ORIGINAL ARTICLE

Nr 2025;15 (2):182-188

Rat Model of Knee Flexion Contracture: Progression of Joint Motion Restriction without Subsequent Changes in Joint Capsule Stiffness

Masahiro Sugahara[1], Yuta Sato[2], Ryoma Ikeo[1], Senma Nagi[1], Takeya Ono[1,2]

[1] *Program in Biological System Sciences, Graduate School of Comprehensive Scientific Research, Prefectural University of Hiroshima, Mihara, Japan*

[2] *Department of Physical Therapy, Faculty of Health and Welfare, Prefectural University of Hiroshima, Mihara, Japan*

CORRESPONDING AUTHOR:
Takeya Ono
Prefectural University of Hiroshima
1-1 Gakuen-machi, Mihara-shi
Hiroshima 723-0053, Japan
E-mail: ono@pu-hiroshima.ac.jp

DOI:
10.32098/mltj.02.2025.08

LEVEL OF EVIDENCE: N/A (Animal study)

SUMMARY

Background. Joint contractures are classified as myogenic or arthrogenic. Capsular ligaments are partially thickened areas of the joint capsule, which are impossible to separate from the joint capsule. The joint capsule is an important factor limiting the range of knee extension; however, its stiffness has not been investigated. This study aimed to investigate changes in joint capsule stiffness over time after the onset of knee flexion contracture.

Methods. Twenty-four 8-week-old male Wistar rats were used. The groups were classified as follows: 0-week (without joint fixation), 2-week fixation, 4-week fixation, and 8-week fixation groups. First, the knee extension range of motion was measured before and after skeletal muscle removal. Next, femur-tibia joint capsule complex samples underwent tensile testing to obtain information on the waveform and stiffness of the length-tension curve of the knee joint capsule. The stiffness was the slope of the waveform calculated from the elongation distance and resistance to elongation.

Results. Despite a significant decrease in the knee extension range of motion after skeletal muscle removal due to the extension of the joint immobilization period, the stiffness of the joint capsule did not change. The length-tension curve for the 0-week group had a sawtooth waveform that repeatedly rose and dropped steeply, which was not observed in the 2-, 4-, and 8-week groups.

Conclusions. The stiffness of the joint capsule did not change during knee flexion contractures.

KEY WORDS

Joint fixation; joint contracture; joint capsule; tensile test; stiffness.

INTRODUCTION

Knee flexion contracture is a clinically significant complication that can occur after trauma, knee surgery, or osteoarthritis of the knee (1-6). When knee flexion contracture occurs, the leg lengths become uneven, and the standing balance worsens (7). In addition, climbing stairs or walking long distances becomes difficult, which significantly impacts social participation and mobility (8). Therefore, effective intervention methods for knee flexion contracture are important.

Myogenic factors, including muscle, tendon, and fascia, and arthrogenic factors, including bone, cartilage, synovial membrane, capsule, and ligaments, have been analyzed in animal experiments using rats (9, 10). Trudel *et al.* reported that arthrogenic contractures are more important than myogenic contractures in causing knee extension restriction after 2 weeks of knee flexion fixation (10). In addition, it is difficult to improve arthrogenic contractures in response to treatment (11-13). Therefore, research on treatment methods for arthrogenic contractures is important (12). Among the arthrogenic factors, the joint capsule causes knee extension restriction. Joint capsule resection improves knee flexion contracture (14, 15). Regarding the morphological changes in the joint capsule observed during knee flexion contracture in rats, Kanaguchi *et al.* (9) reported capsu-

lar thickening, and Trudel *et al*. (16, 17) reported capsular adhesion and shortening. These morphological changes may limit the knee extension range of motion (9, 10). However, no reports have solely evaluated the change in stiffness of the joint capsule during knee flexion contracture.

In this study, we hypothesized that joint capsule stiffness increases when knee flexion contractures occur. Understanding the changes in the stiffness of the joint capsule involved in joint contracture can be useful when considering a treatment plan. This study aimed to clarify changes in joint capsule stiffness after knee flexion fixation.

