International Journal of Cardiology 228 (2017) 900–905

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Echocardiographic comparison between left ventricular non-compaction and hypertrophic cardiomyopathy

Trine F. Haland [a,b,c], Jørg Saberniak [a,b,c], Ida S. Leren [a,b], Thor Edvardsen [a,b,c], Kristina H. Haugaa [a,b,c,*]

[a] Center for Cardiological Innovation, Department of Cardiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway
[b] University of Oslo, Norway
[c] Institute for Surgical Research, Oslo University Hospital, Rikshospitalet, Oslo, Norway

ARTICLE INFO

Article history:
Received 4 September 2016
Accepted 6 November 2016
Available online 09 November 2016

Keywords:
Left ventricular non-compaction
Hypertrophic cardiomyopathy
Strain echocardiography
Regional myocardial function

ABSTRACT

Background: Modern imaging technology has improved detection of left ventricular non-compaction cardiomyopathy (LVNC). Hypertrophic cardiomyopathy (HCM) shares morphological features with LVNC, but prognosis and treatment strategies differ between LVNC and HCM.

Methods and results: We aimed to compare global and regional LV myocardial function in LVNC and HCM. We hypothesized that apical function is reduced in LVNC due to the embryonic reduced compaction of the apex. We studied 25 patients with LVNC (47 ± 14 years) according to current criteria, 50 with HCM (47 ± 14 years) and 50 healthy individuals (49 ± 19 years). By echocardiography, we assessed maximal wall thickness (MWT) and LV ejection fraction (EF). Numbers of trabeculations were counted from 3 apical views. Global longitudinal strain by speckle tracking echocardiography was calculated from a 16 LV segments model. LV basal (6 segments) and apical (4 segments) longitudinal strains were averaged. MWT was thinner, EF lower and trabeculations were more pronounced in LVNC compared to HCM (all $p < 0.001$) but with no significantly differences in LV global longitudinal strain (−15.1 ± 6.1 vs. −16.8 ± 3.7, $p = 0.14$). Function by longitudinal strain increased significantly from base to apex in HCM (−14.9 ± 4.3% vs. −19.5 ± 4.7%, $p < 0.001$) and in healthy controls (−20.0 ± 1.9% vs. −21.8 ± 2.9%, $p < 0.001$), but not in LVNC (−14.7 ± 6.4% vs. −15.7 ± 7.2%, $p = 0.35$).

Conclusions: Increased number of trabeculations, thinner MWT and lower EF were characteristics of LVNC. Myocardial function was homogeneously reduced in LVNC, while an apical to basal gradient with relatively preserved apical function was present in HCM. These characteristics may help to discriminate between LVNC and HCM.

1. Introduction

Left ventricular non-compaction cardiomyopathy (LVNC) is a rare condition with high morbidity and mortality due to malignant arrhythmias, systemic thrombotic embolism and heart failure [1]. LVNC is thought to be caused by an arrest in the normal process of myocardial compaction. Normal compaction of the embryonic myocardium proceeds from the epicardium to the endocardium and from the base to the apex [1,2]. An insufficient compaction of the myocardium will result in multiple prominent ventricular trabeculations and inter trabecular recesses and will predominantly include the ventricular endocardium and the apex of the LV [1]. Both sporadic and familial forms of LVNC have been described [1]. In familial disease, LVNC is a genetically heterogeneous disorder and shares genetic mutations with hypertrophic cardiomyopathy (HCM), including mutations in genes encoding for sarcomere proteins [1]. The prevalence of LVNC is reported between 0.014 and 1.3% [1]. LVNC is diagnosed with increasing frequency which may be due to higher awareness and more sensitive diagnostic tools. The use of modern ultrasound technology and cardiac magnetic resonance (CMR) has increased the detection of morphological features of LVNC. Furthermore, there is a possibility of over-diagnosing LVNC due to the lack of a true gold standard which may challenge the differentiation of LVNC from other cardiomyopathies. Further characterizations of morphological features in LVNC are therefore needed.

LVNC shares morphologic features with HCM which can mimic LVNC by presence of trabeculation and myocardial crypts [3,4]. Also, LVNC can present with increased wall thickness, resembling HCM, a phenotype associated with poor prognosis [5,6]. A true overlap may exist, as reported in genotyped families expressing both with HCM and LVNC phenotypes, and both diseases can occur in the same patient [7]. However, treatment strategies and risk of ventricular arrhythmias differ between LVNC and HCM and there are limited comparative studies on LVNC versus HCM.

