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In vivo kinetic evaluation of an adhesive capsulitis model in rats

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Background and Hypothesis: We hypothesized that extra-articular, internal fixation of the shoulder in rats would result in a subsequent decrease in rotational range of motion (ROM) and an increase in joint stiffness. We further hypothesized that residual kinematic changes would still be present at 8 weeks after immobilization. Extra-articular, internal fixation of the shoulder has been used to induce adhesive capsulitis in rats; however, the effects on in vivo kinematics have not been assessed.

Methods: Baseline measurements of rotational torque and ROM were acquired (n = 10 rats), and the left forelimb of each animal was immobilized with sutures passed between the scapula and the humeral shaft. After 8 weeks, the sutures were removed, and changes in kinematics and kinetics were longitudinally quantified in the follow-up period. Changes in stiffness, defined as the area under the angle-torque curve, were also quantified.

Results: Immediately after suture removal, there was a 63% decrease in total ROM compared with baseline (51° ± 10° vs. 136° ± 0°; $P < .001$). Similarly, total torque was found to increase 13.4 N.mm compared with baseline (22.6 ± 5.9 N.mm vs. 9.2 ± 2.6 N.mm; $P = .002$). Residual total ROM restrictions and an increased torque in internal rotation were still evident at 8 weeks of follow-up (113° ± 8° vs. 137° ± 0°, $P < .001$ and 3.5 ± 0.4 N.mm vs. 2.7 ± 0.7 N.mm, $P = .036$). Stiffness also increased after suture removal and at 8 weeks of follow-up compared with baseline.

Conclusion: This animal model of adhesive capsulitis rendered lasting effects on in vivo kinematics of the shoulder.

Level of evidence: Basic Science Study, In Vivo Animal Study.

Keywords: Adhesive capsulitis; frozen shoulder; contracture; animal model; biomechanics; rat

Adhesive capsulitis is characterized by pain, stiffness, and a prolonged loss of range of motion (ROM) in the glenohumeral joint and affects 2% to 5% of the U.S. population.[8,13,15] This disease is pathologically described by a fibrotic capsule that demonstrates a chronic inflammatory

This study was approved by the Beth Israel Deaconess Medical Center's Institutional Animal Care and Use Committee: Protocol No. 053-2013.

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infiltrate, absence of synovial lining, and subsynovial fibrosis.[14,16,21] Most accounts describe a highly vascularized synovium with abundant granulation tissue that may intrude on the bursa.[2,3] Immunohistochemistry has confirmed the presence of T cells, B cells, synovial cells, fibroblasts, and transforming myofibroblasts along with type I and type III collagen in biopsy samples collected from patients undergoing surgical capsular release.[4,16] However, the exact etiology and natural history of the disease remain uncertain.

Adhesive capsulitis is often described as a self-limited disease, but the course of recovery is arduous and long.[5] Although some patients achieve spontaneous resolution, a significant number fail to recover full ROM after treatment, and up to 60% have residual restrictions of motion years after the onset of symptoms.[18] It has been reported that mild to moderate symptoms can persist after 4.4 years following symptom onset of primary adhesive capsulitis. For those experiencing severe disease, such functional impairment may interfere with daily activities.[6]

Although it is believed that adhesive capsulitis can be treated with physical therapy, the best mode of treatment has been the subject of extreme interest. To evaluate the efficacy of new therapeutic options, it is necessary to develop an accurate animal model of adhesive capsulitis that will achieve the 2 hallmark characteristics of the disease: capsular contracture and a prolonged reduction in ROM. Previous studies have demonstrated that synovial shortening and deposition of type III collagen in the subsynovial area, both typical pathologic findings in adhesive capsulitis, appear in rats after 8 weeks of extra-articular, internal fixation of the glenohumeral joint.[10,12] These studies reportedly achieved a reduction in ROM with this animal model of adhesive capsulitis, as demonstrated by ex vivo measurements of shoulder kinematics. However, they failed to report whether these changes are transient or permanent.

