Osteoarthritis-Related Knee Pain Treated With Genicular Artery Embolization

A Systematic Review and Meta-analysis

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Background: Genicular artery embolization (GAE) is an innovative technique that has been investigated as a supplementary treatment method for chronic pain secondary to knee osteoarthritis (OA).

Purpose: To evaluate the current evidence on the effectiveness and safety of GAE for OA-related knee pain.

Study Design: Systematic review; Level of evidence, 4.

Methods: A systematic literature search was conducted in the PubMed, Web of Science, EMBASE, and Scopus databases to identify studies related to knee OA treated with GAE. Treatment agents were categorized as Embozene, imipenem/cilastatin, resorbable microspheres, and polyvinyl alcohol. The main outcomes were the mean difference (MD) in pre- and postembolization pain based on the visual analog scale (VAS) or the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores as well as changes in the need for pain medication. Random- and fixed-effects models were applied for data analysis.

Results: Of 379 initially inspected publications, 11 (N = 225 patients; 268 knees) were included in the final review. The quality of the studies was fair in 8 and poor in 3—categorized according to the National Institutes of Health quality assessment tool. Overall, 119, 72, 13, and 21 patients were treated with imipenem/cilastatin, Embozene, resorbable microspheres, and polyvinyl alcohol, respectively. Symptomatic improvement was reported in all studies. The pooled effect size, characterized by MD, showed a significant improvement in the VAS and WOMAC pain scores, with better functional status after GAE. Pre- versus postembolization MDs in VAS scores ranged from 32 within the first week to 58 after a 2-year follow-up (equivalent to 54% and 80% improvement, respectively). There was a similar trend in the overall WOMAC scores, with MDs ranging from 28.4 to 36.8 (about 58% and 85% improvement, respectively). GAE resulted in a decreased need for pain medication for knee OA, with a 27%, 65%, and 73% decline in the number of patients who used opioids, nonsteroidal anti-inflammatory drugs, and intra-articular hyaluronic acid injection, respectively ($P < .00001$ for all). No significant difference between embolic agents was seen with regard to post-GAE pain reduction. No severe or life-threatening complications were reported.

Conclusion: OA treated by GAE using different embolic particles can be considered generally safe, with good efficacy and no reported serious complications.

Keywords: osteoarthritis; knee joint; knee pain; genicular artery embolization

Chronic knee pain related to osteoarthritis (OA) is a major cause of disability in the population older than 50 years of age, with a reported prevalence of 25% to 30%.[9] Pain related to OA of the knee necessitates various medical treatments and leads to a decrease in overall quality of life.[25] Various therapeutic approaches have been implemented and investigated for this condition, ranging from nonpharmacological management of symptoms to total knee arthroplasty.[11] Depending on the severity of the OA, the initial recommended management is usually lifestyle modification and nonpharmacological measures, including regular moderate exercise, weight loss, and activity modifications to mitigate risk factors for OA.[4,39] While not without risks, nonsteroidal anti-inflammatory drugs (NSAIDs) are the medications of choice for mild to moderate OA-related pain and can be administered in oral or topical forms. When nonoperative measures fail, more invasive treatment options, such as intra-articular glucocorticoid or hyaluronic acid injection, neurotomy, or neuromodulation techniques, can be considered.[35] Knee arthroplasty is usually reserved for patients with OA who are no longer responsive to nonoperative treatment.[24]

More recently, genicular artery embolization (GAE) has been proposed as an additional, often supplementary,

TABLE 1
Difference Between Embolic Agents Applied in GAE Used for OA[a]

Product	Duration of Action	Size, μm	FDA Approved for Embolization	Specific Properties
Imipenem/cilastatin	Temporary	10-70	No	Small molecule antibiotic, resorbable
Particulate PVA (contour)	Permanent	45-1200	Yes	Irregularly shaped microparticles, nonresorbable
Embozene (Boston Scientific) (polymethylmethacrylate)	Permanent	40-1300	Yes	Calibrated sizes, polymeric, spherical, nonresorbable, biodegradable coating
Gel-Bead (Teleflex Medical) (gelatine)	Temporary	100-300, 300-500, 500-700, 700-1000	Yes	Calibrated sizes, gelatine microspheres degradable in 4-12 weeks

[a]GAE, genicular artery embolization; FDA, Food and Drug Administration; OA, osteoarthritis. PVA, polyvinyl alcohol.

method for management of mild to moderate OA of the knee. Early studies have revealed promising results with only self-limiting minor postprocedure complications.[13] To date, there has been a paucity of cohesive data regarding the effectiveness of GAE techniques for OA-related knee pain, particularly compared with other treatment avenues. Table 1 outlines the embolic agents (all particulates) used in GAE. A comprehensive understanding of the properties of each embolic agent is necessary to optimize its application. The ideal therapeutic embolic agent can be given via any catheter without any prior vortexing and exiting from the catheter tip with no fear of nontarget distal embolization.

The purpose of the present study was to systematically review and evaluate the current evidence for the effectiveness and safety of GAE in the treatment of OA-related knee pain. It was hypothesized that mild to moderate OA treated by GAE using different embolic particles could be considered generally safe with no reported serious complications.

METHODS

Search Strategy

This systematic review was in line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A systematic search in the PubMed, Web of Science, EMBASE, and Scopus databases was conducted to identify relevant studies from the date of inception until April 2020. The applied keywords included [*Osteoarthritis* or *Osteoarthrosis* or *Osteoarthritis-related* knee pain or *Knee pain*] combined with [*Geniculate / Genicular Artery Embolization*, *GAE* or *embolization*]. No language or publication time restrictions were applied. All searches were conducted over a 7-month period from February to August 2020, as detailed in Appendix Table A1.

Study Selection and Data Extraction

The study-selection process is shown in Figure 1. Studies using cadaveric specimen or animal subjects, technical development and review articles without original treatment performance data, studies examining treatment modalities other than GAE, and studies that reported similar data on the same patient population were all excluded. Titles and abstracts of all obtained studies were independently reviewed by 4 investigators (P.T., E.T., A.C., and R.T.), and duplicate studies were eliminated. The same 4 investigators then independently reviewed the full text of all eligible studies. In case of inconsistency, consensus was achieved by discussion. At this stage, those with missing information or insufficient data regarding the evaluation of pain after the procedure or during the follow-up were excluded. The process of search-strategy design, database search, study selection, data extraction, and final inclusion was overseen by a fellowship-trained board-certified musculoskeletal radiologist (M.C.) and 2 interventional radiologists (J.G. and R.T.).

The initial search revealed a total of 379 publications, with 330 unique publications after removing duplicates. Titles and abstracts of these studies were screened for their relevance to the topic of interest. After exclusion, 28 articles focused on GAE, with or without combination of medical treatments, were selected for an in-depth review. After excluding 17 papers because of insufficient data about follow-up, target population, and reports not identifiable with the abstract (n = 8), as well as same patient population (n = 9), 11 and 6 studies were included eventually in the final qualitative and quantitative meta-analysis, respectively.

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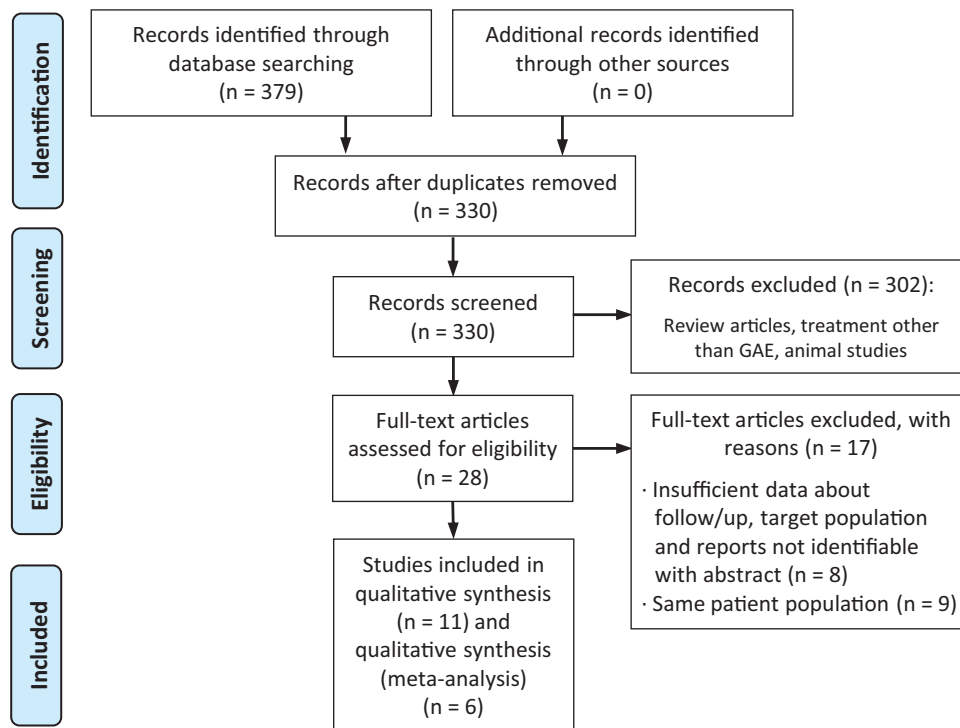†Division of Musculoskeletal Imaging and Intervention, Department of Radiology, University of Washington, Seattle, Washington, USA.
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Figure 1. Flowchart using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines demonstrating the study-selection process for the meta-analysis. GAE, genicular artery embolization.

In addition, we searched for ongoing trials and studies submitted to ClinicalTrials.gov, EU Clinical Trials Register, UMIN Clinical Trials, ANZCTR, CHICTR, and ISRCTN registries up to August 2020, using the following keywords: *Geniculate / Genicular artery embolization* and *Osteoarthritis*. As of this writing (August 2020), we found 12 randomized clinical trials that were underway to evaluate the efficacy and/or safety of GAE for the treatment of OA (see Supplemental Material, available online).

