Transcatheter Arterial Embolization for Musculoskeletal Pain

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Introduction

Approximately 10-22% of people are suffered from chronic pain, most of which involves the musculoskeletal (MSK) system. Chronic MSK pain is caused by various inflammatory, degenerative diseases including adhesive capsulitis, osteoarthritis (OA), tendinopathy and enthesopathy [1-14].

Those patients have been treated by surgical or non-surgical treatment such as anti-inflammatory drugs. However, up to 50% of patients showed persistent symptoms despite of non-surgical treatment [15, 16]. Furthermore, the efficacy of some of nonsurgical treatments has not been clearly confirmed with evidence [17-19]. Although some evidence supports the notion that surgical intervention could benefit these conditions, the results have been disappointing, with failure rates of 20–30% [20, 21].

Therefore, both of non-operative conservative measures including physical therapy, anti-inflammatory medications, corticosteroid injections and surgical treatments are not considered to be satisfactory.

Angiogenesis in chronic musculoskeletal (MSK) pain and Embolization

Recently, angiogenesis is believed to contribute to the genesis of inflammation particularly to its maintenance [22]. The new increased vascular network provides inflammatory cells to the synovium and other joint tissue, and it may promote additional hyperplasia and inflammation leading to bone and cartilage destruction [23]. In addition, studies on OA have shown that angiogenesis may contribute to chronic pain by enabling the growth of new unmyelinated sensory nerves along their path [24, 25].

Okuno et al. investigated the effects of transcatheter arterial embolization (TAE) of abnormal blood vessels about the chronic MSK pain refractory to nonsurgical management [26-30]. TAE for chronic pain has been gradually spread as a treatment option alternative to conservative or surgical treatment.

Transarterial embolization -Basic techniques and Devices-

Treatment options of MSK chronic pain include conservative management (including rest, physical therapy, stretching, muscle strengthening, medication of pain relievers such as acetaminophen or nonsteroidal anti-inflammatory drugs, oral opioid agents, intraarticular injection of corticosteroid or hyaluronic acid), surgical treatments, and TAE.

Indication

General indication for TAE includes chronic joint pain due to OA, synovitis,

overusing, or sports injury resistant to 3 months or more of conservative therapies and persistent pain (visual analog scale [VAS] score > 50). On the other hand, exclusion criteria are local infection, malignancy, advanced atherosclerosis, rheumatoid arthritis, severe mental disorders, severe bone deformation around the joint on radiographs, uncontrollable diabetes, and surgery indication.

Techniques

Arterial access sites are depended upon the location of diseases. Radial or brachial approaches are commonly used for the lesions involving upper limbs, and femoral approach was preferably used for lower limbs lesions. Catheter insertion is performed with 3- or 4-F introducer sheath under local anesthesia. When lower limb, the femoral artery (FA) is punctured in an ipsilateral antegrade fashion under ultrasound guidance. Selective angiography usually reveals abnormal vessels as tumor blush-type enhancement in the arterial phase, often accompanied by early venous drainage. After the abnormal vessels are identified, embolic material; 0.5 g Imipenem/cilastatine sodium (IPM/CS) in 5-10 mL iodinated contrast agent is infused slowly until blood flow stagnated on angiography (Figure 1). IPM/CS forms particles (approximately 50-130μm) have exert as embolic material [31, 32]. If needed, 1.7 - 2.4-F microcatheter is inserted coaxially and selectively placed in the targeted arteries. The patients are discharged on the same day they are treated.

