Cardiac Response to Exercise in Normal Ageing: What Can We Learn from Masters Athletes?

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Abstract: ***Background*****:** Ageing is associated with an inexorable decline in cardiac and vascular function, resulting in an increased risk of Cardiovascular Disease (CVD). Lifestyle factors such as exercise have emerged as a primary therapeutic target in the prevention of CVD, yet older individuals are frequently reported as being the least active, with few meeting the recommended physical activity guidelines. In contrast, well trained older individuals (Masters athletes) have superior functional capacity than their sedentary peers and are often comparable with young non-athletes. Therefore, the 'masters' athlete may be viewed as a unique non-pharmacological model which may allow researchers to disentangle the inexorable from the preventable and the magnitude of the unavoidable 'true' reduction in cardiac function due to ageing.

Conclusion**:** This review examines evidence from studies which have compared cardiac structure and function in well trained older athletes, with age-matched controls but otherwise healthy.

Keywords: Systolic function, diastolic function, cardiac remodelling, healthy ageing, athletes, cardiac response.

1. INTRODUCTION

Improvements in long-term survival have increased the number of older, and elderly individuals worldwide. Indeed, the World Health Organisation estimates that the number of those aged over 60 years of age has doubled since 1980, and will triple by 2050 [1]. Consequently, health span is emerging as a critical public health challenge of our generation. Despite significant improvements in the treatment of Cardiovascular Disease (CVD), it remains the main cause of mortality worldwide [2] and accounts for almost one-third of globally mortality [3]. Moreover, for those who survive with CVD, there are substantial costs financially [4] and in reduced quality of life and reduced functional capacity [5]. While advances in healthcare and survival are welcome, the continued burden of cardiovascular morbidity is substantial. In the UK alone, there are an estimated 7 million people coping with ongoing CVD, requiring more than £9 billion in health care costs [6].

Modifiable lifestyle factors such as exercise and Physical Activity (PA) have emerged as primary therapeutic targets in the prevention of CVD, with extensive epidemiological, pre-clinical, and human interventional studies to support its efficacy [7]. Multiple lines of evidence indicate that those individuals who are most active enjoy superior cardiac function, as well as lower levels of systemic inflammation and oxidative stress [8-11]. Correspondingly, this has resulted in a wealth of health promotion recommendations promoting PA for both children and adults [12, 13]. Despite these such recommendations, older individuals are frequently reported as being the least active, with 1 in four adults failing to meet the weekly PA guidelines for health worldwide, of at least 150 minutes of moderate or 75 minutes of vigorous intensity exercise [14], rising to 85 to 90% of older adults in many developed countries [15].

In contrast, investigations of ageing athletes frequently report that relative to their sedentary counterparts, they exhibit high levels of cardiovascular reserve (*i.e.* Stroke Volume (SV) and a maximal cardiac output; [16]) while simultaneously presenting with minimal risk

factors for CVD [11]. In studies of cardiovascular function, endurance trained masters athletes have superior functional capacity, cardiovascular reserve, than their sedentary peers, which are comparable with much younger non-athletes [17, 18]. In this respect, the 'masters athlete' may be viewed as a unique non-pharmacological model which may allow researchers to disentangle the inexorable from the preventable effects of ageing on cardiac and vascular health. A 'masters' or 'veteran' athlete has been defined as an individual older than 45 or 50 years of age competing regularly in endurance events [19, 20]. A meta-analysis has been performed on structural and functional cardiac adaptation in younger athletes up to 45 years of age [21], therefore, the present review set out to summarise the available literature regarding the effect of exercise on cardiac health in normal ageing, and with specific reference to comparisons between sedentary individuals and masters athletes ≥ 45 years of age.

2. CARDIAC STRUCTURE AND FUNCTION IN RELATION TO EXERCISE AND AGEING

2.1. LV Diastolic Function

2.1.1. The Impact of Healthy Ageing on Diastolic Function

Diastolic function may be divided into 2 components, compliance and relaxation [22]. Myocardial relaxation concerns myocyte calcium handling, whereas ventricular compliance is determined by the interaction of compliant cardiac muscle and less compliant (stiff) connective tissue and extracellular matrix [22]. The inevitability of chronological sedentary yet, healthy ageing seemingly leads to a gradual decline in LV compliance until approximately 64 years of age, at which point LV stiffening may be deemed complete [23]. Similarly, with progressive age, early diastolic function determined by Doppler indices of LV diastolic function show reduced early (E) inflow velocity, ratio of early-to-late inflow velocity (E/A) [24], early

diastolic tissue velocity (e'), and gradual increases in the Isovolumic Relaxation Time (IVRT) and time constant of isovolumic pressure decay (Tau) [25]. Collectively, these functional changes highlight a worsening of LV diastolic function inherent to the ageing process.

