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Prevalence and quantification of left ventricular trabeculation detected by cardiac MR imaging in non-ischaemic primary or secondary cardiomyopathies

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ABSTRACT

Purpose: To assess the prevalence and the qualitative and quantitative characteristics of left ventricular (LV) trabeculation in patients with non-ischaemic primary or secondary cardiomyopathies using detailed cardiac magnetic resonance imaging (MRI) analysis and to ascertain whether left ventricular trabeculations are related to global systolic LV function in different cardiomyopathies.

Material and Methods: One hundred and twenty four patients were studied using cardiac MRI, 10 with isolated left ventricular non-compaction (ILVNC), 24 with dilated cardiomyopathy (DCM), 27 with hypertrophic cardiomyopathy (HCM), 22 with cardiac sarcoidosis and 20 with arrhythmogenic right ventricular cardiomyopathy (ARVC). Twenty one patients with acute onset of myocarditis and no prior or familial history of cardiac disease served as controls.

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Results: Myocardial trabeculations were frequent in cardiomyopathies and were significantly greater in ILVNC and more frequent and extensive at apical segments in all study groups.
Considerable overlapping of trabeculation measures among the other than ILVNC study groups was also found. Trabeculation measures did not negatively correlate with LV ejection fraction (EF) except in sarcoidosis, where end-diastolic (ED) trabeculation thickness at the apical segments (p=0.006), trabeculation thickness on short axis view (p=0.005), trabecular area (p=0.021) and number of trabeculated segments (p=0.038) negatively correlated with LV EF.
Conclusions: Two dimensional and volumetric trabeculation parameters in cardiac MRI show considerable overlapping among primary and secondary cardiomyopathies but are greater in ILVNC. Cardiac sarcoidosis was the only disease in our study in which thickness-based trabeculation measures, trabecular area and number of trabeculated segments were negatively correlated with LV EF.

KEY WORDS
left ventricular trabeculations; cardiomyopathies; non-compaction; sarcoidosis; cardiac MRI; ischaemic cardiomyopathy

1. Introduction

Left ventricular (LV) trabeculation is a common finding in patients undergoing cardiac magnetic resonance imaging (MRI), and a significant variability has been observed between healthy individuals and patients with cardiac disease [1, 2]. Isolated left ventricular non-compaction (ILVNC) is a rare condition classified as a primary genetic cardiomyopathy by the American Heart Association [3], but it is still considered unclassified in the European Society of Cardiology classification [4], as it may be a morphological manifestation of various distinct cardiomyopathies. The diagnosis of ILVNC is based on the identification of thickened myocardium with a 2-layered structure that consists of a thin, compacted epicardial layer and a thick endocardial layer with prominent trabeculation and deep recesses that communicate with the LV cavity but not with the coronary circulation [5-7].

Increased LV trabeculation is not only associated with ILVNC but also with other heart muscle disease [8], congenital heart disease [9], and it has also been observed in healthy individuals [1]. In our clinical experience we have also observed presence of trabeculations in several non-ischaemic disease entities. Many studies have assessed the extent of LV trabeculation in relation to LV function, the results however are controversial [10-15].

The aim of this study was to assess the prevalence and the qualitative and quantitative characteristics of LV trabeculation in patients with non-ischaemic cardiomyopathies performing detailed cardiac MRI analysis, assessing thickness-based, planimetric and volumetric trabeculation measures. In addition, we aimed to evaluate whether LV trabeculations are related to global systolic LV function in different primary and secondary cardiomyopathies.

