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Cyclic Stretch Regulates Matrix Metalloproteinases and Cathepsins in Aortic Valve Leaflets in a Magnitude Dependent Manner

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Objectives:

The hemodynamic environment of the aortic valve is known to play a key role in its continual remodeling. Recent studies have shown that cyclic stretch upregulates collagen synthesis in both valve cells and valve tissue. This study aims at identifying the enzymes involved in the remodeling of aortic valves in response to different levels of cyclic stretch.

Method:

10x15mm segments were isolated from the belly region of porcine aortic valve cusps, and were subject to 10% stretch for 120 hours under: (i) normal DMEM (control); (ii) DMEM with 10⁻⁶M 5HT; and (iii) DMEM with 10⁻⁴M 5HT, and statically incubated under: (iv) DMEM; and (v) DMEM with 10⁻⁴M 5HT. Total soluble collagen content within samples was analyzed using a Sircol collagen assay. Anti-brDu immunostaining was used for cell proliferation.

Results:

Protease expression and activity at 10% stretch was not significantly different compared to fresh controls for all the matrix proteases. MMP-1 expression increased 1.5-fold, while MMP-2 expression increased 2-fold. MMP-1 and -2 activities showed a magnitude-dependent response peaking at 20% stretch. Cathepsin L was most significantly increased under cyclic stretch compared to S and K. A magnitude-dependent response was observed for the cathepsins as well.

Conclusions:

These studies demonstrate that cyclic stretch regulates the remodeling activity of MMPs and cathepsins in a stretch-magnitude dependent manner, resulting in increased turnover of matrix proteins. These results could offer insights into degenerative valve disease observed under hypertension.