We are IntechOpen,
the world's leading publisher of
Open Access books
Built by scientists, for scientists

6,900
Open access books available

186,000
International authors and editors

200M
Downloads

154
Countries delivered to

Our authors are among the

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

BOOK CITATION INDEX
CLARIVATE ANALYTICS
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Echocardiographic Assessment of Myocardial Deformation during Exercise

Eric J. Stöhr and T. Jake Samuel

Abstract

The human heart is an asymmetrical structure that consists of oblique, circumferential, and transmural fibers, as well as laminae and sheets. Sequential electrical activation of all the muscle fibers ultimately results in a coordinated contraction of the heart muscle also referred to as "deformation." This is immediately followed by myocardial relaxation, when the preceding deformation is reversed, and the ventricles fill with blood. Given the complexity of these repetitive motions, it is not surprising that there is great diversity in the myocardial deformation between different individuals and between distinct populations. Exercise presents a natural challenge to determine the full capacity of an individual's heart, and modern imaging technologies allow for the non-invasive assessment of myocardial deformation during exercise. In this chapter, the most relevant anatomical basis for myocardial deformation is summarized and definitions of the most relevant parameters are provided. Then, the general cardiac responses to exercise are highlighted before the current knowledge on myocardial deformation during exercise is discussed. The literature clearly indicates that the echocardiographic evaluation of myocardial deformation during exercise holds great promise for the identification of sub-clinical disease. Future studies should aim to determine the mechanisms of differential expression of myocardial deformation during exercise in health and disease.

Keywords: exercise, heart, stress testing, diagnostics, imaging, echocardiography, VO_2max, CPET, strain, twist, torsion, untwisting rate, blood pressure, LVAD, heart failure, speckle tracking, hypertension

1. Introduction

In recent years, technological advances in the field of echocardiography have allowed for a faster acquisition of images with an improved spatial and temporal resolution. As part of these advances, the advent of speckle tracking imaging has resulted in an explosion of investigations into myocardial deformation, as evidenced by more than 5000 articles on PubMed, increasing exponentially since 2005 (https://pubmed.ncbi.nlm.nih.gov/?term=speckle+tracking, accessed 7th of May 2020). The past two decades has also seen in a shift in "stress echocardiography" from being dominated by acute drug-based interventions to primarily exercise challenges. Therefore, this chapter focuses on the current knowledge related to myocardial deformation during acute exercise stress. Instead of just summarizing the current literature, a careful selection of articles is presented that is then used to provide the reader with a narrative

that highlights important general principles of cardiac physiology, including the responses to exercise. To achieve this aim, first a brief overview of the principles and mechanisms governing myocardial deformation will be provided summarised and the key terminology will be defined. Then, the general role of exercise stress testing will be discussed, before the benefits of obtaining myocardial deformation during exercise in health and disease will be reviewed.

2. Principles of myocardial deformation

During contraction of the heart, deformation of the whole muscle occurs in four quantifiable dimensions. In general, these have been identified as: longitudinal shortening (=longitudinal strain, %), circumferential shortening (circumferential strain, %), radial lengthening (=radial strain, %) and rotation (apical − basal rotation = net twist angle, degrees), as well as the diastolic reversal of all of these indices. In addition, the rate of systolic shortening and diastolic lengthening can be measured, which is referred to as strain rate, twisting rate, and untwisting rate. An important distinction must be made between myocardial deformation and pure "velocities", which do not consider the relative shortening (contraction) or lengthening (relaxation) of heart muscle itself but only consider the linear displacement of single myocardial points. Although myocardial velocities can also be measured, they are not representative of the contraction and relaxation of heart muscle. For these reasons, parameters such as E' ("E prime"), which typically represent myocardial velocities in a single location on the mitral annulus, are not discussed in this chapter.

The conventional categorizations of deformation into strain and twist are logical from a biophysics and bioengineering perspective, since deformation of the heart can indeed be detected in these distinct 2-dimensional echocardiographic imaging planes. However, as will be reviewed in the following section on the anatomy and electrical conductance, the structure of the heart is far from symmetrical and—to achieve the final coordination of all components with each heartbeat—important functional differences in the various regions within the heart are present. These intricate deformational patterns can be conceptually simplified by considering the region-specific deformation in a 2-dimensional plane, allowing for easier evaluation of cardiac mechanics in both the laboratory and the clinic. However, one must consider the 3D deformation of the heart muscle, where the deformation of the four imaging planes occur simultaneously and with many of these aspects anatomically and functionally interwoven. This anatomical complexity is the focus of the next section.

2.1 Anatomy

Historical reviews have often credited Leonardo da Vinci's observations in the 15th century as some of the first to describe the gross anatomy of the heart and his speculations about the resulting function. In his drawings[1], da Vinci refers to the importance of vortices, which necessitate the presence of helical structures and/or motions that were apparent as "clockwise and counterclockwise spirals within the aorta as the outlet of the left ventricle" [1]. More than a century after da Vinci's death, William Harvey published his seminal book *Exercitatio Anatomica De Motu Cordis Et Sanguinis In Animalibus* (An Anatomical Study on the Motion of the Heart and Blood in Living Beings, 1628 [2]), in which he established the circulation—including the anatomy

---

[1] In 2019, an exhibition across the UK celebrated the drawings by Leonardo da Vinci, including some of his anatomical sketches (https://www.rct.uk/collection/themes/exhibitions/leonardo-da-vinci-a-life-in-drawing/the-queens-gallery-palace-of).

and motion of the heart—as we mostly know it today, thereby also popularizing the previous work by Ibn al-Nafis [3]. In 1669, Richard Lower provided remarkable detail on the anatomy of the heart in his publication of *Tractatus de Corde...* (Treatise on the Heart. ... [4]). Despite these early discoveries, it wasn't until the contributions by McCallum and then Mall in the early twentieth century that there were new advancements in this field [5, 6]. During the second World War, Robb & Robb provided an exceptionally detailed overview of the accumulated knowledge that covered five centuries of discoveries [7]. Then, 27 years later, in 1969, Streeter et al. published the much-cited myocardial fiber distribution of the left ventricle (LV) in dogs, and Greenbaum et al. confirmed the observations in human cadavers [8, 9].

Today, after centuries of observations, there is still debate on the exact origins and arrangements of the heart [10]. However, general consensus exists that the mammalian LV consists of oblique fibers in the endocardium that gradually change into circumferential fibers in the midwall and continue to oblique fibers in the sub-epicardium, orientated in the opposite direction to those in the endocardium, thus creating what is often referred to as a helical arrangement [11–14]. Noteworthy insight has also been provided by the description of sheets and laminae, which may not only impact the effect of individual myofibres but also the electrical propagation across the myocardium [15, 16]. With regard to the latter, the coordinated sequence of electrical propagation and activation of the LV occurs in a specific apex-to-base and endocardial-to-epicardial order during systole [17]. Due to these different electrical activation times, each part of the heart muscle is activated for different durations, therefore shortening and lengthening velocities (or systolic and diastolic "strain rates") vary significantly in the different regions of the LV and are not associated with the overall heart rate [18]. A significant addition to the longstanding knowledge on oblique and circumferential fibers was provided by Lunkenheimer et al., who provided evidence for the existence of transmural myofibres that may be of fundamental relevance to the regulation of forces associated with normal myocardial contraction and relaxation [19]. Finally, there is important structural diversity on the myocyte level that contributes to the overall elasticity of the cardiomyocyte, as revealed by different isoforms of the giant protein titin, which may influence myocardial deformation in systole and diastole, not least during exercise [20, 21]. Collectively, the current knowledge indicates a non-uniform, complex mesh of diverse cardiac myofibre arrangements which may be grouped in sheets and laminae, influencing the electrical activation sequence of the heterogeneously distributed autonomic nerves in the heart (**Figure 1**, [22]). In comparison to the LV, the macro-structure of the right ventricle (RV) is not cone-shaped but resembles that of a crescent, almost wrapping around the LV. Yet, the underlying micro-structure is similar to the LV, albeit with some key differences. Like the LV, the epicardial and endocardial fibers are arranged helically, but with a smaller range of oblique angles [23]. The main difference to the LV seems to be in the myofiber arrangement of the midwall. Here, "the circumferentially arranged middle fibres are confined to the LV and septum" [8] and "without such beneficial architectural remodeling [...] seem unsuited structurally to sustain a permanent increase in afterload" [23]. It is probably because of the overall crescent shape (that makes echocardiographic image acquisition in any plane other than the longitudinal challenging), and the lack of an obvious torsional motion, that the assessment of right ventricular deformation has largely focused on longitudinal strain.

