Missing link between aortic wall pathology and aortic diameter: methodological bias or worrisome finding?

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We read with appreciation the article by Leone et al. [1], reporting absent correlation between aortic diameter and degree of medial degeneration (MD) in a surgical cohort of bicuspid aortic valve (BAV) patients. Thirty-eight per cent of patients with aortic diameter ≤4.5 cm had moderate or severe histological alterations, and this highlighted the limitations of the dimensional criterion currently adopted to risk-stratify BAV aortopathy patients.

However, the authors failed to comment on another equally important finding: absent/mild MD was found in >60% patients undergoing ascending aorta replacement, according to official guidelines or intraoperative macroscopic appearance of the aortic wall [1]. Before considering the consequences of this finding, methodological issues should be ruled out: first, the site of sample retrieval might have been a confounding factor. BAV aortopathy can assume different anatomo-clinical phenotypes, each likely subtended by distinct pathogenesis: in an outpatient setting, we distinguished 14% BAV patients (young men, aortic regurgitation) with ‘root-dilatation phenotype’ (enlargement of the sinuses of Valsalva) from another 70% (older age, women, BAV stenosis) with supracoronary dilatation [2]. In a purely surgical series, frequencies can be different; moreover, even in case of initial root localization the disease can extend to the more distal tracts, including the arch, as it progresses, adding to phenotypic variability [3]. How many patients in Leone’s study had a root-dilatation phenotype? The authors stated that six samples were obtained from different sites [1]: did these encompass sinuses and the ascending tract in all patients? Was MD grading performed only in the specimens from the level of maximal diameter? Otherwise, if the reported grades were averaged among the six sites (which would explain the absence of grade 4 cases), the results might be biased.

Although we agree with the choice of excluding atherosclerotic changes from the grading criteria, atherosclerotic lesions should have been separately accounted for, as they could subtend some dilatations showing absent/mild MD: notably, the prevalence of low grades increased with age [1]. Moreover, by using histology alone, without histochemical and biomolecular insights, more subtle cell alterations and extracellular matrix changes might have been overlooked. In our ongoing research...
on BAV aortas with mean diameter as small as 3.9 cm, gene expression analysis is revealing significant alterations in resident cell phenotype and transforming growth factor-beta signalling (unpublished data).

Most likely, the authors’ results were only in part affected by the above flaws, and therefore they deserve serious consideration, as the alarming evidence is presented that we are currently unable to non-invasively detect aortopathy without dilatation, but also we currently replace, according to guidelines, a number of aortas with absent/mild histological alterations! Are those aortas really at risk of dissection or fast growth? Words of caution were recently issued about the current aggressiveness in prophylactic aorta replacement for BAV disease [3, 4].

The paper by Leone et al. [1], as well as our most recent research [5], underscores the need for further investigation on the pre-surgical stages of BAV aortopathy, to identify early predictors of aortic dilatation/dissection, including functional (rather than merely dimensional) imaging measurements [5] and humoral biomarkers [6].

REFERENCES


LETTER TO THE EDITOR RESPONSE

Reply to Della Corte et al.

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We thank Dr Della Corte et al. for their interest in our paper ‘The elusive link between aortic wall histology and echocardiographic anatomy in bicuspid aortic valve: implications for prophylactic surgery’ [1, 2].

(1) Clearly, the absence of correlation between echocardiographic and histological findings (which is the main result of our paper) has two consequences: part of the patients without severe ascending aortic dilatation has advanced histological abnormalities, whereas part of the patients with aortic dilatation leading to surgical intervention lacks histological abnormalities. In our cohort of patients, 18 (14%) had root dilatation (dilatation isolated or prevailing at the sinusal portion), a percentage similar to that reported in Della Corte et al.’s paper [3].

(2) Regarding the site of sample retrieval, the retrospective nature of the paper did not allow us to perform targeted sampling and aortic samples were randomly obtained from the ascending aortic tract, distally to the sino-tubular junction. Additionally, the samples were not oriented or targeted at the level of maximal diameter.

