Multicenter Randomized Sham Controlled Study of Genicular Artery Embolization for Knee Pain Secondary to Osteoarthritis

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ABSTRACT

Purpose: To assess the safety and efficacy of genicular artery embolization (GAE) compared with a sham procedure in the treatment of knee pain secondary to mild to moderate osteoarthritis (OA).

Materials and Methods: A multicenter, single-blinded, randomized controlled trial was conducted to evaluate knee OA symptom reduction after GAE versus sham procedure. Subjects (n = 21) with mild to moderate OA and intractable knee pain were randomized 2:1 to either GAE or a sham procedure. Subjects who were randomized to the sham procedure and did not report clinical improvement in both the total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and visual analog scale (VAS) scores were unblinded and able to crossover to treatment at 1 month. Longitudinal data were collected for 12 months, and subjects were excluded if they required additional analgesics at follow-up. Reductions in the VAS and total WOMAC scores were compared using mixed-effects linear regression models.

Results: All subjects in the sham group failed to show significant improvements at 1 month and crossed over to the treatment arm. There was a statistically significantly greater pain reduction in the treatment group than in the sham group at 1 month (VAS, 50.1 mm; standard error [SE], 10.6; 95% confidence interval [CI], 29.0, 72.3; $P<.01$). Disability improvement was also significantly greater in the treatment group (WOMAC, 24.7 points; SE, 10.4; 95% CI, 3.5, 45.9; $P=.02$). Only minor adverse events were reported. Five subjects were excluded after increased analgesic use. Sensitivity analysis with all excluded patients confirmed significant improvements at 1 and 12 months.

Conclusion: In patients with mild to moderate knee OA, GAE results in symptomatic improvement greater than the sham procedure with clinically significant reduction in pain and disability.

ABBREVIATIONS

CI = confidence interval, DSA = digital subtraction angiography, GAE = genicular artery embolization, MCRI = minimal clinically relevant improvement, OA = osteoarthritis, SE = standard error, VAS = visual analog scale, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Pain and disability secondary to knee osteoarthritis (OA) is a widespread condition affecting over 300 million people worldwide with a prevalence of 10%–13% among adults aged >60 years in the United States (1–3). The mainstays of therapy for knee OA pain are first systemic medications and physical therapy, and then corticosteroid or hyaluronic acid intra-articular injections (4). After failing conservative therapies, patients who advance to severe OA may require total knee arthroplasty, which is the most common inpatient surgery in the United States and is estimated to increase to more than 3.4 million cases by 2030 (5). Many patients are not ideal candidates, including younger patients, patients requiring anticoagulation, and patients with obesity and other surgical comorbidities.

The benefits of minimally invasive therapies such as injections and genicular nerve ablation are inconsistent, and repeat treatments are often required after several months (4,6–8). Therefore, a minimally invasive, durable means of reducing knee OA pain would be a useful addition to the treatment algorithm.

Selective embolization of the genicular arteries has been performed safely for several years to treat hemarthrosis after total knee arthroplasty (9,10). Over the last 2 decades, several studies have demonstrated the role of angiogenesis in the

Supplemental Tables 1 and 2 can be found by accessing the online version of this article on *www.jvir.org* and selecting the Supplemental Material tab.

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RESEARCH HIGHLIGHTS

- A multicenter, single-blinded randomized controlled trial compared genicular artery embolization (GAE) with the sham procedure for the treatment of knee pain from osteoarthritis.
- Twenty-one patients were randomized. All patients in the sham group did not show improvement and crossed over to GAE after 1 month.
- The response rates at 1 month were 79% for the GAE group and 43% for the crossover group.
- GAE resulted in significant pain reduction and improvement of disability at short-term (1 and 12 months) follow-up, with no major adverse events.

STUDY DETAILS

Study type: Prospective, randomized, controlled trial

Study phase: II

Level of evidence: 2 (SIR-B)

setting of OA and its role in the pathophysiology of pain (11–13). Further investigations in the potential for genicular artery embolization (GAE) to reduce knee pain and disability in the setting of OA have demonstrated positive results without major complications (14–18). However, as with any new pain therapy, there is question about how much of the demonstrated symptomatic reduction can be attributed to a placebo effect. This report describes a randomized controlled trial comparing GAE with a sham procedure for the treatment of knee pain secondary to OA.

MATERIALS AND METHODS

This study was performed under an investigational device exemption granted by the Food and Drug Administration and was registered with ClinicalTrials.gov (NCT03362957). This study was approved by the Institutional Review Board and performed under the Health Insurance Portability and Accountability Act regulations.

Study Design

This was a multicenter, single-blinded randomized controlled trial that evaluated knee OA symptom reduction after GAE versus a sham procedure. The primary analysis was performed 1 month after the procedure. At that evaluation, subjects who were randomized to the sham procedure and did not report minimal clinically relevant improvement (MCRI) in both total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and visual analog scale (VAS) measurement were unblinded and able to crossover to treatment (19). An additional evaluation for efficacy and safety was performed 1 month after GAE in the crossover group.

