

higher in the MVR group versus MVr (0 [0–0.4] vs 0[0–0], $p=0.04$). (Table 1)

There was no difference in the mean change in HRQoL during 6 m follow up between patients with peri-operative cerebral microinfarction and those with no detectable embolic events. (Table 2) Within group comparison (MVR group and MVr group) also did not demonstrate any significant difference.

Conclusions Peri-operative cerebral microinfarction occurred in almost a third of patients undergoing mitral valve surgery, with higher volume of lesions following MVR. These lesions however, did not exhibit significant impact on medium term health-related quality of life.

Conflict of Interest None

7 INVESTIGATING A NOVEL ROLE FOR NESPRIN-1 AND THE LINC COMPLEX IN CARDIOMYOCYTE MECHANOTRANSDUCTION

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Introduction Cardiomyopathies are an important cause of heart failure and sudden cardiac death. Emerging evidence demonstrated the importance of the mechanical properties of cardiomyocytes as new causes for dilated cardiomyopathy (DCM). Nesprins-1/2 are highly expressed in cardiac and skeletal muscle and together with SUN1/2, lamin A/C and emerin form the nuclear envelope (NE) Linker of Nucleoskeleton-and-Cytoskeleton (LINC) complex, that mechanically couples the nucleus to cytoskeletal networks. Our recent data showed nesprin-1 mutations in DCM patients cause increased NE fragility and compromise LINC complex function in vitro, leading to disruption of mechanical connections between the plasma membrane and the nucleus, and may potentially affect microtubules (MT), myofibrils and sarcoplasmic reticulum when cells are exposed to mechanical stress accompanying DCM and heart failure. We aim to investigate novel roles of nesprin-1 and the LINC complex in cardiomyocyte mechanotransduction via exploring roles of nesprin-1 in microtubule organisation, nuclear positioning and cardiomyocyte homeostasis. **Methods** and

Results We have generated the first clinically relevant nesprin-1 mutant knock-in (KI) mouse line. Preliminary mouse echocardiography data showed significantly reduced thickness of left ventricle (LV) posterior wall in diastole and reduced % ejection fraction in the KIs at 15 weeks after birth, suggesting left ventricular dysfunction and a tendency of DCM, which is consistent with Echo observations in DCM patients harboring the same mutation. Immunofluorescence showed elongated and reduced nuclear circularity, loss of nesprin-1 NE staining in KI hearts, and also reduced staining of Akap6 and KLC1/2 at the NE as well as reduced perinuclear MT intensity and abnormal nuclear positioning in KI cardiomyocytes compared to the WT. Furthermore, GST-pull down and immunoprecipitation showed nesprin-1 interaction with AKAP6 and KLC1/2 was disrupted in both C2C12 myoblasts and KI heart and muscle tissue.

Conclusion Our model suggests a novel role of nesprin-1, in particular nesprin 1a2 isoform, in MT organization, nuclear positioning and cardiomyocyte homeostasis, thus serving as a platform to investigate novel pathological mechanism of nesprin-1 mutations in DCM. This project has the potential to uncover a novel mechanism that causes cardiomyocyte dysfunction, contributing to the pathogenesis of NE-related cardiomyopathies, which may yield insights into signalling leading to heart failure, with potential to influence the strategies for translational approaches.

Conflict of Interest None

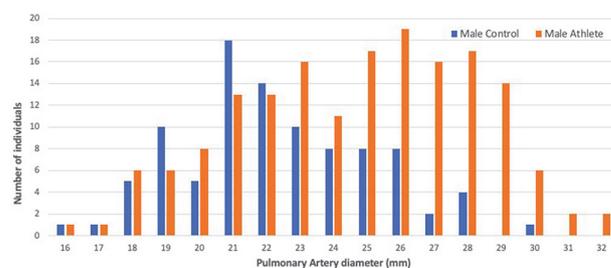
8 THE UTILITY OF EXERCISE-STRESS ECHOCARDIOGRAPHY FOR PRE-PREGNANCY RISK STRATIFICATION IN PATIENTS WITH LEFT HEART OBSTRUCTION

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Introduction All women with cardiac disease wishing to embark on pregnancy require appropriate pre-conception counselling. A variety of risk stratification tools (mWHO, CARPREG II, ZAHARA) have been proposed to inform shared-decision making and positively influence downstream management. Although consensus guidelines recommend pre-pregnancy exercise testing for all patients with known heart disease, thus far exercise stress echocardiography (ESE) has not been routinely advised. There is, however, potential for SE to provide complementary information among patients with left heart obstruction, which confers a high risk of maternal cardiovascular (CV) complications. We sought to determine the relative value of ESE versus exercise ECG testing for the prediction of adverse maternal CV events in patients with left heart obstruction.

Methods This was a retrospective observational cohort study; an electronic database search identified 620 patients referred for ESE by cardiologists with expertise in pregnancy, from January 2010 to July 2021 (Figure 1). Left heart obstruction patients who conceived were included in analysis ($n=44$, age 28 ± 6 y). Baseline demographics were recorded and for each pregnancy, mWHO, CARPREG II and ZAHARA risk scores were calculated. Echocardiography procedures were performed by experienced operators (iE33 or EPIC, Philips Healthcare, Andover, Massachusetts) Patients underwent semi-recumbent



Abstract 8 Figure 1