2. Material and Methods

2.1 Study population

Using the cardiac MRI patient database of our department, we retrospectively selected patients referred with a previously established diagnosis of primary or secondary cardiomyopathies. Diagnosis was based on medical history, physical examination and tests including echocardiogram and electrocardiogram using appropriate established criteria. Those included patients with dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), cardiac sarcoidosis, arrhythmogenic right ventricular cardiomyopathy (ARVC) without MRI findings indicative of LV involvement and patients fulfilling echocardiographic criteria for a diagnosis of ILVNC [7, 16] and also presence of arrhythmias, or a history of thromboembolic events or suspicion/confirmed diagnosis of ILVNC in first degree relatives. Our control group consisted of patients with clinical suspicion of acute onset of myocarditis. These subjects had no prior or familial history of cardiac disease or cardiovascular risk factors

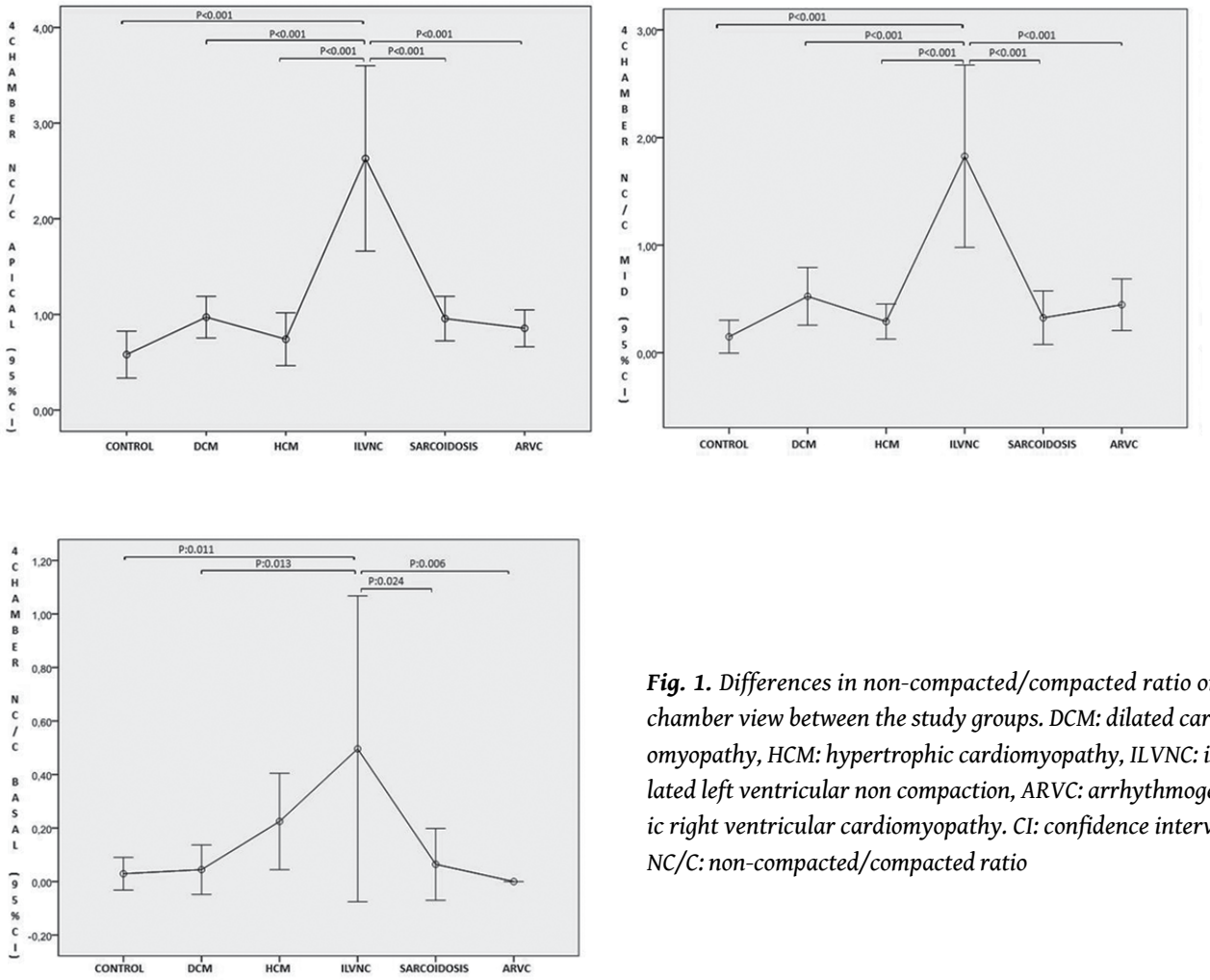

Fig. 1. *Differences in non-compacted/compacted ratio on 4 chamber view between the study groups. DCM: dilated cardiomyopathy, HCM: hypertrophic cardiomyopathy, ILVNC: isolated left ventricular non compaction, ARVC: arrhythmogenic right ventricular cardiomyopathy. CI: confidence interval, NC/C: non-compacted/compacted ratio*

