ESC European Society of Cardiology

European Heart Journal - Cardiovascular Imaging (2024) **25**, 1537–1545
https://doi.org/10.1093/ehjci/jeae155

REVIEW

Diastolic function and dysfunction in athletes

Havard Dalen [1,2,3]*, Jon Magne Letnes[1,2], Morten A. Hoydal[1], and Ulrik Wisløff[1,4]

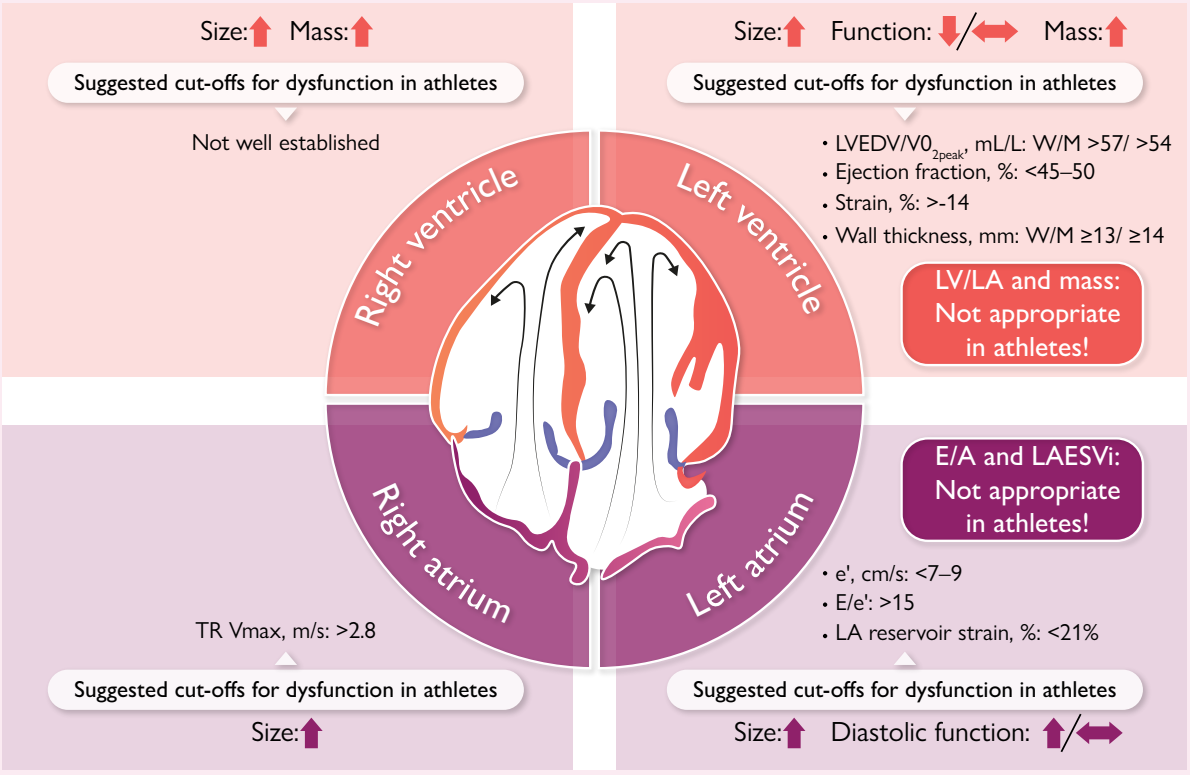
[1]Department of Circulation and Medical Imaging, Norwegian University of Science and Technology, Faculty of Medicine and Health Sciences, Box 8905, NO-7491 Trondheim, Norway; [2]Clinic of Cardiology, St. Olavs hospital, Trondheim University Hospital, Trondheim, Norway; [3]Clinic of Medicine, Levanger Hospital, Nord-Trøndelag Hospital Trust, Levanger, Norway; and [4]School of Human Movement and Nutrition Science, University of Queensland, Saint Lucia, Queensland, Australia

Received 7 June 2024; accepted 15 June 2024; online publish-ahead-of-print 18 July 2024

Cardiac remodelling is often most profound in male athletes and in athletes with the greatest volumes of endurance training and is characterized by chamber enlargement and a mild-to-modest hypertrophy. The diastolic filling of the left ventricle (LV) is a complex process including the early recoil of the contracted LV, the active relaxation of the myocardium, the compliance of the myocardium, the filling pressures, and heart rate. Echocardiography is the cornerstone for the clinical assessment of LV diastolic function. LV diastolic function is usually enhanced in elite endurance athletes characterized by improved early filling of the ventricle, while it is preserved or enhanced in other athletes associated with the type of training being performed. This allows for the high performance of any endurance athlete. Typical findings when using resting echocardiography for the assessment of LV diastolic function in endurance athletes include a dilated LV with normal or mildly reduced LV ejection fraction (EF), significantly enlarged left atrium (LA) beyond the commonly used cut-off of 34 mL/m^2, and a significantly elevated E/A ratio. The early-diastolic mitral annular velocity and the E-wave peak velocity are usually normal. Importantly, interpretation of the echocardiographic indices of LV diastolic function should always consider the clinical context and other parameters of systolic and diastolic functions. In the absence of an underlying pathology, single measurements outside the expected range for similar athletes will often not represent the pathology.

* Corresponding author. E-mail: havard.dalen@ntnu.no

Graphical Abstract



Keywords diastole • echocardiography • exercise • sport • endurance training • imaging

Introduction

Cardiac remodelling in elite athletes such as rowers and skiers was first described 125 years ago.[1,2] Since then, numerous studies have described the typical remodelling of cardiac chambers found in many athletes. According to the European Society of Cardiology, an athlete is defined as a young or adult individual, either amateur or professional, who is engaged in regular exercise training and participates in official sports competition. Most studies on athletes' heart have utilized echocardiography, but the cardiac adaptions in athletes have also been confirmed with other techniques such as cardiac magnetic resonance imaging (MRI). Today, the overview of cardiac adaptions to high-intensity exercise training is well known among clinicians, while the underlying physiology and cellular adaptions may be less known. The main driver for the exercise-induced cardiac adaptions is the direct relationship between the body's demand for oxygen supply and the exercise-related workload.

