Global longitudinal strain differentiates physiological hypertrophy from maladaptive remodeling

Yvonne Bewarder a, *, Lucas Lauder a, Saarraeken Kulenthiran b, Ortwin Schäfer c, Christian Ukena a, Robert Percy Marshall c, Pierre Hepp d, Ulrich Laufs e, Stephan Stöbe e, Andreas Hagendorff f, Michael Böhm a, Felix Mahfoud a, Sebastian Ewen a

a Klinik für Innere Medizin III, Kardiologie, Angiologie und Internistische Intensivmedizin, Universitätsklinikum des Saarlandes, Homburg/Saar, Germany
b Cycling Team Israel Start-Up Nation, 4 Hanechoshet St., 6th Floor, Or Towers, 6971069 Tel Aviv, Israel
c RasenBallsport Leipzig GmbH, Cottaweg 3, 04177 Leipzig, Germany
d Universitätsklinikum Leipzig, Klinik und Poliklinik für Orthopädie, Unfallchirurgie und Plastische Chirurgie, Liebigstrasse 20, 04103 Leipzig, Germany
e Universitätsklinikum Leipzig, Klinik und Poliklinik für Kardiologie, Liebigstrasse 20, 04103 Leipzig, Germany

A R T I C L E   I N F O

Keywords:
- Hypertrophic cardiomyopathy
- E/e’
- Longitudinal strain
- Athletes’ hearts
- Echocardiography
- Left ventricular hypertrophy
- Adaptive and maladaptive remodeling

A B S T R A C T

Aims: Differentiation of left ventricular (LV) hypertrophy in healthy athletes from pathological LV hypertrophy in heart disease is often difficult. We explored whether extended echocardiographic measurements such as E/e’ and global longitudinal strain (GLS) distinguish physiologic from maladaptive hypertrophy in hypertrophic cardiomyopathy, excessively trained athlete’s hearts and normal hearts.

Methods: Seventy-eight professional athletes (cyclists n = 37, soccer players n = 29, handball players n = 21) were compared with patients (n = 88) with pathological LV hypertrophy (hypertrophic obstructive cardiomyopathy (HOCM, n = 17), hypertensive heart disease (HHD, n = 36), severe aortic valve stenosis (AVS, n = 35) and with sedentary healthy individuals as controls (n = 37).

Results: LV ejection fraction (LVEF) was ≥50% in all patients, athletes (median age 26 years, all male) and the controls (97% male, median age 32 years). LV mass index (LVMI) and septal wall thickness was in normal range in controls, but elevated in cyclists and patients with pathological hypertrophy (p < 0.001 for both). E/e’ was elevated in all patients with maladaptive hypertrophy but normal in controls and athletes (p < 0.001 vs. pathological hypertrophy). Furthermore GLS was reduced in patients with pathological hypertrophy compared with athletes and controls (for both p < 0.001). In subjects with septal wall thickness >11 mm, GLS (≥−18%) has a specificity of 79% to distinguish between physiological and pathological hypertrophy.

Conclusion: GLS and E/e’ are reliable parameters unlike left ventricular mass or LV ejection fraction to distinguish pathological and physiological hypertrophy.

1. Introduction

Maladaptive cardiac remodeling in cardiomyopathy and physiological adaptation to exercise both result in increased ventricular mass index on echocardiography [1,2]. Thus, physiological and maladaptive myocardial hypertrophy are difficult to distinguish by standard echocardiography [3]. Herein, we explored whether extended echocardiographic determination employing the diastolic parameter E/e’ and global longitudinal strain can distinguish maladaptive and physiological hypertrophy in cardiomyopathy and following rigorous exercise training, respectively, compared to hearts of non-diseased sedentary individuals. Therefore, we explored myocardial hypertrophy in pressure overload, trained cyclists and normal healthy hearts. As sensitivity analysis, we studied how different forms of pathological hypertrophy such as aortic stenosis, hypertensive heart disease or idiopathic hypertrophic cardiomyopathy compare to other sports disciplines with mixed-training conditions (professional handball players, professional soccer players) and those with hearts of professional cyclists and normal individuals.