2.2 Definitions and selection of myocardial deformation parameters

Because of the increasing number of studies focused on myocardial deformation mentioned in the introduction to this chapter, it has been inevitable that some inconsistencies exist regarding the nomenclature in the literature (**Table 1**). Here, a
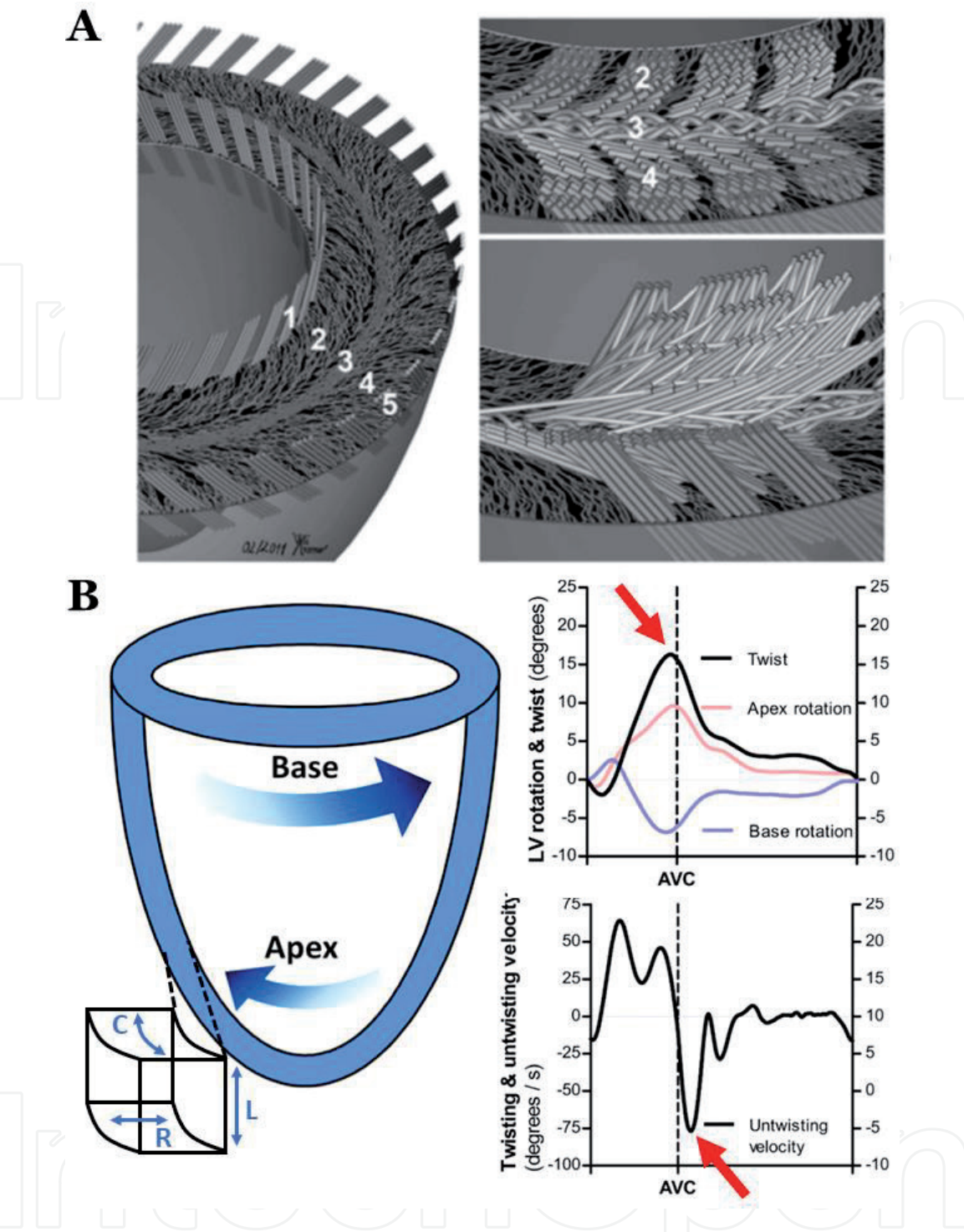
Figure 1.
LV anatomy, strain and twist. (A) Although the detailed anatomy of the heart is still a matter of debate, the most comprehensive, evidence-based model includes a mesh of oblique, circumferential and transmural fibers (1–5). (B) LV strain is typically assessed in three planes, the longitudinal plane (from the apex to the base, L), the circumferential plane, C, and the radial plane (from the endocardium to epicardium, R). Owing to the specific anatomy, contraction of the LV results in a twisting motion around the long-axis, with an opposing rotational movement at the base compared with the apex that is rapidly released in diastole. Resultant twist and twist velocity curves produce a clear signal for peak LV twist and early diastolic untwisting rate (red arrows). Please see further details and the original figures in Refs. [14, 24].

summary of the most common definitions is provided and the reader is also referred to previous review articles for further details on the terminology [24–26].

With regard to the LV, three strain components have been established: longitudinal, circumferential and radial strain [25]. Systolic strain rate was once thought to reflect contractility; however, these hopes have not been sustained. Furthermore, the anatomy of the heart does not support the measurement of radial strain since there are no radial

fibers in the LV or RV. Although the transmural fibers may somewhat relate to this type of strain, they maximally constitute ~20% to overall deformation and do not seem to run strictly in the radial direction. Second, the classification of twist or torsion as a "shear strain" or fourth dimension of deformation does not fit the underlying anatomy of the heart either. There is currently no empirical evidence for the existence of a

Parameter (unit)	Description
Circumferential strain (%)	Percentage shortening of the circumference
Global longitudinal strain (%)	Typically, the average strain of multiple walls obtained from different echocardiographic windows (4-chamber, 2-chamber, 3-chamber)
Longitudinal strain (%)	Shortening along the long-axis of the ventricles in a single 2-dimensional imaging plane (for example a 4-chamber view)
Shear strain	The strain resulting from two different normal strains, for example "longitudinal-circumferential shear strain"
Strain (rate) imaging	Generic term that can refer to strain data obtained with either tissue Doppler or speckle tracking echocardiography
Strain rate (/s)	The rate of shortening (strain) or lengthening (strain) of each strain
Tissue Doppler strain (%)	Strain obtained with tissue Doppler echocardiography, which is more angle-dependent than speckle tracking echocardiography
Tissue velocity imaging (%)	Echocardiographic imaging based upon Doppler modality, often synonymous with tissue Doppler strain
Twist (degrees)	Also called the net twist angle, obtained from the net difference in rotation between the left ventricular base and apex. Not to be confused with torsion or rotation, the latter referring to the local angular deformation at the base and apex
Untwisting rate (°/s)	The maximal early diastolic rate of reversal of twist

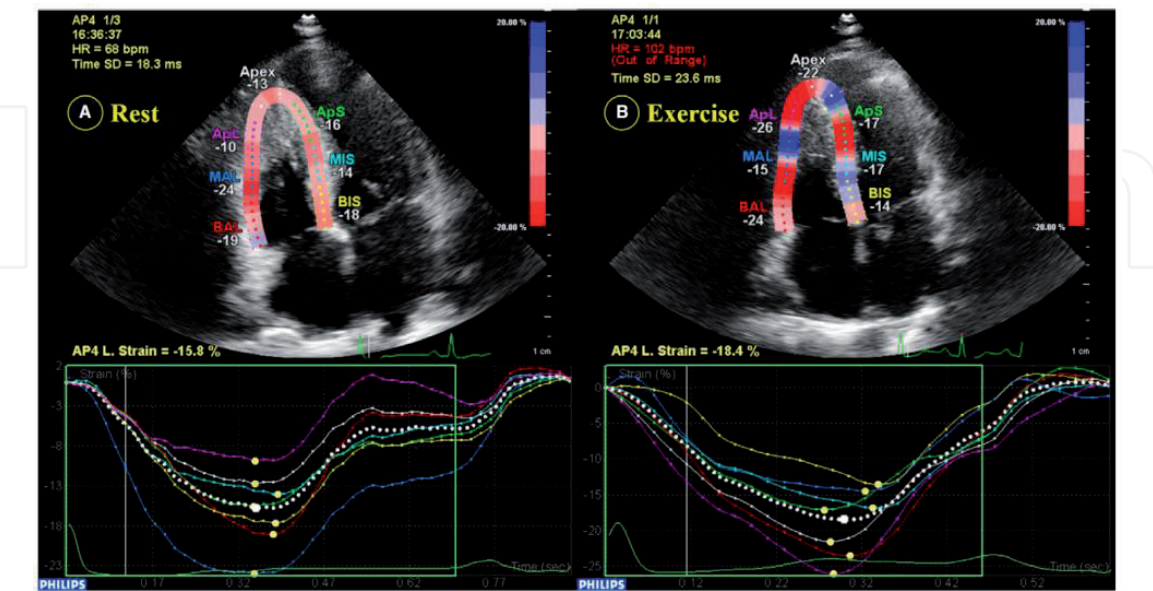**Table 1.**
Deformation parameters.

