A Rat Model of Frozen Shoulder Demonstrating the Effect of Transcatheter Arterial Embolization on Angiography, Histopathology, and Physical Activity

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ABSTRACT

Purpose: To assess the angiographic findings and the effects of transcatheter arterial embolization on physical activity and histopathology using a frozen shoulder rat model.

Materials and Methods: First, the angiographic and histopathologic findings of rats in which the shoulder was immobilized with molding plaster for 6 weeks (n = 4) were compared to control rats with normal non-immobilized shoulders (n = 4). Next, a total of 16 frozen shoulder rats were divided into 2 groups. In the transcatheter arterial embolization group (n = 8), imipenem/cilastatin was injected into the left thoracoacromial artery. The changes of physical activity before and after procedures were evaluated and compared with a saline-injected control group (n = 8). Histopathologic findings were also compared between the 2 groups.

Results: Angiography revealed abnormal shoulder staining in all of the rats with a frozen shoulder. On histopathology, the numbers of microvessels and mononuclear inflammatory cells in the synovial membrane of the joint capsule were significantly higher compared with the control rats (both $P = .03$). In the transcatheter arterial embolization group, the running distance and speed were improved ($P = .03$ and $P = .01$, respectively), whereas there were no significant differences in the control group. The number of microvessels and mononuclear inflammatory cells in the transcatheter arterial embolization group were significantly lower than the control group ($P = .002$ and $P = .001$, respectively).

Conclusions: The rat frozen shoulder model revealed the development of neovascularization. Transcatheter arterial embolization decreased the number of blood vessels and inflammatory changes in the frozen shoulder and increased the moving distance and speed of the rats.

ABBREVIATIONS

IPM/CS = imipenem/cilastatin, MIC = mononuclear inflammatory cells, MV = microvessels

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Frozen shoulder, also referred to as adhesive capsulitis, is a relatively common disorder that affects approximately 2%–5% of the general population (1,2). The associated pain and limited range of joint motion are significant hindrances to the activities of daily living. The majority of patients with frozen shoulder typically experience symptom relief within several months after receiving nonsurgical treatments, such as physical therapy and medication (1,3,4). However, in some cases, the symptoms can persist for over a year before resolving, and frozen shoulder frequently leads to long-term disability (3–5). Surgery is performed in patients who are resistant to the conservative treatment, however this route is highly invasive and might not be an option in all cases (2).

Patients with chronic pain of the shoulder, including frozen shoulder, show abnormal blood vessels in the joint capsule and rotator interval that are not observed in healthy shoulders (6). Okuno et al (7) reported that transcatheter arterial embolization with imipenem/cilastatin (IPM/CS) in patients with adhesive capsulitis resistant to conservative treatments reduced pain and improved the range of motion.

Despite transcatheter arterial embolization with IPM/CS being increasingly used as an effective treatment, the mechanisms underlying its therapeutic effects have not been elucidated (8). Thus, basic research on transcatheter arterial embolization for frozen shoulder using animal models is needed. Although Kim et al and others (9,10) described how to create a rat model of frozen shoulder, there was no description about the angiographic findings. The purpose of this study, therefore, was to assess the angiographic findings using a rat model of frozen shoulder and to investigate the effects of transcatheter arterial embolization on physical activity and histopathology in frozen shoulder rats.

MATERIALS AND METHODS

This laboratory investigation was performed under the observation of an experimental protocol approved by our Institutional Animal Care and Use Committee. Seven-week-old male Sprague-Dawley rats (CLEA Japan, Inc., Tokyo, Japan) with a median weight of 335 g (range, 275–346 g) were used. All procedures were conducted while the rats were anesthetized with isoflurane. The study outline is shown in **Figure 1**.

Experiment 1: Creating a Rat Model of Frozen Shoulder and the Evaluation of Angiographic and Histopathologic Findings

To generate a rat model of frozen shoulder, 8 rats were divided into 2 groups: an experimental group (median weight 344 g; range, 270–357 g) in which the left shoulder was immobilized with molding plaster (n = 4), and a control group without any interventions (median weight 335 g; range, 269–342 g) (n = 4).

According to the methods reported by Kim et al (9), immobilization was accomplished by applying 5-cm-wide molding plaster (Nippon Sigmax Co., Ltd., Tokyo, Japan) around the entire left arm, including the shoulder and thorax. All rats were able to walk, self-feed, and survive for 6 weeks. After 6 weeks, the plaster was removed in the experimental group, and angiography was performed in both the groups (**Fig 2**).

Under general anesthesia, the femoral artery was surgically exposed and punctured with a 20-gauge indwelling needle (Angiocath; Becton Dickinson, Franklin Lakes, New Jersey), using a dissecting microscope. Custom-made 1.5-F, 40-cm-long microcatheters were advanced into the left thoracoacromial arteries over a 0.014-inch guidewire (Transend; Boston Scientific, Marlborough, Massachusetts) under fluoroscopic guidance. Digital subtraction angiography was performed using iodixanol (Visipaque; GE Healthcare, Chicago, Illinois) injected by hand.

