symptoms, for UAE performed with three different agents:

- polyvinyl alcohol particles (PVA)
- gelatin microspheres (GM)
- polyvinyl alcohol spheres (sPVA)

sPVA has a smaller particle size than PVA.

The Yale study involved 247 women treated for UAE between 1999 and 2004. Of these, 101 patients met the inclusion criteria.

The researchers examined gadolinium-enhanced MR studies to assess fibroid volume six months (on average) after the UAE procedure. Residual enhancement on MRI indicated incomplete infarction of fibroids. They also surveyed patients about recurrence of symptoms and quality of life 27 months (on average) after the UAE.

With PVA, there was residual enhancement in 41% of cases and complete infarction in 59%. When sPVA was used, residual enhancement occurred in 75% of cases and complete infarction in 25%. With GM, residual enhancement was evident in 22% of cases and complete infarction in 78%.

The differences between sPVA and PVA, as well as between SPVA and GM, were statistically significant, Galvez said.

"Patients with sPVA were at higher risk of residual enhancement than those with PVA or GM," he said.

The patient survey also showed differences in recurrence of symptoms, but these differences were not statistically significant.

During the session, Galvez was presented with the Trainee Research Prize -- Medical Student for his work on this study.