Figure 2.
RV strain. The measurement of RV strain at rest (left) and during exercise (right) in a patient with hypertrophic cardiomyopathy. Because of the anatomical arrangement of the RV, longitudinal strain is the most commonly investigated parameter, although further clarity is required whether to always include or exclude the septum [28]. From a functional perspective, there is strong evidence that the septal deformation is more similar to that of the LV than the RV free wall, as supported by evidence of a shared morphology [29, 30]. Please see further details and the original figure in: Wu et al. [31].

meaningful number of longitudinal fibers that could determine longitudinal deformation of the ventricles. Instead, the oblique fibers that make up most of the fibers within the left ventricular walls are likely responsible for deformation in the longitudinal direction. Consequently, it does not seem appropriate to calculate twist or torsion from the longitudinal and circumferential shear angle, also because this approach does not capture the potential regional differences that exist between the base and apex in both the LV and RV. Despite these drawbacks to the radial and longitudinal parameters, it must be acknowledged that longitudinal strain has become the most established measure as a clinical marker with diagnostic potential [27]. For these reasons, in the context of this chapter, it seems appropriate to ignore LV radial strain but include LV longitudinal and circumferential strain as well as twist and untwisting rate. Since no clear circumferential fibers or twisting motion have been detected in the RV, the focus for that chamber will be exclusively on longitudinal strain **Figure 2**.

3. Echocardiographic assessment of myocardial deformation during exercise

3.1 Why exercise?

Even if all humans were elite athletes, we would spend most of the time in a day in a biological state of rest—or certainly in a state of low physical activity that only constitutes a fraction of the total capacity of our cardiovascular system. Accordingly, the routine clinical practice of examining cardiac function at rest is a good representation of the condition we find ourselves in most of the time. However, when a person requires an echocardiographic examination, it is typically for clinical reasons initiated by the presence of negative symptoms, often presenting as "exertional dyspnea" or angina. If an echocardiographic examination then detects structural and functional abnormalities of the heart that are congruent with the individual's symptoms, the diagnosis of heart disease is likely. However, resting assessment of cardiac function often fails to recapitulate conditions of exertional dyspnea, and thus can sometimes lead to misdiagnosis. Equally, waiting until the emergence of symptoms postpones clinical treatment. For this reason, "stress testing" has been suggested to offer the opportunity of a "window into the future". By taking the person out of their typical state of rest or low physical activity and stressing the full range of their cardiovascular system until maximum effort, underlying abnormalities may be detected that remain otherwise unknown. Examples for the benefit of exercise testing have been presented in relation to "unmasking masked hypertension" [32, 33]. Similarly, in pregnancy it has been proposed that the cardiovascular responses to exercise tests prior to conception may be indicators of the presence or absence of complications during future pregnancies [34–37]. Furthermore, the complex etiology of heart failure has justified detailed exercise testing to identify the most important contributors out of the numerous cardiac or peripheral factors that may be involved in the development and/or the state of heart failure [38–40].

It is now recognized among clinical practitioners that the investigation of myocardial deformation during exercise can provide additive value, since previous research studies have revealed new (and sometimes surprising) insight into the behavior of the heart during exercise. As will be discussed in detail in Section 3.3, these findings have informed our basic understanding of cardiac function and sometimes guided future clinical investigation. Since myocardial function, including parameters of myocardial deformation, are influenced by the general loading state of the heart, any exercise responses must be seen in the context of general cardiovascular responses, as discussed in the next section.

3.2 General cardiovascular responses to exercise

In the context of myocardial deformation, the most relevant cardiovascular and cardiopulmonary responses to a standardized exercise test pertain to stroke volume, cardiac output, end-diastolic volume, blood pressure, arterial resistance, lactate, and maximal oxygen consumption (VO_2max). In healthy individuals, a clear change in these parameters can be expected at the onset of low intensity dynamic exercise that should continue to change linearly up to moderate intensities. Importantly, dynamic exercise tests cause a disproportionate peripheral vasodilation in relation to the increase in cardiac output, and hence total peripheral resistance drops sharply at the onset of exercise and then remains constant across moderate and high exercise intensities [41]. From a diastolic perspective, end-diastolic volume has been shown to increase in some studies while others have not observed any change with exercise. This is not trivial since an acute increase in end-diastolic volume has been associated with an increased stroke volume, an effect also known as the Frank-Starling mechanism [42]. However, the overall contribution of end-diastolic volume to stroke volume is still relatively low because most of the increase in stroke volume has been attributed to the enhanced contractility that reduces the end-systolic volume.

At workloads above moderate intensity, several important physiological changes occur in healthy individuals. Blood lactate concentrations increase exponentially and CO_2 production rises above O_2 consumption, both reflecting the greater contribution of anaerobic metabolic pathways to overall energy utilization and causing a strong stimulus for vasodilation not least in the cerebral circulation. During the highest effort, stroke volume and VO_2 have been reported to plateau and even decrease, but the exact pattern and the underlying mechanisms to this response remain a matter of debate [43]. Fortunately, this does not seem to impact the interpretation of cardiovascular responses to exercise in patients, since the sub-maximal data are currently thought to be of sufficient clinical value to determine whether exercise performance is normal or impaired [44].

One important distinction between the LV and RV responses to exercise is the potential for a "disproportionate load" on the RV [45], which is perhaps explained by both a greater relative rise in pulmonary blood pressure compared with that in the aorta, and differences in RV intrinsic factors such as force development. The differences between the LV and RV responses to exercise highlight the specific impact exercise has on the cardiovascular system. Consequently, determining the true origin of exercise limitations is challenging because many components of the cardiovascular system may be affected. For example, studies have shown that an exaggerated rise in blood pressure during exercise may be associated with negative outcomes, but whether this is caused by the heart or the periphery may be more difficult to determine [46–48]. Even in heart failure, the reduced exercise tolerance has been suggested to be a result of both central and non-cardiac limitations [38–40, 49]. Consequently, assessing myocardial deformation *in relation* to conventional exercise responses is essential for the quantification of the contributions of the heart muscle itself.

3.3 Myocardial deformation during exercise

Whatever myocardial parameter one chooses to examine during exercise, the interpretation of the responses can be tricky. For example, an increase in myocardial deformation with sub-maximal cycle exercise along with a typical drop in arterial resistance and concomitant reductions in end-systolic volume, in the presence of no adverse structural remodeling would be reflective of a "healthy" response. Equally, it is theoretically possible that the absence of a clear increase in myocardial deformation—which could be interpreted to represent myocardial

dysfunction—may be a normal response if the increase in blood pressure and peripheral resistance were excessively high (or the exercise test did in fact create a condition of increased afterload). In this case, it is conceivable that the origin of the exercise limitation may not be cardiac despite the attenuated deformation, but perhaps peripheral in nature causing an exercise failure before the cardiac reserve is fully used [39]. Therefore, this section provides an overview of the general trend of myocardial deformation during exercise, but the reader is alerted that a qualitative interpretation must be performed after consideration of the wider physiology. Articles in this section were included if the studies had obtained data with echocardiography during exercise (tissue Doppler and tissue velocity imaging data were mostly excluded because both techniques are angle-dependent and typically represent only data from a single segment within the mitral annulus). Although a promising and exciting alternative to echocardiography, myocardial deformation during exercise obtained using MRI is not the focus of this chapter [50, 51]. Studies were also excluded if they obtained data immediately following exercise effort, as discussed in more detail in the section on methodological considerations. Finally, the avid reader is referred to some excellent review articles that cover more of the literature than this book chapter can accommodate [52–55].

3.3.1 Physiological insight from healthy individuals

The physiology of myocardial deformation during exercise in healthy people is the fundamental basis upon which to interpret the responses in patient populations. Although many clinical research studies also include a healthy control group, sometimes these are matched to the patient groups in their demographics and, therefore, may not represent truly "healthy" individuals. Wherever possible, the data presented here will be from populations purposefully recruited as young healthy reference groups. To date, studies have revealed a variety of new perspectives that may be of great importance for the interpretation of clinical populations.