2.1.2. Healthy Ageing and Diastolic Function in Relation to Exercise

Chronic endurance exercise consisting of multiple years of continued training preserves LV compliance [26], which may be 'dose' dependant [27]. In healthy seniors aged >64 years, Bhella *et al.* [27] found an exercise dose of at least 4 to 5 sessions per week, categorised as 'committed exercisers', was sufficient to prevent the age-associated increases in LV stiffness and decreases in distensibility and compliance. Nonetheless, 1 year of aerobic exercise training in previously sedentary, older (71 ± 3 years) individuals did not alter LV compliance or stiffness and therefore, it is possible that exercise initiation prior to reaching 'older' age is necessary to circumvent the detrimental impact of ageing [28]. To advance this theory, mitral inflow and tissue velocity indices were not different between sedentary older men (59 ± 3 years) and exercisers who either began exercising prior to 30 years of age or after 40 years of age, however, LV end-systolic elastance (E_{LV}) was lower in both trained groups compared with their untrained counterparts, suggesting a less stiff ventricle in the trained groups [29].

Long term exercise does not prevent the gradual decline in resting global diastolic function associated with ageing, as measured by conventional Doppler mitral inflow or tissue velocities [30-38]. Nevertheless, when compared with controls of the same age, older (>45 years) endurance-trained athletes have shown superior diastolic function with greater E [19, 37-39], e' [19, 22, 36, 40], lower late mitral inflow velocity (A) [34-36, 40-44], lower late mitral annular tissue velocity (a') [35, 45] and collectively, greater e'/a' [19, 35, 40] and E/A (Table **1**). Equally, in older recreationally active, leisure time athletes, of which sporting discipline was unknown, E/A was greater in trained than untrained [46, 47]. Indeed, the heart

rate and preload dependence of mitral and tissue velocities are known [48, 49]; bradycardia lengthens the diastolic period and reduces the atrial contribution to filling [35, 50]. Therefore, it is possible that superior diastolic function in older athletes may be mediated, in part, by a lower heart rate and/or (to a lesser extent) higher plasma volume. In contrast, a body of evidence disputes a beneficial influence of endurance based exercise on e' [29, 35, 38, 41, 45] or global diastolic function, expressed as E/A (Table **1**) or e'/a' [31, 37, 45], between age-matched athletes and controls. Thus, it is unclear at present whether exercise is a useful mitigant of the inevitable age-related decline in global diastolic function when determined by the profiling of mitral inflow and tissue velocities. Differences in the participant characteristics and training habits between cross-sectional investigations may well contribute to the conflicting findings.

Soccer specific training of 3 hours per week for 12 months in previously sedentary seniors (68 years of age) sufficiently increased E/A and e' by 25% and 12%, respectively, which was not observed during the equivalent strength-based intervention [51]. Similarly, short-term training (12 weeks) elicited an increased [52], or demonstrated a trend toward greater [36] E/A in older adults (>62 years) following High Intensity Interval Training (HIIT); whereas, others found no changes in E/A after 8 weeks HIIT [53]. Nonetheless, 5 days of intensified training in seniors (68 years of age) increased E/A, with the change in E/A significantly related to changes in maximal oxygen uptake ($r=0.52$, $p<0.05$) [54]. Beyond mitral inflow velocities, studies have found that following short term interval training in previously sedentary individuals e' did not change [52, 53], or increased to similar levels as master athletes [36]. Further, after 1 year of vigorous exercise baseline e' decreased, with the suggestion that the effect of exercise training on e' is different between master athletes with a life-long history of exercise training and seniors undergoing short term interventions [28]. It must be noted however, that the masters athletes were slightly younger than sedentary seniors

during the cross-sectional comparison and thus, an influence of age on the greater e' in athletes cannot be ruled out. Nonetheless, taking these findings together, despite some unavoidable decline in diastolic function inherent to progressive ageing and irrespective of the mechanistic underpinning of whether changes reflect altered loading conditions, heart rate or intrinsic functional modifications, these data provide some support for improved diastolic function concomitant with exercise training and/or compared with age-matched sedentary counterparts.