METHODS

Animals and experimental groups

Twenty-four male Wistar rats (290-350 g) were used in this study. The rats were housed in plastic cages in a temperature-controlled room (23 °C) and allowed to move freely and eat food. The rats were divided into four groups: the 0-week group (n = 6), in which the joints were not immobilized; the 2-week group (n = 6), in which the joints were immobilized for 2 weeks; the 4-week group (n = 6), in which the joints were immobilized for 4 weeks; and the 8-week group (n = 6), in which the joints were immobilized for 8 weeks. The left knee joint was used for tensile testing, and the right knee joint was used for the range of joint motion measurements. For all rats, experiments were conducted after confirming that the anesthesia was sufficiently effective and taking care not to cause pain. This experiment was performed according to the Regulations on Animal Experiments of the Prefectural University of Hiroshima and approved by the University's Animal Experiments Committee (approval number: 21A-004-1 – date of approval: July 30, 2021).

Joint fixation

In accordance with a previous study (18), the knee joints of the 2-, 4- and 8-week groups were fixed in an external fixator at 150° flexion. No fixation was performed in the 0-week group. First, holes were drilled into the proximal femur and distal tibia, and a 1.0 mm diameter Kirschner wire was inserted. Next, a wire was placed between the Kirschner wires inserted into the femur and tibia, and a dental treatment resin (UNIFAST III; GC Corporation, Tokyo, Japan) was pressed into place.

Measurement of joint angles

The joint range of motion was measured based on modifications of a previous study (19). Rats were measured in left lateral recumbency with the spine in mid-spine and the hip joint at 90° flexion. A goniometer was used for measurements. The basic axis was the line connecting the greater trochanter of the femur and the lateral femoral condyle, and the moving axis was the line connecting the fibular head and lateral malleolus. The joint angle was 180°, and the femur and tibia were aligned with the knee joint in extension. A load cell (LTS-1KA; Kyowa Dengyo, Japan) was used to equalize the force applied during knee extension. The 1 N force applied during knee extension was applied at the posterior aspect of the lower thigh 3.5 cm below the fibular head (19). In the 0-week group, the joint range of motion was measured on the first day of the experiment without joint fixation, whereas in the 2-, 4-, and 8-week groups, the joint range of motion was measured after the removal of joint fixation. All groups were euthanized, and the joint range of motion was measured after skeletal muscle removal. The measurements were repeated thrice to confirm the intra-examiner reliability of the range of motion measurements. The percentages of myogenic and arthrogenic contractures were calculated according to methods used in previous studies (10).

Tensile test

First, the sample was prepared for tensile testing (**figure 1A**). After the left hind leg was amputated, and all skin and skeletal muscles around the knee joint were removed, the patellar, anterior and posterior cruciate, and medial and lateral collateral ligaments were cut from the ventral side to prepare a sample with a femur-tibia joint capsule complex. Next, a 1.0 mm diameter hole was drilled into the femoral condyle and tibia 10 mm distal to the joint space. A steel wire was inserted into the two holes and attached to the upper and lower sides of the tensile testing machine. The joint capsule was defined as dorsal to the medial and lateral collateral ligaments. Tensile tests were performed using an autograph (AG-50 50kNG; Shimadzu Corporation, Japan). To align the starting position of the tensile test, a steel wire on the femoral side was attached to the upper grip, and the weight of the entire sample was measured. Next, a steel wire on the tibial side was attached to the lower grip, and a tensile load was applied at a speed of 10 mm/min after adjusting it to be equivalent to the weight when the steel wire on the femoral side was attached (20). To prevent the samples from drying out, the test was conducted within 15 min of skeletal muscle removal. The data obtained were converted to AD at a sampling frequency of 100 Hz and then corrected by deleting values < 0.1 N, in accordance with the method of a previous study (21). Stiffness (N/mm) was calculated and compared with the elongation distance every 1 mm, until rupture.

