Transarterial microembolization for the management of refractory chronic joint pain in osteoarthritis

Transarterielle Mikroembolisation zur Behandlung therapierefraktärer chronischer Gelenkschmerzen bei Patienten mit Arthrose

Authors
Lena Marie Wilms, Kai Jannusch, Daniel Weiss, Nilcolas Steinfort, Farid Ziayee, Gerald Antoch, Peter Minko

Affiliations
Diagnostic and Interventional Radiology, Heinrich-Heine-Universitat Düsseldorf, Düsseldorf, Germany

Keywords
embolization, muscular, knee, TAME, genicular artery embolization, osteoarthritis

received 21.11.2023
accepted after revision 9.3.2024
published online 2024

Bibliography
Fortschr Röntgenstr
DOI 10.1055/a-2288-5743
ISSN 1438-9029

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Correspondence
Dr. Peter Minko
Diagnostic and Interventional Radiology, Heinrich-Heine-Universitat Düsseldorf, Düsseldorf, Germany
peter.minko@med.uni-duesseldorf.de

ABSTRACT

Background Osteoarthritis (OA) is a chronic degenerative disease significantly impacting both patient quality of life and socioeconomics. Traditional treatment options, including pharmacological and surgical interventions, are often limited. Advancements in our understanding of the pathological mechanisms behind OA indicate the involvement of pathological angiogenesis. Transarterial microembolization (TAME), a minimally invasive radiological procedure, may present an innovative therapeutic approach. This review aims to consolidate current knowledge and experiences regarding TAME as a therapeutic modality for alleviating chronic joint pain associated with OA. It explores the role of TAME, focusing on its indications, patient selection, clinical outcomes, and future perspectives. Potential complications and associated risks are systematically addressed, alongside proposed strategies for risk mitigation and effective management.

Method The presented patient cases originate from our institution, supplemented by a thorough review of relevant literature retrieved from PubMed.

Conclusion TAME represents a promising therapeutic approach, providing relief from the burden of joint diseases and substantially enhancing patient quality of life. Clinical outcomes emphasize the efficacy and safety of TAME in mitigating pain and improving functional capabilities in patients with chronic joint pain associated with OA. With mounting evidence of its therapeutic benefits and applicability to numerous joint-related pathologies, TAME offers a valuable addition to the arsenal of treatments for these conditions.

Key Points

- TAME is an innovative therapy for treating chronic joint pain related to OA.
- TAME is a technically challenging minimally invasive intervention requiring a high level of expertise.
- Understanding the challenges and complications of TAME can reduce risk and enhance procedural outcomes.

Citation Format

- Wilms LM, Jannusch K, Weiss D et al. Transarterial microembolization for the management of refractory chronic joint pain in osteoarthritis. Fortschr Röntgenstr 2024; DOI 10.1055/a-2288-5743

ZUSAMMENFASSUNG

Hintergrund Arthrose ist eine chronische degenerative Gelenkerkrankung mit erheblichen Auswirkungen auf die Lebensqualität der betroffenen Patienten. Die Möglichkeiten konventioneller Behandlungsoptionen wie Schmerzmanagement und chirurgische Eingriffe kommen häufig an ihre Grenzen. Fortschritte in unserem Verständnis pathologischer Mechanismen, die der Arthrose zugrunde liegen, deuten auf die Beteiligung der pathologischen Angiogenese hin. Die transarterielle Mikroembolisation (TAME), ein minimal-invasives radiologisches Verfahren, könnte daher einen innovativen Therapieansatz darstellen. Diese Übersichtsarbeit soll den aktuellen Wissensstand und die Erfahrungen in Bezug auf die TAME als therapeutische Modalität zur Linderung chronischer Gelenkschmerzen in Zusammenhang mit Arthrose zusammenfassen. Dabei soll der Fokus auf den Indikationen, der Patientenauswahl, verfahrenstechnischen Aspekten, klinischen Ergebnissen und Anwendungsmöglichkeiten liegen. Potenzielle Komplikationen und damit verbundene Risiken sowie Strategien zur Risikominimierung werden beleuchtet.

Methode Die vorgestellten Patientenfälle stammen aus unserem Institut und wurden durch eine sorgfältige Literaturrecherche aus PubMed ergänzt.

Schlussfolgerung TAME ist ein vielversprechender therapeutischer Ansatz, der die Beschwerden von Gelenkerkrankungen lindert und die Lebensqualität der Patienten erheblich verbessert. Die klinischen Ergebnisse unterstreichen die Wirksamkeit und Sicherheit von TAME bei der Linderung von Schmerzen und der Verbesserung der Funktionalität bei Patienten mit chronischen Gelenkschmerzen im Zusammenhang mit Arthrose. Angesichts der zunehmenden wissenschaftlichen Belege für den therapeutischen Nutzen und die Anwendbarkeit bei zahlreichen Gelenkerkrankungen stellt die TAME eine wertvolle Ergänzung des Behandlungsspektrums für diese Erkrankungen dar.

Kernaussagen
- TAME ist eine innovative Therapie zur Behandlung chronischer Gelenkschmerzen im Zusammenhang mit Arthrose.
- Die TAME ist ein technisch anspruchsvoller, minimalinvasiver Eingriff, der eine Expertise erfordert.
- Ein umfassendes Verständnis von Komplikationen mindert Risiken und optimiert die Behandlungsergebnisse des Verfahrens.

Introduction

Affecting over 100 million people worldwide, osteoarthritis (OA) is the most common form of degenerative joint disease and the leading cause of chronic musculoskeletal pain and functional limitations [1]. Chronic musculoskeletal pain often results in reduced daily activities and, consequently, a diminished quality of life for affected patients [2].

Depending on the severity of the disease, therapeutic approaches for OA range from pharmacological interventions, such as anti-inflammatory drugs and pain relievers, to shock-wave therapy, intra-articular corticosteroid injections, and surgical joint replacement [2]. However, alternative treatments like intra-articular glucocorticoid injections could result in significant cartilage tissue loss with prolonged use, thus potentially worsening OA [3]. Moreover, many patients in advanced stages of the disease no longer respond to conservative forms of treatment or exhibit contraindications for long-term pain medication [4]. As a result, patients who are too young for joint replacement or have a high perioperative mortality due to their preexisting medical conditions still pose a challenge for medical treatment today [5, 6].

In response to these challenges, transarterial microembolization (TAME) has emerged as an innovative treatment strategy for patients with chronic joint pain, particularly those resistant to conservative treatments or experiencing persistent pain after surgery.

This review aims to highlight the potential applications of TAME in the treatment of chronic refractory joint pain in OA. The pathophysiology, potential indications, technical aspects, and adverse events are examined, with a specific focus on discussing clinical applications in patients with OA.