The unidimensional motion of tissue velocities does not provide a full description of the LV movements during diastole [38], the assessment of LV rotational mechanics, namely untwisting, can provide further insight into the intrinsic function of the heart at various stages of the cardiac cycle. Recently, studies of middle-aged (~54-57 years) male athletes [35, 55] reported no training effect on E or e' at rest but did identify a significantly greater percentage of untwisting during IVRT. This observation is of particular importance considering the percentage of untwist during early diastole declines with age [56], and may, therefore, suggest a preservation of early diastolic function into old age in aerobically trained individuals. Peak untwisting velocity, however, is contrasting between studies, with some observing greater in athletes than controls [55] and others finding comparable between trained and untrained groups [34, 35]. Carrick-Ranson *et al.* [31] found the larger SV during exercise in older trained men was not the result of faster LV mitral inflow or tissue velocities.

During submaximal exercise, greater E and peak untwisting velocity have been observed in senior trained men than controls [55]. In contrast, Lee *et al.* [34] reported no change in untwisting velocity from rest to exercise in middle-aged trained men, yet an increase in their age-matched untrained counterparts. Still, the trained group achieved peak untwisting velocity earlier than middle-aged untrained. However, because the peak base-to-apex intraventricular pressure gradient is linearly related to peak untwisting velocity [57], superior untwisting mechanics during exercise would likely facilitate greater LV suction within early diastole and

thereby, support LV filling. Yet, given the heterogeneity between studies to data, future studies reporting Speckle Tracking Echocardiographic (STE) derived untwist mechanics, including peak velocities and temporal analysis, will provide a depth of understanding complimentary to conventionally derived Doppler velocities.

2.2. LV Structure

Normal ageing is associated with an increase in the LV wall thickness, likely manifested by cellular ageing and a gradual loss of cardiomyocytes initiating compensatory increase in cardiomyocyte size (LV hypertrophy) [57]. While several cross-sectional studies have documented larger absolute wall thickness in athletes compared with untrained controls, this is not consistent (Table **1**). Baldi *et al.* [30] reported that LV interventricular septal (IVS) and posterior wall thicknesses were 20-22% greater in older athletes than age-matched controls (65 years), whereas a 5% smaller IVS was noted in the young trained compared with untrained. These data may suggest that athletes of the older population exhibit greater adaptations than younger individuals (26 years). Furthermore, prolonged dynamic exercises principally impose a volume overload challenge upon the LV and as a result, older endurance trained athletes have shown larger LV chamber diameters compared to their untrained counterparts (Table **1**). Notably, this is not consistent across available literature. (Table **1**). One explanation for the contrasting findings is a reduction in training stimulus (intensity, duration, volume) which occurs with progressive ageing and could therefore contribute [59]. Moreover, despite the recent suggested that trained-untrained differences in LV hypertrophy (LV mass) diminish or even disappear with advancing age in those beyond 45 years of age [60], the majority of studies have reported significantly larger LV Mass (LVM) in trained individuals, expressed as absolute or allometrically scaled to indices of body size (Table **1**). However, there are inconsistencies in the allometric scaling of LVM between studies. While most have used body surface area,

some have indexed to fat free mass or height$^{2.7}$; this may be important and account for some heterogeneity in the differences between athletes and controls. Further, the influence of chronological age on the magnitude of difference in LV mass between athletes and controls requires further clarification.

Studies of continuous aerobic exercise training in previously sedentary, older males or females [53, 61-67] have largely found unchanged LV morphology from pre-to-post training interventions ranging from 2-9 months. In contrast, three studies in older populations (all 68 years of age) found a statistically significant increase in LVM index of 5-18% following 4-12 months of dynamic exercise training [28, 51, 68] suggestive of an eccentric remodelling [28, 51]. The lack of adaptations in the majority of studies are unlikely to be accounted for by an insufficient exercise intensity since specific HIIT programmes also observed unchanged morphology [53]. Similarly, in a recent study of lifelong sedentary males (63 ± 5 years), Grace *et al.* [52] reported no changes in LV morphology following six weeks of supervised pre-conditioning exercise, which preceded a further 6 weeks of low-frequency HIIT. The training programme duration would likely elicit some influence on the magnitude of adaptation, however, since structural increases were observed after 4 months of football training (small sided games) in elderly men 65-75 years of age [51], suggests adaptations can occur within short periods of HIIT and thus, the programme duration may not be the sole determinant. Greater exercise stimulus including intensity, session duration and frequency, training programme duration, participant age upon recruitment or an interaction of these factors may be necessary to induce modifications within the LV structure. Additionally, and in consideration of the strong evidence from cross-sectional studies of greater LV mass in older trained than untrained adults, with many years of exercise training, suggesting that adaptation may occur earlier in life and is then maintained into older age with continued aerobic exercise training relative to age-matched controls.

