Clinical Predictors of Disease-carrier State in Familial DCM

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Idiopathic dilated cardiomyopathy (DCM) is a major cause of heart failure and heart transplantation in young adults. In about 30% of cases DCM is a familial disease, usually with autosomal dominant inheritance. In most families the disease-causing mutation is unknown and relatives undergo periodic screening to allow early diagnosis and therapy.

We previously identified a TTN Ins59014A mutation in a large Arab family with adult-onset DCM. Genotyping and clinical screening were then extended to include younger first degree relatives in order to identify the earliest predictors of the disease in healthy carriers.

The 11 affected individuals in the original cohort (M/F 6/5, 48±12 years), when compared with their mutation-negative first degree relatives (M/F 11/13, 43±7 years), showed differences in LVSF (21±7 vs. 39±7%, $p<0.0001$), LVEDD (58±9 vs 49±4mm, $p<0.001$), LVESVI (38±10 vs. 21±7, $p<0.0001$) and RVFAC (41±5 vs. 45±5%, $p<0.05$). There were no significant differences in the wall thickness, left atrial size or indexes of diastolic function including E/E' ratio. The DCM group had a higher prevalence of LBBB and left axis deviation ($p<0.01$) on ECG. The second screen identified 14 healthy mutation carriers (M/F 8/6, 29±12 years) who were compared with 16 mutation-negative relatives (M/F 10/6, 30±13years). No differences were recorded between the groups in ECG or echocardiographic parameters, including left ventricular size, and in systolic or diastolic function. Carriers did not differ from non-carriers in serum NT-proBNP, CK or troponin I.

We conclude that genetic diagnosis is instrumental for risk stratification and guided clinical follow-up in familial DCM.