Pathophysiological Mechanisms and Angiogenesis in Osteoarthritis

Pathophysiologically, OA is characterized by irreversible damage to the articular cartilage, remodeling of subchondral bone, formation of osteophytes, and thickening of the joint capsule [7], which ultimately leads to irreversible joint damage [8, 9]. The underlying pathomechanisms of these remodeling processes and the exact causes of chronic joint pain, which is the leading clinical symptom of OA, are very complex and not yet fully understood. Anecdotal evidence suggests that chronic bone and synovial inflammation result in the stimulation of angiogenesis, synovial hyperplasia, and recruitment of inflammatory cells [10, 11]. A variety of factors including altered biomechanics and an increased release of proinflammatory cytokines, chemokines, prostaglandins, matrix-reducing enzymes (e. g., matrix metalloproteases), sphingolipids, and vascular endothelial growth factor play a crucial role in this process in arthritic joints [8, 11, 12]. The resulting imbalance of pro- and anti-angiogenic factors leads to increased angiogenesis in the subintima of the synovial membrane [8], the menisci [7], the osteochondral junction [13], and the deep layers of the articular cartilage of the affected joint [14]. While healthy articular cartilage has a natural resistance to the formation of blood vessels due to the specific structure of its proteoglycan matrix, the loss of proteoglycans in arthritic articular cartilage leads to reduced resistance and thus facilitates the formation of new vascular channels and consequently the penetration of new blood vessels [11, 15, 16]. Via common regulatory signaling pathways, these blood vessels lead to growth stimulation of sensory nerve fibers [9], which penetrate the synovium as well as non-calcified cartilage and osteophytes at the osteochondral junction and are therefore postulated to be the cause of arthritic joint pain [7, 8, 17]. In addition, angiogenesis is an essential stage of endochondral ossification, and the sensory innervation of osteophytes may explain the association between radiographic osteophyte formation and pain perception [7, 8]. Thus, it is hypothesized that pathological angiogenesis contributes to the development of structural damage and pain in osteoarthritic joints [4, 18, 19, 20, 21, 22].

Patient Selection and Assessment

Patient selection and assessment are crucial steps in considering TAME as a viable treatment option. Patients typically include individuals with chronic musculoskeletal pain, particularly those diagnosed with OA, who experience persistent musculoskeletal pain after unsuccessful conservative treatments or even after an endoprosthesis. A further prerequisite is chronic knee pain despite adequate drug therapy (duration of therapy > 6 months) or an intolerance or contraindication to non-steroidal anti-inflammatory drugs and/or opioids. Furthermore, candidates for TAME include patients who are either considered too young or too medically compromised for endoprosthetic joint replacement, as well as those experiencing persistent pain after undergoing joint replacement surgery. In cases involving a joint prosthesis, it is imperative to exclude other causes of pain, such as periprosthetic infection, instability, arthrofibrosis, prosthesis loosening, or implant malposition, before proceeding with TAME. Patients with multiple comorbidities who are deemed unsuitable for joint replacement due to various reasons also qualify for this treatment. Contraindications for TAME encompass acute joint infection (considered an absolute contraindication) and relative contraindications such as renal insufficiency and coagulation disorders, characterized by an INR greater than 1.5. As with any intervention, conducting a comprehensive evaluation of the patient's medical history, pain symptoms, and radiological findings is essential to ensure the safety and efficacy of the procedure. Pre-procedural imaging usually includes standard X-rays and ultrasound as part of the clinical assessment. The use of MRI, while not universally required, is determined based on the specific clinical scenario and the joint under consideration. MRI offers detailed visualization of soft tissues, making it invaluable in cases where comprehensive assessment of synovitis, cartilage integrity, and other soft tissue components is necessary. Its application is particularly pertinent in complex joints or when initial assessments with X-rays and ultrasound yield inconclusive results, and if the clinical examination is ambiguous. Therefore, the decision to incorporate MRI into the diagnostic process is guided by its potential to enhance understanding of the joint's pathology, rather than as a routine requirement for all cases. Examining MRI features before genicular artery embolization (GAE) in knee OA, Choi et al. reported that bone marrow lesions, meniscal injury, and a high Kellgren-Lawrence (KL) grade were associated with poor outcomes [23]. To date, TAME is a promising option for those who are unresponsive to traditional conservative therapies, and patient selection and assessment play a pivotal role in tailoring the treatment to individual needs, thus maximizing the potential benefits of this innovative approach while minimizing potential risks. Given that the indication for treatment is complex and crucial to the success of the procedure, TAME should be meticulously planned in close collaboration between radiologists and orthopedic surgeons. This interdisciplinary approach ensures that patient selection is based on a comprehensive assessment, leveraging the expertise of both specialties to optimize treatment outcomes. However, as the initial studies mainly focused on the feasibility, efficacy, and safety of TAME in various musculoskeletal conditions, there is currently insufficient knowledge about which patients could really benefit most from TAME. Studies including patients with milder symptoms are currently lacking. However, if TAME could notably delay or even prevent joint replacement surgery, the potential economic impact would be enormous. Future research should therefore aim to further identify specific patient groups and diseases that would benefit most from TAME to facilitate future patient selection.

Technical Aspects

Against the background of pathological angiogenesis in OA, TAME, which was initially applied to address bleeding [24] or reduce the size of hypervascular tumors [25], has emerged as a versatile therapeutic approach for various musculoskeletal conditions. By accurately identifying and subsequently embolizing these pathological blood vessels, TAME interrupts and subsequently normalizes blood supply in the affected tissue area. This reduces the influx of inflammatory mediators, interrupting the intricate interplay between angiogenesis, chronic inflammation, and pain, thereby alleviating symptoms and potentially delaying or even preventing further joint damage [10, 11]. While clinical applications such as hemostasis and tumor reduction aim for the complete embolization of the target tissue, in the musculoskeletal context, TAME specifically targets pathological neovessels while simultaneously preserving the larger feeding vessel. Therefore, the endpoint of embolization in TAME is pruning of the neovessels, rather than a complete closure of the feeding vessel.