2.3. LV Systolic Function

LV systolic function is most commonly presented as Ejection Fraction (EF) which is preserved at rest with healthy ageing [24, 69]. The majority of cross-sectional data report similar EF (Table **1**) or fractional shortening (FS) [30,70-72] between older trained and untrained adults. With advancing age, however, EF at maximal exercise is lower while LV End-Diastolic Volume (LVEDV) increases and this counterbalancing results in a lack of overall net change in SV index [24]. Bouvier *et al.* [70] reported that EF was similar between master athletes and controls at rest, yet reported a significant training effect of greater EF at maximal exercise in the trained group. EF improved following 8-12 weeks of interval training in older adults [36, 53], which has not been observed following continuous exercise training [53, 73]. Indeed, the change in EF from pre-to-post exercise intervention was linearly related to the change in maximal oxygen uptake ($\dot{V}O_{2max}$) [53]. Similarly, Fujimoto *et al.* [28] reported 1-year vigorous exercise training improved $\dot{V}O_{2max}$ via favourable changes in maximal cardiac performance, without alterations in arterial-venous oxygen difference. However, another HIIT training study in older adults, of shorter duration and less frequency, reported no changes in EF [52], which may suggest that in addition to intensity, total exercise volume is important.

Alternate measures of LV systolic function include the mitral annular systolic tissue velocity (s') [74], albeit the literature is undecided as to whether this declines which may [30, 35, 36, 38] or not [31, 37] during chronological ageing. The majority of studies have shown homogenous s' between trained and untrained adults [29, 31, 35, 36, 40, 41, 45]. In addition to tissue velocities, newer methods of assessing LV systolic function have been developed, such as STE, with the advantage of being relatively angle independent and not subjected to the tethering effect [75, 76]. Global Longitudinal Strain (GLS) denotes shortening/deformation about its entire long-axis and when averaged across all LV wall segments is used as a measure of global systolic function [77, 78]. Compared with EF, GLS provides a greater means of

directly assessing contractility and is a more sensitive marker of systolic (dys)function [78]. Unlike EF, GLS decreases across the lifespan in healthy participants [68, 79]. Although Schmidt *et al.* [41] found 12% greater (negative) GLS in veteran football players (68 years) compared with age-matched controls, the general consensus from other observational studies is a lack of training effect on GLS in ageing athletes [29, 32, 45, 80]. Participant recruitment might offer an explanation to the unique findings of increased GLS by Schmidt *et al.* [41], where in the veteran footballers (68 years) were still regularly competing throughout the year (26 ± 12 soccer matches) and when compared with participants in the other studies, they were of the oldest age and had the longest training history (52 ± 11 years). Exercise stimulus may also be important. A training study from the same group found that following 12 months of football-specific training in previously lifelong sedentary senior (68 years) males, EF increased and GLS increased (more negative) by 8% [51]. Moreover, recently Howden *et al.* [81] reported a lifelong (at least 25 years) exercise training dose of at least 4 sessions per week in seniors (>60 years) prevented the age-related decline in GLS. Following adjustment for LVEDV however, the training effect was abrogated which, as noted by the authors, highlights the importance of training related changes in LV filling volume in preserving systolic function with ageing. In particular, at similar EDV, GLS was significantly lower in the trained than untrained adults [81]. Taken together, exercise training may improve systolic function. Yet more longitudinal studies are required with GLS as an adjunct to conventional measures as it might offer a more sensitive determinant of interactions between exercise and ageing.

Beyond longitudinal shortening during contraction, the LV also rotates along its long-axis [77]. Systolic twist determined by the opposing rotations at the base and apex in clockwise and counterclockwise directions, respectively [77], increases stepwise with age in a general population of healthy individuals [55]. Maufrais *et al.* [35] documented a lower magnitude of resting twist in senior athletes compared with controls, suggesting a preservation of the age-

related increase in twist, while two studies observed no training effect [34, 54]. With the transition from rest to exercise, Lee *et al.* [34] found middle-aged aerobic athletes were able to increase twist compared with controls, whereas Maufrais *et al.* [54] observed no differences between training levels during submaximal cycling. In younger individuals, LV twist increases with submaximal exercise [82, 83], which is closely coupled with exercise SV [84]. The ability to increase LV twist in older athletes in response to a physiological exercise stress would suggest a greater functional capacity to accommodate the heightened cardiovascular demands by modulating LV output. Nonetheless, further assessment of twisting mechanics in older athletes both at rest and during exercise will provide additional, insightful information to advance our understanding of systolic functioning following long-term exercise training in masters athletes.