Strain echocardiography can assess regional LV function, and be helpful in differentiating between cardiomyopathies [8,9] and reveal changes in myocardial function, also when ejection fraction (EF) is relatively

* Corresponding author at: Department of Cardiology, Oslo University Hospital, Rikshospitalet, PO Box 4950, Nydalen, N-0424 Oslo, Norway.
E-mail address: Kristina.Haugaa@rr-research.no (K.H. Haugaa).

http://dx.doi.org/10.1016/j.ijcard.2016.11.162

preserved [10]. The purpose of this study was to compare echocardiographic parameters in LVNC and HCM patients and to investigate regional cardiac function. We hypothesized that apical function is reduced in LVNC due to the embryonic uncompleted process of compaction.

2. Methods

2.1. Study population

In this cross sectional study, LVNC and HCM patients were consecutively included from our outpatient clinic. Data were analyzed retrospectively. Inclusion criteria were a definite diagnosis of LVNC or HCM, according to definitions [4,11,12] confirmed by two independent investigators. Exclusion criteria were coronary artery disease and myocardial hypertrophy of obvious non-sarcomeric origin [12]. All participants underwent clinical examination including New York Heart Association (NYHA) functional classification.

Healthy individuals were recruited from hospital staff, medical school and research laboratories and underwent clinical examination and echocardiographic examination.

All participants gave written informed consent. The study complied with the Declaration of Helsinki and was approved by the Regional Committees for Medical Research Ethics.

2.2. Definition of LVNC and HCM

Diagnosis of LVNC was defined by echocardiography, according to the criteria of Jenni et al. (Fig. 1) [4,13]. CMR criteria were used if diagnosis was not fulfilled by echocardiography and was defined as end-diastolic ratio between the non-compacted and compacted layer >2.3 [14]. The diagnosis of HCM was fulfilled by an otherwise unexplained hypertrophied LV with a maximal ventricular wall thickness (MWT) of ≥15 mm [12].

2.3. Cardiac imaging and clinical data

Echocardiography was performed at inclusion (Vivid 7 or Vivid E9 GE Healthcare, Horten, Norway) with off-line data analyses (EchoPac® GE Healthcare). The interventricular septum diameter, LV posterior wall diameter, LV end-diastolic diameter and LV end-systolic diameter were determined by M-mode or 2-D imaging. MWT was measured from all LV segments from the base to the apex of the LV in parasternal short-axis view [12]. EF was calculated by modified Simpson's biplane method. Diastolic function was evaluated by transmitral pulsed Doppler and average e′ from septal and lateral tissue Doppler samplings [15]. Atrial area was measured by using the average of apical four-chamber and apical two-chamber views at ventricular end-systole [16]. Myocardial trabeculations were defined as localized protrusions of the endocardial surface ≥3 mm in diameter, associated with intra trabecular recesses on 2-D echocardiography [17]. We manually counted all trabeculations visible in apical 4-chamber, 2-chamber and long-axis view. More than 3 trabeculations apically from the insertion of the papillary muscles were defined as increased LV trabeculation [5,18]. Myocardial longitudinal strain was obtained by speckle tracking technique from the 3 apical views at frame rate >50/s. The region of interest was traced in the compact part of the myocardium [19]. LV global longitudinal strain was averaged from peak longitudinal strains in a 16 segments LV model [20]. LV longitudinal basal strain (6 segments) and longitudinal apical strain (4 segments) were averaged and analyzed separately. The apical-basal gradient (average of apical strains minus average basal strains) was calculated. CMR was performed in a subset of patients on clinical indications as previously described [21].

24 hour Holter monitoring was performed in all participants. Ventricular arrhythmias were defined as aborted cardiac arrests, documented ventricular tachycardia and non-sustained ventricular tachycardia (≥3 consecutive ventricular beats with cycles length >100 beats/min, lasting <30 s) [22]. All patients underwent progressive maximal cardiopulmonary bicycle exercise test with a ramp protocol until exhaustion. Heart rate, blood pressure and maximum achieved Watt were recorded and metabolic equivalents were calculated as $(12 \times (\text{Watt}) + 300) \times (\text{weight} \times 3.5)^{-1}$ [23].

Genetic testing was performed as part of the diagnostic work up in patients with LVNC and HCM. We performed DNA sequencing of the genes encoding the sarcomere proteins MYH7 (NM_000257.2), MYBPC3 (NM_000256.3), TNNI3 (NM_000363.4), TNNT2 (NM_001001430.1), MYL2 (NM_000432.3) and MYL3 (NM_000258.2) as previously described [24]. Patients with variants of unknown significance were defined as genotype negative.