The technical aspects of the TAME procedure can vary greatly depending on the specific anatomical site and the musculoskeletal condition being addressed, which would exceed the scope of this review. However, core principles underlying TAME remain consistent across different anatomical sites: Following local anesthesia with prilocaine (Xylonest 1 %) under sterile conditions, femoral or radial arterial access is established using a guiding catheter (i. e., 3–5F) which is then advanced towards the anatomical target area. Recently, a transpedal arterial access for genicular artery embolization has also been described [26], with limited patient numbers in order to promote this access as a standard, but it might become useful in patients after failed femoral access [27]. Digital subtraction angiography is conducted by manually injecting contrast medium to delineate the vascular anatomy and pathological hypervascularization. Using a 1.7-F microcatheter, for example, smaller branches of the supplying joint vessels are then accessed, evaluating each of those branches individually to identify potential hypervascularization by blush-like contrast medium enhancement and triggering of pain. Once abnormal hypervascularization has been identified and pain could be provoked, permanent or non-permanent embolic agents, diluted with iodinated contrast medium, are slowly injected into the target vessel until complete absence of the previously observed hypervascularization is established. To reduce skin perfusion and thus minimize the risk of skin damage, it is recommended to apply ice to the embolized joint [18, 28, 29, 30]. Since various arterial anastomoses are often present, several branches of the larger supporting vessel must be examined to ensure successful embolization. Once the procedure is completed, the catheter is removed, and hemostasis is achieved by manual compression or the use of a closure device. After a successful procedure, patients are observed depending on the access site for two to six hours to monitor the puncture site, manage pain sensations, and address any post-interventional complications. After this initial observation, patients are discharged on the same day.

To date, a variety of permanent [18, 31] and non-permanent [4, 32] embolic agents have been used. However, the ideal embolic material for TAME in musculoskeletal tissues has yet to be determined. To this end, a recent meta-analysis evaluated the efficacy and safety of GAE using imipenem/cilastatin sodium solution (IPM/CS), microspheres, resorbable microspheres, and polyvinyl alcohol [33]. GAE was effective in improving pain scores using the visual analog scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). No significant difference was found between the different embolic agents in terms of pain relief [33].

Complications and Adverse Events

While TAME offers effective relief from chronic musculoskeletal conditions, patients may experience some mild, transient side effects. Notably, while post-interventional complications have shown a wide range in incidence from 7.1 % [19] to 80 % [26], it's crucial to highlight the absence of major complications that necessitate additional vascular intervention or even surgery. Complication rates, however, appear to be influenced by the size of the embolic particles used. Smaller particles (< 100 µm) have been associated with a higher rate of complications, as seen in both animal models [34] and human studies [26]: In a study in a large animal model, differences in complications were found depending on the size of the embolic particles, with smaller particles (i. e., < 100 µm) leading to more complications [34]. This observation is supported by Bagla et al., who reported two cases of transient plantar sensory paresthesia after GAE with 75 µm microspheres [26]. These events were attributed to non-target embolization, which likely compromised the arterial supply to a branch of the tibial nerve [26]. Although both cases resolved without further intervention, the authors decided to increase the particle size to 100 µm for subsequent cases and found that no further adverse neural consequences occurred [26]. Beyond this, no other major complications were reported. Minor complications, such as subcutaneous hemorrhage at the puncture site [18, 26, 28, 29] or temporary cutaneous color changes in the treated area [4, 19, 20, 21, 26, 30], artery vasospasm [21, 22], and periprocedural pain [4, 20, 21], typically resolved spontaneously. The incidence of post-interventional complications appears to correlate with the size of the embolizing agents used. Studies employing larger particles, specifically 100–300 µm Embospheres, report fewer complications [18], whereas higher complication rates are observed with smaller particles, such as 75 µm or 100 µm microspheres [26]. The increased risk associated with smaller particles is likely due to their propensity to migrate and occlude distal and smaller vessels, leading to non-target embolization and unintended ischemia. Conversely, larger particles are less likely to enter these smaller channels, thus reducing the risk of adverse events. This emphasizes the critical need to select an embolizing agent of appropriate size to ensure a balance between the effectiveness of the embolization and patient safety.

Importantly, these issues resolved without the need for further extensive treatment, emphasizing the overall safety and efficacy of TAME as a valuable therapeutic approach for musculoskeletal diseases [4, 19, 20, 21, 26, 30, 33].

Clinical Application of Transarterial Microembolization in Osteoarthrosis

Pioneered by Okuno et al. in 2013, their successful treatment of tendinopathies and enthesopathies marked the beginning of a series of studies highlighting the efficacy of this technique in musculoskeletal conditions [4]. In addition to its role in hemarthrosis [35], TAME has been shown to offer pain relief in cases of musculoskeletal pain associated with OA. In 2015, its use was extended to patients with musculoskeletal pain in the knee associated with OA, demonstrating sustained pain relief for up to one year after the procedure [19]. Moreover, the benefits of TAME for the shoulder and metacarpophalangeal joints were investigated in further studies, thereby expanding the scope of its therapeutic potential [20, 21, 22, 36].

Osteoarthritis of the Knee Joint

The evidence that newly grown blood vessels and nerves could be potential sources of pain in OA has spurred investigations into the use of TAME for embolization of the genicular artery. While arthroplasty is inevitable in severe cases of knee joint OA, GAE has proven successful in treating chronic knee joint pain that is refractory to conservative treatments in patients with mild to moderate OA [18, 19, 20]. Anatomically, the geniculate arteries originate from the distal segment of the superficial femoral artery, the popliteal artery and anterior tibial artery include the descending genicular artery, the medial and lateral superior genicular artery, the median genicular artery, the medial and lateral inferior genicular artery, and the anterior tibia recurrent artery [20, 37].

Several studies on the effectiveness of GAE for knee OA have consistently shown that GAE is a safe and effective method for alleviating knee pain in patients with mild to moderate knee OA who do not respond to conservative treatment [18, 19, 20, 36, 38]. ► **Table 1** summarizes the patient characteristics and clinical outcomes. In those studies, the technical success rate was reported to range from 84 % [18] to 100 % [20, 26, 38]. GAE rapidly improved pain and physical functioning, as assessed using the VAS and the WOMAC scores. A significant reduction in pain as well as an improvement in physical function were observed at the 3-month [18], 6-month [26, 38], and 1-year follow-up [20] in patients with mild to moderate knee OA. Moreover, a long-term study in 72 patients with mild to moderate knee OA achieved a cumulative clinical success rate in 86.3 % after six months and 79.8 % after three years [20], defined as improvement in pain symptoms six months after the first catheter arterial embolization procedure [20]. Furthermore, MR imaging in 35 knee OA patients revealed a significant reduction in the synovitis score between baseline and two years after the intervention, with no reported osteonecrosis, cartilage loss, or tendinopathy [20]. In a recent multicenter, randomized, controlled trial, Bagla et al. demonstrated that genicular artery embolization (GAE) resulted in significant pain relief and improved functional outcomes in patients with mild to moderate osteoarthritis (OA), as compared to those in the sham group. Functional improvement was quantitatively assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, revealing a mean decrease

▶ **Table 1** Characteristics and clinical outcomes of included studies on genicular artery embolization.

