The bicuspid aortic valve (BAV) is the most common congenital cardiac malformation. Despite being a seemingly simple and harmless anatomic variation, BAV is said to cause more morbidity than any other congenital cardiac defect [52]. BAV may lead to aortic valve stenosis (AS) or regurgitation (AR), endocarditis, an ascending aortic aneurysm, and/or devastating dissection or rupture. Although these potential consequences of BAV were first described long ago [19, 35, 36], only recently have clinicians become fully aware that the presence of a BAV poses a serious health risk. However, the so-called bicuspid aortic valve syndrome [14] is extremely heterogeneous with some patients having rapidly progressive valve and/or aortic disease, while some individuals with BAV remain free of complications throughout their lifetime. In this article, we review current concepts regarding etiology, pathomechanisms, diagnosis, and treatment of BAV with special emphasis on topics relevant for cardiac surgeons.

Etiology

Despite intensive research during recent years, the etiology and mechanisms leading to congenital BAV remain largely unknown. The process of valvulogenesis is complex and begins early during development of the heart [25]. Endothelial-mesenchymal transformation of the endocardium leads to development of endocardial cushions in the outflow tract and in the atrioventricular canal. All four valves are formed from elongations of the endocardial cushions, but cells from the neural crest appear to contribute to the development of the semilunar valves [22–24]. Experiments in Syrian hamsters indicate that a BAV does not result from fusion of two normally developed cusps, but from failure of the anlagen of the three cusps to separate [42]. Thus, involvement of genes and molecular mechanisms responsible for separation and further differentiation of the valve cushions in the etiology of BAV appears likely – and this may include genes encoding transcription factors, extracellular matrix proteins or signaling pathways that regulate cell proliferation, apoptosis, or differentiation. As
such, the Notch signaling pathway, which is extremely conserved evolutionarily and contributes to the differentiation of various organs, has come into the focus of research. Several mutations in the NOTCH1 gene have been described in association with BAV [18, 28], but other chromosomal loci and genes have also been linked to BAV [12, 26, 29]. Thus, BAV syndrome appears to be heterogeneous not only with regard to the clinical phenotype, but also with respect to molecular and cellular events. It is tempting to hypothesize that BAV syndrome is the final common pathway for a variety of genetic defects. This would also serve as an explanation for associated cardiac and vascular malformations (displaced left coronary ostium, short left main artery; malalignment and dilatation of the noncoronary sinus; ventricular septal defect; ascending aortic aneurysm; coarctation of the aorta or aortic interruption; patent ductus arteriosus) which are often, but not always found.

Prevalence

The prevalence of BAV is usually given as 1–2%. This estimation is mainly based on older autopsy series [37], whereas most [20, 30, 33, 50], but not all [49] more recent echocardiographic studies suggest a prevalence of 0.5–1.0%. However, although three of these studies examined echocardiograms from more than 20 000 individuals, none of the studies was population-based. Men are usually found to be more frequently affected than women, but this is not consistent in all studies [21, 38].

While most cases of BAV appear to be sporadic, there is strong evidence of heritability in some families [7, 21]. These findings are often interpreted to show autosomal dominant inheritance with reduced penetrance [15, 17]. Screening of first-degree relatives of patients seems advisable – and is mandatory in relatives of patients who suffered aortic complications.

Diagnosis

Today, the diagnosis of BAV can usually be made with high reliability using echocardiography. It is essential to study the valve in both systole and diastole, as a tall raphe may be mistaken for a commissure. The systolic appearance is less deceptive as a BAV will show a characteristic abnormal fishmouth opening. However, in heavily calcified valves – either bicuspid or tricuspid – the echocardiographic appearance will be so abnormal that the number of cusps cannot be determined.