

**Cardiovascular malformation spectrum of CHD7 mutations in CHARGE syndrome**

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**BACKGROUND:** CHARGE syndrome consists of a combination of congenital malformations including coloboma, heart defects, atresia of choanae, retardation of growth and developmental delay, genital anomalies and ear/semi-circular canal anomalies. A mutation of CHD7 is found in 70 % of CHARGE patients. Cardiovascular malformations are considered a minor criterion for diagnosis because of lack of specificity.

**OBJECTIVES:** Study the panel of congenital heart defects (CHD) among CHARGE patients with a CHD7 mutation; discuss genotype-phenotype correlation and embryological basis of cardiovascular malformations.

**METHODS:**

We report on the spectrum of cardiovascular malformations in 75 CHARGE patients (including 15 fetuses) with CHD7 mutation. Cardiovascular phenotype was precisely assessed by echocardiography, catheterization and CT scan.

**RESULTS:** Sixty-five CHARGE patients with CHD7 mutation (87%) have a CHD. Conotruncal malformations (25%), and atrioventricular septal defects (23%), are the most common. Aortic arch anomalies associated or isolated occur frequently. A rare association of atrioventricular septal defect and discordant ventriculo-arterial connections is described in 2 patients. Our data suggest that hypomorphic mutations are less frequently associated with a heart defect than nonsense and frameshift mutations.

**CONCLUSIONS:** Congenital heart defects are a frequent feature of CHD7 mutated CHARGE patients. The broad observed panel suggests the involvement of neural crest cell as well as cardiac progenitor cells of the second heart field and endocardium in embryological mechanisms leading to CHDs in CHARGE syndrome. More cardiac regulator genes have yet to be identified as potential targets of CHD7.