Adhesive capsulitis / Frozen Shoulder

Patients with adhesive capsulitis with nighttime shoulder pain or painful restriction of motion are good indications for TAE. Suprascapular artery originated from the subclavian artery (SCA), thoracoacrominal artery, corachoid branch, circumflex scapular artery, anterior circumflex humeral artery, and posterior circumflex humeral artery branched from SCA originated from the axillary artery are the target vessels. There are dangerous arteries of ascending cervical artery and deep cervical artery. They have anastomoses to radiculomedullary artery, spinal artery, or vertebral artery [33]. Before and after TAE, numerical rating scale (NRS) at rest, on motion, and at nighttime and range of motion (ROM) should be assessed for effect of TAE. Okuno et al reported 67% of the patients experienced quick improvement of nighttime pain within1 week, and 87% experienced improvement within 1 month and that at 1 year after TAE, 88% of patients were completely pain- free [30]. The results of phase-Ⅱ multicenter trial of MSK embolization for shoulder pain in Japan (UMIN 000021238) are now under submission. There had been total of 100 cases entries for this trial and 80% of them could be followed 6 months after TAE. There were no major procedure-related complications. In this study, 81% patients got initial improvement of nighttime pain score within 1 week. NRS score of nighttime pain was statistically significant improved from 6.4 to 1.8 after 6 months follow-up (P<.001). Mean ROM of forward elevation and external rotation was also improved after TAE.

Knee OA

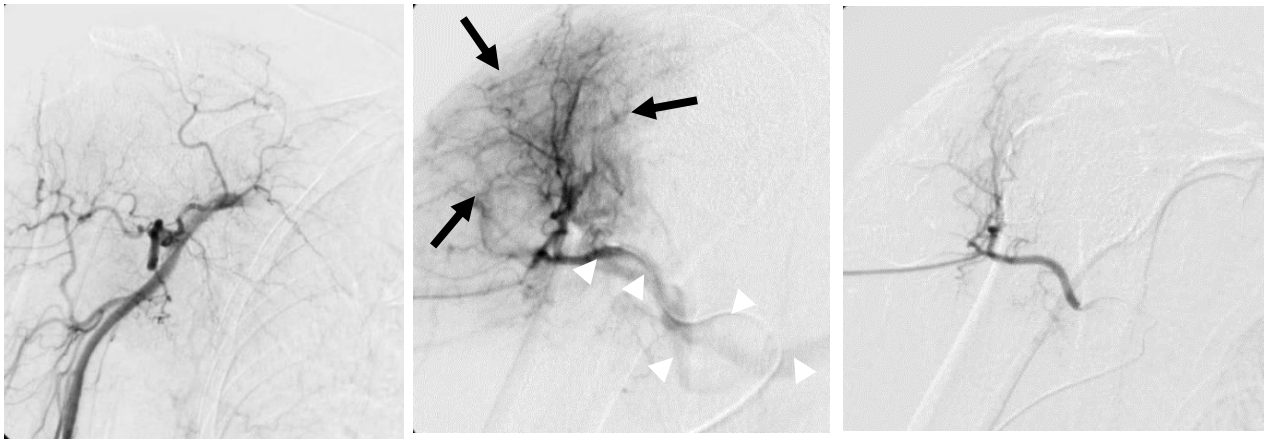
Patients with knee pain due to mild to moderate knee OA changes (Kellgren-Lawrence grade [34] 2 or lower) are also good indications for TAE. In addition to VAS score, Western Ontario and McMaster University Osteoarthritis Index (WOMAC) questionnaire, which includes 24 questions on daily activities is performed before and after the procedure. After catheter insertion from FA, descending genicular artery (DGA) should be selected and embolized at first on digital subtraction angiography (Figure 2). In almost patients with chronic knee pain, DGA embolization is necessary. However, selective angiography shows that other branches of genicular arteries originated from popliteal artery sometimes make anastomosis each other. Therefore, gentle injection of embolic agent is important for avoiding non-target embolization. TAE rapidly improves WOMAC pain scores from 12.2 to 3.3 at 1 month after the procedure and WOMAC total scores from 47.3 to 11.6 at 1 month, and to 6.3 at 4 months [28]. A second TAE procedure should be considered if pain persisted or relapsed within 6 months of the initial procedure. Embolic material used is commonly IPM/CS as mentioned above, but successful genicular artery embolization (GAE) using 75 or 100μm Embozene Microspheres (Boston Scientific, Mariborough, MA) was reported without severe complication [35]. The presented GAE significantly improved pain as measured by VAS and WOMAC (baseline VAS 76 mm, mean decrease -47 mm, $p<0.01$; baseline WOMAC 61, mean decrease 32, $p<0.01$). The optimal embolic material should be researched in the near futures.

