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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Short-term clinical outcomes of transarterial embolization for symptomatic hand osteoarthritis refractory to conservative treatment

Sieh-Yang Lee[1]
Wei-Xiong Lim[1]
Kuan-Ting Wu[2]
Cheng-Ta Wu[2]
Chung-Cheng Huang[1]
Ching-Di Chang[1]

[1]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Department of Diagnostic Radiology, Kaohsiung, Taiwan

[2]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Department of Orthopedic Surgery, Kaohsiung, Taiwan

PURPOSE

The present study aims to assess the short-term clinical outcomes and safety of transarterial embolization (TAE) for symptomatic hand osteoarthritis (OA) refractory to conservative treatment.

METHODS

The present retrospective cohort pilot study included nine patients who underwent TAE for symptomatic OA-associated hand pain in a single tertiary center between November 2022 and January 2023. The baseline and post-procedural OA-associated hand pain and function were assessed using the visual analog scale (VAS) and the Australian Canadian Hand Osteoarthritis Index (AUSCAN). The use of conservative treatment and pain medications was also recorded. Post-procedural adverse events were evaluated according to the Society of Interventional Radiology classification.

RESULTS

Compared with the baseline, the overall VAS scores were significantly decreased at 1-week, 1-month, 3-months, and 6-months after TAE (76 ± 15 mm versus 34 ± 18 mm, $P < 0.001$; 32 ± 11 mm, $P < 0.001$; 21 ± 15 mm, $P < 0.001$; 18 ± 19 mm, $P = 0.002$). Similarly, improvement in the mean total AUSCAN scores (22.0 ± 10.0 versus 13.2 ± 6.6, $P = 0.007$; 14.11 ± 7.3, $P = 0.004$; 9.8 ± 6.8, $P = 0.004$; 9.3 ± 7.4, $P = 0.011$) were documented. The use of other conservative treatment methods also gradually decreased. There were no severe adverse events reported during the follow-up period.

CONCLUSION

TAE is a feasible and safe treatment method for symptomatic hand OA refractory to conservative treatment. This minimally invasive procedure effectively relieves debilitating OA-associated joint pain and restores hand function with a durable treatment effect.

KEYWORDS

Embolization, hand, musculoskeletal, osteoarthritis, pain control

Osteoarthritis (OA) is the most common musculoskeletal disorder among the elderly,[1] with the hands being the most frequently involved site of the disease.[2] In a population aged ≥70 years, 13.2% of men and 26.2% of women suffered from symptomatic hand OA.[3] The debilitating symptoms of hand OA, such as pain, reduction of grip strength, and joint stiffness, have a negative impact on quality of life in the affected individuals.[4-6]

Despite the high prevalence of symptomatic hand OA, optimal treatment for the disease remains unestablished.[7] Conservative management of symptomatic OA is mainly grouped into pharmacological (anti-inflammatory medications, analgesics, and intra-articular injection) and non-pharmacological [exercise, splint, assistive device, physical therapy (PT), etc.] categories. However, current conservative treatments usually provide limited and temporary therapeutic effects to the patients.[8-10] Surgical intervention is reserved for patients with advanced OA and debilitating pain at the expense of motion range and other surgical complications.[11,12]

Recently, transarterial embolization (TAE) has emerged as a safe and effective minimally invasive treatment for chronic musculoskeletal pain.[13-16] Abnormal angiogenesis and ac-

Corresponding author: Ching-Di Chang

E-mail: haaman010@hotmail.com

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companying pain-related nerves have been demonstrated as a possible source of persistent inflammation and pain in OA.[17-20] Thus, eliminating abnormal neovessels by intra-arterially infusing an embolic agent into the target vessels might relieve pain and restore the joint motion in patients with symptomatic OA. Previous studies have described successful treatment of symptomatic hand OA with TAE, specifically focusing on the interphalangeal joint and trapeziometacarpal OA.[10,21-23] However, data regarding the effectiveness and safety profile of TAE use for symptomatic hand OA with isolated or concurrent involvement of digit and wrist joints is still scarce.

