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Left ventricular remodeling in elite and sub-elite road cyclists

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Marked adaptation of left ventricular (LV) structure in endurance athletes is well established. However, previous investigations of functional and mechanical adaptation have been contradictory. A lack of clarity in subjects’ athletic performance level may have contributed to these disparate findings. This study aimed to describe structural, functional, and mechanical characteristics of the cyclists’ LV, based on clearly defined performance levels. Male elite cyclists (EC) (n = 69), sub-elite cyclists (SEC) (n = 30), and non-athletes (NA) (n = 46) were comparatively studied using conventional and speckle tracking 2D echocardiography. Dilated eccentric hypertrophy was common in EC (34.7%), but not SEC (3.3%). Chamber concentricity was higher in EC compared to SEC (7.11 ± 1.08 vs 5.85 ± 0.98 g/(mL)^{2/3}, P < .001). Ejection fraction (EF) was lower in EC compared to NA (57 ± 5% vs 59 ± 4%, P < .05), and reduced EF was observed in a greater proportion of EC (11.6%) compared to SEC (6.7%). Global circumferential strain (GCε) was greater in EC (−18.4 ± 2.4%) and SEC (−19.8 ± 2.7%) compared to NA (−17.2 ± 2.6%) (P < .05 and P < .001). Early diastolic filling was lower in EC compared with SEC (0.72 ± 0.14 vs 0.88 ± 0.12 cm/s, P < .001), as were septal E’ (12 ± 2 vs 15 ± 2 cm/s, P < .001) and lateral E’ (18 ± 4 vs 20 ± 4 cm/s, P < .05). The magnitude of LV structural adaptation was far greater in EC compared with SEC. Increased GCε may represent a compensatory mechanism to maintain stroke volume in the presence of increased chamber volume. Decreased E and E’ velocities may be indicative of a considerable functional reserve in EC.

KEYWORDS
athlete’s heart, cycling, echocardiography, left ventricular geometry, physiological adaptation to exercise

INTRODUCTION

Structural adaptation of the athlete’s heart (AH) has been relatively well characterized, with the greatest dimensions observed in athletes who carry out high volumes of training with high-dynamic and high-static components, as is the case in sports such as cycling, triathlon, and rowing.1 The most notable of these adaptations are proportional increases in left ventricular (LV) chamber volume and wall thickness with concomitant changes in LV mass.3,4 Exposure to extended periods of elevated preload (eliciting ventricular volume overload) and elevated wall stress appear to be the primary drivers of training-induced structural adaptation in the athlete’s heart.5,6 A training-related increase in chamber compliance and size enables the athletes to generate very high cardiac outputs that are required...
to sustain high-dynamic exercise. Although strong correlations between LV end-diastolic volumes (EDV) and aerobic capacity have been reported, the association between functional/mechanical adaptation and athletic performance level is not understood.

While there is some consistency in the extant literature regarding the LV structural phenotype in athletes who engage in high training volumes, this has been based on absolute chamber sizes and a basic linear derivation of LV geometry. In addition, contradictory findings exist regarding the nature and magnitude of physiological adaptation in LV function. This is particularly relevant to the assessment of road cyclists, whereby application of conventional measures of function suggests 7% present with reduced ejection fraction (EF). The application of novel indices of LV mechanics utilizing myocardial speckle tracking echocardiography (STE) may be insightful by facilitating the assessment in LV longitudinal, circumferential and rotational planes of motion. Additionally, STE offers far greater sensitivity than conventional measures of function, with less load-dependence and angle-dependence compared to Doppler and Tissue Doppler, respectively.

Although positive associations between LV Mass Index (LVMi), LV end-diastolic volume (EDV), and STE derived peak global longitudinal ε (GL ε) exist (ie increased LVMi results in decreased GL ε), athletes with the most pronounced structural adaptation can still be expected to present similar peak GL ε values to non-athletes (NA). In contrast, endurance training appears to elicit no change, or mild increases in global circumferential ε (GC ε) and a reduction in LV twist. It is unclear whether alterations in GC ε and LV twist are an acute response to training, or a chronic adaptation required to maintain systolic function in the presence of marked LV structural remodeling.

