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Ascending aorta phenotypic and genotypic changes in bicuspid aortic valve disease

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Bicuspid aortic valve (BAV) with left-right (L-R), right-non coronary (R-NC) and left-non coronary (L-NC) cusp fusion represents distinct pathological entities and the rate of aortic enlargement varies according to the pattern of cusps fusion [1]. Here, we investigated the histological features of aneurysms associated to different BAV phenotypes and we looked for specific microRNAs (miRNA) as biomarkers of medial degeneration severity.

Aortic specimens and blood were obtained from BAV patients treated surgically for the repair of thoracic aortic aneurysm and were divided into two groups: low grade medial degeneration (LGMD, n=10); high grade medial degeneration (HGMD, n=10). A control group (CN, n=10), with tricuspid aortic valve not associated to aortopathy, was also involved in the study. We performed commonly used morphological staining to evaluate medionecrosis, fibrosis, elastic fragmentation and mucoid material accumulation. We detected MMP9 and MMP2 immunoreactivity and tunel assay. Moreover, we measured the expression patterns of miR-122, miR-130, miR-718, miR-486 by RT-qPCR.

MMP2 and MMP9 expression increased in HGMD compared to LGMD and control group. Apoptotic cells were observed in the sub intimal region of the media in HGMD group. The expression levels of miR-718 and miR-122 in aortic specimens significantly decreased in LGMD and HGMD groups compared to CN and negatively correlated with the ascending aorta wall score. Moreover, the expression levels of miR-130 significantly decreased in LGMD group compared to CN. HGMD group showed a significant increase of miR-486 expression levels compared to CN and LGMD. Plasma expression levels of miR-718 significantly decreased in LGMD compared to CN. Interestingly, miR-486 expression levels significantly increased in HGMD group compared to the CN and positively correlated with the ascending aorta wall score.

Our work suggests miR-718 and miR-486 might be considered as new non-invasive biomarkers of aorta wall degeneration in BAV due their association with the morphological features of the vessel. A significant dysregulation of these biomarkers might be associated with high risk of dissection and rupture.

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References

- [1] Pisano et al. (2012) Histological and genetic studies in patients with bicuspid aortic valve and ascending aorta complications. *Interact Cardiovasc Thorac Surg* 14:300-6.

Key words

BAV disease, microRNA.