With increased exercise intensity, the heart ejects more blood per unit of time, which in turn transfers more oxygen to the muscles, aiding mitochondrial oxidative phosphorylation. Each stage in the oxygen pathway plays a crucial role in determining the upper limit of aerobic capacity, defined as the maximal oxygen uptake (VO_{2max}) which is regarded as the gold standard measurement for cardiorespiratory fitness.[3] Often, peak oxygen consumption is used as a proxy for VO_{2max}. In most individuals, the maximal rate of oxygen utilization in skeletal muscle is constrained by the maximum volume of blood that the heart can eject per unit of time.[3] However, in elite endurance athletes where the cardiocirculatory system is well adapted to strenuous exercise, the pulmonary capacity may not be able to accommodate for the high cardiac output, thus potentially restricting their peak performance.[4]

The enlargement of cardiac chambers and subsequent increased capacity of the heart to generate a large stroke volume, and thus, a large cardiac output, are the hallmarks of exercise-induced cardiac remodelling in endurance athletes. The first studies focused on the left ventricular (LV) remodelling,[5] while more recent studies have shown that also the right ventricle (RV), the right atrium (RA), and the left atrium (LA) remodel due to high-intensity exercises. The stroke volume of the enlarged LV is further increased during exercise due to a reduction in end-systolic volume related to the increased sympathetic tone. The haemodynamic alteration during exercise varies with the mode of exercise being performed.[6] Elite endurance athletes who participate in disciplines that involve a high degree of isotonic muscle work such as long-distance running, cycling, rowing, swimming, and cross-country skiing are known for the most pronounced dilatation of cardiac chambers and LV hypertrophy. These changes ensure a sufficient increase in stroke volume, cardiac output, and oxygen supply in response to exercise stress. This has been explained by enhanced venous return of blood to the heart, promoting cardiac preload. Conversely, strength athletes, such as those involved in weightlifting, wrestling, and American football, typically participate in activities characterized by isometric muscle work. This type of activity is traditionally perceived to increase cardiac afterload due to elevated peripheral arterial resistance, leading to a lesser extent of cardiac remodelling. A mixed group, like soccer or tennis players, alternates between isometric and isotonic components. Some sports, like golf or gymnastics, demand less from the cardiorespiratory system and focus on technical skills. These sports are not discussed further due to their lower cardiorespiratory demand.[6]

Almost five decades ago, Morganroth and co-authors suggested that the increased LV mass in endurance athletes compared with non-athletic subjects was mainly due to increased cardiac volumes. In that

study, Morganroth[7] found that eccentric LV hypertrophy was present among the endurance athletes, while concentric LV hypertrophy was found in the strength-trained athletes. Further, the increased LV mass in resistance-trained athletes was due to increased thickness of the ventricular wall. The basis for Morganroth's hypothesis was the comparison of measurements from M-mode echocardiography of 56 athletes with those of non-athletic controls. Haykowsky and others have contended the simplified dichotomized distinction of cardiac remodelling and argue that the hypothesis is obsolete as endurance exercise is linked to increments in both volume load and pressure load.[5,8] However, still the characteristics with a more pronounced eccentric LV hypertrophy in endurance-trained athletes are typical, and a more concentric LV hypertrophy may be present in resistance-trained athletes.[9] Additionally, echocardiographic characteristics accompanying the mild-to-moderate eccentric LV hypertrophy in endurance athletes are among others dilatation of the ventricles and atria, while the LV ejection fraction (EF) and myocardial deformation measures are in the lower part or below the reference ranges for normality.[10–13] Similarly, the concentric LV hypertrophy related to resistance training is usually mild and within normal limits and is not associated with the same degree of RV remodelling.[9] However, it is often accompanied by a mild dilatation of the LA and normal-to-high LV EF.[6,10]

The diastolic filling of the LV is a complex process including the early recoil of the contracted LV, the active relaxation of the myocardium, the compliance of the myocardium, the filling pressures, and heart rate. Echocardiography is the cornerstone for the clinical assessment of LV diastolic function, even though invasive studies can directly assess the LV filling pressure and the pressure–volume relation. Early studies have shown enhanced diastolic function in endurance athletes as evaluated by early-diastolic mitral inflow velocities (E-wave) and early-diastolic mitral annular motion velocities (e') using tissue Doppler.[14,15] Contradictory to these findings, a small study including 35 male university athletics participating in a 90-day training regimen in American-style football found increased LV mass and a mild reduction of early and late diastolic myocardial velocities at post-intervention testing.[16] Whether the latter findings indicate diastolic dysfunction is unknown. Most likely, the explanation relates to the differences in physiological demands and adaptions from different types of sports, highlighting the importance of relating echocardiographic findings with information about the exercise routine of the individual athletes. LV diastolic function, however, is closely associated with cardiorespiratory fitness.[17]

In the clinical diagnostic workflow, the assessment of diastolic function is simplified focusing on the combination of the size of the LA, the peak velocities of the E-wave and e', and the estimated gradient from the RV to the RA in systole calculated from the maximal tricuspid regurgitant jet velocity (TR V_{max}). A well-preserved LV diastolic function is mandatory for the high performance of any endurance athlete. With increasing heart rate, less time is available for filling of the ventricle. Even though the ejection time decreases in parallel with exercise-induced increase in workload and heart rate, the relative reduction is far less than the reduction in filling time, and the emptying rate of the LV increases far less than the filling rate in well-trained athletes.[18] Similarly, the same study showed that the differences in filling rates between endurance athletes and controls are much bigger than the differences in emptying rate.

Cardiac remodelling in athletes

Ventricular remodelling

The ventricular adaption to exercise relates to an increase in both volume and pressure loads. As stated, the enlargement and eccentric hypertrophy of the LV related to participation in endurance sports disciplines with high demands have been recognized for decades.[19] Major signalling pathways are involved in regulating exercise-induced physiological cardiac hypertrophy and cardiac protection.[20] A key step in the evaluation of any athlete with a cardiac symptom is to evaluate whether chamber remodelling is in line with physiological adaption or should be considered part of pathological alterations. Traditionally, measures of LV and RV size have been indexed to body size measures, but this may not be the best way to physiologically assess size of cardiac chambers.

In a recent publication, our research group found a linear relationship between LV end-diastolic volume and the absolute VO_{2max} across the fitness spectrum and sex in healthy individuals.[21] Furthermore, as shown in *Figure 1*, similar LV end-diastolic volume to absolute VO_{2max} ratios were found in several other studies presenting data on both LV volumes and VO_{2max}, and the relationship seems to be valid both during development of young athletes as well as during detraining.[21,22] While eccentric remodelling is most common in endurance athletes,[23] the type of LV remodelling differs between resistance-trained athletes. By reviewing the available literature on resistance training and LV hypertrophy, Haykowsky *et al.*[24] found that the most common findings were no LV hypertrophy (37.5%) or concentric LV hypertrophy (37.5%), while eccentric LV hypertrophy was less common (25%). Similarly, the type of LV hypertrophy was related to the exercise discipline, where two-thirds of those with normal geometry were powerlifters, while weightlifting was associated with concentric hypertrophy.

The relation of LV enlargement with LV hypertrophy has also been studied. Arbab-Zadeh *et al.*[23] found that over 1 year of progressive endurance exercise training, the increase in LV mass was caused by increased LV wall thickness during the low-intensity training period (i.e. concentric hypertrophy), while the increase in LV mass was eccentric due to LV dilatation during the more progressive phase with high-intensity intervals and prolonged endurance exercise. Weiner *et al.*[25] examined the combination of endurance training and resistance training in athletic rowers and found that the increase in LV mass during acute augmentation was related to dilatation of the LV, while the increase in LV mass during a chronic phase of maintenance was related to the increase in LV wall thickness. Both the latter studies showed LV remodelling with phases of concentric and eccentric modes related to the underlying load as well as duration and intensity of endurance exercise.