Quality Assessment

The quality of the included studies was evaluated by using the Quality Assessment Tool for Case Series of the National Institutes of Health (www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). Two investigators (P.T. and E.T.) independently rated 9 items about the aims of the study, case selection, exact definition of their characteristics, and statistical comparisons; in case of disagreement, a joint consensus was achieved through consultation with senior authors (J.G., M.C., and R.T.). The results were almost consistent, indicating fair quality of the included studies (Table 2).

Data Extraction and Outcome Definition

Data extraction regarding type of the study (prospective, case-control, or case series), publication year, country/region of the study, number of patients, patient demographics, pre- and postoperative pain score, pre- and postoperative

pharmacological treatments, type of embolic agents used, technical and clinical success rate, perioperative complications, length of follow-up, and clinical outcomes were performed by 2 independent authors (P.T. and R.T.). Functional improvement was compared between studies that used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire. The WOMAC questionnaire is a self-administered index with 24 items, divided into 3 subscales: 5 items for pain (score range, 0-20 points), 2 for joint stiffness (score range, 0-8 points), and 17 for functional status (score range, 0-68 points). The higher the score indicates the more severe the level of functional limitation. Pain was compared between studies using the visual analog scale (VAS) and WOMAC pain subscale.

The main outcome was defined as the mean difference (MD) between pre- and postembolization values of the pain scales (VAS, WOMAC) as well as the number of patients who consumed analgesic medications for their pain relief.

Statistical Analysis

Data analysis was conducted using Review Manager Version 5.3 (Cochrane Collaboration). Both random- and fixed-effect models were applied to calculate the pooled effect size. The relative weight of each study was determined using inverse variance and Mantel-Haenszel methods for continuous and dichotomous variables, respectively. A subgroup analysis was performed to evaluate the differences in

TABLE 2
Quality Ratings of the Included Studies According to NIH Quality Assessment Tool for Case Series Studies[a]

First Author (Year)	Question Number[b]									Overall Rating	
	1	2	3	4	5	6	7	8	9	Reviewer 1	Reviewer 2
Bagla et al[2] (2020)	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	N/N	Y/Y	Y/Y	Fair	Fair
Okuno et al[27] (2015)	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Fair	Fair
Okuno et al[28] (2017)	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Fair	Fair
Shibuya and Okuno[37] (2018)	Y/Y	N/N	na/N	N/N	Y/Y	N/N	N/N	N/N	N/N	Poor	Fair
Lee et al[21] (2019)	Y/Y	Y/N	na/na	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Y/Y	Fair	Fair
Kumar and Chandrashekhara[19] (2020)	Y/Y	nr/N	Y/Y	Y/Y	nr/nr	Y/N	N/N	nr/N	nr/nr	Fair	Poor
Padia et al[29] (2020)	Y/Y	Y/N	nr/nr	Y/Y	nr/nr	N/N	Y/Y	N/N	nr/nr	Fair	Fair
Bagla et al[3] (2020)	Y/Y	N/N	nr/nr	Y/Y	nr/nr	Y/Y	N/N	N/N	nr/nr	Fair	Fair
Piechowiak et al[31] (2017)	Y/Y	nr/N	nr/nr	Y/Y	nr/nr	Y/Y	N/N	N/N	nr/nr	Fair	Fair
Lauko et al[20] (2020)	Y/Y	Y/Y	na/na	na/na	Y/Y	Y/Y	Y/Y	na/na	Y/Y	Fair	Fair
Little et al[22] (2020)	Y/Y	N/N	N/N	nr/nr	Y/Y	N/N	N/N	N/N	N/N	Poor	Poor

[a]N, no; na, not applicable; NIH, National Institutes of Health; nr, not reported; Y, yes.
[b]Questions: (1)Was the study question or objective clearly stated? (2) Was the study population clearly and fully described, including a case definition? (3) Were the cases consecutive? (4) Were the patients comparable? (5) Was the intervention clearly described? (6) Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? (7) Was the length of follow-up adequate? (8) Were the statistical methods well-described? (9) Were the results well-described?

effectiveness of various embolic agents as well as across different time points. The Egger test was employed to assess publication bias in the Funnel plot using Stata Version 16 (Stata). $P <.05$ indicated statistical significance in all analyses.

RESULTS

Summary of the Included Studies

The characteristics of included studies, such as publication year, number and characteristics of participants, severity grade of knee OA, outcome measuring tools, and follow-up duration, are presented in Table 3. Except for 1 study,[27] all investigations had been published after 2017. Eleven studies with a total of 225 participants (27% men; age range, 48-88 years) and 268 knees were included.[2,3,19-22,27-29,31,37] Different embolic agents were applied, including imipenem/cilastatin (n = 4 studies), Embozene (n = 7 studies), resorbable microspheres (n = 1 study), and polyvinyl alcohol (n = 1 study). Overall, 119, 72, 13, and 21 patients were treated with imipenem/cilastatin, Embozene, resorbable microspheres, and polyvinyl alcohol, respectively. Three studies did not reveal the severity grade of their included patients based on the Kellgren-Lawrence (KL) classification system. However, the majority of participants in 6 other studies were KL grades 1, 2, and 3, which constitute mild to moderate OA involvement on knee radiographs. Most of the reported studies included patients aged 40 to 60 years who had OA with the VAS score >50 mm and refractory to

conservative therapies (NSAIDs, physical therapy, muscle strengthening, and intra-articular hyaluronic acid injection) with KL grades 1 to 3 on their knee radiographs. Patients with a history of rheumatoid arthritis, renal insufficiency, incorrectible coagulopathy, malignancy, advanced atherosclerosis, and previous knee arthroplasty were deemed ineligible to undergo GAE.

All of the studies reassessed their participants with magnetic resonance imaging (MRI)/radiographs postoperatively, with an exception of 1 study that did not mention its follow-up imaging.[19] The mean follow-up time after embolization was at least 6 to12 months for most publications; however, 4 studies continued the follow-up for 1 to 3 months.[3,19,31] Four studies reported the number of participants who concurrently used medications for management of OA, including opioids, NSAIDs, acetaminophen, and intra-articular hyaluronic acid injection, before and after the GAE procedure [2, 21, 27, 28]. No significant publication bias was detected (Egger bias coefficient = -2.17 [95% CI, -10.32 to -5.96]; $P = .45$) (Figure 2).

Effectiveness of GAE

The clinical effectiveness of GAE, including pain reduction based on the VAS and WOMAC scales, is illustrated in Table 4. The impact of GAE on changes in the VAS score was evaluated at 6 different time points; 1 study included day 1 postoperative assessment, which was not included in the pooled analysis, as presented in Figure 3.[21] Pre- and postembolization scores of each study were collected, and the pooled effect size was calculated at 1 week and at 1-, 3-,

TABLE 3
Characteristics of the Included Studies[a]

First Author (Year); Country	Study Design	Imaging	Patients /Knees/ Men, n	Side Affected, Right: Left	Mean Age, y	BMI, kg/m²	KL Grade	Embolic Agent	Agent Dose and Volume	Complications, n Overall/ Severe, n	Based on SIR	Follow-up, mo
Bagla et al[2] (2020); USA	P/MC	MRI (after 1 mo)	20/20/9	11:9	59.4	35	3 (n = 9); 2 (n = 9); 1 (n = 2)	E	75 or 100 μm E spherical particles, 9 mL contrast material added to the 6 mL particles in solution	16/0	A	6
Okuno et al[27] (2015); Japan	P/SC	MRI	14/14/6	5:9	65.2	26.3 ± 6.3	0 or 1 (n = 8); 2 (n = 6)	E (n = 3) and I/C (n = 11)	75 μm E spherical particles (mean volume used: 0.068/2 mL particle volume) plus 10-70 μm I/C (mean volume used: 2.5 mL/5 mL suspension)	1/0	B	12 ± 5
Okuno et al[28] (2017); Japan	P/SC	MRI	72/95/23	49:46	64.4	25.1	1 or 2 (n = 62); 3 (n = 33)	E (n = 7) and I/C (n = 65)	75 μm E plus a suspension of 0.5 g I/CS in 5-10 mL iodinated contrast agent	16/0	B	24-48
Shibuya and Okuno[37] (2018); Japan	P/SC	MRI	2/2/0	1:1	72	nr	3	I/C	0.5-1 mL I/CS plus a suspension of 0.5 g I/CS in 5-10 mL iodinated contrast agent prepared by pumping syringes for 10 s then injected in 0.2-mL increments	nr	nr	2-24
Lee et al[21] (2019); Korea	R/SC	MRI	41/71/17	35:36	67.2	24.9 ± 3.7	4 (n = 12), 1-3 (n = 59)	I/C	0.5 g I/C in 7 mL iodinated contrast medium	10/0	B	12
Kumar and Chandrashekhara[19] (2020); USA	P/SC	nr	21/21/nr	nr	48-71	nr	2 (median)	PVA	nr	0/0	A	1
Padia et al[29] (2020); India	P/SC	MRI (after 3 mo)	26/26/nr	14:12	69 (49-76)	28 (19-47)	nr	E	100 μm E	4/0	B	12
Bagla et al[3] (2020)[3] USA	P/SC	MRI	13/13/3	nr	64	31.4	nr	RM	nr	nr	nr	1
Piechowiak et al[31] (2017); USA	P/SC	MRI	5/5/3	nr	(50-88)	nr	nr	E	75 μm E	5/0	B	3
Lauko et al[20] (2020); USA	P/SC	Radiograph	1/1/0	0:1	64	nr	nr	E	nr	1/0	A	6
Little et al[22] (2020); UK	P/SC	MRI	10/nr/nr	nr	nr	nr	nr	Embosphere	nr	1/0	A	3 (up to now)
Total			225/268		48-88					54/0		

[a]A, no therapy, no consequence; B, nominal therapy, no consequence; BMI, body mass index; E, Embozene; I/C, imipenem/cilastatin; KL, Kellgren-Lawrence; MC, multicenter; MRI, magnetic resonance imaging; nr, not reported; P, prospective; PVA, polyvinyl alcohol; RM, resorbable microspheres; SC, single center; SIR, Society of Interventional Radiology.