Preliminary experiment for sample attachment

Six rats were used in a preliminary experiment. First, a sample with a femur-tibia joint capsule complex was prepared for tensile testing. Two methods were used to attach the specimen to the tensile testing machine. In the non-fixed model (**figure 1A**) (22), the femur and tibia were attached with a jig so that the femur and tibia moved in response to the tensile load, and the direction of the load was aligned with the femur-tibia joint capsule complex. In the fixed model (**figure 1B**) (23), the femur was fixed to the upper grip, and the tibia was fixed to the lower grip, so that the angle of knee flexion did not move in response to the tensile load. However, the effect of the different sample attachment methods on the stiffness results had not been investigated. Therefore, we created non-fixed and fixed models and compared the results. No significant differences were observed between the fixed and non-fixed models (**table I**). The advantage of the non-fixed model was that the sample moved with the load, and the direction of the load was aligned with the sample (22). When multiple fibers running lengthwise and obliquely were mixed in the joint capsule, the results of each fiber breaking were reflected in the length-tension curve. Therefore, a non-fixed model was selected for this study.

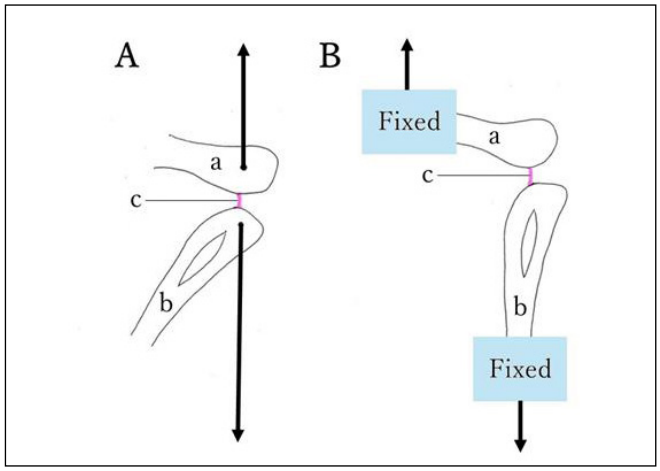


Figure 1. Specimens for tensile testing.

(A) Non-fixed model; (B) Fixed model: a: Femur, b: Tibia, c: Joint capsule, →: tensile direction. The rats were euthanized immediately before the tensile testing, and the right hind limb was amputated from the proximal femur. The skin and skeletal muscles around the knee joint were removed with scissors. The patellar, anterior cruciate, posterior cruciate, medial collateral, and lateral collateral ligaments were cut, and the femur-tibia joint capsule complex specimen was prepared.

Statistics

All data were tested for normality using the Shapiro-Wilk test and analyzed using analysis of variance (ANOVA) with the Bonferroni *post-hoc* test for comparisons between individual groups. The reliability of the joint range of motion measurements was examined using intraclass correlation coefficients (ICC). All data are expressed as mean ± standard deviation (SD). The significance level was set at $p < 0.05$.

RESULTS

Joint fixation

One rat in the 8-week group experienced a femoral fracture when the Kirschner wire was inserted and was excluded. Therefore, five of six rats in the 8-week group were included in the statistical analysis.

Range of motion

The knee extension range of motion after joint fixation removal decreased significantly with an increasing duration of joint fixation (**table II**). The ICC was 0.99, indicating that all measurements had good intra-rater reliability.

Involvement rate of myogenic and arthrogenic contractures

The rate of involvement of myogenic contracture decreased with an increasing duration of joint immobilization, from 72% in the 2-week group to 35% and 19% in the 4-week and 8-week groups, respectively. However, the rate of involvement of arthrogenic contracture increased from

Table I. Effect of different sample mounting methods on stiffness.

	Free model	Fixed model	P-value
Stiffness (N/mm)	3.8 ± 1.0	4.8 ± 2.1	0.8587

All values are presented as mean ± SD. Statistical tests: Shapiro-Wilk test for normality analysis, and t-test for comparisons between two groups. Significance level: $p < 0.05$.