No studies to date have evaluated whether this animal model of adhesive capsulitis affects in vivo shoulder kinetics (i.e., stiffness). Therefore, the aim of this study was to investigate the effects of extra-articular, internal fixation of the glenohumeral joint on shoulder kinetics and kinematics in an in vivo animal model of adhesive capsulitis. To that end, we hypothesized that rotational ROM would decrease and joint stiffness would increase after an 8-week period of immobilization. We further hypothesized that a spontaneous complete recovery would not occur and therefore residual kinematic and kinetic changes would still be present after 8 weeks of follow-up.

Materials and methods

Study design

Following approval by the Institutional Animal Care and Use Committee, a total of 10 Sprague-Dawley rats (250-300 g; Charles River Laboratories, Wilmington, MA, USA) were used in this study. For each animal, torque was measured per degree on the intact left shoulder as a function of rotation angle between 80° of internal rotation (negative values by convention) and 60° of external rotation (positive values by convention) before any surgical intervention (baseline). Rotation was confined within boundaries that were observed to elicit minimal scapular recruitment, as confirmed by fluoroscopy. Torque values at 80° of external rotation (τ_{OUT}) and 60° of internal rotation (τ_{INT}) were recorded for each animal.

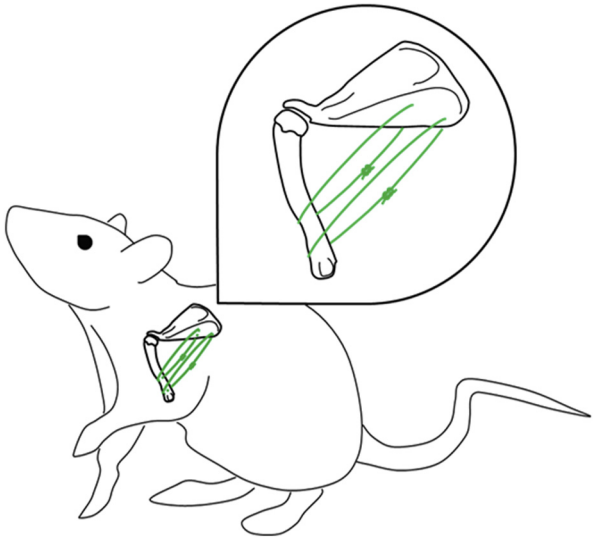

Figure 1 Schematic representation of the model of extra-articular, internal fixation of the glenohumeral joint. Braided polyester sutures were used to firmly tie the scapular edge to the distal third of the humerus.

The left forelimb of each animal was immobilized with a version of the procedure developed by Kanno et al.[10] Briefly, anesthesia was induced with 5% isoflurane inhalation and then maintained with 2% isoflurane. A longitudinal skin incision was made perpendicular to the scapular spine. Two No. 2-0 braided polyester sutures (Ethibond Excel; Ethicon, San Lorenzo, PR, USA) were passed between the medial border of the scapula and the humeral shaft and tightened to immobilize the shoulder joint (Fig. 1). Muscle structures were not manipulated during surgery, and the animals were allowed normal activity in their cages immediately after the procedure.

After 8 weeks of immobilization, the restraining sutures were removed, and the 10 animals were divided into 2 groups to evaluate changes in ROM (ROM group, n = 5) and joint stiffness (stiffness group, n = 5). In the ROM group, changes in kinematics were longitudinally quantified in the follow-up period by measuring the ROM achieved with the τ_{OUT} and τ_{INT} measured at baseline. This was conducted to evaluate whether immobilization mediated a significant reduction in ROM. In the stiffness group, joint kinetics were examined by measuring the differences in τ_{OUT} and τ_{INT} needed to achieve the original 80° of internal rotation and 60° of external rotation, respectively. Measurements for both groups were taken immediately after suture removal (day 0 of follow-up) and at regular intervals thereafter (twice a week until <10% change was observed in 3 consecutive time