This study aims to assess the short-term clinical outcomes and safety of TAE for symptomatic hand OA refractory to conservative treatment.

Methods

The present retrospective study was approved by the Chang Gung Medical Foundation Institutional Review Board Ethics Committee (protocol number: 202300669B0, date: 16.05.2023). Between November 2022 and January 2023, nine patients who underwent TAE for the treatment of symptomatic OA-associated hand pain in a single tertiary center were reviewed. All patients were referred from orthopedic clinics to the interventional radiology outpatient clinics. Hand OA was diagnosed by an orthopedist based on the American Rheumatology College Criteria,[24] and the hand radiography was confirmed by an experienced musculoskeletal radiologist.

The inclusion criteria of the procedure were as follows: (1) age ≥40 years; (2) hand OA with an involvement of single or multiple joints confirmed with plain radiography; (3) visual analog scale (VAS) >50 mm (the pain was rated on a 100 mm scale, with 0 representing no pain and 100 representing the worst pain imaginable); (4) OA-associated hand pain refractory to conservative treatment for ≥3 months, such as intra-articular injection, splint protection, PT, anti-inflammatory medications, or analgesics; and (5) radial artery type A/B/C based on the Barbeau test.

The exclusion criteria were as follows: (1) rheumatoid arthritis; (2) advanced atherosclerosis; (3) allergy to iodinated contrast material/antibiotics; and (4) local infection. After informed consent was obtained, the complete medical history of all patients was recorded, including the disease duration, medication, allergy history, prior conservative treatments, and affected hand joints. The location and severity of the hand OA was assessed via radiography using the Kellgren–Lawrence grading system.

Main points

- Considering abnormal angiogenesis and accompanying sensory nerve growth as a possible source of persistent inflammation and pain in osteoarthritis (OA), angiogenesis might be a new therapeutic target for pain control.
- The percentage of responders (≥50% pain reduction) of hand transarterial embolization (TAE) at the 1-week, 1-month, 3-month, and 6-month follow-ups were 66.7%, 77.8%, 88.9%, and 88.9%, respectively.
- TAE effectively relieved joint pain and restored hand function without major adverse events in patients with symptomatic hand OA refractory to conservative treatment.

Transarterial embolization procedure

The TAE procedures were performed by two experienced interventional radiologists. The treatment protocol was developed based on previous studies.[10,21] All patients received a Barbeau test to assure adequate collateral circulation to the hand (type A to C). To reduce perioperative pain and discomfort, a non-steroidal anti-inflammatory drug (NSAIDs) (Parecoxib, 40 mg) was infused intravenously 10 min before the procedure. Then, under local anesthesia, a 24-gauge needle (BD Insyte Autoguard Becton Dickinson Infusion Therapy system) was inserted in an antegrade direction into the distal radial artery at the level of the wrist. The puncture process was performed under ultrasound guidance. Once brisk backflow of bright red blood was detected, the inner metallic needle was removed, with the outer plastic cannula remaining in the radial artery. Iodinated contrast material (Omnipaque GE healthcare) was injected manually to confirm the proper position of the cannula, and an angiogram with optimal opacification of the deep palmar arch and digital arteries was performed under fluoroscopy. Abnormal neovessels were defined as tumor blush-type opacification during the arterial phase. The embolic agent was prepared by mixing 500 mg imipenem/cilastatin sodium (IPM/CS) powder (Kabi, Facta Farmaceutici S.p.A., Teramo, Italy) with 10 mL iodinated contrast material (Omnipaque). The embolic agent was gradually infused into the radial artery with a maximum dose limit of 5 mL. The endpoint of embolization was stasis of the antegrade blood flow within three heart beats or achievement of the maximal dose limit (Supplementary Video 1). After achieving the endpoint, the cannula was removed. The access site was compressed manually until hemostasis and covered with a band-aid. The patient was discharged after 20 min of observation. A two-session TAE was scheduled for each patient; the second procedure was arranged at 1-month after the first TAE. The maximal dose of the infused embolic agent was decreased to 3 mL for the second session. The pre-TAE and post-TAE angiographies for hand OA are presented in Figure 1.

