

Left ventricular twisting mechanics and exercise in healthy individuals: a systematic review

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Abstract: The aim of this study was to review systematically the effects of exercise on left ventricular (LV) twisting mechanics in healthy individuals. Literature searches were conducted in electronic databases for articles reporting measures of LV twisting mechanics in healthy individuals before and during/after exercise. Upon review, 18 articles were analyzed. Studies were separated by exercise type into the following four categories to allow for detailed comparisons: submaximal, prolonged endurance, maximal, and chronic endurance. Despite an overall methodological quality of low to moderate and within-group variations in exercise intensity, duration, and subject characteristics, important trends in the literature emerged. Most important, the coupling of LV systolic twisting and diastolic untwisting was present in all exercise types, as both were either improved or impaired concomitantly, highlighting the linkage between systole and diastole provided through LV twist. In addition, trends regarding the effects of age, training status, and cardiac loading also became apparent within different exercise types. Furthermore, a potential dose-response relationship between exercise duration and the degree of impairment to LV twisting mechanics was found. Although some disagreement existed in results, the observed trends provide important directions for future research. Future investigations should be of higher methodological quality and should include consistent exercise protocols and subject populations in order to minimize the variability between investigations.

Keywords: twisting mechanics, diastolic untwisting, rotational parameters, exercise intensity and duration

Introduction

The left ventricle (LV) has three planes of motion: longitudinal, radial, and circumferential.¹ Circumferential motion of the LV is the result of the contraction and relaxation of obliquely oriented epicardial and endocardial myofibres.² These oblique contractions in the healthy human heart, when viewed from the apex, result in circumferential clockwise rotation at the base, and counterclockwise rotation at the apex. The net result of these opposing rotations in the basal and apical planes is a wringing motion of the heart during systole, referred to as LV twist.³ A rapid untwisting motion in the opposite direction occurs during diastole,⁴ and is believed to be caused by the release of elastic potential energy accumulated during the systolic contractions⁵ – likely from the compression of spring-like cardiac proteins such as titin.⁶ This early diastolic untwisting enhances the generation of the intraventricular pressure gradient and works to draw blood from the left atrium into the left ventricle, a process known as diastolic suction, and thereby enhances diastolic filling and allows diastolic filling to occur at lower atrial pressures.⁷ Taken together, LV twist, the corresponding diastolic

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untwisting, and the apical and basal components of each can be viewed as the twisting mechanics of the left ventricle and serve as important indicators of LV function.

During exercise, LV twisting mechanics play an important role in augmenting cardiac function. It is well understood that the increases in chronotropic stimulation that occur with exercise result in reduced diastolic filling time, requiring a compensatory increase in diastolic filling in order to maintain cardiac output. As inotropy also increases during exercise, more potential energy is produced during systole through vigorous twisting contractions, resulting in greater diastolic untwisting and therefore allowing for diastolic filling to occur more rapidly.⁸ As diastolic untwisting plays a major role in diastolic filling, and relies heavily on LV twist, it is clear that the twisting mechanics of the left ventricle are integral to cardiac function during exercise. The measurement of these twisting mechanics under exercise conditions is therefore critical to an accurate understanding of the relationship between exercise and heart function.

Recent improvements in echocardiography and cardiac magnetic resonance imaging have allowed the twisting mechanics of the left ventricle to be measured and quantified in healthy individuals.^{9,10} Correspondingly, there has been a rapid increase in the number of papers examining the changes in LV twist and diastolic untwisting resulting from exercise. In light of this, the present authors feel that a systemic assessment of the overall findings from these articles is required. Two recent narrative reviews have discussed changes in various indicators of LV function that occur following acute and prolonged bouts of exercise.^{11,12} However, to the present authors' knowledge, no systematic review exists examining the effects of all forms of exercise on LV twisting mechanics. Accordingly, the primary purpose of this review is to systematically summarize and evaluate the existing literature examining the effects of exercise on LV systolic and diastolic twisting mechanics in healthy individuals. The aim is to provide clarity to the effects of different exercise durations and intensities on LV twisting mechanics, and the present authors hypothesize that acute short-term exercise will induce an increase in these LV parameters, while prolonged exercise will cause a transient decrease.

Methods

Search strategy

An extensive literature search on the effects of exercise on LV systolic and diastolic twisting mechanics was conducted in the following electronic databases: An extensive literature search on the effects of exercise on LV systolic and diastolic twisting mechanics was conducted in the following electronic databases

(from 1950 – January 2012): MEDLINE, EMBASE, and EBSCO (Cochrane Library, ACP Journal Club, DARE, CCTR, CMR, HTA, NHSEED, Academic Search Complete, CINAHL, PsycINFO, and SPORTDiscus). The selected items were published after 1950 and before January 2012. Search terms were divided into three categories: (1) exercise, (2) left ventricle, and (3) twisting mechanics. The exercise search terms used were developed previously in systematic reviews conducted by the authors' research group.¹³ See Table 1 for a complete list of the Medical Subject Headings and keywords used.

Screening

A total of 127 articles were found through the literature search. Duplicates, review articles, conference abstracts, articles not in English, letters to the editor, studies investigating only pathological conditions (without data on healthy individuals), and investigations that did not report data on LV twisting mechanics were excluded, leaving 14 articles remaining. In addition, four articles were found via manual cross-referencing and the authors' knowledge of the subject area, resulting in a total of 18 articles for final review (Figure 1).

Table 1 Results of the MEDLINE literature search using the Ovid interface

Search no	Searches (March 13, 2011)*	Results		
1	exp Physical Fitness/	18,174	Exercise parameters	
2	exp Motor Activity/	93,010		
3	exp Physical Endurance/	19,700		
4	exp Exercise/	54,165		
5	exp Physical Exertion/	50,171		
6	exp Sports/	89,073		
7	exp Exercise Therapy/	22,408		
8	exp Exercise Tolerance/	6138		
9	exp Health Behavior/	75,536		
10	exp Heart Ventricles/	59,094		LV parameters
11	exp Ventricular Function, Left/	22,147		
12	exp Ventricular Function/	39,642		LV twisting parameters
13	Myocardial.mp.	299,096		
14	Rotation\$.mp.	68,499		
15	Recoil\$.mp.	2248		
16	Twist\$.mp.	9749		
17	Untwist\$.mp.	404		
18	Torsion\$.mp.	16,973	329,205	
19	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9			
20	10 or 11 or 12 or 13	353,080	93,704	
21	14 or 15 or 16 or 17 or 18			
22	19 or 20 or 21	43		

Notes: *Use of "/" after an index term indicates that all subheadings were selected; "\$" at the end of a term indicates that this term has been truncated; "exp" before an index term indicates that the term was exploded; ".mp." indicates a free text search for a term.