It has been suggested chronic high training volumes are associated with development of supra-normal diastolic function, and that enhanced ventricular relaxation is an important contributor to LV filling, which in turn facilitates stroke volume generation. That said, large cohort examinations of athletes have described similar diastolic filling (as determined by Doppler imaging) at rest between athletes and non-athletes. Furthermore, recent work has clearly demonstrated larger LV cavity size is associated with a lower E’ velocity.

It is noteworthy that previous investigations of the athletes’ LV mechanics have focused on athlete vs non-athlete comparisons, with little consideration for differences due to athletic performance level. The only cross-sectional comparison between mechanics of elite and sub-elite athletes (to the authors’ knowledge) described significant differences in systolic tissue velocities and diastolic filling, highlighting the importance of characterizing the mechanical phenotypes within these two distinct groups.

Consequently, this study aimed to quantify differences in LV structural remodeling between SEC and EC, and to determine the impact of sub-elite and elite level training on LV function. In view of this, we hypothesized that: (a) greater LV structural remodeling will be observed in EC compared to SEC, and (b) conventional and mechanical measures of systolic and diastolic LV function will be lower in EC compared to SEC.

2 | MATERIAL AND METHODS

2.1 | Study population and design

Male elite-level road cyclists (EC, n = 69) actively competing in UCI World Tour and UCI Pro Continental level events, male sub-elite road cyclists (SEC, n = 30) actively racing under a 1st, 2nd, or 3rd category British Cycling license, and healthy, non-smoking male non-athlete university students/staff (NA, n = 46) engaging in fewer than 3 hours recreational activity per week were recruited into this cross-sectional study. Written, informed consent was provided by all subjects.

A very high proportion of subjects were Caucasian (97%). Of the n = 4 non-caucasian subjects, n = 2 EC athletes were Latin American, and n = 2 NA were mixed Caucasian/Black Caribbean. All subjects were free of known cardiovascular disease and abstained from alcohol and caffeine consumption for at least 24 hours prior to data collection. Subjects also refrained from training activities for at least 6 hours prior to data collection. Ethics approval was granted for this study by the Ethics Committee of Liverpool John Moores University and the National Research Ethics Service, Essex Research Ethics Committee in the United Kingdom.

2.2 | Procedures

Subjects completed a health questionnaire to exclude cardiovascular symptoms, family history of sudden cardiac death (SCD), and other cardiovascular history and/or abnormalities. Body mass (Seca 217, Germany) and height (Seca Supra 719, Germany) were recorded. Body surface area (BSA) was calculated as previously described. A standard, resting 12-lead electrocardiogram was undertaken, and results were reviewed against current international criteria by a sports cardiologist to exclude pathology.

A standard resting echocardiogram was undertaken by one of two experienced sonographers, using a commercially available ultrasound system (Vivid Q, GE, Norway) and a 1.5–4 MHz phased array transducer. All images were acquired in accordance with the American Society of Echocardiography (ASE) guidelines. In the case of borderline LV dilatation or low
EF, exercise echocardiography was used to exclude pathology. Images were analyzed offline (Echopac v202, GE, Norway) by a single experienced researcher. A minimum of three cardiac cycles were averaged for all acquisitions.