After performing digital subtraction angiography, the rats were euthanized, and the left shoulder joint was harvested for histopathologic examination. The specimens were fixed in formalin and decalcified with 10% ethylenediaminetetraacetic acid. Horizontal cuts were made across the bone marrow of the humeral head and scapula, and 2 samples were obtained with a 300-μm interval. Standardized 3-μm-thick sections were created and stained with hematoxylin and eosin. The number of microvessels (MV) and mononuclear inflammatory cells (MIC) per 1 mm^2 field in the synovial membrane of the joint capsule was determined by manual count with a high magnification microscope and compared between the 2 groups. The angiographic findings were assessed in a double-blind manner by 3 interventional radiologists (T.T., H.N., and H.T. with 24, 18, and 8 years of experience, respectively), and the histopathologic findings were assessed in a double-blind manner by 3 pathologists (C.O., K.H. and M.T. with 38, 30, and 19 years of experience, respectively).

Experiment 2: Assessing the Effects of Transcatheter Arterial Embolization on Physical Activity and Histopathology

Eight rats were assigned to each of the transcatheter arterial embolization group (median weight 330 g; range, 275–352 g) and control group (median weight 336.5 g; range, 285–346 g). In all 16 rats, the left shoulder was immobilized for 6 weeks in a plaster cast as described above.

After the immobilizing cast was removed, the behavior of each rat (without any inducements for the rats to move) was observed in an open field of 4 × 4 squares, each 60 × 60 cm in size, that were made of gray polyvinyl chloride. The behavior was captured for each rat on video recorded directly above using a floor illumination of 7 lux for 1200 seconds. The moving distance and the speed of the rats was analyzed using Top Scan software (Primetech Corporation, Tokyo. Japan). The sections of video with noise were omitted, and the parts during which data were recorded were

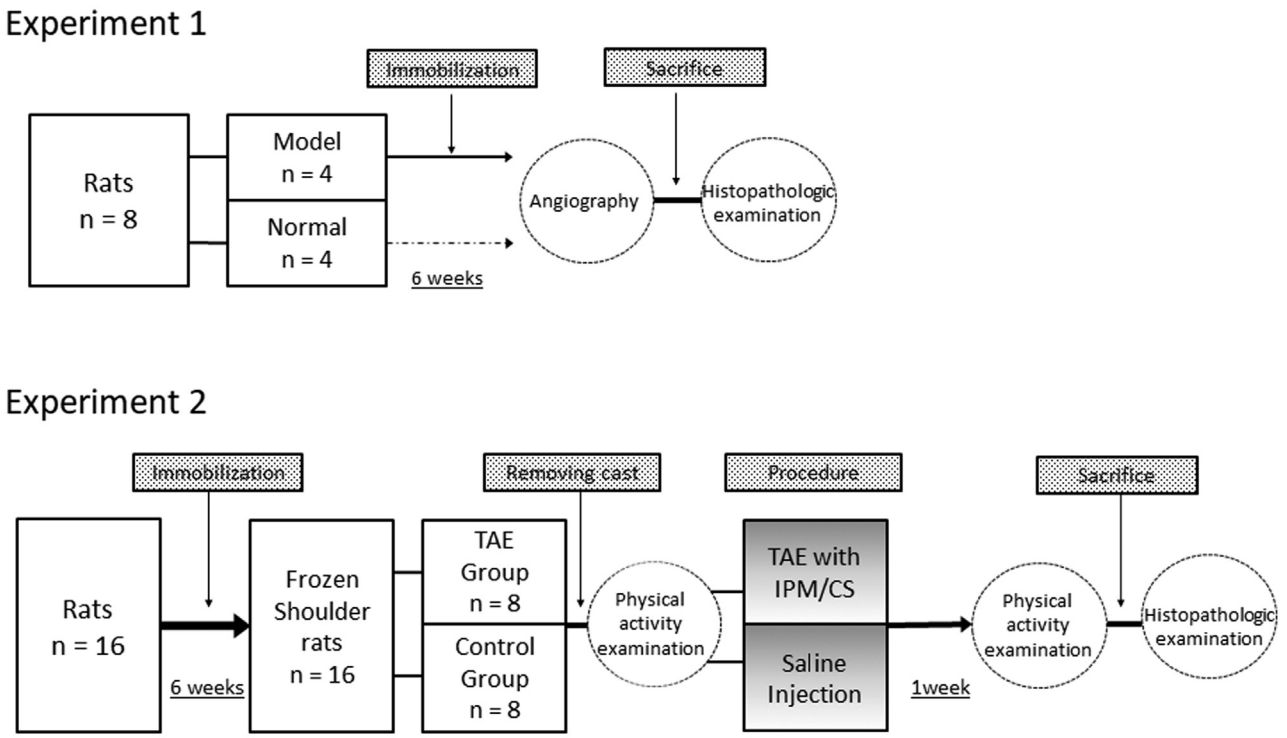

Figure 1. The study outline shows the schedule of experiment 1 and 2.

