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Left Ventricular Speckle Tracking Derived Cardiac Strain and Cardiac Twist Mechanics in Athletes: A Systematic Review and Meta-Analysis of Controlled Studies.

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Abstract

Background The athlete's heart is associated with physiological remodelling as a consequence of repetitive cardiac loading. Exercise training effect on left ventricular (LV) cardiac strain and twist mechanics are equivocal and no meta-analysis has been conducted to date.

Objective The objective of this systematic review and meta-analysis is, (1) to review the literature pertaining to different forms of athletic training on cardiac strain and twist mechanics; (2) to determine the influence of traditional and contemporary sporting classifications on cardiac strain and twist mechanics.

Design Systematic review and meta-analysis.

Data Sources PubMed/MEDLINE, Web of Science and ScienceDirect.

Inclusion criteria Controlled studies of aged matched male participants aged 18-45years that used 2-D speckle tracking with a defined athlete sporting discipline and a control group not engaged in training programmes.

Data Extraction and Analysis Data were extracted independently by two reviewers. Random effects meta-analyses, subgroup analyses and meta-regressions.

Results Thirteen studies of 945 participants; (controls n=355; athletes n=590) were included. Meta-analyses showed no athlete-control differences in LV strain or twist mechanics. However, moderator analyses showed greater LV twist in high static, low dynamic athletes (d= -0.76, 95% CI -1.32 to -0.20, p<0.01) compared with controls. Peak untwisting velocity (PUV) was greater in high static, low dynamic athletes (d= -0.43, 95% CI -0.84 to -0.03, p<0.05) but less than controls in high dynamic, high static athletes (d= 0.79, 95% CI 0.002 to 1.58, p=0.05). Elite endurance athletes had significantly less twist and apical rotation than controls (d= 0.68, 95% CI 0.19 to 1.16, p<0.01; d= 0.64, 95% CI 0.27 to 1.00, p=0.001, respectively) yet no differences in basal rotation compared with controls. Meta-regressions showed LV mass index was positively associated with global longitudinal (b= 0.01, 95% CI 0.002 to 0.02, p<0.05), while systolic blood pressure was negatively associated with PUV (b= -0.06, 95% CI -0.13 to -0.001, p=0.05).

Conclusion Echocardiographic 2-D speckle tracking can identify subtle physiological adaptations to cardiac strain and twist mechanics between athletes and healthy controls. Differences in STE derived parameters can be identified using suitable sporting categorisations.

Key Points

- Without athlete categorisation there is little effect of exercise training on cardiac strain and twist mechanics, but traditional and contemporary methods of sporting categorisation can identify subtle differences in twist mechanics between athletes and controls.

- Elite level endurance athletes demonstrate reduced left ventricular twist and apical rotation, whereas competitive resistance athletes show greater left ventricular twist and peak untwisting velocity compared with controls; additionally athletes also show greater untwisting rate than controls.

- The lack of effect exercise training has on global longitudinal strain may suggest this parameter has potential for distinguishing pathological from physiological remodelling in athletes.

1 Introduction

The concept that the hearts of athletes differ from non-athletes, is one that has aroused medical and public interest for more than a century [1]. Through physical diagnosis using chest percussion in 1899, Henschen provided the first description of an enlarged heart in elite cross-country skiers [2]. Progressive developments in technologies have furthered our understanding of how the heart undergoes morphological changes as consequence of disease (pathological) or exercise training (physiological), with the latter becoming more widely known as 'athlete's heart'. In contrast to the pathological process in heart disease, the athlete's heart is an adaptive remodelling of cardiac tissue that results from the repetitive overload induced by exercise training to accommodate increased physiological demand [3, 4].

The first M-mode echocardiograms where performed by Edler and Hertz in 1953 [5, 6]. Since then rapid technological advances have established two-dimensional (2-D) echocardiography as a standard medical technique [5], identified left ventricular (LV) hypertrophy in athletes [7, 8], and allowed for comprehensive quantitative assessments of cardiac structure and function [9]. 2-D speckle tracking echocardiography (STE) is a newer technology that facilitates the measurement of cardiac deformation by tracking acoustic speckle markers frame-by-frame within the ultrasound image [10, 11]. Although it was initially developed as an expansion of tissue Doppler imaging, it has the advantage of being relatively angle-independent and able to assess movement within any direction of the imaging plane [12, 13]. The development of STE allows the assessment of the LV as it undergoes a multi-planar process of deformation throughout the cardiac cycle [13], across three planes of motion; longitudinal, radial and circumferential [14]. Additionally, 'twist mechanics' can be determined which concerns the cardiac twisting and untwisting occurring during systole and diastole, respectively, and is mechanistically underpinned by myocardial architecture and fibre arrangement [13]. Clockwise rotation at the base and counter-clockwise rotation at the apex of the myocardium constitute net LV twist, upon diastole the directions are reversed to produce untwisting with the myocardium returning to its original shape and resting position [15].

Remodelling of cardiac tissue is considered to differ dependent on the characteristic demands of a given sport which has traditionally been studied between disciplines at polar ends of

a scale i.e. endurance versus resistance athletes. Predominantly dynamic (endurance) sports such as distance running, Nordic skiing and cycling etc, require rapid and voluminous blood supply to working muscles. This is achieved by increased cardiac preload which is typically considered to lead to eccentric ventricular hypertrophy, including chamber dilatation [16] and proportional increases in wall thickness [17]. Sports with a predominantly high static component (resistance) such as weightlifting, martial arts and field throwing events etc, induce elevations in intravascular pressure which enhances afterload with adaptation suggested to cause increased wall thickness in the absence of chamber dilatation, termed concentric hypertrophy [18, 19]; although, there has been some controversy concerning concentric morphology in resistance trained athletes [20, 21].

Nevertheless, cardiac adaptations are relative to the degree of volume and pressure challenges induced by individual sports. Therefore there is likely to be some overlap in the adaptation seen between individual sporting disciplines which represent similar static and dynamic components, accordingly cardiac adaptations should be considered a relative concept [19, 22]. More recently, the traditional, dichotomous classification of exercise has received criticism for its oversimplification [23]. A contemporary sporting categorisation outlined by Mitchell et al. [24] provides a nine box grid system dividing sports in accordance to the dynamic (percentage maximum oxygen consumption) and static (percentage maximum voluntary contraction) components required and provides a more comprehensive division of sports. Detailed separation of athletes into their respective sporting groups may somewhat ameliorate the variability seen using the traditional classification to identify sport-specific cardiac adaptations.

In addition to the possibility of exercise specific alterations in cardiac morphology, athletes of differing sporting disciplines may also present alterations in systolic and diastolic function, including cardiac strain and twist mechanics. Numerous cross-sectional investigations have attempted to establish the deformation profiles of athletes compared with controls, demonstrating conflicting evidence with no overall consensus regarding exercise effects [25-28, 10, 29-36, 23, 37, 38]. These problems are not resolved when comparing functional adaptations using the dichotomous, traditional classification of endurance and resistance athletes versus controls [32, 35, 23, 37]. One study broadly utilised the contemporary framework by subdividing Olympic athletes into four groups in relation to their predominant training characteristics (skill, power, mixed discipline, endurance) [26]. Despite this, each group still consisted of sports with an

assortment of static and dynamic components, thus resulting in heterogeneous samples, which does not truly represent the 'four corners' of Mitchell's classification. Consequently, there is currently limited use of a comprehensive classification system when studying LV strain and twist mechanics. Further to athlete type, training level may provide some explanation for the variation observed in athlete deformation profiles, particularly as past work has demonstrated differing structural and functional adaptations between elite and sub-elite athletes [3], however any dose-response relationship between exercise training and STE derived parameters is currently unknown. Recently, a review presented conflicting athlete-control differences in particularly LV twist and emphasised the necessity for additional data [39]. Together, more data are warranted to explore alterations in athletes as a consequence of chronic training, and with the categorisation of sports into their suited disciplines may aid in establishing potential athletic modifications and expose patterns in cardiac strain and twist mechanics.

To date, no meta-analysis has been conducted to examine whether athlete-control differences occur in LV strain and twist mechanics. In light of this, the present systematic review and meta-analysis aims to, (1) investigate the potential sport-specific dependency using traditional (endurance versus resistance) and contemporary (Mitchell's) classification systems and (2) review how the deformation responses in trained athletes differ from matched controls.

2 Methods

The searching processes, study selection, data collection, analysis and reporting of this systematic review and meta-analysis were conducted in accordance with the Prefereed Reporting Items for Systematic review and Meta-Analyses (PRISMA) guidelines [40]. Consequently the primary research question for this analysis was:

Are there differences in STE characteristics of athletes when grouped using Michell's 9 group model or when using a traditional endurance / resistance exercise model?

A further research question was to assess the degree to which training status (elite v competitive) influenced the deformation characteristics of athletes.

2.1 Information Sources and Search strategy

An electronic database search was conducted to identify 2-D STE studies investigating LV strain in athletic men. Literature searches were conducted up to January 2016 using PubMed/MEDLINE (abstract/title), Web of Science (title only) and ScienceDirect (abstract/title/keywords) to identify studies published from the earliest possible date to 01/01/2016. Further filters were applied to include only human, English language journal articles. Review articles, meta-analyses and longitudinal studies were not included. Search terms associated with the athlete's heart were used in conjunction with Boolean operators (Fig. 1). The initial search was extended through cross-reference, with additional articles sought from the authors' knowledge to obtain records not initially found during the systematic search process.

2.2 Inclusion Criteria

Inclusion criteria to enable eligibility for quantitative analysis consisted of, (1) male participants; (2) aged 18 - 45 years; (3) aged matched; (4) an athlete group from a stated sporting discipline; (5) observational design; (6) 2-D STE; (7) a control group not engaged in training programmes; and (8) at least one or more LV strain parameter. Only males were included based on current knowledge that cardiac strain may be sex dependent [26, 41, 42]. Likewise, twist mechanics are known to be affected by age [43-46]. Therefore, we opted to employ a broad age range to maximise article inclusion whilst attempting to limit potential confounding factors.

2.3 Study Selection and Data Extraction

Literature searching and study selections were performed by two independent authors (AB and NS). All associated data were extracted from each investigation and entered into a spreadsheet (Microsoft Excel 2016, Microsoft Corporation), performed by one author (AB). Nine measures were obtained, including strain measures (1) global longitudinal strain (GLS); (2) basal circumferential strain (BCS); (3) apical circumferential strain (ACS); (4) global circumferential

strain (GCS); (5) global radial strain (GRS); LV twist mechanics (6) basal rotation; (7) apical rotation; (8) twist and (9) untwisting rate/velocity. GLS was determined as the average segmental strain from the apical four-chamber view, a combination of apical four and two-chamber views or apical four, two and three-chamber views. When basal and medium-apical segmental longitudinal strain data were reported, these were used to determine GLS. When specified, GCS was the segmental average strain obtained from the short-axis mid-level or the combination of apical, mid and basal levels. ACS and BCS were presumed to be the average of the automatically generated six segments when not stated. GRS was considered the segmental average strain of the mid-level short-axis view or a combination of the apical, mid and basal levels. Since apical and basal radial strain were not used as independent parameters within this meta-analysis, the two were used to determine GRS. Data were extracted for twist from studies that reported a single time point at peak or at end-systole (aortic valve closure). Studies have often used untwisting rate (UTR) when referring to peak untwisting velocity (PUV) [32, 34, 47], with peak UTR defined as the PUV occurring during early diastole [30, 48]. UTR has also been used to describe the rate of untwisting occurring during the earliest phases of diastole at timing events prior to mitral valve opening (MVO) [10, 37]. Due to terms often used interchangeably, for purposes of this meta-analysis, untwisting indices were separated; peak untwisting markers were categorised as 'PUV', the largest negative deflection following peak twist velocity [49], whereas untwist (°/sec) determined at or prior to MVO were categorised as 'UTR' when clearly detailed. Data were extrapolated from text, tables and figures. When torsion/time graphs were presented, peak measures during systole (0-100% systole) were obtained.

Study means ± standard deviation (SD) were recorded for all variables, however where studies reported the standard error of the mean (SEM), a manual conversion was applied using the formula; $SD = SEM * \sqrt{N}$, where N is the number of participants. Age and cardiac morphology were recorded along with covariates associated with the haemodynamic loading exerted upon the myocardium, consisting of; heart rate (HR), systolic blood pressure (sBP), diastolic blood pressure (dBP) and left ventricular mass index (LVMi).