Assessment of treatment effects and adverse events

The clinical severity of hand OA was assessed using the VAS and the Australian Canadian Hand Osteoarthritis Index (AUSCAN). The AUSCAN is a self-administered questionnaire that assesses pain, disability, and joint stiffness in hand OA with a total of 15 items.[25] Each item is rated on a scale of 0 (none) to 4 (extreme pain/stiffness/difficulty). The authors of the present study documented the following parameters: (1) VAS-night pain; (2) VAS-overall; (3) AUSCAN-pain; (4) AUSCAN-stiffness; and (5) AUSCAN-function at study entry and at 1-week, 1-month, 3-months, and 6-months after TAE. For patients with multiple-joint involvement, the affected joint with the worst pain was assessed. Compared with the baseline, the patient was classified as a responder

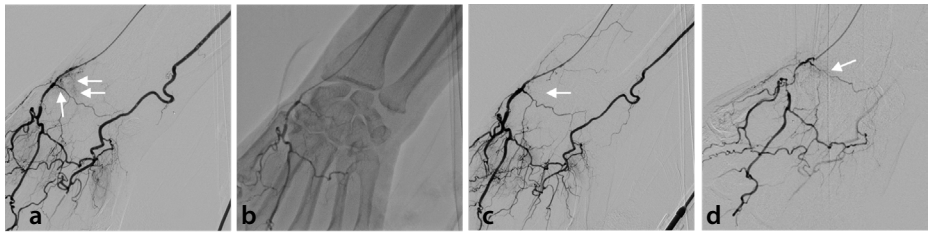

Figure 1. Transarterial embolization for symptomatic scaphotrapeziotrapezoid (STT) joint osteoarthritis. Angiography of **(a)** before, **(b)** during, and **(c)** after intra-arterial infusion of imipenem/cilastatin into the distal radial artery. Abnormal hypervascularity was present at the STT joint before embolization and disappeared after embolization. **(d)** During the second procedure, pre-infusion angiography showed abnormal neovessels in the affected joint; however, the occurrence was lower than in the initial procedure.

(≥50% reduction) or a non-responder (<50% reduction) based on changes in the overall pain VAS score at each time point. Pain recurrence was defined as a higher overall VAS score at 1-month (early recurrence), 3-months, and 6-months after TAE compared with previous recorded VAS scores or the baseline. The self-reported use of conservative treatment and pain medications in the last 3-months was also recorded at outpatient clinics before and after embolization.

Post-procedural adverse events were evaluated according to the Society of Interventional Radiology classification.[26] Possible complications, including tissue necrosis, peripheral paresthesia, and tendon rupture, were assessed during follow-up outpatient visits.

Statistical analysis

The statistical analyses of all data were conducted using the IBM SPSS software (version 22.0; IBM, Armonk, NY, USA). The baseline and outcome variables were compared using repeated-measures analysis of variance and post-hoc multiple comparisons to determine changes in VAS scores, AUSCAN subscores, and AUSCAN total scores at each time point. All parameters were documented as the mean ± standard deviation, and the *P* value for statistical significance was set at <0.05.

Results

A total of nine patients successfully underwent two-session TAE for the unilateral affected hand via the radial artery, with a mean procedural time of 15.7 min (range of 11–20 min; Table 1). Transient radial artery spasm occurred in 4 patients without any sequela. All patients experienced transient skin color changes of the infused hand; the skin turned pale initially and returned to its normal appearance approximately 30 min after infusion of embolic agents (Figure 2). No tissue necrosis, tendon rupture, muscle weakness, paresthesia, or other severe adverse events were reported during the follow-up period.

