Title: Familial Heritability of Rotator Cuff Tears

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Introduction

Rotator cuff tears (RCTs) a common cause of shoulder pain, disability, and has a prevalence between 6.8%-22.4% among people >40 years.[1] Rotator cuff tears are mostly atraumatic caused by degeneration of tendon/s over time, increased cell death and higher fat content. A tear in the tendon whether partial- or full-thickness tear leads to progressive and irreversible fatty infiltration of rotator cuff muscles, encompass a spectrum of pathologic changes and thus, leads to rotator cuff disease (RCD). A familial predisposition to rotator cuff disease has been reported. Genome-wide association studies (GWASs) have enhanced estimates of heritability by leveraging genome-wide single nucleotide polymorphisms (SNPs) among related and unrelated individuals. Considering high prevalence of rotator cuff disease, it is important to elucidate the familial heritability or genetic contribution to the development of RCTs/RCD. Therefore, the present study aimed to assess the familial heritability of rotator cuff tears.

Materials and Methods

We utilized three cohorts: the CuffGEN cohort, UK Biobank and BioVU (Biorepository at Vanderbilt University). The CuffGEN cohort is an ongoing GWA study has recruited 1,282 individuals aged 41-85 years, those with magnetic resonance imaging (MRI) confirmed presence or absence of rotator cuff tears. Subjects were asked to fill-up a baseline questionnaire that elicits the information on family history of rotator cuff tears. We utilized the genetic data from UK Biobank and BioVU to estimate the risk for rotator cuff tears based on genetically determined relatedness and thus, calculated the heritability of rotator cuff tears. We used a natural language processing (NLP) to identify the cases and controls in BioVU as well as UK Biobank. We did quality control on the genetic data, kinship filtering to identify the familial relationships and performed the logistic regression analysis to estimate the effect size and P-values for each SNP.

Results & Discussion

We observed a high risk (AOR: 1.82; 95CI 1.23-2.70) for familial relatedness in the CuffGEN cohort. Similarly, a high risk (AOR: 1.59; 95%CI 1.11-2.26) for rotator cuff tears was observed in first-degree relatives. However, we did not observe any significant risk for second-degree relatives. In BioVU and UK Biobank, we conducted regression modelling to estimate the relatedness associated with the increased risk of rotator cuff tears by adjusting to age, sex, and first ten principal components. We observed an increased risk for rotator cuff tears in familial related individuals in the BioVU (AOR: 1.21; 95CI 1.13-1.30) and UK Biobank (AOR: 1.09; 95CI 1.03-1.16), both. The stratified analysis in BioVU dataset; all BioVU population and white non-Hispanic population revealed a higher risk of developing RCTs/RCD in third-degree relatives followed by first-degree relatives. While in the dataset from UK Biobank, the risk of developing RCTs/RCD appeared higher in second-degree relatives, followed by third-degree relatives. Such differences might stem from variation in population composition. The elevated risk for RCTs/RCD in second-degree and third-degree relatives can be attributed to disparities in gene frequencies and combined influence of environmental factors. We estimated familial heritability to be 0.56% (low heritability) from the meta-analyzed genetic data from UK Biobank and BioVU. Rotator cuff tears/disease is a complex etiology and determining the familial heritability of such complex disease is challenging due to the differences in gene frequencies, environmental factors, health care seeking behavior and occupation/lifestyle influences.[2, 3]

References:

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