2.4 Data Grouping

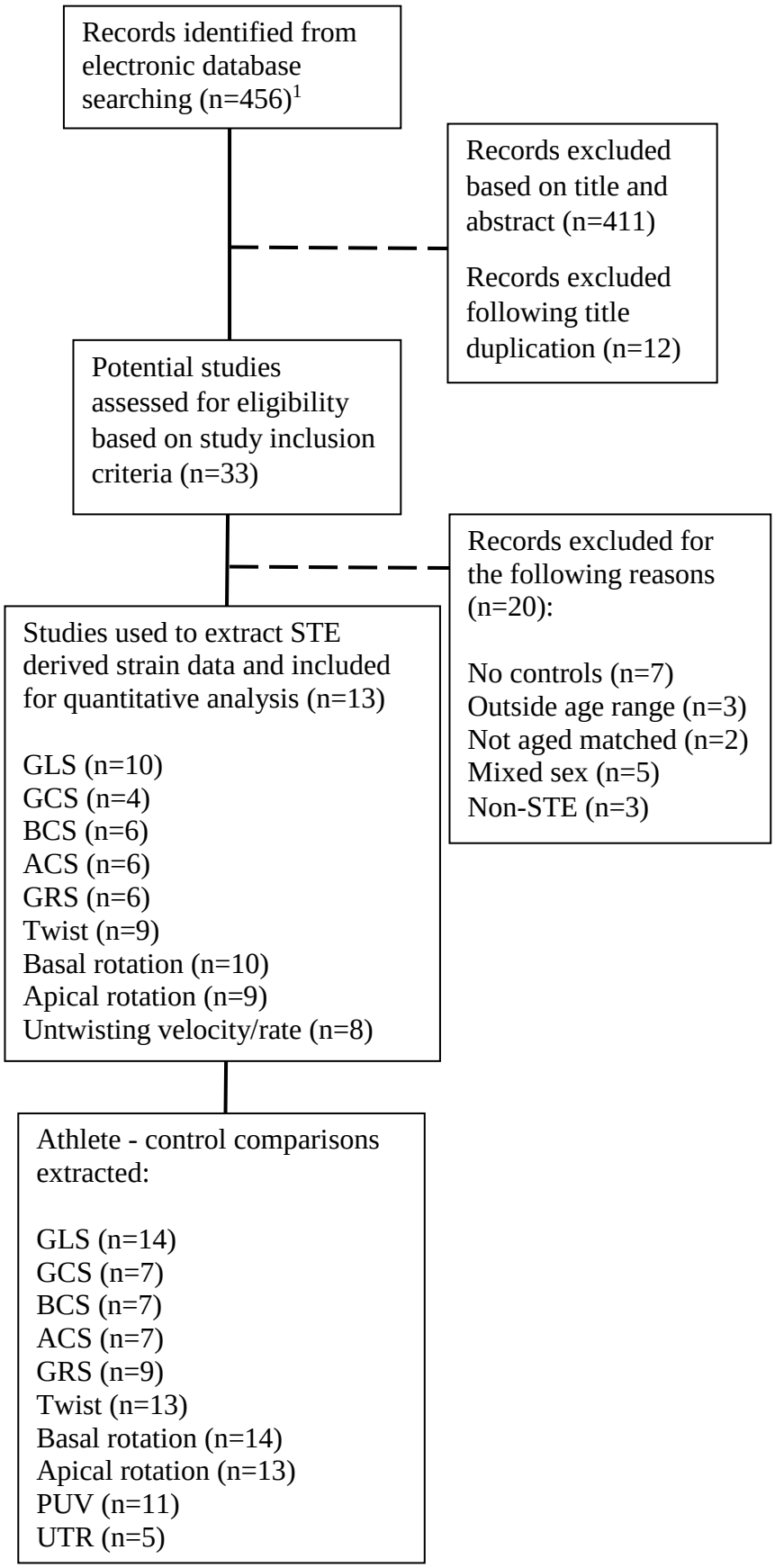
All athlete grouping was conducted by one author (AB) then verified by a second author (NS). Each athlete sample was allocated an assigned group based on Mitchell's classification, when a single sporting discipline was reported, defined as, (1) A1 (low dynamic, low static); (2) A2 (low dynamic, moderate static); (3) A3 (low dynamic, high static); (4) B1 (moderate dynamic, low static); (5) B2 (moderate dynamic, moderate static); (6) B3 (moderate dynamic, high static); (7) C1 (high dynamic, low static); (8) C2 (high dynamic, moderate static); and (9) C3 (high dynamic, high static) [24].

An additional, separate categorisation using a traditional method was utilised to divide sports being either predominantly endurance or resistance in nature. Further subdivision occurred based on athlete training level with athletes considered to be either 'elite' or 'competitive' performers. In this case, the definition of 'elite' consisted of athletes described as elite, participation in professional competitions or at a national/international level. Competitive athletes consisted of 'amateur', 'competitive' or 'highly trained' subjects. Therefore, athlete were allocated into one of four potential groups (elite endurance, competitive endurance, elite resistance, competitive resistance). Fig. 2 illustrates the model used in this meta-analysis for the athlete data grouping according to Mitchell's classification (contemporary) and the traditional, dichotomous model.

2.5 Statistical Analyses

All data analyses were performed using Comprehensive Meta-Analysis (Biostat: V 2.2.064, Englewood, NJ, USA). Pooled data were used to complete the meta-analysis using a random effects model to investigate the athlete-control differences. Standardised difference in means (Cohen's d)/effect sizes were calculated for each individual study, in addition to summary and overall results. Effect sizes in a positive direction indicated greater LV mechanics in controls, whereas negative direction identified greater mechanics in athletes. Moderator analyses were performed by dividing studies using categorical moderator variables (Mitchell's classification and traditional categorisation with training level), performed as separate analyses. Using continuous

moderator variables (age, HR, sBP, dBP, LVMi), we conducted multiple meta-regressions using methods of moments to establish relationships with LV mechanics. Heterogeneity was reported using Cochran's Q and I^2 statistic (the percentage of total variation between studies due to heterogeneity rather than chance), determined as low, moderate and high at 25%, 50% and 75%, respectively [50]. Publication bias was addressed using funnel plots, followed by Egger's regression intercept [51] to test for asymmetry as using funnel plots with fewer than 10 studies in the meta-analysis is not recommended [52]. Statistical significance was granted at $p \leq 0.05$.


Records identified from electronic database searching (n=456)[1]
Records excluded based on title and abstract (n=411)
Records excluded following title duplication (n=12)
Potential studies assessed for eligibility based on study inclusion criteria (n=33)
Records excluded for the following reasons (n=20):
No controls (n=7)
Outside age range (n=3)
Not aged matched (n=2)
Mixed sex (n=5)
Non-STE (n=3)
Studies used to extract STE derived strain data and included for quantitative analysis (n=13)
GLS (n=10)
GCS (n=4)
BCS (n=6)
ACS (n=6)
GRS (n=6)
Twist (n=9)
Basal rotation (n=10)
Apical rotation (n=9)
Untwisting velocity/rate (n=8)
Athlete - control comparisons extracted:
GLS (n=14)
GCS (n=7)
BCS (n=7)
ACS (n=7)
GRS (n=9)
Twist (n=13)
Basal rotation (n=14)
Apical rotation (n=13)
PUV (n=11)
UTR (n=5)

[1] Electronic search was conducted as follows: echocardiography[Title/Abstract] OR ultrasound[Title/Abstract] OR left ventricular[Title/Abstract] OR two dimensional[Title/Abstract] NOT right ventricular[Title/Abstract] AND strain[Title/Abstract] OR speckle tracking[Title/Abstract] OR deformation[Title/Abstract] OR mechanics[Title/Abstract] AND athletes[Title/Abstract] OR exercise[Title/Abstract] OR trained[Title/Abstract] AND Journal Article[pytp] AND "2005/01/01"[PDAT]: "2016/01/01[PDAT] AND "humans"[MeSH Terms] AND English[lang]

Fig. 1 Schematic of literature searching and filtration process used for identification of eligible studies. n= number of studies; STE= speckle tracking echocardiography; GLS= global longitudinal strain; BCS= basal circumferential strain; ACS= apical circumferential strain; GCS= global circumferential strain; GRS= global radial strain; PUV= peak untwisting velocity; UTR= untwisting rate.

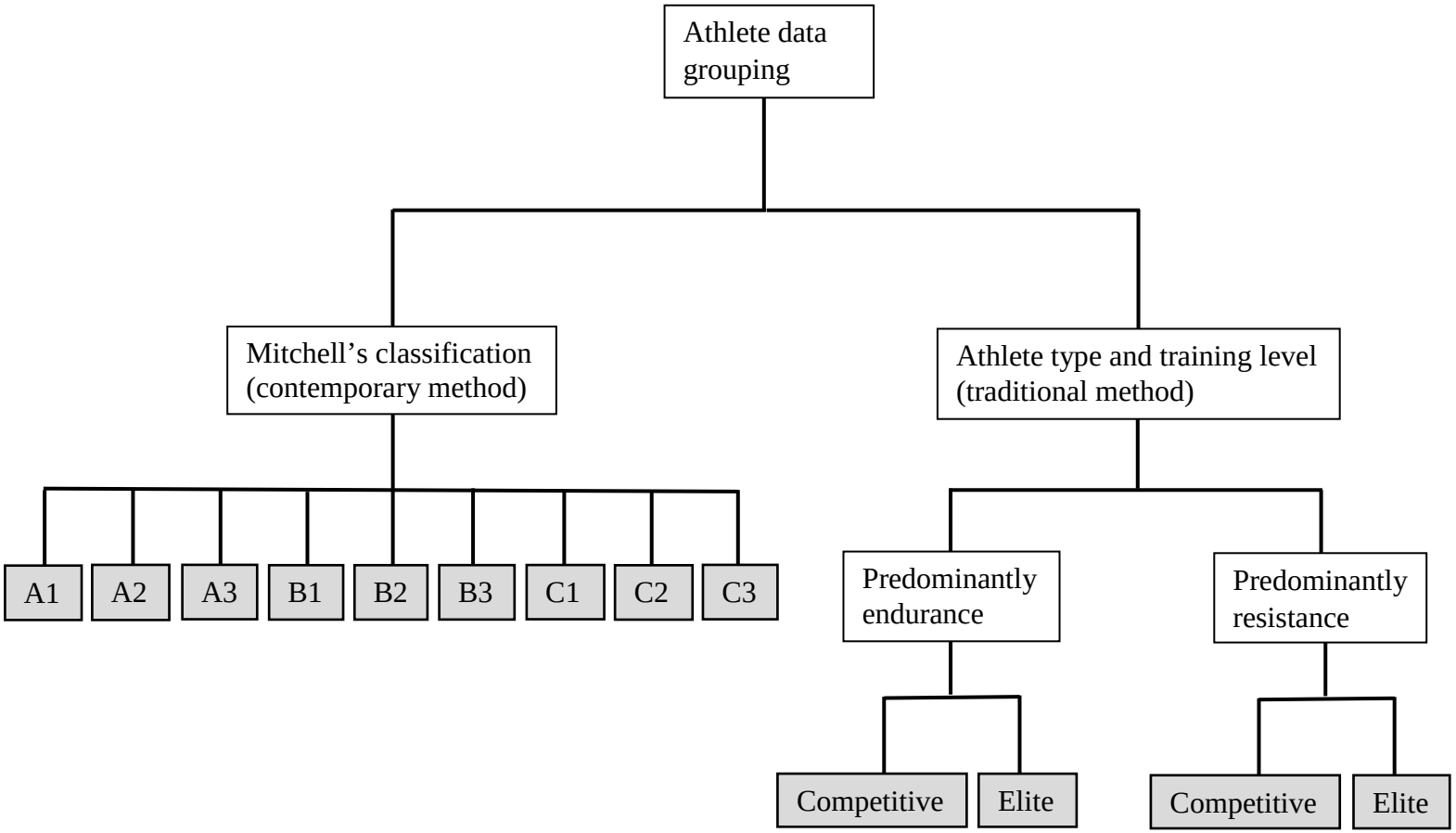


Fig. 2 Model of athlete grouping using the contemporary Mitchell's classification and a traditional dichotomous classification with additional grouping based on athlete training level. Filled boxes indicate end points of the classifications and athletes were allocated into 1 group for each method. A1= low dynamic, low static; A2= low dynamic, moderate static; A3= low dynamic, high static; B1= moderate dynamic, low static; B2= moderate dynamic, moderate static; B3= moderate dynamic, high static; C1= high dynamic, low static; C2= high dynamic, moderate static; C3= high dynamic, high static.

3 Results

3.1 Search Outcome

Following the searching procedures, 456 records were found. Based on title and abstract, 411 studies were disregarded mainly due to a lack of athletic focus. The remaining articles were exported and 12 duplicates were removed. Full texts of potential articles were examined for eligibility, with 20 investigations removed due to, no control group (n=7); group means outside of age range (n=3); athlete and control groups not aged matched (n=2); mixed-sex samples (n=5), and non-STE method of measuring deformation (n=3). Subsequently, 13 studies including 945 participants (590 athletes and 355 controls) fully met the inclusion criteria so were used for statistical analyses [53, 54, 28, 10, 30-34, 36, 23, 37, 38].

Strain variables were identified from the 13 remaining studies used for analysis, which included GLS (n=10) [53, 54, 28, 31-34, 36, 23, 37], BCS (n=6) [53, 28, 31-34], ACS (n=6) [53, 28, 31-34], GCS (n=4) [54, 28, 23, 37], GRS (n=6) [53, 54, 28, 31, 23, 37], twist (n=9) [53, 28, 10, 30-34, 37], basal rotation (n=10) [53, 28, 10, 30-34, 37, 38], apical rotation (n=9) [53, 28, 30-34, 37, 38] and untwisting velocity/rate (n=8) [53, 10, 30-34, 37]. Where more than one athlete-control comparison was reported, this was documented as a separate comparison whereby the control *n* was divided by the number of comparisons available, leading to GLS (n=14), BCS (n=7), ACS (n=7), GCS (n=7), GRS (n=9), twist (n=13), basal rotation (n=14), apical rotation (n=13), PUV (n=11) and UTR (n=5) (Fig. 1). LV strain and twist mechanics data for control and athlete groups are summarised in Tables 1 and 2, respectively. All athlete-control comparisons and heterogeneity for strain measures GLS, GCS, ACS, BCS, GRS and basal and apical rotations are presented in Table 3.

3.2 Global Longitudinal Strain

GLS was analysed overall and in C3 (high dynamic, high static), B3 (moderate dynamic, high static), A3 (low dynamic, high static), C2 (high dynamic, moderate static), C1 (high dynamic, low static), elite endurance, competitive endurance and competitive resistance athlete groups compared with controls.

No athlete-control differences existed for GLS overall, following sporting categorisation or training level. Overall, there was significant heterogeneity with moderate inconsistency. Mitchell's sporting categorisation showed heterogeneity was significant in A3, C1 and C2 groups with inconsistency considered low in C3 and B3, moderate in A3 and C2 and high in C1. Significant heterogeneity was found between sporting groups. Traditional categorisation showed heterogeneity was significant and inconsistency was moderate in all groups. Between groups heterogeneity statistically differed. The funnel plot revealed 3 studies lay outside of the SE funnel, suggesting asymmetry. However, Egger's test did not significantly confirm this visualisation of asymmetry, the intercept was 2.45 (95% CI two-tailed, -0.07 to 4.96; two-tailed p=0.06).

