DETERMINING THE CONTRIBUTION OF NPR3 VARIANTS TO HYPERTENSION IN TREATED COARCTATION OF THE AORTA PATIENTS

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Background

Coarctation of the aorta (CoA) consists of a constriction in the proximal descending thoracic aorta, which often causes elevated blood pressure (BP) proximal to the coarctation. Even after perfectly performed corrective surgery with no residual gradient, hypertension (HTN) requiring chronic antihypertensive medication can occur. Variants of natriuretic peptide receptor 3 (NPR3) are associated with elevated BP in other congenital cardiovascular disease including CoA. This study quantified the frequency of known NPR3 variants in a cohort of patients enriched in CoA and compared to a population based control cohort to ultimately assess whether these variants are associated with HTN.

Methods

Two single nucleotide polymorphisms (SNPs; rs2270915 and rs146301345) in NPR3 were prioritized because they were observed at higher than expected frequencies in a cohort of patients with hypoplastic left heart syndrome (HLHS) in comparison with publicly available databases and based on estimates of functional deleteriousness. CoA patients (n=242) were genotyped using TaqMan SNP Genotyping Assays. The minor allele frequency (MAF) in CoA patients for each SNP was calculated. In a blinded review of patient records, each patient's level of HTN (normal, pre-HTN, HTN) was quantified using the patient's most recent BP measurement and the National High BP Education Program Working Group (<18 yrs) or Joint National Committee 7 guidelines (≥18 yrs). Following unblinding, the relationship between SNP variants and HTN in treated CoA patients will be statistically analyzed as an evaluation field using two-factor cluster analysis.

Results

SNP genotyping revealed allele frequencies in this cohort of CoA patients of MAF G=0.2128/103 (rs2270915) and MAF A=0.0103/5 (rs146301345). These frequencies are higher than expected by dbSNP (NCBI) or 1000 Genomes. The process of unblinding and comparing patient genotypes with their corresponding HTN levels is underway.

Conclusion

Results from this study suggest NPR3 variants may have a role in HTN in this cohort of CoA patients.