Compared with the baseline, the post-procedural mean nighttime VAS scores were significantly decreased at the 1-week, 1-month, 3-month, and 6-month follow-ups (58 ± 22 mm versus 22 ± 19 mm, $P < 0.001$; 20 ± 15 mm, $P < 0.001$; 10 ± 10 mm, $P < 0.001$; 8 ± 12 mm, $P = 0.004$; Figure 3). A significant improvement of the overall VAS score was also documented at 1-week, 1-month, 3-months, and 6-months after TAE (76 ± 15 mm versus 34 ± 18 mm, $P < 0.001$; 32 ± 11 mm, $P < 0.001$; 21 ± 15 mm, $P < 0.001$; 18 ± 19 mm, $P = 0.002$). The percentage of responders at the 1-week, 1-month, 3-month, and 6-month follow-ups were 66.7%, 77.8%, 88.9%, and 88.9%, respectively. The percentage of pain recurrence at the 1-month, 3-month, and 6-month follow-ups were 44.4% (early recurrence), 11.1%, and 11.1%, respectively (Supplementary Table 1).

Improvement was observed in the mean total AUSCAN scores (22.0 ± 10.0 versus 13.2 ± 6.6, $P = 0.007$; 14.11 ± 7.3, $P = 0.004$; 9.8 ± 6.8, $P = 0.004$; 9.3 ± 7.4, $P = 0.011$) and mean AUSCAN-pain subscores (10.0 ± 3.4 versus 5.7 ± 2.8, $P = 0.004$; 5.6 ± 2.7, $P = 0.001$; 3.7 ± 3.3, $P < 0.001$; 3.0 ± 2.6, $P = 0.001$) at every follow-up visit (Figures 4, 5). The mean AUSCAN-function subscores were significantly decreased at the post-procedural 1-week

Table 1. Clinical data and procedural details

Patient no.	Sex	Age (y)	Pain duration (mo)	Prior therapies	Main affected side	Main involved joint*	KL grading#	Embolic volume (mL) (1st/2nd)	Mean procedure time (min)
1	F	62	24	PT	Right	DIP, PIP	4	5 / 3	12
2	M	62	36	CSI	Right	CMC, STT	3	3 / 2	25
3	F	53	3	NSAIDs	Right	DIP	1	4 / 2	18
4	F	78	24	PT, NSAIDs, CSI	Right	DIP, CMC, STT	3	4 / 3	13
5	F	60	120	NSAIDs	Right	FIP, DIP, PIP	4	4 / 2	14
6	F	78	24	NSAIDs	Right	FIP, DIP, PIP	4	4 / 2.5	11
7	M	56	12	PT, CSI	Left	CMC, DIP	3	3.5 / 1.5	20
8	M	70	3	PT	Left	DIP	3	5 / 2.5	15
9	F	61	24	NSAIDs	Left	FIP, DIP	2	4 / 2	13

*The underlined joint indicated the involved joint with the worst pain. The KL grade was assigned to the involved joint with the worst pain. F, female; M, male; CSI, corticosteroid injection; KL: Kellgren–Lawrence system; NSAIDs, non-steroidal anti-inflammatory drugs; PT, physical therapy; DIP, distal interphalangeal joint; CMC, carpometacarpal joint; STT, scaphotrapeziotrapezoid joint; FIP, first interphalangeal joint; PIP, proximal interphalangeal joint.