3.3 Circumferential Strain

3.3.1 Global

GCS was analysed overall and in A3 (low dynamic, high static), C1 (high dynamic, low static), C3 (high dynamic, high static), B3 (moderate dynamic, high static), elite endurance, competitive endurance and competitive resistance athlete groups compared with controls.

Overall, no athlete-control differences existed for GCS; in addition to non-significant heterogeneity and low inconsistency between studies. There were no differences between athletes and controls in the A3, C1 and C3 groups, whereas B3 athletes showed lower GCS than controls. All groups showed non-significant heterogeneity with low inconsistency. Non-significant

heterogeneity was found between groups. Traditional categorisation showed competitive resistance athletes had significantly less GCS than controls, whereas no differences were seen in either endurance groups. Heterogeneity was non-significant in all groups with low inconsistency in endurance elite and resistance competitive yet moderate in endurance competitive, with non-significance between groups. Visual inspection of the funnel plot showed no studies were outside of the funnel, which confirmed no asymmetry by Egger's regression (intercept= 4.72; 95% CI two-tailed, -2.05 to 11.49; two-tailed p=0.13).

3.3.2 Basal

BCS was analysed overall and in A3 (low dynamic, high static), C3 (high dynamic, high static), C2 (high dynamic, moderate static), elite endurance, competitive endurance and competitive resistance athlete groups compared with controls. There were no athlete-control differences found for BCS overall or with Mitchell's classification. Overall, between study heterogeneity was non-significant with low inconsistency. Between study heterogeneity was non-significant within all groups, inconsistency in A3 and C3 was low but moderate in C2. Non-significant between group heterogeneity was observed. Traditional categorisation showed endurance competitive athletes had significantly greater BCS than controls; with no differences found in elite endurance or competitive resistance athletes. Study-to-study heterogeneity in all groups was non-significant with low inconsistency. There was no significant heterogeneity between groups. The funnel plot showed no studies were outside of the funnel, however there was greater weighting to the right side. Asymmetry was confirmed by Egger's regression test (intercept= 1.79; 95% CI two-tailed, -0.03 to 3.62; two-tailed p=0.05).

3.3.3 Apical

ACS was analysed overall and in C3 (high dynamic, high static), B3 (moderate dynamic, high static), A3 (low dynamic, high static), C2 (high dynamic, moderate static), C1 (high dynamic, low static), elite endurance, competitive endurance and competitive resistance athlete groups compared

with controls. ACS did not significantly differ between athletes and controls overall, using Mitchell's or traditional categorisation or training level. Overall, study-to-study heterogeneity was not significant with low inconsistency. Within group heterogeneity was non-significant with low inconsistency in A3 and C2, but significant with moderate inconsistency in C3. Non-significant heterogeneity was found between groups. Heterogeneity within the endurance competitive group was non-significant with low inconsistency. In contrast, endurance elite group showed significant heterogeneity accompanied by moderate inconsistency. In addition, no significant between group heterogeneity was found. The funnel plot showed one study to fall outside of the funnel. In contrast, Egger's regression suggested no asymmetry (intercept= 1.21; 95% CI two-tailed, -1.88 to 4.31; two-tailed p=0.36).

3.4 Global Radial Strain

GRS was analysed overall and in A3 (low dynamic, high static), B3 (moderate dynamic, high static), C1 (high dynamic, low static), C3 (high dynamic, high static), elite endurance, competitive endurance and competitive resistance athlete groups compared with controls.

The overall athlete-control effect indicated no differences. Between study inconsistency was considered low with non-significant heterogeneity. Similarly, with Mitchell's classification no sporting discipline group showed athlete-control differences. Within group heterogeneity was found as non-significant in all cases with low inconsistency in A3, B3 and C1 groups but moderate in C3 group. Between group heterogeneity was non-significant. Traditional categorisation with training level had no effect on the athlete-control differences with non-significant heterogeneity in all groups with low inconsistency in elite endurance and competitive resistance groups but moderate in competitive endurance. Between group heterogeneity was also non-significant. The GRS funnel plot showed no asymmetry which was confirmed by Egger's regression (intercept= --3.32; 95% CI two-tailed, -8.21 to 1.57; two-tailed p=0.15).

3.5 Left Ventricular Twisting Mechanics

3.5.1 Twist

Fig. 3-5 illustrate athlete-control comparisons and heterogeneity statistics overall, based on Mitchell's classification and traditional categorisation with training level. Twist was analysed overall and in A3 (low dynamic, high static), C1 (high dynamic, low static), C2 (high dynamic, moderate static), C3 (high dynamic, high static), elite endurance, competitive endurance and competitive resistance athlete groups compared with controls. Overall, LV twist did not differ between athletes and controls, which was accompanied by significant and highly inconsistent between study heterogeneity. Mitchell's classification showed significantly greater twist in athletes than controls in A3 and C1 groups. In contrast, twist was significantly less in athletes than controls allocated to the C2 group, with no differences found in the C3 group. Between-study heterogeneity was non-significant with low inconsistency in the A3, C1 and C2 groups. On the contrary, significant heterogeneity and high inconsistency occurred in the C3 group; similarly, between-group heterogeneity was also significant.

Traditional categorisation showed elite endurance athletes had less twist than controls, whereas competitive resistance athletes had more twist than controls, with no athlete-control differences in competitive endurance athletes. Heterogeneity was significant in both dynamic groups with high inconsistency, whereas resistance competitive showed non-significant heterogeneity with low inconsistency. Further, between-group heterogeneity was significant. Seven studies exceeded the funnel plot, although Egger's test showed symmetry (intercept= -2.89; 95% CI two-tailed, -7.57 to 1.79; two-tailed p=0.20).

3.5.2 Basal Rotation

Basal rotation was analysed overall and in A3 (low dynamic, high static), C3 (high dynamic, high static), C2 (high dynamic, moderate static), C1 (high dynamic, low static), elite endurance, competitive endurance and competitive resistance athlete groups compared with controls. No

athlete-control differences existed across any comparisons for basal rotation. Heterogeneity was significant with moderate inconsistency overall. Between-study heterogeneity was non-significant in A3 and C3 with moderate inconsistency, yet significant in C2 and C1 with moderate and high inconsistency, respectively. Heterogeneity did not differ between groups overall. Traditional categorisation showed significant study-to-study heterogeneity in the elite endurance group with high inconsistency but non-significant in the competitive endurance and competitive resistance groups accompanied by low and moderate inconsistencies, respectively. No differences between groups occurred. Three studies were outside the funnel plot; however, Egger's test showed symmetry (intercept= 0.60; 95% CI two-tailed -2.41 to 3.62; two-tailed p=0.67).

3.5.3 Apical Rotation

Apical rotation was analysed overall and in A3 (low dynamic, high static), C3 (high dynamic, high static), C2 (high dynamic, moderate static), C1 (high dynamic, low static), elite endurance, competitive endurance and competitive resistance athlete groups compared with controls. Overall, athletes did not differ from controls. Study-to-study heterogeneity was significant and inconsistency high. Sporting categorisation showed that apical rotation did not differ between athletes and controls in A3 and C1 groups. In contrast, C2 and C3 athletes had significantly less apical rotation than controls. Within-group heterogeneity was not significant with low inconsistency in A3, C2 and C3 groups, whereas significant heterogeneity with high inconsistency was found in C1 group. Significant between-group heterogeneity was found. Traditional categorisation with training level showed no differences in competitive endurance and competitive resistance athletes, whereas elite endurance athletes had significantly less apical rotation than controls. Heterogeneity was significant with high and moderate inconsistency in competitive endurance and elite endurance groups, respectively with low and non-significant heterogeneity in competitive resistance. Significant between-group heterogeneity was found. The funnel plot showed 4 studies lay outside the funnel, 2 either side with Egger's regression test proving symmetry (intercept= -1.32; 95% CI two-tailed -4.99 to 2.34; two-tailed p=0.44).

3.5.4 Peak Untwisting Velocity

Fig. 6-8 illustrate athlete-control comparisons and heterogeneity statistics overall, based on Mitchell's and traditional classifications for PUV. PUV was analysed overall and in A3 (low dynamic, high static), C3 (high dynamic, high static), C2 (high dynamic, moderate static), C1 (high dynamic, low static), elite endurance, competitive endurance and competitive resistance athlete groups compared with controls. Pooled analysis demonstrated PUV did not differ between athletes and controls overall; heterogeneity between studies was significant and moderately inconsistent.

The A3 and C1 groups had significantly greater PUV in athletes than controls, whereas PUV in the C3 group was significantly less in athletes. There were no differences in C2 group. A3 and C1 groups showed non-significant heterogeneity with low inconsistency; significant heterogeneity with high and moderate inconsistencies in the C2 and C3 groups, respectively. Further, there was significant between-group heterogeneity. There was no effect when using traditional categorisation on PUV in both endurance (elite and competitive) groups, however, both showed significant heterogeneity with high inconsistencies. In contrast, resistance competitive athletes had significantly greater PUV than controls. Heterogeneity in resistance competitive was non-significant with low inconsistency. There was significant heterogeneity between groups.

Athletes had significantly greater UTR than controls (d= -0.64; 95% CI, -0.99 to -0.30; $p<0.001$); whereas no differences were observed for PUV (d= 0.03; 95% CI, -0.30 to 0.37; $p>0.05$). Within group heterogeneity in UTR group was non-significant with low inconsistency (Q= 5.10; I^2 statistic= 21.61%; $p>0.05$). In contrast, significant heterogeneity with moderate inconsistency was found in PUV group (Q= 35.40; I^2 statistic= 71.75%; $p<0.001$). Similarly, UTR versus PUV heterogeneity was significant (Q= 13.83; $p<0.001$).

PUV funnel plot showed 3 studies lay outside the funnel, however symmetry was proved by Egger's regression test (intercept= 0.41; 95% CI two-tailed -3.25 to 4.06; two-tailed p=0.81).

3.6 Meta-Regressions

All meta-regression associations with strain and LV mechanical parameters are detailed in Table 4. LVMi was indexed to body surface area [53, 32-34, 23] and height [28, 30], with two studies not detailing what left ventricular mass was indexed to [54, 36]. LVMi showed a significant positive relationships with GLS. Also, significant, negative associations was observed between sBP and PUV and GRS with age in the overall sample. No further significant associations were found.

Table 1 Summary of studies assessing left ventricular strain

Author (year of publication)	Study group (Mitchell classification, training level)	*n*	Age (years)	GLS (%)	GCS (%)	BCS (%)	ACS (%)	GRS (%)	Overall findings				
									GLS	GCS	BCS	ACS	GRS
Santoro et al. (2014) [32]	Control	17	24.5 ± 3	-17.7 ± 2.8	-	-16.5 ± 3.4	-27.8 ± 5.6	-					
	Cyclists (C3, E)	33	24.0 ± 3	-16.5 ± 1.7	-	-14.6 ± 3.0	-21.6 ± 4.1	-	↔	-	↔	↓	-
	Weightlifters (A3, C)	36	24.6 ± 5	-16.6 ± 2.1	-	-16.7 ± 2.4	-26.8 ± 7.7	-	↔	-	↔	↔	-
Santoro et al. (2014) [34]	Control	17	40.4 ± 9.2	-20.1 ± 2.3	-	-17.1 ± 3.5	-27.8 ± 1.5	-					
	Water polo players (C2, E)	45	39.2 ± 6.5	-19.2 ± 5.0	-	-16.4 ± 3.2	-25.9 ± 4.3	-	↔	-	↔	↔	-
Santoro et al. (2015) [33]	Control	95	32.0 ± 6.0	-19.3 ± 2.8	-	-16.1 ± 4.2	-23.4 ± 6.4	-					
	Swimmers (C2, C)	125	30.0 ± 9.0	-20.4 ± 2.5	-	-17.6 ± 5.8	-22.7 ± 7.2	-	↑	-	↑	↔	-
Nottin et al. (2008) [31]	Control	23	24.6 ± 4.6	-19.5 ± 2.2	-	-16.2 ± 3.4	-18.6 ± 4.1	46.9 ± 14.4					
	Cyclists (C3, E)	16	22.6 ± 5.4	-19.2 ± 1.9	-	-16.0 ± 3.5	-18.1 ± 2.5	42.2 ± 11.2	↔	-	↔	↔	↔
Szauder et al. (2015) [23]	Control	15	27.0 ± 3.0	-24.1 ± 3.0	-26.4 ± 2.7	-	-	44.1 ± 4.5					
	(ultra)marathoners (C1, E)	24	27.0 ± 3.0	-19.4 ± 3.4	-26.6 ± 3.8	-	-	42.5 ± 5.5	↓	↔	-	-	↔
	Body builders (B3, C)	14	27.0 ± 3.0	-23.3 ± 2.1	-22.4 ± 4.3	-	-	44.2 ± 8.2	↔	↓	-	-	↔
Vitarelli et al. (2013) [37]	Control	35	28.3 ± 11.4	-20.3 ± 2.6	-24.7 ± 3.4	-	-	48.9 ± 9.7					
	Marathoners (C1, C)	35	28.7 ± 10.7	-21.7 ± 2.6	-22.9 ± 3.3	-	-	46.9 ± 9.4	↔	↔	-	-	↔
	Power lifters (A3, C)	35	30.3 ± 9.4	-22.5 ± 2.4	-24.1 ± 2.7	-	-	49.6 ± 8.5	↑	↔	-	-	↔
	Martial artists (A3, C)	35	29.4 ± 9.8	-21.6 ± 2.2	-22.6 ± 3.6	-	-	47.5 ± 8.7	↔	↔	-	-	↔
Stefani et al. (2008) [36]	Control	25	25.0 ± 2.6	-19.4 ± 5.1	-	-	-	-					
	Soccer players (C1, E)	25	26.0 ± 3.5	-18.6 ± 3.3	-	-	-	-	↔	-	-	-	-
Galderisi et al. (2010) [28]	Control	19	28.5 ± 6.6	-21.1 ± 2.0	-17.6 ± 2.9	-16.7 ± 2.7	-17.8 ± 2.9	46.4 ± 15.8					
	Rowers (C3, E)	22	27.7 ± 8.4	-22.2 ± 2.7	-17.7 ± 2.5	-16.8 ± 2.4	-17.8 ± 2.6	47.6 ± 19.1	↔	↔	↔	↔	↔
Cote et al. (2013) [53]	Control	10	28.5 ± 5.9	-19.0 ± 2.9	-	-16.3 ± 5.3	-26.4 ± 10.2	25.7 ± 9.6					
	Cyclists (C3, C)	11	33.0 ± 5.6	-18.5 ± 2.1	-	-16.6 ± 4.3	-25.9 ± 10.7	33.9 ± 12.8	↔	-	↔	↔	↔
Donal et al. (2011) [54]	Control	27	26.2 ± 3.1	-17.7 ± 1.6	-15.9 ± 8.5	-	-	44.1 ± 11.0					
	Cyclists (C3, C)	18	25.2 ± 5.0	-17.0 ± 1.3	-17.4 ± 3.3	-	-	38.7 ± 7.8	↔	↔	-	-	↔

