Institute of Cardiology and Sports Medicine

German Sport University Cologne

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Sports-Cardiological Assessment of Cardiac Health in Elite Athletes Using Strain Analysis by Speckle Tracking Echocardiography

Doctoral thesis accepted for the degree

Doktor der Sportwissenschaft

by

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Affidavits following §7 section 2 No. 4 and 5 of the doctoral regulations from the German Sport University Cologne, February 20th 2013:

Hereby I declare:

The work presented in this thesis is the original work of the author except where acknowledged in the text. This material has not been submitted either in whole or in part for a degree at this or any other institution. Those parts or single sentences, which have been taken verbatim from other sources, are identified as citations.

I further declare that I complied with the actual "guidelines of qualified scientific work" of the German Sport University Cologne.

16.03.2025,

Acknowledgment

To my Masa, who said:

“Du machst doch gerne Sport – studier‘ doch vielleicht an der Sporthochschule Köln!“

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Publications of the Dissertation

Zacher, J., Blome, I., Schenk, A. et al. Cardiac adaptations in elite female football- and volleyball-athletes do not impact left ventricular global strain values: a speckle tracking echocardiography study. Int J Cardiovasc Imaging 36, 1085–1096 (2020). Impact Factor 2.4

Zacher, J., Joisten, N., Schmidt, T. et al. Subacute and long-term effects of COVID-19 on cardiac health and function in German elite athletes assessed by strain analysis: a speckle tracking echocardiography observational trial. Sport Sci Health (2024). Impact Factor 1.2

Summary of the Dissertation

Echocardiography is a common and relatively easily accessible diagnostic tool in cardiology and sports cardiology. In recent years the technique of cardiac strain analysis based on speckle tracking echocardiography has emerged and been established as a highly sensitive means of assessing cardiac health and function. Cardiac strain analysis refers to the assessment of stretching and contracting of heart muscle tissue in different dimensions as measured by specifically designed software. It allows for an analysis of myocardial contractility beyond the classical visual assessment by the cardiologist or planimetric ejection fraction measurement. Thus, for example, left ventricular global longitudinal strain (LVGLS) is commonly used in patients undergoing chemotherapy to detect chemotherapy-induced myocardial damage and consecutive loss of function. It has also proved to be a sensitive tool in the differentiation between physiological (i. e. exercise-induced) or pathological (e. g. hypertension-induced) hypertrophy of the walls of the left ventricle.

While well established in classical cardiology, cardiac strain analysis is not as integrated into sports-cardiological day-to-day athlete care. The overall objective of this dissertation was to further the implementation of strain analysis in the practical athlete care by contributing to closing the data gap regarding cardiac strain values in female athletes and by using the technique of strain analysis in the cardiac assessment of elite athletes after having contracted Covid-19 (Coronavirus disease 2019).

Prior studies demonstrated that left ventricular strain values generally did not change in physiological adaptations to exercise but were reduced in pathological hypertrophy. However, research in this field has focused almost solely on male athletes. Thus, one aim of this dissertation was to investigate strain values in the hearts of female elite athletes with a focus on potential effects of myocardial hypertrophy on strain values. To this end a cross-sectional echocardiography study was performed with 19 female elite football players, 16 female elite volleyball players and 16 physically inactive controls. Conventional echocardiographic data was documented as well as left ventricular longitudinal, radial and circumferential strain values gained by speckle tracking echocardiography. The hearts of the female athletes had a thicker septal wall, a larger overall mass and larger atria than the hearts in the control group. Global longitudinal, radial and circumferential strain values did not differ between the athletes and controls or between sporting disciplines. No correlation between septal wall thickness and global left ventricular strain values could be documented. Thus, cardiac adaptations to elite level exercise in female volleyball and football players apparently do not influence global strain values. While prior studies had documented this for male athletes of several disciplines, this study adds to the very limited control-group comparisons of left ventricular strain values in elite female athletes.

A second aim of this dissertation was to assess cardiac health and function in elite athletes who had undergone Covid-19 using strain analysis derived by speckle tracking echocardiography. During the Covid-19 pandemic most elite athletes were infected with the novel Severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). Initial worries of high rates of multi-organ complications including the heart and ending sporting careers were abated by large studies. However, the effects of Covid-19 on the heart and its function in elite athletes remained unclear, especially in the prolonged post-infection follow-up and during and after return to competition. Thus, a cohort of 127 elite athletes (boasting an accumulated 58 Olympic and world championship medals), 76 of them having recently undergone a SARS-CoV-2 infection, were included. Echocardiography including strain analysis was conducted at baseline for all athletes including the control cohort, as well as longitudinally in the Covid-19 cohort. No pathological changes after the infection were documented, but a small yet significant elevation of LVGLS was documented in athletes shortly after the infection in comparison to healthy controls and in comparison to the later follow-up measurements.