Abbreviation: LV, left ventricular.

Quality assessment and level of evidence

Two reviewers (TD and AP) assessed all articles for methodological quality and level of evidence in duplicate, and any disagreements were settled through consultation with a third reviewer (DW) until 100% consensus was achieved. All systematic review-related processes were overseen and directed by a senior investigator specializing in systematic reviews (SB). Methodological quality was determined using the Downs and Black¹⁴ Quality Index checklist, as the review did not include any randomized controlled trials. The Quality Index checklist was modified according to Prince et al¹⁵ (and used previously by the authors' research group)¹³, to incorporate only the most relevant questions from the original checklist. Each article was assigned a score out of 15, with higher scores indicating greater levels of methodological quality. Level of evidence was assessed using a five-point scale¹⁶ (modified from Sackett et al¹⁷). In brief, Level 1 (the highest level of evidence) corresponds

to a randomized controlled trial of high quality. Level 2 refers to a randomized controlled trial of lower quality, a prospective controlled trial, or a cohort study. Level 3 is a case control study design. Level 4 refers to a pre-post, post-test, or case series study design. Level 5 (the lowest level of evidence) can be of observational, clinical consensus, or case report design.

Results

The 18 included articles involved a total of 324 healthy participants (276 men, 48 women) with an age range of 19–70 years. The articles were categorized by exercise type into four groups: (1) acute submaximal exercise (nine studies, 147 total participants),^{8,18–25} (2) prolonged endurance exercise (five studies, 102 total participants),^{26–30} (3) acute maximal exercise (three studies, 60 total participants),^{31–33} and (3) chronic endurance exercise (one study, 15 total participants).³⁴ See Table 2 for an overall summary and

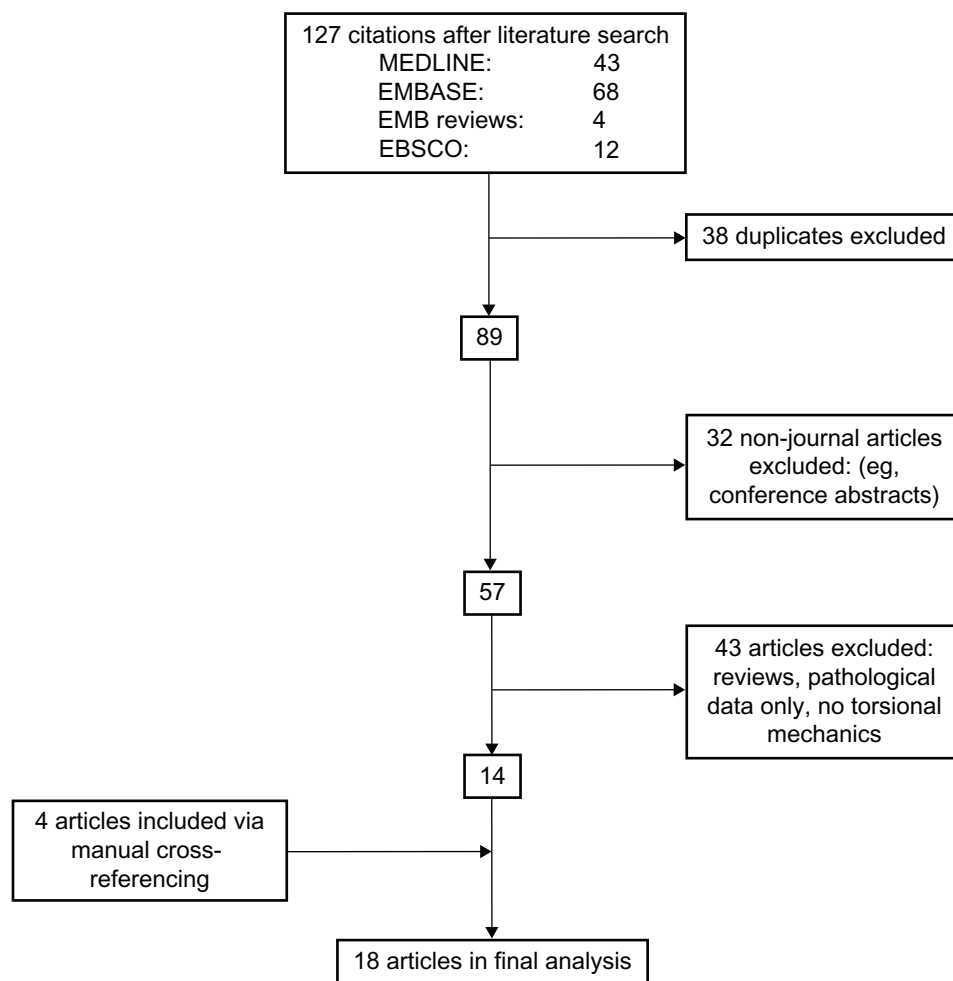


Figure 1 Flowchart of literature search process.
Abbreviation: EMB, evidence-based medicine.

Supplementary Tables 1–4 for a comprehensive summary of the articles in each exercise category. The articles examined were of low to moderate methodological quality, with a mean Downs and Black¹⁴ score of 10.61 ± 0.85 out of 15 (range, 9–12). The articles were published over a 9-year period (2003–2012).

Acute submaximal exercise

Nine studies investigated the effects of acute submaximal exercise on systolic and diastolic LV twisting mechanics (147 total participants; approximate mean ages: 20–70 years). All investigations measured LV function at rest and during exercise. Seven investigations utilized either supine or semi-supine bicycling as their exercise mode,^{8,18–21,24,25} while the two remaining investigations utilized a unilateral knee extensor exercise protocol.^{22,23}

