

Abstract

Several controversies have emerged in recent years with regard to whether left ventricular noncompaction is a distinct pathological entity or a remodeling epiphenomenon. The presence of more than three trabeculations within the left ventricle, accompanied by a two-layered structure, in which a thin compacta has an overlying prominent trabeculation, with an adjacent intertrabecular space, is the distinct phenotypic hallmark of noncompaction.

Left ventricular noncompaction is a distinct anatomical phenotype, which is detected by imaging in a variety of clinical scenarios. These include congenital heart disease, neuromuscular diseases, valvular disease, pregnancy, sickle cell anemia and other cardiomyopathies, such as hypertrophic cardiomyopathy. Whether noncompaction is a distinct genetic disorder, whether the imaging criteria used are accurate, or whether it should be considered a normal variant in certain patient populations is key to diagnoses and clinical management. One such population are individuals of African descent in whom it has been postulated by some authors, that hypertrabeculation is a normal variant. The consequence is that some individuals, particularly those with the phenotype of dilated cardiomyopathy may satisfy current imaging criteria for the diagnosis of left ventricular noncompaction. Exactly what the presence of the left ventricular noncompaction phenotype in these clinical scenarios means, has not been systematically studied until recently. The aforementioned controversies and questions are germane to the key issues that were studied in this thesis.

Therefore, this thesis firstly evaluated normal echocardiographic left and right ventricular parameters in a Black South African population. The study revealed that there was a direct correlation between age, RV A' ($r=0.468$) and inversely correlated with RV E' ($r=-0.431$) but there was no correlation between BMI and RV linear measurements, however TAPSE and RV A' increase with BMI. Secondly, in a large normal Black South African population 4, 7% trabeculations were found, no subjects fulfilled all four criteria for the diagnosis of ILVNC and similar rotation patterns,

quantitative LV rotation patterns and net twist were shown in both individuals with and without trabeculations

Thirdly, the prevalence and predictors of right ventricular dysfunction in ILVNC with reduced ejection fraction and dilated cardiomyopathy (IDCMO) were evaluated using echocardiography. The main findings indicate that ILVNC had more RV dilatation than IDCMO and that RV systolic functional parameters - RV S' TAPSE and RV FAC were decreased compared to IDCMO. In multivariate regression analysis LVEF was the most relevant predictor of RV dysfunction, followed by LVESD ($p=0.013$).

Lastly, the question that was explored was whether ILVNC with low ejection fraction differed from IDCMO with regard to myocardial mechanics and biomarkers of LV remodeling. The results showed that patients with ILVNC had more adverse remodeling, evidenced by increased LV dilatation (66.4 ± 10.1 vs 56.1 ± 10.3), LV mass (295.0 (143.0) vs 234.0 (140.0) and lower EF (ejection fraction) (28.5 ± 9.0 vs 33.3 ± 7.7), when compared to IDCMO. Net twist was higher in IDCMO group vs ILVNC [6.5 (3.0) vs 5.4 (4.6)].

Rigid body rotation and regional longitudinal strain was not statistically significant different between both groups. No statistically significant differences are found between the biomarkers of LV remodeling (Procollagen 1, MMP1, TIMP1, and Fas/APO-1). These results should be considered as preliminary, due to the reduced sample size in both groups.

This thesis has provided key normal reference ranges for several echocardiographic parameters that may define normality in this population group using echocardiography. Furthermore, this thesis highlights that normal individuals in this population group do not satisfy current used echocardiographic left ventricular non compaction criteria and will have normal left ventricular rotational parameters.

With regard to a comparison between ILVNC with the dilated phenotype and a reduced EF and IDCMO, it appears that more adverse left ventricular remodeling and its ensuing functional abnormality are more common in ILVNC. The consequence, is that right ventricular dysfunction is more prevalent in ILVNC and that in both instances, the LVEF was the most important predictor of right ventricular dysfunction. This thesis did not find any significant differences with regard to abnormal rotation patterns or regional longitudinal strain between ILVNC and IDCMO

or with regard to the biomarkers studied.

The strength of this research is that it provides guidance to clinicians with regard to identifying normality in individuals from this population group. Overall, the thesis has unraveled some of the controversies, but several issues remain unresolved with regard to the comparison of ILVNC with IDC MO. This may require future larger studies to address different aspects of ILVNC such as genetic analysis, more extensive biomarkers of heart failure, in addition to speckle tracking parameters.