Inclusion Criteria

The inclusion criteria included the following: Kellgren–Lawrence grade 1–3 findings on knee radiography (20), a score greater than 50/100 on the VAS for pain, pain refractory to 3 months of conservative therapies (medication, physical therapy, or intra-articular injection), and age of >40 years. Two board certified radiologists with approximately 20 years of experience reading radiographs graded the severity of OA. Discrepancies in grading were rare and when presented were discussed with a third experienced radiologist to confirm severity. Patients with local infection, life expectancy of <6 months, severe atherosclerosis seen on prior imaging, rheumatoid arthritis, infectious arthritis, prior knee replacement surgery, international normalized ratio of >2.5, platelets less than 30,000/μL, iodinated contrast medium allergy resulting in anaphylaxis, and estimated glomerular filtration rate of <60 mL/min/1.73 m^2 were excluded.

Procedures

Subjects were screened for enrollment in interventional radiology clinics at the 2 participating centers as well as orthopedic clinics associated with those centers. Thirty subjects were screened, and 21 were enrolled (**Fig 1**). The baseline demographics are presented in **Table 1**. Following written informed consent, a baseline evaluation was performed including the total WOMAC score, VAS score, and magnetic resonance imaging of the knee with contrast. Additionally, a thorough history assessment and physical examination were performed to determine the location of maximal knee pain in the affected joint.

Randomization using REDCap (Nashville, Tennessee) occurred prior to the subjects entering the procedure suite. A 2:1 allocation ratio was used with 14 subjects randomized to undergo embolization and 7 subjects randomized to undergo a sham procedure. Assignments were not disclosed to the subjects, and care was taken by the operators and staff to not reveal the assignment to the subject. All procedures were performed by 3 interventional radiologists with 9, 7, and 7 years of experience performing embolization procedures, respectively.

Sham Procedure

Subjects were provided moderate sedation with intravenous midazolam (Hospira, Lake Forest, Illinois) and fentanyl (Fresenius Kabi, Lake Zurich, Illinois). From a contralateral common femoral artery approach, a 6-F sheath was placed up and over the aortic bifurcation. A 5-F base catheter was advanced into the superficial femoral artery, and digital subtraction angiography was performed to evaluate the origins and courses of the genicular arteries. A 2.4-F microcatheter was inserted, and superselective digital subtraction angiography (DSA) of the genicular arteries was performed with iodinated contrast injection in the genicular arteries. The catheter and sheath were then removed, and hemostasis was obtained with a closure device.