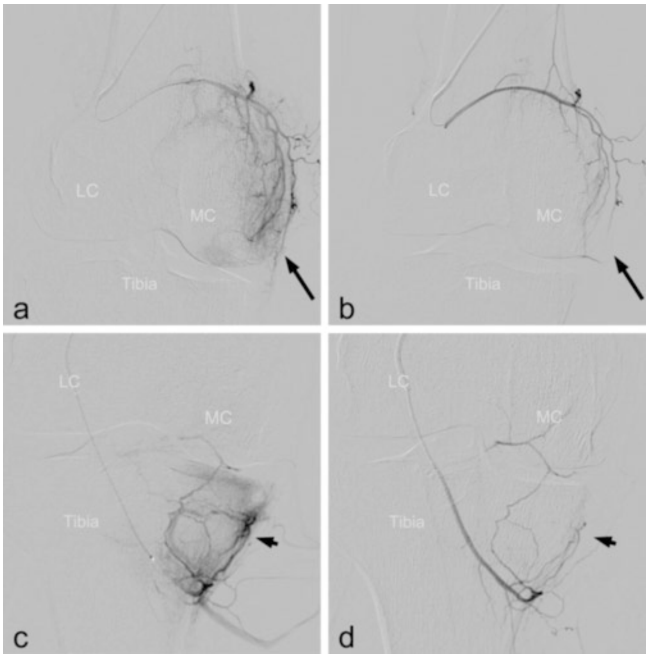
Study Reference	Number of Patients	Duration of Follow-up (Months)	Score Results	Success Rate/Complications
Little et al., 2021 [18]	38	12	Mean VAS improved from 60 (SD = 20.95 % CI 53–66) at baseline to 36 (SD = 24.95 % CI 28–44) at 3 months (p < 0.001) and 45 (SD = 30.95 % CI 30–60) at 1 year (p < 0.05). KOOS subscales significantly improved from baseline to 6 weeks (p < 0.001), 3 months (p < 0.001), and 1 year (p < 0.05).	84 % technical success (6 patients were not embolized); 0 % major adverse events 4 patients with mild self-limiting skin discoloration; 1 patient with small self-limiting groin hematoma.
Okuno et al., 2015 [19]	14	12	Mean WOMAC total scores decreased from 47.3 ± 5.8 at baseline to 11.6 ± 5.4 at 1 month, and to 6.3 ± 6.0 at 4 months.	100 % technical success; 0 % major adverse events 1 patient with self-resolving moderate subcutaneous hemorrhage.
Okuno et al., 2017 [20]	72 (95 joints)	24	Mean VAS score significantly decreased from 72 ± 16 at baseline to 38 ± 23, 29 ± 22, 19 ± 21, 13 ± 21, and 14 ± 17 at 1, 4, 6, 12, and 24 months, respectively (all p < 0.001). The mean total WOMAC score significantly decreased from 43 ± 8.3 at baseline to 24 ± 14, 14.8 ± 11, 11.2 ± 10, 8.2 ± 8.5, and 6.2 ± 6.4 at 1, 4, 6, 12, and 24 months, respectively (all p < 0.001).	100 % technical success; 86.3 % clinical success rate at 6 months; 0 % major adverse events 4 patients with transient cutaneous color change on the treated knee.
Lee et al., 2019 [38]	41 (71 joints)	12	KL 1–3: Mean VAS scores from baseline to 6 months post-GAE improved from 5.5 ± 2.2 to 1.9 ± 1.5 (all P = 0.00). KL 4: Mean VAS scores from baseline to 6 months post- GAE changed from 6.3 ± 2.2 to 5.9 ± 2.0.	100 % technical success; 0 % major adverse events 5 patients with transient cutaneous color change on the treated knee.
Bagla et al., 2020 [26]	20	6	The mean VAS score improved from 76 mm ± 14 at baseline to 29 mm ± 27 at 6 months (p < 0.01). Mean WOMAC score improved from 61 ± 12 at baseline to 29 ± 27 at 6 months (p < 0.01).	100 % technical success; 0 % major adverse events 2 patients with self-resolving plantar sensory paresthesia.

Abbreviations: VAS – Visual Analog Scale; SD – standard deviation; CI – confidence interval; KOOS – Knee Injury and Osteoarthritis Outcome Score; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; KL – Kellgren-Lawrence grading system; GAE – genicular artery embolization

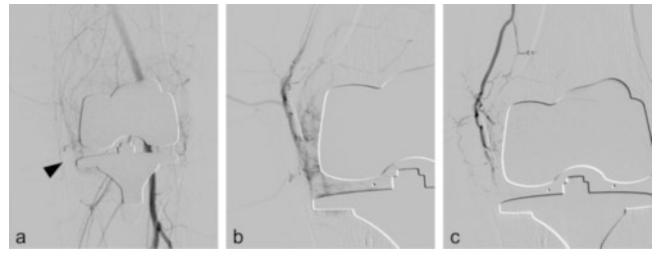
of 24.7 points (Standard Error [SE] = 10.4), with a 95 % Confidence Interval (CI) of 3.5 to 45.9. This change was statistically significant, with a p-value of 0.02, indicating a substantial improvement in patient functionality post-treatment [39]. Minor complications such as a small groin hematoma [18] or transient skin color changes [20] were self-limiting. Importantly, no major complications were observed in these studies. These findings underscore the efficacy of GAE as a treatment option for chronic knee joint pain in mild to moderate knee OA. ▶ **Fig. 1** demonstrates representative images of genicular artery embolization in a 57-year-old female patient with right-sided, medially dominant OA of the knee. The patient had previously undergone multiple treatments, including hyaluronic acid injections and cortisone, which only resulted in a short-term reduction in pain.

However, it is important to note that the severity of knee OA, as assessed using the KL-scale, evidently affects GAE outcomes [38]. While a significant and long-lasting reduction in pain was observed in patients with mild to moderate knee OA (KL grade 1–3) after GAE, patients with severe knee OA (KL grade 4) only experienced a short-term reduction in pain intensity during the first month after the intervention, followed by a gradual return to the original severity level within 3 months after GAE [38]. This phenomenon might be attributed to the substantial loss of articular cartilage in severe knee OA, resulting in direct bone-on-bone and causing significant pain [1]. Furthermore, it should be noted that while TAME has been shown to relieve pain and, to some extent, may improve functional outcomes, it does not alleviate structural limitations such as range of motion restrictions or joint contractures. This distinction is important for physicians to understand the specific benefits of TAME and to set appropriate expectations for patients regarding the procedure's impact on joint mobility and structural abnormalities.