The first study of the dissertation demonstrates that cardiac strain values do not seem to be different in female athletes despite sports-related cardiac changes in comparison to non-athletic controls. This is an important step in expanding reference values from non-athletic cohorts and from male athletes to include female athletes. This helps to establish the use of the highly sensitive tool of cardiac strain analysis in the sports-cardiological care of female athletes. The second study of the dissertation uses cardiac strain analysis to demonstrate that elite athletes seem to recover well from Covid-19 without cardiac injury. All documented global longitudinal strain values were within the normal range for athletes. A return to training and competition had no deleterious effect on cardiac health in athletes after Covid-19 in this trial. The slight but significant elevation of LVGLS values in the Covid-19 cohort shortly after infection may be due to a temporary modulation of the autonomic nervous system, which has previously been documented as a result of Covid-19 disease.

In summary, this dissertation and its included studies furthered the understanding of cardiac strain analysis in elite female athletes and the integration of cardiac strain analysis into the everyday athlete care of the sports cardiologist.

Zusammenfassung der Dissertation

Die Echokardiographie ist eine gut etablierte und leicht verfügbare, nicht-invasive diagnostische Methode in der Kardiologie und Sportkardiologie. In den letzten Jahren hat sich die Strainanalyse auf Basis der Speckle-Tracking-Echokardiographie als hochsensitive Technik zur Beurteilung der Herzfunktion und -gesundheit etabliert. Unter *Strainanalyse* versteht man die Messung der Ausdehnung und Verkürzung des Herzmuskelgewebes in verschiedenen Dimensionen mithilfe einer speziell entwickelten Software. Sie ermöglicht eine Analyse der Myokardkontraktilität, die über die klassische visuelle Beurteilung durch den Kardiologen oder die planimetrische Messung der Ejektionsfraktion hinausgeht. So wird beispielsweise der *left ventricular global longitudinal strain* (linksventrikulärer globaler longitudinaler Strain) (LVGLS) standardisiert bei Krebspatienten eingesetzt, um chemotherapiebedingte Myokardschäden und den daraus resultierenden Funktionsverlust frühzeitig zu erkennen. Zudem hat sich die Strainanalyse als sensitives Instrument zur Differenzierung zwischen physiologischer (d. h. trainingsbedingter) und pathologischer (z. B. Bluthochdruck-bedingter) Hypertrophie der Herzwände erwiesen.

Während die Strainanalyse in der klassischen Kardiologie gut etabliert ist, hat sie noch nicht ausreichend Einzug in die Sportkardiologie gehalten. Das erste Ziel dieser Dissertation bestand darin, die Implementierung der Strainanalyse in der praktischen sportkardiologischen Betreuung von Spitzenathleten zu fördern, indem ein Beitrag zur Schließung der bestehenden Datenlücke hinsichtlich der kardialen Strainwerte von Spitzensportler**innen** geleistet wurde.

Bisherige Studien dokumentierten zumeist unveränderte linkventrikuläre Strainwerte bei physiologischer Anpassung an körperliche Belastung, sowie reduzierte Strainwerte bei pathologischer Hypertrophie. Die Forschung auf diesem Gebiet konzentrierte sich bisher jedoch fast ausschließlich auf männliche Sportler. Ein Ziel dieser Dissertation war daher die Untersuchung der linksventrikulären Strainwerte im Herzen weiblicher Spitzensportlerinnen mit Fokus auf mögliche diesbezügliche Effekte einer Sportherzentwicklung. Zu diesem Zweck wurde eine Querschnitts-Echokardiographie-Studie mit 19 Spitzenfußballerinnen, 16 Spitzenvolleyballerinnen und 16 körperlich inaktiven Kontrollprobandinnen durchgeführt. Es wurden konventionelle echokardiographische Parameter sowie linksventrikuläre longitudinale, radiale und zirkumferenzielle Strainwerte mittels Speckle-Tracking-Echokardiographie gemessen und analysiert. Die Herzen der Athletinnen wiesen eine dickere Septumwand, eine größere Gesamtmasse und größere Vorhöfe auf als die Herzen der Kontrollgruppe. Die globalen longitudinalen, radialen und zirkumferenziellen Strainwerte unterschieden sich weder zwischen den Sportlerinnen und der Kontrollgruppe, noch zwischen den Sportdisziplinen. Es konnte keine Korrelation zwischen einer Septumhypertrophie und den linksventrikulären Strainwerten nachgewiesen werden. Somit haben kardiale Anpassungen an Spitzensport bei Volleyball- und Fußballathletinnen offenbar keinen Einfluss auf die linksventrikulären Strainwerte. Während frühere Studien dies bereits wiederholt für männliche Athleten verschiedener Disziplinen dokumentiert hatten, verbessert diese Studie die sehr begrenzte Datenlage zu linksventrikulären Strainwerten bei Spitzensportlerinnen.