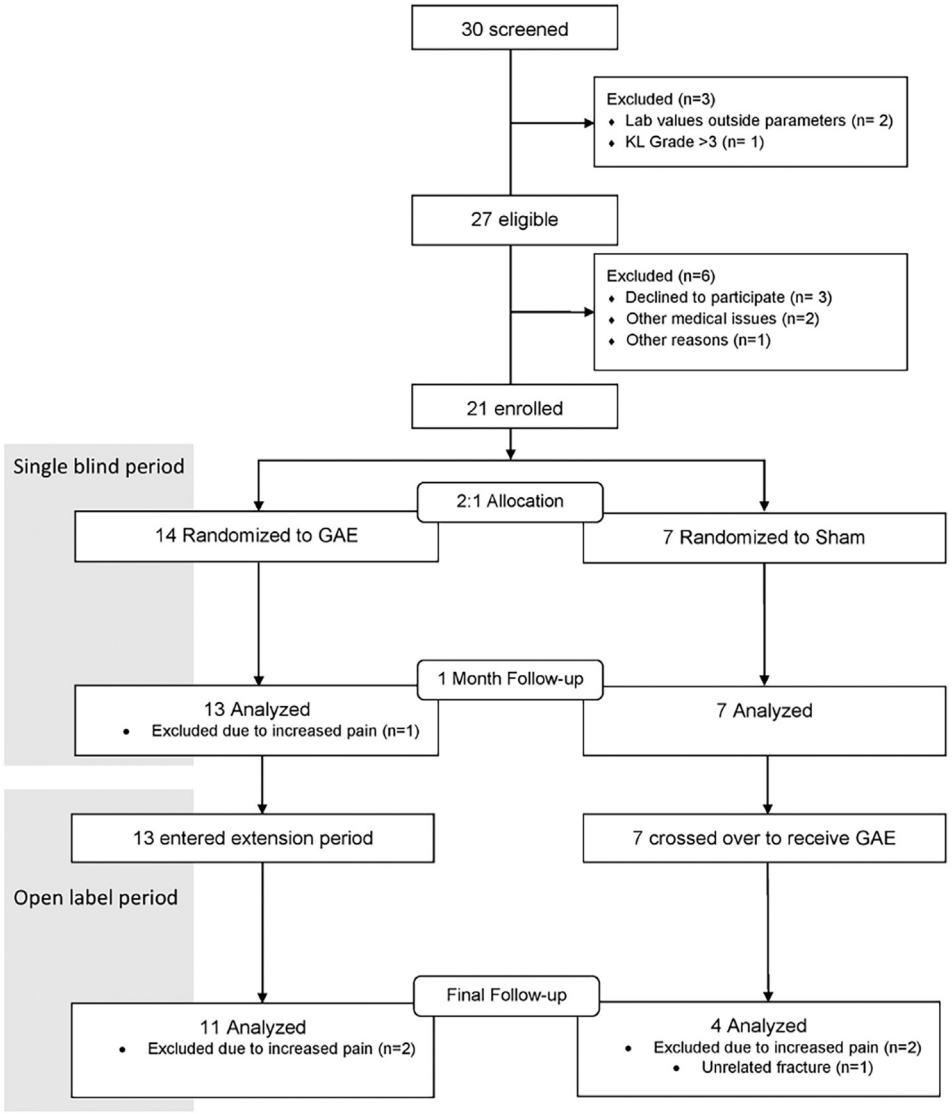

Figure 1. Flow diagram showing the selection, enrollment, and follow-up of participants.

Embolization

The procedural technique and access for the treatment arm were similar to the sham procedure. The 2.4-F microcatheter was used to select the genicular arteries that perfused the side of the knee corresponding to the location of most severe pain (Fig 2). Selective DSA was performed at a low frame rate (1–2 frames/second), and acquisition was continued until "tumor blush" was visible on delayed images. Embolization was then performed using 100–300-micron absorbable particles (OptiSphere; Teleflex, Minneapolis, Minnesota). The embolization technique involved diluting 2 mL of particles in solution with 18 mL of contrast material. After mild agitation to create a homogenous solution, 0.2 mL aliquots were injected, followed each time by repeat DSA. This was continued until the tumor blush was no longer seen on DSA (Fig 3). This process was repeated in each genicular artery perfusing the region of the knee where pain was most severe. Follow-up angiography was performed from the femoral artery to exclude any branches not treated. Once completed, the catheter and sheath were removed, and hemostasis was obtained with a closure device.

All subjects including sham patients received a dose of antibiotics prior to the procedure and for 5 days afterward. Pain medication was prescribed for the postembolization period (up to 1 week after the procedure) in all groups. Subjects were discharged home 2–3 hours after the procedure. An initial follow-up call was made the day after the procedure to assess for acute adverse events. Subsequent follow-up was performed at 1, 3, and 6 months after the procedure. All postprocedural data were collected and recorded by study personnel who were blinded to the subject's allocation. At the 1-month follow-up evaluation, subjects assigned to the sham arm who did not demonstrate the MCRI for both the total WOMAC and VAS were unblinded and able to undergo GAE.

Table 1. Summary of Patient Characteristics, Baseline Scores, and Technical Details

Variables	Sham group (n = 14)			GAE group (n=7)			*P* value
	Mean ± SD	Range	95% CI	Mean ± SD	Range	95% CI	.74*
Patient data							
Age (y)	62.9 ± 7.13	49–71	58.0–67.7	63.9 ± 8.37	49–78	59.6–68.1	.66*
Sex		6F 1M			12F 2M		>.99†
BMI (kg/m^2)	33.4 ± 10.5	21.5–52.9	26.1–40.5	30.8 ± 8.14	16.9–43.8	26.7–34.9	.73*
Laterality		6R 1L			9L 5R		
Kellgren–Lawrence grade	2.3 ± 0.76	1–3	1.8–2.8	2.4 ± 0.51	2–3	2.2–2.7	.54‡
Baseline scores							
WOMAC (0–100 mm)	70.9 ± 13	56–94	61.9–79.8	64.9 ± 17	33–87	56.5–73.2	.68*
VAS (0–100 mm)	78.9 ± 10	69–92	72.2–85.5	81.3 ± 12	55–99	72.9–89.7	.65*
Procedure data							
Procedure time (min)	29.9 ± 15.8	13–55	22.2–37.5	78.9 ± 40.9	31–160	58.2–99.5	.002*
Fluoroscopy time (min)	6.70 ± 4.96	4.05–17.8	4.2–9.1	28.5 ± 15.3	13.4–66.0	20.8–36.2	.0006*
Radiation dose (mGy)	17.9 ± 5.52	8.8 –23.8	15.3–20.4	100.2 ± 95.2	16.9–360	52.2–148.2	.0008*

GAE, n = 14. Sham, n = 7. Two patients underwent previous knee surgery.
BMI = body mass index; CI = confidence interval; GAE = genicular artery embolization; SD = standard deviation; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.
**P* value obtained using the Mann–Whitney U test.
†*P* value obtained using the Fisher exact test.
‡*P* value obtained using the Cochran–Armitage trend test.