2.4. Statistical analyses

Parametric data were presented as mean ± standard deviation and compared by unpaired Student's *t*-test with Bonferroni post-hoc correction for multiple comparisons, Chi-square or Fischer's exact test as appropriate. Number of trabeculations was not normally

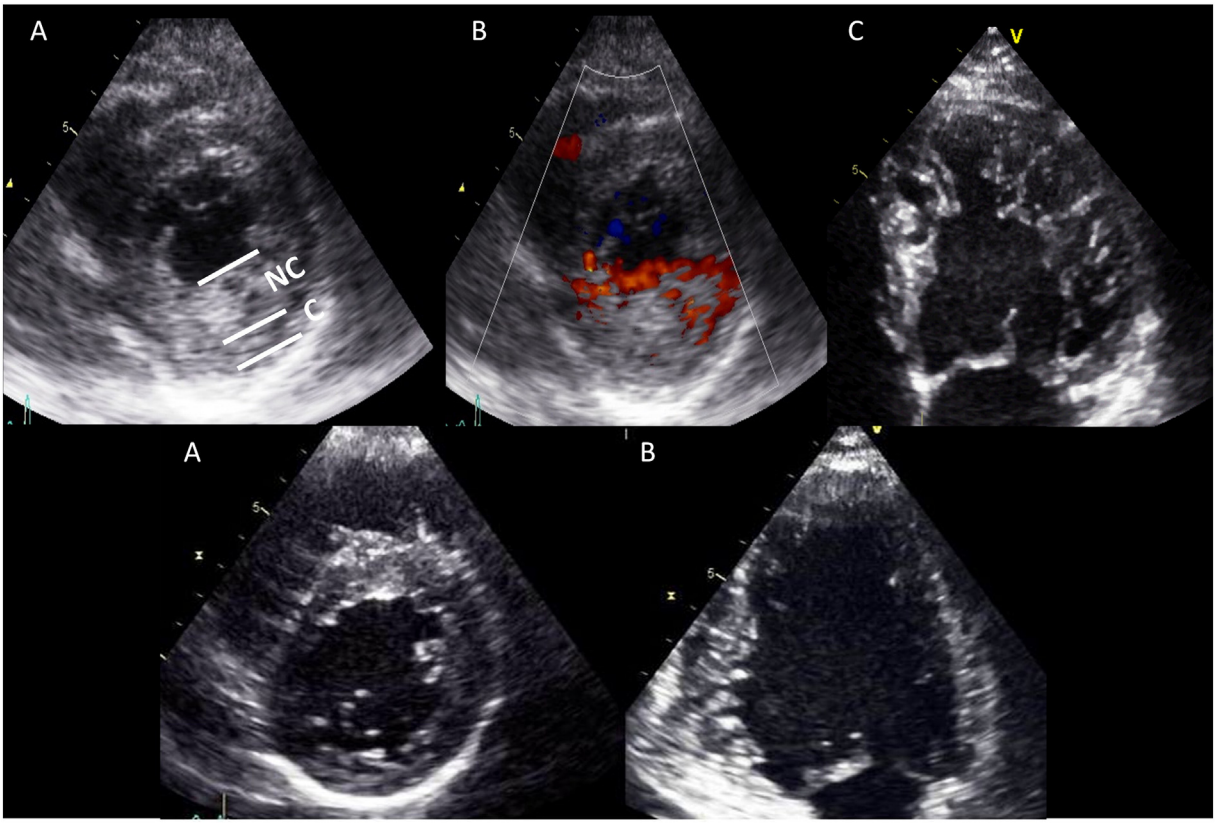

Fig. 1. Echocardiographic images from a patient fulfilling the left ventricular non-compaction (LVNC) criteria (upper panel) and a patient with hypertrophic cardiomyopathy (HCM) (lower panel). Upper panel A. Image from parasternal short-axis showing thickened myocardium consisting of two layers: a thin compacted epicardial layer (C) and a thicker non (N)-compacted (C) endocardial layer. NC/C layer >2 at end-systole. Upper panel B. Trabecular recesses filled with blood from the left ventricular cavity. Panel C. Apical four-chamber view with predominant location of trabeculation in the LV lateral free wall segments. Lower panel A: Posterior wall trabeculations in parasternal short-axis view in a patient with HCM not fulfilling LVNC criteria. Lower panel B: Trabeculations in the inferior wall visible in two-chamber view.

distributed and presented as median [min-max] and compared with non-parametric tests (SPSS 21.0). The incremental value of EF, number of trabeculations and MWT over diagnostic criteria, to assess the diagnosis of LVNC was studied by calculating the improvement in global chi-square. Values of p were two-sided and considered significant if <0.05.