Future Perspectives

Although TAE is a new useful interventional procedure for chronic MSK pain, the indication or effect of the treatment is not well quantitatively established, and pain score is subjective evaluation. As a pre-treatment imaging, X-ray examination is often performed, but there are almost no severe abnormalities and there is no suitable guideline on pain images at present. Comparison the contrast enhanced magnetic resonance imaging (MRI) before and after TAE for the evaluation of contrast effect around the joint and the correlation with therapeutic effect was reported [36] (Figure 3). In the present study, a significant reduction of contrast enhancement on MRI was observed in patients with good therapeutic effect for chronic MSK pain treated with TAE [36] (Table). The indication or effect of the treatment, and details of TAE technique including the optimal embolic material should be validated in the future.

Conclusion

TAE is a potential treatment option in patients with chronic MSK pain resistant to conservative treatment. Scientifically, further investigation is warranted, particularly with prospective studies in comparison with a control group to confirm the effects of TAE.



A B C

Figure 1: A characteristic case of TAE for adhesive capsulitis

57-year-old male with chronic shoulder pain treated with TAE using IPM/CS.

A) Right subclavian arteriography reveals many branches.

B) Selective angiography of the anterior humeral circumflex artery before embolization shows abnormal vessels (black arrows) and early venous drainage (white arrowheads) at a early time point.

C) After embolization, the contrast medium distributes more slowly, and the abnormal vessels and the drainage vein are not evident at the same time point.

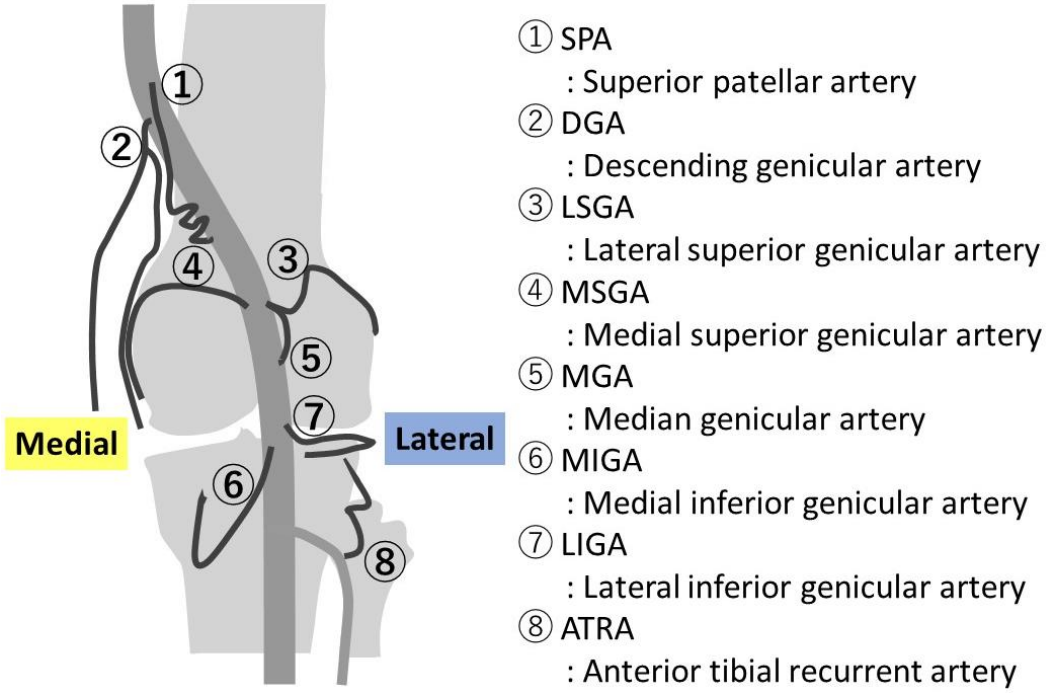
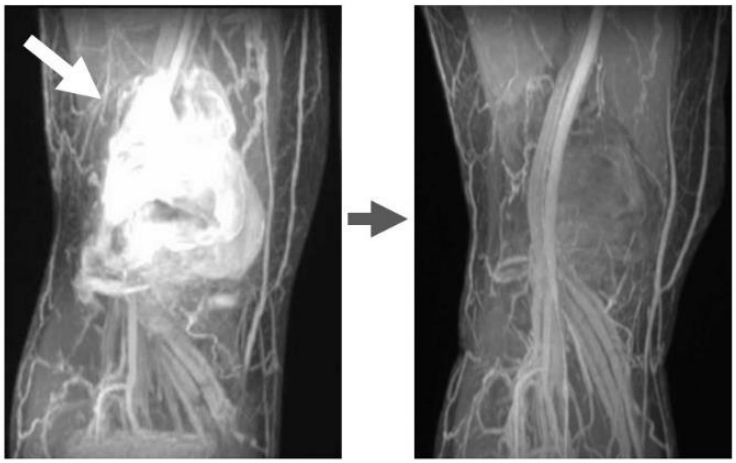