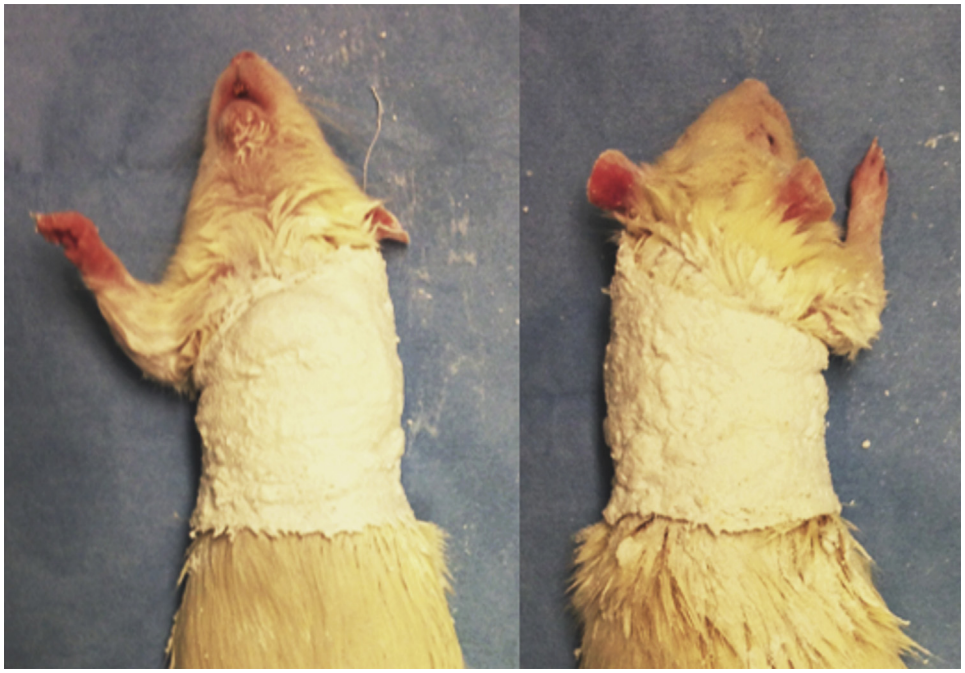

Figure 2. Photograph of an immobilized rat. Immobilization was accomplished by applying 5-cm-wide molding plaster (Nippon Sigmax Co., Ltd., Tokyo, Japan) around the entire left arm, including the shoulder and thorax.

defined as the effective imaging time (in seconds). The mean speed of movement was calculated by dividing the distance of movement (in mm) by the effective imaging time (in seconds).

For all 16 rats, angiography via the left thoracoacromial artery was performed using the same technique as per experiment 1 above. The transcatheter arterial embolization group then underwent embolization of the shoulder joint. A total of 500 mg of IPM/CS was dissolved in 5 mL of contrast agent, then 1 mL of this solution was mixed with 9 mL of contrast agent for a final volume of 10 mL. This solution was drawn into a 1.0-mL syringe and 0.1 mL (1 mg of IPM/CS)

