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The use of 2-D speckle tracking echocardiography in assessing adolescent athletes with left ventricular hypertrabeculation meeting the criteria for left ventricular non-compaction cardiomyopathy

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ABSTRACT

Background: Current echocardiographic criteria cannot accurately differentiate exercise induced left ventricular (LV) hypertrabeculation in athletes from LV non-compaction cardiomyopathy (LVNC). This study aims to evaluate the role of speckle tracking echocardiography (STE) in characterising LV myocardial mechanics in healthy adolescent athletes with and without LVNC echocardiographic criteria.

Methods: Adolescent athletes evaluated at three sports academies between 2014 and 2019 were considered for this observational study. Those meeting the Jenni criteria for LVNC (end-systolic non-compacted/compacted myocardium ratio > 2 in any short axis segment) were considered LVNC+ and the rest LVNC-. Peak systolic LV longitudinal strain (S_l), circumferential strain (S_c), rotation (Rot), corresponding strain rates ($SR_{l/c}$) and segmental values were calculated and compared using a non-inferiority approach.

Results: A total of 417 participants were included, mean age 14.5 ± 1.7 years, of which 6.5% were LVNC+ (n = 27). None of the athletes showed any additional LVNC clinical criteria. All average S_l, SR_l S_c, SR_c and Rot values were no worse in the LVNC+ group compared to LVNC- (p values range 0.0003–0.06), apart from apical SR_c (p = 0.2). All 54 segmental measurements (S_l/S_c SR_l/SR_c and Rot) had numerically comparable means in both LVNC+ and LVNC-, of which 69% were also statistically non-inferior.

Conclusions: Among healthy adolescent athletes, 6.5% met the echocardiographic criteria for LVNC, but showed normal LV STE parameters, in contrast to available data on paediatric LVNC describing abnormal myocardial function. STE could better characterise the myocardial mechanics of athletes with LV hypertrabeculation, thus allowing the transition from structural to functional LVNC diagnosis, especially in suspected physiological remodelling.

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1. Introduction

Left ventricular non-compaction cardiomyopathy (LVNC) is characterised by prominent left ventricle (LV) trabeculae, a thin compacted layer, intertrabecular recesses and the propensity for arrhythmias and cardiac dysfunction [1,2]. The exact causes are not fully understood, being considered to be genetic or embryological [1,2], resulting in abnormal myocardial fibre anatomy and twist mechanics which lead to compensatory hypertrabeculation [3,4]. Clinically, it can present as palpitations or syncope during exertion, ECG changes, heart failure, embolic complications, and as LV dysfunction progresses or arrhythmias occur, sudden cardiac death (SCD) [2,5–7].

Diagnosis of LVNC is based on a combination of personal and family history, clinical and ECG data and echocardiographic [8–10] or cardiac magnetic resonance imaging (CMR) derived criteria [11]. Their major limitation is that hypertrabeculation can also be the result of physiological adaptation to increased preload associated with athletic training [12], rather than a compensatory mechanism to pathological changes in the myocardium [3]. As many as 8% of adult athlete have hypertrabeculation mimicking LVNC [6,13,14], also seen in healthy controls of Black ethnicity [15], or women during pregnancy [16]. To date, there are no data on the prevalence of hypertrabeculation in paediatric populations (healthy controls or athletes), and as such whether somatic growth and length of exposure to training play any role is unknown.

Conventional echocardiographic parameters fall short in differentiating normal from potentially pathologic hypertrabeculation, even when additional tests, like CMR, are indicated [6]. A normal LV size and function is associated with good prognosis in LVNC [2,5,7], but it does not imply that the cardiomyopathy is absent [7,17]. In addition, borderline LV ejection fraction (LVEF) or diastolic dysfunction, used to risk stratify LVNC patients, have been described in healthy athletes [13,18]. Speckle tracking echocardiography (STE) can better characterise cardiac function in these borderline cases, uncovering subclinical changes in myocardial mechanics not limited to global function, in adults [19] and children [17].

In LVNC, LV longitudinal strain (S_l) as well as regional mechanics of the non-compacted areas are abnormal in adults [4,20] and also children [21,22]. STE parameters were abnormal even in LVNC patients with LVEF>50% or normal diastolic LV function [17,19]. Conversely, LVEF is reduced in healthy athletes meeting echocardiographic LVNC criteria [13], to the same degree as in children with confirmed LVNC [21], further complicating the diagnosis when there is no marked LV dysfunction or other non-echocardiographic criteria to clarify the diagnosis.