While partial or complete arthroplasty as a last resort is a possible treatment option in advanced stages of OA, postoperatively, 10 % of patients still complain of persistent joint pain [5, 6]. For these patients, GAE is a potential treatment that may help to alleviate persistent pain, potentially eliminating the need for further revision surgery. However, it is important to clarify that persistent pain in patients with total knee arthroplasty can have a variety of causes, including instability, wear, low-grade infections, and peri-



▶ **Fig. 1** Right knee of a 57-year-old female patient with medially dominant OA of the knee before (**a, c**) and after (**b, d**) transarterial microembolization. **a** Superselective digital subtraction angiography (DSA) from the medial superior genicular artery before embolization indicates abnormal neovessels (arrow) adjacent to the medial condyle (MC). **b** Post-embolization DSA of the medial superior genicular artery demonstrates elimination of the pathological periarticular vascular network around the pain point at the medial joint space (arrow). **c** Superselective DSA of the medial inferior genicular artery reveals hypervascularization around the medial tibial plateau at the pain point (short arrow). **d** Post-embolization DSA of the medial inferior genicular artery with evidence of complete embolization of the hypervascularity (short arrow). Abbreviations: LC – lateral condyle; MC – medial condyle; DSA – digital subtraction angiography.



▶ **Fig. 2** Digital subtraction angiography (DSA) of a 64-year-old female with left knee joint prosthesis and persistent medial knee joint pain. In the overview angiography **a** hypervascularized areas are already visible in projection onto the medial joint space (arrowhead). **b** The DSA after superselective probing of the descending genicular artery clearly demonstrates hypervascularized areas projecting onto the medial joint space. **c** Following embolization with 100–300 µm Embosphere microspheres, the hypervascularized areas are no longer visible.

prosthetic fractures. These causes must be thoroughly investigated and definitively ruled out before considering TAME as a treatment option. As TAME is absolutely contraindicated in these cases, a consultation with an experienced orthopedic surgeon is essential and should be considered mandatory to assess the suitability of TAME for patients with painful total knee arthroplasty. This critical requirement for patient selection protects against inappropriate use of TAME and ensures that treatment is tailored to the underlying pathology. ▶ **Fig. 2** illustrates GAE in a 64-year-old female with persistent pain of the medial knee joint following knee joint prosthesis.

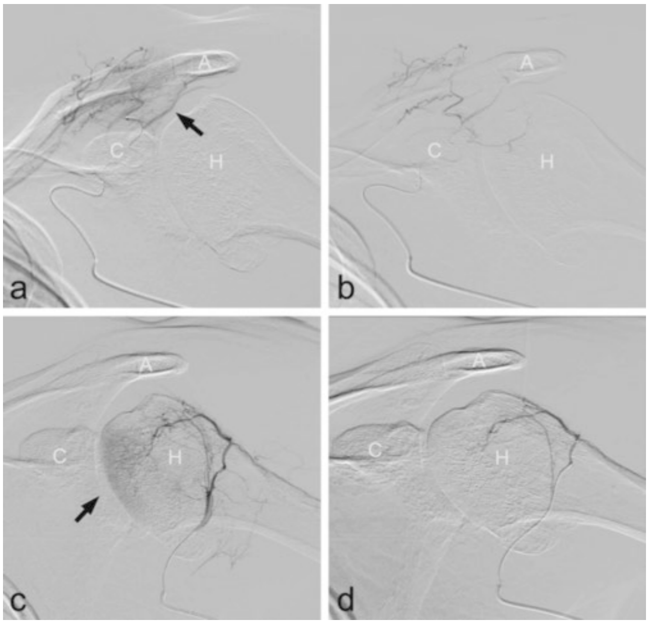
Osteoarthritis of the Shoulder Joint

OA of the glenohumeral joint is estimated to affect over 30 % of people over 60 years of age in the USA [40]. While previous studies have successfully used TAME as a treatment approach for patients with persistent symptoms of adhesive capsulitis [21, 41, 42], there is a lack of studies demonstrating the application of TAME for shoulder joint OA. To date, there is only one report in the literature on the use of TAME for the treatment of OA in the shoulder joint: in their case report Katoh et al. demonstrated transarterial periarticular embolization in a patient with post-traumatic OA of the shoulder [28]. However, although the patient reported significant pain relief as early as one day postintervention, long-term follow-up data is missing [28].

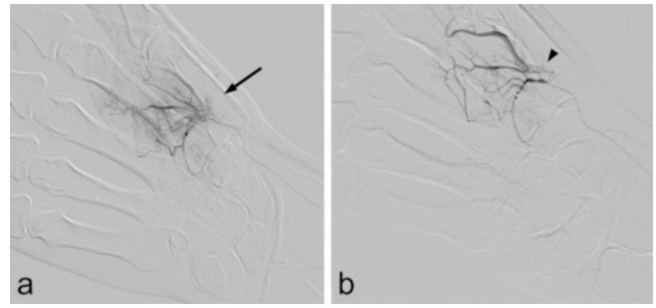
▶ **Fig. 3** shows representative images of TAME in a 51-year-old patient with OA-related pain (KL grade 4) of his left shoulder. Both cortisone and multiple hyaluronic acid injections had previously been unsuccessful and the patient did not want to undergo surgery due to his young age and the fact that he was still mobile and active.

Osteoarthritis of the Trapeziometacarpal Joint

Trapeziometacarpal (TM) OA, occurring at the base of the thumb, is a prevalent form of OA that affects approximately 15 % of adults over 30 years of age [43]. It significantly impairs thumb opposition, leading to considerable movement restrictions. Treating these patients is often challenging due to their relative youth, high activity levels, and demanding requirements for hand mobility [44]. Recently, TAME has been employed as a treatment approach for patients with persistent symptoms of TM-OA. In a first feasibility study involving 31 patients, Inui et al. evaluated intra-arterial IPM/CS infusion for the treatment of TM-OA refractory to conservative treatments [32]. A technical success rate of 100 % and no major adverse events were reported. Intra-arterial infusion of IPM/CS significantly improved pain perception and functional capacity, both short-term at 2 and 6 months and long-term at 24 months, as assessed using the numerical rating scale and the Quick Disabilities of the Arm, Shoulder, and Hand questionnaire. Overall, the clinical success rate was 81 % after 6 months and 74 % after 24 months, thus making intra-arterial IPM/CS infusion a suitable treatment option [32]. These rates were established based on patient-reported outcomes, specifically their self-assessment on the Patient Global Impression of Change (PGIC). A patient's condition was deemed to have met the criteria for "clinical success" if they reported their state as "much improved" or "very much improved" on the PGIC scale at 24 months post-treatment. This high percentage of positive long-term outcomes highlights the potential of intra-arterial IPM/CS infusion as a viable treatment option in this study [32].



▶ **Fig. 3** Left shoulder of a 51-year-old patient with OA of the shoulder (Kellgren/Lawrence grade IV) before (**a, c**) and after (**b, d**) transarterial microembolization. **a** Superselective digital subtraction angiography (DSA) of the ramus acromialis before embolization indicates abnormal neovessels (arrow). **b** Post-embolization DSA demonstrates elimination of the hypervascularized areas, with preservation of the carrier vessel. **c** Superselective probing of the anterior circumflex artery. DSA reveals a hypervascularized area in projection onto the medial part of the humeral head (arrow). **d** Following embolization with 100–300 µm Embosphere microspheres, DSA demonstrates complete elimination of the hypervascularized area.