and cardiac MRI revealed normal LV volumes, a small amount of patchy, non-ischaemic pattern of LGE, no myocardial structural abnormalities and normal global LV systolic function (ejection fraction-EF). This group was selected to serve as controls because coexistence of acute myocarditis and LV non-compacted myocardium is uncommon [17-19]. We deemed conceivable that the onset of acute myocarditis may not per se alter myocardial trabeculations over a brief time interval. A total of 124 individuals constituted the overall study population.

From the 124 individuals, 24 patients had DCM (mean age 42 ± 16 years, 83% men), 27 patients had HCM (mean age 41 ± 16 years, 78% men), 10 patients had ILVNC (mean age 50 ± 11 years, 30% men), 22 patients had cardiac sarcoidosis (mean age 52 ± 12 years, 36% men) and 20 patients had ARVC (mean age 46 ± 18 years, 55% men). The Control group was comprised of 21 individuals (mean age 39 ± 12 years, 76% men) with acute onset of myocarditis.

2.2 Cardiac MRI study

All studies were performed on a 1.5 Tesla MR imaging unit (Philips NT Intera; Philips Medical Systems, Best, The Netherlands) using a five-element phased-array cardiac coil for signal reception. All subjects underwent a detailed cardiac MRI examination and, for the purposes of our study, we used cine steady-state free precession (bFFE) sequences which were acquired on long-axis two-chamber, four chamber, and short-axis views.

2.3 Image analysis

All examinations were transferred to a dedicated workstation (Cardiac Analysis software package provided on a ViewForum workstation, Philips Medical Systems, The Netherlands) for further workup, and calculations of LV volumes, EF, LV mass, and extent of LV trabeculation. In short axis cine bFFE images the end-diastolic (ED) and end-systolic frames (ES) were determined. The epicardial