(3) Finally, we confirm that all patients with advanced atherosclerotic lesions were excluded from this study. Only patients with minor atherosclerotic lesions (including adaptive intimal thickening, intimal xanthoma, pathological intimal thickening or early and small fibroatheroma) were included, according to the morphological classification of the atherosclerotic lesions by Virmani et al. [4] and more recently by Van Dijk et al. [5]. It is highly improbable that these lesions can have significant consequences on the medial layer structure.

REFERENCES


Aortic coaptation in repair

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Thanks to the authors for their article, which teaches us many things [1]. Because the reoperation rate is 10% in the long-term results, we searched and came to the conclusion that, in remodelling and subvalvular annuloplasty, the durability of leaflets worsens due to the inability of aortic expansion [2]; for this reason, the durability of the leafllets should be enhanced.

In the supracoronary graft + annuloplasty method, the expansion property of the aorta is lost [2] and so the flow becomes turbulent due to the expandable ring. This situation begets aneurysm, dissection and leafllet destruction in the graft-free part.

The expandable ring causes turbulent flow. The shape and angular difference in time causes an increase in the turbulent flow.

There are two factors influencing aortic leaflet coaptation:

(i) Microscopic and biochemical structures that prevent leafllet prolapsus [3]
(ii) Aortic commissures are located distally to the leafllet coaptation plane (suspension bridge).

In the subvalvular annuloplasty method, although the ring is expandable, in systole it prevents the aortic root from expanding and thus causes the turbulent flow. This will lead to aneurysm, dissection and deterioration in the leafllet structure.

In cusp remodelling, the diameter of the ring should be carefully calculated. If the ring diameter is greater than the aortic diameter, then shear stress will develop, resistance will occur or in every systole leafllet sail. This will disrupt the leafllet structure.

Reoperation due to leafllet prolapsus in eight patients made us consider it a sign of inadequate leafllet durability.

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We thank Bozok et al. for their comment on our results of aortic valve repair using an aortic ring [1-2]. Reoperation rate was 5.5% (8/144). Intraoperative findings at reoperation were cusp prolapse in all cases, without macroscopic lesions on cusp tissue. As other authors have, we showed that resuspension of cusp effective height should be performed intraoperatively in all cases of aortic valve repair [3-5], which was not the case for the eight reoperated patients in our study. Further analysis showed that ‘repair with gross visual estimation’ repair and absence of per operative effective height resuspension (using Schäfers et al. [4] calliper) were an independent risk factor of reoperation and residual AI ≥ grade II at follow up [5]. The systematic intraoperative resuspension of cusp effective height increased dramatically the rate of cusp repair (70.6 versus 20.3%, \( P < 0.001 \)) and improved significantly the preliminary results since there was no reoperation or AI ≥ grade II at 1-year follow-up [5].

Remodelling of the aortic root offers a physiological reconstruction of the root. Cusp motion and flow patterns across the reconstructed aortic root are more physiologic (1) after remodelling of the aortic root than after reimplantation of the aortic valve, and (2) after procedures using a prosthetic conduit fashioned with neo-sinuses of valsalva than without. However, contrarily to the reimplantation, the remodelling technique does not address the annular base dilation.

Our physiological approach of aortic valve repair is based on reduction in dilated root diameters (aortic annular base through a subvalvular aortic annuloplasty ring and STJ through remodelling of the aortic root); respect of root dynamics (expansibility through the interleaflet triangles and restoration of sinuses of Valsalva) and restoration of cusp coaptation height (measurement of the effective height).

In these series, a Dacron prototype of aortic ring was used. It allowed us to obtain a significant reduction in dilated aortic annular base diameter, without significant transvalvular aortic gradient. To address the need for a dedicated aortic annuloplasty device to facilitate technical standardization, we designed a new expandible aortic ring to achieve complete and calibrated annuloplasty in diastole, while maintaining the systolic expansibility of the aortic root [6]. As such, the cusp coaptation height is increased, reducing stress on the cusps and protecting the repair.

A standardized and physiologic approach to aortic valve repair, considering both the aorta (root remodelling) and the valve (resuspension of the cusp effective height and subvalvular ring annuloplasty), improved the preliminary results and might affect their long-term durability.

REFERENCES