* Corresponding author at: Klinik für Innere Medizin III, Kardiologie, Angiologie und Internistische Intensivmedizin, Universitätsklinikum des Saarlandes, Kirrberger Str. 100, Geb. 41, 66421 Homburg/Saar, Germany.
E-mail address: Yvonne.Bewarder@uks.eu (Y. Bewarder).

https://doi.org/10.1016/j.ijche.2022.101044
Received 13 February 2022; Received in revised form 27 March 2022; Accepted 25 April 2022
2352-9067/© 2022 Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
2. Methods

2.1. Study population

From October 2018 to October 2019, a total of 87 professional athletes (cyclists n = 37; soccer players n = 29; handball players n = 21), aged 18 to 45 years were enrolled. The elite-level athletes included herein participated in international and/or top national level tournaments and trained regularly at least 6 times a week with training sessions of at least 90 min per day. All athletes underwent physical examination, resting and exercise 12-lead ECG as well as 2D and Doppler echocardiography. All athletes were subject to routine anti-doping controls. Professional cyclists were part of the professional team KATUSHA ALPECIN and trained between 15 and 25 h per week. Soccer players were employed by RB Leipzig, a soccer club taking part in the Bundesliga, the highest league in German football. Handball players were part of the team SC DHfK Leipzig, also competing in the highest national handball league as a LVMI in women between 43 g/m² and trained between 15 and 25 h per week. Soccer players were explained by abnormal loading conditions (e.g., hypertension, valvular, congenital disease) or infiltrative cardiomyopathies [4]. Unexplained left ventricular wall thickness of ≥13 mm was sufficient for diagnosis in relatives of individuals with HCM or those who are genotype positive [4]. Controls performed regular exercise trainings <3 times a week and did not participate in any tournaments. All subjects agreed to take part in the study and provided written informed consent in accordance with the declaration of Helsinki.

2.2. Echocardiography

Echocardiographic examinations were performed by experts using the latest ultrasound technology (GE Vivid E9 or E95 or IQ). Two-dimensional assessment of LV end-diastolic diameter, left atrial size, septal wall thickness, and left ventricular ejection fraction (EF) were performed according to the recommendations of the American Society of Echocardiography and the European Association of Cardiac Imaging [5]. Linear internal measurements of the LV were performed in the parasternal long-axis view obtained perpendicular to the LV long axis, and measured at the level of the mitral valve leaflet tips [5]. The current ESC echocardiographic guidelines for cardiac chamber quantification defined the normal range for LV-wall thickness (septal and posterior wall) in women between 6–9 mm and in men between 6–10 mm, as well as a LVM in women between 43–95 g/m² and in men between 49–115 g/m² [5]. However, some athletes have small increases in LV wall thickness and LV cavity diameter outside the normal range [6]. LV mass was determined by using the Devereux formula, which is composed of the septal and posterior wall thickness, the LV end-diastolic diameter, and the body surface area derived from 2D-guided M-mode [5]. 2-D and Doppler methods were used for the assessment of LV diastolic function. Early diastolic peak E-wave velocity (PW-E), late diastolic peak A-wave velocity (PW-A), their ratio (E/A) and mitral valve deceleration time were recorded using PW Doppler in the apical four-chamber view [7,8]. In accordance to the guidelines an annular e’ velocity (septal e’ < 7 cm/sec, lateral e’ < 10 cm/sec) and average E/e’ ratio >14 were used as cutoff values for pathological findings [7]. Analyses of 2D strain imaging were performed offline with a commercially available software version (GE Healthcare GmbH, Echopac, Version 203). For speckle-tracking analysis, apical four-chamber, two-chamber and three-chamber-views were acquired in cardiac cycles with the same length and during the same respiratory phase (expiration) [5,9]. Detection of endocardial and epicardial borders was performed semi-automatically. Manual corrections were used to ensure accurate tracking of the endocardial and epicardial borders and the correct segmentation of the LV. Regional strain parameters are reported for each segment in each apical window. The LV was divided into six segments in each apical window. Herein, the longitudinal component of myocardial strain, the GLS, was measured. GLS was derived as the average of longitudinal strain in all 17 myocardial segments. In accordance to the current recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging average GLS values ≥-18% were considered physiological [5]. Assessment of the echocardiographic images was performed by a cardiovascular imaging specialist blinded to the subject’s characteristics.