A decade ago, two studies revealed the strain and twist responses during incremental exercise. First, Doucende et al. showed that left ventricular twist and circumferential strain increased linearly up to moderate exercise intensities, while longitudinal strain increased initially but then plateaued at low exercise efforts [56]. This study also highlighted the interdependence of systolic and diastolic deformation, the role of untwisting rate in LV filling during exercise and the contribution of the LV apex to the overall myocardial response. Second, it was shown that LV twist and untwisting rate increased linearly up to near-maximal efforts, correlating with stroke volume and, thus, perhaps contributing to maximal exercise capacity in humans [57]. The importance of regional LV deformation, at the LV apex, was again highlighted. Several other studies have revealed similar patterns of LV twist during exercise in pre- and postmenopausal women, in athletes and of humans ascending to high altitude [58–62]. Consequently, it is now generally accepted that an increase in LV twist with exercise up to moderate intensities can be expected as a normal response (**Figure 3**). Surprisingly few studies dedicated to healthy individuals have measured LV strain during exercise, but they agree in general that longitudinal strain also increases with exercise [56, 61–64]. Because of the risk of potential confounders, it is not possible to directly compare the response in LV twist and strain obtained in different studies. But in general, it is of great importance to note that the patters of the responses to exercise are not always the same for the two parameters, reminding us that they do not represent the same myocardial deformation. In agreement with the general physiological response to incremental exercise, LV twist increases linearly while longitudinal strain seems to plateau at low exercise efforts. This was more recently confirmed by Williams et al., who reported the same
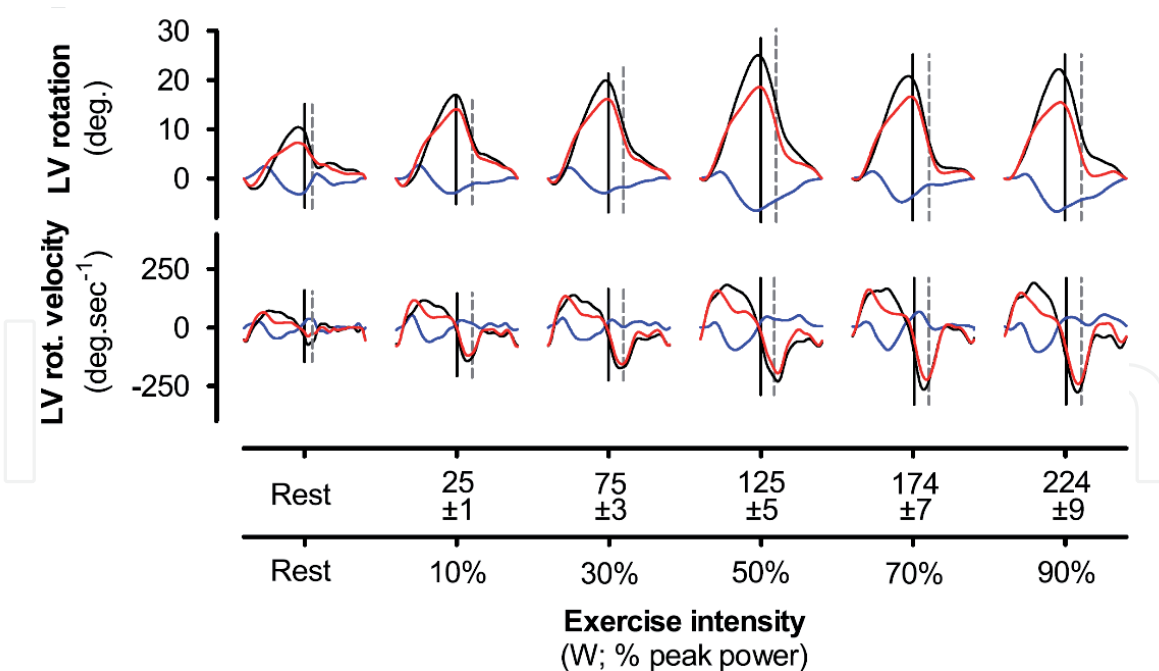
Figure 3.
Myocardial deformation to incremental exercise. LV twist curves during incremental exercise, revealing a linear increase up to 70–80% of maximal individual exercise effort for both peak systolic LV twist (highest value in black lines top row) and peak diastolic untwisting rate (lowest value within black lines bottom row). Red lines represent myocardial deformation at the LV apex, blue lines at the LV base. Black lines are the composite of apical and basal data. Please see further details and the original figure in Ref. [57].

disparity between parameters in young healthy men [62]. Interestingly, in the same study, women seemed to have more of a linear response in longitudinal strain akin to LV twist. The disparity between LV twist and longitudinal strain has also been noted in studies on aging where LV twist consistently increases, but longitudinal strain does not change or decreases. Considering the well-established progression of aortic stiffness with aging [65], longitudinal strain appears to be at odds again with general physiology. Future studies should not only examine the parameters in relation to their sensitivity as a clinical marker but also consider the fit with general physiology.

Studying the acute effects of exercise on myocardial deformation may be influenced by the chronic remodeling that humans have experienced. In this regard, Burns et al. showed that aging seems to be associated with a reduced LV twist reserve during exercise in a population of 60-year old individuals [66]. Similarly, "female aging", as represented by the menopause, seems to impact the myocardial response to exercise, which may be further altered by exercise training [58]. One of the more surprising observations has been that of Cooke et al. who proposed that endurance trained athletes with enlarged "athlete's heart" and a greater stroke volume had a similar systolic LV function, including LV twist, during submaximal exercise compared to untrained humans with smaller stroke volume [67]. Similar to the results presented by Doucende and Williams discussed above [56, 62], this particular exercise response strongly suggests that the mechanical[2] systolic function of the heart may not be strictly associated with its output (stroke volume). Some mathematical calculations support the potentially poor linear association between systolic LV mechanical function and ejection fraction while others suggest a strong relationship [68]. In any case, the previous findings suggest that future investigations into the interaction between systolic deformation and ejection, and diastolic deformation and filling are needed to clarify the current uncertainty. One reason for the existing disagreement between

---

[2] The term mechanical is most commonly used in the literature on myocardial deformation. However, from a biophysical perspective, it may be more appropriate to refer to "kinematics".

mechanical function and associated hemodynamics may be the technical limitations causing restricted views from a 2D echocardiographic window. In the case of exercise responses, this may be particularly evident at the LV apex, since the apex has been proposed as an important contributor to exercise responses (in particular in diastolic function) [56, 57, 69]. However, in the echocardiographic images relevant for the measurement of global longitudinal strain, the representation of the apical segments is proportionately small and their contribution to longitudinal strain and strain rate may be underestimated compared with short-axis views [18]. Thus, some of the insight provided by myocardial deformation during exercise in healthy people relates to our more general understanding of cardiac function.

Compared with LV strain, RV longitudinal strain seems to be ~10 percentage points higher in healthy young humans at rest, likely reflecting the different anatomy combined with a lower pulmonary resistance compared with the aorta. Most studies reporting RV strain in healthy individuals during exercise have done so by including healthy controls as comparators to cardiac patients. From those studies, some patterns have emerged that suggest a consistently increased RV longitudinal strain during submaximal exercise in healthy individuals [28, 31, 70]. The mechanisms for this are probably similar to those of the LV, where an increased sympathetic state increases contractility while peripheral (pulmonary) vasodilation decreases downstream resistance [71]. However, during intense exercise, it seems that right ventricular myocardial deformation increases perhaps less than the LV, and it has even been shown to *decrease*. Given that both ventricles should produce approximately the same stroke volume under stable conditions, the lower RV strain during exercise is another indicator that the interaction between the mechanical function of the ventricles and the circulation may depend as much on the local arterial resistance as it may depend on the muscular performance (and therefore health) of the ventricles, and thus fitting the long-standing concept of a greater afterload-sensitivity of the RV. Recent studies in advanced heart failure patients who were surgically implanted with left ventricular assist devices (LVAD) may support this, since the mechanical pumps "unload" the LV and shift blood volume to the rest of the circulation, maybe creating "A Different Kind of Stress Test for the RV" [72, 73]. The accurate measurement of pulmonary and aortic resistance beyond the measurement or estimation of blood pressure is certainly going to elucidate the differential exposure and performance of the two ventricles [74]. At present, it seems that exercise does indeed cause a greater afterload challenge for the RV compared with the LV. In fact, it is worth noting that the exercise modalities used in the studies presented so far in this section have mostly employed "dynamic" exercise (see Section 3.4). In this context, it is essential to point out that this type of exercise increases sympathetic activation of the myocardium and reduces arterial resistance compared with the resting state, therefore creating an environment for the LV (and at low intensities for the RV) that is characterized by reduced afterload. During higher exercise intensities, pulmonary resistance can increase during dynamic exercise and create an augmented afterload challenge [45]. Strength exercise, also called resistance exercise, and isometric handgrip exercise are two other modalities that can provide an afterload challenge for the LV [75]. Interestingly, studies employing these exercise modalities in a number of different populations have consistently shown that the reduced systolic deformation is in part compensated for by an increase in heart rate, but can also be uncoupled from diastolic function [76–79]. Given that resistance exercise produces a very different challenge to dynamic exercise, and that strength training is an important addition to rehabilitation, future research should consider incorporating responses during high resistive efforts [80, 81].