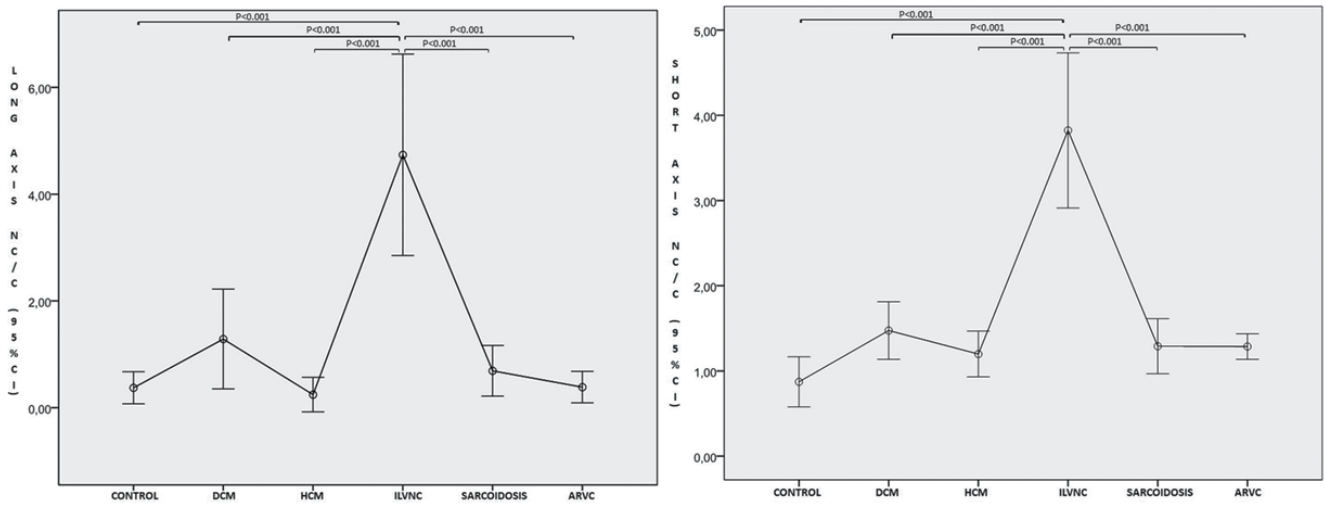

Fig. 2. *Differences in non-compacted/compacted ratio on long axis (left image) and short axis (right image) views between the study groups. DCM: dilated cardiomyopathy, HCM: hypertrophic cardiomyopathy, ILVNC: isolated left ventricular non compaction, ARVC: arrhythmogenic right ventricular cardiomyopathy. CI: confidence interval NC/C: non-compacted/compacted ratio*

and endocardial contours were outlined manually and in all subjects the papillary muscles were included in the calculation of the myocardial mass [20]. In ED and ES frames trabeculations were defined as myocardial protrusions from the wall of the left ventricle into its cavity [20].

The assessment of LV volumes has been previously described by Jacquier et al [20]. To assess LV volumes, EF, and compacted LV mass (CM), the endocardial border was outlined manually to include papillary muscles but exclude trabeculations. To assess global LV volumes and global LV mass (GM), the endocardial border was outlined manually to include papillary muscles and trabeculations. CM and GM were calculated in end-diastole and the trabeculated LV mass (TM) was calculated as GM minus CM [20]. At the location of the most pronounced LV trabeculations the thickness of the trabeculated/non compacted (NC) and the compacted myocardium (C) was assessed perpendicular to C. The ratio of NC/C was assessed in ED at the apex on the central long axis slice, at the apical, mid and basal segments on the central four chamber slice and in short axis view at the location of the most prominent trabeculations but excluding the apex. The papillary muscles were excluded from the above measurement. The calculation of the trabecular area (TA) was derived by planimetry of trabeculations on the central four chamber slice. The presence or absence of trabeculations was qualitatively assessed in all 17 cardiac segments [21].

2.4 Statistical analysis

Continuous variables are presented with mean and standard deviation (SD). Qualitative variables are presented with absolute and relative frequencies. For the comparison of proportions chi-square and Fisher's exact tests were used. Differences in means in study parameters between the different groups were evaluated using analysis of variance (ANOVA). Bonferroni correction was used in all comparisons in order to control for type I error due to multiple testing. Pearson correlation coefficients were used to explore the association of two continuous variables. All p values reported are two-tailed. Statistical significance was set at 0.05 and analyses were conducted using SPSS statistical software (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp).

2.5 Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

2.6 Informed consent

Written informed consent was not required for this study because of the standard policy of our Institutional Review Board to waive approval and informed consent for purely observational studies performed using standardised clinical imaging protocols.

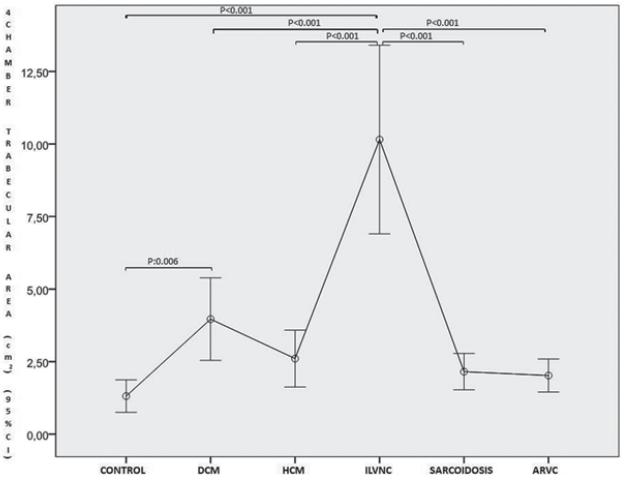

Fig. 3. *Differences in trabecular area between the study groups. DCM: dilated cardiomyopathy, HCM: hypertrophic cardiomyopathy, ILVNC: isolated left ventricular non compaction, ARVC: arrhythmogenic right ventricular cardiomyopathy. CI: confidence interval, NC/C: non-compacted/compacted ratio.*