2.3. Statistical analysis

Data management and statistical analyses were performed using SPSS Statistics version 25.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 8.2.1 (GraphPad Software, La Jolla, CA, USA). Categorical data were presented as numbers (%). Continuous variables were tested for normal distribution using the Shapiro-Wilk test and were expressed as means ± standard deviations (SDs) for normally distributed data or medians and interquartile ranges (IQRs) for non-normally distributed data. For categorical variables, comparisons between independent groups were performed using Pearson’s chi² or Fisher’s exact test. For continuous variables, between-group differences were tested using a one-way analysis of variance (ANOVA) if data were normally distributed or the Kruskal-Wallis test if data were non-normally distributed. If the null hypothesis was rejected, multiple pairwise comparison tests with Bonferroni adjustment were performed. A two-tailed p-value <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

Baseline characteristics of athletes, patients and controls are summarized in Table 1A and Table 2. All athletes were male with a median age of 26 (7) years, a median height of 184 (11) cm and median weight of 80 (17) kg. Among professional athletes, handball players showed the highest body surface area (BSA) with 2.27 (0.17) m² and cyclists the smallest BSA of 1.93 (0.17) m². 36/37 controls were male (97%) with a median age of 32 (17) years and a mean BSA of 1.98 ± 0.19 m². Median age of patients with pathophysiological hypertrophy (HOCM (51 (30) years),
Table 1B Echocardiographic parameters of all professional athletes.

|                          | Pro cyclists | Pro soccer players | Pro handball players | p-value |
|--------------------------|-------------|--------------------|----------------------|---------|
| Septal wall thickness, mm | 13 (2) †‡   | 37 10 (1) *        | 29 10 (2) *          | <0.001 |
| LVEDD, mm                | 51 (5) †‡   | 37 55 (4) †        | 29 57 (3) *          | <0.001 |
| LVEF, %                  | 64.0 7.5   | 37 63.6 4.6        | 29 64.3 4.6         | 0.912  |
| LA size, mm              | 36.7 4.6   | 37 35.8 2.5        | 29 36.6 4.7         | 0.624  |
| LA size/BSA, mm/m²       | 19.0 1.4†‡ | 35 18.0 1.8        | 29 16.2 1.0         | <0.001 |
| LVMi, g/m²               | 160.5 21   | 36 97.0 21         | 29 89.0 21          | <0.001 |
| PW-E, cm/s               | 77.1 91.0 2.3 | 36 78.2 90.1 21 | 70.1 21 0.044       |       |
| PW-A, cm/s               | 46 (14) *  | 36 43 (10) *       | 29 41 (13) 0.42     |       |
| E/A ratio                | 1.72 0.26  | 36 1.83 0.24       | 29 1.52 0.020       |       |
| Deceleration time, ms    | 189.3 31 2.1 | 36 157.2 20.5 31 | 181.5 21 0.010      |       |
| E' septal, m/s           | 12.9 7 2.1 | 7 14.4 2.1         | 29 13.7 21 0.001    |       |
| E' lateral, m/s          | 12.9 7 2.1 | 7 14.4 2.1         | 29 13.7 21 0.001    |       |
| E/e ratio                | 6.5 (1.4) * | 35 4.5 0.9         | 45 21 0.001         |       |
| Strain analyses          |             |                    |                     |        |
| GLS Av, %                | –21.0 2.9 | 37 21.4 2.3       | 29 21 0.001         |       |
| GLS PLAX, %              | –21.0 2.9 | 37 21.4 2.3       | 29 21 0.001         |       |
| GLS 4CH, %               | –21.0 2.9 | 37 21.4 2.3       | 29 21 0.001         |       |
| GLS 2CH, %               | –21.0 2.9 | 37 21.4 2.3       | 29 21 0.001         |       |