3. Results

We included 25 patients with LVNC, 50 patients with HCM and 50 healthy individuals (Table 1). The LVNC diagnosis was established by echocardiography in 21 (84%) of the LVNC cases. Cardiac magnetic resonance imaging was performed in 9 (36%) LVNC patients and determined the final LVNC diagnosis in 4 (16%). A family history of cardiomyopathy was present in 14 (56%) of LVNC and 39 (78%) of HCM patients ($p = 0.06$). HCM associated sarcomere mutations were found in 9 (36%) LVNC patients and in 33 (66%) HCM ($p < 0.01$). Physical capacity was similar in LVNC and HCM patients by NYHA classification ($p = 0.59$) and by exercise capacity testing based on metabolic equivalents ($p = 0.82$) (Table 1). Cardiac arrests occurred more frequently in LVNC compared to HCM patients (6 (24%) vs. 1 (2.0%), $p = 0.05$) and ventricular arrhythmias were more frequent in LVNC patients (14 (56%) vs. 10 (20%), $p < 0.01$). More LVNC patients received an implantable cardioverter defibrillator (13 (52%) vs. 12 (24%), $p = 0.02$).

3.1. LV morphology and function

MWT was thicker in HCM compared with LVNC ($p < 0.001$) (Table 2). All LVNC patients had increased trabeculations (>3) compared to healthy (10 [5–14] vs. 0 [0–3], $p < 0.001$) and these were most frequently located in the apex. Apical trabeculations were present in all ($n = 25$) LVNC patients (Fig. 3). In addition, 23 (92%) had lateral and 12 (48%) had inferior trabeculations and 6 (24%) had trabeculations in the apical part of the septum (Fig. 2). Also HCM patients had increased number of trabeculations compared to the healthy individuals (2 [0–10] vs. 0 [0–3], $p < 0.001$). All LVNC patients (25 (100%)) and 20 (40%) HCM patients had >3 trabeculations ($p < 0.001$). In the 20 HCM patients with >3 LV trabeculations, regional distribution of trabeculations was similar to LVNC patients, except for more prevalent lateral trabeculations in LVNC ($p = 0.002$) (Fig. 2).

LV global systolic functions by EF and by LV global longitudinal strain were reduced in LVNC and HCM compared to healthy individuals (all $p < 0.001$) (Table 2) and EF was reduced in LVNC compared to HCM patients (Table 2). Systolic function by LV global longitudinal strain and diastolic parameters did not differ between LVNC and HCM patients (Table 2). For correct diagnosis, the predictive power of differentiation between LVNC and HCM increased at each step by adding EF, number of trabeculations and MWT, respectively, to clinical evaluation (Fig. 3).

3.2. Regional differences

Apical function was worse in LVNC compared to HCM ($p = 0.01$), while basal function did not differ ($p = 0.82$) (Table 2). In LVNC, LV function was homogenously reduced with no difference between apical and basal function ($-15.7 \pm 7.2\%$ vs. $-14.7 \pm 6.4\%$, $p = 0.35$) (Fig. 4). In contrast, HCM patients had better apical than basal longitudinal function ($-19.5 \pm 4.7\%$ vs. $-14.9 \pm 4.3\%$, $p < 0.001$). The apical-basal gradient was therefore more pronounced in HCM than in LVNC patients ($-4.5 \pm 5.1\%$ vs. $-1.1 \pm 4.6\%$, $p < 0.01$). Also in healthy, apical function was better than basal ($-21.8 \pm 2.9\%$ vs. $-20.0 \pm 1.9\%$, $p < 0.001$), but the apical-basal gradient was less pronounced compared to HCM patients ($-1.7 \pm 2.9\%$ vs. $-4.5 \pm 5.1\%$, $p < 0.01$) (Fig. 3).

There was no difference in apical strain in the subset of HCM patients with apical hypertrophy compared to the HCM without apical hypertrophy ($-19.5 \pm 4.7\%$ vs. $-19.5 \pm 6.0\%$, $p = 0.99$).

4. Discussion

The LVNC phenotype was characterized by more severely and homogeneously reduced myocardial function and the apical function was relatively most reduced in LVNC compared to HCM and healthy. In contrast, HCM patients had preserved EF, but reduced LV global longitudinal strain with more reduced function in basal segments, while apical function was relatively preserved. As expected, trabeculations were most frequent in LVNC. These findings may help to characterize patients with LVNC and HCM in families with overlapping phenotypes. The correct differentiation between LVNC and HCM is important, given the higher incidence of ventricular arrhythmias in LVNC, as also shown in this study.

Evolving imaging techniques have increased the diagnosis of LVNC and patients with a previous HCM diagnosis are occasionally re-diagnosed with LVNC. Whether this reflects a previously overseen LVNC diagnosis or an over-diagnosis of LVNC is unclear. Furthermore, the genetic etiology in the two conditions is overlapping by the presence of both

Table 1
Clinical characteristics in 50 healthy individuals, in 50 patients with hypertrophic cardiomyopathy and in 25 patients with left ventricular non-compaction cardiomyopathy.