Table II. Changes in the knee extension range of motion and stiffness associated with an increased duration of joint immobilization.

Assessment items		Fixed period (W)				P-value
		0	2	4	8	
After removal of the fixture (°)		156 ± 3	118 ± 9*	96 ± 7*†	80 ± 5*†‡	0.001
After removal of skeletal muscle (°)		158 ± 2	146 ± 5*	118 ± 4*†	96 ± 9*†‡	0.001
Stiffness until rupture (N/mm)		3.8 ± 1.0	2.8 ± 1.5	2.8 ± 1.1	2.4 ± 1.3	0.3389
Stiffness at each extension distance (N/mm)	1 mm	1.7 ± 0.9	1.4 ± 1.0	1.2 ± 0.9	1.3 ± 1.3	0.8587
	2 mm	1.7 ± 1.0	2.4 ± 1.7	1.9 ± 1.1	2.0 ± 1.3	0.8597
	3 mm	2.2 ± 1.8	2.7 ± 0.9	2.4 ± 1.1	3.3 ± 2.8	0.7633
	4 mm	2.9 ± 1.9	3.1 ± 1.5	2.7 ± 1.1	2.6 ± 0.9	0.9505
	5 mm	3.0 ± 1.5	2.3 ± 1.2	2.4 ± 0.6	2.8 ± 1.0	0.0989
	6 mm	3.2 ± 0.7	2.5 ± 1.0	2.3 ± 0.6	2.4 ± 0.7	0.2105

The Shapiro-Wilk test was used for normality analysis, and one-way analysis of variance was used for comparisons between the four groups. Significance was set at $p < 0.05$. All values are presented as mean ± SD. W: week; *significant difference compared to the 0 week group; †significant difference compared to the 2 week group; ‡significant difference compared to the 4 week group.

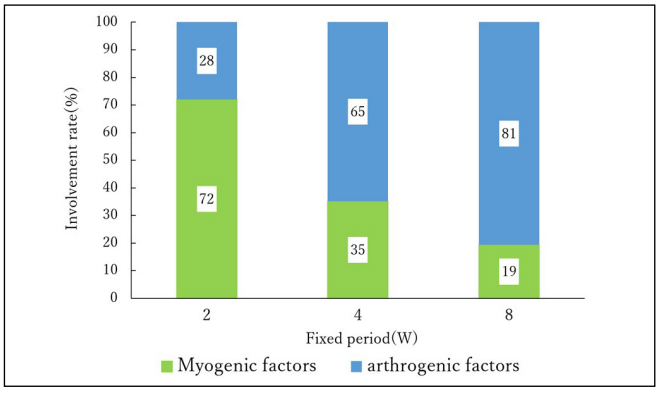


Figure 2. Trends in the incidence of myogenic and arthrogenic factors. The incidence of myogenic contracture decreased with an increasing duration of joint fixation, but the incidence of arthrogenic contracture increased.
W: weeks.