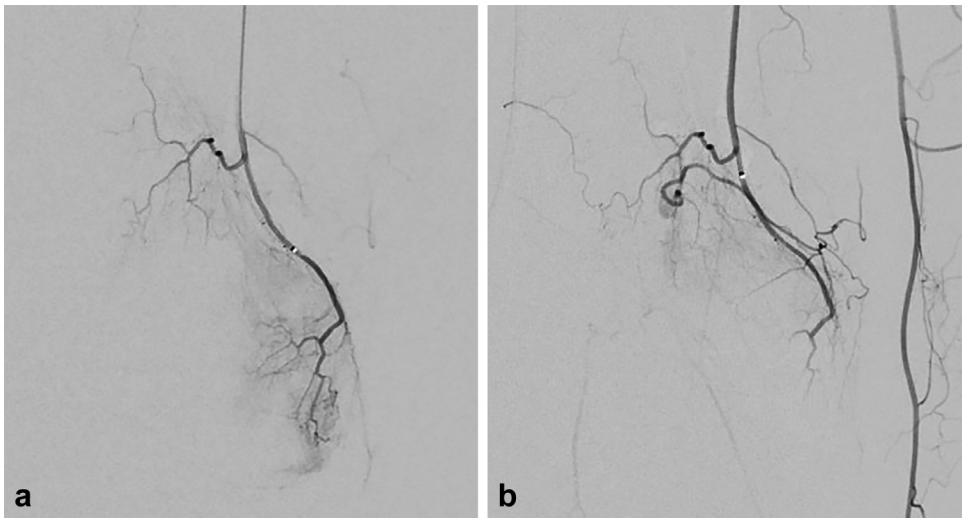

Figure 2. Selective catheterization of the right knee joint. **(a)** Pre-embolization angiogram demonstrating "tumor blush" of the descending genicular artery. **(b)** Postembolization angiogram of the descending genicular artery with reflux into the saphenous branch of the descending genicular artery.

Definitions

MCRI was defined as 16% for the total WOMAC and 12% for the VAS. Technical success was defined as embolization of at least 1 genicular artery for GAE and angiography of the superficial femoral/popliteal artery and its branch vessels for the sham procedure. A subject was labeled as a responder if they demonstrated the MCRI for both the total WOMAC and VAS at 1-month follow-up without increasing their pain therapies over baseline. Nonresponders either did not demonstrate MCRI for both evaluations or increased their pain therapies over baseline. Once a subject was determined to be a nonresponder, they could increase their pain management regimen, and their data were no longer collected to prevent confounding. Recurrence was defined as the increase in both the total WOMAC and VAS to within the MCRI of the baseline value.

Statistical Analysis

The sample size calculation was performed with GPower, version 3.1.9.2, and additional statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

Using baseline scores from a previous study of GAE (15), where there was a mean baseline total WOMAC score

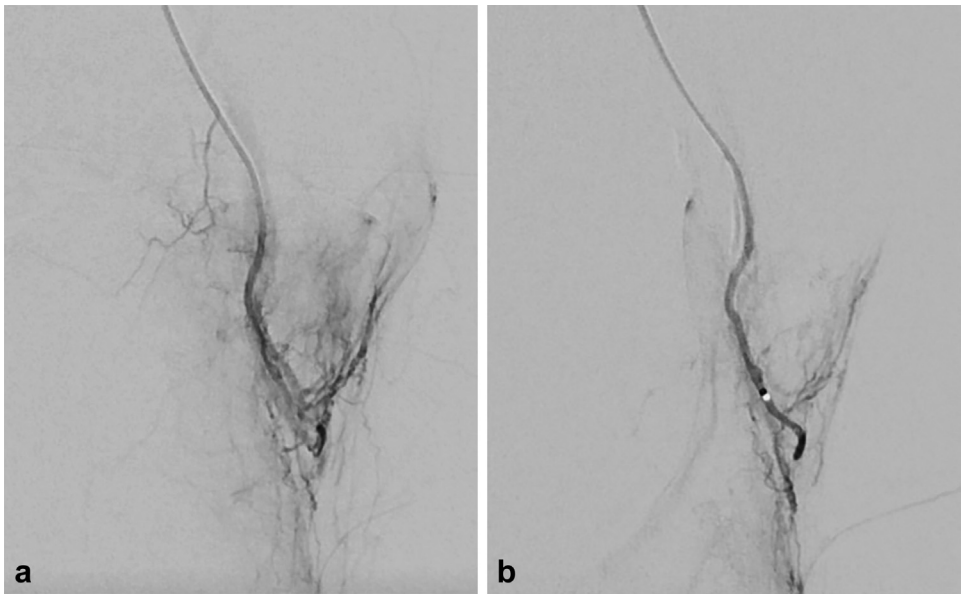

Figure 3. (a) Angiogram from the popliteal artery demonstrating the pre-embolization "tumor blush" in the medial inferior genicular artery. **(b)** Postembolization angiogram of the medial inferior genicular artery.

of 48.5 with a standard deviation of 9.4 and a 2:1 allocation of treatment to sham, a sample size of 21 will have at least 80% power to detect a 26.6% difference in the total WOMAC score from baseline to 1 month, given the crossover study design. This calculation assumes a mixed model analytic approach, controlling for center- and patient-level correlations and modeling WOMAC as a function of time and treatment condition.