6-, 12-, and 24-month follow-up. Results indicated that the MD at those respective time points was 32 (95% CI, 14.9-49), 36.67 (95% CI, 28.2-45), 40.75 (95% CI, 30-51.4), 42.80 (95% CI, 26.5-59), 45.79 (95% CI, 19.7-71.8), and 58 (95% CI, 53.3-62.6). P values were all <.00001; therefore, we could state that knee pain, based on the subjective measure of acute and chronic knee pain, had significantly improved even within the first week after GAE (equivalent to 54% decline). A sustained and downward absolute VAS score

trajectory was observed, which reached about 64% and 80% reduction at the 6- and 24-month follow-up, respectively. This therapeutic trajectory, characterized by percentage change, is shown in Figure 4. This implied a durable pain-control effect across the cohort of studies.

In the present review, postprocedural changes of the WOMAC–pain subscale were congruent with the VAS assessment (Figure 4). Pooled MDs evaluated at 5 different time points (1, 3, 6, 12, and 24 months after GAE) were 28.4
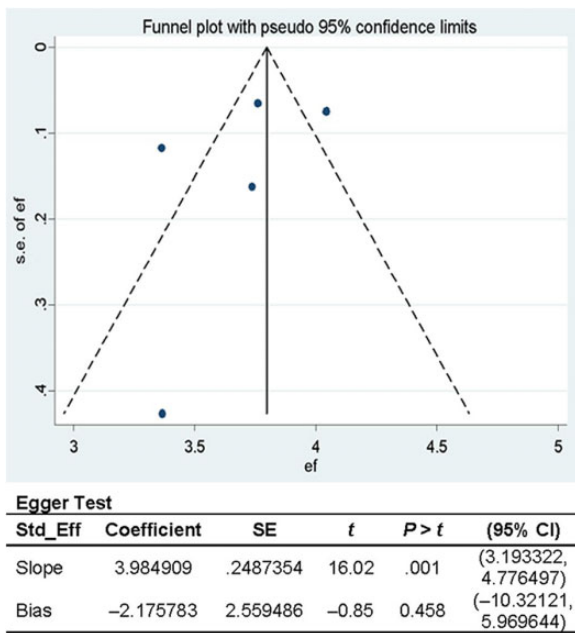
Figure 2. Funnel plot assessing publication bias. Std eff, standard efficiency.

(95% CI, 19.9-36.8), 30.1 (95% CI, 21.0-39.0), 31.7 (95% CI, 29.1-34.2), 34.8 (95% CI, 32.4-37.1), and 36.8 (95% CI, 34.6-38.9), respectively (Figure 5).

Collectively, patient functional status, based on the total WOMAC score (range, 0-96 points), had remarkably improved after the GAE procedure. This reduction in absolute WOMAC scores (implying improved pain/functional status) gradually increased and reached about 73%, 79%, and 85% improvement after 6, 12, and 24 months of follow-up, respectively. Furthermore, P values remained statistically significant at these time points ($P <.00001$). Evidently, the forest plot indicating postoperational changes of the WOMAC pain subscale (Figure 6) confirmed the aforementioned pain reduction based on the VAS assessment. Figure 6 shows that the MD value of the pain subscale was 7.34 at the first month visit and reached 9.50 within 2 years. This amount of improvement (equivalent to 78.5%) was very close to that of the VAS (80%) after a 2-year follow-up. However, the data were not robust enough to calculate effect sizes of other WOMAC subscales. Moreover, we tried to compare the effectiveness of the main types of embolic agents (imipenem/cilastatin vs Embozene) in decreasing total WOMAC scores across the included studies (Figure 7). No statistically significant difference in clinical effectiveness based on the total WOMAC score was observed between these 2 agents ($P = .56$). However, Embozene showed slightly less effectiveness in terms of functional improvement within 1-month follow-up ($P = .56$). The effectiveness of GAE in decreasing the need for medications revealed about 27%, 65%, and 73% decline in the number of patients who used opioids, NSAIDs, and intra-articular hyaluronic acid, respectively ($P < .00001$

for all) (Table 5 and Figure 8). On the other hand, no remarkable decline was observed for acetaminophen consumption (equivalent to 10%; $P = .37$).

Adverse Events

Symptomatic improvement was reported in all studies. All adverse events were evaluated, and no severe or life-threatening complications were reported. To provide a uniform classification system and eliminate the subjective interpretation of complications, studies were evaluated based on the Society of Interventional Radiology classification system for complications.[17] The number of patients with any postembolization adverse events in each study has been depicted in Table 2. A total of 54 out of 214 participants with an overall complication rate of 25.2% mentioned minor adverse events, most commonly self-resolving transient cutaneous ischemia. Other reported minor complications included puncture site hematomas, skin redness, and transient fever in a few cases. No severe adverse events attributable to GAE, such as weakness and joint instability, were reported. There was a statistically significant difference in the risk ratios of complication for Embozene (0.91; $P < .00001$) versus imipenem/cilastatin (0.24; $P < .00001$) (Figure 9).

DISCUSSION

The results of this meta-analysis indicate that OA treated by GAE using Embozene, polyvinyl alcohol, resorbable microspheres, or imipenem/cilastatin could be generally considered a safe treatment with no serious complications. It could be associated with significant and sustained dramatic pain improvement with better functional status. There is no significant difference between embolic agents in regard to post-GAE pain reduction or functional improvement. To date, no randomized controlled trial has evaluated the efficacy of GAE. To the best of our knowledge, this is the first systematic review and meta-analysis to assess the current evidence for the effectiveness and safety of GAE in treatment of OA-related knee pain.

OA is recognized as a highly prevalent and leading cause of disability in adults worldwide.[12,40] This condition imposes a considerable psychosocial, physical, and economic burden on patients who experience OA. Numerous palliative techniques and interventions have been proposed to manage chronic pain, improve knee function, and prolong the time to joint replacement.[1,5,6,11,15] The cornerstone of OA management should include health education, lifestyle modifications coupled with over-the-counter remedies as well as regular moderate physical activity, and weight reduction to protect the articular cartilage against further stress.[10] Pain-relieving medications can be considered an adjunct to core treatments for mild to moderate OA by targeting pain-processing pathways. Local therapies, including intra-articular corticosteroid, viscosupplementation with hyaluronic acid injection, percutaneous neurolysis, and neuromodulation, have been proven to be alternatives in improving mild to moderate symptoms of OA of the knee.[14,16,23,26,32] However, these interventions provide time-limited and

TABLE 4
Summary of Pain and Functional Scores Before and After GAE[a]

| Outcome Measure	Bagla et al[2] (2020)	Okuno et al[27] (2015)	Okuno et al[28] (2017)	Lee et al[21] (2019)	Kumar and Chandrashekhara[19][b] (2020)	Bagla et al[3] (2020)	Piechowiak et al[31] (2017)	Lauko et al[20][c] (2020)
VAS pain								
Baseline	76 ± 14	70 ± 5	72 ± 16	KL grades 1-3: 5.5 ± 2.2 KL grade 4: 6.3 ± 2.2	7.6 out of 10	80.3	6.7 ± 1.6 out of 10	—
1 d	—	—	—	KL grades 1-3: 3.2 ± 2.1 KL grade 4: 4.1 ± 2.1	—	—	—	—
1 wk	—	29 ± 17		KL grades 1-3: 3.1 ± 1.9 KL grade 4: 4.1 ± 2.1	—	—	—	—
1 mo	22 ± 19	21 ± 16	38 ± 23	KL grades 1-3: 2.9 ± 1.7 KL grade 4: 4.4 ± 2.1	3 out of 10	49.82 ± 6.65 lower vs baseline	4 ± 1.6 out of 10	—
3-4 mo	34 ± 26	13 ± 15	29 ± 22	KL grades 1-3: 2.2 ± 1.7 KL grade 4: 5.4 ± 2	—	—	3.8 ± 1.6 out of 10	—
6 mo	31 ± 28	—	19 ± 21	KL grades 1-3: 1.9 ± 1.5 KL grade 4: 5.9 ± 2.1	—	—	—	—
12 mo	—	—	13 ± 21	KL grades 1-3: 1.8 ± 2.1 KL grade 4: 5.3 ± 1.1	—	—	—	—
24 mo	—	—	14 ± 17	—	—	—	—	—
WOMAC–total								
Baseline	61 ± 12	47.3 ± 5.8	43 ± 8.3	—			38.6 ± 9.4	44
1 mo	24 ± 17	11.6 ± 5.4	24 ± 14	—	18 points lower vs baseline	27.15 ± 6.24 lower vs baseline	19.8 ± 9.4	5
3-4 mo	31 ± 21	6.3 ± 6	14.8 ± 11	—	—	—	21.2 ± 9.4	4
6 mo	31 ± 26	—	11.2 ± 10	—	—	—	—	3
12 mo	—	—	8.2 ± 8.5	—	—	—	—	—
24 mo	—	—	6.2 ± 6.4	—	—	—	—	—
WOMAC–pain								
Baseline	14	12.2 ± 1.9	12.1 ± 2.3	—	—	—	—	—
1 mo	5	3.3 ± 2.1	6.2 ± 4	—	—	—	—	—
3-4 mo	7	1.7 ± 2.2	4.4 ± 3.5	—	—	—	—	—
6 mo	5	—	3.7 ± 1.8	—	—	—	—	—
12 mo	—	—	3 ± 3.1	—	—	—	—	—
24 mo	—	—	2.6 ± 3.4	—	—	—	—	—