	Healthy n = 50	HCM n = 50	LVNC n = 25	p-Value
Age (years)	49 ± 19	47 ± 14	47 ± 14	0.67
Women n (%)	15 (60%)	15 (30%)	19 (38%)†	0.04
Heart rate (bpm)	62 ± 10	63 ± 12	66 ± 18	0.48
Systolic blood pressure (mm Hg)		134 ± 22	121 ± 21	0.02
Diastolic blood pressure (mm Hg)		79 ± 13	74 ± 15	0.13
NYHA class		1.7 ± 0.8	1.8 ± 0.6	0.59
NYHA class I (n)		25 (50%)	9 (36%)	0.18
NYHA class II (n)		19 (38%)	13 (52%)	0.18
NYHA class III (n)		4 (8%)	3 (12%)	0.42
NYHA class IV (n)		2 (4%)	0	0.55
Metabolic equivalents (3.5 ml/kg/min)		7.9 ± 2.6	7.8 ± 2.8	0.82
Angiotensin converting enzyme-inhibitor (n)		5 (10%)	10 (40%)	<0.01
Angiotensin II-receptor-antagonist (n)		4 (8%)	4 (16%)	0.42
Beta blocker (n)		43 (86%)	23 (92%)	0.71
Acetylsalicylic acid (n)		6 (12%)	6 (24%)	0.19
Warfarin (n)		6 (12%)	8 (32%)	0.05
Diuretics (n)		2 (4%)	8 (32%)	<0.01
Ventricular arrhythmia (n)		10 (20%)	14 (56%)	<0.01
Cardiac arrest (n)		1 (2%)	6 (24%)	<0.01
Implantable cardioverter defibrillator (n)		12 (24%)	13 (52%)	0.02

Mean ± SD, right column shows p-values for ANOVA and Chi square tests. HCM: hypertrophic cardiomyopathy. LVNC: left ventricular non-compaction NYHA class: New York Heart Association functional classification.
† $p < 0.05$ compared to HCM.

Table 2
Echocardiographic findings in 50 healthy individuals, in 50 patients with hypertrophic cardiomyopathy and in 25 patients with left ventricular non-compaction cardiomyopathy.

	Healthy n = 50	HCM n = 50	LVNC n = 25	p-Value
LV end-diastolic diameter (mm)	52 ± 5.2	48 ± 5.7*	60 ± 9.0*†	<0.001
LV end-systolic diameter (mm)	33 ± 5.2	32 ± 6.4	47 ± 11.9*†	<0.001
Interventricular septum diameter (mm)	7.8 ± 1.6	16.2 ± 4.8*	8.7 ± 2.5†	<0.001
LV posterior wall diameter (mm)	7.5 ± 1.5	9.2 ± 2.4*	8.0 ± 1.7†	<0.001
Maximal wall thickness (mm)	8.5 ± 1.2	18 ± 3.7*	10 ± 2.2†	<0.001
Ejection fraction (%)	61 ± 5	57 ± 7*	40 ± 14*†	<0.001
LV global longitudinal strain (%)	−21.1 ± 1.9	−16.8 ± 3.6*	−15.2 ± 6.1*	<0.001
Basal strain (%)	−20.0 ± 1.9	−14.9 ± 4.3*	−14.6 ± 6.4*	<0.001
Apical strain (%)	−21.8 ± 2.9	−19.5 ± 4.7	−15.7 ± 7.2*†	<0.001
Apical-basal gradient (%)	−1.7 ± 2.9	−4.5 ± 5.1*	−1.1 ± 4.6†	<0.01
Deceleration time (ms)	190 ± 53	191 ± 54	180 ± 69	0.56
E/A	1.4 ± 0.6	1.6 ± 0.9	1.7 ± 1.1	0.31
E (m/s)	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	0.76
E/e′	7.1 ± 2.1	11.8 ± 6.1*	11.5 ± 8.9*	<0.01
Atrial area (cm^2)	17.3 ± 2.9	22.7 ± 6.5*	22.2 ± 5.4*	<0.001
Trabeculations (n)	0 (0–3)	2 (0–10)*	10 (5–14)*†	<0.001

Mean ± SD, right column shows p-values for ANOVA test or Mann-Whitney *U* test. A: atrial transmitral filling velocity. E: early transmitral flow velocity. e′: early diastolic myocardial velocity.GLS: global longitudinal strain. HCM: hypertrophic cardiomyopathy. LV: left ventricle. LVNC: left ventricular non-compaction.
* $p < 0.05$ compared to healthy individuals.
† $p < 0.05$ compared to HCM.