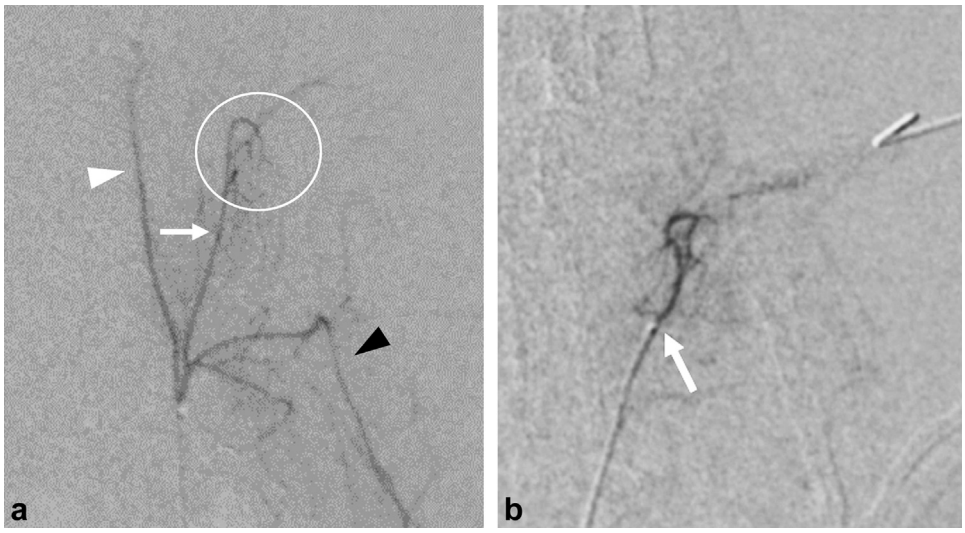

Figure 3. Normal angiographic anatomy of the left subclavian artery (anteroposterior view). (**a**) Digital subtraction angiography of the rat left subclavian artery: thoracoacromial artery (white arrow), vertebral artery (white arrowhead), brachial artery (black arrowhead), and shoulder joint (circle). (**b**) Angiography of the left thoracoacromial artery (arrow) shows no abnormal staining.

was administered via the thoracoacromial artery. The control group received 0.1-mL saline. After administration of IPM/CS or saline, the right femoral artery was ligated to achieve hemostasis, and the wound was closed.

After 1 week, another motion analysis video of all rats was captured under identical conditions without any inducements for the rats to move. The moving distance and the mean speed of rats were compared before and after procedures in the 2 groups. The analysis of physical activity was automatically evaluated using Top Scan software. For the histologic analysis, the specimens with hematoxylin and eosin staining and immunohistochemical staining using anti-CD34 antibody (EP373Y; Abcam, Cambridge, Massachusetts) (diluted at 1:1,000) were created in the same manner as above, and the number of MV and MIC per 1 mm^2 field in the synovial membrane of the joint capsule was compared between the transcatheter arterial embolization and control groups. Immunohistochemical staining using anti-CD34 antibody was also used for MV counting. As indicated above, histopathologic examinations were assessed in a double-blind manner by 3 pathologists with 38, 30, and 19 years of experience.

Statistical Analysis

Statistical analyses were conducted using EZR software for Windows (Saitama Medical Center, Jichi Medical University, Saitama, Japan). The Mann-Whitney U test was used for between-group comparisons. Values were presented as median (interquartile range). Statistical significance was set at a P value no more than .05.

RESULTS

Evaluation of a Rat Model of Frozen Shoulder

Angiography of the left shoulder joint revealed abnormal staining in 4 of 4 rats (100%) in the experimental group, while all rats in the control group appeared normal (Figs 3a, b, 4a, b). Histopathologic examinations revealed decrease in the synovial fold and the subsynovial fat tissue, infiltration of inflammatory cells, proliferation of the synovial lining cells, and fibrosis of the joint capsule (Fig 5a, b). The median number of MV in the experimental group was 46.0 (range, 38.8–50.0), which was significantly different ($P = .03$) from the median value of 7.0 (range, 6.5–9.0) in the control group. The number of MIC was also significantly different between the groups ($P = .03$), with the experimental group having a median of 95.5 (range, 87.0–101.3) and the control group having a median of 3.0 (range, 0.8–5.0) (Table 1).

Transcatheter arterial embolization or saline injection procedures were successful in all cases. Angiography before the procedure revealed abnormal staining in all rats, which disappeared immediately after transcatheter arterial embolization.

Changes in Physical Activity after Transcatheter Arterial Embolization

There were no significant differences in the effective imaging time, moving distance, or speed in either group before treatment. After treatment, the control group had an effective imaging time of 1,132.0 seconds (range, 1,089.5–1,193.3 seconds) as compared to 1,196.5 seconds (range, 1,161.5–1,200.0 seconds) in the transcatheter arterial embolization group. This was not a significant difference.

There were no significant differences in the moving distance or speed in the control group before versus after treatment. The moving distance changed from 16,495.5 mm (range, 14,476.3–17,614.8 mm) before treatment to 17,111.0 mm (range, 12,029.3–19,613.0 mm) after treatment ($P = .96$), whereas the median moving speed was 13.8 mm/s (range, 12.5–14.7 mm/s) before treatment and 15.2

