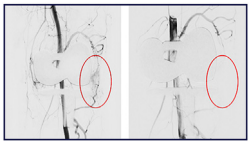

Effectiveness of Geniculate Artery Embolization for Chronic Pain after Total Knee Replacement—A Pilot Study

Yves Chau, MD, Christian Roux, MD, PhD, Jean-François Gonzalez, MD, PhD, Véronique Breuil, MD, PhD, Régis Bernard de Dompsure, MD, Eric Fontas, MD, Alexandre Rudel, MD, and Jacques Sédat, MD

ABSTRACT

Purpose: To evaluate the efficacy and safety of embolization of hyperemic synovial tissue for the treatment of persistent pain after total knee arthroplasty (TKA).

Materials and Methods: Twelve patients with persistent pain after TKA were enrolled in this prospective, single-center pilot study. Genicular artery embolization (GAE) was performed using 75-μm spherical particles. The patients were assessed using a 100-point Visual Analog Scale (VAS) and Knee Injury and Osteoarthritis Outcome Score (KOOS) at baseline and 3 and 6 months thereafter. Adverse events were recorded at all time points.

Results: A mean of 1.8 ± 0.8 abnormal hyperemic genicular arteries were identified and embolized, with a median volume of diluted embolic material of 4.3 mL in all 12 (100%) patients. The mean VAS score on walking improved from 73 ± 16 at baseline to 38 ± 35 at the 6-month follow-up ($P < .05$). The mean KOOS pain score improved from 43.6 ± 15.5 at baseline to 64.6 ± 27.1 at the 6-month follow-up ($P < .05$). At the 6-month follow-up, 55% and 73% of the patients attained a minimal clinically important change in pain and quality of life, respectively. Self-limited skin discoloration occurred in 5 (42%) patients. The VAS score increased by more than 20 immediately after embolization in 4 (30%) patients, who required analgesic treatment for 1 week.

Conclusion: GAE is a safe method of treating persistent pain after TKA that demonstrates potential efficacy at 12 months.

ABBREVIATIONS

GAE = genicular artery embolization, KOA = knee osteoarthritis, KOOS = Knee Injury and Osteoarthritis Outcome Score, STAR = support and treatment after replacement, TKA = total knee arthroplasty, VAS = Visual Analog Scale

In 2011, the United States recorded the highest incidence of total knee arthroplasty (TKA) worldwide, with 235 procedures per 100,000 people (1), translating to 733,447 TKAs that year. The rate of increase in TKA has been slowing in recent years, and models based on data from 2008 to 2014 have projected growth to approximately 935,000 procedures by 2030 in the United States (2). The primary aims of TKAs are to reduce pain and improve function, which relate to a diagnosis of osteoarthritis in 97% of patients (3,4). TKA has been shown to produce good clinical results in 80% of patients during long-term follow-up (5,6). In a randomized controlled trial, Skou et al (7) showed that TKA was superior to nonsurgical treatment alone in providing pain relief and improving function and quality of life after 12 months in patients with moderate-to-severe knee osteoarthritis (KOA) who were eligible for unilateral TKA.

Following TKA, 20% of patients continue to experience pain, although the intensity of this pain typically decreases over time (3,8). In the United Kingdom, nearly 100,000 primary TKAs are performed annually; therefore, 20,000 patients potentially experience chronic pain every year after TKA (4). Chronic pain after TKA can affect all dimensions of health-related quality of life and is associated with functional limitations, depression, anxiety, poorer general health, sleep problems, and long-term opioid use (4,8,9). The sources of pain may be broadly defined as intra-articular (infection and aseptic loosening), periarticular (periprosthetic fractures and neuromas), or extra-articular (hip and/or lumbar spine pathology and complex regional pain syndrome) (4,5). Residual pain, however, remains unexplained in as many as 10%–15% of patients (4,10). Angiogenesis allows the growth of sensory nerve fibers

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RESEARCH HIGHLIGHTS

- In this prospective pilot study, 12 patients with chronic pain 12 months following total knee arthroplasty were treated with embolization using 75-μm permanent spherical particles. Embolization targeted genicular arteries supplying hypervascularity.
- A decrease of at least 20 points in the 100-point Visual Analog Pain Score at 6 months was achieved in 64% of the patients.
- Transient increased pain was experienced by 30% of patients during the 2 weeks following embolization.
- No serious adverse events were observed.

along the pathways of new blood vessels, which may contribute to chronic pain (11). The levels of proinflammatory markers and mediators of angiogenesis are elevated in noninfectious postrevision painful TKA, indicating an active, chronic, and ongoing inflammatory process (12).

