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Combined Atelocollagen and MSC Therapy Enhances Tendon-to-Bone Healing in a Rotator Cuff Repair Rat Model

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Introduction and Background

Rotator cuff repair frequently fails due to insufficient tendon-to-bone healing and incomplete maturation of the enthesis. Biologic augmentation using atelocollagen (ATC) or mesenchymal stromal cells (MSC) has shown potential to improve collagen organization and structural integration. However, the magnitude of benefit and the synergistic effect of combining ATC and MSC remain incompletely defined.

Material and Method

A rotator cuff repair rat model received ATC, MSC, or ATC+MSC treatment with 12 rats assigned to each group. Left shoulders were allocated to histologic evaluation (n = 6) and qPCR (n=6), and right shoulders (n=12) were used for biomechanical testing. Histologic evaluation, qPCR analysis for *COL1A1, COL3A1, BMP2, SOX9, SCX,* and *ACAN, and* biomechanical testing were performed.

Results

Total histologic scores were higher in the ATC and MSC groups than in controls, with no difference compared with each other, and the ATC+MSC group showed the highest score ($p<0.001$). Collagen I/III ratios reflected enhanced maturation, consistent with strong *COL1A1* upregulation, particularly in ATC+MSC (46.5-fold, $p<0.001$). *COL3A1* was reduced in all treated groups ($p<0.001$). *SCX* expression was 2.4-fold and 2.3-fold higher in the ATC+MSC group than in the ATC and MSC groups, and *ACAN* expression was 9.1-fold and 4.2-fold higher than in the ATC and MSC groups, respectively (all $P < 0.05$). Load-to-failure was highest in the ATC+MSC group (4.28±0.87N) and was higher than in the ATC and MSC groups (2.56±0.62N and 1.98±0.54N; $P<0.001$). Ultimate strength was also highest in the ATC+MSC group (2.74±0.75MPa) and was higher than in the ATC and MSC groups (1.62±0.60MPa and 1.47±0.53MPa; $P<0.001$).

Conclusions

ATC+MSC combination therapy produced the strongest tendon-to-bone healing response, characterized by markedly enhanced collagen maturation, upregulation of key tenogenic and fibrocartilaginous genes, and significantly improved biomechanical strength. These findings support ATC+MSC as a compelling biologic strategy for improving rotator cuff repair durability.

Figure & Table 1.