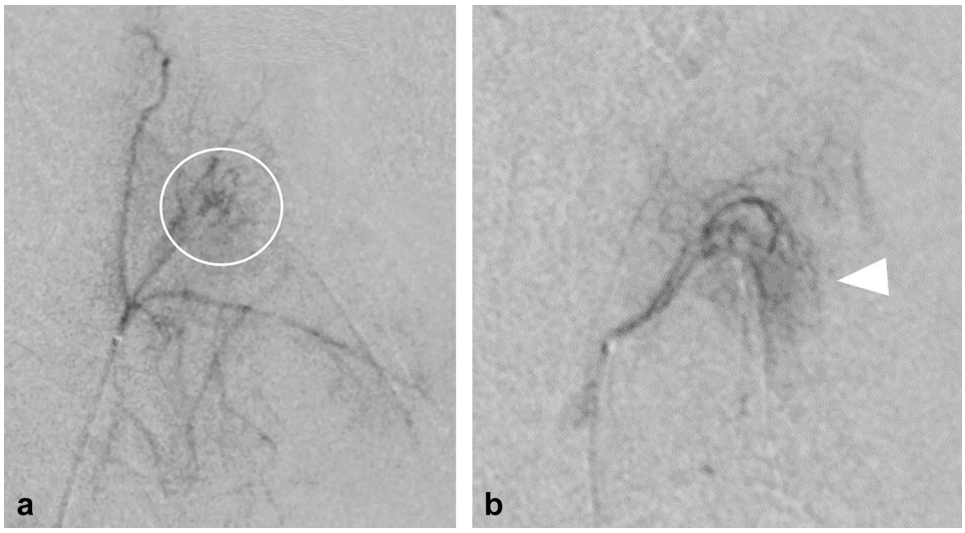

Figure 4. Angiography of a frozen shoulder rat (anteroposterior view). (**a**) Digital subtraction angiography of the left subclavian artery in a frozen shoulder rat shows abnormal staining in the shoulder region (circle). (**b**) Angiography of the left thoracoacromial artery shows abnormal staining in the shoulder region (white arrowhead).

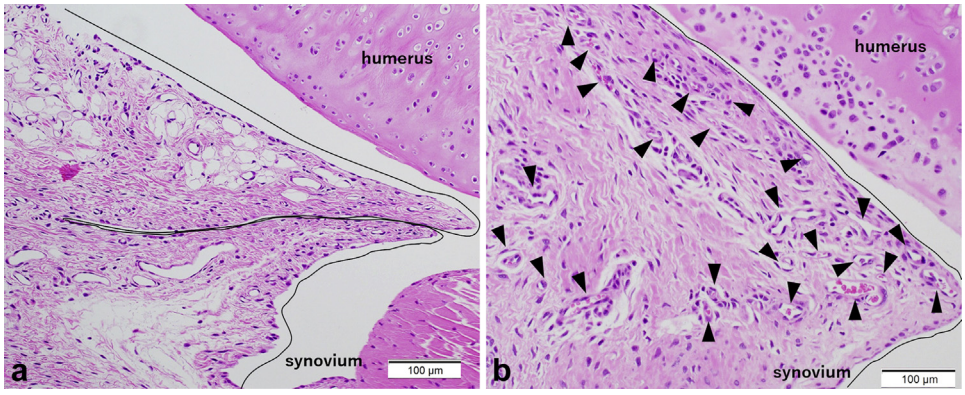

Figure 5. Histopathologic examination in experiment 1. (**a**) Histologic findings of normal rat: The histopathologic examination of normal rat revealed low microvessel density and no inflammation (hematoxylin and eosin, ×200). (**b**) Histologic findings of experimental group: The histopathologic examination revealed the proliferation of microvessels (black arrowhead) and mononuclear inflammatory cells with fibrosis in the subsynovial tissue in the experimental group (hematoxylin and eosin, ×200).

Table 1. Number of Microvessels and Mononuclear Inflammatory Cells in the Synovial Membrane of the Joint Capsule

Experiment 1	Control group n = 4	Frozen shoulder model group n = 4	*P* value
MV	7.0 (6.5–9.0)	46.0 (38.8–50.0)	.03
MIC	3.0 (0.8–5.0)	95.5 (87.0–101.3)	.03

Note–Values are presented as median (interquartile range).
MV = microvessels; MIC = mononuclear inflammatory cells.

mm/s (range, 10.1–19.2 mm/s) after treatment ($P = .65$) (Fig 6a). In contrast, the moving distances and speed of the transcatheter arterial embolization group were significantly improved after treatment. The moving distance increased from 1 to 7,069.5 mm (range, 12,601.8–20,488.5 mm) before treatment to 26,216.5 mm (range, 21,071.5–29,767.3 mm) after treatment ($P = .03$), whereas the median moving speed was 14.3 mm/s (range, 10.5–17.1 mm/s) before treatment and 22.8 mm/s (range, 18.1–25.0 mm/s) after treatment ($P = .01$) (Fig 6b).

