Aortopathy in patients with a bicuspid aortic valve : determining susceptibility for aortic complications

Grewal, N.

CHAPTER

3A

Editorial: The aortic wall with bicuspid aortic valve: immature or prematurely ageing?

Commenting on the paper by Grewal N et al. "Ascending aorta dilation in association with bicuspid aortic valve: a maturation defect of the aortic wall"

Amalia Forte[1], Alessandro Della Corte[2]

[1] Department of Experimental Medicine, Second University of Naples, Naples, Italy
[2] Cardiothoracic and Respiratory Sciences, Second University of Naples, Naples, Italy

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Dear Editor,

We read with interest the study (1) by Grewal and co-workers, suggesting a maturation defect of the aortic wall in patients with bicuspid aortic valve (BAV). A number of recent publications have addressed the pathobiology of BAV-associated aortopathy, however most of them just vaguely concluded that BAV and tricuspid aortic valve (TAV) must have different mechanisms driving aortic dilatation. Grewal *et al.* are commendable for their effort to define the nature of this difference.

However, their data are partially in contrast with previous studies, with which they failed to perform a critical comparison. We have reported (2) increased α-smooth muscle actin (α-SMA) mRNA expression and only mildly and non-homogenously increased overall protein levels, with sub-intimal areas of α-SMA-positive cell loss. This relative stability of the amount of α-SMA (in contrast with Grewal's data) coupled with smoothelin decrease (not absence, unlike in Grewal's results) was consistent with other studies both on samples from patients and on experimental models of aneurysm (discussed in our paper (2)), and suggests a loss of contractile-phenotype SMCs and the emergence of a differentiated myofibroblast line.

In our abovementioned study (2), to minimize confounding factors, we selected BAV and TAV aortic stenosis patients with maximal diameter <4 cm, and analysed both the concavity and the convexity of the vessel, to distinguish constitutive from stress-induced changes. Some of Grewal's co-Authors have previously borrowed in their studies this protocol of sample retrieval from different sites of each aorta, first introduced by us (3), and confirmed that aortic wall changes are asymmetrically expressed with BAV, suggesting a role for longstanding flow and stress pattern alterations in their development. The change of SMC orientation from circumferential to longitudinal direction we observed in the convexity (2) is known to occur in vessels submitted to altered tensile strain. The undefined site of sampling in the present study (1), conversely, could explain the above discrepancies. Similarly, the authors stated that the aortic wall specimens were obtained during full-root stentless implantation in non-dilated BAV patients (1), suggesting that the BAV specimens were taken from the root (sinuses of Valsalva) instead of the ascending tubular tract proper.

Where were the aortic specimens taken in the other patients, also considering that BAV aortopathy usually affects the ascending tract?

How was valve function in the four groups? Also, the mean diameters per subgroup were not acknowledged (1). Intimal thickness data (1) were at odds with previous investigations (2,4): could different diameters between BAV and TAV subgroups explain this?

The paradigms of flow-induced remodeling share many mechanisms with the vascular ageing process, including increased TGF-β receptor-II signalling (5), which has been evidenced in both BAV-associated and non-BAV-associated aortopathies (2). Functionally, one of the early signs of arterial ageing is impaired wall distensibility, which is known to occur in the BAV aorta, even before overt dilation. Thus, with the currently available data, an hypothesis of defective wall maturation is hardly sustainable, without ruling out the contribution of flow induced remodeling: a conceptually opposite theory of premature ageing of the aortic wall, prompted by altered biomechanical environment, could be drawn as well.

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