Data were presented as numbers (%), mean ± standard deviation (SD) or medians (interquartile ranges, IQRs). One-way analysis of variance (ANOVA) and the Kruskal-Wallis test were used for between-group comparisons followed by multiple-comparison (post-hoc) test with Bonferroni adjustment: ‡ indicates an adjusted p <0.05 for comparison with pro cyclists, † indicates an adjusted p <0.05 for comparison with pro soccer players, †‡ indicates an adjusted p <0.05 for comparison with handball players.

3.2. Echocardiographic parameters

Table 1B and Table 3 show the echocardiographic parameters of the study population. In all 212 subjects included, a preserved LV ejection fraction ≥50% was documented (Fig. 1A). Septal wall thickness was in normal range in controls, soccer players and handball players, but elevated in cyclists and patients with pathological hypertrophy (p <0.001 for both). LV end-diastolic diameter (LVEDD) was not elevated in any patient cohort and did not correlate with GLS or any type of hypertrophic disorder. LV mass index (LVMi) in cyclists was significantly higher when compared to soccer players and handball players (p <0.001), HOCM patients showed highest LVMi values when compared to HHD and AV stenosis patients. When compared to controls, LVMi was elevated in patients with pathological hypertrophy and in professional cyclists (Fig. 1B).

In patients with pathological hypertrophy average GLS was reduced when compared to controls and cyclists (p < 0.001 for both, Fig. 1C). Among athletes, normal values for GLS were found regardless of sports discipline, with cyclists showing significantly higher average GLS values than soccer and handball players (p <0.001).

In subjects with septal wall thickness of >11 mm, GLS has a specificity of 79% and a sensitivity of 66% to distinguish between physiological and pathological hypertrophy. Diastolic parameter E/e' was elevated in all patients with maladaptive hypertrophy but normal in controls and athletes (p < 0.001 vs. pathological hypertrophy). Athletes showed lower PW-A velocities, with higher E/A ratios as compared to controls and patients with pathological hypertrophy (p < 0.001). The combination of findings acquired from echocardiography and resting or exercise 12-lead-ECG did not improve the diagnostic accuracy.

4. Discussion

Echocardiographically assessed diastolic function and average GLS help to differentiate between physiological adaption like in professional cyclists and maladaptive pathological hypertrophy in different hypertrophic myocardial diseases.

4.1. Differentiation between pathological and physiological LVH

Some athletes have small increases in LV wall thickness and LV cavity diameter outside the normal range [8,10]. Physiological hypertrophy adaption in highly trained athletes is associated with increased LVM without fibrotic remodelling [4,8,10]. It seems that borderline hypertrophy as adaption to excessive training (athlete’s heart) only develops in distinct sports disciplines that are accompanied with intensive endurance training like cycling, as in our study cyclists had the highest septal wall thickness (12 (2) mm) compared with the other athletes [11]. In addition, we found a significant increase in LVMi among cyclists compared to soccer and handball players. The group of professional cyclists had the smallest body surface area and thickest left ventricular wall thickness (13 (2) mm) compared with the other athletes [11]. Endurance training like cycling, as in our study, has a long-term beneficial effect on left ventricular hypertrophy as adaption to excessive training (athlete’s heart) only develops in distinct sports disciplines that are accompanied with intensive endurance training like cycling, as in our study.