Genicular artery embolization (GAE) of abnormal vessels has been used to treat knee hemarthrosis (13,14) and pain resistant to conservative treatment in patients with KOA. This treatment is based on the theory that neovascularity and accompanying inflamed nerves are a possible source of chronic pain and that occlusion of these abnormal vessels may reduce such pain (15). Because a similar chronic inflammatory state may be observed after TKA, GAE of neovessels might relieve pain in this condition. In a preliminary study, 4 patients with persistent pain after TKA were treated with GAE, without major adverse events, with a 1-month follow-up (16). The aim of this open-label study was to investigate the efficacy of GAE in patients with persistent pain after TKA at 3 and 6 months of follow-up.

MATERIALS AND METHODS

Patients

The study protocol and consent forms were approved by the Comité de Protection des Personnes Sud-Ouest et Outre-Mer II—Toulouse II (2-20-054 id8465). Twelve patients with persistent unexplained pain following TKA were included in this prospective, single-center, single-arm study conducted from January 2021 to April 2022 (**Fig 1**). The study was conducted according to Good Clinical Practice requirements and the tenets of the Helsinki Declaration and registered on ClinicalTrials.gov (NCT04566315). Written informed consent was obtained from all patients.

The inclusion criteria were as follows: age of 40–80 years, 12 months of conservative therapy (oral nonsteroidal anti-inflammatory and/or oral opioid drugs and physical therapy), and knee pain greater than 5 out of 10 (50 out of 100) on the Visual Analog Scale (VAS). Patients with conditions that could cause residual pain were excluded.

STUDY DETAILS

Study type: Prospective, observational, descriptive study

Level of evidence: 4 (SIR-D)

These included low-grade infection; midflexion instability; component malalignment with patellar maltracking; crepitation and patellar clunk syndrome; patellofemoral symptoms, including overstuffing and avascular necrosis of the patella; early aseptic loosening; hypersensitivity to metal or cement; complex regional pain syndrome; and pseudoaneurysms. Patients were assessed for exclusion criteria by an orthopedic surgeon (J-F.G., R.BdD.) and a rheumatologist (C.R.). All patients underwent knee radiography as well as biological and nuclear medicine imaging to exclude septic or aseptic loosening. All patients underwent power Doppler ultrasonography to locate the area of hypervascularization.

Procedure

All GAE procedures were performed by 2 neurovascular interventional radiologists (J.S., Y.C.) with 20 and 15 years of outpatient experience (including 25 GAE procedures performed prior to this study). The procedure was the same in all 12 patients. Before the intervention, a radiopaque marker was applied to the skin overlying the pain site identified on palpation. Under local anesthesia, percutaneous retrograde contralateral femoral access was established in all patients using a 4-F introducer sheath (Radiofocus Introducer II; Terumo, Tokyo, Japan). A 4-F Berenstein angiographic catheter (Cordis, Miami Lakes, Florida) was positioned distally in the contralateral superficial femoral artery. Digital subtraction angiography was performed following injection of 8 mL of iodinated contrast medium (Xenetix 300; Guerbet, France) to enable imaging of the popliteal artery. Initial digital subtraction angiography was performed to identify the appropriate genicular branches supplying the regions of hyperemia near the radiopaque marker (synovial blush). All enlarged hyperemic genicular arteries supplying the regions of maximal tenderness were investigated.

Microcatheter selection was achieved using a 1.3-F Headway Duo (MicroVention; Terumo, Tustin, California) in branches that exhibited "tumor blush"–type vascularity. A dilute embolic solution was created by mixing 100 mL of nonionic contrast material with 6 mL of Embozene microspheres (75 μm), which came in a prepackaged syringe (Boston Scientific, Marlborough, Massachusetts). The embolic agent was selected based on previous reports of GAE in patients with refractory painful KOA (15,17) and persistent pain after TKA (16). This dilution was used to avoid clogging or aggregate formation in the microcatheter, which had an inner diameter of 0.013 inches. Embolization was performed by injecting this dilute embolic solution loaded in a 2-mL syringe to near stasis and resolution of hypervascularity (**Fig 2b**), and care was taken to avoid

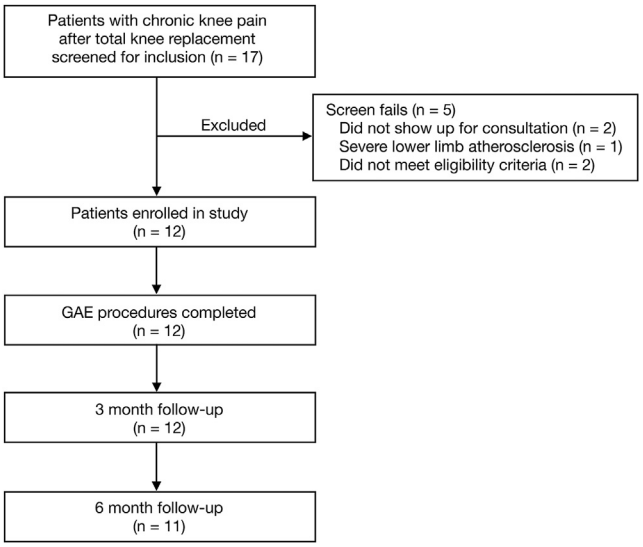

Figure 1. Study flow chart.

reflux. Hemostasis was achieved using manual compression. All patients were discharged on the same day.