▶ **Fig. 4** Right thumb of a 67-year-old female patient with trapeziometacarpal osteoarthrosis (Eaton/Littler Stage III) before **a** and after **b** transarterial microembolization. **a** Digital subtraction angiography (DSA) with contrast injection from small vascular branches from the princeps pollicis artery before embolization. Hypervascularization with a "blush" around the trapeziometacarpal joint at the pain point (arrow). **b** Post-interventional DSA after embolization with 100–300 µm Embosphere microspheres, with evidence of a reduced but still minimally demarcated hypervascularization (arrow head). Due to their small size, those vessels could not be probed.

In the example illustrated in ▶ **Fig. 4**, we present a case of TAME treatment for TM-OA in a 67-year-old female patient. Initially, the patient experienced significant pain, particularly during pressure or forceful movements of the hands. As this case report is drawn from clinical observations within our clinic and does not constitute a formal study, specific quantitative measures such as hand force measurements and clinical scores were not collected. However, following the application of TAME, the patient reported a notable improvement in both pain and functional ability. These qualitative outcomes underscore the potential efficacy of TAME in alleviating symptoms and enhancing hand function in patients with TM-OA, even in the absence of quantifiable metrics typically associated with controlled studies.

Osteoarthritis of the Interphalangeal Joints

OA of the finger most commonly occurs in the distal interphalangeal joint, predominantly in women over 50 years of age [45]. Symptomatic OA of these joints leads to stiffness and compromised hand function, thus impairing daily activities of affected patients. Due to its potential to limit range-of-motion, arthrodesis is a last-resort treatment, typically reserved for those patients suffering from severe pain and joint deformity [46]. While TAME has been explored as a possible intervention for interphalangeal joint OA, the evidence supporting its use is limited and inconclusive. Initial attempts to apply TAME in this context have been documented. However, the lack of comprehensive follow-up data, as seen in studies with high attrition rates, limits the ability to draw definitive conclusions regarding its safety and efficacy. Therefore, such treatments should be considered exploratory, and recommendations for their use cannot be reliably made based on the current literature. There is a clear need for further research, including well-designed clinical trials with substantial follow-up, to fully evaluate the potential of TAME for OA of the interphalangeal joints.

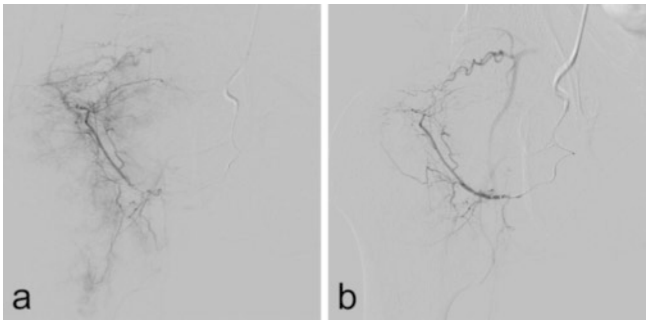
Osteoarthritis of the Hip Joint

With an estimated lifetime risk of symptomatic hip OA at 25 %, it is a highly prevalent form of OA [47]. In a preliminary study involving 13 patients, Correa et al. assessed the effectiveness and safety of TAME of the lateral femoral circumflex artery [48]. The study demonstrated significant improvements in WOMAC and VAS scores over a 6-month follow-up period. However, the cohort was very mixed, with only 3 out of the 13 patients being treated for hip OA, while the other 10 patients suffered from greater trochanteric pain syndrome [48]. Thus, further expanded randomized studies are needed to better evaluate the potential role of TAME in hip OA.

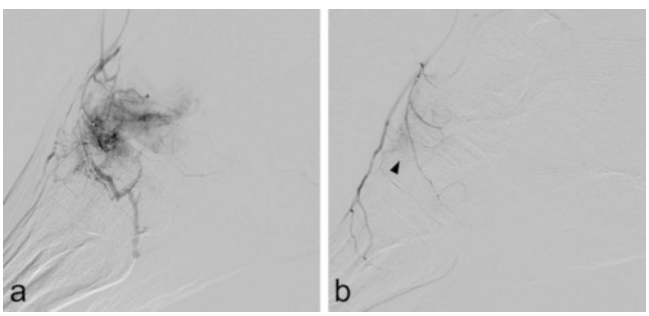
▶ **Fig. 5** demonstrates representative images of circumflex femoral artery embolization in a 59-year-old male patient with symptomatic OA of the right hip (KL grade 2).

Osteoarthritis of the Ankle Joint

While OA of the ankle joint is less common than knee or hip OA, the consequences for the individual patient can be severe [49]. Therapy options are limited and range up to arthrodesis with long recovery times. However, to the best of our knowledge, no report on TAME in OA of the ankle joint has been previously published.



▶ **Fig. 5** Right hip of a 59-year-old male patient with hip OA (Kellgren/Lawrence grade II) before **a** and after **b** transarterial microembolization. **a** Digital subtraction angiography (DSA) with contrast injection from the descending branch of the lateral femoral circumflex artery before embolization. Hypervascularization with a "blush" around the femoral neck. **b** Post-interventional DSA after embolization with 100–300 μm Embosphere microspheres, with evidence of completely reduced hypervascularization.



▶ **Fig. 6** Right foot of a 75-year-old male patient with OA of the lower ankle joint (Kellgren/Lawrence grade IV) before **a** and after **b** transarterial microembolization. **a** Digital subtraction angiography (DSA) with contrast injection from the lateral tarsal artery before embolization. Extensive hypervascularization with a "blush" around the lower ankle joint at the pain point. **b** Post-interventional DSA after embolization with 100–300 μm Embosphere microspheres, with evidence of reduced but still minimally demarcated hypervascularization (arrow head) and patent main feeding arteries.

▶ **Fig. 6** demonstrates a case involving the application of TAME for addressing lower ankle joint OA in a 75-year-old male patient, who initially suffered extensive pain during walking and rolling movements. This clinical case report does not include quantitative metrics like ankle ROM, force measurements, function scores, or gait analysis. However, post-TAME, the patient reported notable pain reduction and improved mobility, demonstrating TAME's potential to enhance quality of life for OA patients, even in the absence of detailed quantitative data.

Conclusion

The presented studies and cases collectively highlight the therapeutic promise of TAME in mitigating chronic musculoskeletal pain linked to OA and its diverse histopathological conditions and anatomical sites. As such, TAME stands as a promising therapeutic approach, providing patient relief from the burdens of joint diseases and significantly enhancing their quality of life. With an expanding evidence base highlighting its therapeutic advantages and the potential for application across a diverse spectrum of joint-related pathologies, TAME is increasingly recognized as a significant enhancement to the treatment options available for these conditions in selected cases. This recognition underscores TAME's role in offering a minimally invasive alternative that can provide relief and improve the quality of life for patients who meet specific criteria for this treatment approach.