3.3.2 Exercise responses in patients with cardiovascular disease

In a seminal study, Notomi et al. provided mechanistic insight into the complex interdependence between systolic and diastolic function in hypertrophic cardio-myopathy [20]. Although the study used Tissue Doppler Imaging, it is a landmark study that has provided new insight and has popularized the use of exercise testing for both basic science and new insight into cardiac performance in patients. The study revealed that LV twist during exercise was significantly reduced in patients with hypertrophic cardiomyopathy. Similarly, two other studies concluded that systolic deformation reserve is reduced in patients with hypertrophic cardiomy-opathy [82, 83]. However, one challenge in patient populations is that the change in heart rate is often different compared with control groups, and therefore it is possible that the groups experienced different physiological stimuli. This is a recurring problem in exercise studies that currently reduces the confidence in some conclusions. Equally, sometimes the matching of the change in heart rate between groups may lead to unequal workloads or changes in blood pressure, highlighting again the need to interpret myocardial deformation during exercise in the context of general physiological responses. Notwithstanding, the overall trend is that LV myocardial deformation in patients is reduced in response to an acute exercise challenge, including in cardiac amyloidosis, hypertension, cancer, coronary artery disease, as well as in patients with valve disease before and after surgical correc-tion [84–89]. Some subtle observations, however, are worthy of discussion. For example, in patients with microvascular angina, only the subendocardial strain was reduced, and diastolic function during exercise was more severely affected than systolic reserve [90]. Similarly, myocardial regions can respond differently dur-ing exercise in coronary artery disease patients, as shown by differential basal vs. apical rotational mechanics [89]. In an elegant study in patients with hypertrophic cardiomyopathy, Soullier et al. showed that there was significant heterogeneity in the response of the different deformation parameters to exercise, and that resting twist was even increased in patients while diastolic untwisting rate was less affected [83]. In patients with a prior heart transplant, the age of the recipients and donors seem to influence the longitudinal and circumferential strain response to exercise [91, 92]. All these observations highlight the very subtle changes that can occur between parameters, and between systolic and diastolic function. To determine the full significance of such differences should be the focus of future investigations. Furthermore, it will be essential to relate myocardial deformation more often to parameters like cardiac output, to enable the meaningful interpretation of deforma-tion indices and their contribution to the overall capacity of the heart. When this was done in previous studies, the myocardial deformation during exercise provided a clear advancement of our general understanding of the etiology and/or progres-sion of cardiac disease [93].

Because of the prevalence and importance of pulmonary hypertension, and the exercise limitations of heart failure patients, myocardial deformation of the RV during exercise has received heightened attention [94]. Similar to the LV response, the expected increase in RV myocardial deformation during exercise is generally blunted, not just in pulmonary hypertension but also in tetralogy of Fallot, sys-temic sclerosis, and hypertrophic cardiomyopathy [31, 95–97]. Most often, there is clear evidence that pulmonary artery pressures increased disproportionately in the groups that had a blunted increase in RV longitudinal strain during exercise. Importantly, these patients often have normal pulmonary artery pressures at rest, which not only emphasizes the diagnostic value of exercise testing, it also highlights the possibility that patients with suspected LV pathology should be tested for the RV myocardial response to exercise.

3.4 Important practical considerations

Any echocardiographic examination consists of two main parts: (1) the acquisition of standardized echocardiographic images, and (2) the analysis of images for the quantification of relevant parameters [98, 99]. When conducting echocardiography during exercise, both parts require modified approaches to ensure that the conclusions drawn remain valid. Here, based upon our extensive practical experience, we present some "take-home-messages" that we consider essential for the echocardiographic assessment of myocardial deformation during exercises.

- Typically, exercise tests are performed in a stepwise (constant intensity for some minutes, then increasing) or incremental (gradually increasing intensity with every second) manner. Because different protocols provoke different physiological responses, the correct protocol must be selected carefully.

- Exercise responses depend on the *relative* workload of an individual. Therefore, exercise intensities should be adjusted to an individual's anticipated capacity and patients' myocardial deformation interpreted in relation to the relative workload [100].

- The individual adjustment of workload increments during the test should also acknowledge fitness, age, sex, medical history, and acute or chronic injuries.

- For the assessment of myocardial deformation during exercise, running or cycling modalities are the most common. For the reason of improved image quality and because it is relatively safe/feasible, the preferred choice for exercise echocardiography may be supine cycling.

- While it is generally accepted that gentle end-expiratory breath holds can be performed to obtain images, it is preferable to obtain echocardiographic cine loops during free breathing and average some cardiac cycles during inspiration and expiration.

- It is important to distinguish between the physiological demands of different exercise modalities, categorized as: dynamic, static, and impact [101]. Consequently, certain types of exercise can be considered more as an "afterload challenge" than others, and the responses of myocardial deformation may vary greatly between these types of exercise. In this context, the reader is reminded that exercise training interventions for health will need to consider the same complexities, as evidenced by the potential for differential effects of moderate continuous exercise training *versus* high-intensity interval training in some cardiac patients [102].

- One concern with regard to exercise testing is the risk of triggering adverse events. Although this will depend on the specific individual being tested and must be decided by qualified personnel on a case-by-case basis, as evidenced by a comprehensive study performed by Rognmo et al. [103], the overall risk for serious adverse events seems to be relatively low. Particular health and safety precautions should be taken in patients with overt or suspected arrhythmia and the decision "not allowed to perform an exercise test" may have to be taken.

- Standardization of echocardiographic data acquisition during exercise is absolutely necessary. Sonographers should minimize the sector width and

depth, maximize imaging frame rates, only use one focal point and position this in the optimal location, and optimize the overall image to maximize the visibility of the endocardial border for speckle tracking analysis. Although 3D echocardiography may solve some of the limitations of 2D echocardiography, at present the frame rates are too low to obtain the necessary temporal resolution for quantification of myocardial deformation during exercise, although this is expected to change in the near future.

- During exercise, when respiration and heart are increased, the quick location of the optimal echocardiographic window is necessary. Marking up the location on the chest after the resting assessment serves as a "quick help" during exercise. The sonographer must, however, still optimize the image and perhaps move the transducer slightly during exercise.

- Since heart rate increases during exercise but imaging frame rates are already maximized, the effective frame rate (data points per cardiac cycle) decreases. Although this cannot be fully corrected, it seems advisable to perform cubic spline interpolation to attenuate some of these limitations [104]. Note that cubic spline interpolation will not only add points in time (for example for the more confident assessment of dyssynchrony), it also slightly adjusts the peak values.

- Data acquisition immediately following exercise is not the same as "during" exercise. With the cessation of exercise, especially after a strenuous effort with strong muscular contractions, instant changes in whole-body hemodynamics set in [105]. Hence, these data do not reflect an exercise challenge but a "exercise recovery" state.

- For the acquisition of LV twist, apical data must be obtained by moving the transducer close to the point of obtaining a 4-chamber view, otherwise severely misrepresentative data will be collected [24].

4. Summary and conclusions

The assessment of LV and RV myocardial deformation during exercise is feasible and has contributed unique insight into cardiac physiology in health and disease. Inherent methodological challenges require appropriate training and a careful approach to image acquisition, analysis and interpretation. However, ongoing technological advancements and an increasing knowledge suggest that the echocardiographic assessment of myocardial deformation during exercise will play an ever-increasing role in future research and the clinical examination of the cardiac patient.