Comparison of Histopathologic Findings

In the transcatheter arterial embolization group, several IPM/CS particles were observed inside the arteries within the subsynovial fat tissue. The number of MV was 19.5 (range, 15.8–23.5) in the transcatheter arterial embolization group, which was significantly lower than that of the control group (52.0 [range, 42.0–56.0], $P = .002$). The number of MIC was also significantly lower in the transcatheter arterial embolization group at 18.5 (range, 16.6–19.4) compared to 69.1 (range, 65.1–76.9) in the control group ($P = .001$)

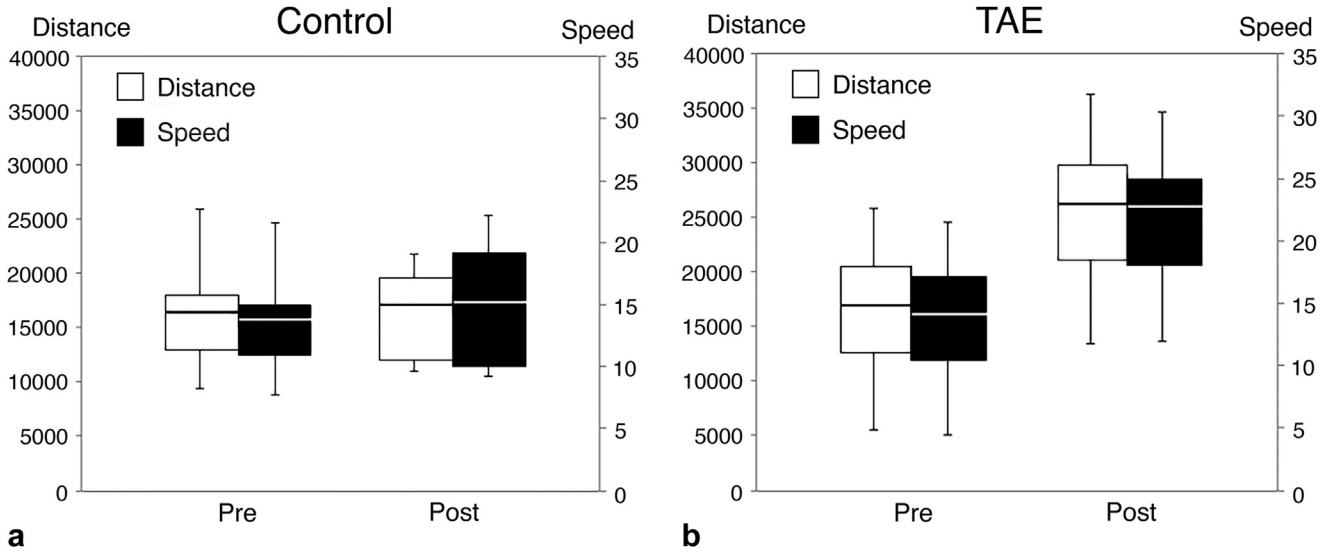

Figure 6. Changes in the physical activity between pre and post procedures. (**a**) No significant changes were observed in the running distance and speed in the control group. (**b**) Significant improvements were observed in the running distance ($P = .03$) and speed ($P = .01$) in the transcatheter arterial embolization group.

Table 2. Number of Microvessels and Mononuclear Inflammatory Cells in the Synovial Membrane of the Joint Capsule 1 Week after the Procedures

Experiment 2	Control group n = 8	Transcatheter arterial embolization group n = 8	*P* value
MV	52.0 (42.0–56.0)	19.5 (15.8–23.5)	.002
MIC	69.1 (65.1–76.9)	18.5 (16.6–19.4)	.001

Note–Values are presented as median (interquartile range).
MV = microvessels; MIC = mononuclear inflammatory cells.

(Table 2). Both groups displayed the evidence of chronic frozen shoulder, with decrease in the synovial fold and subsynovial fat tissue, proliferation of the synovial lining cells, and fibrosis of the joint capsules (Fig 7a–c).

DISCUSSION

Several researchers (9–11) have reported animal models of frozen shoulder using immobilization. Kim et al (9) described a rat model of frozen shoulder using immobilization to simulate a pathophysiologic process of inflammation leading to the fibrosis of the glenohumeral joint. The method of Kim et al (9) was chosen in this study because it seemed much easier to employ and appeared to be more successful than others reported methods. Cho et al (10) also successfully experimented with frozen shoulders using the method of Kim et al (9). Moreover, Kim et al (9) demonstrated that the frozen shoulder begins to manifest after approximately 3 weeks and chronic changes are completed at approximately 6 weeks. Therefore, the shoulder joints of rats were immobilized for a period of 6 weeks in the present study. Histopathologic analyses revealed that fibrotic changes occurred in all cases without failure, similar to the report of Kim et al (9).

In the present study, angiography of frozen shoulders showed abnormal staining. Okuno et al (7) reported that angiography of human shoulder joints with adhesive capsulitis show an increased amount of abnormal neovessels. Angiographic findings in this study were similar to that of human shoulder joints with adhesive capsulitis. This suggests that the model is useful for evaluating frozen shoulder angiographically.

