

#### **P14. Bone Morphogenic Protein Pathway Activation In Sclerotic Human Aortic Valves**

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**OBJECTIVES:** Aortic valve disease is a major cause of cardiac-related deaths globally and is a strong risk factor for additional cardiovascular events. While gross pathological changes and surgical treatments of the diseased valves have received much attention, the molecular mechanisms underlying aortic valve inflammation, calcification and subsequent valve dysfunction are not well understood and remain vastly understudied. Here, we tested the hypothesis that BMPs and BMP antagonists are differentially expressed in the ventricularis and fibrosa endothelium, and that their expression changes as the AV disease develops.

**METHODS:** Both sclerotic and non-sclerotic aortic valves were used in this study; Sclerotic AVs were obtained from valve replacement surgeries while non-sclerotic AVs were obtained from heart transplant surgeries. All AVs were frozen, sectioned and stained with antibodies specific to TGF- $\beta$ 1, BMP2, BMP4, BMP6, BMP antagonists (Crossviesless2, Chordin, Follistatin, or Noggin), or phosphorylated SMAD 1/5/8 or phosphorylated SMAD 2/3.

**RESULTS:** In both sclerotic and non-sclerotic cusps the BMPs were expressed on both the fibrosa and ventricularis endothelium with a 1.5- to 2-fold increase expression on the ventricularis. No difference was seen when staining for TGF- $\beta$ 1 in the endothelium. The BMP antagonists were primarily expressed on the ventricularis endothelium with 2- to 3-fold increases when compared to the fibrosa endothelium. Finally, an increase in phosphorylated SMAD 1/5/8, a marker for activation of the BMP pathway, was observed on the fibrosa of sclerotic cusps when compared to non-sclerotic cusps and the ventricularis of sclerotic cusps.

**CONCLUSIONS:** These results suggest a possible mechanism by which side-specific AV disease occurs.