[a]No data regarding pain score was reported in other studies by Padia et al[29] (2020) and Shibuya and Okuno[37] (2018). Data are presented as mean ± SD. Dashes indicate that the score is not reported. GAE, genicular artery embolization; KL, Kellgren-Lawrence; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
[b]This study was not included in the final meta-analysis because of the lack of data on SD.
[c]This study was not included in the final meta-analysis because it included just 1 case.

moderate pain relief. When repeated, these can deteriorate the integrity of joint structure because of probable complications, including tendon involvement, joint infection, sterile synovitis, and local nerve damage.[26]

OA had been classified as a noninflammatory arthritis for many decades; however, with the recognition of inflammatory mediators and immune processes in OA, the role of inflammation is perceived more strongly.[36,38]
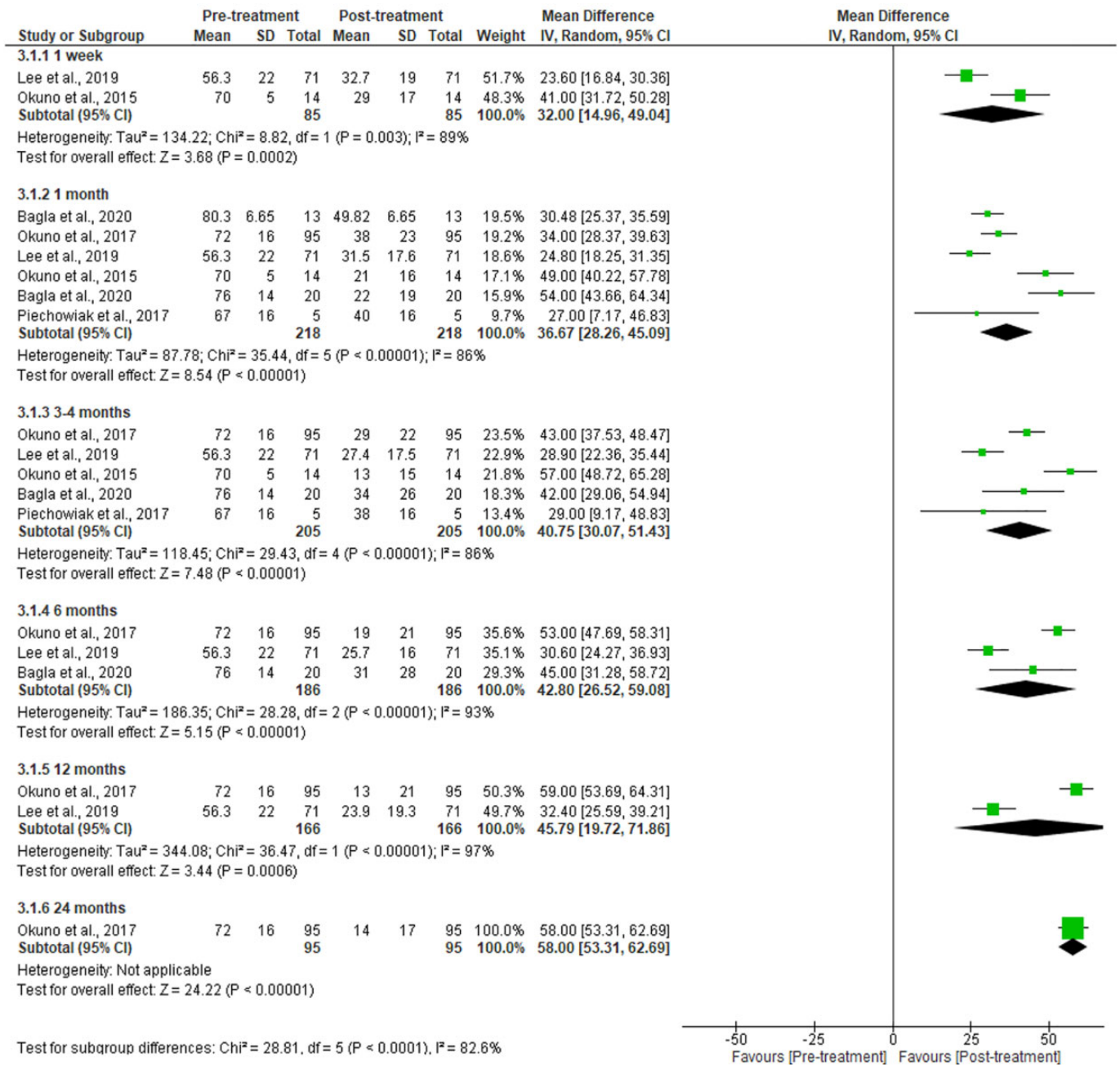
Figure 3. Forest plot demonstrating pre- and postembolization changes in absolute scores of the visual analog scale score at different time points. IV, inverse variance.

Ensuing abnormal neoangiogensis and growing sensory nerves from the pre-existing vasculature are the essential elements in potentiating further inflammation and chemical cascade of pain in OA.[28] These new vascularities have provided a potential target for directed or selective embolization in genicular arteries to alleviate pain.

GAE is an innovative technique that is investigated as an additional, often supplementary, method for palliation of chronic pain secondary to knee OA. While GAE does not appear to completely eliminate pain,[13] its potential to affect GAE's natural progression has yet to be studied. Currently, the available data seem to suggest GAE is a reasonable and safe additional option to alleviate pain, decrease the use of pharmacologic analgesic agents and injection therapies, and improve functional status. Patients undergoing GAE could theoretically experience knee joint replacement at an
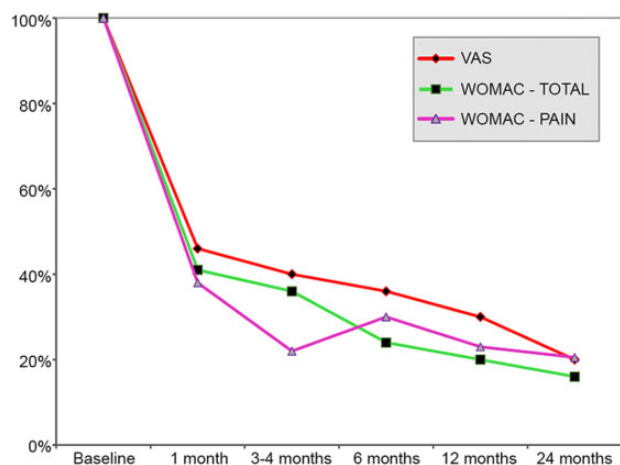
Figure 4. Therapeutic trajectory demonstrating the percentage of improvement in pain and functional scores at different time points (compared with baseline, considered 100%). VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

older age compared with patients without previous GAE,[11] a possible substantial benefit that will require long-term follow-ups for better understanding.