Acknowledgements

Author details

Eric J. Stöhr[1,2]* and T. Jake Samuel[3]

1 School of Sport and Health Sciences, Cardiff Metropolitan University, Cardiff, UK

2 Division of Cardiology, Advanced Heart Failure Program, Columbia University Irving Medical Center, New York City, USA

3 Department of Kinesiology, University of Texas at Arlington, Texas, USA

*Address all correspondence to: estohr@cardiffmet.ac.uk; ejs2212@cumc.columbia.edu

IntechOpen

References

[1] Buckberg GD. Basic science review: The helix and the heart. The Journal of Thoracic and Cardiovascular Surgery. 2002;**124**(5):863-883

[2] Harvey W, Whitteridge G. Anatomical Disputation Concerning the Movement of the Heart and Blood in Living Creatures. Oxford: Blackwell; 1976

[3] Loukas M, Lam R, Tubbs RS, Shoja MM, Apaydin N. Ibn al-Nafis (1210-1288): The first description of the pulmonary circulation. The American Surgeon. 2008;**74**(5):440-442

[4] Grant RP. Notes on the muscular architecture of the left ventricle. Circulation. 1965;**32**:301-308

[5] Mall P. On the muscular architecture of the ventricles of the human heart. The American Journal of Anatomy. 1911;**11**(3):211-260

[6] Mac Callum JB. On the Muscular Architecture and Growth of the Ventricles of the Heart. Welch Festschrift, Johns Hopkins Hospital Reports1900. p. 9

[7] Robb JS, Robb RC. The normal heart—anatomy and physiology of the structural units. American Heart Journal. 1942;**23**(4):455-467

[8] Greenbaum RA, Ho SY, Gibson DG, Becker AE, Anderson RH. Left ventricular fibre architecture in man. British Heart Journal. 1981;**45**(3):248-263

[9] Streeter DD Jr, Spotnitz HM, Patel DP, Ross J Jr, Sonnenblick EH. Fiber orientation in the canine left ventricle during diastole and systole. Circulation Research. 1969;**24**(3):339-347

[10] Lunkenheimer PP, Redmann K, Niederer P, Schmid P, Smerup M, Stypmann J, et al. Models versus established knowledge in describing the functional morphology of the ventricular myocardium. Heart Failure Clinics. 2008;**4**(3):273-288

[11] Harrington KB, Rodriguez F, Cheng A, Langer F, Ashikaga H, Daughters GT, et al. Direct measurement of transmural laminar architecture in the anterolateral wall of the ovine left ventricle: New implications for wall thickening mechanics. American Journal of Physiology. Heart and Circulatory Physiology. 2005;**288**(3):H1324-H1330

[12] Hsu EW, Muzikant AL, Matulevicius SA, Penland RC, Henriquez CS. Magnetic resonance myocardial fiber-orientation mapping with direct histological correlation. The American Journal of Physiology. 1998;**274**(5 Pt 2):H1627-H1634

[13] Poveda F, Marti E, Gil D, Carreras F, Ballester M. Helical structure of ventricular anatomy by diffusion tensor cardiac MR tractography. JACC: Cardiovascular Imaging. 2012;**5**(7):754-755

[14] Lunkenheimer PP, Niederer P, Sanchez-Quintana D, Murillo M, Smerup M. Models of ventricular structure and function reviewed for clinical cardiologists. Journal of Cardiovascular Translational Research. 2013;**6**(2):176-186

[15] Hooks DA, Trew ML, Caldwell BJ, Sands GB, LeGrice IJ, Smaill BH. Laminar arrangement of ventricular myocytes influences electrical behavior of the heart. Circulation Research. 2007;**101**(10):e103-e112

[16] LeGrice IJ, Smaill BH, Chai LZ, Edgar SG, Gavin JB, Hunter PJ. Laminar structure of the heart: Ventricular

myocyte arrangement and connective tissue architecture in the dog. The American Journal of Physiology. 1995;**269**(2 Pt 2):H571-H582

[17] Sengupta PP, Khandheria BK, Korinek J, Wang J, Jahangir A, Seward JB, et al. Apex-to-base dispersion in regional timing of left ventricular shortening and lengthening. Journal of the American College of Cardiology. 2006;**47**(1):163-172

[18] Stöhr EJ, Stembridge M, Esformes JI. *In vivo* human cardiac shortening and lengthening velocity is region-dependent and not coupled with heart rate: 'longitudinal' strain rate markedly underestimates apical contribution. Experimental Physiology. 2015;**100**(5):507-518

[19] Lunkenheimer PP, Redmann K, Florek J, Fassnacht U, Cryer CW, Wubbeling F, et al. The forces generated within the musculature of the left ventricular wall. Heart. 2004;**90**(2):200-207

[20] Notomi Y, Martin-Miklovic MG, Oryszak SJ, Shiota T, Deserranno D, Popovic ZB, et al. Enhanced ventricular untwisting during exercise: A mechanistic manifestation of elastic recoil described by Doppler tissue imaging. Circulation. 2006;**113**(21):2524-2533

[21] Najafi A, van de Locht M, Schuldt M, Schonleitner P, van Williigenburg M, Bollen I, et al. End-diastolic force pre-activates cardiomyocytes and determines contractile force: Role of titin and calcium. The Journal of Physiology. 2019;**597**(17):4521-4531

[22] Kawano H, Okada R, Yano K. Histological study on the distribution of autonomic nerves in the human heart. Heart and Vessels. 2003;**18**(1):32-39

[23] Nielsen E, Smerup M, Agger P, Frandsen J, Ringgard S, Pedersen M, et al. Normal right ventricular three-dimensional architecture, as assessed with diffusion tensor magnetic resonance imaging, is preserved during experimentally induced right ventricular hypertrophy. Anatomical Record. 2009;**292**(5):640-651

[24] Stöhr EJ, Shave RE, Baggish AL, Weiner RB. Left ventricular twist mechanics in the context of normal physiology and cardiovascular disease: A review of studies using speckle tracking echocardiography. American Journal of Physiology. Heart and Circulatory Physiology. 2016;**311**(3):H633-H644

[25] D'Hooge J, Heimdal A, Jamal F, Kukulski T, Bijnens B, Rademakers F, et al. Regional strain and strain rate measurements by cardiac ultrasound: Principles, implementation and limitations. European Journal of Echocardiography. 2000;**1**(3):154-170

[26] Pastore MC, De Carli G, Mandoli GE, D'Ascenzi F, Focardi M, Contorni F, et al. The prognostic role of speckle tracking echocardiography in clinical practice: Evidence and reference values from the literature. Heart Failure Reviews. 2020

[27] Marwick TH, Shah SJ, Thomas JD. Myocardial strain in the assessment of patients with heart failure: A review. JAMA Cardiology. 2019;**4**(3):287-294

[28] Sanz-de la Garza M, Giraldeau G, Marin J, Imre Sarvari S, Guasch E, Gabrielli L, et al.: Should the septum be included in the assessment of right ventricular longitudinal strain? An ultrasound two-dimensional speckle-tracking stress study. The International Journal of Cardiovascular Imaging. 2019; 35 (10): 1853-1860

[29] Addetia K, Takeuchi M, Maffessanti F, Nagata Y, Hamilton J, Mor-Avi V, et al. Simultaneous

longitudinal strain in all 4 cardiac chambers: A novel method for comprehensive functional assessment of the heart. Circulation. Cardiovascular Imaging. 2016;**9**(3):e003895

[30] Hristov N, Liakopoulos OJ, Buckberg GD, Trummer G. Septal structure and function relationships parallel the left ventricular free wall ascending and descending segments of the helical heart. European Journal of Cardio-Thoracic Surgery. 2006;**29**(Suppl 1):S115-S125

[31] Wu XP, Li YD, Wang YD, Zhang M, Zhu WW, Cai QZ, et al. Impaired right ventricular mechanics at rest and during exercise are associated with exercise capacity in patients with hypertrophic cardiomyopathy. Journal of the American Heart Association. 2019;**8**(5):e011269

[32] Peacock J, Diaz KM, Viera AJ, Schwartz JE, Shimbo D. Unmasking masked hypertension: Prevalence, clinical implications, diagnosis, correlates and future directions. Journal of Human Hypertension. 2014;**28**(9):521-528

[33] Schultz MG, Hare JL, Marwick TH, Stowasser M, Sharman JE. Masked hypertension is "unmasked" by low-intensity exercise blood pressure. Blood Pressure. 2011;**20**(5):284-289

[34] Meah VL, Backx K, Davenport MH. International working group on maternal H: Functional hemodynamic testing in pregnancy: Recommendations of the international working group on maternal hemodynamics. Ultrasound in Obstetrics & Gynecology. 2018;**51**(3):331-340

[35] Meah VL, Cockcroft JR, Stöhr EJ. Maternal cardiac twist pre-pregnancy: Potential as a novel marker of pre-eclampsia. Fetal and Maternal Medicine Review. 2013;**24**(4):289-295

[36] Man J, Foo L, Masini G, McEniery CM, Wilkinson IB, Bennett P, et al. Pre-pregnancy exercise stress testing is related to normal physiological adaptation from pre-pregnancy to mid-pregnancy. Ultrasound in Obstetrics & Gynecology. 2017;**50**(Suppl 1):48-153

[37] Bijl RC, Cornette JMJ, van den Bosch AE, Duvekot JJ, Molinger J, Willemsen SP, et al. Study protocol for a prospective cohort study to investigate hemodynamic adaptation to pregnancy and placenta-related outcome: The HAPPO study. BMJ Open. 2019;**9**(11):e033083