3. Results

A total of 124 patients (79 men and 45 women) were recruited with mean age 45.1 years (SD=14.3). Twenty-one patients (mean age 39 ± 12 years, 76% men) with acute onset of myocarditis and normal EF constituted our Control group.

3.1 Assessment of anatomical trabeculation measures and differences between study groups

The mean values of trabeculation thickness ratio (NC/C) measures from four-chamber view and differences between study groups are presented in **Fig. 1**.

At the apical and middle segments mean value of NC/C was 2.63 ± 1.35 and 1.83 ± 1.18 respectively and they were both greater in ILVNC compared to all study groups. At the basal segments mean value of NC/C was 0.50 ± 0.80 and it was greater in ILVNC compared to all groups except ARVC group.

On long axis views, differences in NC/C measures between study groups are shown in **Fig. 2**. Mean value of NC/C in ILVNC was 4.74 ± 2.64 and it was greater compared to values of all other study groups.

On short-axis views, differences in NC/C measures between study groups are shown in **Fig. 2**. Mean value of NC/C in ILVNC was 3.82 ± 1.27 and it was greater compared to values of all other groups.

Mean value of TA in ILVNC was 10.15 ± 4.55, and it was significantly greater compared to that of controls and all other study groups. Mean value of TA in DCM was 3.96 ± 3.37, greater compared to controls (**Fig. 3**).

Fig. 4 presents differences between trabecular/compacted mass ratio (TM/CM) and trabecular/global mass ratio (TM/GM) among study groups. Mean value of TM/CM and TM/GM in ILVNC was 0.31 ± 0.14 and 0.23 ± 0.08 respectively, both higher in ILVNC compared to values of all other groups. Furthermore, mean value of TM/CM in DCM was 0.11 ± 0.07, higher when compared to values of control group. Finally, mean value of TM/GM in DCM was 0.09 ± 0.05, higher when compared to values of control and HCM groups.

In ILVNC patients mean value of trabeculated segments was 10.3 ± 2.7, significantly higher (p<0.001) when compared to values of all other study groups. No differences were observed among values of all other groups.

3.2 Functional assessment and correlation with trabeculation measures

Mean LVEF ranged within normal limits in controls (64.83 ± 4.86%), HCM (71.72 ± 11.69%), ILVNC (59.02 ± 18.37%), cardiac sarcoidosis (67.01 ± 11.22%) and ARVC (63.59 ± 10.54%). Mean LVEF was low in DCM (38.33 ± 16.77%) while in ARVC mean right ventricular EF ranged at 59.58 ± 8.3%.

No correlation between trabeculation measures and the LVEF was observed in Control, DCM and ILVNC groups.

In patients with HCM, there was a positive correlation between LVEF and the NC/C measured on the four chamber projection in all LV segments from apical to basal segments, as well as on long axis (r=0.55, p=0.004) and short axis (r=0.43, p=0.026) planes. There was also a positive correlation between EF and TA (r=0.49, p=0.009) and between EF and TM/CM (r=0.43, p=0.025), the TM/GM (r=0.41, p=0.036) and the number of trabeculated segments (r=0.48, p=0.012).

In patients with cardiac sarcoidosis there was a negative correlation between LVEF and trabeculation thickness at the apical segments (r=-0.57, p=0.006), the TA (r=-0.49, p=0.021), as well as the trabeculation thickness on short axis planes (r=-0.57, p=0.005) and the number of trabeculated segments (r=-0.44, p= 0.038).