Table 2 Baseline characteristics.

|                          | Control | HOCM | HHD | Pro cyclists | AV stenosis | p-value |
|--------------------------|---------|------|-----|-------------|-------------|---------|
| Male, n (%)              | 36 (97) | 37  | 9 (53) | 17 22 (61) | 36 37 (100) | 36 22 (63) | <0.001 |
| Age, years               | 32 (17) *| 37  | 51 (30) *| 17 60 (18) *| 36 29 (7) *| 37 81 (5) *| <0.001 |
| Height, cm               | 178.7 7.9 | 37 | 171.5 9.8 | 17 172.0 10.2 | 36 182.8 6.2 | 35 169.9 8.6 | <0.001 |
| Weight, kg               | 80 (16) | 37  | 75 (27) | 17 91 (19) | 36 73 (12) | 35 78 (24) | <0.001 |
| BSA, m²                  | 1.98 ± 0.19 | 37  | 1.94 ± 0.25 | 21 2.10 ± 0.21 | 35 1.93 ± 0.12 | 35 1.91 ± 0.24 | <0.001 |
| Diabetes, n (%)          | 0 (0) | 37 | 1 (6) | 17 8 (22) | 36 0 (0) | 35 9 (26) | <0.001 |
| Hypertension, n (%)      | 0 (0) | 37 | 6 (35) | 17 36 (100) | 36 0 (0) | 35 13 (37) | <0.001 |

Data were presented as mean ± standard deviation (SD) or medians (interquartile ranges, IQRs). One-way analysis of variance (ANOVA) and the Kruskal-Wallis test were used for between-group comparisons followed by multiple-comparison (post-hoc) test with Bonferroni adjustment: * indicates an adjusted p <0.05 for comparison with control, † indicates an adjusted p <0.05 for comparison with HOCM, ‡ indicates an adjusted p <0.05 for comparison with HHD, § indicates an adjusted p <0.05 for comparison with AV stenosis.

Abbreviations: AV, aortic valve; HHD, hypertensive heart disease; HOCM, hypertrophic obstructive cardiomyopathy; pro cyclists, professional cyclists.
Abbreviations: AV, aortic valve; HHD, hypertensive heart disease; HOCM, hypertrophic obstructive cardiomyopathy; pro cyclists, professional cyclists.

With the echocardiography technologies used in this study (GE tation. We did not observe specific differences in diastolic function be function showed no deviations from normal in cyclists in contrast to cric septum compared with the other athletes and controls. Elevated wall thickness and LVEDD can indicate heart disease. In our study that focused on myocardial hypertrophy, LVEDD did not correlate with a specific disease or hypertrophy in athletes.

4.2. Diastolic function

Our data on athletes indicate “normal”/physiological diastolic values in line with data from the literature, in which normal diastolic values were found in Olympic athletes [12-14]. In our cohorts, only the professional cyclists presented with hypertrophic or borderline hypertrophic hearts. Echocardiographic parameters evaluation diastolic function showed no deviations from normal in cyclists in contrast to patients with pathological LVH, who showed impaired diastolic function. We did not observe specific differences in diastolic function between patients with HOCM, HHD and AV stenosis. The evaluation of diastolic function can be regarded as diagnostic tool in distinguishing physiological from pathological LV hypertrophy.