Data are mean ± SD. *n*= participant number; GLS= global longitudinal strain; GCS= global circumferential strain; BCS= basal circumferential strain; ACS= apical circumferential strain; GRS= global radial strain; C3= high dynamic, high static; A3= low dynamic, high static; C2= high dynamic, moderate static; C1= high dynamic, low static; B3= moderate dynamic, high static; E= elite athletes; C= competitive athletes; ↔ = no athlete-control differences; ↓= significantly less in athletes; ↑ significantly greater in athletes.

Table 2 Summary of studies assessing left ventricular twist mechanics

Author (year of publication)	Study group (Mitchell classification, training level)	*n*	Age (years)	Systolic parameters			Diastolic parameters		Overall findings				
				Brot (°)	Arot (°)	Twist (°)	PUV (°/sec)	UTR (°/sec)	Brot	Arot	Twist	PUV	UTR
Santoro et al. (2014) [32]	Control	17	24.5 ± 3	-8.5 ± 7.4	6.3 ± 2.8	10.0 ± 3.1	-103.3 ± 29.3	-					
	Cyclists (C3, E)	33	24.0 ± 3	-6.4 ± 2.1	4.2 ± 1.9	6.2 ± 1.1	-67.3 ± 22.9	-	↔	↓	↓	↓	-
	Weightlifters (A3,C)	36	24.6 ± 5	-5.8 ± 2.3	7.6 ± 5.4	12.0 ± 2.1	-122.5 ± 52.8	-	↔	↔	↑	↔	-
Santoro et al. (2014) [34]	Control	17	40.4 ± 9.2	-4.3 ± 1.2	6.5 ± 1.1	10.3 ± 2.4	-108.4 ± 39.5	-					
	Water polo Players (C2, E)	45	39.2 ± 6.5	-4.9 ± 1.6	6.1 ± 0.3	8.8 ± 3.6	-79.9 ± 35.9	-	↔	↓	↔	↓	-
Santoro et al. (2015) [33]	Control	95	32.0 ± 6.0	-6.7 ± 3.8	8.2 ± 4.0	12.2 ± 5	-96.2 ± 48.7	-					
	Swimmers (C2, C)	125	30.0 ± 9.0	-5.9 ± 3.4	6.1 ± 3.4	9.0 ± 3.8	-94.5 ± 40.3	-	↔	↓	↓	↔	-
Nottin et al. (2008) [31]	Control	23	24.6 ± 4.6	-4.8 ± 3.2	4.0 ± 2.9	9.2 ± 3.2	-72.9 ± 20.7	-					
	Cyclists (C3, E)	16	22.6 ± 5.4	-5.2 ± 2.4	1.7 ± 1.9	6.0 ± 1.8	-68.2 ± 33.5	-	↔	↓	↓	↔	-
Vitarelli et al. (2013) [37]	Control	35	28.3 ± 11.4	-6.7 ± 2.3	10.1 ± 3.6	14.6 ± 4.3	-78.9 ± 15.0	-61.7 ± 24.0					
	Marathoners (C1, C)	35	28.7 ± 10.7	-7.7 ± 2.2	14.2 ± 4.3	21.5 ± 5.2	-93.9 ± 21.0	-94.2 ± 29.0	↔	↑	↑	↑	↑
	Power lifters (A3,C)	35	30.3 ± 9.4	-6.8 ± 1.9	10.8 ± 3.7	15.8 ± 4.5	-83.1 ± 16.0	-64.2 ± 23.0	↔	↔	↔	↔	↔
	Martial artists (A3,C)	35	29.4 ± 9.8	-7.6 ± 2.4	13.8 ± 3.9	20.8 ± 5.4	-92.2 ± 22.0	-80.6 ± 31.0	↔	↑	↑	↔	↔
Cote et al. (2013) [53]	Control	10	28.5 ± 5.9	-11.7 ± 21.3	12.9 ± 5.2	17.8 ± 6.2	-139.9 ± 44.5	-					
	Cyclists (C3, C)	11	33.0 ± 5.6	-5.8 ± 1.7	12.2 ± 3.9	17.4 ± 4.9	-108.7 ± 33.0	-	↔	↔	↔	↔	-
Galderisi et al. (2010) [28]	Control	19	28.5 ± 6.6	-3.7 ± 0.5	6.2 ± 1.4	9.7 ± 1.8	-	-					
	Rowers (C3, E)	22	27.7 ± 8.4	-2.9 ± 1.5	6.1 ± 2.3	9.2 ± 2.0	-	-	↓	↔	↔	-	-
Kovacs et al. (2014) [10]	Control	13	30.0 ± 5.0	-2.1 ± 1.0	-	6.0 ± 2.2	-	AVC:					AVC:
	Kayak, canoe and rowers (C3, E)	28	26.0 ± 8.0	-2.7 ± 1.2	-	6.4 ± 2.1	-	-7.4 ± 9.3 -12.2 ± 8.8 MVO: -23.2 ± 8.2 -32.7 ± 12.7	↔	-	↔	-	↔ MVO: ↑
Maufrais et al. (2014) [30]	Control	30	21.3 ± 3.0	-5.6 ± 2.5	5.6 ± 2.9	8.9 ± 3.3	-66.7 ± 27.5	-					
	Marathoners, triathletes and cyclists (n/a, E)	25	23.0 ± 2.0	-4.9 ± 2.2	4.9 ± 2.0	8.0 ± 3.2	-76.7 ± 34.0	-	↔	↔	↔	↔	-
Maufrais et al. (2014) [30]	Control	19	38.0 ± 5.0	-5.9 ± 3.5	7.2 ± 3.4	11.5 ± 4.5	-69.5 ± 29.0	-					
	Marathoners, triathletes and cyclists (n/a, E)	46	38.0 ± 5.0	-4.2 ± 1.5	6.2 ± 2.6	8.5 ± 3.0	-74.9 ± 24.1	-	↓	↔	↓	↔	-
Zocalo et al. (2008) [38]	Control	10	27.0 ± 6.0	-7.4 ± 0.9	6.9 ± 2.5	-	-	-					
	Soccer players (C1, E)	17	25.0 ± 5.0	-2.7 ± 2.8	3.1 ± 1.8	-	-	-	↓	↓	-	-	-

Data are mean ± SD. *n*= participant number; Brot= basal rotation; Arot= apical rotation; PUV= peak untwisting velocity; UTR= untwisting rate; C3= high dynamic, high static; A3= low dynamic, high static; C2= high dynamic, moderate static; C1= high dynamic, low static; B3= moderate dynamic, high static; E = elite athletes, C = competitive athletes; AVC= aortic valve closure; MVO= mitral valve opening; ↔ = no athlete-control differences; ↓= significantly less in athletes; ↑ significantly greater in athletes.

Table 3 Meta-analyses of athlete-control comparisons for left ventricular strain and twist mechanics

Parameter	Number of studies	d	95% CI		p value	Heterogeneity		
			Lower bound	Upper bound		Cochran's Q	I^2 statistic (%)	p value
Global longitudinal strain								
Overall	14	0.04	-0.25	0.33	0.80	39.75	67.30	**<0.001**
Mitchell classification								
A3	3	-0.34	-1.13	0.45	0.40	7.29	72.58	**0.03**
B3	1	0.33	-0.58	1.24	0.48	-	-	-
C1	3	0.32	-0.67	1.30	0.53	12.24	83.66	**0.002**
C2	2	-0.16	-0.76	0.44	0.61	3.84	73.93	**0.05**
C3	5	0.17	-0.21	0.55	0.38	6.16	35.03	0.19
Between	-	-	-	-	-	10.23	-	**0.04**
Athlete and training level								
Endurance $_{competitive}$	4	-0.13	-0.60	0.35	0.61	8.58	65.05	**0.04**
Endurance $_{elite}$	6	0.29	-0.14	0.72	0.18	12.91	61.26	**0.02**
Resistance $_{competitive}$	4	-0.20	-0.86	0.47	0.56	9.24	67.53	**0.03**
Between	-	-	-	-	-	9.03	-	**0.01**
Global circumferential strain								
Overall	7	0.24	-0.07	0.54	0.12	7.96	24.60	0.24
Mitchell classification								
A3	2	0.39	-0.09	0.87	0.11	0.62	0.00	0.43
B3	1	1.03	0.08	1.99	**0.04**	-	-	-
C1	2	0.29	-0.29	0.87	0.33	1.27	21.03	0.26
C3	2	-0.13	-0.56	0.30	0.56	0.17	0.00	0.68
Between	-	-	-	-	-	5.90	-	0.12

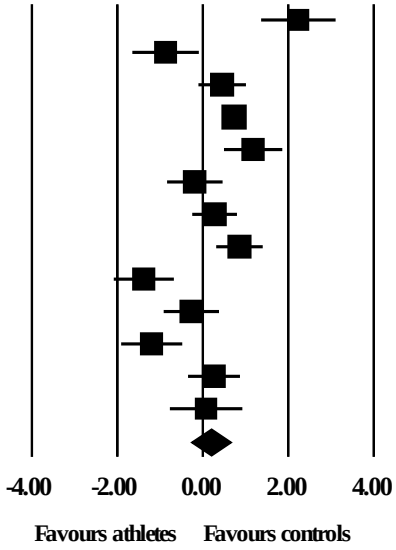
Parameter	Number of studies	d	95% CI		p value	Heterogeneity		
			Lower Bound	Upper Bound		Cochran's Q	I^2 statistic (%)	p value
Athlete and training level								
Endurance $_{competitive}$	2	0.15	-0.59	0.89	0.67	2.76	63.77	0.10
Endurance $_{elite}$	2	-0.04	-0.53	0.44	0.86	0.00	0.00	0.97
Resistance $_{competitive}$	3	0.52	0.09	0.95	**0.02**	2.01	0.57	0.37
Between	-	-	-	-	-	3.19	-	0.20
Apical circumferential strain								
Overall	7	0.29	-0.02	0.59	0.06	10.89	44.91	0.09
Mitchell classification								
A3	1	0.14	-0.63	0.90	0.73	-	-	-
C2	2	0.22	-0.14	0.59	0.23	1.60	37.41	0.21
C3	4	0.37	-0.24	0.99	0.23	8.78	65.82	**0.03**
Between	-	-	-	-	-	0.52	-	0.77
Athlete and training level								
Endurance $_{competitive}$	2	0.10	-0.16	0.35	0.46	0.02	0.00	0.90
Endurance $_{elite}$	4	0.47	-0.07	1.01	0.09	8.41	64.31	**0.04**
Resistance $_{competitive}$	1	0.14	-0.63	0.90	0.73	-	-	-
Between	-	-	-	-	-	2.47	-	0.29
Basal circumferential strain								
Overall	7	-0.05	-0.27	0.18	0.68	6.92	13.35	0.33
Mitchell classification								
A3	1	-0.08	-0.84	0.69	0.84	-	-	-
C2	2	-0.10	-0.58	0.38	0.68	2.53	60.47	0.11
C3	4	0.13	-0.22	0.48	0.47	2.14	0.00	0.54
Between	-	-	-	-	-	2.25	-	0.32
Athlete and training level								
Endurance $_{competitive}$	2	-0.27	-0.53	-0.01	**0.04**	0.26	0.00	0.61

Parameter	Number of studies	d	95% CI		p value	Heterogeneity		
			Lower Bound	Upper Bound		Cochrane's Q	I^2 statistic (%)	p value
Endurance $_{elite}$	4	0.18	-0.14	0.50	0.26	1.95	0.00	0.58
Resistance $_{competitive}$	1	-0.08	-0.84	0.69	0.84	-	-	-
Between	-	-	-	-	-	4.72	-	0.10
Global radial strain								
Overall	9	0.13	-0.11	0.36	0.29	6.97	0.00	0.54
Mitchell classification								
A3	2	0.04	-0.44	0.51	0.89	0.24	0.00	0.62
B3	1	-0.01	-0.92	0.89	0.98	-	-	-
C1	2	0.25	-0.26	0.76	0.34	0.03	0.00	0.86
C3	4	0.09	-0.40	0.58	0.71	6.24	51.91	0.10
Between	9	-	-	-	-	0.46	-	0.93
Athlete and training level								
Endurance $_{competitive}$	3	0.08	-0.59	0.75	0.82	5.40	62.98	0.07
Endurance $_{elite}$	3	0.17	-0.22	0.56	0.38	0.99	0.00	0.61
Resistance $_{competitive}$	3	0.02	-0.39	0.44	0.91	0.25	0.00	0.88
Between	-	-	-	-	-	0.32	-	0.85
Basal rotation								
Overall	14	0.22	-0.06	0.51	0.13	40.17	67.63	**<0.001**
Mitchell classification								
A3	3	0.08	-0.54	0.69	0.81	4.55	56.04	0.10
C1	2	0.75	-1.65	3.15	0.54	17.32	94.23	**<0.001**
C2	2	-0.04	-0.64	0.57	0.91	3.84	73.95	**0.05**
C3	5	0.18	-0.29	0.65	0.45	8.99	55.53	0.06
Between	-	-	-	-	-	0.92	-	0.82