No severe or life-threatening perioperative complications were reported after the GAE procedure, which may be attributable to the small amount of embolic material utilized. Early pain reduction, self-resolution, and the low minor complication rate may warrant increased interest in GAE. These findings, however, should be interpreted with caution until larger prospective randomized trial data become available. Current limitations include the large heterogeneity in the follow-up time, with most of the studies having <2 years' follow-up and only 1 study having about 4 years' follow-up. Therefore, understanding of the long-term effects of GAE is limited, and results regarding sustained symptom relief and delay in need of total knee joint arthroplasty were inconclusive. The pooled analysis data in this study did not show any significant difference in the effectiveness and clinical outcomes of Embozene compared with imipenem/cilastatin based on the total WOMAC scale. Therefore, as imipenem/cilastatin has not
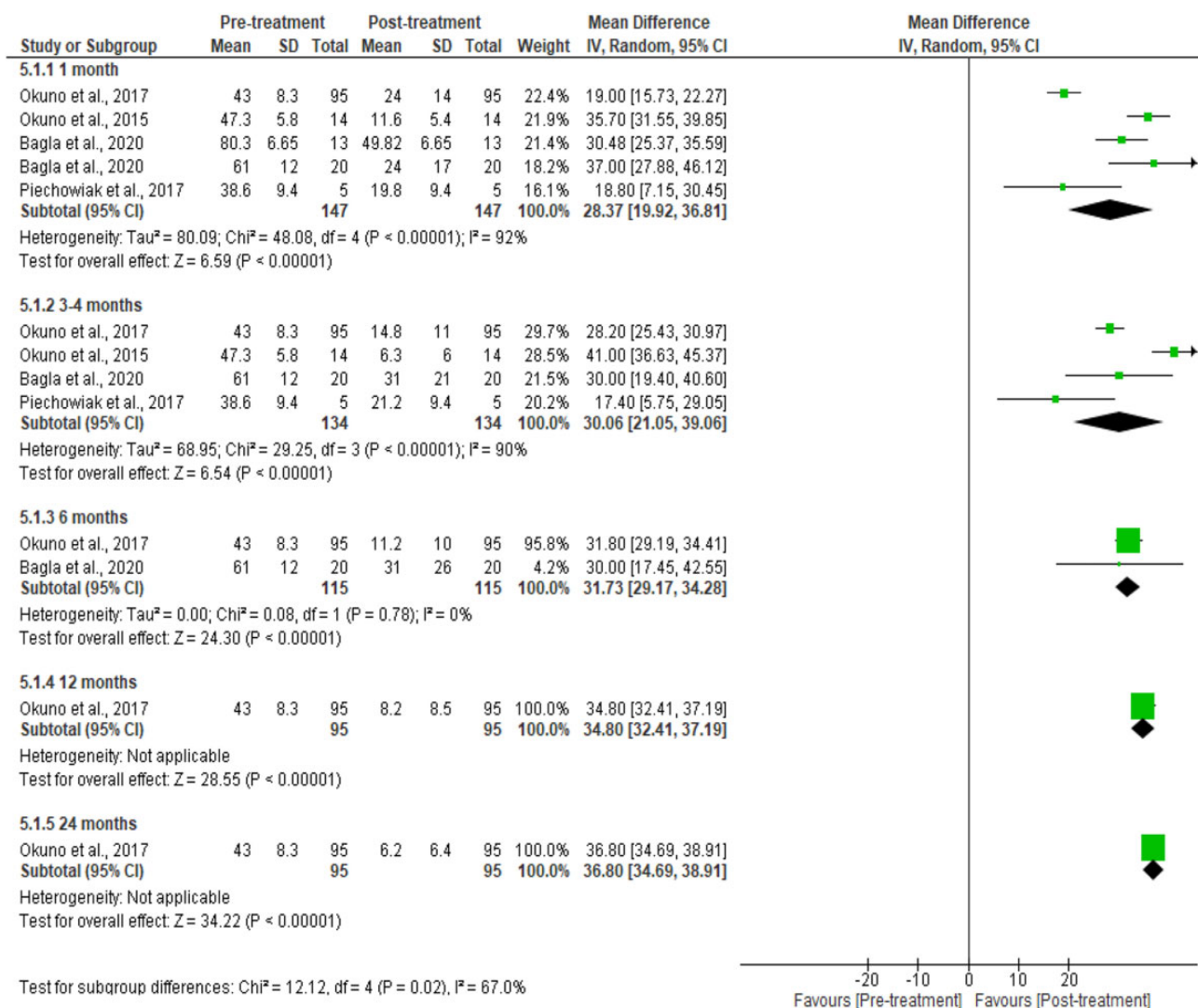
Figure 5. Forest plot demonstrating pre- and postembolization changes in patient-reported function based on the Western Ontario and McMaster Universities Osteoarthritis Index—total scores at different time points. IV, inverse variance.
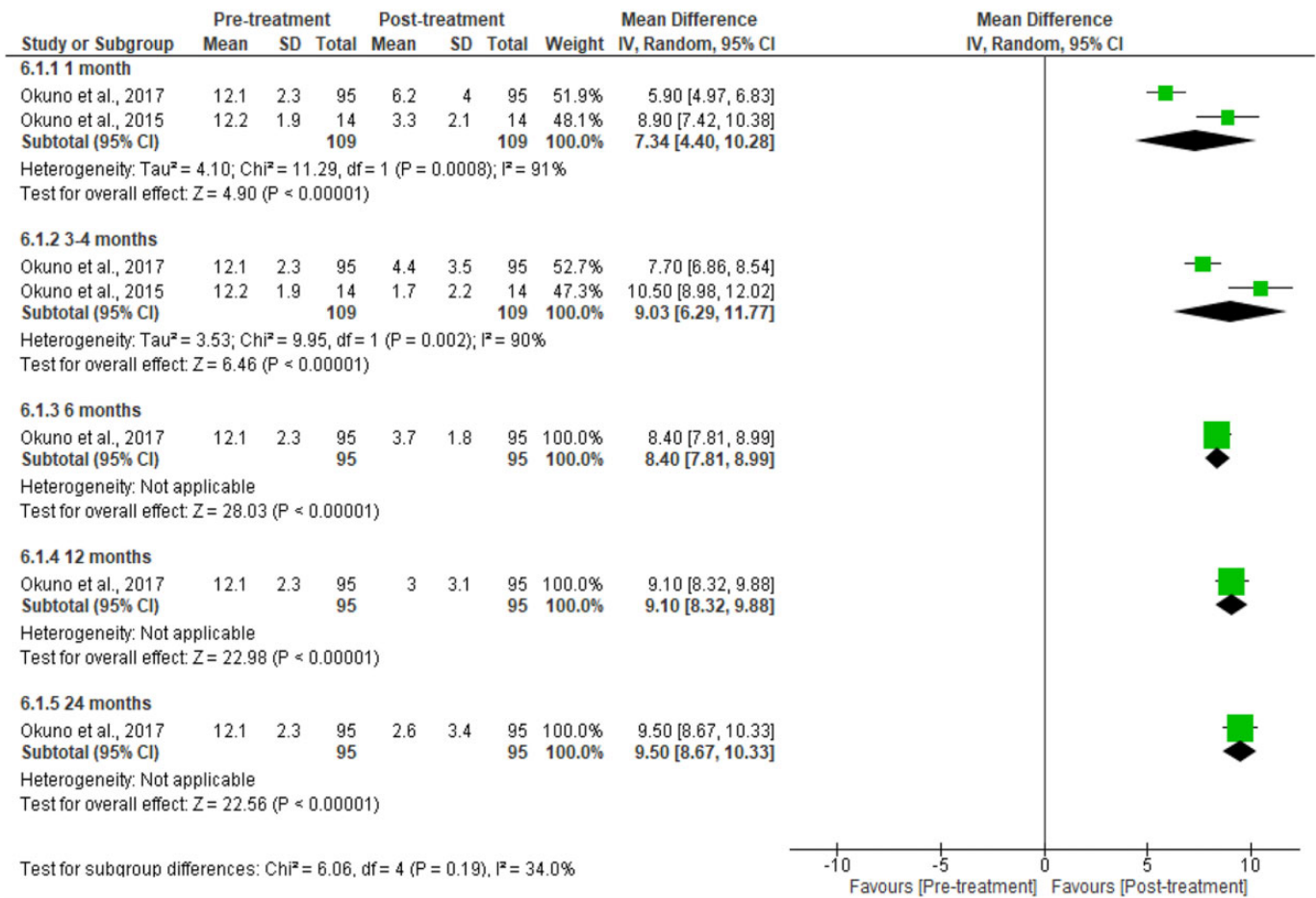
Figure 6. Forest plot demonstrating pre- and postembolization changes in the absolute scores of the Western Ontario and McMaster Universities Osteoarthritis Index–pain subscales at different time points.

yet been approved by the US Food and Drug Administration, it seems to be an equivalent embolic material for US patients. However, embolization performed by Embozene showed a higher minor complication rate compared to imipenem/cilastatin (0.24) ($P < .00001$), which may be attributable to particle size, suggesting a need for further investigation analysis. An alternative explanation for differences in outcomes (minor complication rates and effectiveness) could be attributed to the various techniques used by different institutions. As GAE evolves into a more established technique, angiographic technical details and intraprocedural endpoints will need to be further discussed and possibly consensus will be reached; however, at this stage, technical differences could be a source for higher effectiveness and lower complication rates among cases.

Other possibilities include the self-resorbable nature of imipenem/cilastatin versus the permanent presence of Embozene in the blood vessel, leading to different ischemic time of involved cutaneous branches. Additionally, differences in embolization technique or desired angiographic endpoints result in more aggressive embolization, which can increase the possibility of nontarget embolization.

To date, outcome measures include patient-reported pain/function changes and image-based assessments. Patient-reported outcome measures are used across trials to evaluate health status, and disease course or monitor patient progress after the intervention.[8,18] The widely used WOMAC has been suggested as one of the highest-performing outcome measures for knee and hip OA in terms of reliability, validity, responsiveness, and feasibility.[34] By evaluating included researches, we found that there was a lack of clarity and uniformity in how an outcome measure was used, making it more difficult to accurately interpret results between studies. Reporting the WOMAC total score should also contain results for the individual subscales of pain, stiffness, and physical activity. Results of OA trials treated with GAE should clearly report the specific subscale used for the WOMAC and the associated score range. This would allow readers to see whether the treatment effect is consistent across the 3 domains. Alternatively, the Knee injury and Osteoarthritis Outcome Score as an extension of the WOMAC can be used to compare the functional outcomes of all types of knee ailments, from traumatic injuries to OA, while the WOMAC score is used to compare the functional outcomes of OA treatments.[33]
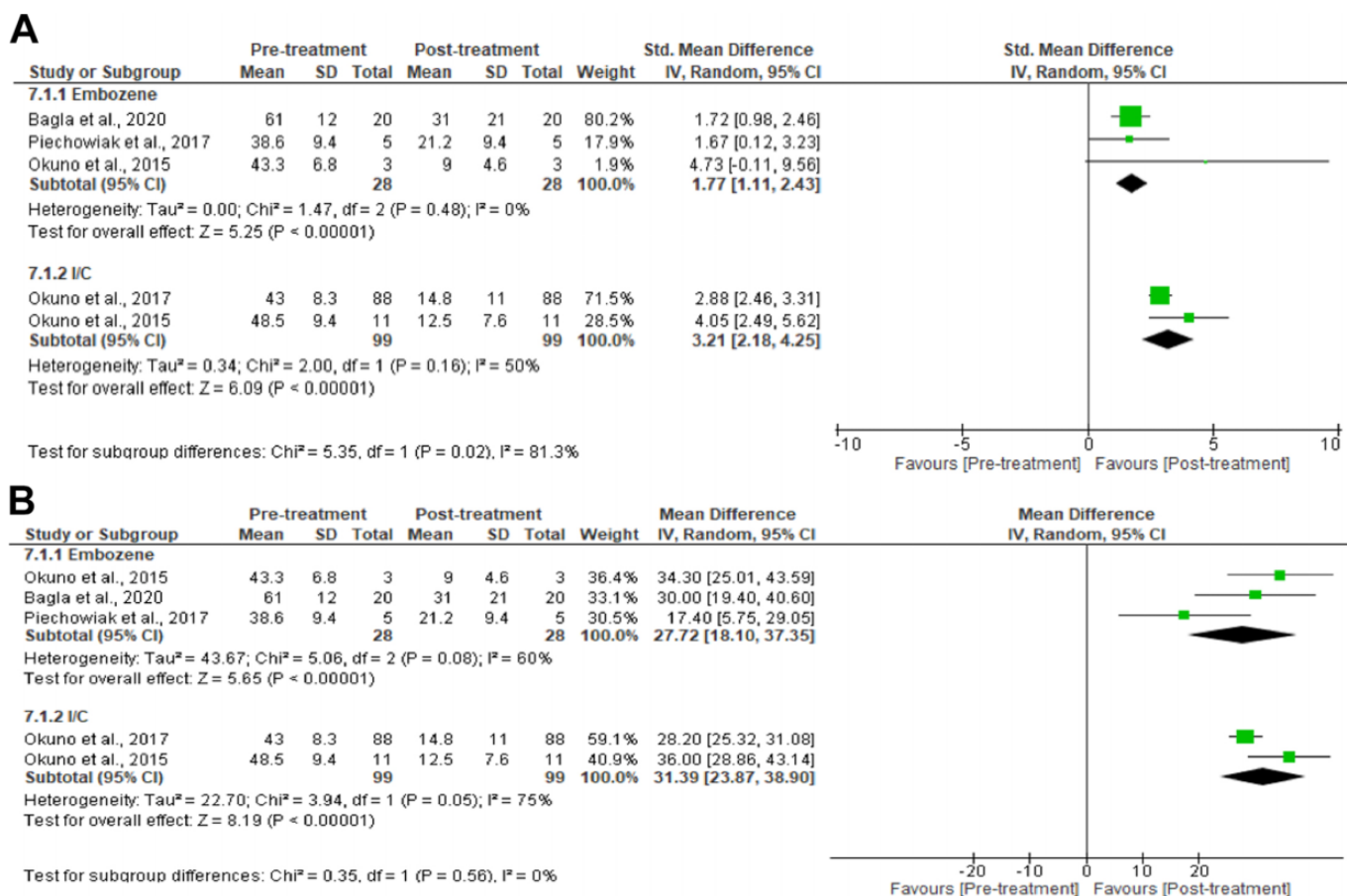
Figure 7. Forest plots demonstrating (A) the overall functional improvement (standard mean difference of WOMAC scores) and (B) the overall functional improvement (mean difference of WOMAC scores) between different embolic agents within 1-month follow-up. WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index. IV, inverse variance.