HCM and LVNC phenotypes within families with sarcomere mutations. However, the arrhythmic risk seems to be higher in patients with LVNC compared to HCM, making correct diagnosis important. MWT was thicker in HCM compared to LVNC, as expected. Furthermore, numbers of trabeculations were most frequent in LVNC. Trabeculations are common in LVNC, but importantly, not specific for LVNC (Fig. 1). Prominent trabeculations may be present also in patients with dilated cardiomyopathy, hypertensive heart disease and may increase during pregnancy [4,19,25,26]. Prominent trabeculations are included in the diagnostic criteria for LVNC by Jenni [4], and by Stöllberger, including >3 trabeculations visible in a single image plane [5]. We counted trabeculations from all 3 apical echocardiographic views. Our findings support that trabeculations are frequent in LVNC, although >3 trabeculations were also found in 40% of HCM patients. EF was relatively preserved in HCM as previously reported [27]. However, a depressed global longitudinal LV function was found in both diseases as supported by previous reports [28,29]. A reduced LV global longitudinal strain could therefore not be used to separate between the two diagnoses.

Compaction of the embryonic myocardium proceeds from the epicardium to the endocardium and from the base to the apex [1,2]. An arrest in compaction will therefore predominantly include the ventricular endocardium and the apex of the LV [1]. From this, the apical segments should be most frequently involved in the non-compaction pathology. We found a homogeneously reduced function in basal and apical segments in LVNC patients. In healthy individuals, we observed a mild gradient with better apical than basal function, also described by others [30]. No such gradient was observed in LVNC. Therefore, apical function was relatively more reduced than basal function in LVNC compared to healthy individuals. Our findings are in line with previous observations

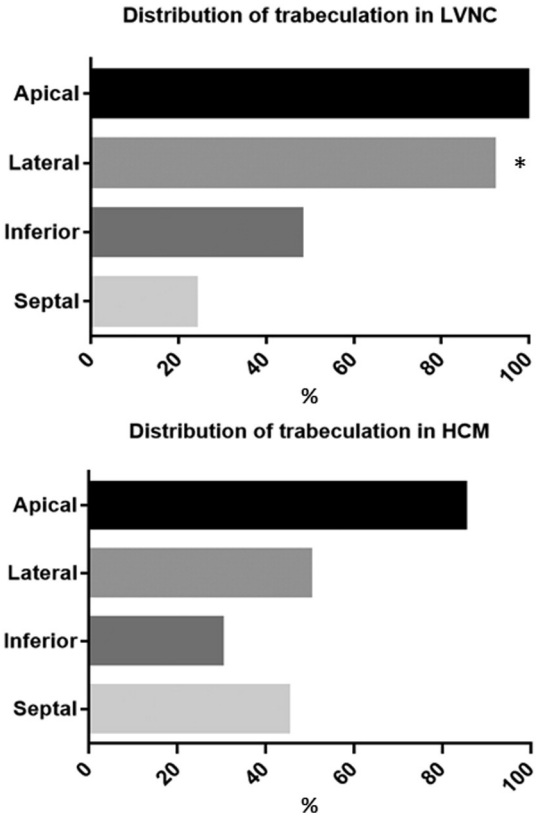

Fig. 2. Distribution of trabeculations among the left ventricular segments in patients with left ventricular non-compaction (LVNC) and in patients with hypertrophic cardiomyopathy (HCM). All patients with left ventricular non-compaction had trabeculations in apical segments. The distribution was not significantly different between the two groups, except in the lateral segments, where trabeculations were more prevalent those with LVNC *($p < 0.01$). LVNC = left ventricular non-compaction, HCM = hypertrophic cardiomyopathy.

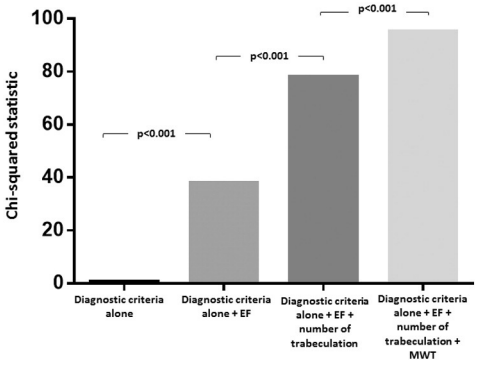

Fig. 3. Incremental value of EF, number of trabeculation and MWT over conventional diagnostic parameters. Addition of EF, number of trabeculation and MWT to conventional diagnostic criteria in a Likelihood ratios test resulted in a significant improvement in predictive value of differentiation between left ventricular non-compaction and hypertrophic cardiomyopathy. EF = ejection fraction, MWT = maximal wall thickness.

