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The Genetic Architecture Underlying Dilated Cardiomyopathy in Singaporeans

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Abstract : Dilated cardiomyopathy (DCM) is a common cause of heart failure. Genetic mutations account for 50% of DCM cases with TTN mutations being the most common, accounting for up to 25% of DCM cases. However, the genetic architecture underlying Asian DCM patients is unknown. We evaluated 68 patients (female= 17) with DCM who underwent follow-up at the National Heart Centre, Singapore from 2013 through 2014. Clinical data were obtained and analyzed retrospectively. Genomic DNA was subjected to next-generation targeted sequencing. Nextera Rapid Capture Enrichment was used to capture the exons of a panel of 169 cardiac genes. DNA libraries were sequenced as paired-end 150-bp reads on Illumina MiSeq. Raw sequence reads were processed and analysed using standard bioinformatics techniques. The average age of onset of DCM was 46.1±10.21 years old. The average left ventricular ejection fraction (LVEF), left ventricular diastolic internal diameter (LVIDd), left ventricular systolic internal diameter (LVIDs) were 26.1±11.2%, 6.20±0.83cm, and 5.23±0.92cm respectively. The frequencies of mutations in major DCM-associated genes were as follows TTN (5.88% vs published frequency of 20%), LMNA (4.41% vs 6%), MYH7 (5.88% vs 4%), MYH6 (5.88% vs 4%), and SCN5a (4.41% vs 3%). The average callability at 10 times coverage of each major gene were: TTN (99.7%), LMNA (87.1%), MYH7 (94.8%), MYH6 (95.5%), and SCN5a (94.3%). In conclusion, TTN mutations are not common in Singaporean DCM patients. The frequencies of other major DCM-associated genes are comparable to frequencies published in the current literature.

Keywords : heart failure, dilated cardiomyopathy, genetics, next-generation sequencing
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