Osteoarthritis (OA) is a leading cause of disability and chronic pain that reduces physical activity and quality of life. The prevalence of knee OA has been rising because of the increasing aging population and the obesity epidemic. Treatment options for OA include nonpharmacologic and pharmacologic therapies and knee joint replacement surgery, depending on the severity of OA and degree of pain. However, a large number of patients are resistant to conventional nonsurgical therapies. In addition, 15% of patients have persistent severe to extreme pain after knee joint replacement surgery.

OA has long been recognized as a "wear and tear" disease; it is now considered a much more complex disease of low-grade inflammation induced by inflammatory mediators released by cartilage, bone, and synovium. Angiogenesis contributes to synovial inflammation and promotes the destruction of cartilage and bone. Furthermore, increased vessels and accompanying sensory nerves into osteochondral, synovium, and meniscus are a cause of chronic pain in knee OA.

We have previously reported the safety and efficacy of transcatheter arterial microembolization (TAME) for mild to moderate knee OA that was resistant to conservative treatment for short-term and midterm clinical outcomes. This article describes which patients with OA may be the best candidates for TAME as well as the proper techniques and follow-up.

PATIENT SELECTION

Signs and symptoms of OA are essential for determining which patients are suitable for TAME. Patients with chronic knee pain refractory to conventional therapies (eg, oral nonsteroidal anti-inflammatory drugs, oral opioid agents, physical therapy, muscle strengthening, intra-articular injection of hyaluronic acid) for at least 3 months are selected in principle. Spontaneous pain, including nighttime pain and rest pain, strongly suggests the presence of an abnormal neovessel at the origin of pain. Local tenderness during physical examination at the synovium and periosteum around the medial/lateral condyle, the infrapatellar fat pad, the medial/lateral meniscus base, and the medial/lateral side of the joint capsule also point to the presence of an abnormal neovessel, and thus, these patients are good candidates for TAME.

Pain that occurs when climbing the stairs is a good indicator of the existence of abnormal neovessel. However, patients with pain while walking on flat ground should be carefully evaluated because the pain in this situation mainly comes from the overload on the weight-bearing joint or anatomic joint incongruence, not from an abnormal neovessel. These patients often have severe/end-stage degenerative changes and should be considered for knee joint surgery. However, TAME can be performed in patients with chronic pain after successful total joint arthroplasty. In addition, patients with algodystia and swelling concomitant with pain have obtained significant pain relief with TAME.

MRI

Recent advances in MRI enable imaging of joints with great anatomic detail, which is essential for accurate morphologic assessment of OA. Additionally, new quantitative MRI techniques provide numeric outcomes related to vascularity such as short tau inversion recovery and enhancement after paramagnetic contrast agent administration (gadolinium). We use dynamic contrast-enhanced MRI to detect abnormal hypervascularity (Figure 1).
PROCEDURAL TECHNIQUE

Before the catheterization procedure, the locations of tenderness (indicating the presence of abnormal neovessel) are confirmed to determine the key arteries to be treated. The common femoral artery is penetrated in an ipsilateral antegrade fashion under local anesthesia with ultrasound guidance, and a 3-F introducer sheath (Super Sheath, Boston Scientific Corporation) is inserted toward the superficial femoral artery. The recommended puncture site is immediately above the femoral head in order to effectively obtain hemostasis after the procedure. A contralateral approach is not recommended because low torque transmissibility makes it difficult to manipulate the angiographic catheter to select the branch vessel.

After intravenous administration of 2,000 IU of heparin, a 3-F Judkins right 2.5 angiographic catheter is inserted and moved distally to the superficial femoral artery. This angiographic catheter is used for selective embolization because it can adapt to acute angle branches from the parent vessel. Digital subtraction angiography, obtained by injecting 3 to 5 mL of iodinated contrast medium (Hexabrix, Guerbet LLC), shows the entire image of the branch vessel at the knee joint area to confirm the diagnosis (Figure 2).