Previously, less focus was on the RV, but more recently, RV remodelling has been shown across several athletic disciplines. Compared with the LV, the RV has a thin, crescent-like shape which is only one-sixth of the muscle mass and shortens mainly due to the contraction of longitudinal fibres. In the study by Arbab-Zadeh *et al.*,[23] RV remodelling was non-cyclic with an increase in volume and mass with a constant relationship, i.e. eccentric hypertrophy. It has been shown that the RV adaptions to exercise also include prominent trabeculations.[26] As for the LV, the most pronounced RV remodelling is present in the endurance sports disciplines with the highest demands.

At rest, the RV does minimal work to maintain blood flow through the low-pressure pulmonary circulation, and the wall stress in the RV is lower than in the LV. During exercise, there is also a physiological increase in systolic blood pressure and systolic pulmonary artery pressure. It has been shown that the increase in the systolic pulmonary artery pressure during exercise is relatively higher than the increase in systolic blood pressure. Aligned with these changes, the relative increase in RV wall stress during exercise is higher than the LV.[27] The wall stress does not differ between athletes and non-athletic controls at the same workload, but as athletes may achieve a much higher workload, the relative increase in wall stress from rest to high-intensity efforts is higher in endurance athletes.[27]

Any kind of exercise training is transient, and thus, it is not surprising that ventricular remodelling will be greater by spending more time exercising. It has been shown that athletes who spend the longest time in

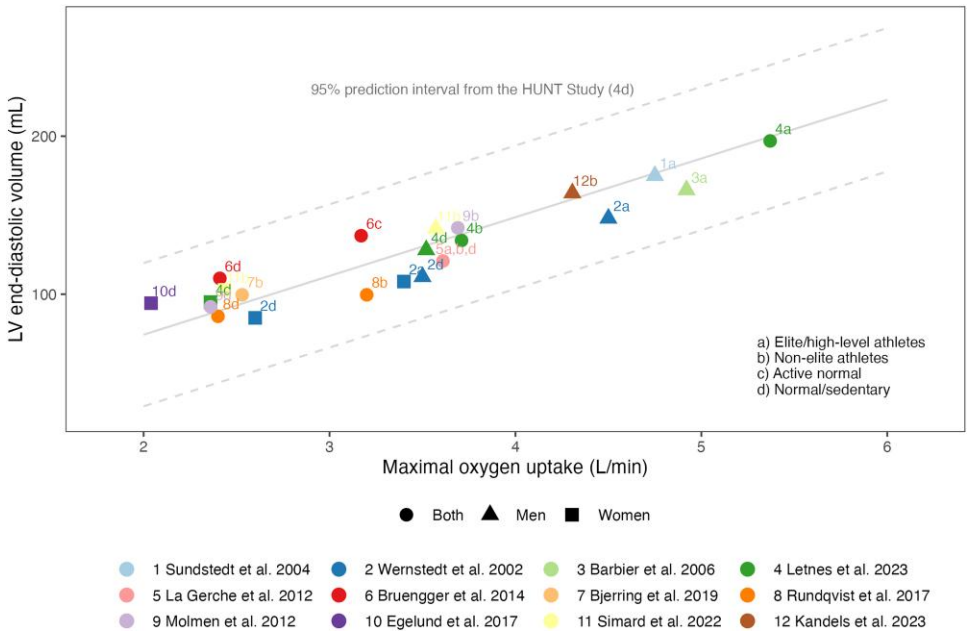


Figure 1 Overview of studies presenting LV end-diastolic volume and VO_{2max}. LV end-diastolic volume according to absolute VO_{2max} from different publications plotted on the 95% prediction interval based on 1190 healthy subjects from Letnes *et al.*[21]

training or competing, such as cyclists and other endurance athletes, show the most profound exercise-induced remodelling.[19] In healthy subjects, this remodelling is expected to be proportional to the fitness level.[21] In a recently published study by Claessen *et al.*[13] evaluating 281 elite endurance athletes, it was shown that those with enlarged ventricles and subnormal LV EF, GLS, and/or RV EF more often had genetic variants associated with dilated cardiomyopathy. Interestingly, the group of athletes with reduced ventricular function at rest had excellent exercise capacity and relatively higher increments in LV EF and RV EF during exercise compared with those with normal cardiac function at rest. Moreover, cardiac MRI findings of fibrosis outside the RV hinge points were only found among a few athletes [4 (1.7%)] with preserved ventricular function. Thus, beyond providing data indicating that LV remodelling is not exclusively related to the type, intensity, and duration of the exercise being performed, this study indicates that the degree of LV remodelling also relates to some genetic predisposition.

Atrial remodelling

The atria has a key role in optimizing LV function due to its function as a reservoir, conduit, and pump optimizing the ventricular filling.[28] To adapt to the body's metabolic demands, it is a close relation between the function of the atria and the ventricles. Endurance athletes have larger LA and RA compared with non-athletes.[21,29] In marathon runners, a close relation between atrial enlargement and the number of marathon participations has been shown. Moreover, both baseline and peak exercise levels of pro–atrial natriuretic peptide has been shown to be higher in marathon runners than controls.[29,30]

According to the law of Laplace, wall tension is related to wall thickness and the radius of the cavity. Thus, the stress on the atrial walls during exercise-induced volume overload will be higher compared with the ventricles as the wall thickness is lower. This may at least partly explain some of the acute differences in remodelling across chambers. It has been shown that the LA dilatation in soccer athletes, as well as the general population and physically fit normal individuals, depends on age.[17,31,32] Chamber dilatation due to long-lasting intensive exercise sessions seems to be more pronounced for RA compared with the LA,[30,33] while the ventricular volumes seems more closely related to the actual fitness level.[21,26] In recent studies, we showed that the relation of VO_{2max} to indexed LA end-systolic volume (LAESVi) was most pronounced at younger age, and the LA-to-LV volume ratio increased by age due to a reduction in LV volumes associated with reduced VO_{2max}.[21,34] Both studies indicate that the reverse remodelling of the LA follows a different pattern than the LV with less ability to reversely remodel accompanied with reductions in exercise volumes and metabolic demands. One hypothesis may be that the reverse remodelling of the LA is limited by the adjacent anatomical structures such as the pulmonary veins or the thinner myocardial wall compared with the LV.