Systolic parameters

Acute submaximal exercise was found to result primarily in augmented LV systolic twisting mechanics (including LV twist, twisting rate, systolic apical and basal rotation, and apical and basal rotation rate) in individuals below the age of 40.^{8,18–20,24–25} However, two investigations reported no change in any of these parameters in response to sub-maximal exercise in individuals of this age group.^{22,23} This disagreement is most likely due to the use of a weak exercise stimulus in these two outlying investigations, as unilateral knee extensor exercises did not induce increases in either stroke volume or ejection fraction,^{22,23} two indices of cardiac function that were found to increase in all other investigations in this category. Interestingly, one investigation examined the changes in LV twisting mechanics during submaximal exercise between endurance-trained and normally active individuals.²⁵ This investigation reported that all measured systolic LV twisting mechanics increased from rest to exercise in both groups, but found no evidence of group differences in any LV twisting mechanic parameter, aside from lower apical rotation, and the endurance-trained group had a slightly lower LV twist ($P = 0.09$) at rest and during exercise than the normally active group.²⁵ In addition, submaximal exercise was also found to primarily result in no change in LV systolic twisting mechanics in individuals above the age of 40,^{18,20} although one investigation did report increased peak apical rotation in an older population during semi-recumbent cycling.²¹ This discrepancy is potentially attributable to differences in the selected sample populations, as the older populations examined by Burns et al¹⁸ and Esch et al²⁰ were on various cardiac and blood pressure-lowering medications,

while the population examined by Tan et al²¹ was free of any cardiovascular medications. The absence of medication possibly reflects a healthier cardiovascular system in which LV function may more closely resemble that of younger individuals in the ability to augment systolic twisting mechanics. In support of this theory, the peak heart rates elicited by the exercise protocols used by Burns et al¹⁸ and Esch et al²⁰ were greater than that reported by Tan et al²¹ (140 and 110 bpm, respectively, versus 90 bpm). Observing an increase in peak apical rotation despite a lower peak exercising heart rate²¹ suggests that a greater intrinsic LV function, such as that found in younger individuals, was present in the sample population.

Diastolic parameters

Consistent with the increase in LV systolic twisting mechanics, diastolic twisting mechanics (including untwisting rate, time to peak untwisting rate, and diastolic apical and basal rotation rates) were generally reported to increase during submaximal exercise in individuals below the age of 40.^{8,18–20,24–25} The same two investigations which utilized a lower exercise intensity reported no change in diastolic twisting mechanics.^{22,23} In endurance-trained and normally active individuals, submaximal exercise induced an increase in all measured LV diastolic twisting mechanics, yet there was no difference in any diastolic twisting mechanic parameter between groups at rest or during exercise.²⁵ In individuals above the age of 40, submaximal exercise resulted primarily in impaired diastolic untwisting (increased time to peak untwisting rate, failure to augment peak untwisting rate).^{18,20} However, the same investigation that reported contradictory improvements in systolic twisting mechanics in a potentially healthier older population also found conflicting evidence of increased peak untwisting rate in these individuals.²¹ The percentage of LV untwisting that occurred prior to mitral valve opening, a marker of early diastolic function and an essential aspect of diastolic suction, was found to be primarily unchanged in individuals below the age of 40.^{8,19,20} The two studies to report this measure in those older than 40 years found conflicting evidence, as Esch et al²⁰ reported a decrease – further supporting their finding of impaired diastolic twisting mechanics – while Tan et al²¹ reported no change in the amount of untwisting occurring at any point during diastole. The percentage of LV untwisting occurring prior to mitral valve opening is of great interest, because any LV untwisting that occurs after mitral valve opening does not contribute to LV pressure decay and is therefore less efficient.⁸

Table 2 Overall summary table of the effects of exercise on systolic and diastolic LV twisting mechanics

Study	# Subjects (male)	Exercise mode	Mean age (SD)	Systolic parameters			Diastolic parameters		
				Twist	Apical rotation	Basal rotation	TTP Twist	Untwisting rate	TTP untwisting rate
Acute submaximal exercise									
Notomi et al ⁸	n = 20 (12)	Supine cycling	34 (7)	↑	↑	↑	↑	↑	↓
Burns et al ¹⁸	n = 14 (9)	Supine cycling	Young: 40 (NR) Old: 60 (NR)	↑	↑	↑	↑	↑	↑
Esch et al ²⁰	n = 11 (11)	Semi-supine cycling	Young: 35 (8) Old: 60 (12)	↔	↔	↔	↓	↔	↔
Prolonged endurance exercise									
Tan et al ²¹	n = 27 (8)	Semi-supine cycling	70 (7)	↔	↔	↔	↔	↔	↔
Doucende et al ¹⁹	n = 20 (20)	Semi-supine cycling	25 (9)	↑	↑	↑	↔	↔	↔
Stöhr et al ²²	n = 10 (10)	Knee Extensions	21 (2)	↔	↔	↔	↔	↔	↔
Stöhr et al ²⁴	n = 9 (9)	Supine cycling	26 (4)	↑	↑	↑	↑	↑	↓
Stöhr et al ²³	n = 8 (8)	Knee Extensions	20 (2)	↔	↔	↔	↔	↔	↑
Stöhr et al ²⁵	n = 28 (28)	Supine cycling	ET: 21 (3) NA: 21 (2)	↑	↑	↑	↑	↑	↑
Prolonged endurance exercise									
Nottin et al ²⁷	n = 23 (23)	Triathlon	40 (9)	↔	↓	↓	↑	↓	↑
Chan-Dewar et al ²⁶	n = 14 (14)	Marathon	32 (10)	S-epi S-end	↔ ↔	↔ ↔	↔ ↔	↔ ↔	↔ ↔
Oxborough et al ²⁹	n = 17 (17)	Marathon	33 (6)	↔	↔	↔	↔	↓	↔
Hanssen et al ³⁰	n = 28 (28)	Marathon	41 (5)	↑	↔	↔	↔	↔	↔
Nottin et al ²⁸	n = 20 (20)	Upright cycling	25 (5)	↔	↔	↔	↔	↔	↑
Acute maximal exercise									
Tischler and Nigge ³³	n = 25 (14)	Treadmill	35.6 (9)	↑	↔	↔	↔	↔	↔
Neilan et al ³¹	n = 17 (12)	Rowing	37 (NR)	↑	↔	↑	↑	↓	↑
Scott et al ³²	n = 18 (18)	Upright cycling	ET: 29 (6) NA: 35 (7)	↔	↓	↔	↔	↔	↔
Chronic endurance exercise									
Weiner et al ³⁴	n = 15 (15)	Endurance exercise training	18.6 (0.5)	↑	↑	↔	↔	↑	↔

Abbreviations: TTP, time to peak; ET, endurance-trained athletes; NA, normally active untrained individuals; S-epi, sub-epicardium; S-end, sub-endocardium; EET, endurance exercise training; NR, not reported.

Conclusion

There is consistent support from level 4 and level 2^{18,20,24,25,28} evidence that sub-maximal exercise results in enhanced systolic and diastolic LV twisting mechanics in individuals below age 40. The conflicting results present in the two level 4 studies likely arise from the use of low intensity exercise protocols.^{22,23} As eight investigations have examined the effects of sub-maximal exercise on LV twisting mechanics in younger individuals, the results can be interpreted to be relatively conclusive. However, the evidence in older individuals is less clear, and more work is needed examining LV twist during exercise across the human life span. Regardless, future studies should utilize comparable modes of exercise, and they should pay close attention to the clinical health of their participants. However, it is evident that the changes in systolic and diastolic LV twisting mechanics during submaximal exercise are influenced by age, as younger individuals are able to augment their LV function during exercise, while older individuals are not.