Figure 2: Relevant arterial anatomy for TAE of knee chronic pain

Descending genicular artery (DGA) should be selected and embolized at first on digital subtraction angiography. In almost patients with chronic knee pain, DGA embolization is necessary.



A B

Figure 3: Contrast-enhanced MRI before and after TAE for chronic pain in the right knee (T1-weighted fat suppression image (3D image))

The contrast effect of the synovium on the right knee (abnormal blood vessels) (A) (white arrow) disappeared completely after treatment (B), and pain improved significantly (NRS: 10→0).

Group	N (lesions)	NRS pre-TAE	NRS post-TAE	P value
A : invariant	37 (17.7%)	8.1	5.9	0.571
B : mild	74 (34.4%)	8.3	4.3	0.241
C : marked	104 (48.2%)	9.2	2.5	0.026
total	215	8.5 (average)	4.3 (average)	

Table: Contrast reduction of enhancement on MRI after TAE was classified into three groups; A: invariant, B: mild, and C: marked

The NRS value decreased significantly in group C compared with group A ($P<0.05$). A significant reduction of contrast enhancement on MRI was observed in patients with good therapeutic effect for chronic MSK pain treated with TAE.

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References

1) Gureje O, Von Korff M, Simon GE & Gater R. Persistent pain and well-being: a World Health Organization Study in Primary Care. JAMA 1998; 280:147-151.
2) Breivik H, Collett B, Ventafridda V, Cohen R & Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain 2006; 10:287-333.
3) Wada K, Arakida M, Watanabe R, Negishi M, Sato J & Tsutsumi A. The economic impact of loss of performance due to absenteeism and presenteeism caused by depressive symptoms and comorbid health conditions among Japanese workers. Ind Health 2013; 51:482-489.
4) Takura T, Ushida T, Kanchiku T, Ebata N, Fujii K, DiBonaventura Md & Taguchi T. The societal burden of chronic pain in Japan: an internet survey. J Orthop Sci 2015; 20:750-760.
5) Malmberg-Ceder K, Haanpää M, Korhonen PE, Kautiainen H & Soinila S. Relationship of musculoskeletal pain and well-being at work – Does pain matter? Scand J Pain 2017; 15:38-43.
6) Hattori S, Takeshima N, Kimura N, Yamamoto H, Mizutani A & Noguchi T. The clinical perspective on chronic pain management in Japan. Pain Clinic 2004; 25:1541-1551, 2004.
7) Matsudaira K, Takeshita K, Kunogi J, Yamazaki T, Hara N, Yamada K & Takagi Y. Prevalence and characteristics of chronic pain in the general Japanese population. Pain Clinic 2011; 32:1345-1356.
8) Hsu JE, Anakwenze OA, Warrender WJ, Abboud JA. Current review of adhesive capsulitis. J Shoulder Elbow Surg 2011; 20:502-514.
9) Bijlsma JW, Berenbaum F, Lafeber FP. Osteoarthritis: an update with relevance for clinical practice. Lancet 2011; 377:2115-2126.
10) Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. Ann Rheum Dis 2001; 60:91-97.
11) Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis 2014; 73:1323-1330.
12) Abate M, Silbernagel KG, Siljeholm C, et al. Pathogenesis of tendino- pathies: inflammation or degeneration? Arthritis Res Ther 2009; 11:235.
13) Lian OB, Engebretsen L, Bahr R. Prevalence of jumper's knee among elite athletes from different sports: a cross-sectional study. Am J Sports Med 2005; 33:561-567.
14) Hyman GS. Jumper's knee in volleyball athletes: advancements in diagnosis and treatment. Curr Sports Med Rep 2008; 7:296-302.
15) van der Windt DA, Koes BW, Boeke AJ, et al. Shoulder disorders in general