This study aims to report the prevalence of positive LVNC echocardiographic criteria in healthy adolescent athletes and evaluate the potential role of STE in characterising cardiac function in the presence of hypertrabeculation. The hypothesis is that myocardial mechanics, including LV longitudinal/circumferential strain and rotation parameters, will be no worse, within a relevant margin in healthy adolescent athletes who meet the criteria for non-compaction (LVNC+) compared to those who do not (LVNC-). These findings would complement the current literature describing abnormal LV global and regional mechanics in children with LVNC or hypertrabeculation [22,23].

2. Methods

2.1. Participant assessment and classification

Male athletes under 18 years of age evaluated at three sport academies (Manchester United Football Club, United Kingdom, Doha Aspire Academy, Qatar and Barcelona Football Club, Spain) between 2014 and 2019 were considered. Evaluations were done at the beginning of the season (n = 388, 93%), while a small proportion had to be performed either mid-season or after the season end (n = 29, 7%). UK National Research Ethics Service approval was obtained, and local ethics approval for participating centres (Qatar Anti-Doping Laboratory IRB #E2013000003 and #E20140000012; Hospital Clinic Barcelona HCB/2018/0068), and parent/carer and adolescents signed procedure consent forms and/or assent forms, respectively, when not covered by the local institutional consent framework. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

All athletes underwent a detailed evaluation, including health questionnaire, anthropometric measurements and 12-lead ECG, as recommended by the local and institutional protocols and were cleared for sports participation based on the current recommendations [24]. Practiced sport was classified by type (endurance, power, skill or mixed) [25]. All athletes were reviewed by the local clinical team if a cardiomyopathy was suspected, underwent the recommended testing (including CMR if indicated), and the most recent follow-up information was reviewed.

Based on previous literature, the echocardiographic criteria described by Jenni et al. [8] were selected as being the most restrictive in athletes (lowest probability of false positive) [6,13–15]. Those having a ratio of non-compacted (NC) to compacted (C) myocardium of NC/C > 2 during end-systole in any short axis view segment, with prominent trabeculations and deep intratrabecular recesses were considered as LVNC+, and the rest LVNC- [8]. Individuals where an adequate apical short axis (SAX) view was not available were excluded (Fig. A.1).

2.2. Echocardiography

Echocardiography at rest was performed using either an Artida or an Aplio i900 machine (Canon Medical Systems, Japan) and a 2.0–4.8 MHz transducer. LV chamber quantification was performed: LV end diastolic diameter (LVEDD), LV end systolic diameter (LVESD), interventricular septum thickness (IVS), posterior wall thickness (PW). LV systolic and diastolic function was quantified as follows: LV ejection fraction (LVEF) using the modified Quinones formula (%ΔD2 + [(1-%ΔD2)x(%ΔL)], %ΔD2 = LVEDD [2] - LVESD [2]/LVEDD [2], %ΔL = 15% for normal apical function), peak septal and lateral mitral annulus velocity at pulsed wave tissue Doppler Imaging (LV septal and lateral S′), peak mitral E and A wave velocities, peak mitral E' velocities (mean of lateral and septal values when both are reported), E/A ratio, E/E' ratio. All measurements were performed by an experienced clinician (G.E.P., A.G.S., D.M.D) either at the time of the clinical evaluation or offline, following current echocardiographic guidelines [26–28].

NC and C myocardium thickness was measured offline in all three short axis views (basal, mid, apical) by DMD and CR, using the Ultra Extend Package v3.2 (Canon Medical Systems, Japan) or Radiant DICOM Viewer 2020 (Medixant, Poland).

2.3. Speckle tracking echocardiography (STE)

Apical 4 chamber (A4C) and short axis (SAX basal, mid and apical) views were acquired for STE analysis (three cardiac cycles at 50–100 frames per second). The endocardial border was traced (automatically in A4C, otherwise manually), myocardial thickness adjusted and automated tracking used on one manually selected best cardiac cycle. Tracking quality and strain curves were visually inspected, and tracking was adjusted if necessary.

Average LV peak systolic longitudinal A4C strain (A4C S_l), average LV basal, mid and apical circumferential peak systolic strain (basal, mid and apical S_c), the corresponding peak systolic strain rates (SR_l and SR_C) as well as peak systolic basal (negative) and apical (positive) rotation (basal and apical Rot) were measured and reported [29]. All STE analyses were performed offline by an experienced clinician (DMD) using the Vitrea 7.11.5.29 (Canon Medical Systems, Japan). The end systole frame was automatically selected as corresponding to the smallest ventricular volume. All peak systolic strain values were extracted from the output using an in-house script (R version 4.1.0).

2.4. Statistical analyses

Frequencies are given as numbers and percentages, continuous values as means±standard deviation (SD). Population characteristics were compared using the *t*-test with Welch's approximation (continuous variables) and Fisher's test (categorical variables). Associations between patient factors and LVNC+ were explored based on descriptive data, with age, BSA, sport group, ethnicity being co-variates in a multivariable logistic regression (adjusted by centre) and reported as odds ratio (OR).