Prolonged endurance exercise

The effects of prolonged endurance exercise on resting LV systolic and diastolic twisting mechanics were investigated by five studies (102 total participants; approximate mean ages: 30–40 years). The exercise protocols included three marathon races (involving 42.2 km of running),^{26,29,30} one ultra-long triathlon race (involving 3.8 km of swimming, 186 km of cycling, and 42.2 km of running),²⁷ and one 120-minute continuous cycling protocol.²⁸ All investigations examined the changes in LV twisting mechanics pre- and post-exercise, with one investigation specifically examining the changes in the subendocardial and subepicardial layers of the myocardium.²⁶

Systolic parameters

Prolonged endurance exercise primarily resulted in impaired LV systolic twisting mechanics. This was evident in the form of decreased peak systolic apical and basal rotations,²⁷ increased time to peak apical and basal rotation,²⁷ increased time to peak apical and basal rotation rates,²⁸ a slight decrease in peak LV twist ($P=0.09$),²⁷ delayed time to peak LV twist,²⁶ and a decreased amount of LV twist occurring at the time of aortic valve closure.^{27,28} In contrast, however, one investigation reported augmented systolic twisting mechanics (increases in peak LV twist and twisting rate).³⁰ As preload has been previously demonstrated to influence systolic twisting mechanics,³⁵ this disagreement could be the result of changes in preload before and after exercise. Accordingly, the two investigations that reported impaired systolic twisting mechanics also reported decreases in preload,^{27,29} while

the investigation that reported augmented systolic twisting mechanics reported no change in preload.³⁰ Finally, prolonged endurance exercise was also found to largely exert no effect on systolic twisting mechanics in the subendocardial and subepicardial layers of the myocardium, apart from an increase in peak subendocardial apical rotation rate.²⁶

Diastolic parameters

Prolonged endurance exercise resulted primarily in impaired diastolic twisting mechanics. This was evident through a decrease in peak untwisting rate,^{27–29} an increase in time to peak untwisting rate,^{27–29} a decrease in peak diastolic apical and basal rotation rates,²⁹ and a decrease in the amount of LV untwisting that occurred during isovolumic relaxation (indicating less efficient diastolic filling).²⁹ Interestingly, the diastolic impairments observed after 120 minutes of endurance exercise²⁸ were less severe than those observed after 850 minutes,²⁸ suggesting a potential dose-response relationship between exercise duration and diastolic impairment. In addition, LV twist²⁹ and systolic apical rotation³⁰ were reported to remain elevated during early diastole, indicating a reduction in LV relaxation time and therefore a reduced time for diastolic untwisting and subsequent filling. These findings could also be interpreted as an increased time to peak LV twist, therefore suggesting an impairment in systolic twisting mechanics. Furthermore, Hanssen et al³⁰ reported no evidence of impaired diastolic twisting function yet found a global decrease in diastolic filling. This finding, coupled with the elevated systolic apical rotation during early diastole, suggests that diastolic impairment may not always manifest in altered diastolic twisting mechanics. Finally, prolonged endurance exercise resulted in no changes in the twisting mechanics of the subendocardium and subepicardium.²⁶

Conclusion

Level 4 evidence (indicating available evidence but without comparable groups) exists indicating that prolonged endurance exercise induces impaired systolic and diastolic LV twisting mechanics.^{27–29} Also, conflicting level 4 evidence exists indicating that prolonged endurance exercise results in augmented systolic twisting mechanics and unaltered diastolic twisting mechanics.³⁰ However, this investigation also reported elevated measures of systolic twisting mechanics during diastole, suggesting a form of diastolic impairment consistent with previous reports. Finally, Level 4 evidence demonstrates that prolonged endurance exercise largely exerts no change in either systolic or diastolic twisting mechanics in the subendocardial and subepicardial layers

of the myocardium. As there have only been five studies examining the changes in twisting mechanics after prolonged endurance exercise, the need for further research is clear. However, the relative consistency in the observed results tends to support the observed trends in the data. Of particular interest is the apparent effect of changes in preload on LV systolic twisting mechanics, a finding potentially resulting from excessive fluid loss or exercise-induced hypotension, which can occur during exercise of this duration and intensity.

Acute maximal exercise

Three articles investigated the effects of acute maximal exercise on resting LV twisting mechanics (60 total participants; approximate mean ages: 30–40 years). All investigations measured LV function before and after exercise and each utilized a different exercise intervention, yet all reported achieving a maximal effort from their respective participants.

Systolic parameters

In response to maximal exercise, LV systolic twisting mechanics were found to increase, in the form of increases in peak LV twist,^{31,33} peak basal rotation,³¹ and slightly increased peak apical rotation ($P = 0.07$).³¹ Interestingly, one investigation that examined repeated bouts of maximal intensity exercise showed differing results. After performing 14 1-minute bouts at maximal exercise (separated by 2 minutes of recovery), no change in LV systolic twisting mechanics occurred in their untrained group, while the endurance-trained group experienced decreases in peak apical rotation rate and a delay in the time to peak twist.³² This disagreement is potentially due to the increased duration and intensity of the exercise protocol in comparison with the protocols involving single bouts at maximal intensity, and it draws similarities to the apparent dose-response relationship between twisting mechanics and exercise duration found during prolonged endurance exercise.

Diastolic parameters

Diastolic LV twisting mechanics were only examined in one investigation, which reported evidence of reduced peak untwisting rate and an increased time to peak untwisting rate in endurance-trained individuals but not in untrained participants.³² This investigation also reported a reduced time interval between peak diastolic untwisting and LV filling (measured as peak circumferential strain rate) in endurance-trained individuals. As noted by the authors, peak diastolic untwist and LV filling are distinctly separated under normal resting conditions, as myocardial relaxation occurs before ventricular filling,³⁶ and a reduction in this time interval therefore indicates

impaired diastolic function. Interestingly, additional evidence exists that maximal exercise can also result in an attenuation of more traditional markers of LV diastolic function in endurance-trained participants. Neilan et al³¹ showed that there is a reversal in diastolic filling pattern in these individuals, perhaps suggesting that highly trained athletes are more susceptible to diastolic impairment following maximal exercise.