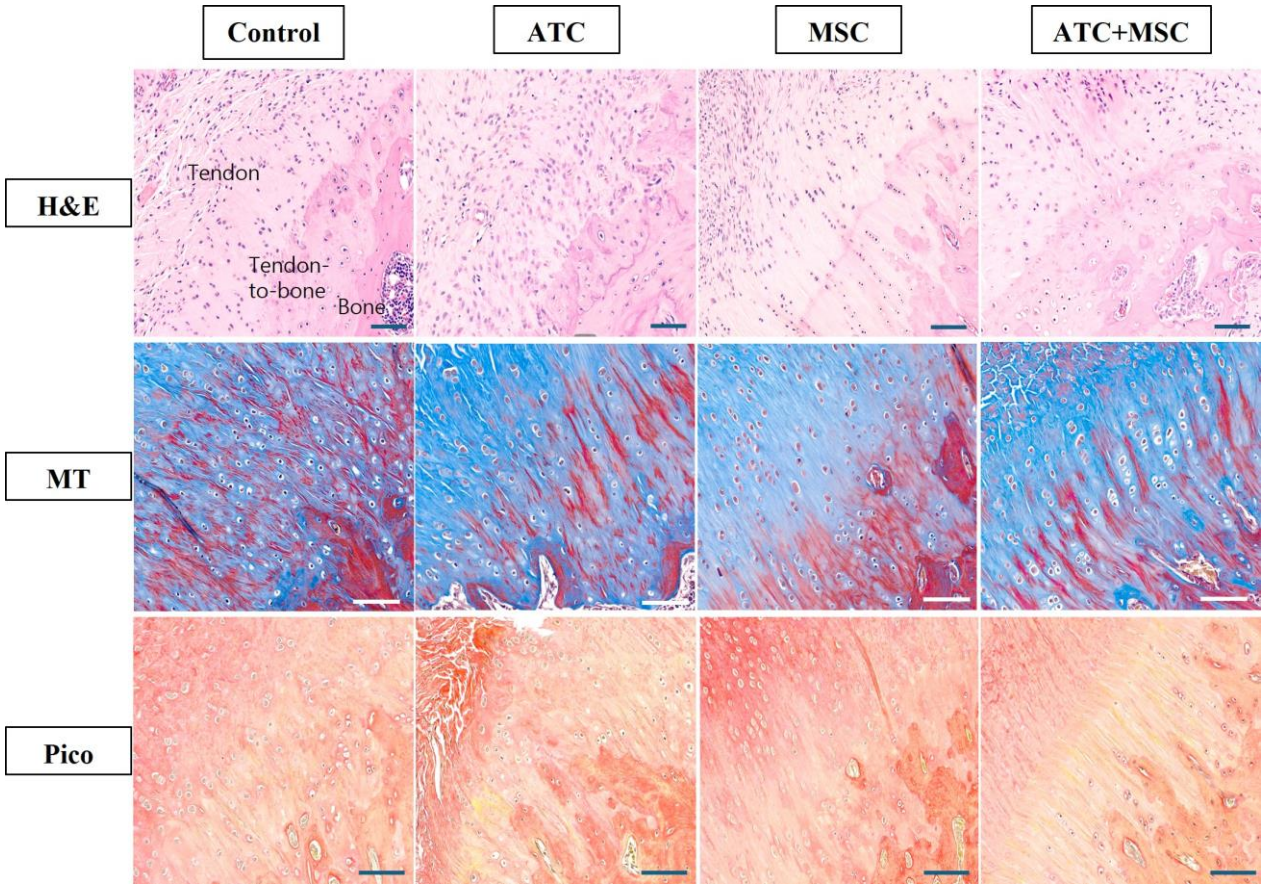

Figure & Table 2.

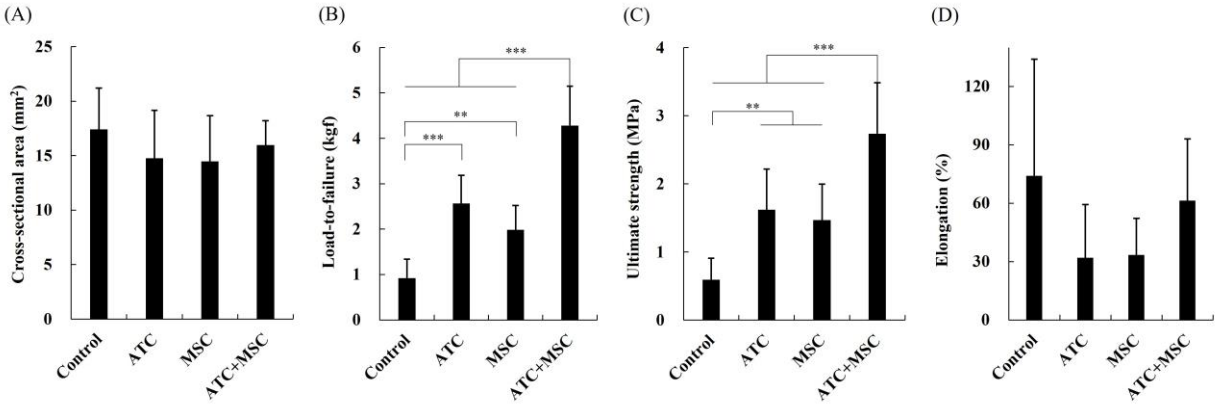

Figure. Biomechanical properties of the repaired tendon–bone interface at 8 weeks. (A) Cross-sectional area showed no significant differences among groups (ANOVA $p = 0.270$). (B) Load-to-failure differed significantly among groups (ANOVA $p < 0.001$). Tukey post-hoc testing showed that the ATC+MSC group had significantly higher load-to-failure than ATC, MSC, and Control, and both ATC and MSC were significantly higher than Control (all $p < 0.01$). (C) Ultimate tensile strength also differed significantly among groups (ANOVA $p < 0.001$). The ATC+MSC group exhibited significantly greater tensile strength than all other groups, and both ATC and MSC exceeded Control ($p < 0.01$). (D) Elongation at failure showed a significant overall group effect (ANOVA $p = 0.033$), but no pairwise differences reached statistical significance in Tukey post-hoc testing. Data are presented as mean ± SD. Statistical comparisons were performed using one-way ANOVA with Tukey post-hoc testing. **p < .01 and ***p < .001.