LOW PREVALENCE OF CLINICALLY APPARENT CARDIAC AMYLOIDOSIS AMONG CARRIERS OF TRANSTHYRETIN V122I VARIANT IN A LARGE ELECTRONIC MEDICAL RECORD

Poster Contributions
Poster Hall B1
Sunday, March 15, 2015, 3:45 p.m.-4:30 p.m.

Session Title: Genetic Interactions in Heart Failure
Abstract Category: 14. Heart Failure and Cardiomyopathies: Clinical
Presentation Number: 1215-182

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Background: Transthyretin (TTR) gene mutations are the most common cause of hereditary amyloidosis. Valine replaced by isoleucine in position 122 (V122I) variant is common in the United States, present in up to 4% of the black population. V122I carriers are reported to be at high risk for development of cardiac amyloidosis and cardiomyopathy, particularly at older age. Despite a relatively high prevalence, the penetrance of V122I is not firmly established. In this study we sought to determine the prevalence of clinically apparent cardiac amyloidosis among carriers of the TTR V122I variant.

Methods: BioVU, a Vanderbilt University resource linking DNA samples and pre-existing genetic data to de-identified electronic medical records was used to identify TTR V122I mutation carriers. Automated billing code queries (ICD-9 codes), problem list searches, and manual chart reviews were used to identify subjects with clinically diagnosed cardiac amyloidosis. Analysis was limited to black and white subjects. Statistical analysis was performed using Fisher’s exact test.

Results: Amongst 28,429 subjects with available genotype data, 129 were V122I carriers. Carriers were 95% black, 61% female, median age of 42 years [IQR 16 to 64], age range 4 to 96 years. Non-carriers were 11% black, 53% female, median age of 62 years, [IQR 41 to 77], age range 3 to 109 years. The carrier rate was 3.7% in blacks and 0.02% whites. Overall, the prevalence of clinically apparent cardiac amyloidosis was 0.8% in carriers and 0.04% in non-carriers (p=0.05). Above age 60 (N= 15,671, 7.8% black, 51% female, median age=75 [IQR 67 to 75.3 years) the prevalence of cardiac amyloidosis was 2.6% in carriers and 0.06% in non-carriers (p=0.03).

Conclusion: Carriers of the TTR V122I variant are at a higher risk for development of cardiac amyloidosis, particularly at age>60 years. However, clinically apparent cardiac amyloidosis in this population was uncommon. Though limited by reliance on clinically acquired data and possible under-ascertainment, these results support that the penetrance of TTR V122I is age dependent and suggest it may be significantly lower than previously reported.