4.3. Speckle-tracking

Speckle-tracking echocardiography allows quantification of myocardial deformation by analyzing standard B-mode images and is mainly used for functional assessment of the LV [15]. In contrast to the biplane EF, strain echocardiography allows a more sensitive detection of functional disorders with lower interobserver variability [16]. Several components of the contractile deformation can be distinguished: i) longitudinal shortening, ii) circumferential shortening (the radius of the ventricle decreases in cross-section) and iii) radial thickening [17]. Average GLS represents the best-validated strain parameter, which has been established in various pathologies such as coronary heart disease, heart failure, or HCM [18,19]. Reduced GLS has been associated with poor prognosis and increased risk of adverse cardiovascular events, independent of other clinical and echocardiographic risk factors [9,20]. With the echocardiography technologies used in this study (GE Healthcare), a GLS <16% is considered as pathologic and a GLS >18% as normal. Because GLS varies with age, gender and LV load, the range between −16% and −18% is considered borderline or slightly impaired [5]. GLS analysis measures the mobility of the longitudinally arranged subendocardial myocardial fibers of the left and right ventricles [21]. It has been shown that GLS is reduced in patients with HCM [22]. Our findings are in agreement with this and maladaptive LVH in patients with HOCM, HHD and AV stenosis was associated with a significant reduction of GLS compared with controls. As athletes exhibit adaptive physiological hypertrophy, the differentiation between maladaptive and adaptive hypertrophy can be challenging, especially with a septal wall thickness in the “grey zone” (IVSD 12-15 mm). The Maron’s criteria recommend the evaluation based on family history, ECG, gender and functional capacity in HCM [6,8]. There are only few studies on GLS in athletes [11,23-25] and there have been no reference values proposed for the definition of an athlete’s heart. Most of these studies included one single sport discipline and often used different software tools with individual ranges to evaluate GLS [21,26,27]. This study, is the first to compare GLS in different professional sports (cycling, soccer, or handball) with various exercise burdens and training focus (excessively trained endurance training vs. ball sport) to controls and patients with different forms of hypertrophic heart disease. In all athletes, the median GLS was in normal ranges (~19 (4) %). The investigated game sports including a ball herein are comparable to Olympic athletes [23] (~18.1 (2.2) %), grouped into skill, power, mixed, and endurance disciplines, or professional NBA athletes (~18.5 (2.5) %) [25]. Particularly the cyclists had a median GLS above normal ranges (~21.0 (3.5) %) which was higher than the GLS value in the other sports disciplines and the control group. Our data generated in professional cyclists are in line with top-level rowers [11]. In parallel to diastolic function evaluation, GLS easily discerns physiological cardiac hypertrophy in athletes from pathological changes. GLS seems especially suited for this task since GLS values were highest in cyclists who on the other hand showed the most pronounced hypertrophy with increased septal wall thickness and LVMI. This also raises the interesting question of whether “above normal” values could be evaluated to assess cardiac fitness in extreme athletes.

5. Limitations

Group sizes vary, which is related to the different group sizes of the individual sport teams. Also, in this study only male individuals were explored and the data cannot be extrapolated to female athletes, since we were not able to obtain data from female athletes subjected to similar exercise schedules. In our study, only patients with echocardiographically clear etiological findings were included as a control group.

Table 3

| Echocardiographic data. | Control | HOCM | HHD | Pro cyclists | AV stenosis | p-value |
|-------------------------|---------|------|-----|-------------|-------------|---------|
| Control | HOCM | HHD | Pro cyclists | AV stenosis | p-value |
| Septal wall thickness, mm | 11 (2) | 37 | 18 (4) | 37 | 13 (2) | 36 | 13 (2) | 37 | 14 (2) | 35 | <0.001 |
| LVEDD, mm | 49 (5) | 37 | 43 (6) | 37 | 44.5 (6) | 36 | 51 (5) | 37 | 48 (10) | 35 | <0.001 |
| LVEDD/BSA, mm/m² | 24.4 (3.7) | 37 | 22.3 (3.1) | 37 | 22.0 (17.8) | 36 | 26.7 (2.8) | 35 | 25.1 (4.8) | 35 | <0.001 |
| LVF, % | 61 (4) | 37 | 61 (5) | 37 | 62.5 (9) | 36 | 64 (10) | 37 | 57 (10) | 35 | <0.001 |
| LA size, mm | 34.7 ± 5.3 | 37 | 41.5 ± 5.6 | 37 | 44.6 ± 7.9 | 36 | 36.7 ± 4.6 | 37 | 41.8 ± 5.5 | 35 | <0.001 |
| LA size/BSA, mm² | 17.5 ± 2.2 | 37 | 21.8 ± 4.1 | 37 | 21.2 ± 3.5 | 36 | 19.0 ± 2.3 | 35 | 22.2 ± 3.5 | 35 | 0.002 |
| LVMi, g/m² | 89 (31) | 37 | 159 (33) | 37 | 125 (31) | 36 | 160.5 (42) | 35 | 137 (62) | 35 | <0.001 |
| PW-E, cm/s | 72 (21) | 37 | 74 (34) | 37 | 73 (27) | 36 | 76 (20) | 36 | 81 (36) | 35 | 0.249 |
| PW-A, cm/s | 57 (10) | 37 | 87 (45) | 37 | 74.5 (18) | 8 | 46 (14) | 37 | 109 (61) | 27 | <0.001 |
| E/A ratio | 1.2 (0.5) | 37 | 0.7 (0.4) | 37 | 0.85 (0.4) | 33 | 1.6 (0.6) | 36 | 0.7 (0.3) | 26 | <0.001 |
| Deceleration time, ms | 190 (55) | 37 | 216 (127) | 37 | 279 (72) | 33 | 190.5 (76) | 36 | 186 (165) | 35 | <0.001 |
| E/e’ | 20.0 (4.0) | 37 | 18.0 (3.0) | 37 | 19.0 (3.0) | 37 | 21.0 (4.0) | 35 | 21.0 (2.0) | 35 | <0.001 |
| E/e’ | 14.0 (4.0) | 37 | 14.0 (9.0) | 37 | 13.8 (5.7) | 35 | 14.0 (9.0) | 36 | 16.0 (7.0) | 34 | <0.001 |
| LVMI, g/m² | 4.1 | 37 | 5.6 | 37 | 5.6 | 17 | 4.6 | 37 | 21.2 | 35 | <0.001 |
| LA size, mm | 16% and 18% is considered borderline or slightly impaired [5]. GLS analysis measures the mobility of the longitudinally arranged subendocardial myocardial fibers of the left and right ventricles [21]. It
However, it would be interesting to also evaluate patients with borderline LV hypertrophy compared to athletes. This would be an interesting thesis for a further evaluation.