Outcome Measures

Technical success was defined as selective catheterization and embolization of at least 1 artery responsible for hypervascularization in the area of pain. The patients were clinically evaluated at 3 months based on total pain, symptoms, activities of daily living, sport and recreation function, and knee-related quality of life according to the Knee Injury and Osteoarthritis Outcome Score (KOOS) and VAS pain scores. KOOS is a 42-item self-reported questionnaire that contains 5 dimensions: pain (9 items), other symptoms and stiffness (7 items), function in daily living (17 items), function in sport and recreation (5 items), and knee-related quality of life (4 items). KOOS uses a 5-point Likert scale, with anchors ranging from 0 (no problems) to 4 (extreme problems). The KOOS scores were transformed to a scale of 0–100, with zero representing extreme knee problems and 100 representing no knee problems. The 5 outcomes (pain, other symptoms and stiffness, function in daily living, function in sports and recreation, and knee-related quality of life) were assessed separately and summarized as a total score. This score is appropriate for measuring self-reported physical function in patients undergoing TKA (18). The primary end point was KOOS at 3 months. The secondary end point was the VAS score (also transformed to a 100 point scale, 0 representing no pain and 100 representing extreme pain) at 3 months. Clinical success was defined as an improvement in KOOS (pain) by 18 points from baseline according to the threshold defined by Lyman et al (19) or a decrease in the VAS score of 20 from baseline (20). Adverse events were reported according to the Society of Interventional Radiology classification system (21).

Statistical Analysis

Continuous data are reported as mean ± standard deviation and categorical data as absolute and relative frequencies. The evolution of VAS scores and KOOS was defined as the difference between values at 3 months and those at the baseline and between values at 6 months and those at the baseline. The normality of these differences was tested using the Shapiro–Wilk test. In cases with normal distribution, the paired Student *t* test was performed to compare the mean values; otherwise, the Wilcoxon signed rank test was used. All tests were 2 sided, and the significance level was set at 5%. Statistical analyses were performed using SPSS version 11.0 (IBM, Armonk, New York).

RESULTS

Twelve patients (8 women and 4 men) were included, with a mean age of 69 years ± 9 and a mean interval since TKA of 2.8 years ± 0.9, and all patients had experienced pain since that date. Six patients were taking pain medications without adequate relief: 200 mg of ibuprofen 3 times a day for 4 patients, 1,000 mg of acetaminophen 3 times a day for 1 patient, and 50 mg of tramadol 3 times a day for 1 patient. Seven TKAs involved the left knee (**Table 1**). The mean number of arteries embolized per patient was 1.8 ± 0.8 (1 superior patellar artery, 4 descending genicular arteries, 9 lateral superior genicular arteries, 2 median genicular arteries, 4 lateral inferior genicular arteries, and 1 anterior tibial recurrent artery). The technical success rate was 100% (all vessels that were intended to be catheterized were successfully catheterized). Abnormal synovial hypervascularity was observed in all patients (**Fig 2a**). The median amount of the diluted embolic material used to treat the knee was 4.25 mL (range, 2–10 mL). The mean procedure duration, radiation dose, and contrast media used were 68 minutes (range, 26–112 minutes), 92,791 mGy/cm^2 (range, 19,600–214,496 mGy/cm^2), and 90 mL (range, 40–150 mL), respectively. No adverse events were observed during the procedure.

At 3-month follow-up, the mean KOOS (pain) improved significantly from 45.1 ± 15.6 to 64.1 ± 26.6 ($P < .05$); mean VAS score at rest decreased significantly from 32 ± 33 to 9 ± 14 ($P < .05$), and mean VAS score on walking decreased significantly from 72 ± 15 to 42 ± 24 ($P < .05$) (**Table 2**). At 6-month follow-up, 1 patient was lost to follow-up, the mean KOOS (pain) improved significantly from 43.6 ± 15.5 to 64.6 ± 27.1 ($P < .05$), mean VAS score at rest decreased significantly from 35 ± 33 to 11 ± 21 ($P < .05$), and mean VAS score on walking decreased significantly from 73 ± 16 to 38 ± 35 ($P < .05$) (**Table 3**).

