Genetic and personalized approach to valvular heart disease

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Valve diseases have a large share in the total morbidity and mortality of the adult population, and can be congenital or acquired. The last few decades have seen a predominance of degenerative (calcified) heart valve diseases due to a prolonged life expectancy in economically developed countries. The therapeutic approach has remained unchanged and in the case of severe dysfunction, the valve is replaced with a mechanical or biological prosthesis, balloon valvuloplasty or valve reconstruction. The findings in understanding the development of heart valves along with human genome sequencing have led to the discovery of a genetic basis in valvular diseases[1]. Also, there are numerous evidence to suggest that heart valve diseases which develop in adulthood has its source in embryonic development. In this review authors will display the genetic basis of the two most common inherited valvular diseases: bicuspid aortic valve and mitral valve prolapse, as well as a review of the findings suggesting a genetic contribution to calcified aortic valve disease[2]. In addition, this review will include a review of the guidelines and benefits of genetic testing, as well as highlight the need to include genetic counseling in families with proven or suspected malformations. Linking genetic information to the clinical phenotype (**Table 1**) and potential outcomes of surgical treatment leads to a personalized approach to each patient[3].

TABLE 1. Gene mutations associated with valvular heart disease.

	Location	Gene	Inheritance	Phenotype
Bicuspid aortic valve				
Syndromic	17q24.3	*KCNJ2*	AD	Andersen syndrome
Nonsyndromic	9q34.3	*NOTCH1*	AD	AOVD1
	20q13.33	*GATA5*	AD, AR	CHTD5
	15q22.31	*SMAD6*	AD	AOVD2
	11q24.2	*ROBO4*	AD	AOVD3
Mitral valve prolapse				
Syndromic	15q21.1	*FBN1*	AD	Marfan syndrome
	9q22.33	*TGFBR1*	AD	Loeys-Dietz syndrome 1
	3p24.1	*TGFBR2*	AD	Loeys-Dietz syndrome2
	7q21.3, 12q13.1, 2q32.2,9q34.3	*Collagen types I–III, V/ XI*	AR,AD AD,AD	OI 1,Ehlers-Danlos syndrome, cardiac valvular type
Nonsyndromic	Xq28	*Filamin A*	XL	Cardiac valvular dysplasia
Aortic valve stenosis				
CAVD	9q34.3	*NOTCH1*	AD	AOVD1

AD – autosomal dominant, AR – autosomal recessive, AOVD – aortic valve disease, CHTD – congenital heart disease, OI – osteogenesis imperfecta, XL – X-linked, CAVD - calcified aortic valve disease.

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