**Introduction:** Rotator cuff disease is the most common cause of shoulder pain in adults (1). Although several studies have documented the pathological changes associated with rotator cuff disease (2), the exact etiology of the disease remains unclear. The role of intrinsic (vasculature, intrinsic degeneration, tendon overload) versus extrinsic (mechanical impingement, secondary impingement) factors remains unknown. The subacromial bursa is commonly involved in patients with rotator cuff disease and has been suggested to be a source of healing during rotator cuff repair (3). However, its possible contribution to tendon degeneration is unknown.

**Purpose:** The purpose of this study was to determine if matrix metalloproteinase (MMP) and tissue inhibitors of metalloproteinase (TIMP) mRNA levels were altered in the bursa of normal versus torn rotator cuffs.

**Hypothesis:** We hypothesized that the subacromial bursa would demonstrate increased MMP mRNA levels in the bursa of torn versus normal rotator cuffs.

**Methods:** Tissue was obtained from 10 patients undergoing rotator cuff repair for full thickness rotator cuff tears. Bursal tissue was harvested immediately adjacent to the tear site. Care was taken to ensure that there was no contamination of tissue from adjacent structures. The mean age of the patients was 60 +/- 5 years. In addition, tissue was obtained post-mortem from donors adjacent to the tear site. Care was taken to ensure that there was no contamination of tissue from adjacent structures. The mean age of the patients was 60 +/- 5 years. Reverse transcription polymerase chain reaction (RT-PCR) was performed as previously described (4) for the collagenases (MMP-1, MMP-8, MMP-13), the gelatinases (MMP-2, MMP-9), the membrane type MMPs (MMP-14, MMP-15, MMP-16) and the TIMPs (TIMP-1, TIMP-2, TIMP-3, TIMP-4) and normalized to the housekeeping gene GAPDH using human-specific primer sets (5). The ethics review board from our institution approved the study.

**Results:** All of our no RT controls were negative. Results for collagenase mRNA levels demonstrated a significantly increased MMP-13 mRNA levels in the bursa from torn rotator cuffs (Fig 1). There were no significant differences in the other collagenases (MMP-1 or MMP-8). There were also no significant differences in gelatinase mRNA levels (MMP-2 or MMP-9).

Discussion: The etiologic factors involved in tendon degeneration remain controversial. Our study suggests that the subacromial bursa may also play an active role in tendon degeneration. Collagenases (MMP-1, MMP-8, MMP-13) are known to degrade type I collagen the most common extracellular matrix protein within the rotator cuff (6). In particular, MMP-13 is known to degrade type I collagen with equal efficiency to MMP-1 or MMP-8. MMP-13 mRNA levels were increased in the bursa from torn rotator cuffs. In addition, there were no corresponding increases in mRNA levels for endogenous inhibitors of MMPs, the TIMPs. These results collectively suggest that the subacromial bursa may be actively involved in tendon degeneration or remodeling and is consistent with pathological studies, which have demonstrated alterations in collagen architecture and organization and a decrease in collagen content in degenerated rotator cuffs (7,8). In addition, MMP-15 and MMP-16 mRNA levels were also increased in the bursa of torn rotator cuffs. In addition to acting on various extracellular matrix components, the membrane type MMPs are known to activate various pro-MMPs to their active form including MMP-13. Thus these two membrane type MMPs may also be involved in the pathogenesis of degeneration. Interestingly, the high mRNA levels of MMP-13 and MMP-15 are also more consistent with the chronic inflammatory MMP expression profile seen in rheumatoid arthritis versus a traumatic MMP expression profile (9). Thus the MMP profile seen in the bursa of torn rotator cuffs may similarly facilitate inflammatory tissue destruction.

Assuming these mRNA changes are not secondary effects from rotator cuff tearing and are reflected by protein synthesis these findings may have several clinical implications. These results suggest that partial bursectomy may play a role in the treatment of rotator cuff disease by removing a source of potentially degradative MMPs and thus may inhibit the progression of tendon degeneration. In addition, the decision to routinely preserve the bursa during rotator cuff repair due to its potential contribution to the healing process must be considered in light of its possible degradative effects (3).

**Conclusion:** Elucidating the pathogenesis of rotator cuff disease is important in rationalizing treatment decisions and providing an avenue for novel therapeutic interventions. Our results suggest that there is an increase in MMP-13, MMP-15 and MMP-16 mRNA levels in the bursa of torn rotator cuff tendons. This suggests that the subacromial bursa may play an active role in the degeneration and remodeling of the rotator cuff.

**References:**

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