In order to evaluate whether the STE parameters measured in the LVNC+ were comparable to those in the LVNC- group, a non-inferiority statistical approach was used. The "two one-sided t-test" with Welch approximation test (TOST package) [30] was used, which determines whether the difference between two means is between a lower and upper set limit (equivalence limit, or delta). This limit was chosen empirically, based on the limited available data [21], to be 2% for S_l and proportionally 2.5% for S_c, 0.1 for SR_l, 0.15 for SR_c, and 0.5^O for basal/apical rotation. Since only a non-inferiority test was relevant, the *p* value for the upper limit test was used for the negative values (S_l, SR_l and basal rotation) and the lower limit test for positive values (apical Rot). This methodology is further detailed in the Supplemental Material (Statistical analyses).

Evaluating differences in average and segmental STE measurements between LVNC+/− groups required 68 statistical tests (same test family), for which a Benjamini-Hochberg (BH) critical value (false discovery rate set at 0.1) was calculated as an adjusted statistical significance level [31], to correct for multiple testing. Thus, an alpha value of $p \leq 0.05$ was considered statistically significant unless an adjusted Benjamini-Hochberg critical value is specified.

Inter- and intra-observer agreement were expressed as Cohen's kappa

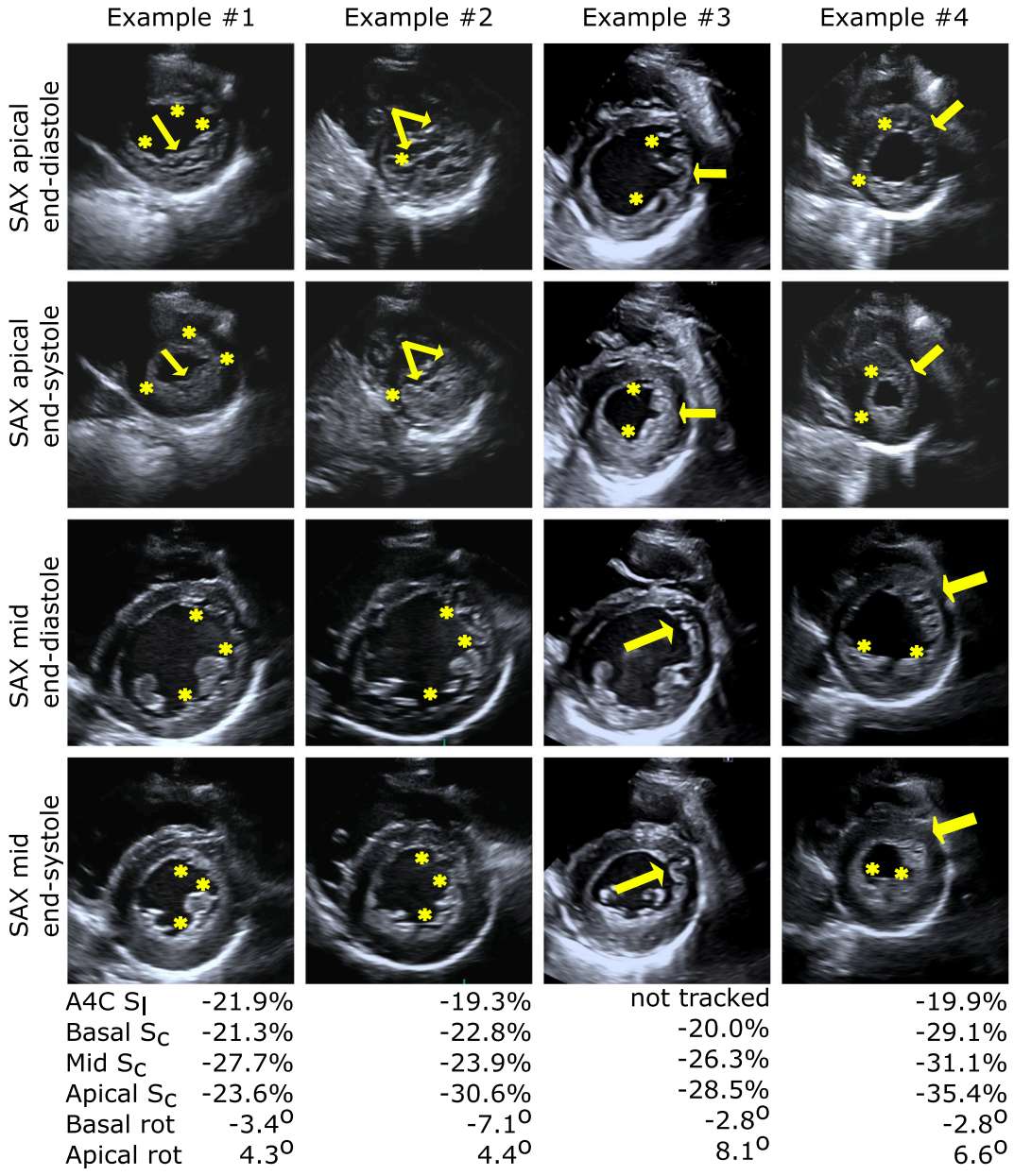

Fig. 1. Examples of athletes meeting the left ventricular non-compaction criteria [8]. Each column represents one example (#1-#4) and shows the short axis (SAX) apical and mid views (in end-diastole and end-systole), as well as peak systolic longitudinal apical 4 chamber (A4C) strain (S_l), circumferential strain (S_c), basal rotation (Rot) and apical rotation (Rot). Arrows point to the myocardial segments with hypertrabeculation having an end-systolic non-compacted/compacted (NC/C) ratio ≥ 2, while asterisks show segments with hypertrabeculation and a NC/C ratio < 2.

statistic for LVNC classification (random sample of $n = 40$, DMD and CR) and as inter-class-coefficient (ICC) for STE parameters (random sample of $n = 30$, DMD and ND). All Statistical analyses were done using the STATA 16 SE (Stata Corp, Texas, USA).

3. Results

A total of 417 healthy male athletes under 18 years of age were included (mean age 14.5 ± 1.7, range 11.6–18 years), from the total of 447 eligible participants (exclusions with reasons in Fig. 1). Of these, 6.5% ($n = 27$) met the Jenni criteria for LVNC (LVNC+).