Longitudinal changes in the VAS score, total KOOS, KOOS (pain), and quality-of-life score are shown in **Figure 3a–d**, respectively. At the 3-month follow-up,

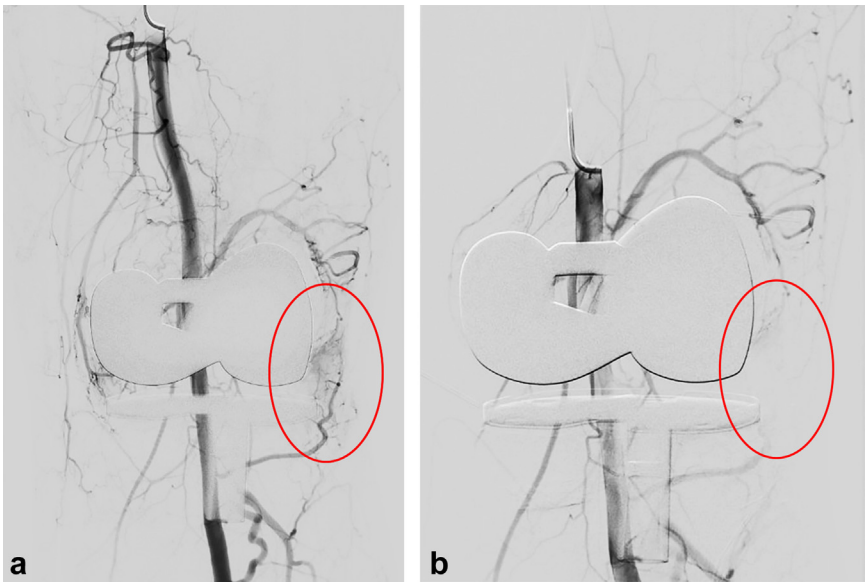

Figure 2. Example of angiographic findings before and after endovascular occlusion of neovascularization of the left lateral superior genicular and inferior lateral arteries of a 52-year-old patient. The Visual Analog Scale score at rest was 0 before and after embolization; the Visual Analog Scale score on walking was 90 before and after embolization; and the Knee Injury and Osteoarthritis Outcome Score pain improved from 19 to 36, on a scale normalized to 0-100. **(a)** Before embolization, nonselective angiography showed neovascularity supplied by the left median genicular artery (ellipse). **(b)** Postembolization angiography showed the disappearance of hypervascularity (ellipse).

Patient 7 presented with an increase in VAS score at rest (0 vs 20), Patient 10 had the same VAS score at rest (20), Patient 5 presented with an increased VAS score on walking (80 vs 90), and Patient 8 had the same VAS score on walking (60); however, 3 patients (Patients 1, 3, and 8) did not show an improvement in KOOS (pain). At the 6-month follow-up, the VAS scores at rest had decreased or were the same as those at the baseline for all patients, VAS scores on walking scores increased for 2 patients (Patients 1 and 5) and were the same as those at the baseline for 2 patients (Patients 8 and 10), and all except 1 patient (Patient 1) presented with amelioration of their KOOS (pain) (Fig 4a–d). Patients who did not show any improvement did not receive further treatment.

At the 3-month follow-up, 58% and 67% of the patients achieved a minimal clinically important change in pain and quality of life, respectively. Substantial clinical benefit (the smallest change that a patient considered meaningful) was observed in 42% of the patients for pain and 25% for quality of life (Table 4). Six (50%) and 8 (67%) patients had VAS scores decreased by greater than 20 at rest and while walking, respectively.

At the 6-month follow-up, 55% and 73% of the patients achieved a minimal clinically important change in pain and quality of life, respectively. Substantial clinical benefit was observed in 45% and 64% of the patients for pain and quality of life, respectively (Table 5). Four (36%) and 7 (64%) patients had VAS scores decreased by greater than 20 at rest and while walking, respectively.

Adverse Events

No major adverse events were reported. Tissue necrosis or dermal ulcers were not observed. Five patients presented with transient cutaneous color change, which resolved spontaneously within 1.5 months. The VAS score increased by more than 20 immediately after embolization in 4 (30%) patients, leading to the need for level 2 (according to World Health Organization Analgesic Ladder) analgesic treatment for 1 week. No transient nerve injury was observed during follow-up.

DISCUSSION

In this study, 58% of the patients demonstrated clinical improvement as measured using KOOS (pain) and 67% as measured using VAS at the 3-month follow-up. This was maintained at the 6-month follow-up in 55% and 64% of the patients, as demonstrated by KOOS (pain) and VAS score improvements, respectively. The median total KOOS, KOOS (pain), and quality-of-life KOOS in this study increased by 40%, 42%, and 80%, respectively, at the 3-month follow-up. The mean VAS score at rest and walking decreased by 72% and 41%, respectively. At the 6-month follow-up, the median total KOOS, KOOS (pain), and quality-of-life KOOS increased by 56%, 48%, and 138%, respectively. The mean VAS score at rest and walking decreased by 69% and 48%, respectively. GAE had already been performed in 4 patients with persistent pain after TKA, with a 1-month follow-up (16). The present study, which involved a larger number of patients, confirmed that the

Table 1. Baseline Patient Characteristics

Variable	Value
Age (y)	69 (52–82)
Sex	
Female	8
Male	4
Pain duration (y)	2.8 (1.3–4.4)
Affected knee	
Right	5
Left	7
BMI (kg/m^2)	30.6 (22.6–36.4)
Oral acetaminophen	1
Oral NSAIDs	4
Oral opioids	1

Note–Values are presented as mean (range) where applicable.
BMI = body mass index; NSAID = nonsteroidal anti-inflammatory drug.