CONCLUSION

There is growing evidence that undertaking regular exercise training results in improved indices of diastolic performance. In addition, lifelong exercisers exhibit moderate remodelling to support greater SV and cardiac output. However, differences in systolic function are less clear, therefore, much of this comparative data has been acquired at rest, and it is possible that larger differences may be evident during exercise, as the greater functional reserve of masters athletes becomes apparent. There is a need for more observational studies, to include exercise measures, as well as wider use of novel imaging technologies within this cohort.

The non-pharmacological model of the 'master athlete' enables researchers to extract the inexorable from the preventable effects of ageing on cardiac structure and function. The superior findings in those who have sustained exercise training into old age, suggest that the waning assumed to occur with age are less precipitous than previously suspected, and that while some functional impairment seems inevitable, partaking in regular exercise may result

in a significant slowing in the rate of decline. However, there is a need for more research to help elucidate the mechanisms of true age-related decline and the mechanisms of decline due to sedentariness and that which can be mitigated by physical exercise. In addition, more data are needed to determine the most effective prescription to improve cardiac function.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Table 1. Summary of studies including echocardiographic derived left ventricular structure, systolic and diastolic function in athletes and controls.

Study (Year of Publication)	Participant Characteristics		Echocardiographic Measures						
	Sport (Gender- M/F)	Age (Years)	Wall Thickness			LVEDD	LVM	E/A	EF
			IVS	PWT	MWT				
Baldi *et al*. [30]	Controls (M) Aerobic (M)	65.7 ± 3.7 65.2 ± 4.2	↔	↔		↑	↑ ↑ *	↔	
Bhella *et al*. [27]	Controls (M+F) Endurance (M+F)	68.8 ± 5.1 67.8 ± 2.9						↔	
Bohm *et al*. [45]	Controls (M) Runners, rowers, triathletes (M)	46.0 ± 9.0 47.0 ± 8.0	↑	↑		↑			
Bouvier *et al*. [70]	Controls (-) Orienteers, runners (M)	74.9 ± 2.4 72.8 ± 2.9	↔	↑		↔	↔ *	↑	
Carrick-Ranson *et al*. [31]	Controls Cyclists, runners, dual/triathletes (M)	66.0 ± 5.0 66.0 ± 4.0				↔	↑ ↑ *	↑	
Child *et al*. [71]	Controls (M) Runners (M)	56.3 ± 7.8 53.7 ± 10.6	↑ *	↑ *		↑ *	↑ *		
Cottini *et al*. [39]	Controls (-) Aerobic (-)	61.0 ± 7.0 60.0 ± 10.0	↔	↔		↔		↑	↑
D'Andrea *et al*. [19]	Controls (M) Swimmers (M)	47.4 ± 2.2 48.2 ± 3.4	↔	↔		↑	↑ *	↑	
Di Bello *et al*. [72]	Controls (M) Runners (M)	69.7 ± 8.4 65.7 ± 7.1	↑	↑		↔ ↔ *	↑ ↑ *	↑	↔
Donal *et al*. [32]	Controls (M) Cyclists (M)	58.9 ± 8.6 61.5 ± 5.6	↑	↑		↔	↑ *	↔	↔
Douglas and O'Toole. [43]	Controls (M+F) Ultra-endurance (M+F)	65.0 ± 6.0 58.0 ± 6.0		↔ ↔		↑ ↑ *	↔ ↔ *	↑	
Fleg *et al*. [42]	Controls (M) Runners (M)	63.0 ± 6.0 65.0 ± 8.0	↔ *	↔ *		↔ *	↔ *	↔	
Galetta *et al*. [85]	Controls (M) Runners (M)	66.9 ± 4.6 67.6 ± 4.5	↑	↑		↑	↑ ↑ *	↔	↔
Galetta *et al*. [40]	Controls (M) Runners (M)	68.3 ± 3.2 69.4 ± 3.8	↑	↑		↑	↑ ↑ *	↑	↔
Gates *et al*. [33]	Controls (M) Aerobic (M)	65.0 ± 6.6 68.0 ± 6.9			↑ *	↑ *	↑ *	↑	
Giada *et al*. [86]	Controls (M) Cyclists (M)	58.0 ± 6.0 55.0 ± 5.0	↑ *	↑ *		↑ *	↑ *	↔	↔
Grace *et al*. [52]	Controls (M) Endurance (M)	62.7 ± 5.2 61.1 ± 5.4	↔	↔		↔	↔ ↔ *	↔	↔
Jungblut *et al*. [87]	Controls (M) Runners (M)	69.0 ± 3.0 69.0 ± 5.0	↔	↔		↑	↑ *	↔	