[38] Pieske B, Tschope C, de Boer RA, Fraser AG, Anker SD, Donal E, et al. How to diagnose heart failure with preserved ejection fraction: The HFA-PEFF diagnostic algorithm: A consensus recommendation from the heart failure association (HFA) of the European Society of Cardiology (ESC). European Heart Journal. 2019;**40**(40):3297-3317

[39] Tucker WJ, Haykowsky MJ, Seo Y, Stehling E, Forman DE. Impaired exercise tolerance in heart failure: Role of skeletal muscle morphology and function. Current Heart Failure Reports. 2018;**15**(6):323-331

[40] Dhakal BP, Malhotra R, Murphy RM, Pappagianopoulos PP, Baggish AL, Weiner RB, et al. Mechanisms of exercise intolerance in heart failure with preserved ejection fraction: The role of abnormal peripheral oxygen extraction. Circulation. Heart Failure. 2015;**8**(2):286-294

[41] González-Alonso J, Calbet JA. Reductions in systemic and skeletal muscle blood flow and oxygen delivery limit maximal aerobic capacity in humans. Circulation. 2003;**107**(6):824-830

[42] Helmes M, Lim CC, Liao R, Bharti A, Cui L, Sawyer DB. Titin determines the Frank-Starling relation

in early diastole. The Journal of General Physiology. 2003;**121**(2):97-110

[43] Gonzalez-Alonso J. Point: Stroke volume does/does not decline during exercise at maximal effort in healthy individuals. Journal of Applied Physiology. 2008;**104**(1):275-276; discussion 9-80

[44] Guazzi M, Bandera F, Ozemek C, Systrom D, Arena R. Cardiopulmonary exercise testing: What is its value? Journal of the American College of Cardiology. 2017;**70**(13):1618-1636

[45] La Gerche A, Heidbuchel H, Burns AT, Mooney DJ, Taylor AJ, Pfluger HB, et al. Disproportionate exercise load and remodeling of the athlete's right ventricle. Medicine and Science in Sports and Exercise. 2011;**43**(6):974-981

[46] Schultz MG, Otahal P, Picone DS, Sharman JE. Clinical relevance of exaggerated exercise blood pressure. Journal of the American College of Cardiology. 2015;**66**(16):1843-1845

[47] Park C, Fraser A, Howe LD, Jones S, Davey Smith G, Lawlor DA, et al. Elevated blood pressure in adolescence is attributable to a combination of elevated cardiac output and total peripheral resistance. Hypertension. 2018;**72**(5):1103-1108

[48] Falkner B. Cardiac output versus total peripheral resistance. Hypertension. 2018;**72**(5):1093-1094

[49] Morris RI, Sobotka PA, Balmforth PK, Stöhr EJ, McDonnell BJ, Spencer D, et al. Iliocaval venous obstruction, cardiac preload reserve and exercise limitation. Journal of Cardiovascular Translational Research. 2020

[50] La Gerche A, Claessen G, Van de Bruaene A, Pattyn N, Van Cleemput J, Gewillig M, et al. Cardiac MRI: A new gold standard for ventricular volume quantification during high-intensity exercise. Circulation. Cardiovascular Imaging. 2013;**6**(2):329-338

[51] Beaudry RI, Samuel TJ, Wang J, Tucker WJ, Haykowsky MJ, Nelson MD. Exercise cardiac magnetic resonance imaging: A feasibility study and meta-analysis. American Journal of Physiology. Regulatory, Integrative and Comparative Physiology. 2018;**315**(4):R638-RR45

[52] Celutkiene J, Plymen CM, Flachskampf FA, de Boer RA, Grapsa J, Manka R, et al. Innovative imaging methods in heart failure: A shifting paradigm in cardiac assessment. Position statement on behalf of the heart failure Association of the European Society of cardiology. European Journal of Heart Failure. 2018;**20**(12):1615-1633

[53] Crowe T, Jayasekera G, Peacock AJ. Non-invasive imaging of global and regional cardiac function in pulmonary hypertension. Pulmonary Circulation. 2018;**8**(1):2045893217742000

[54] Donal E, Lund LH, Oger E, Reynaud A, Schnell F, Persson H, et al. Value of exercise echocardiography in heart failure with preserved ejection fraction: A substudy from the KaRen study. European Heart Journal Cardiovascular Imaging. 2016;**17**(1):106-113

[55] Gupta DK, Solomon SD. Imaging in heart failure with preserved ejection fraction. Heart Failure Clinics. 2014;**10**(3):419-434

[56] Doucende G, Schuster I, Rupp T, Startun A, Dauzat M, Obert P, et al. Kinetics of left ventricular strains and torsion during incremental exercise in healthy subjects: The key role of torsional mechanics for systolic-diastolic coupling.

Circulation. Cardiovascular Imaging. 2010;**3**(5):586-594

[57] Stöhr EJ, González-Alonso J, Shave R. Left ventricular mechanical limitations to stroke volume in healthy humans during incremental exercise. American Journal of Physiology. Heart and Circulatory Physiology. 2011;**301**(2):H478-H487

[58] Nio AQX, Rogers S, Mynor-Wallis R, Meah VL, Black JM, Stembridge M, et al. The menopause alters aerobic adaptations to high-intensity interval training. Medicine and Science in Sports and Exercise. 2020

[59] Stöhr EJ, McDonnell B, Thompson J, Stone K, Bull T, Houston R, et al. Left ventricular mechanics in humans with high aerobic fitness: Adaptation independent of structural remodelling, arterial haemodynamics and heart rate. The Journal of Physiology. 2012;**590**(9):2107-2119

[60] Stembridge M, Ainslie PN, Hughes M, Stöhr EJ, Cotter J, Tymko M, et al. Impaired myocardial function does not explain reduced left ventricular filling and stroke volume s0at rest or during exercise at high altitude. Journal of Applied Physiology. 2015;**117**:334-343

[61] Vitiello D, Cassirame J, Menetrier A, Rupp T, Schuster I, Reboul C, et al. Depressed systolic function after a prolonged and strenuous exercise. Medicine and Science in Sports and Exercise. 2013;**45**(11):2072-2079

[62] Williams AM,Shave RE, Coulson JM, White H, Rosser-Stanford B, Eves ND. Influence of vagal control on sex-related differences in left ventricular mechanics and hemodynamics. American Journal of Physiology. Heart and Circulatory Physiology. 2018;**315**(3):H687-HH98

[63] Unnithan VB, Rowland TW, George K, Lord R, Oxborough D. Left ventricular function during exercise in trained pre-adolescent soccer players. Scandinavian Journal of Medicine & Science in Sports. 2018;**28**(11):2330-2338

[64] von Scheidt F, Kiesler V, Kaestner M, Bride P, Kramer J, Apitz C. Left ventricular strain and strain rate during submaximal semisupine bicycle exercise stress echocardiography in healthy adolescents and young adults: Systematic protocol and reference values. Journal of the American Society of Echocardiography. 2020

[65] McEniery CM, Yasmin, Hall IR, Qasem A, Wilkinson IB, Cockcroft JR. Normal vascular aging: Differential effects on wave reflection and aortic pulse wave velocity: The Anglo-Cardiff collaborative trial (ACCT). Journal of the American College of Cardiology. 2005;**46**(9):1753-1760

[66] Burns AT, La Gerche A, Mac Isaac AI, Prior DL. Augmentation of left ventricular torsion with exercise is attenuated with age. Journal of the American Society of Echocardiography. 2008;**21**(4):315-320

[67] Cooke S, Samuel TJ, Cooper SM, Stöhr EJ. Adaptation of myocardial twist in the remodelled athlete's heart is not related to cardiac output. Experimental Physiology. 2018;**103**(11):1456-1468

[68] Lipiec P, Wisniewski J, Kasprzak JD. Should we search for linear correlations between global strain parameters and ejection fraction? European Heart Journal Cardiovascular Imaging. 2014;**15**(11):1301

[69] Stöhr EJ, Gonzalez-Alonso J, Bezodis IN, Shave R. Left ventricular energetics: New insight into the plasticity of regional contributions at rest and during exercise. American Journal of Physiology. Heart and Circulatory Physiology. 2014;**306**(2):H225-H232

[70] Claeys M, Claessen G, Claus P, De Bosscher R, Dausin C, Voigt JU, et al. Right ventricular strain rate during exercise accurately identifies male athletes with right ventricular arrhythmias. European Heart Journal Cardiovascular Imaging. 2020;**21**(3):282-290

[71] Kovacs G, Olschewski A, Berghold A, Olschewski H. Pulmonary vascular resistances during exercise in normal subjects: A systematic review. The European Respiratory Journal. 2012;**39**(2):319-328