Parameter	Number of studies	d	95% CI		p value	Heterogeneity		
			Lower Bound	Upper Bound		Cochrane's Q	I^2 statistic (%)	p value
Athlete and training level								
Endurance $_{competitive}$	3	0.08	-0.38	0.52	0.74	3.78	47.02	0.15
Endurance $_{elite}$	8	0.36	-0.12	0.83	0.14	30.56	77.09	**<0.001**
Resistance $_{competitive}$	3	0.08	-0.54	0.69	0.81	4.55	56.04	0.10
Between	-	-	-	-	-	1.28	-	0.53
Apical rotation								
Overall	13	0.25	-0.10	0.60	0.17	52.67	77.22	**<0.001**
Mitchell classification								
A3	3	-0.47	-0.96	0.02	0.06	2.88	30.62	0.24
C1	2	0.39	-2.35	3.13	0.78	22.90	95.63	**<0.001**
C2	2	0.59	0.34	0.83	**<0.001**	0.05	0.00	0.83
C3	4	0.52	0.03	1.02	**0.04**	5.64	46.84	0.13
Between	-	-	-	-	-	21.16	-	**<0.001**
Athlete and training level								
Endurance $_{competitive}$	3	-0.06	-1.06	0.94	0.91	17.43	88.52	**<0.001**
Endurance $_{elite}$	7	0.64	0.27	1.00	**0.001**	13.71	56.24	**0.03**
Resistance $_{competitive}$	3	-0.47	-0.96	0.02	0.06	2.88	30.62	0.24
Between	-	-	-	-	-	18.65	-	**<0.001**

CI= confidence intervals; A3= high static, low dynamic; B3= high static, moderate dynamic; C1= high dynamic, low static; C2= high dynamic, moderate static; C3= high dynamic, high static.

Study name	Sport discipline	Std diff in means	Lower limit	Upper limit	p-Value	Control	Intervention
Santoro et al. [32] 1	Cyclists	2.235	1.357	3.114	0.000	9	33
Santoro et al. [32] 2	Weight lifters	-0.871	-1.658	-0.083	0.030	8	36
Santoro et al. [34]	Water polo players	0.451	-0.112	1.015	0.116	17	45
Santoro et al. [33]	Swimmers	0.734	0.459	1.010	0.000	95	125
Nottin et al. [31]	Cyclists	1.176	0.487	1.866	0.001	23	16
Kovacs et al. [10]	Rowers	-0.188	-0.847	0.471	0.577	13	28
Maufrais et al. [30] 1	Marathoners, triathletes and cyclists	0.276	-0.257	0.810	0.310	30	25
Maufrais et al. [30] 2	Marathoners, triathletes and cyclists	0.858	0.304	1.413	0.002	19	46
Vitarelli et al. [37] 1	Marathoners	-1.381	-2.094	-0.669	0.000	12	35
Vitarelli et al. [37] 2	Powerlifters	-0.270	-0.927	0.388	0.422	12	35
Vitarelli et al. [37] 3	Martial artists	-1.199	-1.920	-0.479	0.001	11	35
Galderisi et al. [28]	Rowers	0.262	-0.355	0.878	0.405	19	22
Cote et al. [47]	Cyclists	0.078	-0.779	0.934	0.859	10	11
Overall		0.171	-0.285	0.626	0.462		

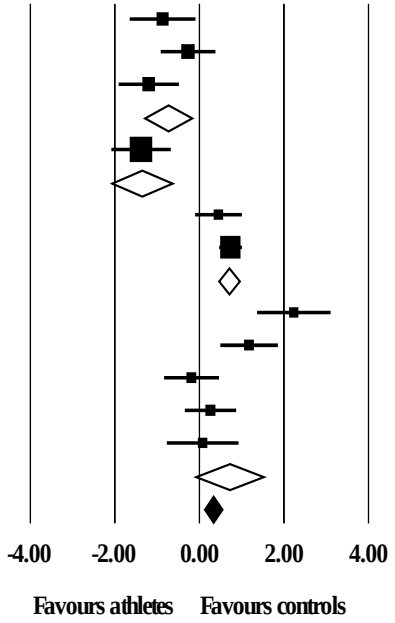


Heterogeneity

Overall: Q= 90.16, df= 12, p<0.001, I^2= 86.69%

Fig. 3 Forest plot showing meta-analysis of overall athlete-control differences in left ventricular twist. CI= confidence intervals; *Forest Plot Symbols* Closed square= study effect size. Size of symbol and confidence intervals represents study weight and precision, respectively in the meta-analysis; Closed diamond= overall summary effect. Diamond width represents overall summary effect precision; 1, 2 and 3 denote multiple athlete-control comparisons from the same study.

Study name	Group by Mitchell classification	Sport discipline	Statistics for each study				Sample size	
			Std diff in means	Lower limit	Upper limit	p-Value	Control	Intervention
Santoro et al. [32] 2	A3	Weight lifters	-0.871	-1.658	-0.083	0.030	8	36
Vitarelli et al. [37] 2	A3	Powerlifters	-0.270	-0.927	0.388	0.422	12	35
Vitarelli et al. [37] 3	A3	Martial artists	-1.199	-1.920	-0.479	0.001	11	35
	A3		-0.760	-1.320	-0.200	0.008		
Vitarelli et al. [37] 1	C1	Marathoners	-1.381	-2.094	-0.669	0.000	12	35
	C1		-1.381	-2.094	-0.669	0.000		
Santoro et al. [34]	C2	Water polo players	0.451	-0.112	1.015	0.116	17	45
Santoro et al. [33]	C2	Swimmers	0.734	0.459	1.010	0.000	95	125
	C2		0.680	0.432	0.927	0.000		
Santoro et al. [32] 1	C3	Cyclists	2.235	1.357	3.114	0.000	9	33
Nottin et al. [31]	C3	Cyclists	1.176	0.487	1.866	0.001	23	16
Kovacs et al. [10]	C3	Rowers	-0.188	-0.847	0.471	0.577	13	28
Galderisi et al. [28]	C3	Rowers	0.262	-0.355	0.878	0.405	19	22
Cote et al. [47]	C3	Cyclists	0.078	-0.779	0.934	0.859	10	11
	C3		0.690	-0.108	1.488	0.090		
	Overall		0.305	0.097	0.513	0.004		

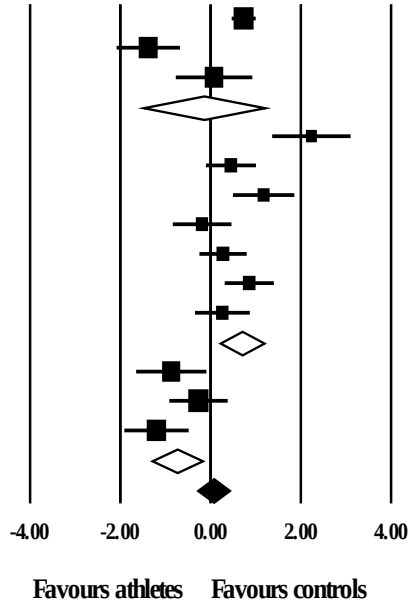


Heterogeneity

A3:	Q= 3.63,	df= 2,	p= 0.16,	I^2= 44.90%
C1:	Q= 0.00,	df= 0,	p= 1.00,	I^2= 0%
C2:	Q= 0.78,	df= 1,	p= 0.38,	I^2= 0%
C3:	Q= 24.06,	df= 4	p< 0.001,	I^2= 83.38%
Between:	Q= 57.95,	df= 3,	**p< 0.001**	

Fig. 4 Forest plot showing meta-analysis of athlete-control differences in left ventricular twist categorised by Mitchell's classification. CI= confidence intervals; *Forest Plot Symbols* Closed square= study effect size. Size of symbol and confidence intervals represents study weight and precision, respectively in the meta-analysis; Closed diamond= overall summary effect; Open diamond= overall summary effect within category. Diamond width represents overall summary effect precision; A3= high static, low dynamic; C1= high dynamic, low static; C2= high dynamic, moderate static; C3= high dynamic, high static; 1, 2 and 3 denote multiple athlete-control comparisons from the same study.

Study name	Group by Athlete type and training level	Sport discipline	Statistics for each study: Std diff in means	Lower limit	Upper limit	p-Value	Sample size: Control	Intervention
Santoro et al. [33]	END Competitive	Swimmers	0.734	0.459	1.010	0.000	95	125
Vitarelli et al. [37] 1	END Competitive	Marathoners	-1.381	-2.094	-0.669	0.000	12	35
Cote et al. [47]	END Competitive	Cyclists	0.078	-0.779	0.934	0.859	10	11
	END Competitive		-0.167	-1.511	1.176	0.807		
Santoro et al. [32] 1	END Elite	Cyclists	2.235	1.357	3.114	0.000	9	33
Santoro et al. [34]	END Elite	Water polo players	0.451	-0.112	1.015	0.116	17	45
Nottin et al. [31]	END Elite	Cyclists	1.176	0.487	1.866	0.001	23	16
Kovacs et al. [10]	END Elite	Rowers	-0.188	-0.847	0.471	0.577	13	28
Maufrais et al. [30] 1	END Elite	Marathoners, triathletes and cyclists	0.276	-0.257	0.810	0.310	30	25
Maufrais et al. [30] 2	END Elite	Marathoners, triathletes and cyclists	0.858	0.304	1.413	0.002	19	46
Galderisi et al. [28]	END Elite	Rowers	0.262	-0.355	0.878	0.405	19	22
	END Elite		0.678	0.192	1.163	0.006		
Santoro et al. [32] 2	RES Competitive	Weight lifters	-0.871	-1.658	-0.083	0.030	8	36
Vitarelli et al. [37] 2	RES Competitive	Powerlifters	-0.270	-0.927	0.388	0.422	12	35
Vitarelli et al. [37] 3	RES Competitive	Martial artists	-1.199	-1.920	-0.479	0.001	11	35
	RES Competitive		-0.760	-1.320	-0.200	0.008		
	Overall		0.045	-0.309	0.398	0.805		

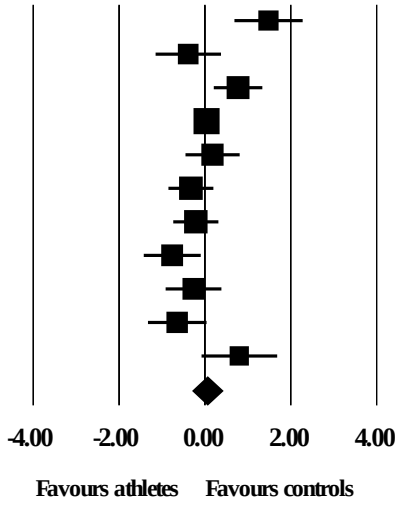


Heterogeneity

END Competitive:	Q= 30.16,	df= 2,	p< 0.001,	I^2= 93.37%
END Elite:	Q= 25.15,	df= 6,	p< 0.001,	I^2= 76.14%
RES Competitive:	Q= 3.63,	df= 2,	p= 0.16**,**	I^2 = 44.90%
Between:	Q= 31.23	df= 2	**p< 0.001**	

Fig. 5 Forest plot showing meta-analysis of athlete-control differences in left ventricular twist using traditional categorisation and athlete training level. CI= confidence intervals; *Forest Plot Symbols* Closed square= study effect size. Size of symbol and confidence intervals represents study weight and precision, respectively in the meta-analysis; Closed diamond= overall summary effect; Open diamond= overall summary effect within category. Diamond width represents overall summary effect precision; END= endurance; RES= resistance; 1, 2 and 3 denote multiple athlete-control comparisons from the same study.

Study name	Sport discipline	Statistics for each study				Sample size	
		Std diff in means	Lower limit	Upper limit	p-Value	Control	Intervention
Santoro et al. [32] 1	Cyclists	1.481	0.678	2.283	0.000	9	33
Santoro et al. [32] 2	Weight lifters	-0.387	-1.157	0.384	0.325	8	36
Santoro et al. [34]	Water polo players	0.772	0.198	1.347	0.008	17	45
Santoro et al. [33]	Swimmers	0.039	-0.228	0.305	0.777	95	125
Nottin et al. [31]	Cyclists	0.176	-0.463	0.816	0.589	23	16
Maufrais et al. [30] 1	Marathoners, triathletes and cyclists	-0.327	-0.861	0.208	0.231	30	25
Maufrais et al. [30] 2	Marathoners, triathletes and cyclists	-0.211	-0.747	0.325	0.440	19	46
Vitarelli et al. [37] 1	Marathoners	-0.761	-1.435	-0.088	0.027	12	35
Vitarelli et al. [37] 2	Powerlifters	-0.266	-0.924	0.391	0.427	12	35
Vitarelli et al. [37] 3	Martial artists	-0.645	-1.335	0.045	0.067	11	35
Cote et al. [47]	Cyclists	0.802	-0.088	1.692	0.077	10	11
Overall		0.034	-0.301	0.368	0.844		

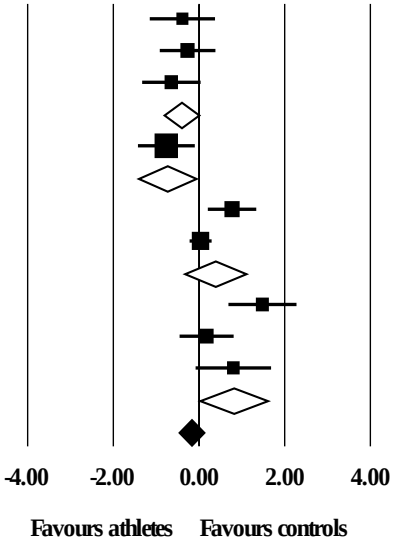


Heterogeneity

Overall: Q= 35.40, df= 10, p<0.001, I^2= 71.75%

Fig. 6 Forest plot showing meta-analysis of overall athlete-control differences in left ventricular peak untwisting velocity. CI= confidence intervals; *Forest Plot Symbols* Closed square = study effect size. Size of symbol and confidence intervals represents study weight and precision, respectively in the meta-analysis; Closed diamond = overall summary effect. Diamond width represents overall summary effect precision; 1, 2 and 3 denote multiple athlete-control comparisons from the same study.