Ein zweites Ziel dieser Dissertation war der Einsatz der myokardialen Strainanalyse zur Beurteilung der Herzgesundheit und -funktion bei Spitzensportlern, die eine Covid-19-Erkrankung durchgemacht hatten. Während der Covid-19-Pandemie infizierten sich auch die meisten Spitzensportler mit dem *Severe acute respiratory syndrome coronavirus type 2* (SARS-CoV-2). Anfängliche Sorgen in der Sportmedizin, dass in großem Umfang Karrieren von Spitzensportlern durch eine Infektion mit Multiorgankomplikationen beendet werden würden, konnten im Verlauf durch groß angelegte Studien weitestgehend zerstreut werden. Die genauen Auswirkungen von Covid-19 auf das Herz und seine

Funktion bei Spitzensportlern blieben jedoch weiterhin unklar, insbesondere im mittel- und längerfristigen postinfektiösen Intervall, sowie im Kontext der Rückkehr zu Training und Wettkampf. Daher wurde eine Kohorte von 127 Spitzensportlern (mit insgesamt 58 Olympia- und Weltmeisterschaftsmedaillen) inkludiert, von denen 76 eine SARS-CoV-2-Infektion durchgemacht hatten. Eine Echokardiographie einschließlich Strainanalyse wurde zu Studienbeginn bei allen Athleten, einschließlich der bis dato nicht infizierten Kontrollkohorte, sowie longitudinal bei der Covid-19-Kohorte durchgeführt. Es wurden keine pathologischen Veränderungen nach der Infektion dokumentiert, jedoch wurde bei Sportlern kurz nach der Infektion im Vergleich zu gesunden Kontrollathleten und im Vergleich zu den späteren Nachuntersuchungen eine kleine, aber signifikante Erhöhung der LVGLS-Werte dokumentiert.

Die erste Studie dieser Dissertation zeigt, dass sich die linksventrikulären globalen Strainwerte in einer kleinen Kohorte aus Spitzensportlerinnen trotz sonstiger signifikanter, sportassoziierter myokardialer Anpassungen im Vergleich zu einer nicht-sportlichen Kontrollgruppe nicht zu unterscheiden scheinen. Dies ist ein wichtiger Schritt zur Ausweitung der Referenzwerte aus der Allgemeinbevölkerung und von männlichen Athleten auf Sportlerinnen. Dies trägt dazu bei, den Einsatz des hochsensitiven Instruments der kardialen Strainanalyse in der sportkardiologischen Versorgung von Spitzenathletinnen zu etablieren. Die zweite Studie der Dissertation nutzt die Strainanalyse um zu demonstrieren, dass sich Spitzensportler in der Regel ohne myokardiale Folgeschäden von einer Covid-19-Erkrankung erholen. Alle in dieser Kohorte dokumentierten globalen longitudinalen Strainwerte lagen im für Sportler normalen Bereich. Die Rückkehr zu Training und Wettkampf hatte in dieser Studie keine negativen Auswirkungen auf die Herzgesundheit von Sportlern nach Covid-19. Der dezente signifikante Anstieg der LVGLS-Werte in der Covid-19-Kohorte kurz nach der Infektion könnte auf eine vorübergehende Modulation des autonomen Nervensystems zurückzuführen sein, was in anderen Studien als mögliche Folge einer Covid-19-Erkrankung dokumentiert wurde.

Zusammenfassend lässt sich sagen, dass diese Dissertation und die darin enthaltenen Studien das Verständnis der myokardialen Strainanalyse bei weiblichen Spitzensportlerinnen verbessert und die Integration der Strainanalyse in die alltägliche sportkardiologische Athletenbetreuung gefördert haben.

Abbreviations

2D-STE	2-dimensional speckle tracking echocardiography
AVC	aortic valve closure
AH	athlete's heart
BSA	body surface area
C	controls
CON	elite athletes in the control group without prior SARS-CoV-2 infection
COV	elite athletes with prior SARS-CoV-2 infection
Covid-19	Coronavirus disease 2019
EF	ejection fraction
FP	football players
GCS	global circumferential strain
GLS	global longitudinal strain
GRS	global radial strain
IVSd	interventricular septum diameter in diastole
LV	left ventricle
LVEF	left ventricular ejection fraction
LVGLS	left ventricular global longitudinal strain
LVPWd	left ventricular posterior wall in diastole
LVSV	left ventricular stroke volume
LVVED	left ventricular volume end diastolic
MRI	magnetic resonance imaging
Publication 1	The first publication included in this dissertation
Publication 2	The second publication included in this dissertation
RVDl	right ventricular diastolic length
SARS-CoV-2	Severe acute respiratory syndrome coronavirus type 2
T0	measurement time-point 1 month after SARS-CoV-2 infection
T1	measurement time-point 4 months after SARS-CoV-2 infection
T2	measurement time-point 8 months after SARS-CoV-2 infection
VP	volleyball players

Images

Image 1: Anatomical image of the heart with visualized planes of echocardiographic image acquisition.

