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# Pattern of Ascending Aortic Dimensions Predicts the Growth Rate of the Aorta in Patients With Bicuspid Aortic Valve

Alessandro Della Corte, MD, PhD,* Ciro Bancone, MD, PhD,* Marianna Buonocore, MD,* Giovanni Dialetto, MD,* Franco E. Covino, MD,* Sabrina Manduca, MD,* Giancarlo Scognamiglio, MD,† Veronica D'Oria, MD,* Marisa De Feo, MD, PhD*
*Naples, Italy*

**OBJECTIVES** This study sought to identify risk factors for rapid growth of the ascending aorta in patients with bicuspid aortic valve (BAV) disease, taking into account its phenotypic variability.

**BACKGROUND** Phenotypic heterogeneity of BAV-related aortopathy has recently been widely recognized. However, few studies have addressed the determinants of aortic growth so far, not distinguishing among morphological phenotypes.

**METHODS** Serial retrospective data on 133 adult outpatients with BAV undergoing echocardiographic follow-up were analyzed to search for factors associated with aortic diameter growth over time and with rapid aortic growth (fifth quintile of growth rate distribution), focusing on the impact of different valve morphotypes (i.e., cusp fusion pattern: right-left coronary [RL] and right-noncoronary [RN]) and previously defined aortic phenotypes (nondilated aorta, ascending dilation, root dilation).

**RESULTS** The RL pattern was present in 69% of patients with BAV and RN in 31%. At baseline, an ascending dilation phenotype was observed in 57% of patients and a root phenotype in 13.5%. No patient with RN-BAV had a root dilation phenotype at either baseline or last examination. Follow-up time averaged 4.0 $\pm$ 2.7 years (535 patient-years). The mean growth rate was 0.3 mm/year at the sinuses and 0.6 mm/year at the ascending level. Aortic regurgitation predicted an increase in ascending diameter over time (odds ratio [OR]: 2.3; $p = 0.03$). Root phenotype at presentation, not absolute baseline diameter, was an independent predictor of fast progression (>0.9 mm/year) for the ascending tract (OR: 14; $p = 0.001$). Fast growth was rarely seen in patients with the RL morphotype and ascending phenotype (6% at the root and 10% at the ascending level).

**CONCLUSIONS** In patients with BAV, the root phenotype (aortic dilation predominantly at the sinuses, with normal or less dilated ascending tract) may be a marker of more severe aortopathy, warranting closer surveillance and earlier treatment. The more common ascending phenotype proved to be a more stable disease entity, generally with slower progression. (J Am Coll Cardiol Img 2013;6:1301–10)


From the *Cardiac Surgery Unit and Echocardiography Service, Department of Cardiothoracic Sciences, Second University of Naples, V. Monaldi Hospital, Naples, Italy; and the †Cardiology Unit, Department of Cardiothoracic Sciences, Second University of Naples, V. Monaldi Hospital, Naples, Italy. Funded by a "Ricerca Finalizzata" grant (GR09-1580434) from the Italian Ministry of Health. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Although first pointed out as early as 1999 (1), the heterogeneity of bicuspid aortic valve (BAV) in terms of aortopathy risk and features remain often disregarded, both in research and clinical guidelines (2,3). The natural course of bicuspid aortopathy can vary, ranging from indolent aortic diameter growth to rapid progression or earlier occurrence of life-threatening aortic complications (4,5). So far, no established risk marker is available to help define the prognosis of aortopathy in individual patients with BAV, especially in terms of expected rapidity of aortic growth.

Two sources of BAV disease heterogeneity are the morphology of the aortic valve and the shape of the aorta. Valve morphology has been classified by Sievers and Schmidtke (6) according to the number of cusps and the pattern of congenital cusp fusion. The 2 most frequent morphotypes are believed to have distinct underlying developmental defects and to potentially imply different risks and features of aortopathy (7). There is no consensus classification of the shapes that a dilated or aneurysmal ascending aorta can assume; the use of different criteria and imaging methods has led to diverging nomenclature (8–10). In 2006, based on the analysis of 552 patients with aortic dilation, we suggested the distinction between a "root type" of dilation (i.e., with sinuses of Valsalva enlarged to a greater extent than the tubular portion) and an "ascending type" (i.e., dilation predominantly located distal to the sinotubular junction [STJ]) (11). Subsequently, the distinction between root phenotype and ascending phenotype has been adopted in several studies on BAV (8,12,13). Of note, the smooth muscle cells in the sinus portion embryologically derive in part from the secondary heart field, whereas those in the tubular tract originate from the neural crest (14).

**ABBREVIATIONS AND ACRONYMS**

**AR** = aortic regurgitation
**BAV** = bicuspid aortic valve
**MVP** = mitral valve prolapse
**RL** = right-left coronary
**RN** = right-noncoronary
**STJ** = sinotubular junction

The aim of the present retrospective longitudinal study was to assess the determinants of bicuspid aorta growth rates over time, focusing on the possible impact of valve morphotypes and aortic phenotypes on the progression of the aortopathy.

## METHODS

**Patient cohort.** Our echocardiography database was reviewed to select serial examinations performed in outpatients with isolated BAV. Forty-eight percent of patients were first referred for symptoms, 24% for radiological evidence of increased aortic diameter, 22% were known to have a "congenital murmur," and none had been previously followed up systematically. We also included patients with undefined valve morphology at pre-operative serial echocardiography (usually for severely calcific stenosis) but who later received intraoperative inspective and pathology diagnosis of congenital BAV. Exclusion criteria were unicuspid aortic valve, associated significant congenital or acquired cardiac diseases (e.g., moderate or worse dysfunction of another valve, endocarditis, coarctation), systemic syndromes (e.g., Marfan, Loeys-Dietz, Ehler-Danlos, Turner), and previous cardiac surgery. From a total of 726 echocardiograms recorded between January 2000 and May 2011 in 150 outpatients with BAV who fulfilled the inclusion/exclusion criteria, 716 were serial examinations in 143 patients with at least 1 year of follow-up. Three patients were then excluded because of left-coronary to noncoronary leaflet fusion (the rare left-noncoronary morphotype); another 7 were excluded because of pediatric age at presentation. The definitive study group included 133 patients (age range 18 to 77 years). The study conformed to the Declaration of Helsinki and received local institutional review board approval.

**Variables.** Three experienced operators performed all echocardiographic examinations. Aortic stenosis severity was graded by integration of Doppler methods, continuity equation, and planimetry; aortic regurgitation (AR) degree was defined by composite evaluation of proximal jet width, abdominal aortic Doppler imaging, and left ventricular end-diastolic dimension (15,16). Bicuspidy of the aortic valve was defined by a systolic fish-mouth appearance of the orifice in parasternal short-axis views (1). Valve morphotype (i.e., the pattern of cusp fusion) was categorized as right-left coronary (RL) (fusion between right and left coronary cusps) or right-noncoronary (RN) (between right and noncoronary cusps) (6). Initially doubtful definitions of the morphotype (37 patients) were resolved by collegial review, cardiac magnetic resonance, or 3-dimensional echocardiography.

The aorta was measured twice (inner-edge to inner-edge method) by bidimensional imaging in parasternal long-axis views at the root (maximal dilation of the sinuses of Valsalva), STJ, and ascending aorta (at its maximal diameter). The tubular tract was routinely visualized as much distally (at least 2 to 3 cm) to the STJ as possible. A random sample of 55 examinations was repeated by a blinded operator, showing good reproducibility (Spearman's r between 0.88 and 1.0 and Bland-Altman p values $>0.05$). For each patient, the expected normal aortic