Association between phenotype and deletion size in 22q11.2 microdeletion syndrome: Systematic review and meta-analysis

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Background: Chromosome 22q11.2 microdeletion syndrome, a disorder caused by heterozygous loss of genetic material in chromosome region 22q11.2, has a broad range of clinical symptoms. The most common congenital anomalies involve the palate in 80% of patients, and the heart in 50-60% of them. The cause of the phenotypic variability is unknown. Patients usually harbor one of three common deletions sizes: 3, 2 and 1.5 Mb, between low copy repeats (LCR) designated A-D, A-C and A-B, respectively. This study aimed to analyze the association between these 3 deletion sizes and the presence of congenital cardiac and/or palatal malformations in individuals with this condition. A systematic review and meta-analysis were conducted, merging relevant published studies with data from Chilean patients to increase statistical power. Results: Eight articles out of 432 were included; the data from these studies was merged with our own, achieving a total of 1514 and 487 patients to evaluate cardiac and palate malformations, respectively. None of the compared deleted chromosomal segments were statistically associated with cardiac defects (ORAB v/s AC-AD: 0.654 [0.408-1.046]; OR AD v/s AB-AC: 1.291 [0.860-1.939]) or palate anomalies (ORAB v/s AC-AD: 1.731 [0.708-4.234]; OR AD v/s AB-AC: 0.628 [0.286-1.382]). Conclusions: The lack of association between deletion size and CHD or PA found in this meta-analysis suggests that deletion size does not explain the incomplete penetrance of these 2 major manifestations, and that the critical region for the development of heart and palatal abnormalities is within LCR A-B, the smallest region of overlap among the three deletion sizes.

Chromosome 22q11.2 deletion syndrome

Congenital heart defects

DiGeorge syndrome

Meta-analysis

Palate anomalies

Systematic review

Velocardiofacial syndrome

aortic arch interruption

Article

Chilean

chromosome deletion 22q11

cleft lip palate

cleft palate

congenital heart disease

disease course

Fallot tetralogy

gene deletion

genetic association

heart atrium septum defect

heart right ventricle double outlet

heart ventricle septum defect

human

palate malformation

palatopharyngeal incompetence

phenotype

pulmonary valve atresia

segmental duplication

systematic review

arachnodactyly

chromosome deletion

craniofacial synostosis

genetics

Marfan syndrome

meta analysis

phenotype

Arachnodactyly

Chromosome Deletion

Craniosynostoses

Humans

Marfan Syndrome

Phenotype