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ARTICLE

POSTER ABSTRACT PRESENTATIONS
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Abstract P332: Microfluidic Model Of Late-stage Calcific Aortic Valve Disease Develops Calcium Phosphate Mineralizations

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Abstract

Introduction: Calcific aortic valve disease (CAVD) is an active pathological process leading to severe valve calcification. Late-stage CAVD is characterized by increased leaflet stiffness, disorganized collagen bundles and the deposition of glycosaminoglycans, such as chondroitin sulfate (CS), in the fibrosa layer. However, many details of the cellular pathological cascade remain unknown. Animal models such as mice, rabbits, and pigs are used in understanding human CAVD, but mice do not have similar anatomy, rabbits cannot spontaneously develop atherosclerotic lesions, and pigs require long, expensive and complex studies. Here we utilize microfluidic devices of the aortic valve fibrosa to model late-stage CAVD.

Hypothesis: We assessed the hypothesis that microfluidic calcification will increase with increased shear rates and CS content.

Methods: Valve-on-a-chip devices contained a hydrogel of 1.5 mg/mL collagen I-only healthy controls or 1.5 mg/mL collagen I with 1 mg/mL or 20 mg/mL CS. Porcine aortic valve interstitial cells (PAVIC) were embedded within and endothelial cells (PAVEC) were seeded onto the matrix. Steady shear stress at 1 dyne/cm^2 and 20 dyne/cm^2 were applied using a peristaltic pump for 14 days. Alizarin Red S (ARS), an assay to assess calcium deposition, was used to quantify calcific nodule formation. Scanning electron microscopy with energy dispersive x-ray (SEM/EDX) was used to further analyze sample mineralization.

Results: Co-cultures in the presence of increasing shear stress and CS exhibit increased calcific nodule formation compared to static controls, both qualitatively and quantitatively (n≥3). SEM revealed the microstructure of calcified nodules and EDX confirmed calcium phosphate mineralization with physiologically-relevant calcium to phosphorous ratios (Ca/P= 0.88 - 1.4).

Conclusions: These results show that *in vitro* calcification is driven by shear stress in the presence of PAVEC and CS. As seen in *ex vivo* studies of human calcification, these microfluidic-derived nodules are similarly composed of a range of naturally-occurring calcium phosphates. Given that CAVD has no targeted therapy, the creation of a physiologically relevant model of the aortic valve can provide a test bed for novel therapeutic interventions.

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Footnotes

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