Demographic, anthropometric and practiced sport data within the LVNC+/LVNC- groups are shown in Table 1. LVNC+ athletes were older ($p = 0.03$), had higher BSA ($p = 0.002$), and a higher probability of being of Black ethnicity ($p = 0.005$). Due to the risk of selection bias, the associations between LVNC+ and subject characteristics were further evaluated. Only Black ethnicity was found to be associated with LVNC+ status after adjusting for age, weight, height, BSA, practiced sport type and centre (adjusted OR = 2.9 versus non-Black ethnicity, 95% CI [1.1;8], $p = 0.04$). At the time of writing, no cases of cardiomyopathies were reported in this cohort as part of usual care at the participating centres. The prevalence of abnormal ECG changes and borderline ECG findings [32] was similar in both groups ($p = 0.8$, Table 1). None of the athletes had physical examination, personal or family history suggestive of LVNC.

3.1. Left ventricular structure, size and function by conventional echocardiography

LV size, systolic function or diastolic function parameters measured by conventional echocardiography were normal, and similar between LVNC+ and LVNC- groups (Table A.1).

Table 1
Demographic, anthropometric, ECG and practiced sports data.

	LVNC+n = 27	LVNC-n = 390	Total$n$ = 417	p value
Age, mean ± SD (y)	15.2 ± 1.5	14.5 ± 1.7	14.5 ± 1.7	0.03
BSA, mean ± SD (m^2)*	1.72 ± 0.15	1.61 ± 0.26	1.62 ± 0.26	0.002
Ethnicity, n (%)				
Arab	6 (22.2)	188 (48.2)	194 (46.5)	0.005
Black	11 (40.8)	73 (18.7)	84 (20.1)	
White	7 (25.9)	73 (18.7)	80 (19.2)	
Other**	2 (7.4)	9 (2.3)	11 (2.7)	
Missing	1 (3.7)	47 (12.1)	48 (11.5)	
Practiced sport type, n (%)				
Mixed	19 (70.4)	285 (73.1)	304 (72.9)	0.3
Power	5 (18.5)	44 (11.3)	49 (11.7)	
Endurance	1 (3.7)	31 (7.9)	32 (7.7)	
Skill	0	18 (4.6)	18 (4.3)	
Unclassifiable***	2 (7.4)	12 (3.1)	14 (3.4)	
ECG findings, n (%)****				
Normal	23 (85.2)	294 (80.1)	317 (80.5)	0.3
One borderline finding	3 (11.1)	68 (18.5)	71 (18)	
Abnormal	1 (3.7)	5 (1.4)	6 (1.5)	

BSA, body surface area; SD, standard deviation.
Abnormal ECG:
LVNC+: anterior T wave inversion ($n = 1$) LVNC-: pathological Q wave (n = 2), lateral T wave inversion (n = 1), ST segment depression (n = 1), >2 premature ventricular complexes on a 10s period (n = 1).
* using the DuBois formula, missing n = 2
** $n = 7$ (mixed) and n = 4 (south Asian).
*** $n = 13$ (referee), n = 1 (missing)
**** ECG changes were classified by current criteria [32]. Missing in $n = 23$.