The ages and body mass indices between the sham and treatment groups were compared using the Mann–Whitney U test. The Kellgren–Lawrence scores were compared with the Cochran–Armitage test to determine if there was a significant difference in the trend of severity scores by treatment group. The Kellgren–Lawrence scores may only take on 3 values; thus, it is more appropriate to analyze it as a categorical variable, specifically using the Cochrane Armitage trend test since the values are ordinal. The percentage of females in the sham and treatment groups was compared using the Fisher exact test.

Reductions in the VAS and total WOMAC scores after treatment, sham, or crossover treatment were compared using mixed-effects linear regression models. The crossover group was treated as a separate treatment group due to the possibility of carryover effects. The mixed models controlled for center- and person-level correlations by including these terms as random effects since the levels of these variables are considered samples from a larger population. We also included the fixed effects of the treatment group, time, and interaction of the treatment group and time. The test of the time treatment group interactions in these models was analogous to the test of whether the difference in the outcomes differed by treatment group. A P value of $<.05$ was considered evidence of a significant treatment difference, and a P value of $>.05$ but $<.10$ was considered evidence of a marginal difference. In addition, 95% confidence intervals (CIs) were calculated for the treatment differences in reduction.

RESULTS

Between June 2018 and May 2019, 21 subjects with mild to moderate OA of the knee were enrolled into the study. Fourteen subjects were randomized to GAE, and 7 subjects were randomized to the sham procedure. No significant differences were noted when comparing the baseline attributes of the treatment and sham groups (Table 1). Technical success was achieved in all GAEs and sham procedures. The 1-month analysis excluded 1 patient from the GAE group but included the patients who were ultimately excluded from the study at 12 months (n = 4) A sensitivity analysis was performed at 1 and 12 months to assess the significance of the missing data points.

One-Month Primary Endpoint Data

None of the subjects who underwent the sham procedure demonstrated the MCRI for both the total WOMAC and VAS scores at 1-month follow-up. All subjects in the sham group opted to undergo GAE and were described as the crossover group. One subject who received GAE reported increased pain prior to the 1-month follow-up and was withdrawn from the trial. Physical examination and imaging workup did not reveal any evidence of adverse sequelae from the GAE other than increased pain. Given her increased medication requirement, she was labeled as a nonresponder, and her follow-up data were not collected. The response rates at 1 month were 79% (11/14), 0% (0/7), and 43% (3/7) for the treatment, sham, and crossover groups, respectively.

Table 2. Comparison of the First-Month VAS and WOMAC Scores

GAE vs sham	GAE group mean, SE			Sham group mean, SE			Difference in change
	Baseline (n = 14)	1 month (n = 13)	Change	Baseline (n = 7)	1 month (n = 7)	Change	
VAS	81.3, 3.1	30.5, 7.4	50.8	78.9, 3.4	78.4, 3.6	0.7	50.1 (95% CI, 29.0, 72.3; $P < .01$)
WOMAC	64.9, 4.3	34.7, 6.4	30.2	70.9, 4.6	65.9, 4.0	5.0	25.2 (95% CI, 3.5, 45.9; $P = .02$)
Crossover vs sham	**Crossover group mean, SE**			**Sham group mean, SE**			**Difference in change**
	Baseline (n = 7)	1 month (n = 7)	Change	Baseline (n = 7)	1 month (n = 7)	Change	
VAS	78.4, 3.6	39.8, 10.8	38.6	78.9, 3.4	78.4, 3.6	0.7	38.1 (95% CI, 13.3, 62.9; $P < .01$)
WOMAC	65.9, 4.0	46.3, 10.4	19.6	70.9, 4.6	65.9, 4.0	5.0	14.6 (95% CI, –9.7, 38.8; $P = .23$)

CI = confidence interval; GAE = genicular artery embolization; SE = standard error; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Treatment Group versus Sham Group

Among responders, the difference in baseline for the treatment group compared with the sham group was not significant for the WOMAC (difference, −6.0; standard error [SE], 9.1; 95% CI, −24.5, 12.5) or VAS (difference, 2.4; SE, 9.1; 95% CI, −16.2, 21.1) When comparing the reduction in global disability among responders, the total WOMAC score at 1 month in the treatment group (n = 13) was statistically greater than that in the sham group (n = 7). The difference was 24.7 (SE, 10.4; 95% CI, 3.5, 45.9; $P = .02$) (Table 2). The WOMAC subscore comparisons between the treatment and sham groups revealed significant differences in all 3 subscores. Similarly, when comparing the reduction in the VAS score at 1 month in the treatment (n = 13) and sham (n = 7) groups, the difference was 50.1 (SE, 10.6; 95% CI, 29.0, 72.3; $P < .01$) and was statistically significant.

Because the WOMAC and VAS scores were not obtained for the subject who required more pain medication prior to the 1-month follow-up, a sensitivity analysis was performed in which no improvement in either metric was assumed for the missing subject to determine if overall significance would be affected. However, both the differences in the reduction in the WOMAC (21.7; $P = .045$) and VAS (46.6; $P < .001$) scores when comparing the treatment (n = 14) and sham (n = 7) groups using this methodology were still statistically significant.