Study name	Group by Mitchell classification	Sport discipline	Statistics for each study				Sample size	
			Std diff in means	Lower limit	Upper limit	p-Value	Control	Intervention
Santoro et al. [32] 2	A3	Weight lifters	-0.387	-1.157	0.384	0.325	8	36
Vitarelli et al. [37] 2	A3	Powerlifters	-0.266	-0.924	0.391	0.427	12	35
Vitarelli et al. [37] 3	A3	Martial artists	-0.645	-1.335	0.045	0.067	11	35
	A3		-0.430	-0.835	-0.025	0.037		
Vitarelli et al. [37] 1	C1	Marathoners	-0.761	-1.435	-0.088	0.027	12	35
	C1		-0.761	-1.435	-0.088	0.027		
Santoro et al. [34]	C2	Water polo players	0.772	0.198	1.347	0.008	17	45
Santoro et al. [33]	C2	Swimmers	0.039	-0.228	0.305	0.777	95	125
	C2		0.360	-0.354	1.073	0.323		
Santoro et al. [32] 1	C3	Cyclists	1.481	0.678	2.283	0.000	9	33
Nottin et al. [31]	C3	Cyclists	0.176	-0.463	0.816	0.589	23	16
Cote et al. [47]	C3	Cyclists	0.802	-0.088	1.692	0.077	10	11
	C3		0.791	0.002	1.580	0.050		
	Overall		-0.196	-0.486	0.094	0.186		

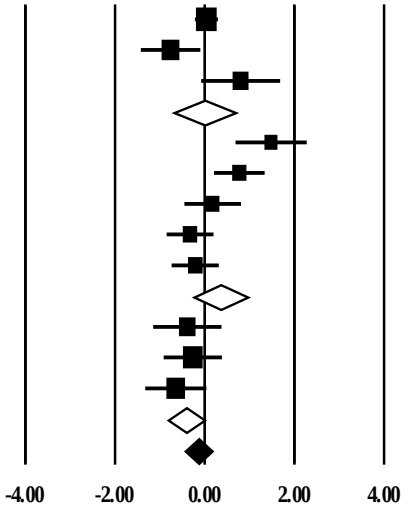


Heterogeneity

A3:	Q= 0.62,	df= 2,	p=0.73,	I^2= 0%
C1:	Q= 0.00,	df= 0,	p=1.00,	I^2= 0%
C2:	Q= 5.16,	df= 1,	p=0.02,	I^2= 80.62%
C3:	Q= 6.26,	df= 2,	p=0.04,	I^2= 68.06%
Between:	Q= 20.67,	df= 3,	**p<0.001**	

Fig. 7 Forest plot showing meta-analysis of athlete-control differences in left ventricular peak untwisting velocity categorised by Mitchell's classification. CI= confidence intervals; *Forest Plot Symbols* Closed square = study effect size. Size of symbol and confidence intervals represents study weight and precision, respectively in the meta-analysis; Closed diamond = overall summary effect; Open diamond = overall summary effect within category. Diamond width represents overall summary effect precision; A3= high static, low dynamic; C1= high dynamic, low static; C2= high dynamic, moderate static; C3= high dynamic, high static; 1, 2 and 3 denote multiple athlete-control comparisons from the same study.

Study name	Group by Athlete type and training level	Sport discipline	Std diff in means	Lower limit	Upper limit	p-Value	Control	Intervention
Santoro et al. [33]	END Competitive	Swimmers	0.039	-0.228	0.305	0.777	95	125
Vitarelli et al. [37] 1	END Competitive	Marathoners	-0.761	-1.435	-0.088	0.027	12	35
Cote et al. [47]	END Competitive	Cyclists	0.802	-0.088	1.692	0.077	10	11
	END Competitive		-0.018	-0.705	0.669	0.960		
Santoro et al. [32] 1	END Elite	Cyclists	1.481	0.678	2.283	0.000	9	33
Santoro et al. [34]	END Elite	Water polo players	0.772	0.198	1.347	0.008	17	45
Nottin et al. [31]	END Elite	Cyclists	0.176	-0.463	0.816	0.589	23	16
Maufrais et al. [30] 1	END Elite	Marathoners, triathletes and cyclists	-0.327	-0.861	0.208	0.231	30	25
Maufrais et al. [30] 2	END Elite	Marathoners, triathletes and cyclists	-0.211	-0.747	0.325	0.440	19	46
	END Elite		0.339	-0.260	0.938	0.268		
Santoro et al. [32] 2	RES Competitive	Weight lifters	-0.387	-1.157	0.384	0.325	8	36
Vitarelli et al. [37] 2	RES Competitive	Powerlifters	-0.266	-0.924	0.391	0.427	12	35
Vitarelli et al. [37] 3	RES Competitive	Martial artists	-0.645	-1.335	0.045	0.067	11	35
	RES Competitive		-0.430	-0.835	-0.025	0.037		
	Overall		-0.156	-0.457	0.146	0.311		



Heterogeneity

END Competitive:	Q= 8.10,	df= 2,	p= 0.02,	I^2= 75.33%
END Elite:	Q= 19.56,	df= 4,	p= 0.001,	I^2= 79.55%
RES Competitive:	Q= 0.62,	df= 2,	p= 0.73,	I^2 = 0.00%
Between:	Q= 7.11	df= 2	**p= 0.03**	

Fig. 8 Forest plot showing meta-analysis of athlete-control differences in left ventricular peak untwisting velocity using traditional categorisation and athlete training level. CI= confidence intervals; *Forest Plot Symbols* Closed square= study effect size. Size of symbol and confidence intervals represents study weight and precision, respectively in the meta-analysis; Closed diamond= overall summary effect; Open diamond= overall summary effect within category. Diamond width represents overall summary effect precision; END= endurance; RES= resistance; 1, 2 and 3 denote multiple athlete-control comparisons from the same study.

Table 4 Meta-regressions of athlete-control differences in left ventricular strain and twisting mechanics with covariates.

Covariate parameter	Number of studies	Cochran's Q	SE	β	95% CI		p value
					Lower bound	Upper bound	
Global longitudinal strain							
Age	14	1.03	0.04	-0.04	-0.11	0.03	0.31
HR	13	0.33	0.03	0.01	-0.04	0.07	0.57
sBP	14	1.57	0.03	-0.03	-0.09	0.02	0.21
dBP	14	0.20	0.03	0.01	-0.04	0.07	0.66
LVMi	10	5.41	0.005	0.01	0.002	0.02	**0.02**
Basal circumferential strain							
Age	7	0.02	0.03	-0.003	-0.05	0.05	0.90
HR	7	0.86	0.02	-0.02	-0.06	0.02	0.36
sBP	7	1.07	0.02	-0.02	-0.06	0.01	0.30
dBP	7	2.99	0.03	0.06	-0.01	0.12	0.08
LVMi	6	2.52	0.004	0.01	-0.001	0.01	0.11
Apical circumferential strain							
Age	7	0.02	0.03	-0.005	-0.07	0.06	0.88
HR	7	0.12	0.03	-0.01	-0.06	0.04	0.73
sBP	7	0.52	0.03	-0.02	-0.07	0.03	0.47
dBP	7	0.22	0.06	0.03	-0.09	0.14	0.64
LVMi	6	3.47	0.004	0.01	-0.0004	0.02	0.06
Global circumferential strain							
Age	7	1.57	0.09	0.11	-0.06	0.28	0.21
HR	6	0.48	0.03	0.02	-0.04	0.08	0.49
sBP	7	0.20	0.04	0.02	-0.07	0.11	0.65
dBP	7	2.60	0.03	0.04	-0.01	0.10	0.11

LVMi	4	0.02	0.01	0.001	-0.02	0.02	0.90

Parameter	Number of studies	Cochran's Q	SE	β	95% CI		p value
					Lower bound	Upper bound	
Global radial strain							
Age	9	4.19	0.04	-0.09	-0.17	0.004	**0.04**
HR	8	0.10	0.02	0.01	-0.04	0.05	0.75
sBP	9	0.54	0.02	0.02	-0.03	0.06	0.46
dBP	9	0.39	0.02	-0.01	-0.06	0.03	0.53
LVMi	5	0.04	0.01	0.002	-0.01	0.02	0.84
Twist							
Age	13	0.01	0.05	-0.01	-0.10	0.09	0.91
HR	13	1.25	0.04	-0.05	-0.13	0.04	0.26
sBP	13	0.08	0.04	-0.01	-0.08	0.06	0.77
dBP	13	0.74	0.08	-0.07	-0.23	0.09	0.39
LVMi	8	0.35	0.01	0.005	-0.01	0.02	0.56
Basal rotation							
Age	14	0.38	0.03	-0.02	-0.08	0.04	0.54
HR	14	0.96	0.03	0.03	-0.03	0.08	0.33
sBP	14	0.10	0.02	-0.01	-0.05	0.04	0.75
dBP	14	0.02	0.05	0.01	-0.10	0.12	0.88
LVMi	8	0.07	0.005	-0.001	-0.01	0.01	0.79
Apical rotation							
Age	13	0.21	0.04	-0.02	-0.09	0.05	0.65
HR	13	0.003	0.03	0.002	-0.06	0.07	0.96
sBP	13	0.004	0.04	0.002	-0.07	0.07	0.95
dBP	13	0.92	0.06	-0.06	-0.18	0.06	0.34

LVMi	8	0.31	0.004	0.002	-0.01	0.01	0.58

Parameter	Number of studies	Cochran's Q	SE	β	95% CI		p value
					Lower bound	Upper bound	
Peak untwisting velocity							
Age	11	0.18	0.03	0.01	-0.05	0.08	0.67
HR	11	1.28	0.03	-0.03	-0.09	0.03	0.26
sBP	11	3.95	0.03	-0.06	-0.13	-0.001	**0.05**
dBP	11	1.35	0.06	-0.07	-0.18	0.05	0.25
LVMi	7	0.84	0.01	0.01	-0.02	0.04	0.36

SE= standard error; CI= confidence intervals; HR= heart rate; sBP= systolic blood pressure; dBP= diastolic blood pressure; LVMi= left ventricular mass index.

4 Discussion

The main findings from the present study are that when sporting categorisations are ignored then there are no differences in LV strain and twisting mechanics, besides UTR, in athletes compared with non-exercising controls. However, when athletes are categorised according to the static and dynamic demands of their individual sports using Mitchell's classifications, then differences emerge, predominantly in twist mechanics. Cardiac twist was greater in low dynamic, high static (A3 – weightlifting, martial arts etc) and high dynamic, low static (C1 – distance running, soccer etc) athlete groups compared with their untrained counterparts. In contrast, twist was lower in high dynamic, moderate static (C2 – swimming, water polo etc) athletes, which was driven by alterations in apical rotation but not basal rotation. PUV was found to be greater in athletes in A3 (weightlifting, martial arts etc) and C1 (distance running, soccer etc) groups but less than controls in high dynamic, high static (C3 – rowing, cycling etc) athletes. Additionally, using the traditional method of categorisation endurance athletes showed a trend towards reduced LV twist than controls, therefore subdivision of training level revealed that elite endurance athletes demonstrate significantly less twist than controls which was accompanied by lower apical rotation which was not found in competitive endurance athletes. In contrast, competitive resistance athletes show increased twist compared with controls and subsequent PUV than controls. Athletes demonstrated significantly increased UTR compared with controls. Finally, LVMi, a measure of cardiac adaptation, was significantly and positively associated with GLS. This is the first meta-analysis to investigate the influence of athletes on 2-D STE derived LV mechanics. These data provide further understanding of athlete-control differences in LV STE derived indices.

4.1 Global Longitudinal Strain

Collectively, GLS did not differ in athletes compared with matched controls. The lack of overall effect may be explained by significant inter-study heterogeneity. Further, subgroup analyses showed GLS in athletes remained unchanged, which suggests GLS does not alter in trained athletes, at least at rest. Previous work has demonstrated that during incremental exercise GLS

remained unchanged after the initial workload (20% maximum aerobic power) [55]. Further, longitudinal strain did not change during afterload elevated exercise using isometric hand-grip [56]. GLS has shown limited augmentation during exercise, whereas other myocardial STE parameters (i.e. circumferential strain, LV twist mechanics) may play a more pivotal role in augmenting myocardial function during effort, and thus, changes in GLS may not be necessary in athletic populations.