The relationship between neovascularization and pain remains unclear. Okuno et al (7,12,13) speculated that an increase in the number of small blood vessels and nerve fibers could cause pain, and they performed transcatheter arterial embolization under the hypothesis that embolizing newly developed vessels would cause nerve fibers to withdraw and thereby alleviate pain. In the present study, histopathologic analyses revealed that the number of new blood vessels decreased after transcatheter arterial embolization. In addition, the decreased number of MIC could demonstrate that transcatheter arterial embolization also improved the inflammatory reaction in the frozen shoulder. Although changes in the nerve fibers and neurotransmitters were not assessed in the present study, it would be informative to elucidate the mechanism by which transcatheter arterial embolization relieves the pain.

Evaluating the changes in the pain visual analog scale and the range of motion is often used clinically to assess the effectiveness of therapeutic treatments for frozen shoulder (7). In a previously reported rat model of frozen shoulder, the range of motion was also used to assess the therapeutic effects (11,14). It is, however, inherently difficult to consistently apply a defined external force to the small shoulder joint of an individual rat and accurately measure the resulting angle. Therefore, an open field test was used in

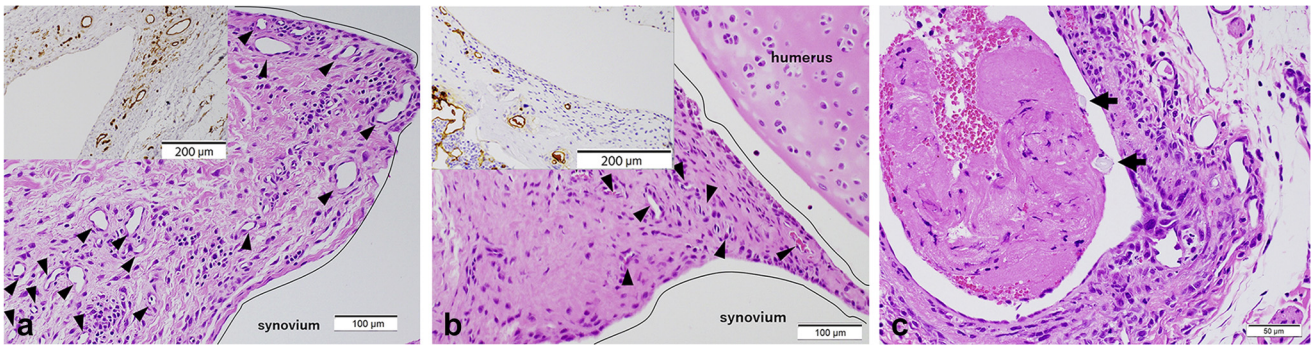

Figure 7. Histopathologic examination in experiment 2. (**a**) Histologic findings of control group: In the control group, the proliferation of microvessels (black arrowhead) and mononuclear inflammatory cells with fibrosis in the subsynovial tissue was almost the same as in the experimental group in experiment 1 (hematoxylin and eosin, ×200). In-slide shows CD34+ vascular endothelial cells (immunohistochemical staining for CD34, ×200). (**b**) Histologic findings of transcatheter arterial embolization group: Microvessels (black arrowhead) and mononuclear inflammatory cells were significantly deceased in the transcatheter arterial embolization group compared with the control group (hematoxylin and eosin, ×200). In-slide shows CD34+ vascular endothelial cells (immunohistochemical staining for CD34, ×200). (**c**) Histologic findings of foreign materials: A thrombus and 10–15 μm foreign materials (IPM/CS particles) (black arrow) were found in the small artery in the fat tissue near the joint (hematoxylin and eosin, ×400).

the present study, with the expectation of obtaining more objective data. An open field test is a method of assessing animal behavior in a space without barriers, as in a maze, and has been widely used in previous studies assessing pharmacological effects or surgeries for spinal injury (15,16). This study demonstrated that the physical activity of rats in the transcatheter arterial embolization group was significantly higher after treatment as compared to the control group. Thus, transcatheter arterial embolization could alleviate pain and allowed a better range of motion in the shoulder.

To date, the optimal embolic material to use in transcatheter arterial embolization for frozen shoulder remains unclear. Okuno et al (7) performed transcatheter arterial embolization with IPM/CS in 24 patients with adhesive capsulitis resistant to conservative treatments. They found that 16 (67%) patients experienced rapid improvement of nighttime pain within 1 week and 21 (87%) patients improved within 1 month. In addition, they used IPM/CS to treat other chronic pain (12,13), and other authors (8,17) used IPM/CS for transcatheter arterial embolization to treat chronic pain. IPM/CS is a slightly soluble powder detergent with a particle diameter of 10–70 μm. Due to its low solubility, it retains the crystalline structure, without dissolving for a certain length of time (18). This property has resulted in its use, for example, as a hemostatic agent in the treatment of oozing blood (19). The transient effect and the particle size of IPM/CS is considered sufficient to embolize and reduce the number of new blood vessels found in tissues with chronic inflammation (7,12,13). The short duration of embolization makes IPM/CS less likely to cause ischemic complications, even if the particles end up in vessels supplying healthy tissue (7,19). However, there is still no accurate data on the time it takes for the particles to dissolve. In the present study, several foreign matter particles, approximately 10 μm in size, in addition to thrombi were found in the transcatheter arterial embolization group, and these were considered to be IPM/CS particles. This may suggest that IPM/CS remains even 1 week after transcatheter arterial embolization.