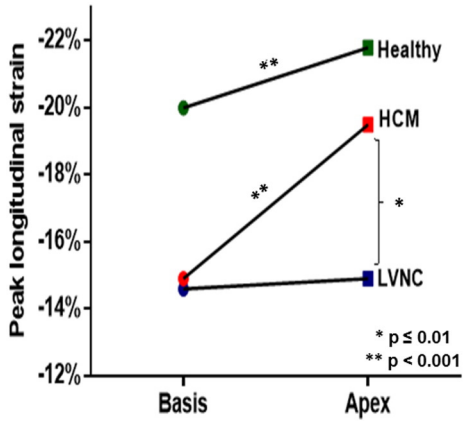

Fig. 4. Diagram of left ventricular basal and apical longitudinal strain in patients with hypertrophic cardiomyopathy (red), in patients with left ventricular non-compaction cardiomyopathy (blue) and in healthy individuals (green). Patients with hypertrophic cardiomyopathy had better strain in apical segments compared to basal segments, while there was no difference in basal and apical function in patients with left ventricular non-compaction. Furthermore, apical function was significantly better in patients with hypertrophic cardiomyopathy compared to left ventricular non-compaction ($p = 0.01$). *$p \leq 0.01$, **$p < 0.001$. Basal = average of peak longitudinal strain from 6 basal segments, Apical = average of peak longitudinal strain from 4 apical segments. LVNC = left ventricular non-compaction, HCM = hypertrophic cardiomyopathy. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

by Niemann et al. [19] who showed lower function in the LV apex compared to base by tissue Doppler imaging in LVNC patients. We suggest that reduced apical function may be a specific finding in LVNC and may originate from the specific embryonic mechanism of progressing myocardial compaction from base to apex. HCM patients had a significant apical to basal functional gradient with preserved apical function compared to a greater loss of basal function. This gradient was more pronounced in HCM compared to the mild apical-basal gradient observed in our healthy individuals. The pronounced functional gradient in HCM patients may be explained by the more frequent location of hypertrophy in the basal and septal segments, however apical strain did not differ between HCM patients with septal versus apical hypertrophy, supporting our hypothesis that reduced apical function is specific for LVNC.

4.1. Limitations

An important limitation of this study was that no gold standard exists in the definition of LVNC. We defined our LVNC patients according to the Jenni criteria with thickened myocardium and the two-layer structure of non-compacted/compacted ratio >2. Other definitions include hypertrabeculation defined as >3 trabeculations protruding from the left ventricle [1,5]. Strain analyses are challenging in both LVNC and in HCM due to the varying intra individual wall thickness which may influence strain measurements. We carefully placed the measurements in the compacted area in LVNC and in the midventricular wall in HCM patients to obtain reproducibility.

5. Conclusion

We found homogeneously reduced LV function in LVNC, as opposed to preserved apical and more reduced basal function in HCM, which may represent specific differences in embryogenesis and pathogenesis in the two cardiomyopathies. LVNC patients had increased number of trabeculations, thinner MWT, and lower EF compared to HCM patients and assessment of these parameters may help to characterize LVNC in patients with overlapping phenotypes.

Disclosures

The authors have no conflicts of interest to disclose.

Funding sources

This work was supported by the Center for Cardiological Innovation, funded by the Research Council of Norway.

Acknowledgements

We thank all participants in this study.