Table 2. Results at 3 Months in 12 Patients

Clinical parameters	Before	After	Difference	*P*
VAS score (100-point scale)				
At rest	32 ± 33	9 ± 14	23 ± 31	.026
On walking	72 ± 15	42 ± 24	29 ± 26	.003
KOOS				
Total	37.7 ± 12.0	52.6 ± 19.8	14.9 ± 15.2	.006
Pain	45.1 ± 15.6	64.1 ± 26.6	19.0 ± 18.6	.005
Symptoms	66.0 ± 19.2	71.9 ± 16.7	5.9 ± 10.2	.069*
Function in daily living	41.1 ± 13.1	59.4 ± 24.5	18.3 ± 16.5	.003
Function in sport and recreation	12.1 ± 14.8	28.7 ± 18.6	16.7 ± 21.1	.022
Knee-related quality of life	24.5 ± 13.5	44.0 ± 24.6	19.5 ± 24.9	.020

Note–Values are presented as mean ± standard deviation.
KOOS = Knee Injury and Osteoarthritis Outcome Score; VAS = Visual Analog Scale.
*Nonsignificant value.

Table 3. Results at 6 Months in 11 Patients

Clinical parameters	Before	After	Difference	*P*
VAS score (100-point scale)				
At rest	35 ± 33	11 ± 21	24 ± 29	.022
On walking	73 ± 16	38 ± 35	35 ± 34	.024
KOOS				
Total	35.8 ± 10.6	56.0 ± 21.9	20.2 ± 14.6	.001
Pain	43.6 ± 15.5	64.6 ± 27.1	21.0 ± 16.7	.001
Symptoms	64.5 ± 19.2	70.3 ± 19.1	5.7 ± 14.9	.001
Function in daily living	39.5 ± 13.1	61.4 ± 25.6	21.9 ± 16.4	.001
Function in sport and recreation	9.5 ± 12.5	28.2 ± 23.4	18.6 ± 24.4	.030
Knee-related quality of life	22.2 ± 11.3	52.9 ± 28.9	30.7 ± 26.5	.003

Note–Values are presented as mean ± standard deviation.
KOOS = Knee Injury and Osteoarthritis Outcome Score; VAS = Visual Analog Scale.

effect of embolization was maintained for 6 months. However, 30% of patients experienced a transient increase in pain for 2 weeks after embolization.

Chronic postsurgical pain is defined as pain that persists for at least 3 months after surgery beyond the healing process (22). At the authors' institution, patients with chronic pain 3 months after total knee replacement surgery are managed according to the Support and Treatment After Replacement (STAR) care pathway protocol (23). The STAR intervention aims to identify the underlying causes of chronic pain and enable onward referrals for targeted treatment through a 3-month postsurgery assessment with an extended scope practitioner and telephone follow-up over 12 months (3,23). The STAR care pathway is a clinically effective and cost-effective intervention for reducing pain severity and interference in patients with pain 3 months after total knee replacement (3). If pain persisted for 12 months after TKA, the STAR care pathway was considered a failure and GAE was proposed to the patient. Pain outcomes may improve for up to 1 year after surgery (24).

Several treatments have been proposed for chronic post-TKA pain. The literature suggests that the currently available pharmacologic and intra-articular treatments have demonstrated limited efficacy (3–5,8,25). Although the STAR care pathway is clinically effective in reducing pain intensity in patients with pain 3 months after TKA, 25% of patients reported having the same, a bit worse, or much worse pain than they did before TKA (3). Singh et al (26) evaluated the short-term efficacy of a single intra-articular botulinum toxin injection based on antinociceptive and anticholinergic activities in a randomized controlled trial. Patients in the trial had undergone total knee replacement at least 6 months earlier and experienced pain in their replaced knees for more than 3 months. Responder status was defined as clinically meaningful pain relief of a 2-point reduction in the 0–10 VAS pain score. Reduced pain intensity was apparent for the intervention compared with that after a placebo after 2 and 3 months, although the authors suggested that meaningful pain relief was evident up to approximately 40 days, with no increase in adverse events. This was the only randomized trial identified by Beswick et al (25) in their systematic review of interventions for predicting and managing chronic postsurgical pain after total knee replacement.