TABLE 5
Summary of Pain and Disability Scores Including the VAS and WOMAC Scores Before and after GAE[a]

| First Author, Year	Opiate (Daily + as needed)		NSAID (Daily + as needed)		Acetaminophen (Daily + as needed)		Hyaluronic Acid Injection	
	Baseline	Final Follow-up	Baseline	Final Follow-up	Baseline	Final Follow-up	Baseline	Final Follow-up
Bagla et al[2] (2020)	6	1	13	6	4	2	nr	nr
Okuno et al[27] (2015)	nr	nr	10	1	nr	nr	6	0
Okuno et al[28] (2017)	22	2	39	4	nr	nr	43	2
Lee et al[21] (2019)	nr	nr	56	12	nr	nr	49	3
Total	28	3	118	25	4	2	98	5

[a]No data regarding conservative treatment before and after GAE were reported in the studies by Shibuya and Okuno[37] (2018), Kumar and Chandrashekhara[19] (2020), Padia et al[29] (2020), Bagla et al[3] (2020), and Piechowiak et al[31] (2017). GAE, genicular artery embolization; nr, not reported; NSAID, nonsteroidal anti-inflammatory drug; VAS, visual analog scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

The most sensitive imaging modality in the assessment of knee OA is MRI. The multifeatured Whole-Organ Magnetic Resonance Imaging Score (WORMS) was the first scoring system published and has been commonly utilized in research for more than a decade in the OA and orthopaedic literature. WORMS scores should be used at baseline and long-term GAE follow-up to assess the markers of baseline knee joint pathology and treatment response.[30] Among included studies, only Okuno et al[28] showed modifications of the knee structure after GAE at
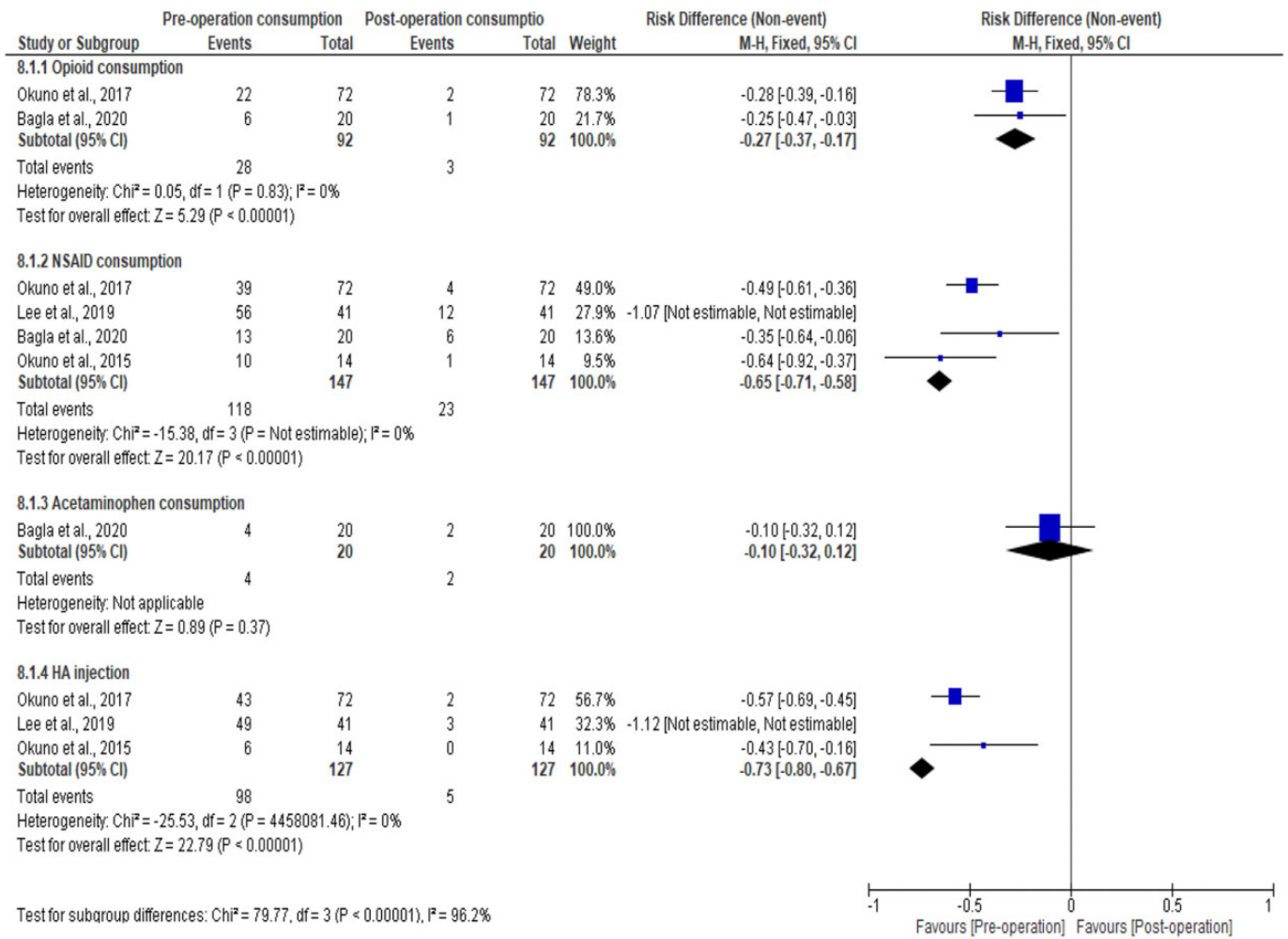
Figure 8. Forest plot demonstrating overall changes in consumption proportion of concurrent pharmacologic medications pre- and postoperatively. M-H, Mantel-Haenszel.
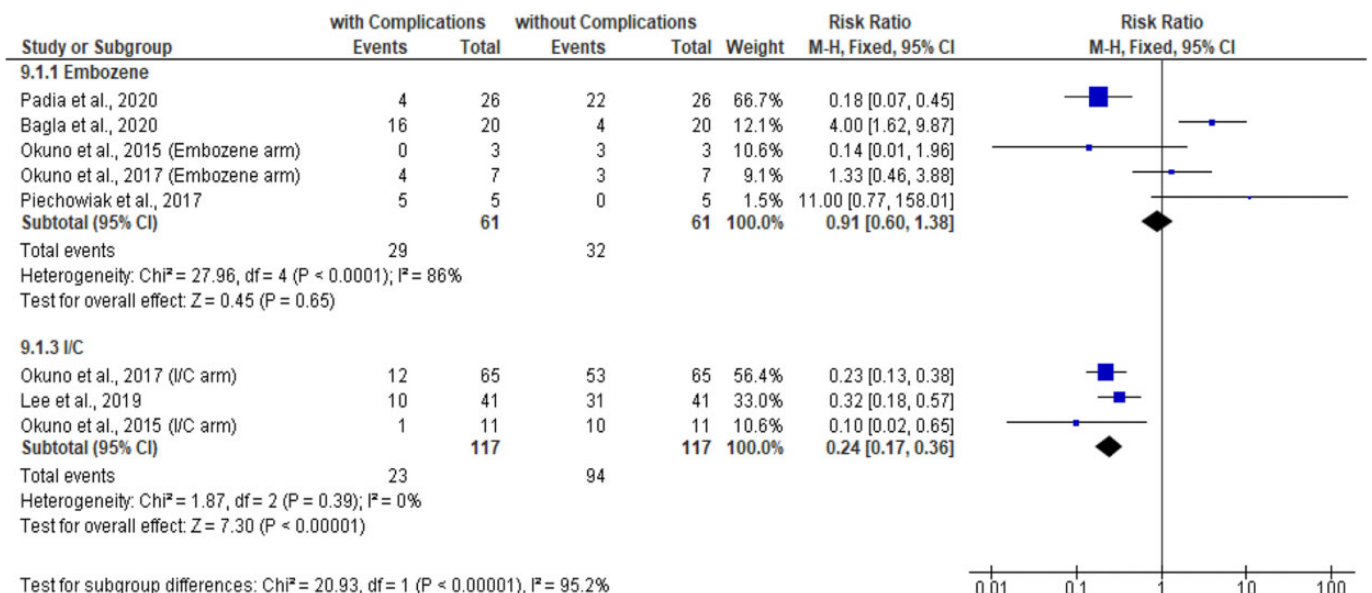
Figure 9. Forest plot demonstrating overall complications risk ratio (event vs nonevent) across different embolic agents. I/C, imipenem/cilastatin; M-H, Mantel-Haenszel.