Conclusion

There is level 4 evidence that acute maximal exercise can result in augmented LV systolic twisting mechanics.^{30,32} Further to this, there is level 2 evidence that this same exercise type, albeit a more intense exercise protocol, can impair both systolic and diastolic twisting mechanics in endurance-trained individuals while exerting no changes in untrained participants.³² As only three studies exist examining the effects of acute maximal exercise on LV twisting mechanics, and as each investigation utilized a different exercise protocol and varying subject populations, more research is necessary that incorporates standardized exercise protocols and consistent population samples. However, despite these inconsistencies, it appears that endurance-trained individuals may experience a reduction in both systolic and diastolic LV twisting mechanics after maximal exercise while untrained individuals do not.

Chronic endurance exercise

One study investigated the effects of chronic endurance exercise on resting LV systolic and diastolic twisting mechanics in elite athletes (15 total participants; mean age: 19 years),³⁴ utilizing 90 days of endurance exercise training (approximately 13.6 hours per week) as their exercise protocol. Measures of LV twisting mechanics were taken at rest before and after the training program.

Systolic parameters

Systolic LV twisting mechanics were found to be augmented following chronic endurance exercise in the form of increases in peak LV twist and peak systolic apical rotation.³⁴

Diastolic parameters

Chronic endurance exercise resulted in enhanced LV diastolic twisting mechanics in the form of increased peak untwisting rate, increased peak diastolic apical rotation rate, and an increase in the percentage of untwisting occurring during isovolumic relaxation.³⁴ This increase in early diastolic untwisting is likely the result of the increased LV systolic twist, which would generate greater elastic potential energy for release during early diastole.

Conclusion

There is level 4 evidence that chronic endurance exercise results in augmented LV systolic and diastolic twisting mechanics.³⁴ Although this is the only study of its kind, previous investigations have examined resting LV systolic and diastolic twisting mechanics in elite athletes and untrained individuals, reporting reduced peak LV twist^{37,38} and both reduced³⁸ and unchanged³⁷ LV diastolic untwisting in elite athletes. This disagreement, recognized by Weiner et al,³⁴ was attributed to differences in study populations and study designs, as Nottin et al³⁷ and Zócalo et al³⁸ examined slightly older individuals and used a cross-sectional study design that could have collected data from the athletes while they were in a period of detraining.

Discussion

Significant contention exists regarding changes in LV twisting mechanics occurring in response to exercise. This debate has resulted in several publications (see References section for examples).^{1,11,12,39,44} The purpose of this review was to systematically summarize the existing published evidence examining the influence of exercise on LV twisting mechanics. Separation of the articles according to exercise type was essential in order to adequately compare investigations, and this yielded mixed results, with no category having complete agreement. However, despite these observed inconsistencies, some intriguing trends were found in the literature.

First, sub-maximal exercise appears to result in augmented LV systolic and diastolic twisting mechanics in only younger individuals (below age 40). Given that exercise produces increases in heart rate and contractility, both previously demonstrated to increase LV twisting mechanics,^{40,41} this finding can be expected. However, the increases in venous return (preload) and systolic blood pressure (often used as an indicator of afterload) that also occur with exercise, and have been demonstrated to influence LV twisting mechanics through opposing mechanisms,^{42,43} could account for some of the observed result variability. With regards to the effects of age on LV twisting mechanics during exercise previous research has demonstrated the influence of age on resting LV twisting mechanics,^{45,46} yet the inability of older individuals to enhance LV twisting mechanics has not been fully explained. One theory attributes this age-related change to a decreased 'twisting reserve' in older individuals due to higher resting LV twist, therefore reducing the capacity of the LV to further twist/untwist during exercise,¹⁸ yet more research is needed to thoroughly investigate this theory.

Second, prolonged endurance exercise appears to impair both LV systolic and diastolic twisting mechanics. LV function during systole and diastole has been well documented to decrease following endurance exercise through traditional measures such as ejection fraction and E/A ratio (the ratio between the early maximal ventricular filling velocity and the late filling velocity),^{12,47} thereby providing support for this observed decrease in twisting mechanics. Interestingly, there also appears to be a dose-response relationship between the duration and intensity of endurance exercise and the level of twisting impairment. Again, this is supported by previous research using traditional measures of LV function that demonstrate that increases in exercise duration and intensity are proportional to the level of cardiac function impairment.⁴⁸ Changes in cardiac loading after endurance exercise were also found to potentially exert an effect on systolic twisting mechanics, supporting the idea that LV twisting mechanics are indeed load-dependent, manifested in these studies as changes in end diastolic volume.

Finally, a general trend found throughout all exercise types is the linkage between the systolic and diastolic components of LV twisting and untwisting. In other words, if systolic twisting was impaired (or improved), it resulted in impaired (or improved) diastolic untwisting. This finding suggests that the systolic-diastolic rotational coupling of the left ventricle, through the production and release of elastic potential energy,⁸ holds true for the various exercise modalities. In fact, systolic-diastolic LV rotational coupling has also been widely reported in various heart diseases.¹ As it appears that systolic function cannot be altered without similar implications on diastolic function, or vice versa, the connectedness between systole and diastole through LV twisting mechanics provides an important avenue for future cardiac research.⁴⁹

Methodological considerations

The presence of conflicting evidence in many of the exercise categories is potentially explained by some important methodological considerations. The methodological quality of the analyzed investigations was low to moderate and the evidence was primarily rated at level 4. Methodological quality could be improved in future studies through the use of control groups (absent in 15 of the 18 studies), and their absence in the current body of literature is difficult to explain – perhaps because of unreported challenges such as an increased amount of time required to analyze echocardiographic images, or difficulty with participant recruitment. In addition, there was significant variability in the exercise protocols and subject characteristics present within each exercise

type. The inconsistent durations and intensities of the exercise protocols across studies of the same exercise type are likely to account for some of the observed conflicting results. As increases in exercise duration and intensity have already been demonstrated to directly relate to changes in cardiac function during endurance exercise,⁴⁸ it is conceivable that variations in the duration and intensity of the exercise protocols used in the other exercise types could exert similar effects. The use of different exercise protocols also creates different conditions of cardiac loading. In the submaximal exercise category, for example, participants exercised in the supine, semi-supine, and upright postural positions – each resulting in differing levels of venous return and therefore preload. Given the aforementioned influence of changes in cardiac loading on LV twisting mechanics, the use of inconsistent exercise protocols is an important methodological consideration. Furthermore, previous research has demonstrated that the LV twisting mechanics of endurance-trained athletes and untrained individuals are affected differently by reductions in preload resulting from an orthostatic challenge.⁵⁰ This finding highlights the importance of not only cardiac loading but also participant training status, as variations in the level of participant fitness between studies may further contribute to the disagreement. Another potential confounding factor and methodological consideration is the use of sample populations consisting of mixed sexes, as females are known to exhibit altered cardiac responses to both acute⁵¹ and prolonged⁵² exercise in comparison with males. Finally, variations in transducer probe position during the collection of apical short-axis echocardiographic images have been demonstrated to significantly alter the calculation of LV apical rotation.⁵³ The use of trained personnel to collect and analyze the data in order to reduce measurement error and result variability is therefore essential.