While TAME is recognized as a safe and effective option for selected cases of chronic musculoskeletal pain, it is imperative to acknowledge that its applicability and efficacy are contingent upon the specific conditions of individual patients. This tailored approach necessitates comprehensive understanding of potential challenges that may arise during the intervention, as well as the importance of vigilant management of post-treatment complications. The implementation of preventive measures, along with early detection and adept management strategies by experienced interventional radiologists are pivotal for optimizing patient outcomes and mitigating the likelihood of complications.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

[1] Bhatia D, Bejarano T, Novo M. Current interventions in the management of knee osteoarthritis. J Pharm Bioallied Sci 2013; 5: 30–38. doi:10.4103/0975-7406.106561

[2] Litwic A, Edwards MH, Dennison EM et al. Epidemiology and burden of osteoarthritis. Br Med Bull 2013; 105: 185–199. doi:10.1093/bmb/lds038

[3] McAlindon TE, LaValley MP, Harvey WF et al. Effect of Intra-articular Triamcinolone vs Saline on Knee Cartilage Volume and Pain in Patients With Knee Osteoarthritis: A Randomized Clinical Trial. JAMA 2017; 317: 1967–1975. doi:10.1001/jama.2017.5283

[4] Okuno Y, Matsumura N, Oguro S. Transcatheter Arterial Embolization Using Imipenem/Cilastatin Sodium for Tendinopathy and Enthesopathy Refractory to Nonsurgical Management. J Vasc Interv Radiol 2013; 24: 787–792. doi:10.1016/j.jvir.2013.02.033

[5] Klit J, Jacobsen S, Rosenlund S et al. Total Knee Arthroplasty in Younger Patients Evaluated by Alternative Outcome Measures. J Arthroplasty 2014; 29: 912–917. doi:10.1016/j.arth.2013.09.035

[6] Parvizi J, Nunley RM, Berend KR et al. High Level of Residual Symptoms in Young Patients After Total Knee Arthroplasty. Clin Orthop Relat Res 2014; 472: 133–137. doi:10.1007/s11999-013-3229-7

[7] Ashraf S, Wibberley H, Mapp PI et al. Increased vascular penetration and nerve growth in the meniscus: a potential source of pain in osteoarthritis. Ann Rheum Dis 2011; 70: 523–529. doi:10.1136/ard.2010.137844

[8] Bonnet CS. Osteoarthritis, angiogenesis and inflammation. Rheumatology 2005; 44: 7–16. doi:10.1093/rheumatology/keh344

[9] Goldman DT, Piechowiak R, Nissman D et al. Current Concepts and Future Directions of Minimally Invasive Treatment for Knee Pain. Curr Rheumatol Rep 2018; 20: 54. doi:10.1007/s11926-018-0765-x

[10] Casadaban LC, Mandell JC, Epelboym Y. Genicular Artery Embolization for Osteoarthritis Related Knee Pain: A Systematic Review and Qualitative Analysis of Clinical Outcomes. Cardiovasc Intervent Radiol 2021; 44: 1–9. doi:10.1007/s00270-020-02687-z

[11] Mapp PI, Walsh DA. Mechanisms and targets of angiogenesis and nerve growth in osteoarthritis. Nat Rev Rheumatol 2012; 8: 390–398. doi:10.1038/nrrheum.2012.80

[12] Cherifi C, Latourte A, Vettorazzi S et al. Inhibition of sphingosine 1-phosphate protects mice against chondrocyte catabolism and osteoarthritis. Osteoarthritis Cartilage 2021; 29: 1335–1345. doi:10.1016/j.joca.2021.06.001

[13] Suri S, Gill SE, de Camin SM et al. Neurovascular invasion at the osteochondral junction and in osteophytes in osteoarthritis. Ann Rheum Dis 2007; 66: 1423–1428. doi:10.1136/ard.2006.063354

[14] Fransès RE, McWilliams DF, Mapp PI et al. Osteochondral angiogenesis and increased protease inhibitor expression in OA. Osteoarthritis Cartilage 2010; 18: 563–571. doi:10.1016/j.joca.2009.11.015

[15] Fenwick SA, Gregg PJ, Rooney P. Osteoarthritic cartilage loses its ability to remain avascular. Osteoarthritis Cartilage 1999; 7: 441–452. doi:10.1053/joca.1998.0238

[16] Eisenstein R, Sorgente N, Soble LW et al. The Resistance of Certain Tissues to Invasion. Am J Pathol 1973; 73: 765–774

[17] Walsh DA, Bonnet CS, Turner EL et al. Angiogenesis in the synovium and at the osteochondral junction in osteoarthritis. Osteoarthritis Cartilage 2007; 15: 743–751. doi:10.1016/j.joca.2007.01.020

[18] Little MW, Gibson M, Briggs J et al. Genicular artEry embolizatioN in patiEnts with oSteoarthrItiS of the Knee (GENESIS) Using Permanent Microspheres: Interim Analysis. Cardiovasc Intervent Radiol 2021; 44: 931–940. doi:10.1007/s00270-020-02764-3

[19] Okuno Y, Korchi AM, Shinjo T et al. Transcatheter Arterial Embolization as a Treatment for Medial Knee Pain in Patients with Mild to Moderate Osteoarthritis. Cardiovasc Intervent Radiol 2015; 38: 336–343. doi:10.1007/s00270-014-0944-8

[20] Okuno Y, Korchi AM, Shinjo T et al. 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: 995–1002. doi:10.1016/j.jvir.2017.02.033

[21] Okuno Y, Iwamoto W, Matsumura N et al. Clinical Outcomes of Transcatheter Arterial Embolization for Adhesive Capsulitis Resistant to Conservative Treatment. J Vasc Interv Radiol JVIR 2017; 28: 161–167.e1. doi:10.1016/j.jvir.2016.09.028

[22] Iwamoto W, Okuno Y, Matsumura N et al. Transcatheter arterial embolization of abnormal vessels as a treatment for lateral epicondylitis refractory to conservative treatment: a pilot study with a 2-year follow-up. J Shoulder Elbow Surg 2017; 26: 1335–1341. doi:10.1016/j.jse.2017.03.026

[23] Choi JW, Ro DH, Chae HD et al. The Value of Preprocedural MR Imaging in Genicular Artery Embolization for Patients with Osteoarthritic Knee Pain. J Vasc Interv Radiol 2020; 31: 2043–2050. doi:10.1016/j.jvir.2020.08.012