Transcutaneous electrical nerve stimulation, pulsed radiofrequency, and spinal cord stimulation have been used to treat chronic pain after TKA (27,28). Although a meta-analysis (27) demonstrated some evidence supporting the management of chronic pain after TKA using these modalities, the small sample sizes and lack of comparisons did not results in definitive treatment recommendations.

Revising the prosthesis is risky and does not ensure pain resolution (5). Revision TKA is generally not recommended for unexplained pain. Revision TKA in the absence of knee pathology may not relieve pain and could result in a worse

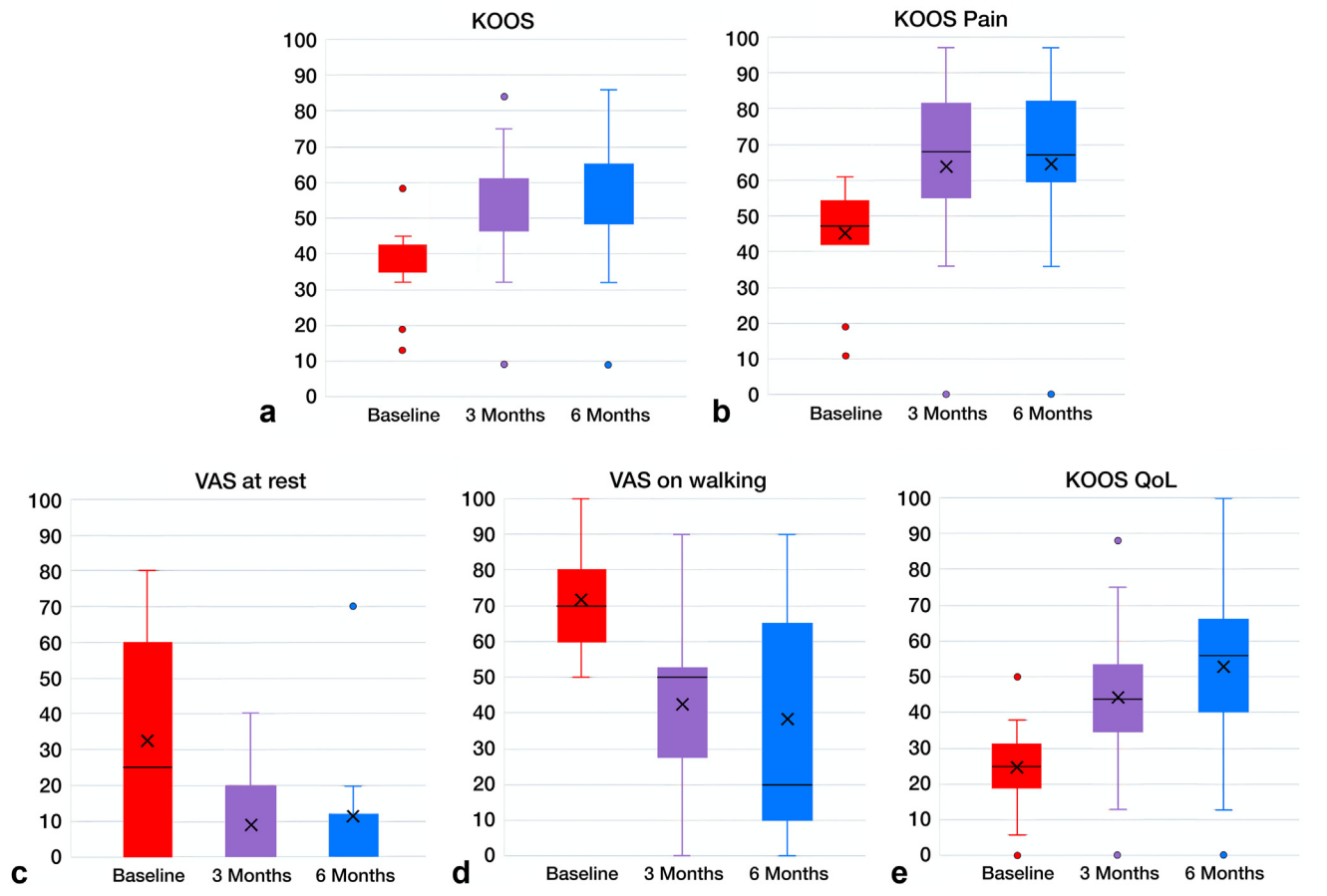

Figure 3. Box plots depicted longitudinal changes in symptom metrics: **(a)** total Knee Injury and Osteoarthritis Outcome Score (KOOS), **(b)** KOOS pain, **(c)** Visual Analog Scale at rest, **(d)** Visual Analog Scale on walking, and **(e)** KOOS quality of life score. QoL = quality of life; VAS = Visual Analog Scale. KOOS and KOOS Pain scores were normalized to a scale from 0-100, with 100 being no knee problems and 0 being extreme problems.

outcome and higher rates of rerevision compared with TKA revision for more established indications such as "aseptic loosening." Petersen et al (29) reported persistent pain in 47% of patients after revision TKA for any indication as opposed to 19% after primary TKA. Neurolysis of the genicular nerves has been used; however, fewer than 50% of patients treated in this manner reporting pain reduction and improvement generally experienced return to baseline after 12 months (30).

