Changes of Matrix Metalloproteinase and Tissue Inhibitors of Metalloproteinase in Patients with Rotator Cuff Tears

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Introduction

Rotator cuff tears are common cause of pain and disability in shoulder pathologies. However, pathogenesis and natural history of rotator cuff tear still remains to be unclear. And despite the successful clinical outcomes of surgical repair of rotator cuff tears, biological status of torn cuff has not been clearly understood. Therefore, molecular changes of torn rotator cuff would be expected to provide the information regarding disease process. The purpose of this study is to measure matrix metalloproteinase and tissue inhibitor of metalloproteinase level in rotator cuff tears and evaluate correlation between molecular changes and clinical parameters such as age, duration of symptom, range of motion, tear size.

Methods

The human ethics review committee of our institution approved the protocol of this study. The purpose and methods of the study were explained to all the patients and all agreed informed consent. We studied 20 patients with rotator cuff tears; 13 full thickness tears, 7 partial thickness tears. Each patient had arthroscopic rotator cuff surgery between May 2007 and May 2008. Among those patients, 12 were male and 8 were female. Their mean age was 59 years (range, 39-76). Average duration of symptoms was 10 months (range, 3-24). Defect of full thickness tear was measured with a linear measuring probe notched 1-mm increments under arthroscopic view. Average size of the full thickness tear was 439 mm2 (range, 150-600). Rotator cuff tissue was obtained from edge of torn tendon after debridement by motorized shaver. All specimens were snap frozen and stored at-70°C until further analysis by RT-PCR. MMP-2 and TIMP-2 mRNA expression was evaluated as follows: Total RNA was extracted from each specimen using Trizol kit (Invitrogen, USA). The RNA (2 μg) was then reverse transcribed into complementary DNA (cDNA) using Superscript system from Invitrogen (Carlsbad, USA). For PCR, initial incubation was performed at 94°C 3min, then total 35 cycles were used for denaturation at 94°C for 1min, primer annealing at 65oC for 1min, and extension 72°C for 1 min. All PCR products were analyzed by eletrophoresis in a 1.5% agarose gel at 70 V for 1.5 hours and photographed using UV-Transiluminator. Relative band intensities were quantified by densitometric scanning of the photographic negatives.using Image J program (NIH, USA). Spearman's correlation coefficients were used to determine correlation and significant

differences between clinical variables and mRNA levels.

Results

There was inverse correlation between MMP-2 and TIMP-2 from torn rotator cuff tendon regardless of clinical variables. Comparison of mRNA levels versus clinical parameters such as age, defect size, range of motion and duration of symptoms revealed a number of findings. There was significant correlation between age and mRNA levels of MMP-2 from torn cuff (r=.513, P=.021). Evaluation of the mRNA levels from rotator cuff margin showed a correlation between MMP-2 levels and defect in the full thickness tears (r=.454, P=.045). There was insignificance between levels of MMP-2 and range of motion or duration of symptom.

Discussion

Matrix metalloproteinase (MMP) is zinc-dependent protease well known to participate in the degradation and remodeling of the extracellular matrix of connective tissues through their broad proteolytic capabilities in both normal and pathologic status. The activity of MMP is inhibited by tissue inhibitors of metalloproteinase. Especially, MMP-2 rapidly degrades denatured collagen and native collagen types. MMP-2 activity was essential for collagen degradation in soft connective tissue. Despites their role in connective tissue healing, there are few studies on the role of MMPs in tendon bone healing. One study showed MMP-2 and TIMP-1 were expressed in both edge of tendon defect and reparative tissue in a rotator cuff defect model in rabbit. It suggested that MMP-2 and TIMP-2 play a role in the remodeling of a torn supraspinatus tendon during the healing process. Another study exhibited altered MMP-13 mRNA levels in torn rotator cuff tendons. We have limitations in this study. Total number of sample was small and it was difficult to obtain normal healthy tendon from young subject as control group due to ethical matters. Our results suggest that both MMP-2 and TIMP-2 may be involved in disease process of rotator cuff tears with constant relationship pattern in torn rotator cuff irrespective of clinical variables and mRNA levels of MMP-2 and TIMP-2 could be influenced by age and defect size in tendon degradation and healing process.