[24] Wang K, Zhou J, Chen X-S et al. Transcatheter arterial embolization for postoperative arterial complications after pelvic or hip surgery. Diagn Interv Radiol 2019; 25: 219–224. doi:10.5152/dir.2019.18212

[25] Kishore S, Friedman T, Madoff DC. Update on Embolization Therapies for Hepatocellular Carcinoma. Curr Oncol Rep 2017; 19: 40. doi:10.1007/s11912-017-0597-2

[26] Bagla S, Piechowiak R, Hartman T et al. Genicular Artery Embolization for the Treatment of Knee Pain Secondary to Osteoarthritis. J Vasc Interv Radiol 2020; 31: 1096–1102. doi:10.1016/j.jvir.2019.09.018

[27] Marmagkiolis K, Sardar P, Mustapha JA et al. Transpedal Access for the Management of Complex Peripheral Artery Disease. J Invasive Cardiol 2017; 29: 425–429

[28] Katoh M, Schott P, Freyhardt P et al. Transarterial Periarticular Embolization (TAPE): Indications and Initial Experience in Germany. Fortschr Röntgenstr 2020; 192: 1046–1052. doi:10.1055/a-1212-6149

[29] Padia SA, Genshaft S, Blumstein G et al. Genicular Artery Embolization for the Treatment of Symptomatic Knee Osteoarthritis. JB JS Open Access 2021; 6: e21.00085. doi:10.2106/JBJS.OA.21.00085

[30] Lin HY, Liang KW, Wang B et al. Challenges and complications and their management of the transarterial microembolization for chronic musculoskeletal pain. Eur Radiol 2023. doi:10.1007/s00330-023-10328-5

[31] Bhatia S, Jalaeian H, Kumar J et al. Two-year outcomes comparing Embosphere® microspheres versus Imipenem Cilastatin for genicular artery embolization in patients with moderate to severe knee osteoarthritis. The Knee 2023; 41: 38–47. doi:10.1016/j.knee.2022.12.008

[32] Inui S, Yoshizawa S, Shintaku T et al. Intra-Arterial Infusion of Imipenem/Cilastatin Sodium through a Needle Inserted into the Radial Artery as a New Treatment for Refractory Trapeziometacarpal Osteoarthritis. J Vasc Interv Radiol JVIR 2021; 32: 1341–1347. doi:10.1016/j.jvir.2021.06.024

[33] Torkian P, Golzarian J, Chalian M et al. Osteoarthritis-Related Knee Pain Treated With Genicular Artery Embolization: A Systematic Review and Meta-analysis. Orthop J Sports Med 2021; 9. doi:10.1177/23259671211021356

[34] Ghelfi J, Soulairol I, Stephanov O et al. Feasibility of Neovessel Embolization in a Large Animal Model of Tendinopathy: Safety and Efficacy of Various Embolization Agents. J Pers Med 2022; 12: 1530. doi:10.3390/jpm12091530

[35] Waldenberger P, Chemelli A, Hennerbichler A et al. Transarterial embolization for the management of hemarthrosis of the knee. Eur J Radiol 2012; 81: 2737–2740. doi:10.1016/j.ejrad.2011.11.016

[36] Hwang JH, Park SW, Kim KH et al. Early Results of Transcatheter Arterial Embolization for Relief of Chronic Shoulder or Elbow Pain Associated with Tendinopathy Refractory to Conservative Treatment. J Vasc Interv Radiol 2018; 29: 510–517. doi:10.1016/j.jvir.2017.11.013

[37] O'Grady A, Welsh L, Gibson M et al. Cadaveric and Angiographic Anatomical Considerations in the Genicular Arterial System: Implications for Genicular Artery Embolisation in Patients with Knee Osteoarthritis. Cardiovasc Intervent Radiol 2022; 45: 80–90. doi:10.1007/s00270-021-02978-z

[38] 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: 1530–1536. doi:10.1007/s00270-019-02289-4

[39] Bagla S, Piechowiak R, Sajan A et al. Multicenter Randomized Sham Controlled Study of Genicular Artery Embolization for Knee Pain Secondary to Osteoarthritis. J Vasc Interv Radiol 2022; 33: 2–10.e2. doi:10.1016/j.jvir.2021.09.019

[40] Kerr R, Resnick D, Pineda C et al. Osteoarthritis of the glenohumeral joint: a radiologic-pathologic study. AJR Am J Roentgenol 1985; 144: 967–972. doi:10.2214/ajr.144.5.967

[41] Fernández Martínez AM, Baldi S, Alonso-Burgos A et al. Mid-Term Results of Transcatheter Arterial Embolization for Adhesive Capsulitis Resistant to Conservative Treatment. Cardiovasc Intervent Radiol 2021; 44: 443–451. doi:10.1007/s00270-020-02682-4

[42] Okuno Y, Oguro S, Iwamoto W et al. Short-term results of transcatheter arterial embolization for abnormal neovessels in patients with adhesive capsulitis: a pilot study. J Shoulder Elbow Surg 2014; 23: e199–e206. doi:10.1016/j.jse.2013.12.014

[43] Haara MM, Heliövaara M, Kröger H et al. Osteoarthritis in the Carpometacarpal Joint of the Thumb: Prevalence and Associations with Disability and Mortality. JBJS 2004; 86: 1452

[44] Patel TJ, Beredjiklian PK, Matzon JL. Trapeziometacarpal joint arthritis. Curr Rev Musculoskelet Med 2012; 6: 1–8. doi:10.1007/s12178-012-9147-6

[45] Kalichman L, Hernández-Molina G. Hand osteoarthritis: an epidemiological perspective. Semin Arthritis Rheum 2010; 39: 465–476. doi:10.1016/j.semarthrit.2009.03.001

[46] Kloppenburg M, Kroon FP, Blanco FJ et al. 2018 update of the EULAR recommendations for the management of hand osteoarthritis. Ann Rheum Dis 2019; 78: 16–24. doi:10.1136/annrheumdis-2018-213826

[47] Murphy NJ, Eyles JP, Hunter DJ. Hip Osteoarthritis: Etiopathogenesis and Implications for Management. Adv Ther 2016; 33: 1921–1946. doi:10.1007/s12325-016-0409-3

[48] Correa MP, Motta-Leal-Filho JM, Junior EB et al. 6-Month Follow-up of Lateral Femoral Circumflex Artery Embolization to Control Pain Related to Hip Osteoarthritis and Greater Trochanteric Pain Syndrome. Cardiovasc Intervent Radiol 2022; 45: 1710–1715. doi:10.1007/s00270-022-03253-5

[49] Herrera-Pérez M, Valderrabano V, Godoy-Santos AL et al. Ankle osteoarthritis: comprehensive review and treatment algorithm proposal. EFORT Open Rev 2022; 7: 448–459. doi:10.1530/EOR-21-0117