Characteristics of VCP Mutation-Associated Cardiomyopathy

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Abstract

VCP associated inclusion body myopathy, Paget's disease of bone, and Frontotemporal Dementia (IBMPFD, VCP disease, or multisystem 77 type 1 (MSP1)) is an autosomal dominant disease caused by missense mutations in the *VCP* gene, which plays a crucial role in ubiquitin-proteasome dependent degradation of cytosolic proteins. Those diagnosed with the disorder often suffer from cardiovascular complications in the advanced stages. We conducted an observational cross-section study to investigate echocardiographic features of asymptomatic carriers and those affected by the disease to determine the differences and potential early features of the VCP-associated cardiomyopathy. The study cohort constituted of 32 patients with *VCP* mutations including 23 affected individuals diagnosed with myopathy +/- Paget disease of bone, and 9 asymptomatic carriers. Among the affected individuals, 95.7% had myopathy, 43.5% had Paget's disease of bone, and none had frontotemporal dementia, and the carriers were asymptomatic. Not surprisingly the carriers were younger (mean age 38.4±3.8 years), than the affected cohort (mean age 50.6±9.1 years; $p < 0.001$). There was a 43.5% prevalence of diastolic dysfunction on echocardiogram among patients who were symptomatic from VCP disease, whereas none of the two asymptomatic carriers manifested diastolic dysfunction ($p=0.017$). Among the 5 affected individuals who had consequential echocardiogram 2-3 years apart, three affected developed diastolic dysfunction, and two already had diastolic dysfunction on the initial study. The two carriers did not develop diastolic function changes. This present study represents the largest series of echocardiograms performed in patients and asymptomatic carriers with VCP myopathy, and will pave the way for future, large-scale studies that may include other imaging modalities such as cardiac MRI and strain evaluation, in patients at all stages of the disease.