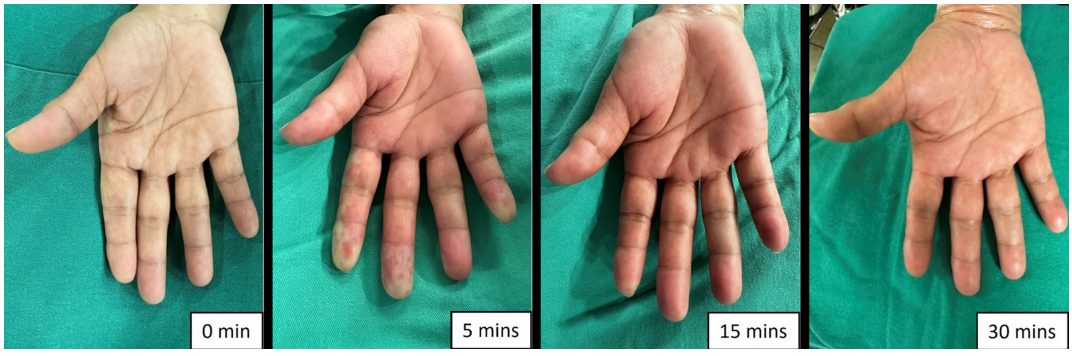

Figure 2. Skin color changes of the hand after intra-arterial infusion of imipenem/cilastatin sodium. The skin turned pale initially (5 min) and turned into hyperemia when reperfusion occurred (15 min). The skin color returned to normal appearance approx. 30 min after infusion of an embolic agent.

and 1-month follow-ups (11.1 ± 7.5 versus 6.8 ± 4.7, $P < 0.05$; 7.8 ± 5.5, $P < 0.05$); however, the differences were statistically insignificant at the 3-month and 6-month follow-ups (5.6 ± 5.1, $P = 0.072$; 5.8 ± 5.6, $P = 0.103$). There were also no differences in the mean AUSCAN-stiffness among all the timepoints (10.0 ± 3.4 versus 5.7 ± 2.8, $P = 0.347$; 5.6 ± 2.7, $P = 0.347$; 3.7 ± 3.3, $P = 0.195$; 3.0 ± 2.6, $P = 0.282$).

After initial embolization, the use of other conservative treatments gradually decreased (Table 2). Before TAE, 33% of the patients received corticosteroid injection (CSI), 44% of the patients received PT, and 55.6% of the patients took oral NSAIDs daily or almost daily. The rates of regular use of oral NSAIDs at the 1-week, 1-month, 3-month, and 6-month follow-ups were 33.3%, 22.2%, 11.1%, and 11.1%, respectively. No patients received PT or CSI after embolization.

Discussion

The present study demonstrated that TAE effectively relieved OA-associated joint pain and restored hand function with a durable treatment effect. After initial embolization, rapid reduction of nighttime and overall pain was documented (62% and 55% within 1-week, respectively), followed by gradual pain improvement up to the final 6-month follow-up. Similarly, the early improvement of hand function could also be observed within 1-week and 1-month after TAE, followed by a trend toward improved, albeit statistically insignificant, function scores. Moreover, most patients gradually decreased the use of other conservative treatments. There were no severe adverse events reported during the follow-up period.

Mounting evidence suggested that inflammation and hypervascularization played crucial roles in the pathogenesis of OA.[17,18,20] During OA, cartilage degradation products initiate synovial inflammation, inducing the release of the pro-inflammatory mediators and recruitment of immune cells. The increased macrophage infiltration drives synovial angiogenesis and excessive production of proteolytic enzymes

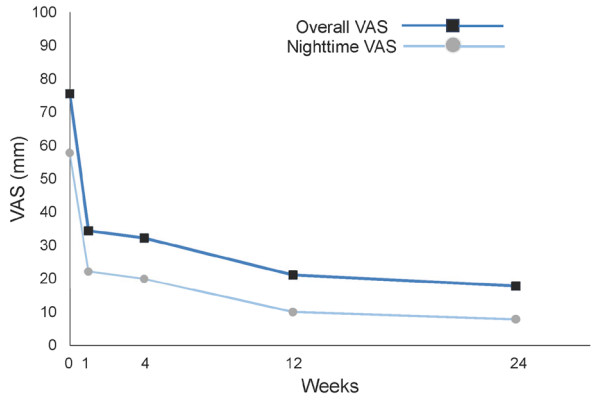

Figure 3. Reduction of the visual analog scale score after transarterial embolization (TAE). Both mean nighttime and overall pain decreased rapidly at 1-week after TAE, followed by gradual improvement at 4, 12, and 24-weeks after TAE (all $P < 0.01$). VAS, visual analog scale.