2.3 Conventional 2D Echocardiography

Standard measurements were made in accordance with ASE guidelines. LV linear dimensions (LVIDd and LVIDs) facilitated calculation of LV mass using the ASE corrected equation. To provide a comprehensive assessment of LV wall thickness, eight measurements were made from a parasternal short-axis orientation at basal and mid-levels from the antero-septum, infero-septum, posterior wall, and lateral wall. Mean wall thickness (MWT) was calculated as an average of all eight segments. Conventional relative wall thickness (RWT) was calculated using the formula [(IVSWTd + PWTd)/LVd] (where IVSWTd denotes diastolic basal interventricular wall thickness and PWTd denotes diastolic basal posterior wall thickness). LV end-diastolic volume (LV EDV) and LV end-systolic volume (LV ESV) were calculated using a Simpsons biplane method, and LV eccentricity was calculated as [LV mass/LV EDV'(2/3)]. LV geometry was assessed using a four-tier method, whereby geometry was defined as (a) normal (LV mass < 116 g/m², eccentricity < 9.1 g/mL(2/3)), (b) concentric remodeling (LV mass < 116 g/m², eccentricity ≥ 9.1 g/mL(2/3) and LV EDV/BSA < 76 mL/m²), (c) concentric non-dilated LVH (LV mass ≥ 116 g/m², eccentricity ≥ 9.1 g/mL(2/3)), (d) eccentric non-dilated LVH (LV mass ≥ 116 g/m², eccentricity ≥ 9.1 g/mL(2/3) and LV EDV/BSA < 76 mL/m²), (e) concentric dilated LVH (LV mass ≥ 116 g/m², eccentricity ≥ 9.1 g/mL(2/3)), and (f) eccentric dilated LVH (LV mass ≥ 116 g/m², eccentricity ≥ 9.1 g/mL(2/3) and LV EDV/BSA ≥ 76 mL/m²).

2.4 Myocardial speckle tracking

All images were acquired at a frame rates between 40 and 90 frames per second, and settings were adjusted to provide optimal endocardial delineation. During offline analysis (Echopac v202, GE, Norway), the endocardial border was manually traced, and the region of interest was adjusted to encompass the full myocardium. GL ε was calculated using apical four-chamber, two-chamber, and three-chamber orientations, which provided a global value based on the average of 18 segments (6 basal-apical segments per orientation). The parasternal short-axis orientation facilitated assessment of circumferential ε and rotation at basal (mitral-valve), mid- (papillary muscle), and apical (the point immediately above the point of systolic cavity obliteration) levels. GC ε values were calculated as an average of all basal and mid-level regional segments, and LV twist was calculated as the net difference between apical and basal rotation. Previous data collected in our laboratory has demonstrated very good agreement for peak GL ε (CoV 6%, ICC 0.807) and LV Twist (CoV 10%, ICC 0.954), and good agreement for GC ε (CoV 7%, ICC 0.781).

2.5 Statistical analysis

Study data were collected and managed using REDCAP electronic data capture tools hosted at Liverpool John Moores University. All echocardiographic data were presented as mean ± SD (range). Statistical analyses were performed using the commercially available software package SPSS (SPSS, version 23.0 for Windows). A one-way analysis of variance (ANOVA) with an alpha value set to P = 0.05 was used to examine differences between groups.

3 RESULTS

Age and height were similar between EC (27 ± 5 years and 1.80 ± 0.06 m), SEC (25 ± 5 years and 1.80 ± 0.07 m), and NA (22 ± 3 years and 1.78 ± 0.07 m), respectively. Body mass was significantly lower in EC and SEC, compared to NA (P < .001 and P < .05, respectively) (71.0 ± 5.9 and 73.2 ± 8.4 vs 78.1 ± 9.8 kg) resulting in BSA being significantly lower in EC compared to NA (P < .001) (1.88 ± 0.10 and 1.96 ± 0.14 m²). Resting HR was also significantly lower in EC and SEC compared with NA (both P < .001) (51 ± 8, 53 ± 7, and 69 ± 10 beats.min⁻¹, respectively). No non-training-related ECG changes were observed in any subjects.

3.1 Left ventricular structure

Conventional LV structural parameters are presented in Table 1. Absolute LVd, MWT, LV mass, LV EDV, and LV ESV were significantly greater in EC compared with SEC (P < .05, P < .001, P < .001, P < .05, and P < .001, respectively) and NA (all P < .001). Absolute parameters were also significantly greater in SEC compared with NA (P < .05, P < .05, P < .001, P < .001, and P < .001, respectively). LV...
structural indices remained significantly greater in EC compared with SEC ($P < .05$, $P < .001$, $P < .001$, $P < .05$, and $P < .001$, respectively) following allometric scaling to BSA (LVD index, MWT index, LV mass index, LV EVD index, LV ESV index). All scaled parameters were also greater in SEC compared with NA (all $P < .001$).