The distribution of segments with NC/C ratio ≥ 2, 0 < NC/C ratio < 2 and no NC layer is shown in Fig. A.2. The LV segments most likely to exhibit a NC/C layer ratio ≥ 2 were: apical lateral (16/27, 59.3%), apical anterior (6/27, 22.2%), apical inferior (6/27, 22.2%), mid anterior (4/26, 15.4%) and basal anterior (3/27, 11.1%). Examples of athletes meeting the LVNC+ criteria in our cohort are presented in Fig. 1, along with their corresponding main STE measurement values.

3.2. Left ventricle STE measurements

The overall mean A4C-S_l was −20.7 ± 2% (range − 16.4% to −27.6%), mean basal S_c − 26.1 ± 3.7% (range − 16.5% to −37.4%), mid S_c − 28 ± 3.6% (range − 17.9% to −39.6%) and apical S_c − 30.3 ± 4.9% (range − 19.4% to −45.3%). Mean A4C S_l, A4C SR_l, basal, mid and apical S_c, basal, mid and apical SR_c, basal and apical rotation were numerically similar in both LVNC+ and LVNC- groups, and also statistically non-inferior in the LVNC+ compared to the LVNC-, with the exception of the apical SR_c where the comparison was underpowered (Fig. 2 and Table A.2).

Segmental measurements were also numerically similar between the two groups, absolute differences ranging from 0.001 to 1.34% for S_l/S_c, 0.002–0.134 s^{-1} for SR_l/SR_c and 0.04–1.1^O for basal/apical Rot. Of all 54 segmental values comparisons done (Fig. 3), 37 (69%) were statistically non-inferior in the LVNC+ group compared to LVNC-, while in 17 (31%) the comparison was underpowered, but with mean differences being below the predefined margin (Fig. 3 and Table A.3). None of the LVNC+ measurements were found to be significantly worse than those in the LVNC- group.

3.3. Interobserver and intraobserver reliability

Inter-observer agreement for classification into LVNC+/LVNC- groups was 96.7% (Cohen Kappa coefficient = 0.87), while intra-observer agreement was 100%. The majority of average and segmental STE measurements showed good or excellent intraobserver and interobserver agreement (ICC range 0.61–0.99, ICC > 0.7 in 95.3% of measurements), fully detailed in Table A.4.

4. Discussion

In a large group of healthy adolescent athletes from diverse ethnic and sports backgrounds, 6.5% met the echocardiographic criteria for LVNC, more prevalent in those of Black ethnicity, as seen in adult athlete data [6,13,14]. LV regional S_l, S_c, rotation, as well as strain rate and segmental measurements were no worse in those with hypertrabeculation meeting the LVNC criteria, compared to those without. This contrasts with paediatric cohorts with diagnosed LVNC, where LV strain and rotation ware abnormal, even when conventional myocardial function parameters were preserved [17]. As such, documenting normal LV function and mechanics, including regional assessment, could differentiate physiological training adaptations from pathological changes seen in LVNC, where abnormal regional function has been shown to be present. This would improve the current diagnostic criteria which still focus on quantifying the degree of hypertrabeculation, rather than the myocardial function, and would offer additional tools during athlete screening and follow-up.

4.1. LV hypertrabeculation in athletes – an issue of over diagnosis

Current imaging criteria for LVNC diagnosis are based on showing hypertrabeculation and ventricular dysfunction [8–11]. In athletes, hypertrabeculation is an adaptation to increased preload associated with training, reducing myocardial work for the same cardiac output [12,33], a phenomenon also observed during pregnancy [16]. In LVNC this could be to compensate for rigid rotation patterns caused by abnormal myocardial fibre disposition [3,4]. Similar structural findings could thus