Assessment of diastolic function

LV diastolic function is characterized by restoring forces supporting the early-diastolic suction, the LV active relaxation, and the compliance of the LV. Impairment in any of the components may lead to diastolic dysfunction that may limit filling, and the filling pressure may be increased to compensate. According to the current recommendation by the American Society of Echocardiography and European Association of Cardiovascular Imaging,[35] LV diastolic dysfunction in resting subjects with LVEF $\geq$ 50% is present if more than 50% of the following variables have values in line with the following cut-offs: (i) septal e' < 7 cm/s or lateral e' < 10 cm/s, (ii) ratio of the E-wave to the averaged septal e' and lateral e' (E/e') > 14, (iii) LAESVi >34 mL/m^2, and (iv) TR V_{max} > 2.8 m/s. Previously, several other Doppler blood flow measurements such as the ratio of early-to-late mitral inflow velocity, deceleration time of the early-diastolic mitral inflow, and pulmonary venous flow was regularly considered. After the publication of the 2016 recommendations for evaluation of diastolic function, most clinician consider the four major characteristics, while the additional characteristics included in the previous recommendations are rarely a part of the diastolic assessment.[36]

The revision of the recommendations for evaluation of diastolic function were among other reasons motivated by an overdiagnosis of

diastolic dysfunction in the grey zone not well-defined as normal or abnormal using the previous recommendations. Even though the European Association of Cardiovascular Imaging found that the current recommendations were well adopted into clinical practice, the recommendations have been debated and several publications have highlighted important limitations.[36–38] Some of the concerns relate to reproducibility and validity, as well as the cut-off to identify LA enlargement. The agreement between operators may be influenced by measurement variability in cases where the measurements for any of the four characteristics are close to the cut-offs.[37] Also the role of the E/e' ratio has been debated, and the algorithm for identifying diastolic dysfunction in individuals with normal LV EF has been shown to have a low sensitivity to identify individuals with invasively detected LV diastolic dysfunction [prolonged time constant (τ) and/or elevated LV end-diastolic pressure] even though the specificity was high in a study of 94 patients.[38] Two recently published large-scale population studies have shown that the upper limit of normal reference ranges for LAESVi significantly exceeds the recommended cut-off of 34 mL/m^2.[2,32,39] It has been shown that focusing the echocardiographic recordings to the chamber in focus influences the related measurements and, thus, provides larger volume estimates than unfocused acquisitions.[40] Based on recent population studies, the latter relates in special to estimates of the size of the LA and RV.[39] Together with the knowledge of atrial remodelling in athletes, it should be expected that the cut-off for LAESVi of 34 mL/m^2 does not apply to athletes. However, in physiological adaption, LA enlargement should be expected to be in proportion to LV enlargement, keeping the impact of age on the LA to LV ratio in mind.[34]

Several studies have shown a close correlation between e' and the invasively measured time constant (τ) as a measure of the LV relaxation rate.[41,42] The group of Smiseth found that both active relaxation of the myocardium, restoring forces from the systolic shortening contributing

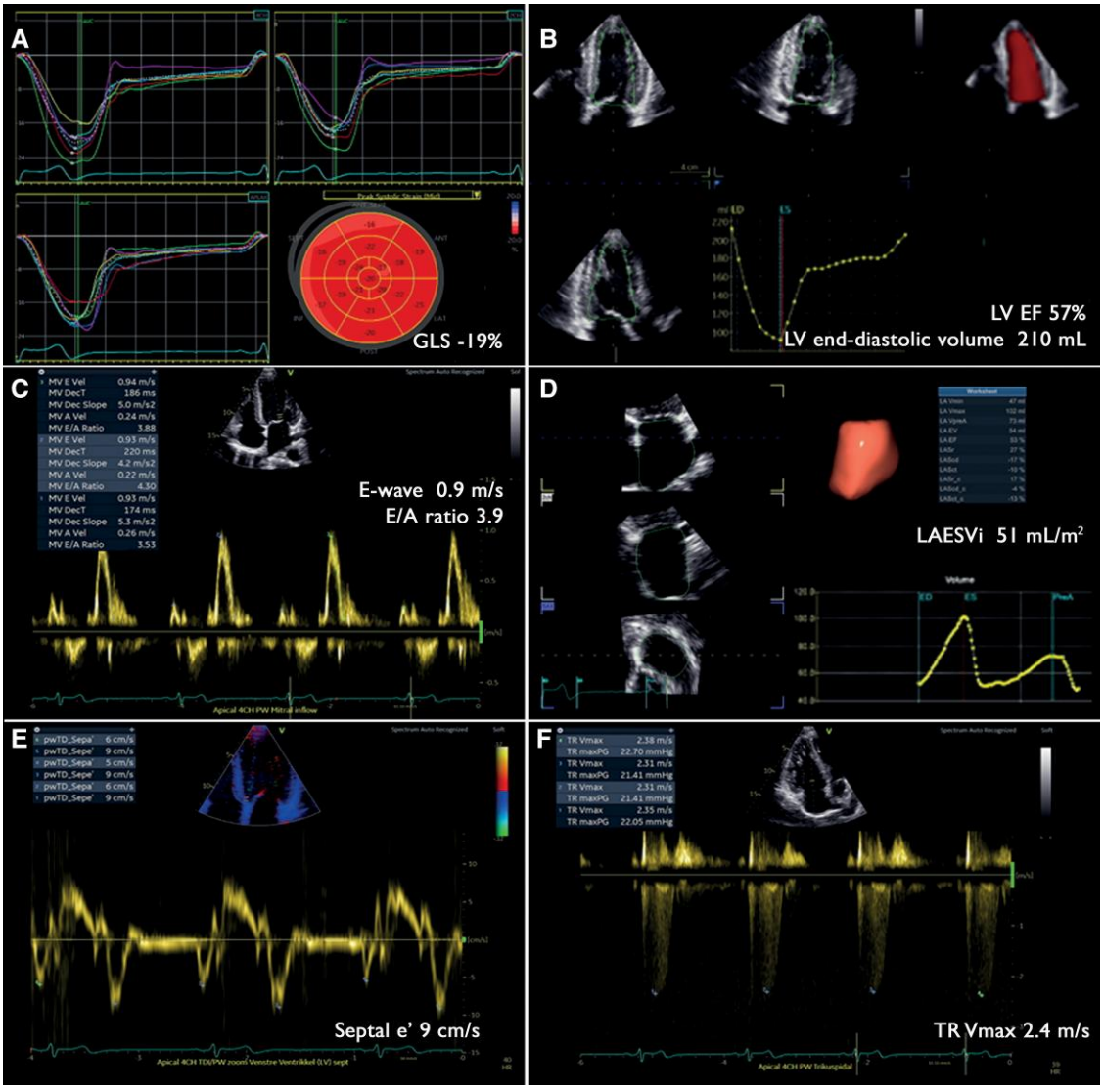


Figure 2 Extracts from echocardiographic evaluation of diastolic function in an endurance athlete. (*A*) Normal GLS. (*B*) Dilated LV, normal LV EF. (*C*) Normal peak E-wave, elevated E/A ratio. (*D*) Dilated LA. (*E*) Normal septal e'. (*F*) Normal TR Vmax. E/A ratio, peak early-to-late diastolic mitral inflow velocity ratio; E-wave, peak early-diastolic mitral inflow velocity; e', peak early-diastolic mitral annular velocity; GLS, global longitudinal strain; LAESVi, indexed left atrial end-systolic volume; LA, left atrium; LV, left ventricle; TR V_{max}, tricuspid regurgitant peak velocity.

to recoiling of the myocardial fibres to their original length after systole, and the early-diastolic lengthening load contributed independently to e'.[42] They also showed that both LV relaxation, restoring forces, and LV early-diastolic load were independent determinants of left ventricular untwisting rate, another sensitive measure of diastolic function.[43] Validation of echocardiographic indices of diastolic function in athletes is limited by the fact that invasive procedures would provide the best reference measurements.[44] The latter is challenging due to ethical issues in healthy individuals and even more challenging in elite athletes.