GAE has been previously shown to treat KOA-related knee pain effectively, with a limited adverse event profile (15,17,31–33). GAE has also been previously shown to treat recurrent spontaneous hemarthrosis after arthroplasty effectively (14,34) and 2 cases complicated by joint infection requiring arthroplasty revision (13). Patients treated with GAE for KOA rarely report mild transient knee pain (15,31–33). In the present study, 30% of the patients presented with mild transient knee pain after the procedure. This may have been due to increased neovascularity in patients after TKA compared with that in patients with KOA. The neovascularity after TKA seems more intense distally but involves fewer arteries than KOA, which seems to involve more arteries but seems less intense distally. This may explain why the mean number of embolized arteries after TKA was lower than that after KOA.

Heller et al (14) reviewed and analyzed 5 retrospective studies evaluating recurrent hemarthrosis after TKA with sample sizes of more than 10 patients. The size of embolic agents varied from 100 to 700 μm, and they were microspheres or polyvinyl alcohol particles eventually associated with *n*-butyl cyanoacrylate or coils. Okuno et al (15) used a nonpermanent embolic material, imipenem/cilastatin sodium, to treat patients with KOA; however, 75-μm Embozene spheres were used for patients who had contraindications to imipenem/cilastatin sodium. There was no significant difference in clinical success between the 2 groups. They hypothesized that the use of a small amount of Embozene or a nonpermanent embolic agent reduces the risk of significant tissue inflammation and symptomatic active foreign body reactions while maintaining a sufficient occluding effect to suppress small-caliber neoangiogenesis (15). Embolization was performed with either 75-μm (9 patients) or 100-μm Embozene (11 patients) particles by