Study (Year of Publication)	Participant Characteristics		Echocardiographic Measures						
	Sport (Gender- M/F)	Age (Years)	Wall Thickness			LVEDD	LVM	E/A	EF
			IVS	PWT	MWT				
Kozakova *et al*. [88]	Controls (M) Marathoners, triathletes (M)	46.5 ± 16.0 53.1 ± 20.0	↑	↑		↔	↑ ↑ *		
Lee *et al*. [34]	Controls (M) Cyclists, triathletes, speed-skaters (M)	54.8 ± 4.3 53.8 ± 4.1	↔	↔		↔	↑ *	↔	↔
Lindsey and Dunn [89]	Controls (M) Runners (M)	52.0 ± - 52.0 ± 11.4	↑	↑		↑	↑ *	↔	
Maessen *et al*. [80]	Controls (M) Endurance (M)	58.0 ± 7.0 61.0 ± 7.0						↔	
Matelot *et al*. [29]	Controls (M) Runners, cyclists (M)	59.0 ± 3.0 62.0 ± 3.0	↔	↑		↔ ↑ *		↔	↔
Maufrais *et al*. [35]	Controls (-) Runners, triathletes, cyclists (M)	56.0 ± 6.0 54.0 ± 7.0			↑	↑	↑ *	↑	
Maufrais *et al*. [55]	Controls (M) Cyclists (M)	55.0 ± 8.0 57.0 ± 8.0				↑	↑ *		
Miki *et al*. [90]	Controls (-) Cyclists (-)	49.0 ± 7.6 49.4 ± 6.4			↑ *	↑ *	↑ *		
Molmen *et al*. [36]	Controls (M) Cross-country skiers (M)	71.7 ± 1.3 74.3 ± 1.8						↔	↔
Nishimura *et al*. [91]	Controls (M) Bicyclists (M)	46.9 ± 3.3 45.6 ± 2.3	↑	↑		↑	↑		↓
Northcote *et al*. [92]	Controls (M) Runners (M)	56.0 ± 7.0 56.0 ± 7.0	↔ ↑ *	↑ ↑ *		↔ ↔ *	↑ ↑ *		
Nottin *et al*. [37]	Controls (M) Cyclists (M)	55.9 ± 4.1 58.6 ± 4.8	↔ *	↔ *		↑ *	↔ *	↑	↔
Olsen *et al*. [38]	Controls (M) Runners (M)	66.3 ± 3.8 65.0 ± 4.6			↑ ↑ *	↑ ↑ *	↑ ↑ *	↑	↔
Prasad *et al*. [22]	Controls (M+F) Marathoners, triathletes, middle-distance runners (M+F)	69.8 ± 3.0 67.8 ± 3.0			↔		↑ *	↑	↔
Seals *et al*. [93]	Controls (M) Runners (M)	63.0 ± 3.0 64.0 ± 6.0		↑ *		↑ *			
Schmidt *et al*. [41]	Controls (M) Soccer players (M)	68.2 ± 3.2 68.1 ± 2.1	↔	↔		↔	↔	↔	↑
Takemoto *et al*. [44]	Controls (M+F) Runners (M+F)	60.0 ± 5.0 60.0 ± 7.0						↑	
Vianello *et al*. [94]	Controls (M+F) Marathoners (M+F)	57.0 ± 10.0 58.0 ± 6.5	↑	↑		↑	↑ *	↑	↓

M, male; F, female; IVS, interventricular septal thickness; PWT, posterior wall thickness; MWT, mean wall thickness; LVEDD, left ventricular end-diastolic diameter, LVM, left ventricular mass; E/A, early-to-late mitral inflow velocity; EF, ejection fraction. *, indicates allometrically scaled indices; ↑, significantly greater in athletes as reported by study; ↓,

significantly lower in athletes as reported by study; ↔, no significant difference between athletes and controls as reported by study. Data presented as means ± standard deviation.