Figure 2 shows examples from a resting echocardiographic examination of an elite-level endurance athlete with findings of a dilated LV of 210 mL with normal LV EF and global longitudinal strain (GLS). As shown by the Doppler spectrum of the mitral inflow and the volume curves from three-dimensional analyses of the LV and the LA, the early-diastolic function was enhanced with very rapid filling of the LV. The E/A ratio varied from 3.5 to 4.3 between cardiac cycles, and the E-wave was within the normal range. Such findings are most coherent with improved early-diastolic function with enhanced ventricular suction due to the enhanced recoil of the enlarged LV combined with a well-preserved or enhanced early relaxation. In *Figure 3*, some expected findings when imaging the athletes' heart are shown.

A large study of 1145 Olympic athletes and 154 healthy controls provided important data regarding diastolic echocardiographic findings across sport disciplines.[6] Main Doppler findings in athletes at rest compared with controls were higher values for E/e', early-to-late mitral inflow (E/A) ratio, isovolumetric relaxation time, and mitral early inflow deceleration time, while the E-wave and TR V_{max} velocities were equal to controls. Both e' and a' assessed from the basal septal wall were somewhat lower among the athletes compared with controls, however both being well within the normal range. D'Andrea[14] found significantly higher resting values for e' averaged from the basal septal and lateral wall being ≥16 cm/s in the majority of 650 highly trained athletes examined during cardiovascular pre-participation screening. In a population study, we found a positive association, although modest, with higher e' associated with higher VO_{2max} adjusted for sex and age.[17] Moreover, it has also been shown that LV measurements as strain and EF at rest are in the normal or lower range in athletes.[14,21] However, it is important to remember that in healthy athletes the low-to-normal measures of systolic function normalize with exercise stress.[13] LA strain has been introduced as a tool that may aid in the identification of LV diastolic dysfunction, and some studies indicate that LA strain may be lower in athletes than controls.[45]

Cardiovascular risk factors and associated patterns

Atrial fibrillation and atrial flutter have been linked to atrial remodelling, supraventricular ectopic beats, and imbalances of the autonomic nervous system.[46,47] Endurance training increase the risk of atrial fibrillation and atrial flutter by influencing both remodelling, ectopy, and the autonomic nervous system. In a meta-analysis by Abdulla *et al.*[48], endurance athletes had a five-fold increased risk for atrial fibrillation and atrial flutter. The risk of atrial arrhythmias seems to be most pronounced for long-term endurance athletes.[46,49] It has been discussed whether the increased risk for atrial fibrillation and atrial flutter is due to chamber dilatation, exercise-related inflammation, acute stress, or fibrosis. In a couple of studies, long duration and excessive exercise training was associated with inflammation and markers of fibrosis.[47] The latter may support the possibility of cumulative, and possibly irreversible, changes to the atria over time. The male predominance in exercise-related atrial arrhythmias combined with larger LA volume in males also support that the stretching of the LA wall may be important.

High-intensity or prolonged endurance exercise like ultra-marathon has been associated with reduced RV and LV functions as well as elevated cardiac biomarkers as troponins and natriuretic peptides.[50–52] Moreover, some previous studies have indicated that a significant

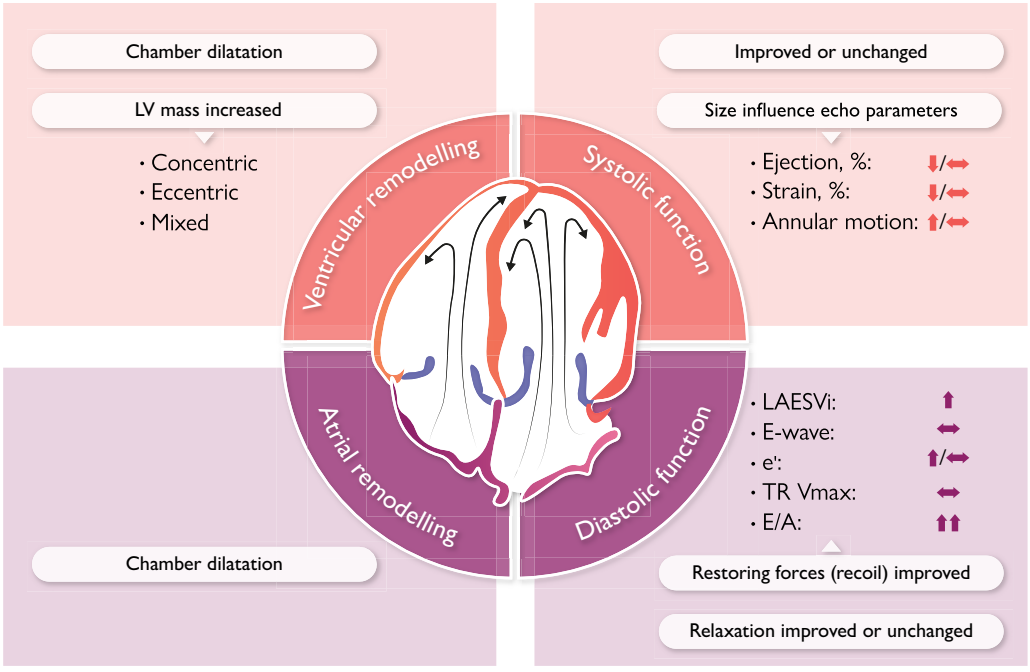


Figure 3 Exercise-induced adaptions to cardiac structure and function evaluated by echocardiography at rest. E/A, peak early-to-late diastolic mitral inflow velocity ratio; E-wave; peak early-diastolic mitral inflow velocity; e', peak early-diastolic mitral annular velocity; LAESVi, indexed left atrial end-systolic volume; LV, left ventricle; TR V_{max}, tricuspid regurgitant peak velocity.

Table 1 Selection of echocardiographic measurements of size and function with corresponding expectations and suggested cut-offs that may indicate cardiac dysfunction in young adult athletes

Variables	Expectations vs. controls	Suggested cut-offs indicating cardiac dysfunction
LV wall thickness	Athletes higher	W, ≥13 mm/M, ≥14 mm
LV volume	Athletes higher	LVEDV/VO_{2peak}: W, >57 mL/L/M, >54 mL/L
LV EF%	Athletes somewhat lower	<45–50%
GLS	Athletes somewhat lower	>-14%
LV mass index	Athletes higher	Varies between studies
LAESVi	Athletes higher	Not appropriate for diastolic evaluation
E/A ratio	Athletes higher	Not appropriate for diastolic evaluation
e' averaged	Athletes a little higher/equal	<7–9 cm/s
E/e' ratio	Athletes a little lower/equal	>15
TR V_{max}	Equal	>2.8 m/s
LA:LV ratio	Athletes lower	Not well defined
LA reservoir strain	Athletes somewhat lower	<21%