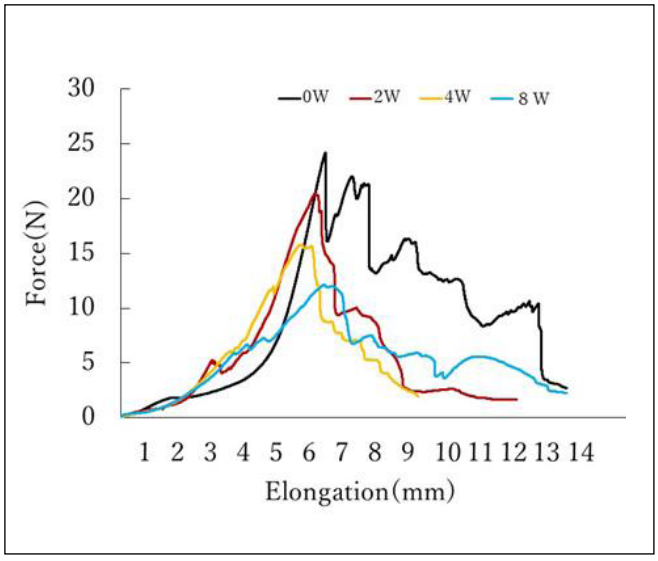


Figure 3. Representative examples of length-tension curves for each group. The oblique popliteal and arcuate popliteal ligaments are mixed within the knee joint capsule of rats in the 0-week group. The sawtooth-like waveform is caused by the shorter ones breaking in order of length. The decrease in serrated waveforms in the 2, 4, and 8-week groups is caused by the decrease in the stiffness of the oblique popliteal and arcuate popliteal ligaments due to joint fixation.
W: week.

28% in the 2-week group to 65% and 81% in the 4-week and 8-week groups, respectively (**figure 2**).

Tensile testing

In the waveform of the length-tension curve for the 0-week group, a sawtooth waveform was observed with repeated increases and steep drops. However, in the 2-, 4-, and 8-week groups, the sawtooth waveform became less prominent (**figure 3**).

Knee joint capsule stiffness

The stiffness until rupture tended to decrease with an increasing duration of joint fixation but was not significantly different between the groups (**table II**). Statistical processing showed no significant differences in the stiffness of all groups at each extension distance from 1 to 6 mm (**table II**).

DISCUSSION

A condition in which joint flexibility moves beyond the normal physiological range of motion is referred to as generalized joint hypermobility. However, it is reportedly not due to increased muscle flexibility (24). This suggests the importance of the joint capsule and ligaments as anatomical sites that determine the final joint range of motion. This study hypothesized that the stiffness of the joint capsule increases when knee flexion contracture occurs. However, the results of this study differed from our hypothesis and showed that the stiffness of the joint capsule did not change, despite an increase in the range of knee extension restriction.

We first investigated the range of motion. The knee extension range of motion restriction increased with an increasing duration of joint immobilization, and the rate of arthrogenic involvement increased. These results are consistent with the findings of previous studies (9, 10, 13) and show that arthrogenic factors increase with an increasing duration of joint immobilization.

Furthermore, we found that the joint capsule stiffness did not change. This result may be related to the stiffness change in the joint capsule owing to knee immobilization, which has not been previously reported. The joint capsule is composed of a highly elastic inner synovial membrane layer and an outer fibrous membrane layer comprising tough collagen fibers (25). In the human joint capsule, a portion of the fibrous membrane thickens to form oblique and arcuate popliteal ligaments, which are inseparable from the ligaments and fibrous membranes (25). The oblique and arcuate popliteal ligaments are involved in knee stability (26). Additionally, the anterior cruciate, posterior cruciate, and internal and external collateral ligaments are involved in knee stability (26). Furthermore, the stiffness of these ligaments, including the anterior cruciate (27), posterior cruciate (28), and internal and external collateral (27) ligaments, reportedly decreases with joint immobilization. However, there are no reports on the stiffness of fibrous membranes, other than those of the oblique and arcuate popliteal ligaments of the knee. In conclusion, the reason for the lack of change in the stiffness of the joint capsule is assumed to be the decrease in stiffness of the ligamentous portions of the joint capsule, such as the oblique and arcuate popliteal ligaments, offset by an increase in the stiffness of the fibrous membrane. No studies to date have examined the physiological range of extension of the rat joint capsule. Therefore, in this study, we compared the stiffness of the joint capsule in 1 mm intervals and found no change in stiffness up to 6 mm. Therefore, the stiffness of the joint capsule may not change in vivo, even with knee flexion contractures.

The findings of this study suggest that the rat joint capsule contains multiple ligaments. This was observed in the length-tension curve of the 0-week group in the form of a sawtooth waveform. Normally, in muscles and ligaments, a sharp decline is observed once the sample is completely broken (20, 27). The reason for the repeated appearance of the sawtooth waveform in the length-tension curve in this study is thought to be the rupture of the multiple ligaments in the joint capsule. Furthermore, the sawtooth waveform became less noticeable in the groups that underwent joint fixation at 2, 4, and 8 weeks, which is thought to be due to the decreased stiffness of the ligaments in the joint capsule with an increasing duration of joint fixation.

