Accumulation of Advanced Glycation End-Products and Expression of Estrogen Receptor in Tendinopathy

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Disclosure

The authors declare no conflict of interests related to this presentation.
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The pathology of tendinopathy is considered as a continuum of tendon degeneration but the precise molecular pathology of tendinopathy is still lacking.

Accumulation of advanced glycation end-products (AGEs) happens during connective tissue aging and affects tendon viscoelasticity. Estrogen, which functions via estrogen receptor (ER), is essential for metabolism and plays a role in tendon health and aging.
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**Study Goal:**
This preliminary study investigated the accumulation and expression of AGEs, RAGE and ER in tendinopathic tendons, in comparison with normal tendons, for their potential roles in the pathogenesis of tendinopathy.
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Study Design:

1. **Patient information:** This study included six patients with posterior tibial tendon (PTT) tendinopathy (age from 20 to 72 years, 5 male and 1 female). Normal flexor digitorum longus (FDL) tendon samples were collected from three donors (female, age from 42 to 51 years, approved by IRB).

2. **Immunohistochemistry and western blot:** Tissue samples of tendinopathy and normal tendon were sectioned. Picrosirius Red stain was used for collagen structure. Immunohistochemistry of AGEs, AGEs receptor (RAGE) and ER was performed for protein localization. Proteins were extracted from the collected tendinopathic and normal tendons. Western blot for AGEs, RAGE and ER was performed for quantification of proteins in the tissue.
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**Histology:**
Tendinopathy of PTT was confirmed by a disorderly organized collagen network and highly heterogeneous collagen contents. Cellularity was greatly increased in the pathological region.
Estrogen Receptor (ER) in Tendinopathy

Immunohistochemistry of ER: While ER was negatively expressed in normal tendon, it was positive in the tenocytes, particularly around the tendinopathic lesion.

Western blot of ER: The amount of ER was significantly increased in tendinopathic tendons, compared with normal tendons.
Advanced Glycation End-Products (AGEs) in Tendinopathy

Immunohistochemistry of AGEs: While accumulation of AGEs was present in the tendon tissue normally, it was more concentrated intracellularly in tendinopathy.

Western blot of AGEs: The amount of AGEs was not significantly changed between the normal and tendinopathic tendons.
Receptor of Advanced Glycation End-Products (RAGE) in Tendinopathy

Immunohistochemistry of RAGE: While the staining of RAGE was more diffused in normal tendon, its expression was more intracellular in tendinopathy.

Western blot of RAGE: The amount of RAGE was not significantly changed between the normal and tendinopathic tendons.
Discussion:

- ER regulates tendon tension and is relevant to tendon healthy. This study found an increased expression of ER in tendinopathy tissue and localized ER in tenocytes around the lesion. Future investigation will focus on the pathological role of ER in regulation of tenocytes.

- Compared with normal tendon, the accumulation of AGEs and expression of RAGE in tendinopathy were not significantly increased but their distributions were more intracellular, suggesting their possible involvement in the pathogenesis of tendinopathy.
Conclusion:
This preliminary study revealed the features of expression and tissue localization of AGEs, RAGE and ER, which are associated with connective tissue aging, in tendinopathy. Molecular pathology is key for developing disease-modifying therapies for tendinopathy.
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