References

[1] E. Oechslin, R. Jenni, Left ventricular non-compaction revisited: a distinct phenotype with genetic heterogeneity? Eur. Heart J. 32 (2011) 1446–1456.
[2] D. Sedmera, T. Pexieder, M. Vuillemin, R. Thompson, R.H. Anderson, Developmental patterning of the myocardium, Antarct. Rec. 258 (2000) 319–337.
[3] M.S. Maron, E.J. Rowin, D. Lin, et al., Prevalence and clinical profile of myocardial crypts in hypertrophic cardiomyopathy, Circ. Cardiovasc. Imaging 5 (2012) 441–447.
[4] R. Jenni, Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: a step towards classification as a distinct cardiomyopathy, Heart 86 (2001) 666–671.
[5] C. Stöllberger, J. Finsterer, Left ventricular hypertrabeculation/noncompaction, J. Am. Soc. Echocardiogr. 17 (2004) 91–100.
[6] J.A. Towbin, Left ventricular noncompaction: a new form of heart failure, Heart Fail. Clin. 6 (2010) 453–469.
[7] A. Kelley-Hedgepeth, J.A. Towbin, M.S. Maron, Images in cardiovascular medicine. Overlapping phenotypes: left ventricular noncompaction and hypertrophic cardiomyopathy, Circulation 119 (2009) e588–e589.
[8] T. Edvardsen, B.L. Gerber, J. Garot, D.A. Bluemke, J.A.C. Lima, O.A. Smiseth, Quantitative assessment of intrinsic regional myocardial deformation by Doppler strain rate echocardiography in humans: validation against three-dimensional tagged magnetic resonance imaging, Circulation 106 (2002) 50–56.
[9] D. Phelan, P. Collier, P. Thavendiranathan, et al., Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis, Heart 98 (2012) 1442–1448.
[10] K.H. Haugaa, J.P. Amlie, K.E. Berge, T.P. Leren, O.A. Smiseth, T. Edvardsen, Transmural differences in myocardial contraction in long-QT syndrome: mechanical consequences of ion channel dysfunction, Circulation 122 (2010) 1355–1363.
[11] B.J. Maron, W.J. McKenna, G.K. Danielson, et al., American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy, J. Am. Coll. Cardiol. 42 (2003) 1687–1713.
[12] P.M. Elliott, A. Anastasakis, M.A. Borger, et al., 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC), Eur. Heart J. 35 (2014) 2733–2779.
[13] B.S. Frischknecht, C.H. Attenhofer Jost, E.N. Oechslin, et al., Validation of noncompaction criteria in dilated cardiomyopathy, and valvular and hypertensive heart disease, J. Am. Soc. Echocardiogr. 18 (2005) 865–872.
[14] S.E. Petersen, J.B. Selvanayagam, F. Wiesmann, et al., Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging, J. Am. Coll. Cardiol. 46 (2005) 101–105.
[15] S.F. Nagueh, C.P. Appleton, T.C. Gillebert, et al., Recommendations for the evaluation of left ventricular diastolic function by echocardiography, J. Am. Soc. Echocardiogr. 22 (2009) 107–133.
[16] R.M. Lang, M. Bierig, R.B. Devereux, et al., Recommendations for chamber quantification, Eur. J. Echocardiogr. 7 (2006) 79–108.
[17] S. Gati, N. Chandra, R.L. Bennett, et al., Increased left ventricular trabeculation in highly trained athletes: do we need more stringent criteria for the diagnosis of left ventricular non-compaction in athletes? Heart 99 (2013) 401–408.
[18] M.T. Boyd, J.B. Seward, A.J. Tajik, W.D. Edwards, Frequency and location of prominent left ventricular trabeculations at autopsy in 474 normal human hearts: implications for evaluation of mural thrombi by two-dimensional echocardiography, J. Am. Coll. Cardiol. 9 (1987) 323–326.
[19] M. Niemann, D. Liu, K. Hu, et al., Echocardiographic quantification of regional deformation helps to distinguish isolated left ventricular non-compaction from dilated cardiomyopathy, Eur. Heart J. 14 (2012) 155–161.
[20] M.D. Cerqueira, Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association, Circulation 105 (2002) 539–542.
[21] T.F. Haland, V.M. Almaas, N.E. Hasselberg, et al., Strain echocardiography is related to fibrosis and ventricular arrhythmias in hypertrophic cardiomyopathy, Eur. Heart J. Cardiovasc. Imaging. (2016).
[22] C.T. Pedersen, G.N. Kay, J. Kalman, et al., EHRA/HRS/APHRS expert consensus on ventricular arrhythmias, Europace 16 (2014) 1257–1283.
[23] G.F. Fletcher, G.J. Balady, E.A. Amsterdam, et al., Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association, Circulation 104 (2001) 1694–1740.

[24] V.M. Almaas, K.H. Haugaa, E.H. Strom, et al., Increased amount of interstitial fibrosis predicts ventricular arrhythmias, and is associated with reduced myocardial septal function in patients with obstructive hypertrophic cardiomyopathy, Europace 15 (2013) 1319–1327.
[25] S.K. Kohli, A.A. Pantazis, J.S. Shah, et al., Diagnosis of left-ventricular non-compaction in patients with left-ventricular systolic dysfunction: time for a reappraisal of diagnostic criteria? Eur. Heart J. 29 (2008) 89–95.
[26] S. Gati, M. Papadakis, N.D. Papamichael, et al., Reversible de novo left ventricular trabeculations in pregnant women: implications for the diagnosis of left ventricular noncompaction in low-risk populations, Circulation 130 (2014) 475–483.
[27] L.C. Afonso, J. Bernal, J.J. Bax, T.P. Abraham, Echocardiography in hypertrophic cardiomyopathy: the role of conventional and emerging technologies, JACC Cardiovasc. Imaging 1 (2008) 787–800.
[28] N. Cardim, M. Galderisi, T. Edvardsen, et al., Role of multimodality cardiac imaging in the management of patients with hypertrophic cardiomyopathy: an expert consensus of the European Association of Cardiovascular Imaging Endorsed by the Saudi Heart Association, Eur. Heart J. Cardiovasc. Imaging 16 (2015) 280.
[29] D. Bellavia, H.I. Michelena, M. Martinez, et al., Speckle myocardial imaging modalities for early detection of myocardial impairment in isolated left ventricular noncompaction, Heart 96 (2010) 440–447.
[30] T. Edvardsen, K.H. Haugaa, Imaging assessment of ventricular mechanics, Heart 97 (2011) 1349–1356.