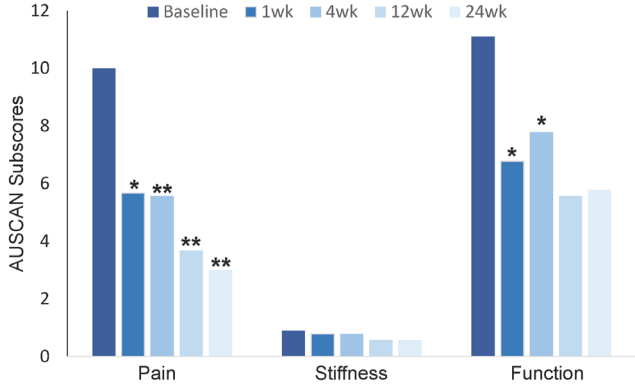

Figure 4. Changes in the Australian Canadian Hand Osteoarthritis Index pain, stiffness, and physical function subscores after embolization. A single asterisk indicates $P < 0.05$ and a double asterisk indicates $P < 0.01$.

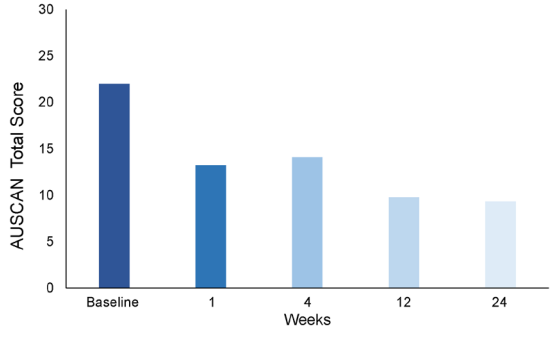

Figure 5. Changes in the total Australian Canadian Hand Osteoarthritis Index (AUSCAN) score after embolization. The AUSCAN score significantly decreased at the 1-week, 4-week, 12-week, and 24-week follow-ups compared with baseline (all $P < 0.05$).

Table 2. Summary of patients undergoing other conservative treatments during the study period

Treatment options	Baseline	1-week	1-month	3-months	6-months
Physical therapy	4	0	0	0	0
Oral NSAIDs	5	3	2	1	1
Corticosteroid injection	3	0	0	0	0

NSAIDs, non-steroidal anti-inflammatory drugs.

responsible for aggravated osteochondral damage and further synovial inflammation, creating a positive feedback loop.[27] The sensory nerves grow along neovessels into the synovium, cartilage, osteophytes, and other joint tissues, contributing to the structural damage and pain in the OA joint.[20] Thus, as a key component in the pathogenesis of OA, angiogenesis might be a new therapeutic target for breaking the vicious cycle. Inui et al.[21] and Liang et al.[23] demonstrated the treatment outcome of intra-arterial infusion of IPM/CS in refractory trapeziometacarpal and interphalangeal OA, respectively. However, hand OA usually involves multiple digits and wrist joints, including interphalangeal joints, carpometacarpal joints, and scaphotrapeziotrapezoid joints. Transarterial embolization is not limited to treating isolated joints, and multiple affected interphalangeal and wrist joints can be treated simultaneously by intra-arterial infusion of IPM/CS into the distal radial artery. The present study demonstrated that TAE is an efficient method for relieving OA-associated pain and improving hand function in patients with isolated or concurrent joint involvement.