practice: prognostic indicators of outcome. Br J Gen Pract 1996; 46: 519-523.
16) Shaffer B, Tibone JE, Kerlan RK. Frozen shoulder. A long-term follow-up. J Bone Joint Surg Am 1992; 74:738-746.
17) Andres BM, Murrell GA. Treatment of tendinopathy: what works, what does not, and what is on the horizon. Clin Orthop Relat Res 2008; 466:1539-1554.
18) Skjong CC, Meininger AK, Ho SS. Tendinopathy treatment: where is the evidence? Clin Sports Med 2012; 31:329-350.
19) Rees JD, Maffulli N, Cook J. Management of tendinopathy. Am J Sports Med 2009; 37:1855-1867.
20) Radwan YA, ElSobhi G, Badawy WS, Reda A, Khalid S. Resistant tennis elbow: shock-wave therapy versus percutaneous tenotomy. Int Orthop 2008; 32:671-677.
21) Marcheggiani Muccioli GM, Zaffagnini S, Tsapralis K, et al. Open versus arthroscopic surgical treatment of chronic proximal patellar tendinopathy. A systematic review. Knee Surg Sports Traumatol Arthrosc 2013; 21:351-357.
22) Ashraf S, Mapp PI, Walsh DA. Contributions of angiogenesis to inflammation, joint damage, and pain in a rat model of osteoarthritis. Arthritis Rheum 2011; 63:2700-2710.
23) Pap T, Distler O. Linking angiogenesis to bone destruction in arthritis. Arthritis Rheum 2005; 52:1346-1348.
24) 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.
25) Ashraf S, Wibberley H, Mapp PI, et al. Increased vascular penetration and nerve growth in the meniscus: a potential source of pain in isteoarthritis. Ann Rheum Dis 2011; 70:523-529.
26) 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.
27) 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; 23:199-206.
28) Okuno Y, Korchi AM, Shinjo T, Kato S. Transcatheter arterial embolization as a treatment for medial knee pain in patients with mild to moderate osteoarthritis. Cardiovasc Intervent Radiol 2015; 38:336-343.
29) Okuno Y, Iwamoto W, Matsumura N, Oguro S, Yasumoto T, Kaneko T, Ikegami H. Clinical Outcomes of Transcatheter Arterial Embolization for Adhesive Capsulitis Resistant to Conservative Treatment. J Vasc Interv Radiol 2017; 28:161-167.
30) 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.

31) Woodhams R. et al. Presented at the 10th Asia-Pacific Congress of Cardiovascular and Interventional Radiology; May 30, 2012; Kobe, Japan.
32) Aihara TA. Kawasaki Igakkaishi 1999; 25:47-54.
33) Geibprasert S, Pongpech S, Armstrong D, Krings T. Dangerous extracranial-intracranial anastomoses and supply to the cranial nerves: vessels the neurointerventionalist needs to know. AJNR Am J Neuroradiol 2009; 30:1459-68.
34) Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthritis. Ann Rheum Dis 1957; 16:494-502.
35) Bagla S, Piechowiak R, Hartman T, et al. Geniculate artery embolization (GAE) for osteoarthritis (OA)-related knee pain: results from a multicenter US trial. Presented at the Society of Interventional Radiology (SIR) 2018, March 17-22 Los Angeles, Calif. USA.
36) Yasumoto T, Uemoto K, Yamada K, et al. Impact of contrast-enhanced magnetic resonance imaging on clinical outcomes of transcatheter arterial embolization for chronic musculoskeletal pain. Presented at the Society of Interventional Radiology (SIR) 2018, March 17-22 Los Angeles, Calif. USA. J Vasc Interv Radiology 2018; 29: S89.