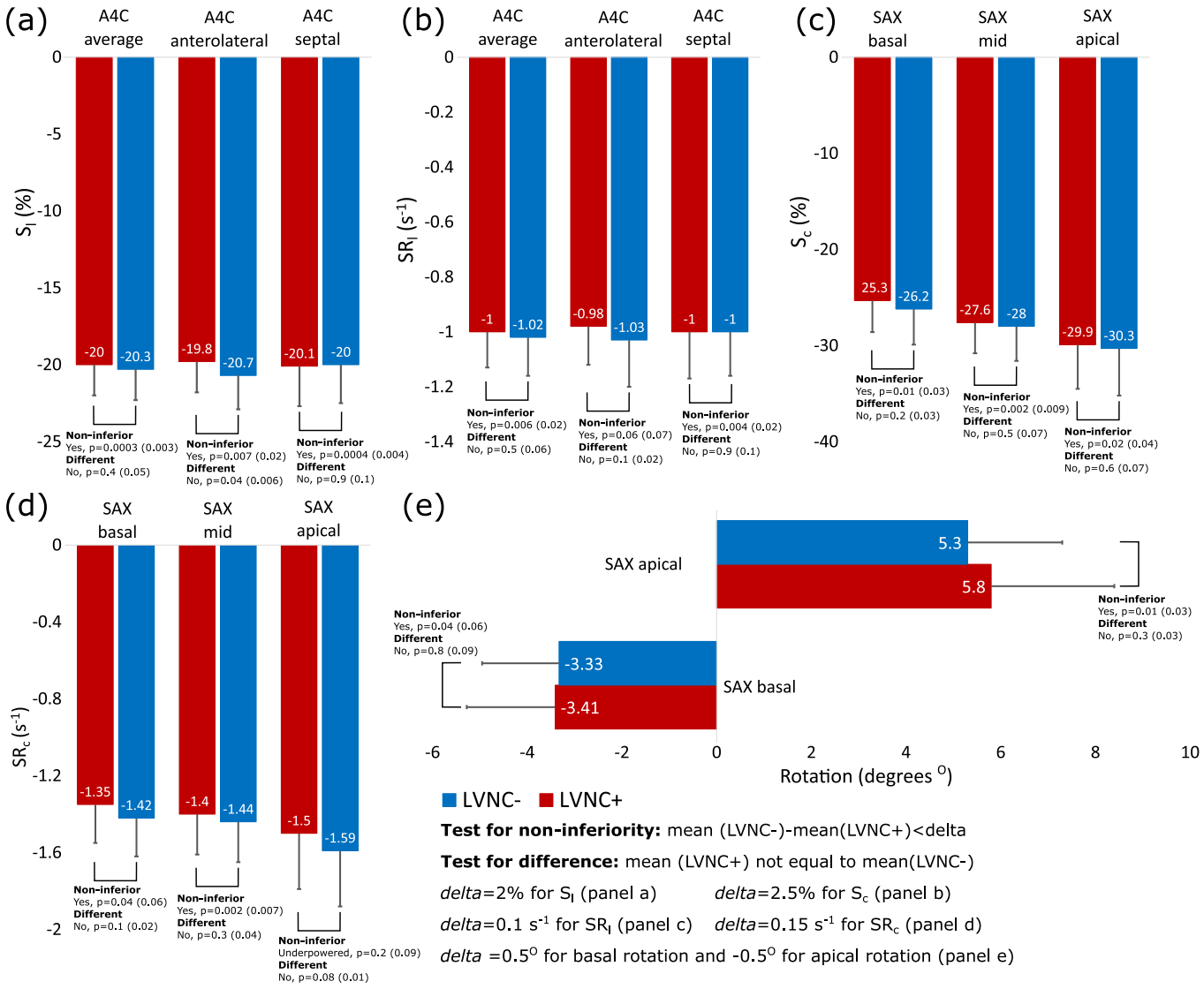

Fig. 2. Global and regional left ventricle speckle tracking echocardiography parameters in LVNC+ and LVNC- athletes. Panel a: longitudinal strain (Sl); Panel b: longitudinal strain rate (SR_l,); Panel c: circumferential strain (S_c); Panel d: circumferential strain rate (SR_c); Panel e: basal and apical rotation (Rot). All mean S_l and SR_l in the LVNC+ group are numerically comparable to those in the LVNC- group and statistically non-inferior, within the predefined margins, except for the apical SR_c region (where the comparison is underpowered).
Values are expressed as means, with confidence interval bars representing standard deviation, detailed in Table A.2. Reported are *p* values (Benjamini-Hochberg critical values) for non-inferiority test and *t*-test. For statistical tests detailed output and interpretation, see Table A.2 and Supplementary Material – Statistical analysis.

be secondary to physiological adaptation or pathological development, without any criteria to differentiate the two, outside of when overt LV dysfunction occurs or other non-imaging findings confirm LVNC [3,6].

This issue is common among athletes, especially in those of Black ethnicity, with >18% of adult athletes showing some degree of LV hypertrabeculation, and 1.3%–8.1% fulfilling the Jenni criteria for LVNC [6,13,14]. In our cohort of healthy adolescent athletes, 6.5% met the Jenni criteria, also more prevalent in Black athletes, showing that over-diagnosis of hypertrabeculation is as prevalent in this age group, as in adults. Looking at the affected LV areas, the majority were distributed around the apex, some were mid antero-lateral, and few also had basal involvement, which is uncommon in LVNC [22]. Echocardiographic alternatives to the Jenni criteria, the Chin and Stöllberger criteria, also have even higher prevalence among athletes [8–10]. Using inaccurate criteria in an athlete is problematic, since even just the suspicion of a cardiomyopathy can significantly affect their eligibility and participation in competitive sports.

