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A randomized clinical trial to compare the effectiveness of rotator cuff repair with or without augmentation using porcine small intestine submucosa for patients with moderate to large rotator cuff tears: a pilot study

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Background: The rate of rotator cuff repair failure is between 13% and 67%. Porcine small intestine submucosa (SIS) may be suitable to augment the repair.
Methods: There were 62 patients with moderate and large cuff tears randomized to repair alone (control) or augmentation with SIS (Restore Orthobiologic Implant; DePuy, Warsaw, IN, USA). Primary outcome was repair failure using magnetic resonance arthrography. Randomization occurred on completion of the repair. Patients and assessors were blind to group. Assessments occurred preoperatively and postoperatively at 2 and 6 weeks and 3, 6, 12, and 24 months.
Results: There were 62 patients randomized (34 SIS, 28 control). Patient demographics, rotator cuff tear characteristics, and repair details were similar between groups. At 1 year, risk of failure was 52.9% (18/34) in the SIS group and 65.4% (17/26) in the control group for a risk difference of 12% (80% confidence interval, −7% to 32%) or relative risk of 0.81 (95% confidence interval, 0.53-1.24, $P = .33$) in favor of SIS. At 1 and 2 years, the mean difference between groups for patient-reported outcomes was small and consistent with chance but did not exclude the possibility of a clinically important difference. There was no statistically significant difference ($P = .50$) between the SIS group (59.6 ± 38.9; range, 3-112) and the control group (52.7 ± 38.6; range, 5-112) in number of days to being narcotic and pain free (<20 mm on a 100-mm visual analog scale).

Institutional Review Board approval was provided by St Joseph's Healthcare, McMaster University Research Ethics Board: Study No. 03-2244.

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Conclusion: We found no evidence that SIS-augmented rotator cuff repair provides superior outcomes in patients with moderate rotator cuff tears.
Level of evidence: Level I; Randomized Controlled Trial; Treatment Study

Keywords: Rotator cuff repair; porcine intestine submucosa; augmentation; randomized clinical trial; patient-reported outcomes; MRI; shoulder; restore

Disability related to rotator cuff tears is an increasing problem in an aging population. The prevalence of full-thickness tears has been reported to increase from 50% in the fourth decade of life to 80% in the eighth decade.[25,26,37,39] The theory of tendon failure speculates that an increased functional demand coupled with persistent altered use causes a stress response within the cells of the tendon matrix, from which the cells may become injured.[21] In some cases, injury may be irreversible such that cell death and denaturation cause tendon degeneration and microtearing, which eventually lead to full-thickness tendon failure.[21] Microinjection studies of the rotator cuff support the concept of a hypovascular zone within the tendinous portion of the supraspinatus[27,30,32,38] and have shown that vascularization is diminished in older individuals, which is consistent with the observed pattern of age-related tendon degeneration.[9] Thus, strategies that promote the intrinsic capacity of the tendon to repair itself may result in superior outcomes.

A biologic scaffold derived from submucosal and basilar mucosal layers of small intestine submucosa (SIS, Restore Orthobiologic Implant; DePuy, Warsaw, IN, USA) provides numerous structural and functional proteins that may direct cell growth and signal cell differentiation. In vivo, the submucosa and basilar layers of the mucosa support a rapidly dividing cell population (small intestine enterocytes) as they are repeatedly subjected to insults originating in the intestinal lumen. The complex composition of the small intestine is responsible for the in vivo signals, which cause cell attachment, migration, proliferation, and differentiation of new cells. SIS is relatively acellular, and the bulk of its material consists of extracellular connective tissue matrix, approximately 90% collagen (mainly type I), fibronectin, 5 different glycosaminoglycans,[15] growth factors (such as transforming growth factor β, fibroblast growth factor, and vascular endothelial growth factor), and various proteoglycans and glycoproteins.

There are a number of examples of successful remodeling in tissue locations throughout the body, including the lower urinary tract dermis and epidermis,[29] tendon and ligament,[14] abdominal wall,[29] and blood contact surfaces such as small- and large-diameter arteries and veins.[2,3,7,13,19,20,28,33,34] There is specific evidence from animal studies[8,35,42] and case series in humans[36] that supports the use of SIS for augmentation of rotator cuff repairs.

Iannotti et al published a randomized trial to determine the effectiveness of an SIS-augmented repair to a standard repair of 30 chronic 2-tendon rotator cuff tears (15 per group).[16] All patients underwent magnetic resonance imaging (MRI) with intra-articular administration of gadolinium 1 year after repair, which showed that 11 of the 15 cuffs in the SIS group compared with 5 of the 15 cuffs in the control group had failed (risk difference of −33% [95% confidence interval (CI), −73% to 7%] or relative risk of 1.83 [95% CI, 0.92-3.66]). The difference between groups in the Penn shoulder-specific questionnaire was not statistically significant ($P = .07$); however, this study's small sample size meant that the results of the study were inconclusive.

A biologic scaffold provides numerous structural and functional properties that may direct cell growth and aid in tendon healing. Therefore, we conducted a pilot multicenter randomized clinical trial (1) to obtain a preliminary estimate of the likely success of SIS, (2) to formally evaluate our ability to successfully recruit eligible patients into this study, (3) to determine a more accurate estimation of sample size for the full trial using quality of life as a primary outcome, (4) to determine the frequency with which surgeons comply with the surgical protocol, and (5) to determine the frequency with which patients and physiotherapists comply with the suggested physiotherapy protocol.

Methods

This study was a parallel-groups randomized clinical trial that included 4 centers and 6 surgeons (R.H., K.W., R.L., D.D., and 2 nonauthors).

Eligibility criteria

We systematically reviewed incoming referrals of patients with complaints of shoulder pain or disability. The surgeon reviewed the patient's eligibility during history and physical examination, taking into account information provided from preconsultation MRI. We excluded patients who had (1) previous shoulder surgery, excluding acromioplasty or diagnostic arthroscopy; (2) other significant shoulder disease, including type II-IV superior labral anterior-posterior lesion requiring repair, Bankart lesion, Hill-Sachs lesion, and grade III or greater osteoarthritis according to Kellgren and Lawrence[17]; (3) active joint or systemic infection; (4) significant shoulder girdle muscle paralysis; (5) major medical illness; (6) unwillingness to be assessed for 1 year after surgery; or (7) major psychiatric illness, developmental handicap, or inability to read and to understand the English language. Eligible and consenting patients underwent a baseline assessment not more than 1 month before surgery. Diagnostic arthroscopy was performed at the time of surgery. Patients were excluded if the surgeon was unable to repair the tear