24 months by using the WORMS. A significant improvement for synovitis was depicted with no other significant changes in cartilage, marrow abnormality, bone cysts, bone attrition, osteophyte, menisci, and ligaments compared with the baseline. Hence, the utilization and standardization of a specific imaging protocol for semiquantitative whole-organ assessments will be central to future meticulous GAE research.

In terms of health economy, surgical procedures are the major driver of the high total cost compared with routine medications among patients with OA-related knee pain. Little data exist to draw a definite conclusion, especially when it comes to cost-effectiveness analysis and comparison for quality-adjusted life years of GAE. In a study by Davies and Isaacson,[7] GAE for knee OA was shown to be more expensive than NSAIDs, but less than cyclooxygenase-2–selective drugs when expected future complication costs were considered. However, for a better comparison, quality-adjusted life years, long-term follow-up, and available prices of a wide variety of products will be needed in future trials.

As far as the general limitations of the study are concerned, available studies lacked a control group (other treatment modalities). Additionally, the studies have been reported from a limited number of geographical regions. Thus, further patient-centered investigations of the GAE safety and effectiveness in other geographical regions, with a larger sample size from different ethnic groups and longer duration of follow-up, is needed to improve the quality of evidence in terms of durability, efficacy, and safety of this treatment. If true and sufficiently robust, GAE can have significant implications on the current treatment paradigm for patients who experience OA of the knee.

CONCLUSION

Our systematic review revealed that mild to moderate OA treated by GAE using different embolic particles could generally be considered safe, with no reported serious complications. The procedure resulted in significant and sustained pain improvement as well as better functional status in the studies reviewed. However, because of the paucity of high-quality trials, further research is warranted to evaluate GAE's long-term outcomes, its comparative efficacy with other treatment modalities, and its role in the therapeutic approach.

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REFERENCES

1. Alcaraz MJ, Guillén MI, Ferrándiz ML. Emerging therapeutic agents in osteoarthritis. *Biochem Pharmacol*. 2019;165:4-16.
2. Bagla S, Piechowiak R, Hartman T, Orlando J, Del Gaizo D, Isaacson A. Genicular artery embolization for the treatment of knee pain secondary to osteoarthritis. *J Vasc Interv Radiol*. 2020;31(7):1096-1102.
3. Bagla S, Piechowiak R, Hartman T, et al. 3:00 PM Abstract No. 3. DISTINGUISHED ABSTRACT multicenter prospective, randomized, sham-controlled study of genicular artery embolization. *J Vasc Interv Radiol*. 2020;31(3):S6.
4. Cao P, Li Y, Tang Y, Ding C, Hunter DJ. Pharmacotherapy for knee osteoarthritis: current and emerging therapies. *Expert Opin Pharmacother*. 2020;21(7):797-809.
5. Charlesworth J, Fitzpatrick J, Perera NKP, Orchard J. Osteoarthritis: a systematic review of long-term safety implications for osteoarthritis of the knee. *BMC Musculoskelet Disord*. 2019;20(1):151.
6. Collins NJ, Hart HF, Mills KAG. Osteoarthritis year in review 2018: rehabilitation and outcomes. *Osteoarthritis Cartilage*. 2019;27(3):378-391.
7. Davies E, Isaacson A. 3:27 PM Abstract No. 204 Cost analysis of geniculate artery embolization versus conservative therapy for pain secondary to knee osteoarthritis. *J Vasc Interv Radiol*. 2018;29(4):S89.
8. Dobson GP, Letson HL, Grant A, et al. Defining the osteoarthritis patient: back to the future. *Osteoarthritis Cartilage*. 2018;26(8):1003-1007.
9. Driban JB, Harkey MS, Liu SH, et al. Osteoarthritis and aging: young adults with osteoarthritis. *Curr Epidemiol Rep*. 2020;7(1):9-15.
10. Filardo G, Kon E, Longo UG, et al. Nonsurgical treatments for the management of early osteoarthritis. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(6):1775-1785.
11. Filippiadis D, Charalampopoulos G, Mazioti A, et al. Interventional radiology techniques for pain reduction and mobility improvement in patients with knee osteoarthritis. *Diagn Interv Imaging*. 2019;100(7-8):391-400.
12. Georgiev T, Angelov AK. Modifiable risk factors in knee osteoarthritis: treatment implications. *Rheumatol Int*. 2019;39(7):1145-1157.
13. Goldman DT, Piechowiak R, Nissman D, Bagla S, Isaacson A. Current concepts and future directions of minimally invasive treatment for knee pain. *Curr Rheumatol Rep*. 2018;20(9):54.
14. Huskin JP, Vandekerckhove B, Delincé P, et al. Multicentre, prospective, open study to evaluate the safety and efficacy of hylan G-F 20 in knee osteoarthritis subjects presenting with pain following arthroscopic meniscectomy. *Knee Surg Sports Traumatol Arthrosc*. 2008;16(8):747-752.
15. Jones IA, Togashi R, Wilson ML, Heckmann N, Vangsness CT Jr. Intra-articular treatment options for knee osteoarthritis. *Nat Rev Rheumatol*. 2019;15(2):77-90.
16. Jüni P, Reichenbach S, Trelle S, et al. Efficacy and safety of intraarticular hylan or hyaluronic acids for osteoarthritis of the knee: a randomized controlled trial. *Arthritis Rheum*. 2007;56(11):3610-3619.
17. Khalilzadeh O, Baerlocher MO, Shyn PB, et al. Proposal of a new adverse event classification by the Society of Interventional Radiology Standards of Practice Committee. *J Vasc Interv Radiol*. 2017;28(10):1432-1437.e3. doi: 10.1016/j.jvir.2017.06.019
18. Kloppenburg M, Berenbaum F. Osteoarthritis year in review 2019: epidemiology and therapy. *Osteoarthritis Cartilage*. 2020;28(3):242-248.
19. Kumar S, Chandrashekhara S. 3:27 PM Abstract No. 6 Feasibility, safety, and efficacy of genicular artery embolization for relief of knee pain related to osteoarthritis. *J Vasc Interv Radiol*. 2020;31(3):S7.
20. Lauko K, Tangchaiburana S, Padia S. Transarterial genicular artery embolization as treatment of painful knee osteoarthritis in a 64-year-old woman. *J Radiol Nurs*. 2020;39:89-91.
21. Lee SH, Hwang JH, Kim DH, et al. Clinical outcomes of transcatheter arterial embolisation for chronic knee pain: mild to moderate versus severe knee osteoarthritis. *Cardiovasc Intervent Radiol*. 2019;42(11):1530-1536.

22. Little M, Gibson M, Davies N, et al. Geniculate artery embolisation in patients with osteoarthritis of the knee (genesis): preliminary results. *Cardiovasc Intervent Radiol*. 2020;43(2):S57-S58.

23. Liu SC, Qiao XF, Tang QX, et al. Therapeutic efficacy of extracorporeal shock wave combined with hyaluronic acid on knee osteoarthritis. *Medicine (Baltimore)*. 2019;98(8):e14589.

24. Lonner JH, Hershman S, Mont M, Lotke PA. Total knee arthroplasty in patients 40 years of age and younger with osteoarthritis. *Clin Orthop Relat Res*. 2000;380:85-90.

25. Mandl LA. Osteoarthritis year in review 2018: clinical. *Osteoarthritis Cartilage*. 2019;27(3):359-364

26. Nguyen C, Rannou F. The safety of intra-articular injections for the treatment of knee osteoarthritis: a critical narrative review. *Expert Opin Drug Saf*. 2017;16(8):897-902.

27. Okuno Y, Korchi AM, Shinjo T, Kato S. Transcatheter arterial embolization as a treatment for medial knee pain in patients with mild to moderate osteoarthritis. *Cardiovasc Intervent Radiol*. 2015;38(2):336-343.

28. Okuno Y, Korchi AM, Shinjo T, Kato S, Kaneko T. Midterm clinical outcomes and MR imaging changes after transcatheter arterial embolization as a treatment for mild to moderate radiographic knee osteoarthritis resistant to conservative treatment. *J Vasc Interv Radiol*. 2017;28(7):995-1002.

29. Padia S, Plotnik A, Blumstein G, et al. 4:12 PM Abstract No. 11 Prospective investigational device exemption trial of genicular artery embolization for the treatment of knee osteoarthritis: interim safety results. *J Vasc Interv Radiol*. 2020;31(3):S9.

30. Peterfy CG, Guermazi A, Zaim S, et al. Whole-Organ Magnetic Resonance Imaging Score of the knee in osteoarthritis. *Osteoarthritis Cartilage*. 2004;12(3):177-190.

31. Piechowiak R, Garcia-Monaco R, Smirniotopoulos J, Bagla S. Geniculate artery embolization for osteoarthritis-related knee pain: preliminary results from a pilot experience. *J Vasc Interv Radio*. 2017;2(28):S28-S29.

32. Richards MM, Maxwell JS, Weng L, Angelos MG, Golzarian J. Intra-articular treatment of knee osteoarthritis: from anti-inflammatories to products of regenerative medicine. *Phys Sportsmed*. 2016;44(2):101-108.

33. Roos EM, Toksvig-Larsen S. Knee injury and Osteoarthritis Outcome Score—validation and comparison to the WOMAC in total knee replacement. *Health Qual Life Outcomes*. 2003;1:17.