With the use of TAE for chronic musculoskeletal joint pain, concerns regarding adverse events, especially ischemia and non-target embolization, might arise. IPM/CS sodium is slightly water soluble and has a short half-life of approx 1 h. When suspended in an iodinated contrast material, it forms a crystalline compound, with a particle size of 10–130 μm.[28] With a transient embolic effect and peripheral accessibility, IPM/CS has been used in the embolization of gastrointestinal bleeding and chronic musculoskeletal pain. In several studies,[29-32] IPM/CS demonstrated its excellent safety profile, with no severe adverse event reported. In the present study, all patients experienced transient skin color changes of the infused hand; the skin turned pale initially and returned to its normal appearance approximately 30 min after infusion of embolic agents. There were no severe ischemic adverse events in the target and non-target areas of embolization. To avoid non-target embolization in the hand, several modified methods, such as manual compression and the use of a rubber band, might be useful for limiting the blood flow to the non-symptomatic joint. The decreased distribution of particles in the non-target areas might help improve post-procedural hand swelling and discomfort. However, further investigation on the effects of these methods is warranted.

In this study, early recurrence of joint pain was observed in 4 patients (44%) at the 1-month follow-up visit; however, the recurring pain was milder than before treatment. Previous literature reported early recurrence of local tenderness after successful initial TAE for chronic musculoskeletal pain.[31] This phenomenon might be explained by partial recanalization of abnormal vessels or revascularization after initial TAE.[31] The temporary embolic agent IPM/CS was used for TAE in this study due to its safety profile. During the second procedure, abnormal vessels were present in the affected joint; however, the occurrence was lower than in the initial procedure. These findings supported the present authors' hypothesis that the presence of partial recanalization or revascularization after the initial TAE procedure might lead to early recurrence of joint pain in some affected patients. Thus, a two-session procedure might be an appropriate regimen to maintain the effectiveness of the treatment.

Several limitations of this study should be addressed. First, the patients were allowed to receive conservative therapy after embolization, possibly confounding the treatment outcome of TAE. However, the use of conservative therapy was evidently decreased after TAE. This finding highlighted the effectiveness of TAE in the treatment of symptomatic hand OA. Secondly, the best endpoint of embolization has yet to be established. In this study, the endpoint of embolization was determined based on the achievement of the antegrade blood flow stasis within three heart beats or achievement of the maximal dose limit. Third, this small-scale study lacked a control group as a comparator arm, possibly leading to the occurrence of the placebo effect. Transarterial embolization is a novel treatment for symptomatic hand OA, and data regarding the treatment effectiveness and safety profile are currently limited. The present authors' initial experience might help introduce TAE as a potentially effective and safe treatment for symptomatic hand OA refractory to conservative treatment. Therefore, future sham-controlled randomized controlled studies are warranted to validate the preliminary results of this study.

In conclusion, TAE is a feasible and safe treatment for symptomatic hand OA refractory to conservative treatment. This minimally invasive procedure effectively relieves debilitating OA-associated joint pain and restores hand function with a durable treatment effect.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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Supplementary Table 1. Changes in overall VAS pain score and total AUSCAN scores after embolization

No.	VAS pain score					Total AUSCAN score				
	Baseline	1 w	1 m	3 m	6 m	Baseline	1 w	1 m	3 m	6 m
1	6	6	3	2	2	10	9	6	11	13
2	10	6	4	4	3	33	20	16	7	1
3	7	5	1	1	0	18	15	6	3	4
4	7	2	4	2	0	29	20	25	14	18
5	9	3	4	2	2	32	8	23	16	5
6	6	3	2	5	2	22	16	16	22	21
7	9	2	4	1	1	32	21	16	9	13
8	8	3	3	0	0	7	6	5	0	0
9	6	1	4	2	6	15	4	14	6	9

VAS, visual analog scale; AUSCAN, Australian Canadian Hand Osteoarthritis Index; PIP, proximal interphalangeal joints; CMC, carpometacarpal joint; DIP, distal interphalangeal joints; IP, interphalangeal joint.

Supplementary Video 1 link: http://glns.co/m7w4u

Supplementary Video 1. Angiography demonstrated the endpoint of embolization when stasis of the antegrade blood flow within three heart beats was achieved after intra-arterial infusion of imipenem/cilastatin sodium.