6. Conclusion

Differentiation of LV hypertrophy in healthy athletes from pathological LV hypertrophy in heart disease is often difficult. Neither the LV
ejection fraction nor the LVMI can distinguish physiological from pathological hypertrophy. The diastolic parameter E/e' was elevated in all patients with maladaptive hypertrophy but normal in controls and athletes. Furthermore, GLS was reduced in patients with pathological hypertrophy compared with athletes and controls. Therefore, assessment of diastolic function and average GLS helps to differentiate between athletes’ hearts and pathologic left ventricular hypertrophy.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: L. L. received speaker honoraria from Medtronic and ReCor Medical, outside the submitted work. M.B. reports support from Abbott, Amgen, Astra-Zeneca, Bayer, Boehringer-Ingelheim, Medtronic, Novartis, Recor, Servier, and Vifor outside the submitted work. All other authors have declared no conflict of interest. S.E. received speakers or consultant relationships which may be considered as potential competing interests: L. L. received speaker honoraria from Medtronic and ReCor Medical, outside the submitted work. All other authors have declared no conflict of interest. S.E. received speakers or consultant relationships which may be considered as potential competing interests: L. L. received speaker honoraria from Medtronic and ReCor Medical, outside the submitted work. All other authors have declared no conflict of interest.

Y.B., S.K., M.B. and S.E. wrote the original draft of the manuscript; F.M., performed by Y.B., S.K., O.S., C.U., R.P.M., P.H., U.L., S.S., A.H. and L.L.; research project; data curation and formal analysis of the data were Y.B., S.K., O.S., C.U., R.P.M., P.H., U.L., S.S., A.H. and L.L.; research project; data curation and formal analysis of the data were Y.B., S.K., O.S., C.U., R.P.M., P.H., U.L., S.S., A.H. and L.L.; research project; data curation and formal analysis of the data were performed by Y.B., S.K., O.S., C.U., R.P.M., P.H., U.L., S.S., A.H. and L.L.; research project; data curation and formal analysis of the data were performed by Y.B., S.K., O.S., C.U., R.P.M., P.H., U.L., S.S., A.H. and L.L.; research project; data curation and formal analysis of the data were

Acknowledgements

The authors are grateful to Armin Schweitzer for his help in artwork.

Funding

M.B. and F.M. are supported by the Deutsche Forschungsgemeinschaft (DFG, TTR 219, S-01, M-03, M-05).