Concentricity and RWT were significantly greater in EC compared with SEC (both $P < .001$) and NA (both $P < .001$); however, no differences were observed between SEC and NA. The distribution of LV geometry across all groups is presented in Figure 1. A predominance of normal LV geometry was observed across EC, SEC, and NA (60.9%, 96.7%, and 100%, respectively). Eccentric dilated LV hypertrophy was more common than eccentric non-dilated LV hypertrophy in EC (33.3%) compared to SEC (3.3%). There were no cases of eccentric non-dilated LVH in SEC. Concentric non-dilated LV hypertrophy and concentric dilated LV hypertrophy remained rare in EC (1.4% and 2.9%, respectively), and no cases of this geometry were observed in SEC.

### 3.2 Left ventricular function

Conventional indices of LV function are presented in Table 2. LV EF was lower in EC compared with NA only ($P < .05$). Reduced LV EF occurred in 11.6% of EC and 6.8% of SEC. Septal S’ was lower in EC compared with NA only ($P < .05$).

GC and GL ε, and twist data are presented in Table 3. No differences existed between groups in peak GL ε. Peak GC ε was greater in EC and SEC compared with NA ($P < .05$ and $P < .001$, respectively). No differences existed between groups in peak LV twist or basal rotation; however, peak apical rotation was lower in EC compared with SEC ($P < .05$).

Transmitral E and A were both lower in EC compared with SEC ($P < .001$ and $P < .05$) and NA ($P < .05$ and $P < .001$). E/A ratio was significantly higher in EC and SEC compared with NA (both $P < .05$). Septal E’ and A’ were lower in EC compared with NA (both $P < .05$). In addition, septal E’ was lower in EC compared to SEC ($P < .001$), and greater in SEC compared to NA ($P < .05$) while lateral E’ was lower in EC, compared to SEC ($P < .05$) and NA ($P < .05$).

### 4 DISCUSSION

The main findings of this study are (a) Marked structural remodeling was observed in EC, who presented with significantly greater LV chamber volume and wall thickness compared to SEC. Over one-third of EC presented with eccentric hypertrophy, compared to just 3.3% in SEC. 2) Reduced LV EF was observed in a greater proportion of EC compared to SEC, despite similar conventional and STE measures of systolic function. Conventional measures of diastolic function were lower in EC compared with SEC.

### 4.1 Left ventricular structure

In keeping with previous findings, we observed significantly greater LV chamber size in EC and SEC compared with NA, providing further support for sustained periods of elevated preload and hemodynamic volume overload acting as a primary stimulus for structural adaptation of the
LV in endurance athletes. Although we observed increased MWT in EC, none of our cohort presented thicknesses greater than 12 mm. This is in stark contrast to the work of Abergel et al,\(^4\) who found 8.7% of elite cyclists presented a MWT exceeding 13 mm. It is difficult to speculate as to the reason for this disparity, however, the authors themselves report the potential confounding impact of performance-enhancing drugs used by cyclists during the 1990s and early 2000s, many of which are known to elicit concentric LVH.\(^3^5\) Better endocardial border differentiation from a combination of improvement in echocardiography technology and experience in defining true endocardium from LV trabeculation may potentially have also contributed to previously erroneous measurements.

Although like Utomi et al,\(^3\) the majority of our EC cohort presented with normal LV geometry, a greater proportion of our cohort presented with eccentric hypertrophy (34% compared to 30%). These differences may be due to the sporting disciplines represented by the endurance-trained cohort of Utomi et al,\(^3\) as the influence of static (% maximal voluntary