Because knee extension restriction caused by fixation of the knee joint in flexion is improved by resection of the joint capsule (14, 15), the joint capsule is a cause of knee extension restriction. Therefore, it is necessary to consider why the knee joint capsule, which does not experience stiffness changes with an increasing duration of joint fixation, is related to the range of motion restriction during knee extension. In this study, we did not perform a morphological analysis of the joint capsule. However, many studies have reported on morphological changes in the knee joint capsule due to knee joint flexion fixation (9, 12, 13, 16, 17, 29-31). According to Ando *et al.*, rats experienced morphological changes in the joint capsule after knee fixation in the flexed position over time, with joint capsule thickening and changes in the lengths of the synovial and fibrous membranes. They reported that joint adhesion and shortening, which causes shortening of the synovial and fibular membranes, are involved in restricting knee extension (32). In conclusion, joint capsule adhesion and shortening, which does not alter stiffness, causes the restriction of knee joint extension.

The results of this study are also clinically significant. If adhesion and shortening of the joint capsule cause restricted knee extension range of motion, intra-articular hydraulic distension may be effective (33). Intra-articular hydraulic distension has been utilized to treat stiff shoulders by distending the joint capsules (34). In addition, knee joint intra-articular pressure increases during knee extension (35); as a non-invasive method, knee joint range of motion exercise could be

a potential prevention/treatment for joint capsule adhesion and shortening. Future studies should investigate whether intra-articular hydraulic distension and range of motion exercises effectively prevent adhesions in the knee joint capsule.
This study had several limitations. First, the presence of oblique and arcuate popliteal ligaments has only been confirmed in the joint capsule of humans, and whether the ligaments are also present in the joint capsule of rats requires further study. Second, the stiffness of knee joint capsule thickening, other than that of the ligaments, has not been clarified. Finally, how the adhesion and shortening of the joint capsule specifically limit the range of knee extension has not been fully elucidated.

CONCLUSIONS

This study hypothesized that joint capsule stiffness would increase as one of the causes of knee flexion contractures. However, in our experimental results we found a new finding that the stiffness of joint capsule did not change with increasing knee flexion limitation.

FUNDINGS

Financial support was provided by the Prefectural University of Hiroshima in Hiroshima, Japan.

DATA AVAILABILITY

Data are available under reasonable request to the corresponding author.

CONTRIBUTIONS

MS: conceptualization, data curation, formal analysis, interpretation, visualization, writing – original draft, writing – review & editing. YS, RI, SN: formal analysis, interpretation, visualization. OT: supervision, funding, writing – review & editing.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

