Age-related Accumulation of Advanced Glycation End Products and Enzymatic Cross-links in the Human Meniscus

Hiroki Katagiri[1], Rena Hagiwara[2], Shoutaro Arakawa[3], Yusuke Nakagawa[2], Tomomasa Nakamura[2], Kunikazu Tsuji[2], Toshitaka Yoshii[2], Mitsuru Saito[3], Hideyuki Koga[2]
[1]Dokkyo Medical University Saitama Medical Center, [2]Institute of Science Tokyo, [3]The Jikei University School of Medicine
Email of Presenting Author katagiri.orj@tmd.ac.jp

Disclosures: All authors (N)

INTRODUCTION:
Advanced glycation end products (AGEs) have been implicated in age-related tissue degeneration. While pentosidine accumulation in the meniscus has been shown to increase with aging, little is known about other AGEs or enzymatic cross-links. This study aimed to clarify age-related changes in AGEs and collagen cross-links in meniscus obtained during total knee arthroplasty (TKA).

METHODS:
Menisci were obtained from patients undergoing TKA for osteoarthritis. The medial meniscus (MM), lateral meniscus (LM), and medial and lateral meniscal posterior roots (MMPR, LMPR) were dissected. AGEs (pentosidine, CML, CEL, MG-H1) and enzymatic cross-links (LNL, HLNL, DHLNL, PYD, DPD) were quantified by mass spectrometry and normalized to hydroxyproline (Hyp). Correlations with age were analyzed using Spearman's rank coefficient.

RESULTS:
Thirty-three patients (mean age 74 ± 6 years; 7 males, 26 females) were included. Pentosidine, CML, and CEL tended to accumulate with age in the LM posterior horn, although the correlations were not statistically significant (Figure 1). Among immature cross-links, DHLNL was most abundant. LNL, HLNL, and DHLNL each showed significant positive correlations with age in the LMPR ($r=0.37, 0.33, 0.35$; $p<0.05$ Figure 2). DHLNL also correlated positively with age in the LM ($r=0.39$; $p<0.05$). Conversely, the mature cross-link PYD showed a significant negative correlation with age in the LM ($r=-0.34$; $p<0.05$ Figure 3).

DISCUSSION:
AGEs tended to accumulate with age in the LM, whereas no consistent trend was observed in the MM. Menisci obtained from TKA specimens may be affected by osteoarthritic remodeling to varying degrees, suggesting future multivariate analyses incorporating OA severity are needed. The reduction in mature cross-links, in combination with AGE accumulation, may contribute to meniscal degeneration.

SIGNIFICANCE/CLINICAL RELEVANCE:
This study demonstrates that aging is associated with altered collagen cross-linking in the lateral meniscus, with increased AGEs and immature cross-links and decreased mature cross-links. These changes may represent a potential mechanism underlying age-related meniscal degeneration and its contribution to osteoarthritis progression.

IMAGES AND TABLES:

Figure1: Correlation between AGEs and age.

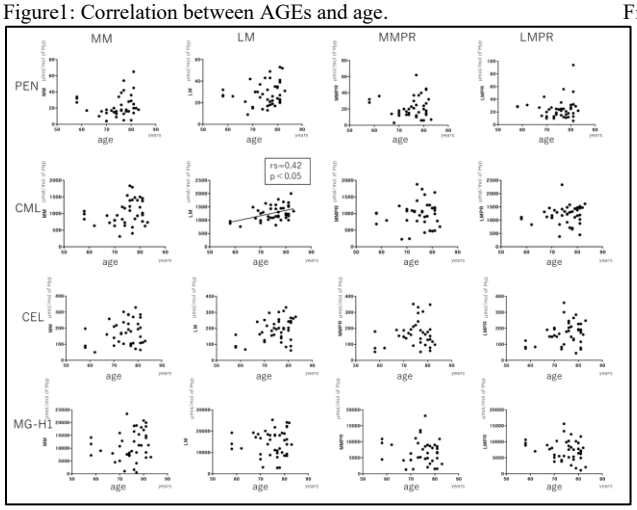

Figure2: Correlation between immature cross-links and age.

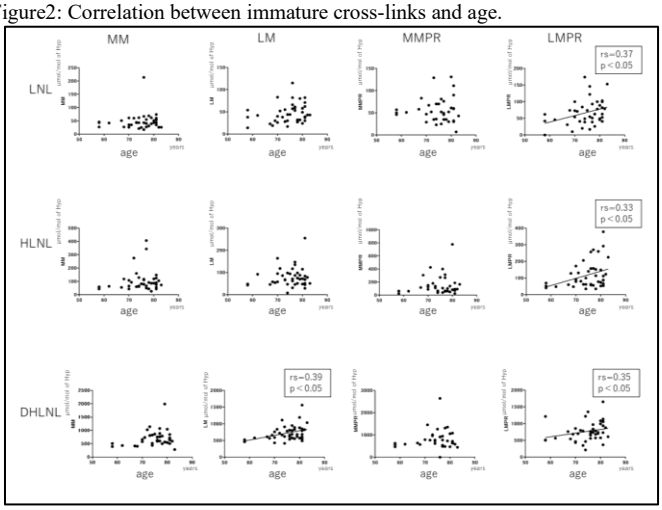

Figure3: Correlation between mature cross-links and age.