[72] Stöhr EJ. Left ventricular assist device therapy - a different kind of stress test for the right ventricle. Med Sci sports Exerc. 2019. In: Symposium Presentation at the 2019 Annual Meeting of the American College of Sports Medicine. p. 48. Available from: https://www.acsm. org/docs/default-source/annual-meeting-documents/acsm-annual-meeting-2019-full-program.pdf? sfvrsn=5f858f5c_12

[73] Houston BA, Kalathiya RJ, Hsu S, Loungani R, Davis ME, Coffin ST, et al. Right ventricular afterload sensitivity dramatically increases after left ventricular assist device implantation: A multi-center hemodynamic analysis. The Journal of Heart and Lung Transplantation. 2016;**35**(7):868-876

[74] Pahuja M, Burkhoff D. Right ventricular afterload sensitivity has been on my mind. Circulation. Heart Failure. 2019;**12**(9):e006345

[75] Samuel TJ, Beaudry R, Haykowsky MJ, Sarma S, Nelson MD. Diastolic stress testing: Similarities and differences between isometric handgrip and cycle echocardiography. Journal of Applied Physiology. 2018;**125**(2):529-535

[76] Balmain B, Stewart GM, Yamada A, Chan J, Haseler LJ, Sabapathy S. The

impact of an experimentally induced increase in arterial blood pressure on left ventricular twist mechanics. Experimental Physiology. 2016;**101**(1):124-134

[77] Weiner RB, Weyman AE, Kim JH, Wang TJ, Picard MH, Baggish AL. The impact of isometric handgrip testing on left ventricular twist mechanics. The Journal of Physiology. 2012;**590**(20):5141-5150

[78] Meah VL, Shave R, Backx K, Stöhr EJ. Cardiovascular responses to increased pressure during healthy pregnancy. Artery Research. 2019;**20**:109-110

[79] Stöhr EJ, Stembridge M, Shave R, Samuel TJ, Stone K, Esformes JI. Systolic and diastolic left ventricular mechanics during and after resistance exercise. Medicine and Science in Sports and Exercise. 2017;**49**(10):2025-2031

[80] Bjarnason-Wehrens B. Recommendations for resistance exercise in cardiac rehabilitation: Do they need reconsideration? European Journal of Preventive Cardiology. 2019;**26**(14):1479-1482

[81] Hansen D, Abreu A, Doherty P, Voller H. Dynamic strength training intensity in cardiovascular rehabilitation: Is it time to reconsider clinical practice? A systematic review. European Journal of Preventive Cardiology. 2019;**26**(14):1483-1492

[82] Badran HM, Faheem N, Ibrahim WA, Elnoamany MF, Elsedi M, Yacoub M. Systolic function reserve using two-dimensional strain imaging in hypertrophic cardiomyopathy: Comparison with essential hypertension. Journal of the American Society of Echocardiography. 2013;**26**(12):1397-1406

[83] Soullier C, Obert P, Doucende G, Nottin S, Cade S, Perez-Martin A, et al.

Exercise response in hypertrophic cardiomyopathy: Blunted left ventricular deformational and twisting reserve with altered systolic-diastolic coupling. Circulation. Cardiovascular Imaging. 2012;**5**(3):324-332

[84] Cusma Piccione M, Zito C, Khandheria B, Madaffari A, Oteri A, Falanga G, et al. Cardiovascular maladaptation to exercise in young hypertensive patients. International Journal of Cardiology. 2017;**232**:280-288

[85] Clemmensen TS, Eiskjaer H, Molgaard H, Larsen AH, Soerensen J, Andersen NF, et al. Abnormal coronary flow velocity reserve and decreased myocardial contractile reserve are main factors in relation to physical exercise capacity in cardiac amyloidosis. Journal of the American Society of Echocardiography. 2018;**31**(1):71-78

[86] Kaneko S, Tham EB, Haykowsky MJ, Spavor M, Khoo NS, Mackie AS, et al. Impaired left ventricular reserve in childhood cancer survivors treated with anthracycline therapy. Pediatric Blood & Cancer. 2016;**63**(6):1086-1090

[87] Kearney MC, Gallop-Evans E, Cockcroft JR, Stohr EJ, Lee E, Backx K, et al. Cardiac dysfunction in cancer survivors unmasked during exercise. European Journal of Clinical Investigation. 2017;**47**(3):213-220

[88] Magne J, Mahjoub H, Dulgheru R, Pibarot P, Pierard LA, Lancellotti P. Left ventricular contractile reserve in asymptomatic primary mitral regurgitation. European Heart Journal. 2014;**35**(24):1608-1616

[89] Peteiro J, Bouzas-Mosquera A, Broullon J, Sanchez-Fernandez G, Barbeito C, Perez-Cebey L, et al. Left ventricular torsion and circumferential strain responses to exercise in patients with ischemic coronary artery disease. The International Journal of Cardiovascular Imaging. 2017;**33**(1):57-67

[90] Cadeddu C, Nocco S, Deidda M, Pau F, Colonna P, Mercuro G. Altered transmural contractility in postmenopausal women affected by cardiac syndrome X. Journal of the American Society of Echocardiography. 2014;**27**(2):208-214

[91] Cifra B, Dragulescu A, Brun H, Slorach C, Friedberg MK, Manlhiot C, et al. Left ventricular myocardial response to exercise in children after heart transplant. The Journal of Heart and Lung Transplantation. 2014;**33**(12):1241-1247

[92] Esch BT, Scott JM, Warburton DE, Thompson R, Taylor D, Cheng Baron J, et al. Left ventricular torsion and untwisting during exercise in heart transplant recipients. The Journal of Physiology. 2009;**587**(Pt 10):2375-2386

[93] Pugliese NR, Fabiani I, Santini C, Rovai I, Pedrinelli R, Natali A, et al. Value of combined cardiopulmonary and echocardiography stress test to characterize the haemodynamic and metabolic responses of patients with heart failure and mid-range ejection fraction. European Heart Journal Cardiovascular Imaging. 2019;**20**(7):828-836

[94] Taylor BJ, Shapiro BP, Johnson BD. Exercise intolerance in heart failure: The important role of pulmonary hypertension. Experimental Physiology. 2020

[95] Bhatt SM, Wang Y, Elci OU, Goldmuntz E, McBride M, Paridon S, et al. Right ventricular contractile reserve is impaired in children and adolescents with repaired tetralogy of Fallot: An exercise strain imaging study. Journal of the American Society of Echocardiography. 2019;**32**(1):135-144

[96] Chia EM, Lau EM, Xuan W, Celermajer DS, Thomas L. Exercise testing can unmask right ventricular

dysfunction in systemic sclerosis patients with normal resting pulmonary artery pressure. International Journal of Cardiology. 2016;**204**:179-186

[97] Bourji KI, Hassoun PM. Right ventricle dysfunction in pulmonary hypertension: Mechanisms and modes of detection. Current Opinion in Pulmonary Medicine. 2015;**21**(5):446-453

[98] Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Journal of the American Society of Echocardiography. 2015;**28**(1):1-39.e14

[99] Harkness A, Ring L, Augustine DX, Oxborough D, Robinson S, Sharma V, et al. Normal reference intervals for cardiac dimensions and function for use in echocardiographic practice: A guideline from the British Society of Echocardiography. Echo Research and Practice. 2020;**7**(1):G1-G18

[100] Armstrong C, Samuel J, Yarlett A, Cooper SM, Stembridge M, Stöhr EJ. The effects of exercise intensity vs. metabolic state on the variability and magnitude of left ventricular twist mechanics during exercise. PLoS One. 2016;**11**(4):e0154065

[101] Levine BD, Baggish AL, Kovacs RJ, Link MS, Maron MS, Mitchell JH, et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task force 1: Classification of sports: Dynamic, static, and impact: A scientific statement from the American Heart Association and American College of Cardiology. Circulation. 2015;**132**(22):e262-e266

[102] Wisloff U, Stoylen A, Loennechen JP, Bruvold M, Rognmo O, Haram PM, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: A randomized study. Circulation. 2007;**115**(24):3086-3094

[103] Rognmo O, Moholdt T, Bakken H, Hole T, Molstad P, Myhr NE, et al. Cardiovascular risk of high-versus moderate-intensity aerobic exercise in coronary heart disease patients. Circulation. 2012;**126**(12):1436-1440

[104] Burns AT, La Gerche A, Prior DL, MacIsaac AI.s Reduced and delayed untwisting of the left ventricle in patients with hypertension and left ventricular hypertrophy: A study using two-dimensional speckle tracking imaging. European Heart Journal. 2008;**29**(6):825-826

[105] Laugshlin MH. Cardiovascular response to exercise. The American Journal of Physiology. 1999;**277**(6 Pt 2): S244-S259