Crossover Group versus Sham Group

When comparing the reduction in the VAS score at 1 month in the crossover group and that in the sham group, the difference was 38.1 (SE, 12.2; 95% CI, 13.3, 62.9; $P < .01$) and was significant. When comparing the reduction in the total WOMAC score at 1 month in the crossover group (n = 7) and that in the sham group (n = 7), the difference was 14.6 (SE, 11.9; 95% CI, −9.7, 38.8; $P = .23$) and was not significant. Additionally, the WOMAC subscore comparison between the crossover and sham groups was significant for stiffness.

To determine if the placebo effect swayed significance in the crossover versus sham group analysis, a sensitivity analysis was performed in which the difference in the WOMAC score for the crossover group was calculated using the baseline value from before the sham procedure (in lieu of after the sham but before the crossover treatment). The 1-month scores for the crossover group were compared with the baseline value at the beginning of the study rather than the postsham values. There was a near significant difference, measuring 21.7 (SE, 11.3; 95% CI, −1.3, 44.8; $P = .06$).

Longitudinal Data

The 12-month data are summarized in Figure 4. The median follow-up period for all groups was 12 months. Among the responders in the GAE group, the mean VAS score improved from 81.3 at baseline to 30.5, 21.7, 20.3, and 26.7 at 1, 3, 6, and 12 months, respectively. Similarly, the mean total WOMAC score among responders improved from 64.9 at baseline to 34.7, 19.8, 29.3, and 17.9 at 1, 3, 6, and 12 months, respectively. As described earlier, 1 subject in the GAE group was excluded from the study within the first month because of persistent pain after the 1-week postprocedural period that required increased pain medication from what she was taking at baseline. Additionally, 2 subjects who received GAE reported increased pain (1 patient between 1- and 3-month follow-ups and 1 patient between 6- and 12-month follow-ups) was withdrawn from the trial. **Supplemental Tables 1** and **2** (available online on the article's Supplemental Material page at *www.jvir.org*.) summarize all patient data for 12 months.

In the crossover group, the mean total WOMAC score among responders improved from 65.9 at baseline to 46.3, 40.9, 26.0, and 16.3 at 1, 3, 6, and 12 months, respectively. One subject in the crossover group sustained a traumatic injury to her leg that was deemed unrelated to the study procedures and withdrew from the study between the 3- and 6-month follow-up evaluations Additionally, 2 subjects who received GAE reported increased pain between the 6- and 12-month follow-ups and were withdrawn from the trial.

The mean reductions in the VAS and WOMAC scores from baseline to 6 and 12 months among responders are summarized in Table 3. The reduction from the baseline of