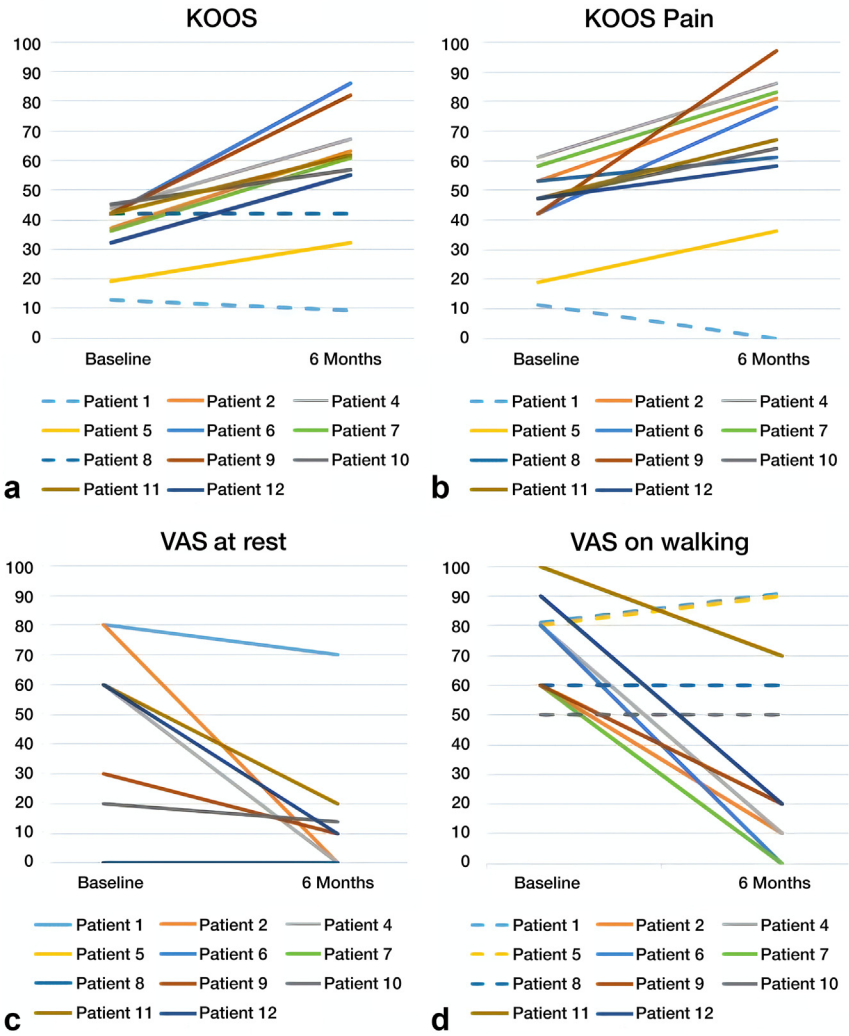

Figure 4. Individual evolution of **(a)** total Knee Injury and Osteoarthritis Outcome Score, **(b)** Knee Injury and Osteoarthritis Outcome Score pain, **(c)** Visual Analog Scale score at rest, and **(d)** Visual Analog Scale score on walking between baseline and at the 6-month follow-up. The solid lines indicate favorable evolution, and the dotted lines indicate unfavorable evolution. KOOS = Knee Injury and Osteoarthritis Outcome Score; VAS = Visual Analog Scale. All KOOS scores were normalized to a scale of 0-100, with 100 representing no knee problems, and all VAS scores were normalized to a scale of 0-100, with 0 representing no pain.

Table 4. Minimal Detectable Change, Minimal Clinically Important Change, and Substantial Clinical Benefit at 3 Months of Follow-up (12 Patients)

Clinical parameters	Minimal detectable change			Minimal clinically important change		Substantial clinical benefit: anchor based
	MDC80	MDC90	MDC95	Distribution based	Anchor based	
Pain	9 (75) [10]	9 (75) [13]	8 (67) [15]	9 (75) [8]	7 (58) [18]	5 (42) [22]
Symptoms	4 (33) [10]	3 (25) [12]	2 (17) [16]	4 (33) [9]	4 (33) [7]	1 (8) [21]
ADL	8 (67) [10]	7 (58) [13]	6 (50) [15]	9 (75) [9]	6 (50) [16]	6 (50) [15]
QoL	8 (67) [9]	8 (67) [12]	8 (67) [14]	8 (67) [8]	8 (67) [17]	3 (25) [23]

Note–Values are represented as the number of patients (%) whose score was higher than the value defined (in square brackets) by Lyman et al (11).
ADL = activities of daily living; MDC80 = minimal detectable change calculated with CI reflecting 80%; MDC90 = minimal detectable change calculated with CI reflecting 90%; MDC95 = minimal detectable change calculated with CI reflecting 95%; QoL = quality of life.

Bagla et al (17) to treat patients with KOA. A particle size of 75 μm was used by Chau et al (16) to treat 4 patients with persistent pain after TKA, without adverse events. Embozene particles are uniform in size, and they seem to reach vessels closely corresponding to their nominal size; thus, the transient skin discoloration was a consequence of the use of 75-μm particles (35).

The limitations of the present study include its short follow-up period, the small number of patients, and the absence of a control or sham group. No

Table 5. Minimal Detectable Change, Minimal Clinically Important Change, and Substantial Clinical Benefit at 6 Months of Follow-up (11 Patients)

Clinical parameters	Minimal detectable change			Minimal clinically important change		Substantial clinical benefit: anchor based
	MDC80	MDC90	MDC95	Distribution based	Anchor based	
Pain	9 (82) [10]	8 (73) [13]	8 (73) [15]	9 (82) [8]	6 (55) [18]	5 (45) [22]
Symptoms	3 (27) [10]	2 (18) [12]	2 (18) [16]	3 (27) [9]	3 (27) [7]	2 (18) [21]
ADL	9 (82) [10]	8 (73) [13]	7 (64) [15]	9 (82) [9]	7 (64) [16]	7 (64) [15]
QoL	8 (73) [9]	8 (73) [12]	8 (73) [14]	8 (73) [8]	8 (73) [17]	7 (64) [23]

Note–Values are represented as the number of patients (%) whose score was higher than the value defined (in square brackets) by Lyman et al (11).
ADL = activities of daily living; MDC80 = minimal detectable change calculated with CI reflecting 80%; MDC90 = minimal detectable change calculated with CI reflecting 90%; MDC95 = minimal detectable change calculated with CI reflecting 95%; QoL = quality of life.

comparisons with other treatment modalities was performed.

In conclusion, the results of the present study suggest that GAE is safe and effective for providing pain relief at 12 months in patients with chronic pain after TKA. Further randomized, comparative studies are needed to determine the true treatment effect versus the placebo effect.

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AUTHOR INFORMATION

From the Neurointerventionnal and Interventional Vascular Unit (Y.C., J.S.), Department of Rheumatology (C.R., V.B.), Department of Orthopedics (J.-F.G, R.B.d.D.), Department of Osteo-Articular Radiology (A.R.), and Department of Clinical Research and Innovation (E.F.), CHU de Nice, Pasteur 2 Hospital, Nice, France. Received September 28, 2022; final revision received May 19, 2023; accepted June 20, 2023. Address correspondence to Yves Chau; Neurointerventional and Interventional Vascular Unit, Pasteur 2 Hospital, 30 voie romaine, 06000 Nice, France; E-mail: chau.y@chu-nice.fr

None of the authors have identified a conflict of interest.

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