Selection of echocardiographic measurements for assessment of diastolic function and other relevant measures of LV size and function with corresponding expectations and suggested cut-offs suggestive of cardiac dysfunction in young adult athletes. As age is of high importance for e', values among the youngest athletes below 9 cm/s will be rare.
E/A ratio, peak early-to-late diastolic mitral inflow velocity ratio; EF, ejection fraction; E-wave, peak early-diastolic mitral inflow velocity; e', peak early-diastolic mitral annular velocity; GLS, global longitudinal strain; LAESVi, indexed left atrial end-systolic volume; LV, left ventricle; M, men; TR V_{max}, tricuspid regurgitant peak velocity; W, women, VO_{2peak}, peak oxygen consumption.

proportion of tachyarrhythmias in endurance athletes originate from the RV possibly in response to the excessive haemodynamic stress placed on the RV during intense endurance exercise.[53] Endurance exercise training also significantly influences the regulation of cellular excitation-contraction coupling. One key adaptation is the handling of calcium ions (Ca^{2+}), which facilitates enhanced contraction and relaxation of cardiomyocytes.[54] Alterations in Ca^{2+} handling has also been linked to transient cardiac dysfunction related to exhaustive exercise.[55] The transient exercise-induced ventricular dysfunction may furthermore be related to an increased permeability of the cardiomyocyte sarcolemma during exercise.[56] The clinical importance of these findings is uncertain.

In healthy populations, there are positive associations of male sex with LV wall thickness, systolic blood pressure, and an unfavourable lipid profile.[57] D'Ascenzi[58] found that dyslipidaemia (found in 32%) was the most common cardiovascular risk factor among more than 1000 Olympic athletes, while a positive cardiovascular family history, cigarette smoking, or waist circumference above 94 cm for men and 80 cm for women were found in some (8–25%). In this study, both hypertension and hyperglycaemia were rare, even though hypertension previously has been shown more prevalent in other studies.[59] In the study by D'Ascenzi,[58] the group without elevated risk factors constituted 40% of the total, and endurance athletes were overrepresented within this group. Resistance training is associated with higher acute blood pressures than endurance training, and strenuous resistance exercise to fatigue combined with Valsalva's manoeuvre has been related to the highest acute blood pressure.[60] It has also been shown that marathon runners with a mean age 38[9] years had higher systolic blood pressure and higher pulsed-wave velocities than controls.[61] Even though this study could indicate an association of increased arterial stiffness with long-term prolonged endurance sporting activities, the role of arterial stiffness for cardiac remodelling and diastolic dysfunction in athletes over the long-term is not known. Furthermore, prohibited substances like anabolic steroids are associated with hypertension, LV hypertrophy, and LV dysfunction. In the clinical context, a history of doping or other drugs may indicate a higher risk of LV diastolic as well as systolic dysfunction.[62]

Conclusions

Exercise training leads to cardiac remodelling characterized by chamber enlargement and a mild-to-modest hypertrophy, often most profound in male athletes and in athletes with the greatest volumes of endurance training. LV diastolic function is usually enhanced in elite endurance athletes characterized by improved early filling of the ventricle, while it is preserved or enhanced in other athletes associated with the type of training being performed. The improved early filling allows for sufficient filling of the ventricle when the relative diastolic time is reduced at higher heart rates.

Table 1 shows a summary of expected findings in athletes compared with non-athletes and suggested echocardiographic cut-offs that may indicate diastolic dysfunction in athletes. Typical findings when using resting echocardiography for assessment of LV diastolic function in endurance athletes include a dilated LV with normal or mildly reduced LV EF, significantly enlarged LA beyond the commonly used cut-off of 34 mL/m2, and a significantly elevated E/A ratio. The early-diastolic mitral annular velocity and the E-wave peak velocity are usually normal. Importantly, interpretation of the echocardiographic indices of LV diastolic function should always consider the clinical context and other parameters of systolic and diastolic function. In the absence of an underlying pathology, single measurements outside the expected range for similar athletes will often not represent pathology. Considering the athletes in perspective, dilatation of the LA and a significantly altered E/A ratio are often appropriate due to exercise-induced cardiac remodelling, and thus, care should be taken to avoid misinterpretation of such findings as markers of pathology. In cases suspect of diastolic or systolic dysfunction, a stress test by echocardiography or cardiac MRI may be appropriate. In the context of elevated cardiovascular risk factors, use of prohibited substances or worsening of symptoms during exercise findings of elevated tricuspid regurgitant jet velocity or reduced early-diastolic mitral annular velocities may indicate that LV diastolic and systolic dysfunction is present.

The LA has various geometries and is commonly enlarged in athletes. Thus, the LA size should be assessed by volumetric measurements rather than dimensions or area. Importantly, it will be expected that most

athletes present with LAESVi above the recommended cut-off indicating that it is not appropriate to use LAESVi > 34 mL/m^2 as an indicator of LV diastolic dysfunction in athletes. An asymmetrical dilatation of the LA compared with the LV may indicate diastolic dysfunction, but further studies are warranted. Similarly, chamber volumes and dimensions should in general be measured in recordings focusing on the chamber of interest and measuring in recordings not targeting the chamber specific optimal axis should be avoided.

And further, *E/A* > 2 would be common as both findings relate to physiological adaptations and not pathology. The high E/A ratio does not mean there is an increased reliance on early-diastolic filling, but more likely it relates to enhanced diastolic properties of the LV associated with a higher recoil from the enlarged contracted LV and a more rapid myocardial untwisting and relaxation.

Aligned to LV enlargement, some endurance athletes will present with borderline low LV EF, which also may be below 50%. The recommendation for evaluating diastolic dysfunction states the importance of interpreting the echocardiographic parameters in a wider context including clinical status. Thus, the recommendations may not be directly applicable to athletes. To best evaluate diastolic function in athletes, the physician needs to interpret echocardiographic measurements considering the athletes' exercise-induced remodelling.

Funding

No specific funding was raised for this manuscript.

Conflict of interest: None declared.

Data availability

Data will be made available upon reasonable request to the authors.