An abnormal neovessel appears as a tumor blush–type enhancement in the arterial phase. A 1.7-F Asahi Veloute microcatheter (Asahi Intecc Co. Ltd.) is inserted to the corresponding vessel (including the descending genicular artery, superior and inferior lateral genicular arteries, superior and inferior medial genicular arteries, median genicular artery, and anterior tibial recurrent artery) to the site of tenderness. Embolization is performed in each artery sequentially, and the presence of pain is checked by injecting imipenem/clasatatin sodium (IPM/CS; Primaxin IV, Merck & Co., Inc.) \(^{8,9}\). A suspension of 0.5 g of IPM/CS in 5 to 10 mL of iodinated contrast agent is prepared by pumping syringes for 10 seconds and then injected in 0.2-mL increments. IPM/CS is a crystalline compound that is slightly soluble in water and forms small-sized particles that exert an embolic effect when suspended in contrast agent. The volume of embolic agents for each branch is adjusted based on the amount of abnormal neovessel and perfusion area.

Treatment is stopped after determining a reduction or elimination of abnormal neovessel as well as the mitigation of tenderness. Hemostasis is achieved with 10 minutes of hands-on pressure. Patients are discharged on the same day after 1 hour of rest and are advised to refrain from excessive exercise for 2 weeks. Previous conservative therapies are allowed to continue.

FOLLOW-UP ASSESSMENTS

Follow-up assessments are performed every 3 to 4 weeks after the TAME procedure. Pain relief occurs gradually and varies depending on the individual, duration of pain, and the severity of OA. To support quick pain relief, 0.25 mL of triamcinolone acetonide (10 mg/mL) mixed with 2 mL of lidocaine 1% can also be locally injected.

Case 1

A 69-year-old woman presented to the clinic with painful swelling in the left knee joint for more than 2 years. Her symptoms mainly appeared spontaneously at night. Radiography revealed moderate degenerative changes, corresponding to Kellgren-Lawrence grade 3 (ie, multiple osteophytes, definite joint space narrowing, sclerosis, possible bony deformity). She had undergone several treatments for pain, such as intra-articular hyaluronic acid injection, nonsteroid anti-inflammatory drugs, and physical therapy; however, they did not provide adequate pain relief. Physical examination revealed local tenderness at the infrapatellar fat pad. Selective angiography demonstrated an abnormal neovessel in the inferior lateral genic-
cular artery (Figure 3). A total of 0.5 to 1 mL of IPM/CS was injected in each branch of the inferior lateral genicular artery using a microcatheter. Pain relief was obtained immediately after procedure, and almost no residual pain was observed at 2-month follow-up.

Case 2
A 75-year-old woman presented to the clinic with chronic residual right knee pain 2 years after total knee arthroplasty. Nighttime pain was her main complaint, and she also noted pain that occurs when stepping down stairs. Conservative treatment had not been effective.

TAME was performed 3 years after arthroplasty. The presence of an abnormal neovessel supplied from the descending genicular artery was confirmed by selective angiography (Figure 4). Subsequently, 0.5 mL of IPM/CS was injected using a microcatheter. A significant reduction of the abnormal neovessel was confirmed by angiography (Figure 4). The patient reported that her pain had completely resolved at 1-month follow-up and has been maintained for 2 years.

DISCUSSION
Although the symptoms of the two presented cases improved and these results have been maintained over time, we have to be aware that OA is an age-related disease with no prospect for spontaneous recovery. It is thus expected that structural changes and associated inflammation will continue to progress and that pain can recur, especially in patients with severe degenerative changes. A subset of our patients experienced pain recurrence after initial clinical success. Combining TAME with other conservative treatments, such as physiotherapy, local steroid injection, and/or weight management, is required to manage residual or recurrent pain after knee embolization procedures.

CONCLUSION
TAME is a potential treatment option in patients with mild to moderate knee OA that is resistant to conservative treatment. However, further investigation, such as a larger longitudinal comparative study, is warranted.


Masahiko Shibuya, MD, PhD
Chief Researcher, Musculoskeletal Intervention Center
Okuno Clinic
Tokyo, Japan
Disclosures: None.

Yuji Okuno, MD, PhD
Chief Director, Musculoskeletal Intervention Center
Okuno Clinic
Tokyo, Japan
contact@okuno-y-clinic.com
Disclosures: None.