**FIGURE 1** Four-tier LV geometry classification distribution for EC ⚫, SEC ⊙, and NA ○.

**TABLE 2** Ejection fraction, transmitial and tissue Doppler (TDI) echocardiographic parameters

<table>
<thead>
<tr>
<th></th>
<th>Elite Cyclists</th>
<th>Sub-Elite Cyclists</th>
<th>Non-Athletes</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV EF (%)</td>
<td>57 ± 5 (^1) [45:70]</td>
<td>59 ± 7 [48.74]</td>
<td>59 ± 4 [54:68]</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>0.72 ± 0.14*(\ast)(\ast) [0.42:1.04]</td>
<td>0.88 ± 0.12 [0.63:1.14]</td>
<td>0.82 ± 0.15 [0.49:1.19]</td>
</tr>
<tr>
<td>A (cm/s)</td>
<td>0.37 ± 0.08*(\ast)(\ast) [0.23:0.67]</td>
<td>0.44 ± 0.07 [0.28:0.61]</td>
<td>0.49 ± 0.10 [0.31:0.81]</td>
</tr>
<tr>
<td>E/A</td>
<td>1.98 ± 0.50(^1) [1.17:3.56]</td>
<td>2.05 ± 0.40(^1) [1.36:3.17]</td>
<td>1.80 ± 0.48 [0.78:2.91]</td>
</tr>
<tr>
<td>Septal S’ (cm/s)</td>
<td>9 ± 1 (^1) [6:13]</td>
<td>9 ± 1 [7:11]</td>
<td>10 ± 2 [7:13]</td>
</tr>
<tr>
<td>Septal A’ (cm/s)</td>
<td>7 ± 2 (^1) [4:10]</td>
<td>8 ± 2 [4:13]</td>
<td>8 ± 2 [5:12]</td>
</tr>
<tr>
<td>Lateral S’ (cm/s)</td>
<td>12 ± 2 [8:18]</td>
<td>12 ± 3 [7:17]</td>
<td>13 ± 3 [7:19]</td>
</tr>
<tr>
<td>Lateral A’ (cm/s)</td>
<td>7 ± 2 [4:18]</td>
<td>7 ± 2 [5:12]</td>
<td>8 ± 2 [3:16]</td>
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</tbody>
</table>

*\(P < .05\) vs sub-elite.
**\(P < .001\) vs sub-elite.
\(^1\)\(P < .05\) vs non-athletes.
\(^\ast\)\(P < .001\) vs non-athletes.
contraction) demands of highly dynamic sports on adaptation of LV geometry has previously been highlighted. As previously demonstrated in other sporting disciplines, concentric hypertrophy was rare in EC (4%).

The changes we observed in LV geometry highlight the contribution of LV dilatation to the increase in LV mass between NA and SEC while the development of a concomitant increase in wall thickness (ie concentricity) drives the further increase in LV mass observed in EC. This appears to be in contrast with previous studies of the endurance training process, which have either described concurrent development of LV mass and chamber volume over a period of 3-6 months or increases in LV mass preceding those of chamber volume over a period of 12 months. Our findings appear to have captured a longer-term adaptation in LV geometry, very similar to that observed by Weiner et al in their 3-year longitudinal examination of competitive rowers, albeit in a cross-sectional design with a different cohort.

4.2 Left ventricular function

Previous research has highlighted decreased resting systolic function in endurance cyclists, which, in addition to the marked cavity dilation presented by this population, increases the potential for a false-positive diagnosis of dilated cardiomyopathy. Our finding that 11.6% of EC and 6.7% of SEC present with reduced EF emphasizes the challenge of differentiating physiological and pathological adaptation in this group. Claessen et al have previously demonstrated that a low EF in this population is simply a function of increased cavity volume, which requires a lower contractile force to produce the necessary stroke volume.

Previous studies have identified GL peak ε as a potential tool to aid differentiation between physiological and pathological adaptation, as healthy athletes and non-athletes present similar GL ε values and significant decreases are observed in several pathological conditions. Our findings provide further support for the clinical application of GL peak ε, as we observed similar values across all groups.

The work of MacIver et al identified GC peak ε as having a far greater influence on EF than that of GL peak ε at rest (67% and 33%, respectively). It therefore seems the increased GC peak ε we observed in EC and SEC represents a compensatory mechanism which facilitates normal function at rest, despite vastly increased chamber volume.