References

1. Darling EA. The effects of training–a study of the Harvard University crews. *Boston Med Surg J* 1899;**141**:205–9.
2. Henschen SE. Skilanglauf und skiwettlauf. Eine medizinische sportstudie. *Mitt Med Klin Upsala (Jena)* 1899;**2**:15–8.
3. Ross R, Blair SN, Arena R, Church TS, Després J-P, Franklin BA *et al.* Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. *Circulation* 2016;**134**:e653–99.
4. Dempsey JA, La Gerche A, Hull JH. Is the healthy respiratory system built just right, overbuilt, or underbuilt to meet the demands imposed by exercise? *J Appl Physiol* 2020;**129**:1235–56.
5. Pluim BM, Zwinderman AH, van der Laarse A, van der Wall EE. The athlete's heart. A meta-analysis of cardiac structure and function. *Circulation* 2000;**101**:336–44.
6. Caselli S, Di Paolo FM, Pisicchio C, Pandian NG, Pelliccia A. Patterns of left ventricular diastolic function in Olympic athletes. *J Am Soc Echocardiogr* 2015;**28**:236–44.
7. Morganroth J, Maron BJ, Henry WL, Epstein SE. Comparative left ventricular dimensions in trained athletes. *Ann Intern Med* 1975;**82**:521–4.
8. Haykowsky MJ, Samuel TJ, Nelson MD, La Gerche A. Athlete's heart: is the Morganroth hypothesis obsolete? *Heart Lung Circ* 2018;**27**:1037–41.
9. Boraita A, Díaz-Gonzalez L, Valenzuela PL, Heras ME, Morales-Acuna F, Castillo-García A *et al.* Normative values for sport-specific left ventricular dimensions and exercise-induced cardiac remodeling in elite Spanish male and female athletes. *Sports Med Open* 2022;**8**:116.
10. Caselli S, Montesanti D, Autore C, Di Paolo FM, Pisicchio C, Squeo MR *et al.* Patterns of left ventricular longitudinal strain and strain rate in Olympic athletes. *J Am Soc Echocardiogr* 2015;**28**:245–53.
11. Abergel E, Chatellier G, Hagege AA, Oblak A, Linhart A, Ducardonnet A *et al.* Serial left ventricular adaptations in world-class professional cyclists: implications for disease screening and follow-up. *J Am Coll Cardiol* 2004;**44**:144–9.
12. Żebrowska A, Mikołajczyk R, Waśkiewicz Z, Gąsior Z, Mizia-Stec K, Kawecki D *et al.* Left ventricular systolic function assessed by speckle tracking echocardiography in athletes with and without left ventricle hypertrophy. *J Clin Med* 2019;**8**:687.
13. Claessen G, De Bosscher R, Janssens K, Young P, Dausin C, Claeys M *et al.* Reduced ejection fraction in elite endurance athletes: clinical and genetic overlap with dilated cardiomyopathy. *Circulation* 2024;**149**:1405–15.
14. D'Andrea A, Cocchia R, Riegler L, Scarafile R, Salerno G, Gravino R *et al.* Left ventricular myocardial velocities and deformation indexes in top-level athletes. *J Am Soc Echocardiogr* 2010;**23**:1281–8.
15. Caso P, D'Andrea A, Galderisi M, Liccardo B, Severino S, De Simone L *et al.* Pulsed Doppler tissue imaging in endurance athletes: relation between left ventricular preload and myocardial regional diastolic function. *Am J Cardiol* 2000;**85**:1131–6.
16. Baggish AL, Wang F, Weiner RB, Elinoff JM, Tournoux F, Boland A *et al.* Training-specific changes in cardiac structure and function: a prospective and longitudinal assessment of competitive athletes. *J Appl Physiol* 2008;**104**:1121–8.
17. Letnes JM, Nes B, Vaardal-Lunde K, Slette MB, Mølmen-Hansen HE, Aspenes ST *et al.* Left atrial volume, cardiorespiratory fitness, and diastolic function in healthy individuals: the HUNT study, Norway. *J Am Heart Assoc* 2020;**9**:e014682.
18. Gledhill N, Cox D, Jamnik R. Endurance athletes' stroke volume does not plateau: major advantage is diastolic function. *Med Sci Sports Exerc* 1994;**26**:1116–21.
19. Pelliccia A, Culasso F, Di Paolo FM, Maron BJ. Physiologic left ventricular cavity dilatation in elite athletes. *Ann Intern Med* 1999;**130**:23–31.
20. Bernardo BC, Ooi JYY, Weeks KL, Patterson NL, McMullen JR. Understanding key mechanisms of exercise-induced cardiac protection to mitigate disease: current knowledge and emerging concepts. *Physiol Rev* 2018;**98**:419–75.
21. Letnes JM, Nes BM, Langlo KAR, Aksetøy IA, Lundgren KM, Skovereng K *et al.* Indexing cardiac volumes for peak oxygen uptake to improve differentiation of physiological and pathological remodeling: from elite athletes to heart failure patients. *Eur Heart J Cardiovasc Imaging* 2023;**24**:721–9.
22. Bjerring AW, Landgraff HE, Stokke TM, Murbræch K, Leirstein S, Aaeng A *et al.* The developing athlete's heart: a cohort study in young athletes transitioning through adolescence. *Eur J Prev Cardiol* 2019;**26**:2001–8.
23. Arbab-Zadeh A, Perhonen M, Howden E, Peshock RM, Zhang R, Adams-Huet B *et al.* Cardiac remodeling in response to 1 year of intensive endurance training. *Circulation* 2014;**130**:2152–61.
24. Haykowsky MJ, Dressendorfer R, Taylor D, Mandic S, Humen D. Resistance training and cardiac hypertrophy: unravelling the training effect. *Sports Med* 2002;**32**:837–49.
25. Weiner RB, DeLuca JR, Wang F, Lin J, Wasfy MM, Berkstresser B *et al.* Exercise-Induced left ventricular remodeling among competitive athletes: a phasic phenomenon. *Circ Cardiovasc Imaging* 2015;**8**:e003651.
26. D'Ascenzi F, Pisicchio C, Caselli S, Di Paolo FM, Spataro A, Pelliccia A. RV remodeling in Olympic athletes. *JACC Cardiovasc Imaging* 2017;**10**:385–93.
27. La Gerche A, Heidbüchel H, Burns AT, Mooney DJ, Taylor AJ, Pfluger HB *et al.* Disproportionate exercise load and remodeling of the athlete's right ventricle. *Med Sci Sports Exerc* 2011;**43**:974–81.
28. Blume GG, McLeod CJ, Barnes ME, Seward JB, Pellikka PA, Bastiansen PM *et al.* Left atrial function: physiology, assessment, and clinical implications. *Eur J Echocardiogr* 2011;**12**:421–30.
29. Wilhelm M, Nuoffer JM, Schmid JP, Wilhelm I, Saner H. Comparison of pro-atrial natriuretic peptide and atrial remodeling in marathon versus non-marathon runners. *Am J Cardiol* 2012;**109**:1060–5.
30. Wilhelm M, Roten L, Tanner H, Schmid JP, Wilhelm I, Saner H. Long-term cardiac remodeling and arrhythmias in nonelite marathon runners. *Am J Cardiol* 2012;**110**:129–35.
31. Wilhelm M, Brem MH, Rost C, Klinghammer L, Hennig FF, Daniel WG *et al.* Early repolarization, left ventricular diastolic function, and left atrial size in professional soccer players. *Am J Cardiol* 2010;**106**:569–74.
32. Singh A, Carvalho Singulane C, Miyoshi T, Prado AD, Addetia K, Bellino M *et al.* Normal values of left atrial size and function and the impact of age: results of the World Alliance Societies of Echocardiography Study. *J Am Soc Echocardiogr* 2022;**35**:154–164.e3.
33. Trivax JE, Franklin BA, Goldstein JA, Chinnaiyan KM, Gallagher MJ, deJong AT *et al.* Acute cardiac effects of marathon running. *J Appl Physiol* 2010;**108**:1148–53.
34. Sabo S, Dalen H, Nyberg J, Grenne BL, Jakobsen EO, Nes BM *et al.* Left atrial to ventricular volume ratio and relation to fitness, cardiovascular risk factors and diastolic function in healthy individuals. The HUNT study. *Eur Heart J Imaging Methods Practice* 2024;**2**:qyae028.
35. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF III, Dokainish H, Edvardsen T *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2016;**17**:1321–60.
36. Sitges M, Ajmone Marsan N, Cameli M, D'Andrea A, Carvalho RF, Holte E *et al.* EACVI survey on the evaluation of left ventricular diastolic function. *Eur Heart J Cardiovasc Imaging* 2021;**22**:1098–105.
37. Hubert A, Coisne A, Dreyfus J, Bohbot Y, Lavie-Badie Y, Aghezzaf S *et al.* Reproducibility of the 2016 American Society of Echocardiography-European Association of Cardiovascular Imaging algorithm for estimation of left ventricular filling pattern: not perfect but good enough. *Ultrasound Med Biol* 2022;**48**:856–61.
38. Yamamoto J, Wakami K, Muto K, Kikuchi S, Goto T, Fukuta H *et al.* Verification of echocardiographic assessment of left ventricular diastolic dysfunction in patients with preserved left ventricular ejection fraction using the American Society of Echocardiography and European Association of Cardiovascular Imaging 2016 recommendations. *Circ Rep* 2019;**1**:525–30.
39. Eriksen-Volnes T, Grue JF, Hellum Olaisen S, Letnes JM, Nes B, Løvstakken L *et al.* Normalized echocardiographic values from guideline-directed dedicated views for