In the ARVC group, there was a positive correlation between LVEF and the thickness of the compacted myocardium at the basal segment (r=0.54, p=0.014), but no nega-

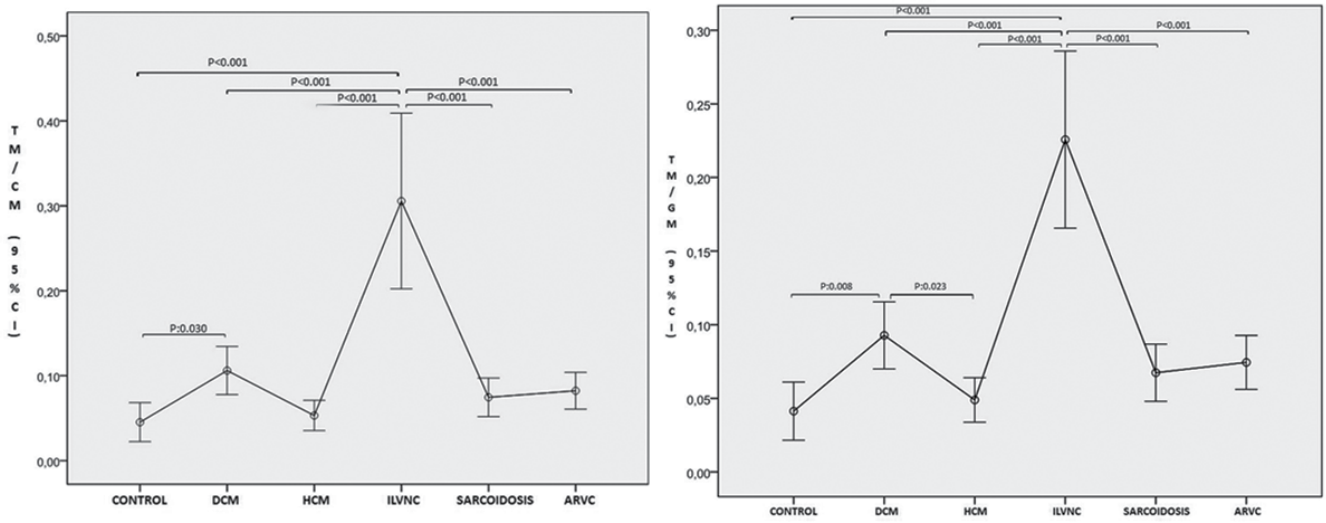

Fig. 4. *Differences in trabecular/compacted mass ratio (left image) and trabecular/global mass ratio (right image) between the study groups. TM: trabecular mass, CM:compacted mass, GM: global mass, DCM: dilated cardiomyopathy, HCM: hypertrophic cardiomyopathy, ILVNC: isolated left ventricular non compaction, ARVC: arrhythmogenic right ventricular cardiomyopathy, CI: confidence interval.*

tive correlation between trabeculation measures and the LVEF was observed.

4. Discussion

In this study using cardiac MRI, we have found that the presence of myocardial trabeculations is a frequent finding, not only in ILVNC but also in patients with other types of non-ischaemic primary and secondary cardiomyopathies, as well as in patients with acute onset of myocarditis, who served as controls. In our daily practice we had observed the presence of trabeculations in different primary or secondary cardiomyopathies, a fact that triggered the planning of this retrospective, mainly morphological, study regarding trabeculations in these diseases.

Our results show that trabeculations are present in all disease groups included in our study, as well as in our control population comprised of acute myocarditis with no previous history of cardiac disease or cardiovascular risk factors. Differences in LV trabeculations measures were found between ILVNC and all other study groups, and in addition, patients with DCM showed greater TA, TM, TM/GM and TM/CM compared to controls. This finding has also been reported in previous studies [20, 22-26]. Interestingly, the spatial distribution of trabeculation in the ILVNC group was similar to the patterns of trabeculation in patients with DCM [20]. However, the number of trabeculated segments was greater in the ILVNC group compared to DCM, a finding consistent with a previous study [15].