Conclusion

The measurement of LV twisting mechanics during exercise is becoming increasingly prevalent and has resulted in considerable debate. The study of the rotational properties of the left ventricle provides important insight into cardiac function during exercise that traditional measures of LV function cannot. Despite some important methodological considerations present in the available literature, there are significant trends in each exercise category that should be considered. Most important, the rotational coupling of the left ventricle between systole and diastole holds true in all exercise types, as LV systolic and diastolic twisting mechanics were impaired (or improved) concomitantly. Future research

should include standardized exercise protocols and consistent subject characteristics in order to limit the methodological-induced variability in the observed results.

Disclosure

The authors report no conflicts of interest in this work.

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Table S1 Effects of acute submaximal exercise on systolic and diastolic left ventricular (LV) twisting mechanics

Study, country, study design and level of evidence, quality score	Population	Methods	Outcome	Additional notes	Interpretations
Notomi et al ⁸ United States Pre-post = level 4 D&B score = 11/15	N = 20 (12 males) Mean age: 34 ± 7 yrs Characteristics: healthy volunteers	Ei: submaximal supine bicycle (25 W start with 25 W increases every 2 minutes) MP: before and during exercise (HR = 100 bpm) OMs: LV systolic apical and basal rotation, twist, twisting rate, time to peak twist, diastolic untwisting rate, time to peak untwisting rate MT: Doppler tissue imaging	LV systolic apical and basal rotation, twist, twisting rate and diastolic untwisting rate increased; time to peak untwisting rate decreased	No change in percentage of LV untwisting occurring prior to mitral valve opening	Submaximal exercise enhances LV systolic and diastolic twisting function
Burns et al ¹⁸ Australia Pre-post = level 4 D&B score = 11/15	N = 14 (9 males) Mean age: old, 60 yrs; young, 40 yrs Characteristics: patients undergoing clinically indicated stress tests	Ei: submaximal supine bicycle (50 W start with 25 W increases every 3 minutes) MP: before and at peak exercise OMs: LV twisting, twisting rate, diastolic untwisting rate MT: 2D echocardiogram with STA	Old: no change in LV twist, diastolic untwisting rate, or time to peak untwisting rate Young: LV twist and diastolic untwisting rate increased; time to peak twist decreased	Older population on various cardiac medications to treat hypertension and lipid problems	Submaximal exercise enhances twisting function in younger populations and impairs systolic and diastolic twisting function in older populations
Esch et al ²⁰ Canada Prospective controlled trial = level 2 D&B score = 10/15	N = 11 (all males, 6 old and 5 young) Mean age: old, 60 ± 9 yrs; young, 35 ± 8 yrs Characteristics: old = $VO_{2,peak} = 36.3 \pm 10.7$ mL/kg/min; young = $VO_{2,peak} = 51.1 \pm 10.4$ mL/kg/min	Ei: submaximal semi-supine bicycle (20 minutes at 80% ventilatory threshold) MP: before and at peak exercise OMs: LV systolic apical and basal rotation, twist, twisting rate, diastolic untwisting rate MT: 2D echocardiogram with STA	Old: no change in twist and diastolic untwisting rate Young: LV twist and diastolic untwisting rate increased; time to peak twist decreased	Percentage of LV diastolic untwisting occurring prior to mitral valve opening decreased in old group, no change in young group Older population on various cardiac medications to treat hypertension and lipid problems	Submaximal exercise enhances twisting function in younger populations and impairs systolic and diastolic twisting function in older populations
Tan et al ²¹ United Kingdom Pre-post = level 4 D&B score = 12/15	N = 27 (8 males) Mean age: 70 ± 7 yrs Characteristics: no prior medical history and receiving no medications	Ei: symptom limited, fatigue or dyspnea, submaximal semi-recumbent bicycle (to a maximum HR of 100 bpm) MP: before and during submaximal exercise OMs: LV systolic apical rotation, diastolic untwisting rate MT: 2D echocardiogram with STA	LV systolic apical rotation and diastolic untwisting rate increased	No change in percentage of LV untwisting occurring prior to mitral valve opening Population was not on any medications	Submaximal exercise enhances systolic and diastolic twisting function in older populations Disagreement potentially because of sampling of healthier older population

(Continued)

Table S1 (Continued)
Study, country, study design and level of evidence, quality score

Study, country, study design and level of evidence, quality score	Population	Methods	Outcome	Additional notes	Interpretations
Doucende et al ¹⁹ France Pre-post = level 4 D&B score = 11/15	N = 20 (all males) Mean age: 25 ± 9 yrs Characteristics: sedentary males, no reported regular training habits	EI: submaximal semi-supine bicycle (6-minute stages at 20% (W1), 30% (W2), and 40% (W3) VO ₂ max) MP: before exercise and during each stage (W1, W2, W3) OMs: LV systolic apical and basal rotation, apical and basal rotation rate, twist, untwisting rate, time to peak twist, diastolic apical and basal rotation rate, untwisting rate, time to peak untwisting rate MT: 2D echocardiogram with STA	LV systolic apical and basal rotation, apical and basal rotation rate, twist, untwisting rate, diastolic apical and basal rotation rate, and untwisting rate increased with each stage	No change in percentage of LV untwisting occurring prior to mitral valve opening	“-Submaximal exercise does not result in changes to systolic and diastolic twisting function -Weak exercise stimulus potential reason for this finding”
Stöhr et al ²⁰ United Kingdom Pre-post = level 4 D&B score = 10/15	N = 10 (all males) Mean age: 21 ± 2 yrs Characteristics: recreationally active individuals	EI: submaximal unilateral knee extensor exercises (12 minutes at 21 ± 2 W) MP: before and during last 8 minutes of exercise OMs: LV systolic apical and basal rotation, apical and basal rotation rate, twist, untwisting rate, diastolic apical and basal rotation rate, untwisting rate MT: 2D echocardiogram with STA	No change in any LV systolic or diastolic twisting mechanic measurement	Exercise stimulus did not induce increases in stroke volume or ejection fraction	Submaximal exercise does not enhance systolic or diastolic twisting function Disagreement potentially due to weak exercise stimulus
Stöhr et al ²² United Kingdom Pre-post = level 4 D&B score = 9/15	N = 9 (all males) Mean age: 26 ± 4 yrs Characteristics: recreationally active individuals	MT: 2D echocardiogram with STA EI: submaximal supine bicycle (4-minute stages at 10%, 30%, 50%, 70%, and 90% peak power) MP: before and during each stage OMs: LV systolic apical and basal rotation, apical and basal rotation rate, twist, untwisting rate, time to peak twist, diastolic apical and basal rotation rate, untwisting rate MT: 2D echocardiogram with STA	LV systolic apical and basal rotation, apical and basal rotation rate, twist, untwisting rate, diastolic apical and basal rotation rate, and untwisting rate increased LV twist, untwisting rate, and untwisting rate plateaued at ~50% peak power Time to peak diastolic apical rotation rate and untwisting rate decreased Time to peak diastolic basal rotation rate increased	Stroke volume and end-diastolic volume plateaued at ~30% and ~50% peak power, respectively	The enhancement of systolic and diastolic twisting function during exercise plateaus at submaximal intensities