REFERENCES

1. Wong K, Trudel G, Laneuville O. Noninflammatory Joint Contractures Arising from Immobility: Animal Models to Future Treatments. Biomed Res Int. 2015;2015:848290. doi: 10.1155/2015/848290.
2. Born CT, Gil JA, Goodman AD. Joint Contractures Resulting From Prolonged Immobilization: Etiology, Prevention, and Management. J Am Acad Orthop Surg. 2017;25(2):110-16. doi: 10.5435/JAAOS-D-15-00697.
3. Saito T, Takeuchi R, Yamamoto K, et al. Unicompartmental Knee Arthroplasty for Osteoarthritis of the Knee: Remaining Postoperative Flexion Contracture Affecting Overall Results. J Arthroplasty. 2003;18(5):612-8. doi: 10.1016/s0883-5403(03)00196-7.
4. Campbel TM, Trudel G. Knee Flexion Contracture Associated With a Contracture and Worse Function of the Contralateral Knee: Data From the Osteoarthritis Initiative. Arch Phys Med Rehabil. 2020;101(4):624-32. doi: 10.1016/j.apmr.2019.11.018.
5. Campbel TM, McGonagle D. Flexion contracture is a risk factor for knee osteoarthritis incidence, progression and earlier arthroplasty: Data from the Osteoarthritis Initiative. Ann Phys Rehabil Med. 2021;64(2):101439. doi: 10.1016/j.rehab.2020.09.005.
6. Ritter MA, Lutgring JD, Davis KE, et al. The Role of Flexion Contracture on Outcomes in Primary Total Knee Arthroplasty. J Arthroplasty. 2007;22(8):1092-6. doi: 10.1016/j.arth.2006.11.009.
7. Fischer U, Muller M,Strobl R, et al. Prevalence of functioning and disability in older patients with joint contractures: a cross-sectional study. Eur J Phys Rehabil Med. 2015;51(3):269-79.
8. Bartoszek G, Fischer U, Grill E, et al. Impact of joint contracture on older persons in a geriatric setting: A cross-sectional study. Z Gerontol Geriatr. 2015;48(7):625-32. doi: 10.1007/s00391-015-0895-y.
9. Kaneguchi A, Ozawa J, Minamimoto K, et al. Active exercise on immobilization-induced contractured rat knees develops arthrogenic joint contracture with pathological changes. J Appl Physiol. 2018;124(2):291-301. doi: 10.1152/japplphysiol.00438.2017.
10. Trudel G, Uhthof HK. Contractures Secondary to Immobility: Is the Restriction Articular or Muscular? An Experimental Longitudinal Study in the Rat Knee. Arch Phys Med Rehabil. 2000;81(1):6-13. doi: 10.1016/s0003-9993(00)90213-2.
11. Fox P, Richardson J, Mclnnes B, et al. Effectiveness of a Bed Positioning Program for Treating Older Adults With Knee Contractures Who Are Institutionalized. Phys Ther. 2000;80(4):363-72.
12. Trudel G, Uhthoff HK, Goudreau L, et al. Quantitative analysis of the reversibility of knee flexion contractures with time: an experimental study using the rat model. BMC Musculoskelet Disord. 2014;15(338):1-7. doi: 10.1186/1471-2474-15-338.
13. Kaneguchi A, Ozawa J, Yamamoto K. The effects of immobilization duration on joint contracture formation after anterior cruciate ligament reconstruction in rats. Clin Biomech (Bristol). 2023;103:105926. doi: 10.1016/j.clinbiomech.2023.105926.
14. Chimoto E, Hagiwara Y, Ando A, et al. Progression of an arthrogenic motion restriction after immobilization in a rat experimental knee model. Ups J Med Sci. 2007;112(3):347-55. doi: 10.3109/2000-1967-207.

