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Bone Morphogenic Proteins and Their Antagonists in Human Aortic Valve Disease

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Objectives:

Aortic valve (AV) diseases preferentially occur in the fibrosa side, which is exposed to unstable hemodynamic conditions. DNA microarray studies carried out using normal porcine AV or pig AV endothelial cells showed bone morphogenic protein-4 (BMP4) is downregulated by laminar shear (LS), while a BMP antagonist chordin is upregulated in the ventricularis endothelium. Here, we tested the hypothesis that BMPs and BMP antagonists are differentially expressed in the endothelium of ventricularis and fibrosa, and that their expression changes as the AV disease develops.

Method:

Human AVs were obtained from two sources: Diseased human AVs were harvested from AV replacement patients, while non-diseased human AVs were obtained from heart transplantation patients. Collected AV's were frozen, sectioned, and stained with antibodies to BMP4, BMP6, and three BMP antagonists (CV2, noggin, DAN and follistatin).

Results:

In both diseased and non-diseased human leaflets, endothelial BMP4 and BMP6 expression was not significantly side-specific. In non-diseased human AV leaflets, similar levels of CV2 and DAN were expressed on both sides of the leaflet. In diseased AV leaflets, however, CV2 and noggin levels were significantly lower in the fibrosa endothelium compared to the ventricularis.

Conclusions:

These results indicate a positive correlation between the decreased BMP antagonists in fibrosa endothelium and AV calcification. The balance between the BMPs and their antagonists may play an important role in the development of AV calcification, and could be considered as a target of diagnosis and treatment of the AV disease.