34. Salaffi F, Leardini G, Canesi B, et al. Reliability and validity of the Western Ontario and McMaster Universities Osteoarthritis Index in Italian patients with osteoarthritis of the knee. *Osteoarthritis Cartilage*. 2003;11(8):551-560.

35. Sarı S, Aydın ON, Turan Y, Özlülerden P, Efe U, Ömürlü İK. Which one is more effective for the clinical treatment of chronic pain in knee osteoarthritis: radiofrequency neurotomy of the genicular nerves or intra-articular injection? *Int J Rheum Dis*. 2018;21(10):1772-1778.

36. Scanzello CR, Goldring SR. The role of synovitis in osteoarthritis pathogenesis. *Bone*. 2012;51(2):249-257.

37. Shibuya M, Okuno Y. Embolization for OA: which patients are the most suitable candidates? *Endovascular Today*. 2018;17(4):54-56.

38. Sohn DH, Sokolove J, Sharpe O, et al. Plasma proteins present in osteoarthritic synovial fluid can stimulate cytokine production via toll-like receptor 4. *Arthritis Res Ther*. 2012;14(1):R7.

39. Vaishya R, Pariyo GB, Agarwal AK, Vijay V. Nonoperative management of osteoarthritis of the knee joint. *J Clin Orthop Trauma*. 2016;7(3):170-176.

40. Zhao X, Shah D, Gandhi K, et al. Clinical, humanistic, and economic burden of osteoarthritis among noninstitutionalized adults in the United States. *Osteoarthritis Cartilage*. 2019;27(11):1618-1626.

APPENDIX

TABLE A1
Search Strategy[a]

Search	Query	Results, n
PubMed		
#1	"Osteoarthritis"[MeSH] OR "Osteoarthritis, Knee"[MeSH] OR "Osteoarthritides"[All Fields] OR "Osteoarthrosis"[All Fields] OR "Osteoarthroses"[All Fields] OR "Degenerative Arthritides"[All Fields] OR "Degenerative Arthritis"[All Fields] OR "Arthrosis"[All Fields] OR "Arthroses"[All Fields] OR "Osteoarthrosis Deformans"[All Fields] OR "Knee Osteoarthritides"[All Fields] OR "Knee Osteoarthritis"[All Fields] OR "Osteoarthritis of Knee"[All Fields] OR "Osteoarthritis of the Knee"[All Fields] OR "knee pain"[All Fields] OR "pain of knee"[All Fields] OR "knee joint pain"[All Fields] OR "pain of knee joint"[All Fields] OR "knee disabilit*"[All Fields] OR "disability of knee"[All Fields] OR "disabilities of knee"[All Fields] OR "disability of knee joint"[All Fields] OR "disabilities of knee joint"[All Fields] OR "disability of the knee"[All Fields] OR "disabilities of the knee"[All Fields] OR "disability of the knee joint"[All Fields] OR "disabilities of the knee joint"[All Fields] OR "pain of the knee"[All Fields] OR "pain of the knee joint"[All Fields]	77,671
#2	"Embolization, Therapeutic"[MeSH] OR "Embolotherapy"[All Fields] OR "Embolotherapies"[All Fields] OR "Therapeutic Embolization*"[All Fields] OR "geniculate artery embolization*"[All Fields] OR "geniculate arteries embolization*"[All Fields] OR "embolization of geniculate arter*"[All Fields] OR "GAE"[All Fields] OR "embolization of the geniculate arter*"[All Fields] OR "genicular artery embolization"[All Fields] OR "genicular arteries embolization"[All Fields] OR "embolization of genicular arter*"[All Fields] OR "embolization of the genicular arter*"[All Fields] OR "arterial embolization"[All Fields] OR "embolization of arter*"[All Fields] OR "geniculate artery embolisation*"[All Fields] OR "geniculate arteries embolisation*"[All Fields] OR "embolisation of geniculate arter*"[All Fields] OR "embolisation of the geniculate arter*"[All Fields] OR "genicular artery embolisation"[All Fields] OR "genicular arteries embolisation"[All Fields] OR "embolisation of genicular arter*"[All Fields] OR "embolisation of the genicular arter*"[All Fields] OR "arterial embolisation"[All Fields] OR "embolisation of arter*"[All Fields]	46,003
#3	#1 and #2	24

(continued)

Table A1 (continued)

Search	Query	Results, n
EMBASE		
#1	"Osteoarthritis"/mj OR "knee osteoarthritis"/mj OR "Osteoarthritides": ti, ab, kw OR "Osteoarthrosis": ti, ab, kw OR "Osteoarthroses": ti, ab, kw OR "Degenerative Arthritides": ti, ab, kw OR "Degenerative Arthritis": ti, ab, kw OR "Arthrosis": ti, ab, kw OR "Arthroses": ti, ab, kw OR "Osteoarthrosis Deformans": ti, ab, kw OR "Knee Osteoarthritides": ti, ab, kw OR "Knee Osteoarthritis": ti, ab, kw OR "Osteoarthritis of Knee": ti, ab, kw OR "Osteoarthritis of the Knee": ti, ab, kw OR "knee pain": ti, ab, kw OR "pain of knee": ti, ab, kw OR "knee joint pain": ti, ab, kw OR "pain of knee joint": ti, ab, kw OR "knee disabilit*": ti, ab, kw OR "disability of knee": ti, ab, kw OR "disabilities of knee": ti, ab, kw OR "disability of knee joint": ti, ab, kw OR "disabilities of knee joint": ti, ab, kw OR "disability of the knee": ti, ab, kw OR "disabilities of the knee": ti, ab, kw OR "disability of the knee joint": ti, ab, kw OR "disabilities of the knee joint": ti, ab, kw OR "pain of the knee": ti, ab, kw OR "pain of the knee joint": ti, ab, kw	90,368
#2	"arterial embolization"/mj OR "Embolotherapy": ti, ab, kw OR "Embolotherapies": ti, ab, kw OR "Therapeutic Embolization*": ti, ab, kw OR "geniculate artery embolization*": ti, ab, kw OR "geniculate arteries embolization*": ti, ab, kw OR "embolization of geniculate arter*": ti, ab, kw OR "GAE": ti, ab, kw OR "embolization of the geniculate arter*": ti, ab, kw OR "genicular artery embolization": ti, ab, kw OR "genicular arteries embolization": ti, ab, kw OR "embolization of genicular arter*": ti, ab, kw OR "embolization of the genicular arter*": ti, ab, kw OR "arterial embolization": ti, ab, kw OR "embolization of arter*": ti, ab, kw OR "geniculate artery embolisation*": ti, ab, kw OR "geniculate arteries embolisation*": ti, ab, kw OR "embolisation of geniculate arter*": ti, ab, kw OR "embolisation of the geniculate arter*": ti, ab, kw OR "genicular artery embolisation": ti, ab, kw OR "genicular arteries embolisation": ti, ab, kw OR "embolisation of genicular arter*": ti, ab, kw OR "embolisation of the genicular arter*": ti, ab, kw OR "arterial embolisation": ti, ab, kw OR "embolisation of arter*": ti, ab, kw	14,210
#3	#1 and #2	40
Scopus		
#1	((TITLE-ABS-KEY ("Osteoarthritis" OR "knee osteoarthritis" OR "Osteoarthritides" OR "Osteoarthrosis" OR "Osteoarthroses" OR "Degenerative Arthritides" OR "Degenerative Arthritis" OR "Arthrosis" OR "Arthroses" OR "Osteoarthrosis Deformans" OR "Knee Osteoarthritides" OR "Knee Osteoarthritis" OR "Osteoarthritis of Knee" OR "Osteoarthritis of the Knee" OR "knee pain" OR "pain of knee" OR "knee joint pain" OR "pain of knee joint" OR "knee disabilit*" OR "disability of knee" OR "disabilities of knee" OR "disability of knee joint" OR "disabilities of knee joint" OR "disability of the knee" OR "disabilities of the knee" OR "disability of the knee joint" OR "disabilities of the knee joint" OR "pain of the knee" OR "pain of the knee joint")) AND (TITLE-ABS-KEY ("arterial embolization" OR "Embolotherapy" OR "Embolotherapies" OR "Therapeutic Embolization*" OR "geniculate artery embolization*" OR "geniculate arteries embolization*" OR "embolization of geniculate arter*" OR "GAE" OR "embolization of the geniculate arter*" OR "genicular artery embolization" OR "genicular arteries embolization" OR "embolization of genicular arter*" OR "embolization of the genicular arter*" OR "arterial embolization" OR "embolization of arter*" OR "geniculate artery embolisation*" OR "geniculate arteries embolisation*" OR "embolisation of geniculate arter*" OR "embolisation of the geniculate arter*" OR "genicular artery embolisation" OR "genicular arteries embolisation" OR "embolisation of genicular arter*" OR "embolisation of the genicular arter*" OR "arterial embolisation" OR "embolisation of arter*")))	34
Web of Science		
#1	ALL=(Osteoarthritis OR Osteoarthr* OR Arthr* OR Osteoarthritis of the Knee OR knee pain OR pain of knee OR knee joint pain OR pain of knee joint OR knee disabilit* OR disability of knee OR disabilities of knee OR disabilities of knee joint OR disability of the knee OR disabilities of the knee OR pain of the knee OR pain of the knee joint) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years	663,784
#2	ALL=(arterial embolization* OR Embolotherap* OR geniculate artery embolization* OR geniculate arteries embolization* OR embolization of geniculate arter* OR GAE OR genicular artery embolization OR embolization of genicular arter* OR embolization of the genicular arter* OR embolization of arter* OR geniculate artery embolisation* OR geniculate embolisation) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC Timespan=All years	42,151
#3	#1 and #2	281

[a]All searches were performed on August 11, 2020. MeSH, Medical Subject Headings.