



GEN73 – Identifying Rare Variants as Genetic Risk Factors for Bicuspid Aortic Valve

OBJECTIVE: To perform whole exome sequencing (WES) to identify rare genetic variants that are specifically associated with the BAV phenotype.

ORGANIZATION

Lead Investigator: Michael Silberbach MD

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Other sources, pending.

BACKGROUND AND RATIONALE

BAV is the most common congenital heart malformation, occurring in 1-2% of the general population making it more common than all other congenital heart malformations combined. Malformation of the cardiac valves can fundamentally alter cardiovascular hemostasis and lead to significant morbidity and mortality.

In girls and women with TS, BAV occurs in 25 to 50% of cases, with TS acting as a risk factor. However, TS alone is not sufficient to cause the defect. Other contributing risk factors are likely to exist in the rest of the genome and are likely to be the same genes/pathways as those that confer risk to the general population.

Because TS contributes substantially to the risk for BAV, the number of additional predisposing risk factors is reduced. This study has the added significance of potentially identifying genetic risk factors for BAV in TS, but also in the population in general.

DESIGN

Inclusion criteria:

- Female
- Subjects with confirmed TS diagnosis
- Non-Hispanic white

Methods

- The investigators will compare individuals with TS+BAV (XO+BAV; cases) with TS and a normal heart (XO; controls)
- Mutations in several genes and gene pathways will be evaluated to identify variants that are significantly associated with BAV.
- Non-specific variants will be tested by two-sided Fisher's Exact Test ($p < 0.05$ significance cutoff) to determine if there is a significant difference in allele frequency between cases and controls.

Samples:

- Genetic

Data:

- Image data

CONCLUSIONS

Results:

- Pending