Author contributions

Y.B., S.E., F.M. and M.B. contributed to conceptualization of the research project; data curation and formal analysis of the data were performed by Y.B., S.K., O.S., C.U., R.P.M., P.H., U.L., S.S., A.H. and L.L.; research project; data curation and formal analysis of the data were performed by Y.B., S.K., O.S., C.U., R.P.M., P.H., U.L., S.S., A.H. and L.L.; research project; data curation and formal analysis of the data were performed by Y.B., S.K., O.S., C.U., R.P.M., P.H., U.L., S.S., A.H. and L.L.; research project; data curation and formal analysis of the data were

References

[1] A. Pelliccia, B.J. Maron, A. Spataro, M.A. Froshchan, P. Spirito, The upper limit of physiologic cardiac hypertrophy in highly trained elite athletes, N. Engl. J. Med. 324 (5) (1991) 295–301.
[2] A. Pelliccia, F. Culasso, F.M. Di Paolo, B.J. Maron, Physiologic left ventricular cavity dilatation in elite athletes, Ann. Intern. Med. 150 (1) (1999) 23–31.
[3] A.L. Baggish, R.W. Battle, T.A. Beaver, W.L. Border, P.S. Douglas, C.M. Kramer, M.W. Martiner, J.H. Mercandetti, D. Phelan, T.K. Singh, R.B. Weiner, E. Williamson, Recommendations on the Use of Modularity Cardiovascular Imaging in Young Adult Competitive Athletes: A Report from the American Society of Echocardiography in Collaboration with the Society of Cardiovascular Computed Tomography and the Society for Cardiovascular Magnetic Resonance, J. Am. Soc. Echocardiogr. 33 (5) (2020) 523–549.
[4] F.M. Elliott, A. Anastasakis, M.A. Borger, M. Borggrefe, F. Cecchi, P. Charron, A. D’Ascenzo, A. Dewaele, J. Ginis, G. Guedj, G. Gehr, M. Olibet, R. Raia, M. Di Nardo, M. Shen, Z. Tan, K. Tabata, S. Ueda, J. Voigt, S. Zalawadiya, A. Pinheiro, T.P. Abraham, Cardiac hypertrophy: Definitions for a common language, J. Am. Coll. Cardiol. 71 (15) (2018) 1615–1629.
[5] R.M. Lang, L.P. Badano, V. Mor-Avi, J. Afilalo, A. Armstrong, L. Ernande, F.A. Flachskampf, T.C. Gillebert, A.L. Klein, P. Lancellotti, P. Marino, A. Avierinos, K. Cramariuk, M. D’Ascenzo, A. Devereux, J. D’hooge, G. Errico, S. Fagiolini, A. Finn, J. Fontana, A. Ghione, M. Gimenez, N. Glogauer, D. Gomes, A. Granger, N. Granger, A. Groeninckx, F. Guidera, L. Guigliarelli, G. Gurevich, J. Hadjibayev, T. Hasegawa, J.M. Hezel, D. Hernandez, D. Ho, G. Hopfer, M. Horie, J. Huber, J. Iolascon, A. Jirsa, M. Kihara, J. Kim, S. Klimow, M. Kobayashi, S. Komuro, Y. Kusumoto, H. Kuroda, K. Kwon, S. Leipsic, J. Lewis, J. Li, D. Liu, R. Libby, J. Lim, P. Luzi, M. Macchi, S. Marchitelli, A. Marchi, T. Martelli, S. Matsuda, R. Matsuda, S. Matsuoka, J. Mayer, W. Martinez, J.C. Mccabe, J.H. Mercandetti, D. Phelan, T.K. Singh, R.B. Weiner, E. Williamson, Recommendations on the Use of Modularity Cardiovascular Imaging in Young Adult Competitive Athletes: A Report from the American Society of Echocardiography in Collaboration with the Society of Cardiovascular Computed Tomography and the Society for Cardiovascular Magnetic Resonance, J. Am. Soc. Echocardiogr. 33 (5) (2020) 523–549.
[6] B.J. Maron, Distinguishing hypertrophic cardiomyopathy from athlete heart, Ann. Intern. Med. 127 (11) (1997) 833–845.