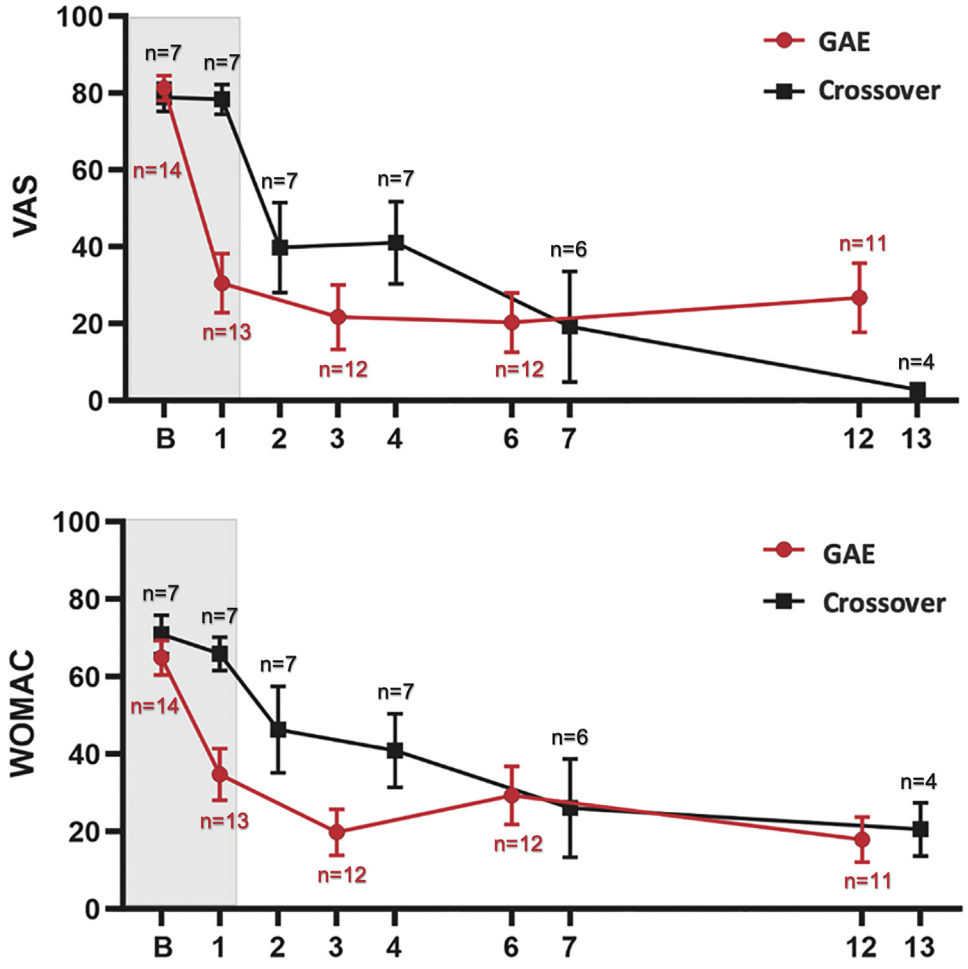

Figure 4. Visual analog scale and Western Ontario and McMaster Universities Osteoarthritis Index scores measured over the course of the study. The genicular artery embolization group (n = 14) data begin at baseline (B) to 12 months. The shaded region includes the sham group (n = 7) as part of the crossover cohort from baseline to 1 month. The crossover group (n = 7) begins at the 1-month mark and concludes at the 13-month mark. Five patients were excluded after reporting increased pain medication use. All data are included until the follow-up appointment with increased medication use resulting in exclusion.

Table 3. Summary of the Mean Reduction in the VAS and WOMAC Scores from Baseline to 6 and 12 Months

Group	Scale	Mean pain score reduction from baseline	
		6 months	12 months
GAE	VAS	61.01 (n = 12)	54.59 (n = 11)
	WOMAC	35.58 (n = 12)	46.96 (n = 11)
Crossover	VAS	59.19 (n = 6)	75.61 (n = 4)
	WOMAC	39.86 (n = 6)	45.36 (n = 4)

GAE = genicular artery embolization; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

the combination of both groups (crossover and GAE) is also shown. In total, 5 subjects (3 from the GAE group and 2 from the sham/crossover group) were removed from the study due to increased pain requiring additional therapy. The 12-month reduction calculations were made excluding these data points with a total of 11 treatment and 4 sham patients at the last checkpoint.

Because the WOMAC and VAS scores were not available for the subjects who required more pain medication at 12 months (n = 5, 2 from sham/crossover and 3 from treatment), a sensitivity analysis was again performed in which no improvement in either metric was assumed for the missing subjects to determine if overall significance would be affected. The missing VAS and WOMAC scores at 12 months were substituted with baselines scores, and the mean scores were compared. The difference in mean from baseline to 12 months for both the WOMAC and VAS scores was still statistically significant ($P < .0001$) using this research methodology.

Adverse Events

All adverse events were classified as Clavien–Dindo grade 1 and were self-limiting. The rates of adverse events by group are displayed in Table 4.

Table 4. Summary of Adverse Events

Adverse event	Post-sham (n = 7)	Sham Crossover (n = 7)	GAE (n = 14)	Total (n = 21)
Knee pain	0	1	1	2
Purpura	0	3	2	5
Nausea/vomiting	0	1	0	1
Hematoma	1	0	0	0
Skin changes	0	0	1	1
Skin ischemia	0	0	1	1
Pruritus	0	0	1	1
Ecchymosis	1	0	0	0
Bleeding at access site	1	0	0	0

GAE = genicular artery embolization.

DISCUSSION

This study demonstrates that the improvement of symptoms observed after GAE are not merely due to the placebo effect. Within the study population, there was a significantly greater reduction in disability and pain, as measured by the total WOMAC and VAS scores, in the GAE group than in the sham group at 1 month after the procedure. Additionally, none of the subjects who received the sham procedure demonstrated MCRIs in both the total WOMAC and VAS scores, allowing them to crossover to treatment at 1 month per the study protocol. For comparison, 11 of 14 (79%) subjects in the GAE arm met this benchmark in both scores at 1 month.

Interestingly, the crossover group did not demonstrate a significant reduction in the total WOMAC score compared with the sham group at 1 month. Because these 2 arms were comprised of the same subjects, it could be argued that this is the best comparison of placebo to treatment. However, when performing the same analysis in regard to the VAS score, there was a significantly greater reduction for the crossover subjects after GAE compared with after the sham procedure. One explanation for the lack of significant reduction in the WOMAC score is that the subjects experienced a mild placebo effect after the sham procedure that limited the improvement observed after treatment. This theory is corroborated by a sensitivity analysis that showed that when the placebo effect was corrected for, the difference in reductions between the crossover and sham groups approached significance.

Also of interest were the WOMAC subscore analyses. In the GAE versus sham comparison, the differences in all 3 subscores (pain, stiffness, and physical function) were significant. In the crossover versus sham analysis, only the difference in stiffness was significant. It was surprising that the pain subscore difference was not significant given the significant difference observed in the VAS score also measuring pain. Previous studies (14,15) have shown that the WOMAC pain subscore is highly correlated with VAS responses on the knee OA population. Again, this may be due to the placebo effect in the crossover group, or perhaps the sample size (n = 7) was not large enough to detect this change.