Transcatheter arterial embolization improved the physical activities and decreased the numbers of MV and MIC. However, there were no changes in the chronic histopathologic findings of fibrosis in the joint capsule. These results suggest that although transcatheter arterial embolization may alleviate pain by decreasing both the number of abnormal vessels and the inflammatory response, it might not directly treat frozen shoulder.

This study had several limitations. First, a rat model was employed, which differs in various respects from humans. The blood vessels, in particular, are considerably different in size. Therefore, the catheter diameter and the size of the embolic materials must be adjusted. Second, transcatheter arterial embolization was assessed after only 1 week of treatment. Longer-term results, therefore, remain unclear. Third, the present study did not prove any causal relationship between decrease in the number of MV/MIC and the alleviation of pain. This is a topic for further study.

In conclusion, the rat model of frozen shoulder used in the present study was able to replicate the growth of new blood vessels observed in patients, as confirmed by angiography and histopathology. Rats that underwent treatment with transcatheter arterial embolization exhibited a decrease in new blood vessels and inflammation after treatment and an increase in the moving distances and speed as compared to untreated rats.

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REFERENCES

1. Hsu JE, Anakwenze OA, Warrender WJ, Abboud JA. Current review of adhesive capsulitis. J Shoulder Elbow Surg 2011; 20:502–514.
2. Robinson CM, Seah KT, Chee YH, Hindle P, Murray IR. Frozen shoulder. J Bone Joint Surg Br 2012; 94:1–9.
3. Vastamäki H, Kettunen J, Vastamäki M. The natural history of idiopathic frozen shoulder: a 2- to 27-year followup study. Clin Orthop Relat Res 2012; 470:1133–1143.
4. Levine WN, Kashyap CP, Bak SF, Ahmad CS, Blaine TA, Bigliani LU. Nonoperative management of idiopathic adhesive capsulitis. J Shoulder Elbow Surg 2007; 16:569–573.
5. Shaffer B, Tibone JE, Kerlan RK. Frozen shoulder. A long-term follow-up. J Bone Joint Surg Am 1992; 74:738–746.
6. Xu Y, Bonar F, Murrell GA. Enhanced expression of neuronal proteins in idiopathic frozen shoulder. J Shoulder Elbow Surg 2012; 21:1391–1397.
7. 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 2017; 28:161–167.
8. 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.
9. Kim DH, Lee KH, Lho YM, et al. Characterization of a frozen shoulder model using immobilization in rats. J Orthop Surg Res 2016; 11:160.
10. Cho CH, Lho YM, Hwang I, Kim DH. Role of matrix metalloproteinases 2 and 9 in the development of frozen shoulder: human data and experimental analysis in a rat contracture model. J Shoulder Elbow Surg 2019; 28:1265–1272.
11. Okajima SM, Cubria MB, Mortensen SJ, et al. Rat model of adhesive capsulitis of the shoulder. J Vis Exp 2018; 28:58335.
12. Okuno Y, Oguro S, Iwamoto W, Miyamoto T, Ikegami H, Matsumura N. 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.
13. Okuno Y, Korchi AM, Shinjo T, Kato S, Kaneko T. 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.
14. Ochiai N, Ohtori S, Kenmoku T, et al. Sensory innervation of rat contracture shoulder model. J Shoulder Elbow Surg 2013; 22:158–164.
15. Chen J-X, Li W, Zhao X, Yang J-X. Effects of the Chinese traditional prescription Xiaoyaosan decoction on chronic immobilization stress-induced changes in behavior and brain BDNF, TrkB, and NT-3 in rats. Cell Mol Neurobiol 2008; 28:745–755.
16. Martinez M, Brezun J-M, Bonnier L, Xerri C. A new rating scale for open-field evaluation of behavioral recovery after cervical spinal cord injury in rats. J Neurotrauma 2009; 26:1043–1053.
17. 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.
18. Aihara T. Establishment of an animal model for super-selective transcatheter arterial chemotherapy and preparation for appropriate suspension of microembolization. Kawasaki Igakkaishi 1999; 25:47–54.
19. Woodhams R, Nishimaki H, Ogasawara G, et al. Imipenem/cilastatin sodium (IPM/CS) as an embolic agent for transcatheter arterial embolisation: a preliminary clinical study of gastrointestinal bleeding from neoplasms. Springerplus 2013; 2:344.