In contrast to the recent meta-analysis of Beaumont et al, which found significantly decreased LV twist in endurance athletes, we observed no differences between EC, SEC, and NA groups. We did, however, observe a lower apical contribution to LV twist in EC, compared with SEC. Although parallels can be drawn between this adaptation and a previous cross-sectional examination, these results are in contrast to the longitudinal training study of Weiner et al. The disparity in findings between cross-sectional assessments and acute training studies may be explained by the phasic nature of training-induced adaptations in LV twist. We propose, the differential acute and chronic adaptations apparent in competitive rowers could extend to sub-elite and elite cyclists, as both processes are characterized by the accumulation of training volume over time and phasic structural adaptation of the LV.

Although we observed increased transmitral E/A in both EC and SEC, in agreement with previous descriptions of the endurance athlete’s heart, Doppler and TDI analysis shows a clear divergence in the nature of this finding between EC and SEC. SEC presented with a similar E velocity, and increased septal E’ compared to NA, suggestive of enhanced chamber relaxation assisting early diastolic filling. In contrast, E velocity and E’ velocity were both lower in EC (compared to NA), which indicate lower diastolic function. The most likely explanation for these lower values may be a significantly greater reserve volume and

<table>
<thead>
<tr>
<th>TABLE 3 Speckle tracking LV echocardiographic parameters</th>
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<tbody>
<tr>
<td>Elite cyclists</td>
</tr>
<tr>
<td>Global longitudinal</td>
</tr>
<tr>
<td>Peak ε (%)</td>
</tr>
<tr>
<td>Global circumferential</td>
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<tr>
<td>Peak ε (%)</td>
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<tr>
<td>LV rotation</td>
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<tr>
<td>Peak twist (°)</td>
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<tr>
<td>Peak basal rotation (°)</td>
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<td>Peak apical rotation (°)</td>
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*P < .05 vs sub-elite.
†P < .05 vs non-athletes.
‡P < .001 vs non-athletes.
lower resting HR in comparison to both SEC and NA, resulting in a decreased need for enhanced relaxation/suction at rest.39

4.3 Limitations

Due to the cross-sectional nature of this study, it is not possible to directly assess any cause-effect relationships between exercise and physiological cardiac remodeling. Although the performance levels of subjects are well defined, data pertaining to maximal aerobic capacity, or volume and intensity of training were not available. As such, characterization of training within this group was based on previous reports using athletes of a similar performance level.44 Radial \( \varepsilon \) was not reported in this study, due to poor reproducibility of this parameter (CoV 19%, ICC 0.714).33 It should also be noted that findings of this study are specific to males aged 20-30 years, and as such, should not be extrapolated to female, junior, or veteran athletic populations. All subjects denied use of illicit performance-enhancing drugs, however, it is impossible to quantify this claim, and as such, this should be considered a limitation of the study.

5 CONCLUSIONS

A significantly greater LV mass was observed in EC compared to SEC, who presented with greater LV mass compared to NA. Differences in LV mass between EC and SEC are primarily driven by increased wall thickness (and therefore concentricity), whereas chamber dilatation differentiates SEC and NA. Increased GC \( \varepsilon \) in EC and SEC may represent a compensatory mechanism to maintain stroke volume at rest in the presence of increased chamber volume, unchanged GL \( \varepsilon \), and unchanged LV twist. Decreased E and E’ velocities in EC are a novel finding and may be indicative of a considerable functional reserve. Future research is required to elucidate this complex relationship between structural adaptation and function in elite endurance athletes.

6 PERSPECTIVES

In this study, we highlighted a considerable difference in the magnitude of structural remodeling presented by elite and sub-elite cyclists. We also showed marked structural adaptation is often accompanied by functional and mechanical alterations, which could appear atypical in a pre-participation screening setting. The potential application of STE for differential diagnosis in these situations should be noted, particularly in the case of localized adaptations (ie apical rotation). This investigation prompts further research into identification and quantification of the functional reserve observed in elite endurance athletes. Future work may develop our understanding of this area utilizing stress echocardiography, and examining intra-individual variability of function and mechanics in relation to training status.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest. The authors alone are responsible for the content and writing of this manuscript.

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