cardiac dimensions and left ventricular function. *JACC: Cardiovascular Imaging* 2023;**16**:1501–15.
40. Genovese D, Mor-Avi V, Palermo C, Muraru D, Volpato V, Kruse E *et al.* Comparison between four-chamber and right ventricular-focused views for the quantitative evaluation of right ventricular size and function. *J Am Soc Echocardiogr* 2019;**32**:484–94.
41. Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM *et al.* Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. *Circulation* 2000;**102**:1788–94.
42. Opdahl A, Remme EW, Helle-Valle T, Lyseggen E, Vartdal T, Pettersen E *et al.* Determinants of left ventricular early-diastolic lengthening velocity: independent contributions from left ventricular relaxation, restoring forces, and lengthening load. *Circulation* 2009;**119**:2578–86.
43. Opdahl A, Remme EW, Helle-Valle T, Edvardsen T, Smiseth OA. Myocardial relaxation, restoring forces, and early-diastolic load are independent determinants of left ventricular untwisting rate. *Circulation* 2012;**126**:1441–51.
44. Edvardsen T, Smiseth OA. Evaluation of diastolic function by echocardiography: important progression, but issues to be resolved. *Eur Heart J Cardiovasc Imaging* 2018;**19**:387–8.
45. Trivedi SJ, Claessen G, Stefani L, Flannery MD, Brown P, Janssens K *et al.* Differing mechanisms of atrial fibrillation in athletes and non-athletes: alterations in atrial structure and function. *Eur Heart J Cardiovasc Imaging* 2020;**21**:1374–83.
46. Myrstad M, Løchen ML, Graff-Iversen S, Gulsvik AK, Thelle DS, Stigum H *et al.* Increased risk of atrial fibrillation among elderly Norwegian men with a history of long-term endurance sport practice. *Scand J Med Sci Sports* 2014;**24**:e238–44.
47. Wilhelm M. Atrial fibrillation in endurance athletes. *Eur J Prev Cardiol* 2014;**21**:1040–8.
48. Abdulla J, Nielsen JR. Is the risk of atrial fibrillation higher in athletes than in the general population? A systematic review and meta-analysis. *Europace* 2009;**11**:1156–9.
49. Baldesberger S, Bauersfeld U, Candinas R, Seifert B, Zuber M, Ritter M *et al.* Sinus node disease and arrhythmias in the long-term follow-up of former professional cyclists. *Eur Heart J* 2008;**29**:71–8.
50. Neilan TG, Januzzi JL, Lee-Lewandrowski E, Ton-Nu TT, Yoerger DM, Jassal DS *et al.* Myocardial injury and ventricular dysfunction related to training levels among nonelite participants in the Boston marathon. *Circulation* 2006;**114**:2325–33.
51. Ness HO, Ljones K, Gjelsvik RH, Tjønna AE, Malmo V, Nilsen HO *et al.* Acute effects of high intensity training on cardiac function: a pilot study comparing subjects with type 2 diabetes to healthy controls. *Sci Rep* 2022;**12**:8239.
52. Kleiven Ø, Omland T, Skadberg Ø, Melberg TH, Bjørkavoll-Bergseth MF, Auestad B *et al.* Race duration and blood pressure are major predictors of exercise-induced cardiac troponin elevation. *Int J Cardiol* 2019;**283**:1–8.
53. Heidbuchel H, Prior DL, La Gerche A. Ventricular arrhythmias associated with long-term endurance sports: what is the evidence? *Br J Sports Med* 2012;**46**:i44–50.
54. Kemi OJ. Exercise and calcium in the heart. *Curr Opin Physiol* 2023;**32**:100644.
55. Ljones K, Ness HO, Solvang-Garten K, Gaustad SE, Andre Høydal M. Acute exhaustive aerobic exercise training impair cardiomyocyte function and calcium handling in Sprague-Dawley rats. *PLoS One* 2017;**12**:e0173449.
56. Mair J, Lindahl B, Hammarsten O, Müller C, Giannitsis E, Huber K *et al.* How is cardiac troponin released from injured myocardium? *Eur Heart J Acute Cardiovasc Care* 2018;**7**:553–60.
57. Dalen H, Thorstensen A, Romundstad PR, Aase SA, Stoylen A, Vatten LJ. Cardiovascular risk factors and systolic and diastolic cardiac function: a tissue Doppler and speckle tracking echocardiographic study. *J Am Soc Echocardiogr* 2011;**24**:322–32.
58. D'Ascenzi F, Caselli S, Alvino F, Digiacinto B, Lemme E, Piepoli M *et al.* Cardiovascular risk profile in Olympic athletes: an unexpected and underestimated risk scenario. *Br J Sports Med* 2019;**53**:37–42.
59. De Matos LD, Caldeira Nde A, Perlingeiro Pde S, dos Santos IL, Negrao CE, Azevedo LF. Cardiovascular risk and clinical factors in athletes: 10 years of evaluation. *Med Sci Sports Exerc* 2011;**43**:943–50.
60. Heitmann KA, Dalen H, Holmen Gundersen G, Ingvaldsen RP, Welde B. Intra-arterial blood pressure traits during and after heavy resistance exercise in healthy males. *Transl Sports Med* 2019;**2**:325–33.
61. Vlachopoulos C, Kardara D, Anastasakis A, Baou K, Terentes-Printzios D, Tousoulis D *et al.* Arterial stiffness and wave reflections in marathon runners. *Am J Hypertens* 2010;**23**:974–9.
62. Carbone A, D'Andrea A, Riegler L, Scarafile R, Pezzullo E, Martone F *et al.* Cardiac damage in athlete's heart: when the "supernormal" heart fails!. *World J Cardiol* 2017;**9**:470–80.