The limitations of this study included the small number of subjects in the sham group. Although the sample size resulted in adequate power to evaluate the subject receiving treatment versus the subjects receiving the sham procedure, it was likely too small to generate adequate power for the comparison of the crossover group with the sham group, which was the not the primary intent of the study. Additionally, the lack of data collection once a subject was determined to be a nonresponder also decreased the strength of the study. However, all of these subjects required additional pain therapy over their baseline regimen. There was a concern that if their data were included, any improvement from additional therapy could be false attributed to GAE. For the primary endpoint, a sensitivity analysis was performed that assumed no improvement in the nonresponder to determine if the overall result would be affected.

A sensitivity analysis was also conducted at the 12-month data point given the exclusion of 5 total subjects for increased analgesic use (n = 1 at 1 month, n = 1 at 3 months, and n = 3 at 12 months). One additional patient was also excluded after an unrelated traumatic injury. The sensitivity analysis used the baseline VAS and WOMAC scores for the 12-month follow-up. Assuming that the VAS and WOMAC scores did not worsen, the sensitivity analysis strengthens the treatment effect. The exclusion of nonresponders remains a weakness, and symptomatic improvement noted by the reduction in the total WOMAC and VAS scores should be interpreted as what can be expected for responders and not for the entire population undergoing GAE. The authors recognize the flaw in excluding failures but highlight the use of the sensitivity analysis to address this weakness. Finally, this study could have been strengthened by a longer follow-up period to determine the durability of the improvement of symptoms after GAE.

In conclusion, in patients with mild to moderate OA of the knee, GAE results in a greater pain and disability improvement than a comparable sham procedure. Further investigation comparing GAE with other pain therapies such as systemic medications, joint injection, and nerve ablation should be considered to determine which provides the best risk-to-benefit ratio as well as overall value for treating pain secondary to knee OA.

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S.B. is a consultant for Boston Scientific, Varian Medical Systems, Medtronic, Embolx, IMBiotechnologies, and Philips Medical System. A.I. is a consultant for Terumo, ABK Biomedical, and CrannMed. The other authors have not identified a conflict of interest.

From the 2020 SIR Annual Meeting, Abstract #3 "Multicenter prospective, randomized, sham-controlled study of genicular artery embolization."

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Supplemental Table 1. Supplemental Data: Patient-Level Demographic Data

Study ID	Sex	Age	BMI	Knee	Kellgren–Lawrence grade	Arm
1	F	66	27.1	R	3	Sham/CRO
2	F	71	21.5	R	2	Sham/CRO
3	F	62	52.9	L	2	Sham/CRO
4	F	60	41	R	3	Sham/CRO
5	F	68	28.1	R	2	Sham/CRO
6	M	64	30.9	R	3	Sham/CRO
7	F	49	32	R	1	Sham/CRO
8	F	65	32.9	R	2	GAE
9	F	55	37.7	L	3	GAE
10	F	62	27.6	L	3	GAE
11	F	72	43.8	R	3	GAE
12	M	65	25.1	L	2	GAE
13	F	50	16.9	L	3	GAE
14	F	64	28.4	L	3	GAE
15	F	66	24.5	L	2	GAE
16	F	73	41.9	R	2	GAE
17	M	49	29.3	R	2	GAE
18	F	59	42.2	R	2	GAE
19	F	68	33.6	L	2	GAE
20	F	78	24.9	L	3	GAE
21	F	68	23	L	2	GAE

Note–BMI = body mass index; CRO = crossover; GAE = genicular artery embolization.

Supplemental Table 2. Summary of Individual Scores

Subject	WAC_B	VAS_B	WAC_1	VAS_1	WAC_3	VAS_3	WAC_6	VAS_6	WAC_12	VAS_12
1	64	74	54	40	49	40	29	17	16	0
2	51	67	67	52	53	48	22	6	F	F
3	76	97	93	92	61	46	86	90	F	F
4	83	84	9	0	2	0	8	0	30	6
5	71	70	13	8	7	8	2	1	3	5
6	58	82	50	55	57	73	9	1	33	0
7	58	75	38	32	57	72	Fx			
8	72	72	30	25.4	23	46	32	26	36	40
9	55	82	37	67	8	7	9	13	7	6
10	87	67	63	40	34	21	52	6	6	18
11	78	89	44	35	25	7	32	19	12	14
12	80	84	9	8	1	0	4	7	8	78
13	66	75	54	0	5	3	42	0	52	30
14	83	90	F	F						
15	39	55	9	17	4	5	4	0	5	0
16	33	85	0	0	0	0	0	0	0	0
17	75	99	69	60	F	F				
18	60	76	11	14	27	62	30	20	43	72
19	69	88	38	31	9	7	36	32	10	9
20	66	99	68	91	74	90	83	88	F	F
21	45	77	19	8	27	12	28	32	18	27

Note–The first 7 patients were in the sham/crossover group, while the remaining 14 patients were in the treatment group.
F = treatment failure; Fx = fracture; VAS = visual analog scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.