4.2. LV strain in the assessment of athletes with LV hypertrabeculation

Current LVNC echocardiographic criteria focus on quantifying the degree of hypertrabeculation, less on evaluating global or regional cardiac function [8–10], despite growing evidence of the role of myocardial mechanics in this pathology. STE has been shown to be useful in the early diagnosis [19] as well as risk stratification of LVNC [20]. Reduced apical S_c [22,23], rigid-body rotation or reduced twist [4,19,21], and a lack of S_c basal-apical gradient [22] were all associated with LVNC, even in those with LVEF>50% [17,19]. These findings support using STE in athletes with hypertrabeculation, to describe the LV function in greater detail, and differentiate physiological from pathological remodelling. There is sufficient data at present to show reduced LV strain parameters, including regional measurements, in non-athlete children with LVNC, or hypertrabeculation [22,23], and in our study we complement this by showing that athletes with similar structural criteria have normal LV function.

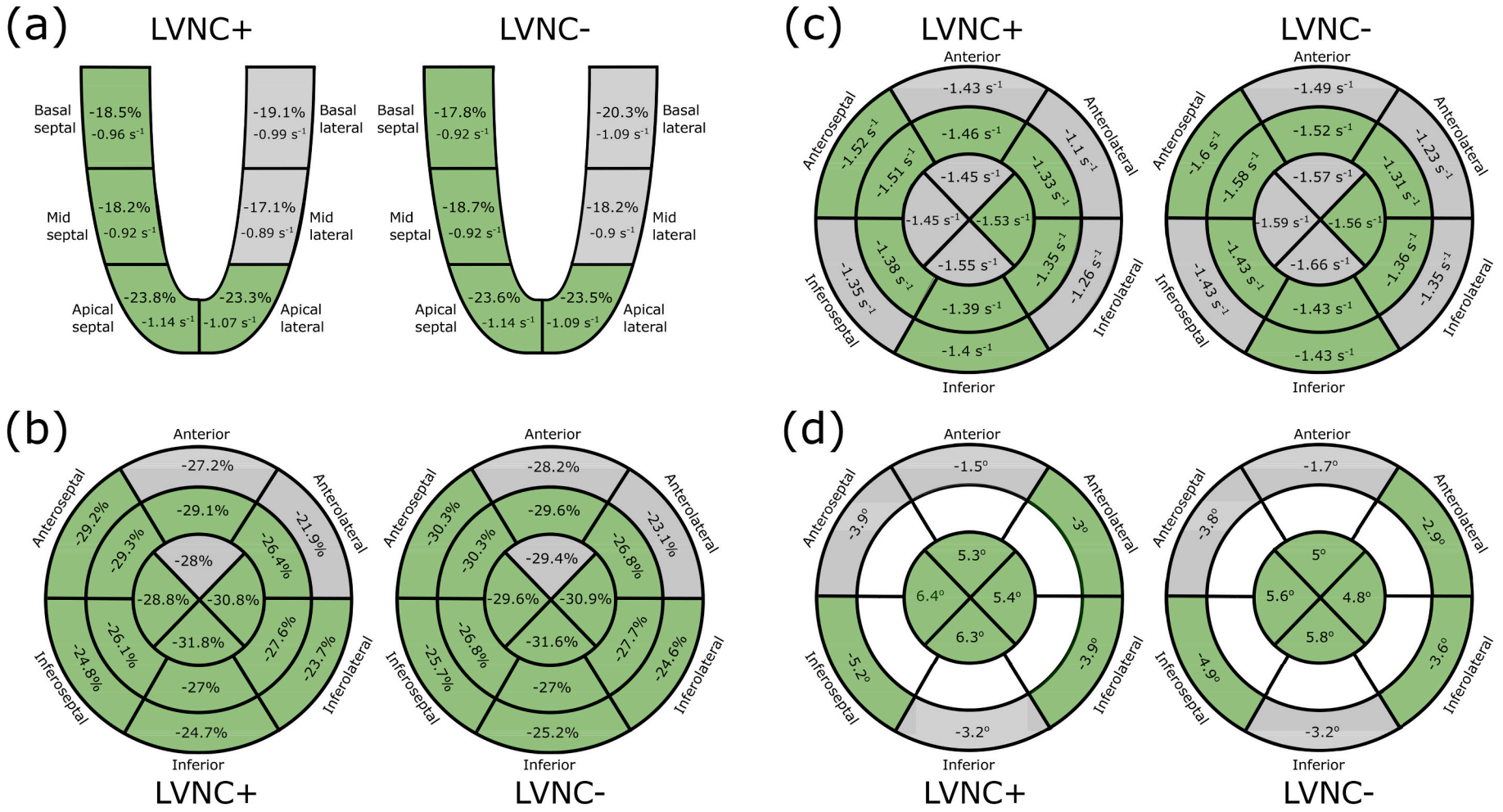

Fig. 3. Left ventricular segmental speckle tracking echocardiography measurements in athletes with left ventricular non-compaction criteria (LVNC+) and without (LVNC-). Panel a: Apical 4 chamber view - peak systolic longitudinal strain (S_l) and longitudinal strain rate (SR_l); Panel b: peak systolic circumferential strain (S_C); Panel c: peak systolic circumferential strain rate (SR_C); Panel d: peak systolic basal and apical rotation (Rot);

Panels a, b, c represents the 16 segments LV model short axis views, and panel d the 6 apical-4-chamber view segments [28]. All values are expressed as means, standard deviations and detailed statistical data in Table A.3. Segments where LVNC+ mean was statistically non-inferior to the LVNC- mean are coloured in green, those with an underpowered comparison in grey.

It was proposed that when suggestive hypertrabeculation is observed in an athlete, as found in our group (Fig. 1), a LVEF<50% could guide the decision for sports participation [6], given that worse outcomes are strongly associated with LV dysfunction [2,5]. Nevertheless, in a small group of 22 athletes with LVNC criteria, half had LVEF<55% or LV dilation, but only two had other abnormalities, and none had sufficient criteria for diagnosis [34]. This leaves the majority of these cases in a "grey area", with little evidence to inform a decision to clear as normal physiology, or perform further testing. All 27 LVNC+ athletes in our study fall into this category, and yet had comparable LV strain and rotation to those without LVNC echocardiographic criteria. Furthemore, in large general population studies, isolated LV hypertrabeculation was not found to be associated with adverse outcomes [35]. This supports the notion that in athletes, LV hypertrabeculation with normal regional, segmental function and rotation is unlikely to be related to cardiomyopathy, or of clinical consequence, highlighting the role STE could play in their assessment.

4.3. Limitations