Despite the lack of differences between controls and athletes in this meta-analysis, studies have demonstrated increased longitudinal strain following exercise training programmes ranging from 3 to 39 months in duration [57-61]. If longitudinal strain is altered in athletes it is likely to be increased, since a reduction is not a common feature of the athlete's heart [39]. Lower GLS may be attributed to predominately unhealthy patients, whereby healthy subjects regardless of training status (i.e. both trained and untrained) possess normal longitudinal strain at rest, observed to be -19.7% (95% CI -18.9% to -20.4%) in a previous meta-analysis [62]. Indeed, a review suggested that in the presence of significantly reduced GLS when accompanied by LV hypertrophy, individual athletes should be carefully evaluated [39]. This meta-analysis supports those suggestions given the lack of effect that exercise training appears to have on GLS, and is thus not decreased in athletes.

Since GLS is measured on a negative scale, the positive association between LVMi and GLS indicates that as LVMi increased, GLS decreased in athletes relative to controls. The interaction is indicative of reduced GLS with increasing cardiac hypertrophy; suggesting an enhancement of a reserve with increasing relative cardiac mass. However, any such functional reserve may be small given the lack of overall difference in GLS between athletes and controls.

In terms of cardiovascular disease, past work has demonstrated reduced GLS in hypertensive and hypertrophic cardiomyopathy populations [63, 25, 28, 64, 34], supporting the contention that reductions in GLS may be maladaptive and associated with cardiovascular disease abnormalities. Therefore, reduced longitudinal strain could be considered an early sign of dysfunction, such as myocardial fibrosis, which is associated with a 3.4-fold increased risk of major adverse events [65]. In hypertrophic cardiomyopathy patients with normal conventional systolic and diastolic function, GLS was significantly lower in those with late gadolinium enhancement (a quantifiable tool to assess myocardial fibrosis) than those without [66]. This

suggests a link between the extent of fibrosis and GLS, and thus GLS may be considered a sensitive, superior marker for early detection of dysfunction in the absence of global abnormalities. This also supports the current guidelines that recommend GLS as a reproducible and feasible tool for clinical use, and provides incremental data over traditional measures of systolic function [67].

Consideration of these findings and our growing understanding of the changes in longitudinal strain under various conditions may prompt the translation of GLS into clinical practice to aid in the detection of adverse remodelling and distinguishing pathological from physiological functional remodelling prior to major cardiovascular events.

4.2 Circumferential Strain

Neither basal nor GCS demonstrated significant athlete-control differences; however, there was a trend for reduced ACS in athletes relative to controls. Circumferential strain progressively increases with exercise [55], while other work has shown that during exercise ACS increases but BCS remains unchanged [68]. Since the apex permits a more dynamic behaviour than the base when the myocardium is subjected to physiological demands, and thus may have a greater reserve to respond to exercise [49], it is possible that any adaptive reductions in ACS at rest may contribute a functional reserve which could become available for utilisation during effort to enhance GCS.

ACS and BCS are uninfluenced by sport-specificity as no alterations were observed following the Mitchell's categorisation. Conversely, GCS was significantly reduced in the B3 (body building, wrestling etc) group. This finding comes from a sole study using trained body builders [23], thus interpretation of this finding should be treated with caution. Although exclusion for use of performance enhancing drugs was implemented, previous work has demonstrated significantly diminished ACS in anabolic steroid users [69]. Any undisclosed use of anabolic steroids may have contributed to the observed GCS reductions.

Competitive endurance athletes demonstrated greater BCS than controls. Despite this observation, the summary effect was heavily influenced by a single investigation (relative weight – 91.07%), being the only study to show a significant effect, containing a large sample size and high precision [33]. Consequently, whether competitive endurance athletes have greater BCS

remains inconclusive and further large population based studies are warranted to provide further insight into the initial observations found.

4.3 Global Radial Strain

GRS did not differ between athletes and controls during any comparisons; overall, Mitchell's or traditional classifications. Further, no individual studies showed significant effects between athletes and controls with the study sample considered homogenous. GRS is a surrogate measure of cardiac contractility as it represents strain in a plane orthogonal to the direction of sarcomere shortening. In addition, previous analysis of GRS has shown it to be the most variable strain measure with test-retest reproducibility of 19% coefficient of variation [70] and measurement variability of 35.9% [71]. The large variance inherent in the measurement of GRS may explain the lack of athlete-control differences observed to date due to much variability within the measure itself, potentially owing to out-of-plane motion [70].

4.4 Left Ventricular Twisting Mechanics

4.4.1 Twisting

Overall twist was not different between athletes and controls, accompanied by a large and highly significant heterogeneous sample. Following Mitchell's classification, the present data showed multiple intriguing observations. The A3 (weightlifting, martial arts etc) and C1 (distance running, soccer etc) athletic groups had greater twist than controls, whereas twist in C2 athletes was less than controls. Although the C1 (distance running, soccer etc) group demonstrated significantly greater twist in the athletes, these findings came from a single study; whereas the A3 (weightlifting, martial arts etc) group was determined to be homogenous from multiple studies.

Despite literature frequently disputing concentric morphological adaptations in resistance trained athletes [20, 21], the findings of this meta-analysis show that functional STE derived

alterations are present. Afterload conditions may partly explain greater twist in the high static, low dynamic sporting disciplines. Unlike the C2 group, compensatory twist in A3 athletes could become necessary to overcome the aortic pressure, providing a more forceful contraction for ejection. With advancing levels of afterload in diseased patients (hypertension and aortic stenosis), LV twist progressively increased [34]. In this meta-analysis, we show a trend towards significantly greater apical rotation in A3 (weightlifting, martial arts etc) athletes. Experimental studies inducing afterload with isometric hand-grip exercise have shown impaired LV twist via reductions in apical rotation [56, 48]. Repeated exposure to acute afterload increases may lead to chronic adaptations in twist to maintain systolic function mediated by increased baseline apical rotation, a compensatory mechanism in high static, low dynamic (A3) athletes. Coupled with enhanced afterload, the unchanged [32, 21, 72, 73] or modestly increased [22, 74] LV chamber size typically associated with concentric morphological adaptations, with unchanged end-diastolic volume [74], could further accentuate twist in order to eject a stroke volume adequate for supporting baseline cardiovascular functioning. Additionally, geometry alterations with greater wall thickness, relative to short-axis cavity dimensions, may provide an explanation for greater twist. It is well established that the longer lever arm of the subepicardium than the subendocardium dominates the direction of rotation due to its larger radius [31]. In previous work, increased wall thickness was associated with greater apical rotation and thus LV twist [75]; amplifying the distance between the two contour layers as a result of thicker walls could cause even greater dominance of epicardial rotation and potentially explain increased twist in highly static, low dynamic athletes.

Lower twist and apical rotation in C2 group, which is the opposite to that observed in A3 athletes, could be explained by LV volume changes and chronic adaptations. Both studies recruited water based sports (water polo players [34] and swimmers [33]), showing increased LV internal diameter [33, 34] and end-diastolic volume [33]. Underwater exercise induces greater hydrostatic pressure, central volume and thus preload [76] in which may contribute to the observed enlargements [77]. Although increases in LV twist with preload manipulation has been observed following saline administration [78, 79] which artificially increases LV end-diastolic volume and internal diameter and activates the Frank-Starling mechanism, this may not cause the same twisting responses compared with pre-existing LV structural alterations brought about by training induced physiological adaptations. Greater LV chamber adaptations to training may facilitate a functional reserve in systolic mechanics. In support, two longitudinal studies of relatively short duration

(acute) endurance exercise training (3 months [61] and 6 months [57]) led to increased LV twist and apical rotation. More recently, a chronic maintenance programme (36 months) showed LV twist and apical rotation regressed to baseline levels [60]. Given the aforementioned influence that heightened preload has on twist [78, 79], facilitated by the Frank-Starling mechanism, these responses following the acute phases may be mediated by greater plasma and thus volume expansion leading to larger end-diastolic volumes [60]. In contrast, the morphological adaptations observed consequent to the chronic phase including increased LV length and wall thickness may therefore accommodate heightened blood volume and contribute to reduced twist. LV sphericity index and twist are related in a parabolic manner [75]; with increased LV length, demonstrating a more elliptical ventricle, chronically trained athletes may represent the lower right side of the curve whereby twist will become reduced potentially due to alterations in myocardial fibre angle, as shape and fibre orientation are closely associated [80]. Irrespective of mechanistic underpinning, these longitudinal observations suggest that in athletes, cardiac twisting profiles follow a phasic response to training, which therefore may also assist in explaining potential causes of heterogeneity as found in this meta-analysis.

When categorised according to traditional methods, alongside the level of athletic accomplishment, the elite endurance group demonstrated significantly reduced twist with no differences seen in the competitive endurance group compared with controls. Further, apical rotation was reduced in elite athletes but basal rotation did not differ. The apex is suggested to be more ‘free’ than the base due to its greater elasticity and not tethered to the right ventricle, which may therefore permit more rotation at the apex [81]. In laboratory based settings, literature has frequently documented greater apical augmentation with submaximal exercise than at the base [55, 82, 49], potentially owing to its greater β receptor density and responsiveness to adrenergic stimulation [83], greater augmentation in response to heightened preload [79] or a combination of both. The apex is suggested to have a greater functional reserve to respond to exercise than the base [49] and considering the superior sensitivity of the apex with the onset of increased cardiovascular demand, it is unsurprising that the more caudal region of the myocardium presents a baseline adaptation. Along with the potential cardiac geometry changes and their influential effects on twist mechanics, LV twist is lower with a decreased resting HR [31] and following exercise training, changes in sympathovagal balance cause decreases and increases in sympathetic and parasympathetic activity, respectively [32]. Greater β adrenergic receptor concentration within

the apex might explain reduced apical rotation and twist due to heightened sensitivity to Ca^{2+} release and uptake [33], whereby normal functioning is maintained with decreased systolic twist at rest. Another mechanism concerns alterations in the myocardial fibres, elite athletes may present greater contractility of the subendocardial layer, thereby reducing the net twist. In contrast, reductions in both the inner and outer layers may also partly explain reduced LV twist and thus apical rotation, as demonstrated by Nottin et al. [31] in elite cyclists.

Dynamic exercise induces elevations in preload and consequently exercise performance may benefit from greater twist during effort, especially with elite participation. It is commonly known that endurance athletes demonstrate functional reserves in basic physiological measures including heart rate, blood pressure etc, at rest compared with untrained populations. Given this meta-analysis found reduced twist in elite endurance athletes, it may be plausible that there exists a necessary functional reserve of apical rotation and thus twist to attain a superior level of sporting performance. Nevertheless, more research is still required to establish the 'true' nature of reduced twist mechanics in elite athletes and its interaction with global LV function; this is likely to require study of twist mechanics during exercise. For example, LV twist plateaued during incremental exercise at moderate intensities, which is a suggested mechanical limitation to stroke volume in recreationally active individuals [49]. LV twist is linearly related to stroke volume [78, 49] and since stroke volume progressively increases to maximum in endurance athletes [84], it is plausible that reduced resting twist in elite endurance athletes may facilitate continual LV output to high intensity exercise, however in light of the available literature, this remains an assertion. Clarification will require determining if the baseline physiological adaptation is because athletes possess a functional reserve that may be called upon during exercise. Indeed, limited work indicates that even in non-athletic individuals, apical rotation was lower at rest and during submaximal exercise (40% peak power output) in those with high aerobic fitness compared to those with moderate aerobic fitness [68]. This reduction may be indicative of a functional reserve even during submaximal exercise and additionally supports that twist may have capabilities of increasing beyond moderate intensities. Conducting further studies in elite endurance individuals will aid in bridging the gap between global, traditional measures of systolic function and 'novel' measures (twist mechanics).

Despite numerous studies with competitive endurance athletes reporting increased structural adaptations [53, 33, 37], the lack of overall effect in twist mechanics could suggest structural adaptations precede those of functional STE derived indices in competitively trained athletes. Although, in two of the studies LV twist was significantly different between athletes and controls but in opposing directions [33, 37], therefore further data are necessary to expose the large heterogeneity in studies with competitive athletes to further establish the dose-response relationship between exercise training and twist mechanics. However, from the literature to date and thus the findings of this meta-analysis, alterations in LV twist appear to be attributed to elite level populations performing predominantly high dynamic exercise. Competitive resistance athletes on the other hand showed a compensatory increase in twist compared with controls. There were no elite resistance studies available in this meta-analysis, which prevented a direct comparison between training levels in resistance trained performers, therefore it remains unknown to date if athletes of a greater training level within static disciplines demonstrate a further increased twist than seen in the competitive performers.

4.4.2 Untwisting

Untwisting velocity was not different in athletes to controls overall. Similar to LV twist, heterogeneity was significant but sport-specific alterations were found. The A3 (weightlifting, martial arts etc) and C1 (distance running, soccer etc) athletes showed greater PUV to controls, suggesting a systolic-diastolic coupling (i.e. concomitantly increased twist and PUV compared to controls). In contrast, the C3 (rowing, cycling etc) group, consisting all of cyclists, showed significantly reduced PUV in athletes. Although the findings of the present meta-analysis did not show a twist-PUV coupling in C3 (rowing, cycling etc) group, when additional LV twist analysis was conducted using the same studies used for PUV analysis [53, 31, 32], a significant reduction in athlete's twist was apparent ($p=0.05$) (data not presented), indicating a systolic-diastolic mechanical coupling (i.e. concomitantly decreased twist and PUV compared to controls).

Stored energy following systolic twist prompts the release of energy within the spring like titin protein [85] to cause untwisting. Untwisting produces a 'suction' effect by creating an intraventricular pressure gradient (IVPG) [82] with the ability to create this gradient and facilitate

passive filling providing superior diastolic function [86]. Lower ventricular pressure facilitates passive LV filling with low atrial pressures [87], with the relationship between IVPG and untwisting shown to be positive [88]. The LV twist/untwist interaction is also documented as positive [88] and thus, the increased twist found in the A3 (weightlifting, martial arts etc) group may explain greater PUV as a compensatory mechanism in order to enhance filling.