Stöhr et al ²³ United Kingdom Pre-post = level 4 D&B score = 10/15	N = 8 (all males) Mean age: 20 ± 2 yrs Characteristics: active individuals	EI: submaximal unilateral knee extensor exercises (15 minute at 23 ± 2 W) MP: before and during last 10 minutes of exercise OMs: LV systolic apical and basal rotation, apical and basal rotation rate, twist, twisting rate, diastolic apical and basal rotation rate, untwisting rate, time to peak untwisting rate MT: 2D echocardiogram with STA	No change in any LV systolic or diastolic twisting mechanic measurement Time to peak untwisting rate increased	Exercise stimulus did not induce an increase in stroke volume	Submaximal exercise does not result in changes to systolic and diastolic twisting function Weak exercise stimulus potential reason for this finding
Stöhr et al ²⁵ United Kingdom Pre-post = level 4 D&B score = 11/15	N = 28 (all males, 14 ET and 14 NA) Mean age: ET, 21 ± 3 yrs; NA, 21 ± 2 yrs Characteristics: groups divided post hoc ET = VO ₂ peak = 63 ± 7 mL/kg/min; NA = VO ₂ peak = 49 ± 5 mL/kg/min	EI: submaximal supine bicycle (5 minutes at 40% peak power) MP: before and during last 3 minutes of exercise OMs: LV systolic apical and basal rotation, apical and basal rotation rate, twist, twisting rate, diastolic apical and basal rotation rate, untwisting rate MT: 2D echocardiogram with STA	LV systolic apical and basal rotation, apical and basal rotation rate, twist, twisting rate, diastolic apical and basal rotation rate, and untwisting rate increased in both ET and NA subjects LV systolic apical rotation was lower at rest and during exercise in ET subjects than in NA subjects	Slightly lower LV twist at rest and during exercise in ET than NA subjects ($P = 0.09$) No between-group differences in LV structure, HR, or stroke volume	ET individuals have reduced twisting function during submaximal exercise compared with NA individuals despite similar hemodynamics

Abbreviations: 2D, two-dimensional; D&B score, Downs and Black¹³ score; EI, exercise intervention; ET, endurance-trained individuals; HR, heart rate; MP, measurement period; MT, measurement technique; NA, normally active individuals; OM, outcome measure; STA, speckle tracking analysis; yrs, years; VO₂, oxygen consumption; VO₂max, maximal aerobic power.

Table S2 Effects of prolonged endurance exercise on left ventricular (LV) systolic and diastolic twisting mechanics

Study, country, study design and level of evidence, quality score	Population	Methods	Outcome	Additional notes	Interpretation
Nottin et al ²⁷ France Pre-post = level 4 D&B score = 11/15	N = 23 (all males) Mean age: 40 ± 9 yrs Characteristics: trained individuals (mean training, 12 ± 3 hours/week for 12 ± 6 yrs)	EI: ultra-long triathlon (3.8 km swim, 186 km cycle, 42.2 km run) MD: 858 minutes MP: before and 40 ± 15 minutes after race completion OMs: LV systolic apical and basal rotation, apical and basal rotation rate, twist, time to peak twist, time to peak systolic apical and basal rotation, diastolic apical and basal rotation rate, untwisting rate, time to peak untwisting rate MT: 2D echocardiogram with STA EI: marathon (42.2 km) MD: 229 ± 38 minutes MP: before and within 60 minutes after race completion OMs: LV systolic apical and basal rotation, apical and basal rotation rate, twist, diastolic apical and basal rotation rate in subendocardium and subepicardium MT: 2D echocardiogram with STA	LV systolic apical and basal rotation, and diastolic untwisting rate decreased Time to peak twist, times to peak systolic apical and basal rotation, and time to peak untwisting rate increased	LV twist increased but not significantly ($P = 0.09$) Twist at aortic valve closure decreased Loss of rapid LV untwisting during isovolumic relaxation time	Ultra-long triathlon induces impaired systolic and diastolic twisting function
Han-Dewar et al ²⁶ United Kingdom Pre-post = level 4 D&B score = 11/15	N = 14 (all males) Mean age: 32 ± 10 yrs Characteristics: nonelite runners (range of personal best marathon times: 157–268 minutes; range of training mileage in month prior to race: 10–60 miles)	MT: 2D echocardiogram with STA EI: marathon (42.2 km) MD: 229 ± 38 minutes MP: before and within 60 minutes after race completion OMs: LV systolic apical and basal rotation, apical and basal rotation rate, twist, diastolic apical and basal rotation rate in subendocardium and subepicardium MT: 2D echocardiogram with STA	Systolic apical rotation rate in the subendocardium increased	Irregular trends in remaining indexes of twisting function	Marathon running induces sporadic changes in twisting function in the subendocardium and subepicardium
Oxborough et al ²⁹ United Kingdom Pre-post = level 4 D&B score = 10/15	N = 17 (all males) Mean age: 33 ± 6 yrs Characteristics: recreational runners	EI: marathon (42.2 km) MD: 209 ± 19 minutes MP: before, within 60 minutes, and after 6 hours of race completion OMs: LV systolic apical and basal rotation, twist, diastolic apical and basal untwisting rate, untwisting rate MT: 2D echocardiogram with STA EI: marathon (42.2 km) MD: 245 ± 55 minutes MP: before, within 1 hour of race completion and 1 day after race completion OMs: LV systolic apical and basal rotation, twist, diastolic apical and basal rotation rate, twist, diastolic apical and basal rotation rate MT: cardiac MRI	LV diastolic apical and basal rotation rate and untwisting rate decreased	LV twist decreased slightly but not significantly Twist at aortic valve closure decreased Twist remained elevated during early diastole LV systolic apical rotation remained elevated during early diastole	Marathon running impairs diastolic twisting function and induces slight depressions in systolic function
Hanssen et al ³⁰ Germany Pre-post = level 4 D&B score = 11/15	N = 28 (all males) Mean age: 41 ± 5 yrs Characteristics: amateur marathon runners (completed ≥ 1 marathon; mean training mileage 10 weeks prior to race: 43 ± 17 km/week)	EI: marathon (42.2 km) MD: 245 ± 55 minutes MP: before, within 1 hour of race completion and 1 day after race completion OMs: LV systolic apical and basal rotation, twist, diastolic apical and basal rotation rate, twist, diastolic apical and basal rotation rate MT: cardiac MRI	LV twist and twisting rate increased	LV systolic apical rotation remained elevated during early diastole	Marathon running enhances systolic twisting function but impairs diastolic twisting function