To summarise the above, in our cohort, comprised of different cardiomyopathies, ILVNC was the only group that fulfilled both Petersen's [27] and Jacquier's [20] criteria. These criteria differentiated ILVNC from the other entities but, despite the extensive assessment of two-dimensional and volumetric parameters of trabeculations, we were not able to draw any firm conclusions regarding cut-off values of the aforementioned parameters to permit accurate distinction between hypertrabeculated individuals with different cardiomyopathies apart from ILVNC, as there was considerable overlap of these values. Nevertheless, our data showed that trabeculations exist in a wide range of primary and secondary cardiomyopathies.

Although a correlation between the extent of trabeculations and ventricular function has been reported in the literature, results are conflicting [10-15, 28-30]. Cheng et al [15] found that the number of trabeculated segments and NC/C ratio had negative correlation with the EF, while Nucifora et al [30] did not.

In our study, trabeculation measures didn't negatively correlate with LVEF in ILVNC, DCM, ARVC and Control groups. Although ILVNC patients had a significant amount of trabeculations particularly located at the apex, the apical and the middle LV segments, the pres-

ence and extent of trabeculations did not correlate with EF. Recently in a similar study that has been published by Choi et al [31] no correlation was observed between trabeculated LV volume and LVEF in ILVNC and Control groups. The absence of correlation between the number of segments with presence of trabeculation, trabecular area, TM/CM and TM/GM and the EF in the aforementioned groups questions the efficacy of two dimensional measurements on cardiac MRI in predicting systolic dysfunction in these subjects.

The paradoxical positive correlation between increased trabeculation measures and EF in patients with HCM indicates that in these patients with LV hypercontractility, the presence of trabeculation may not have significant impact on global LV systolic function.

To our knowledge, this is the first study assessing LV trabeculations with cardiac MRI to include patients with cardiac sarcoidosis and also to show the presence of trabeculations and a negative association between their extent and left ventricular EF. In patients with cardiac sarcoidosis, there was a negative correlation between trabeculation thickness, TA, the number of trabeculated segments and EF. However, no negative correlation between trabecular area and TM/CM and TM/GM and the EF was observed. Although an inverse correlation between trabeculations and EF was found, in these patients mean LVEF was measured within expected normal limits.

As the study population of this retrospective study was relatively limited these results need to be addressed by further prospective studies. These might include patients with cardiac sarcoidosis to investigate the influence of trabeculations in myocardial contractility, using additionally strain-based imaging techniques, as in the setting of a normal EF myocardial strain can be impaired [32], and also to clarify the possible prognostic implications of the above correlations. Increased LV trabeculations have been suggested in the literature to be an epiphenomenon and their extent has no additional prognostic value in individuals with normal LVEF [33].

In conclusion, presence of LV trabeculations detected by MRI is not rare in non-ischaemic primary and secondary cardiomyopathies and there is considerable overlapping of trabeculation measures among different cardiomyopathies. The negative correlation of trabeculations with mean LVEF in cardiac sarcoidosis merits further investigation in larger prospective follow-up studies.

5. Limitations

Our study was retrospective and limited by a selection bias as the patient populations were provided from a single tertiary referral centre. In addition patient numbers were relatively small, which in the case of ILVNC is due to its nature as a rare disease and thus the LV trabeculations may not apply to the entire spectrum of cardiomyopathies. Mean age of individuals in the control group was younger than in other groups. For ILVNC genetic testing and neuromuscular findings were not available. The ILVNC and cardiac sarcoidosis groups were dominated by female subjects in comparison to the other groups. Radiologists were not blinded to the echocardiographic diagnosis. Our Control group consisted by patients with acute onset of myocarditis and normal global LV systolic function with no history of cardiomyopathies, it is conceivable, however, that this acute presentation may not per se alter myocardial trabeculations. R

Conflict of interest

The authors declared no conflicts of interest.

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