15. Malinowski K, Mostowy M, Kozlak M, et al. Complete Arthroscopic Posterior Knee Capsulotomy in Patients With Knee Extension Deficit: Preliminary Results of a Clinical Trial. Orthop J Sports Med. 2023;11(12):1-10. doi: 10.1177/23259671231203606.
16. Trudel G, Seki M, Uhthoff HK. Synovial Adhesions Are More Important Than Pannus Proliferation in the Pathogenesis of Knee Joint Contracture After Immobilization: An Experimental Investigation in the Rat. J Rheumatol. 2000;27(2):351-7.
17. Trudel G, Jobi M,Uhthoff HK. Localized and Adaptive Synoviocyte Proliferation Characteristics in Rat Knee Joint Contractures Secondary to Immobility. Arch Phys Med Rehabil. 2003;84(9):1350-6. doi: 10.1016/s0003-9993(03)00233-8.
18. Nagai M, Aoyama T, Itoi A, et al. Contributions of biarticular myogenic components to the limitation of the range of motion after immobilization of rat knee joint. BMC Musculoskelet Disord. 2014;15(224):1-10. doi: 10.1186/1471-2474-15-224.
19. Baranowski A, Schlemmer L, Forster K, et al. A novel rat model of stable posttraumatic joint stiffness of the knee. J Orthop Surg Res. 2018;13(1):185. doi: 10.1186/s13018-018-0894-y.
20. Sato Y, Ono T, Ishikura H, et al. Study on change of rat soleus extensibility caused by reduction in joint movement with unweighting of the hind limbs. J Phys Ther Sci. 2018;30(1):53-7. doi: 10.1589/jpts.30.53.
21. Lujan T, Underwood CJ, Henninger HB, et al. Effect of Dermatan Sulfate Glycosaminoglycans on the Quasi-Static Material Properties of the Human Medial Collateral Ligament. J Orthop Res. 2007;25(7):894-903. doi: 10.1002/jor.20351.
22. Kokubun T, Kanemura N, Murata K, et al. Effect of Changing the Joint Kinematics of Knees With a Ruptured Anterior Cruciate Ligament on the Molecular Biological Responses and Spontaneous Healing in a Rat Model. Am J Sports Med. 2016;44(11):2900-10. doi: 10.1177/0363546516654687.
23. Kaneguchi A, Ozawa J, Minamimoto K, et al. Three-week joint immobilization increases anterior-posterior laxity without alterations in mechanical properties of the anterior cruciate ligament in the rat knee. Clin Biomech (Bristol, Avon). 2020;75:104993. doi: 10.1016/j.clinbiomech.2020.104993.
24. Tas S, Dikici TF, Araci A, et al. Mechanical Properties of Muscles and Tendons in Asymptomatic Individuals with Generalized Joint Hypermobility. Muscles Ligaments Tendons J. 2021;11(4):641-47. doi: 10.32098/mltj.04.2021.05.
25. Drake RL, Vogl AW, Mitchell AWM.Gray's Anatomy for Students, 5th ed. Amsterdam: Elsevier; 2024: pp. 598-607.
26. Abulhasan JF, Grey MJ. Anatomy and Physiology of Knee Stability. J. Funct. Morphol. Kinesiol. 2017;2(4):34. doi: 10.3390/jfmk2040034.
27. Nordin M, Frankel VH. Basic Biomechanics of the Musculoskeletal System,5th ed. Philadelphia: Lipincott Williams & Wilkins; 2022: pp. 86-112.
28. Larsen NP, Forwood MR, Parker AW. Immobilization and retraining of cruciate ligaments in the rat. Acta Orthop Scand. 1987; 58(3): 260-4. doi: 10.3109/17453678709146480.
29. Lee S, Sakurai T, Ohsako M, et al. Tissue stiffness induced by prolonged immobilization of the rat knee joint and relevance of AGEs (pentosidine). Connect Tissue Res. 2010;51(6):466-77. doi: 10.3109/03008201003686941.
30. Ozawa J, Kaneguchi A, Tanaka R, et al. Cyclooxygenase-2 inhibitor celecoxib attenuates joint contracture following immobilization in rat knees. BMC Musculoskelet Disord. 2016;17(1):446. doi: 10.1186/s12891-016-1303-5.
31. Tokuda K, Yamaoka Y, Mano Y, et al. Effect of metformin treatment and its time of administration on joint capsular fibrosis induced by mouse knee immobilization. Sci Rep. 2021;11(1):17978. doi: 10.1038/s41598-021-97445-7.
32. Ando A, Hagiwara Y, Onoda Y, et al. Distribution of type A and B synoviocytes in the adhesive and shortened synovial membrane during immobilization of the knee joint in rats. Tohoku J Exp Med. 2010;221(2):161-8. doi: 10.1620/tjem.221.161.
33. Lee JH, Kim K, Chung SG.Intra-articular pressure characteristics of the knee joint: Anexploratory study. J Orthop Res. 2022;40(9):2015-24. doi: 10.1002/jor.25236.
34. Lee KJ, Lee JH, Chung SG. Real-time pressure monitoring of intraarticular hydraulic distension for painful stiff shoulders. J Orthop Res. 2008;26(7):965-70. doi: 10.1002/jor.20535.
35. Wood L, Ferrell WR, Baxendale RH. Pressures in normal and acutely distended human knee joints and effects on quadriceps maximal voluntary contractions. Q J Exp Physiol. 1988;73(3):305-14. doi: 10.1113/expphysiol.1988.sp003147.