Mucosa/Submucosa Remodeling in Aging

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Prevalence of a number of urinary bladder disorders—increases with age

Significance: The process of ‘aging’ can lead to changes in bladder structure and function - and this can be influenced by remodeling.
State of the Art Knowledge / Gaps

Age-related dysfunctions in the bladder (i.e. fibrosis) can make the elderly more vulnerable to developing incontinence.

Mechanisms proposed to explain voiding dysfunction in the elderly include collagen deposition / fibrosis.

The causes of fibrosis remain unknown - however may involve ischemia and oxidative stress.
Along with smooth muscle, the complex network of the extracellular matrix (collagen/elastin) forms the primary load bearing structural components of the bladder wall.

**Urinary Bladder** - made up of multiple layers/cell types
In pathology and aging, there is a loss of organization and function of the extracellular matrix. Limited understanding as to cause/effect.
We used mechanical loading (biaxial stretching) and multi-photon microscopy to examine collagen organization; re-alignment and recruitment. Overall goal — to examine how ECM components (collagen) contribute to mechanical behavior of the bladder in aging.
Collagen fibers are oriented differently through the bladder wall

ECM (collagen): mucosal fibers are more uniform versus SM fibers

Mucosal versus muscle ECM (collagen) fibers exhibit different responses to mechanical loading (stretch)
Stretch-induced collagen (orientation/recruitment) is altered in aging bladder.

The ECM ‘stiffness’ can be modulated in disease and aging.
Vascular changes (ischemia) often accompany the development of fibrosis.

Lower Urinary Tract Symptoms (instability, impaired contractility, changes in bladder volume and flow rate) - can increase in frequency with age.

Underlying mechanisms can include changes in blood flow and oxidative stress - this can impact neuronal and non-neuronal targets.
The ECM balances mechanical loads throughout the bladder wall (involved in structural support; cellular function).

Differences in mucosal/SM collagen orientation/recruitment - suggest different roles in bladder health and disease.

Aging alters remodeling of vasculature and ECM proteins (ECM fibers may break, thicken, stiffen, clump together and lose elasticity with increased stretch).

Additional studies may lead to insights into biomechanical properties of the bladder wall and how sensory properties may be altered in aging.