Nortin et al ²⁸ France Pre-post = level 4 D&B Score = 9/15	N = 20 (all males) Mean age: 25 ± 5 yrs Characteristics: healthy	Ei: continuous cycling (cadence: 70–80 rpm; HR > 150 bpm) MD: 120 minutes MP: before, within 30–45 minutes after protocol completion OMs: LV systolic apical and basal rotation, apical and basal rotation rate, twist, twisting rate, diastolic apical and basal rotation rate, untwisting rate MT: 2D echocardiogram with STA	Time to peak systolic apical rotation rate and time to peak diastolic untwisting rate increased	Reduction in rapid LV untwisting during early diastole	Prolonged cycling impairs diastolic twisting function and slightly reduces systolic twisting function
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Abbreviations: 2D, two-dimensional; D&B score, Downs and Black¹³ score; Ei, exercise intervention; HR, heart rate; MD, mean exercise duration; MP, measurement period; MRI, magnetic resonance imaging; MT, measurement technique; OM, outcome measure; STA, speckle tracking analysis; yrs, years.

Table S3 Effects of acute maximal exercise on systolic and diastolic left ventricular (LV) twisting mechanics

Study, country, study design and level of evidence, quality score	Population	Methods	Outcome	Additional notes	Interpretation
Tischler and Niggel ³³ United States Pre-post = level 4 D&B score = 11/15	N = 25 (14 males) Mean age: 35.6 yrs Characteristics: 15 healthy volunteers, 10 referred for stress echocardiography	EI: maximal exercise test – bruce protocol MD: 14 ± 4 minutes MP: before and immediately after exercise OM: LV twist MT: 2D echocardiogram with image angle calculations	LV twist increased	LV end-systolic volume decreased, ejection fraction increased	Maximal exercise augments LV systolic function
Neilan et al ³¹ United States Pre-post = level 4 D&B score = 11/15	N = 17 (12 males) Mean age: 37 yrs Characteristics: elite rowers	EI: 2000 m rowing sprint to exhaustion on ergometer MD: males: 6.6 ± 0.45 minutes; females: 7.2 ± 0.15 minutes MP: before and within 5–10 minutes after exercise OMs: LV systolic apical and basal rotation, LV twist MT: 2D echocardiogram with STA	LV basal rotation and twist increased	LV apical rotation increased but not significantly ($P = 0.07$) Evidence of reversed diastolic filling (reduced early passive filling and increased late active filling)	Maximal exercise augments LV systolic function but may impair LV diastolic function
Scott et al ³² Canada Prospective controlled trial = level 2 D&B score = 10/15	N = 18 (all males, 9 ET and 9 NA) Mean age: ET, 29 ± 6 yrs; NA, 35 ± 7 yrs Characteristics: ET = $VO_{2max} > 50$ mL/kg/min, regular training; NA = $VO_{2max} < 50$ mL/kg/min, no regular training	EI: 15 1-minute workloads at 100% VO_{2max} power output, separated by 2-minute recoveries at 20% VO_{2max} power output on a cycle ergometer MD: approximately 45 minutes MP: before, 6.2 ± 2.6 minutes after, and 38.4 ± 3.8 minutes after exercise OMs: LV systolic apical and basal rotation rates, twist, time to peak twist, diastolic untwisting rate, time to peak untwisting rate MT: cardiac MRI	ET: LV systolic apical rotation rate and diastolic untwisting rate decreased; time to peak twist and time to peak untwisting rate increased NA: no change in twisting mechanics	ET: evidence of impaired diastolic function (reduced time period between diastolic untwisting and LV filling – in normal hearts there is distinct separation)	Maximal exercise impairs LV systolic and diastolic function in ET but not NA individuals

Abbreviations: 2D, two-dimensional; D&B score, Downs and Black³³ score; EI, exercise intervention; ET, endurance-trained individuals; MD, mean exercise duration; MP, measurement period; MRI, magnetic resonance imaging; MT, measurement technique; NA, normally active individuals; OM, outcome measure; STA, speckle tracking analysis; VO_{2max} , oxygen consumption; VO_{2max} , maximum volume of oxygen utilized; yrs, years.

Table S4 Effects of chronic endurance exercise on left ventricular (LV) systolic and diastolic twisting mechanics

Study, country, study design and level of evidence, quality score	Population	Methods	Outcome	Additional notes	Interpretation
Weiner et al ³⁴ United States Pre-post = level 4 D&B score = 12/15	N = 15 (all males) Mean age: 18.6 ± 0.5 yrs Characteristics: first-year university student members of the competitive rowing program	EI: 90 days of EET MD: 13.6 ± 0.9 hours/week of organized, primarily endurance-oriented training (12.6 ± 0.7 versus 1.0 ± 0.9 hours/week EET and strength training, respectively) MP: before and after 90 days of EET OMs: LV systolic apical and basal rotation, twist, time to peak twist, diastolic apical and basal rotation rate, untwisting rate MT: 2D echocardiogram with STA	LV systolic apical rotation, twist, diastolic apical rotation rate, and untwisting rate increased	Percentage of LV untwisting that occurred during isovolumic relaxation time increased	EET results in improved systolic and diastolic twisting function

Abbreviations: 2D, two-dimensional; D&B score, Downs and Black¹³ score; EET, endurance exercise training; EI, exercise intervention; MD, mean exercise duration; MP, measurement period; MT, measurement technique; OM, outcome measure; STA, speckle tracking analysis; yrs, years.

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