(age 63 ± 16) were used as reference group Non-synonymous EMD variants were associated with non-ischemic cardiomyopathy, cardiac conduction disease and atrial fibrillation (OR: 7.2, 95% CI 3.3-15). Forty-two patients had a cardiac phenotype, 14 individuals had symptomatic SND and/or advanced AV block, 8 patients had DCM, 6 patients had LV dysfunction, 2 patients had ARVC, 2 patients had HCM, 9 patients had isolated AF and a patient with a EMD frameshift variant who had EDMD1. Overall 32% had AF; 22% had a cardiac implantable electronic device. Interestingly, individuals with non-synonymous variants had a higher incidence of tendon rupture and tendinopathy when compared to reference group (OR 3.4, 95%CI 1.3 to 9.2). Among patients in the PMBB, EMD related cardiac disease was detected in 1 out of every 520 male patients.

Conclusion: Missense EMD variants contribute to a cardiac emerinopathy in male patients. The disease spectrum includes LV dysfunction, cardiac conduction disease and atrial arrhythmias.

**HF-566-04**

PATHOGENIC VARIANTS IN EMD ARE ASSOCIATED WITH AN ISOLATED CARDIAC EMERINOPATHY

Ahmed Alsalem MD; Erica S. Zado PAC, FHRS; Rajat Deo MD; Pasquale Santangeli MD, PhD; Fermin C. Garcia MD; Francis E. Marchlinski MD, FHRS and Matthew Craig Hyman MD, PhD

**Background:** Emerin (EMD) is an inner nuclear envelope protein critical to the integrity of the nucleoskeleton and mechanotransduction. Loss-of-Function (LoF) variants in EMD results in Emery-Dreifuss muscular dystrophy type 1 (EDMD1). This syndrome is characterized by a proximal skeletal myopathy associated with joint contractures and cardiac conduction disease. Several small reports have suggested that pathogenic EMD variants are associated with a cardiac emerinopathy (cardiomyopathy without evidence of skeletal myopathy). The full clinical spectrum of these EMD variants is poorly understood.

**Objective:** To characterize the clinical spectrum of cardiac emerinopathies (CE) and evaluate the impact of EMD variant effect on disease presentation.

**Methods:** We reviewed the literature, internal and publicly available databases (HGMD, PubMed, ClinVar) for patients with identified EMD pathogenic variants without skeletal muscle or joint involvement. A total of 106 individuals were identified and included in the analysis.

**Results:** Of the 106 individuals, 75 were males, due to X-linked nature of this disease males and females were analyzed separately. The presentation in male patients were cardiac conduction disease (39%), dilated cardiomyopathy (33%), isolated LV dysfunction without dilation (6.6%), left ventricular non-compaction (LVNC, 4%), and ARVC (3%). Atrial fibrillation was diagnosed in 35%. Patients with predicted loss-of-function (pLOF) variants developed symptoms at a younger age when compared to patients with missense or in-frame deletions (pLOF: mean 26.4 years, non-LOF: mean 44.1, p =< 0.0001, 95% CI:12.3 to 23 ). Of the 31 female carriers of pathogenic variants in EMD, 13 individuals were found to have a cardiac pathology. Sudden cardiac death was reported in 1 out of 5 male patients (mean age=38 years, SD = 8.4 years). Cardiac device implantation was reported in 35% (mean age=39 years, SD=12.4 years) in the reviewed cohort.

**Conclusion:** In a review of published cases, cardiac emerinopathies are commonly associated with diverse cardiac pathologies including cardiac conduction disease, atrial tachyarrhythmias, dilated cardiomyopathy, LV dysfunction, LVNC and ARVC.