Reduced PUV may be due to reductions in twist at rest, with the myocardium requiring less twist and thus untwisting to attain sufficient resting cardiovascular function [38]; a suggested reserve mechanism for exercise [32, 38]. Lower HR, elongated diastolic filling periods consequent to preserved LV pressure decay (tau) and diastasis may facilitate reduced PUV. A strong, negative association has been observed between untwist and tau in dogs ($r = -0.66$, $p<0.0001$) [88]. Greater parasympathetic activity could preserve untwisting until inotropic stimulation occurs during exercising conditions. In support, progressive administration of dobutamine caused proportional increases in twist and PUV, whilst tau progressively decreased and HR remained unchanged from baseline [88]. As with systolic twist, further research on the untwisting responses in athletes, both at rest and during exercise, will help establish whether a functional reserve in PUV is present in high dynamic, high static sports, as suggestive by the results of this meta-analysis.

Limited data are available on diastolic twist mechanics following longitudinal exercise training. Following 3 months rowing training in University athletes, Weiner et al. [61] showed early diastolic PUV and %untwist during isovolumic relaxation time (IVRT) increased, with no further changes in early diastolic PUV after the ensuing chronic maintenance programme, unlike twist which regressed to baseline [60]. The initial increase probably occurred due to volume expansion since past work has demonstrated the preload dependency of early diastolic PUV [60, 79]. After the chronic phase however, adaptive hypertrophic remodelling occurred, therefore the preserved supernormal diastolic function may reflect an intrinsic functional adaptation in untwisting mechanics. Additional mechanistic contributions for altered mechanics other than HR and sympathovagal balance are suggested. Changes in the titin isoforms could be responsible for potential compensatory increases and functional reserves in rotational mechanics as found in this meta-analysis. Titin, a bidirectional myocardium filament contributes a crucial role in storing forces necessary for early diastolic function [89]. Different spring compositions alter passive stiffness, this variation influences passive and restoring forces. Methawasin et al. [90] showed that

greater titin compliance attenuated the Frank-Starling mechanism, whereas stiffer isoforms showed greater length-dependant activation. Diastolic function is influenced by increases in titin-based compliance which manifests in increased LV chamber compliance [90]. Shifts to more elastic isoforms could increase the quantity of energy released during early diastole prior to MVO [30], as was found in elite endurance athletes who demonstrated significantly greater peak kinetic energy during early diastole [91]. Titin phosphorylation and isoform shifts have shown alterations with cardiac disease [92]; adjustments in athletes may in part explain divergent athlete-control differences in LV twist mechanics. Findings from this meta-analysis showed greater UTR in athletes, suggesting facilitation for early LV filling, in addition to other investigations having shown greater UTR [37], %untwist during IVRT [30] and shorter time-to-PUV [29] in athletes without differences in PUV compared with controls. Thus, athletes may present noticeable enhancements in diastolic function as measured during the earliest phases of relaxation (i.e. before MVO) even when PUV differences are absent. During resting conditions in those with normal diastolic function, alterations in PUV may not be obviously different between trained and untrained individuals, potentially due to the long durations of diastole at rest, thus PUV may become a more influential parameter for assessment when the filling period diminishes, i.e. during exercise. Due to the significant proportion of untwist which occurs during the IVRT (~50-70%) [13], parameters reflecting the earliest phases of relaxation may be considered more sensitive markers of diastolic function when distinguishing trained and untrained populations. Athletes often have normal or superior global diastolic function as measured using conventional markers such as the E, A and E/A ratio [93, 22]. These observations may be underpinned by early untwisting allowing the generation of a sufficient pressure gradient and thus, measurements of untwisting mechanics before mitral inflow may provide a precursor to the traditional, well established parameters. However, it is clear that further substantiation is required in athletic populations to fully understand how exercise training influences untwisting mechanics, with particular interest in potential differences between UTR and PUV. Consequently, until untwisting mechanics are understood to a greater extent, conventional global measures of diastolic function may remain more suitable parameters to differentiate pathology and physiology in athletic patients.

Following meta-regression analysis, as sBP increased, the difference in PUV effect size between athletes and control diminished. This association is suggestive of increased afterload

exerting influences on LV twist mechanics, thus reducing the functional reserve in diastolic function.

4.5 Study Limitations and Future Studies

There are several limitations which must be addressed within this meta-analysis. The first concerns the use of the random effects model which does not assume all studies are equal but the true effect varies between studies, and the analysis estimates the mean distribution of effects [94]. Smaller studies become more influential and reduce the relative weight of larger studies, to account for the within study variability and 'balance' the outcome [94]. Between-study variances may be influenced by echocardiographic inconsistencies with techniques of image acquisition and analysis. LV twist mechanics have greater variability ((apical rotation (8% - 50%) [55, 31, 70, 95, 49], basal rotation (5% - 21%) [55], twist (10% - 20%) [96, 70, 49] and PUV (26%) [96]) than longitudinal and circumferential strain (<8%) [55, 70]. When the high variability of STE derived measures is compounded by small sample sizes, as is the case in several studies included within this meta-analysis, it is likely that studies are underpowered to detect subtle differences between athletes and controls. Consequently, this may explain why, in some cases, only minimal differences between athletes and controls were noted in the present meta-analysis. Moreover, when assessing the apex, progressive caudal transducer movement is associated with increased apical rotation [95, 97]. Given that the present meta-analysis indicates alterations in LV twist with concomitant changes in apical rotation, the importance of consistent and accurate apical acquisition, allied to consistent and accurate reporting of the location of apical measures, in reducing study-to-study heterogeneity is clear. Publication bias only occurred for BCS, therefore findings from this meta-analysis for all remaining measures suggest an unbiased, thorough collection of sample studies and are representative of completed literature. Nevertheless, in common with many systematic reviews, it is possible that we have missed some data, particularly those published in languages other than English.

Our use of Mitchell's classification, although widely accepted as a method of categorising sporting activities, has several inherent limitations. Firstly, sporting categorisation is not position

specific, which has implications for team games. For example, the dynamic and static loading experienced by a goalkeeper and midfielder in soccer should not be considered equal. Secondly, the model classifies the activity not the athlete. This may be an issue, particularly in elite level sport where athletes likely undertake additional strength and conditioning training to supplement competition training. Clearly there is the possibility of this altering the dynamic and static components and thus cardiac loading [24]. In conjunction with our findings, it is suggested training level be considered when interpreting study findings. Further, when including two or more athlete groups, studies should obtain participants of a similar competition standard and training level.

Furthermore, the inclusion criteria for this analysis included healthy males aged 18-45 years so our findings cannot be extended to female, older (>45 years), child or adolescent (<18 years) populations. A broad age range was adopted to maximise study inclusion, however, no associations were evident between age and STE derived measures following meta-regression analysis in LV twist mechanics. Therefore, the study age range used in this meta-analysis can be considered homogenous and is unlikely to account for some of the between-study heterogeneity.

Although still controversial, LV systolic twist mechanics and rotations appear to be sex independent [53, 42, 44], while past work has shown sex to influence GLS [26, 41, 42]. Twist mechanics however, are repeatedly documented to be affected by age [44-46], therefore to eliminate any confounding factors and for homogeneity purposes it is suggested that future studies recruit single sex groups that are aged matched.

We analysed data on global indices of LV strain; therefore, whether athletes develop regional alterations in specific segments of the myocardium, where global differences were undetected, is beyond the scope of this study and future work may wish to explore this potential.

Training level subdivision was only conducted when using the traditional method of categorisation, since additional division of elite and competitive athletes when using Mitchell's classification would have resulted in few studies within each groups as 18 available categories would become apparent. The effect of training duration and protocols may also be important. In particular, this meta-analysis did not take into consideration the stage or duration of training, and most studies did not report the training phase of athletes during data collection. Given the possibility of a phasic response of exercise training on LV twist [60] this may account for some of the between-study heterogeneity observed in this meta-analysis. Future studies should

acknowledge and consider the phase, volume and intensity of training, in addition to the time-point within a season that athletes are tested. Accordingly, we recommend that more longitudinal studies are conducted which may eliminate much of the heterogeneity observed between existing observational studies. More studies are required to establish additional sources of between-study heterogeneity, for example Oxborough et al. [98] recently used novel strain - volume/area loops to study simultaneous strain and structure, suggesting differences in peak longitudinal strain are a reflection of chamber size following the finding of normalised strain for % end-diastolic volume. Future work may wish to explore the interaction between LV mechanics and volume/area in chronically trained athletes. Further to this, few studies have investigated the effect of body size on LV mechanics. Since it is currently recommended that traditional, structural measures be scaled to body surface area [67], to enable direct comparisons, more studies are required to understand the influence of body size and thus scaling on LV mechanics.

Inter-vendor differences were not taken into account during the present meta-analyses, and it is possible that vendor differences in the algorithms and thus analysis of speckle tracking measurements may account for some heterogeneity observed, as previously acknowledged [13, 74]. Therefore, these differences should be considered when interpreting associated LV mechanics data.

There has been some recent attention directed towards strain of the right ventricle (RV) following prolonged exercise [99] and although the focus of this meta-analysis is primarily related to LV mechanics, it is important to acknowledge the possible impact of training on the RV. It has been well established that athletes develop enlargement of the RV albeit this is in the presence of normal systolic and diastolic function as determined by conventional indices such as RV fractional area change and tricuspid plane systolic excursion (TAPSE). In view of this, few studies have attempted to define RV longitudinal regional and global strain [100-104]. Teske et al. [104] demonstrated reduced basal systolic strain rate in athletes with a dilated RV while others have demonstrated values similar to non-athletic controls. These heterogeneous findings are likely a consequence of variable athlete demographics similar to those seen in studies of the LV. The parallel interaction of RV size and function on the LV is equally important and may, in part, explain some of the findings that are presented in this review, particularly in the septal regions and

ventricular insertion points. It is apparent that further work to systematically explore the literature in this area is warranted.

There are also limitations in the available literature. Within the included studies, limited reporting of anthropometric data prevented additional meta-regression or moderator analyses which may have further identified sources of heterogeneity between comparisons. Future investigators may wish to consider reporting basic anthropometric data along with cardiac data associated with the athlete's heart.

A further important limitation is the different criteria used to classify the control or non-trained group used to compare against athletes. The quantity of exercise ranged from those untrained and sedentary [10, 32-34, 37] to performing < 2 hours/week [54], < 3 hours/week [23] and recreationally active subjects (3.9 ± 1.5 days/week) [53]. Given that there were differences between dynamic training levels, it is important that control groups are as homogenous as possible and preferably sedentary, which may eliminate some between-study heterogeneity and provide more clarity on exercise training on LV mechanics. However, when recruitment of completely sedentary participants is not possible, studies should report data detailing exercise volume and intensity.

From the available literature within this meta-analysis, only one study attempted to differentiate sports based on the variation of static and dynamic components [37]. However, the intermediate group (martial artists), considered by the authors as combined strength and endurance is actually classified as a high static, low dynamic sport in accordance with Mitchell's classification. Consequently, it is recommended that future studies incorporate a spread of athlete types alongside Mitchell's framework as opposed to dichotomous athlete grouping to expand on the sport-specific alterations in cardiac twist mechanics.

When investigating LV untwist and consequently diastolic function, studies should assess both UTR (early diastole) and PUV, as separate parameters, to provide more useful insights into athlete's diastolic response at various timing events as only one study to date has done so [37], which will further enable a greater understanding of the relative importance of each measure especially during resting conditions. Additionally, the measurement point of diastolic markers should be more clearly identified, which may eradicate some heterogeneity via the use of consistent terminology.

Due to the large heterogeneity observed throughout, future research is warranted while considering sporting discipline, training level and covariates as identified from this meta-analysis. At present, without additional knowledge regarding the direction of alterations in LV strain and twist mechanics, aside from GLS, the findings of this analysis are supportive of the suggestion that it may not be feasible to use baseline LV mechanics clinically to differentiate pathological and physiological remodelling [37].

5 Conclusion

Apart from UTR, when sporting categorisation was not implemented, no differences between trained athletes and untrained healthy controls exist in any LV STE derived parameters. However, the use of GLS may have potential to become a promising parameter to aid in the diagnosis between pathological and physiological remodelling due to the lack of effect that exercise training has. This meta-analysis has shown the use of 2-D STE is able to distinguish cardiac functional changes when taking athletic type and training level into consideration. Elite level endurance athletes demonstrate reduced LV twist, accompanied by lower apical rotation at rest, which may not be present in competitive level athletes. Thus, it is plausible that there may exist a dose-response relationship between endurance exercise training level and alterations in LV twist. Athletes exposed to differing cardiac loading associated with the dynamic and static components of sports possess divergent twisting mechanical profiles, with low dynamic, high static sports presenting a potential compensated increase in twist. Further, PUV were greater in low dynamic, high static sports but lower in high dynamic, high static sports. The results of the meta-regressions suggest that relative cardiac size and haemodynamic loading conditions should be taken into account when interpreting data from future studies. Each of these covariates may also in part explain some inter-study heterogeneity and inconsistency.

LV twist mechanics are dependent on sporting type, training level or a combination of both. Suitable athlete categorisation using both traditional and contemporary methods have proved to be potentially useful tools for extrapolating LV twisting mechanics in athletes, thus sporting type and athlete training level should be considered simultaneously in future studies. With the promising use of 2-D STE coupled with improved data reporting leading to homogenous athlete and control

samples, greater certainty regarding alterations in STE derived LV mechanics consequent to exercise training can be elucidated.

Compliance with Ethical Standards

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Alexander Beaumont, Fergal Grace, Joanna Richards, John Hough, David Oxborough and Nicholas Sculthorpe declare that they have no conflicts of interest relevant to the content of this review.

Ethical approval

Ethical approval was not required to complete this review.

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