**CONGENITAL HEART ABNORMALITIES ASSOCIATED WITH LOSS OF FUNCTION FILAMIN A GENE MUTATIONS**

**M. Chen**1, M. Hirata2, C. Walsh1, S. Choudhury1

1Boston Children’s Hospital, Boston, MA, Boston, MA, USA

2Tokyo Women's Medical University, Tokyo, Japan

Loss of function (LOF) mutations in the Filamin A (FLNA) gene, which encodes an actin binding protein, are associated with thoracic aortic aneurysm in young patients and also a brain disease associated with epilepsy, called X-linked periventricular nodular heterotopia (Chen et al, 2018, AJMG 176:337-35). However, other types of congenital heart disease (CHD) associated with LOF FLNA mutations have been less well-defined, and their frequency unknown. METHODS: Therefore, from our FLNA registry of 69 study patients and 66 literature patients with known cardiac assessment, we characterized the range and frequency of cardiac structural abnormalities. All but 4 patients had a cardiac echocardiogram. RESULTS: 135 patients (107 F, 28 M, median age 19 yrs, range 0-71 yrs), both children and adults of both gender, with LOF FLNA mutation formed our cohort. 95 patients had structural CHD, which included ventricular septal defect (n=14), atrial septal defect (n=12), patent ductus arteriosus (PDA) (n=30), and valve disease (n=66). 47 of 95 CHD patients (49%) had ≥ 1 myxomatous/dysplastic or dysfunctional valve, with the mitral valve being most commonly affected (25/66); 15 patients had mitral valve prolapse (MVP). The aortic valve was frequently regurgitant, with mild to severe regurgitation present in 27 subjects; only 4 had a bicuspid aortic valve. 9 patients had a dysplastic/dysfunctional tricuspid valve, and 8 had a dysplastic pulmonic valve. Serial follow-up over >15 yrs found at least 2 patients who developed MVP over time, during their teenage years. Non-valvular CHD included 30 patients with a PDA, of which 16 required surgical ligation during early childhood. CONCLUSIONS: In this largest cohort of LOF FLNA patients, CHD was present in 70.4% of all patients. Given the frequency of structural cardiac abnormalities, echocardiography should be considered in neonates with PVNH with LOF FLNA mutations. Children and adults with FLNA mutations should have serial echocardiograms to assess change in their disease.