This is a retrospective analysis of data gathered both prospectively and retrospectively, and shares both the strengths and limitations of both designs. The echocardiography reports were issued by more than one clinician, with an expected degree of variability, affecting non-primary measurements. Since these are healthy participants, for simplicity S_l was reported only for A4C, and segmental analysis was performed using SAX views and S_c. We could evaluate only male athletes, so could not analyse sex differences, although the study did have the advantage of diverse ethnicities. This study did not include a confirmed disease as positive control group, or a non-athlete negative control group, as that was not our primary hypothesis. Instead, we relied on the already published data on these topics. We had follow-up data showing no diagnosis of cardiomyopathy, but this cannot be a guarantee none will be seen in the future, although we estimate the probability as very low. In addition, routine CMR evaluation for LVNC were not planned for this study, as that would have posed ethical considerations for professional adolescent athletes, instead all further tests were performed as recommended by the local clinical team. Segmental analysis had higher variability, and higher SD, so the statistical power for the non-inferiority testing was lower than for regional parameters, for the same delta value, resulting in some statistically inconclusive results. Choosing an equivalence limit for the non-inferiority test was done empirically, based on clinical reasoning, and limited previous data, and this impacted the statistical power of the tests. Nevertheless, since this methodology only adds to the standard testing of difference, choosing slightly different limits would not have impacted the interpretation of the results. In addition, sensitivity analysis on the impact of participant factors, such as type of sport or ethnicity couldn't not be performed reliably due to low sample size. A small proportion of athletes were evaluated mid-season, or at the end of sports season, but this did not result in a difference in the main outcomes, or likely significant bias.

5. Conclusion

Among healthy adolescent athletes, 6.1% met the echocardiographic criteria for LVNC, highlighting the limitations of the current criteria which focus on quantification of hypertrabeculation degree. These LVNC+ athletes showed LV STE parameters comparable to those in the LVNC- group, in contrast to abnormal STE parameters in paediatric LVNC cohorts. STE would allow for a more accurate characterisation of myocardial mechanics and transition from a mostly structural evaluation of LVNC criteria, to a more functional approach. Adding a comprehensive LV evaluation, not limited to global function or structure, to current LVNC diagnostic criteria could improve athlete pre-participation screening and follow-up. This would be most important when physiological remodelling is suspected, such as cases with hypertrabeculation and no other signs of cardiomyopathy, as it could allow for fewer additional tests and false positive diagnoses.

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Declaration of Competing Interest

The Author(s) declare(s) that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2022.09.076.

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