Image 2: Left: Apical 4-chamber view of the heart. Right: Transverse image of the left ventricle in the parasternal short axis at the level of the papillary muscles.

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Image 6: Measurement of left ventricular longitudinal strain in a 4-chamber view. The image at the bottom left depicts the peak systolic strain per segment of myocardium. The image at the top right depicts the systolic strain over time; note the high level of synchronicity of the colored lines (each representing one myocardial segment) with a synchronous strain peak at the moment of aortic valve closure (AVC). Bottom right: Color-coded strain values over time.

Image 7: Parasternal short axis transverse view of the left ventricle at the level of the papillary muscles. The strain analysis depicts regional peak radial strain values per segment (bottom left); radial strain throughout the selected cardiac cycle for each segment (line graph, top right; color-coded, bottom right).

Image 8: Bull's eye view (bottom right) of left ventricular longitudinal strain, depicted for each segment (LV-apex in the center, LV-base in the periphery), derived by averaging all apical peak longitudinal strain measurements as shown in the three line graphs representing the 4-chamber (top left), 2-chamber (top right) and 3-chamber (bottom left) view measurements.

Introduction

Objective of the Dissertation

Sports-medical and sports-cardiological athlete care is one of the key functions of the Institute of Cardiology and Sports Medicine at the German Sport University Cologne. The day-to-day care of elite athletes -incorporating the expertise of sports scientists and medical specialists in internal medicine, sports medicine, orthopaedics and cardiology- ranges from routine pre-participation screenings and preventive measures to the acute diagnostic and therapeutic support of athletes during and after illness or injury. Echocardiography (see chapter *Echocardiography* for details) plays a key role in this task. One function of modern echocardiography machines and the software therein is cardiac strain analysis by speckle tracking echocardiography, which allows for the assessment of different aspects of the function of the heart muscle using automated programs (see chapter *Speckle Tracking Echocardiography and Strain Analysis* for details). While this technique is by now relatively well incorporated into classical cardiology and patient care, its integration into sports cardiology is less well established. One reason for this has been the lack of sports-specific research regarding the technique: The heart of the athlete may differ from non-athletic persons (see chapter *Athlete's heart* for details), making the transfer of well-established reference ranges for different cardiac measurements from the general population to the cohort of elite athletes difficult. This has, for example, been recognized and compensated by specific research in athletes regarding myocardial hypertrophy, so that the wall thickness and chamber dimensions in the hearts of athletes are assessed against different reference values than the hearts of non-athletes. To allow for this kind of specific use of the tool of cardiac strain analysis in the elite athlete population many evidence gaps need to be closed and its implementation in the day-to-day athlete care practiced. Thus, the objective of this dissertation is to contribute to collecting data in female elite athletes -as most of the limited data sets focus on male athletes- and to integrate the technique into the practical athlete care in the controlled setting of a prospective study. To this end, primarily a cross-sectional study was initiated comparing the hearts of elite female football and volleyball athletes to non-athletic controls. The extensive echocardiographic assessment included different types of left ventricular strain analysis. As the Covid-19 pandemic developed shortly thereafter, the necessity to closely monitor the cardiac health of elite athletes during and after the initial infection allowed for the integration of cardiac strain analysis into the practical day-to-day athlete care. Thus, the second study for this dissertation was designed to focus on a cross-sectional comparison between athletes after Covid-19 disease in comparison to healthy control athletes without prior infection, as well as on a longitudinal follow-up assessment of cardiac strain values in the weeks and months after the infection. Based on these studies, this dissertation aimed to further the understanding of cardiac strain analysis in elite athletes as well as its implementation into the practical sports-cardiological care of these elite athletes.

Echocardiography

In 1954 the use of ultrasound to assess the function of the heart was scientifically documented for the first time by Swedish cardiologist Inge Edler and German physicist Carl Hertz, thus creating the technique of echocardiography [1]. Since then echocardiography has developed into one of the most important diagnostic tools in cardiology, allowing for a multitude of non-invasive insights into the human heart, its function and the assessment of its health. Generally, ultrasound in medicine refers to a technique of detecting tissues of different densities by sending out ultrasound waves from a probe and measuring the time and intensity of their return to said probe. Thus, morphological images and changes therein over time can be visualized, allowing for the detection of the exact position of organs and -where applicable- their movement [2]. By directing and receiving ultrasound waves from different positions and in different planes throughout the heart, an accurate anatomical depiction can be created. Image 1 shows a picture of a human heart partly including large veins and arteries. The three planes in blue, green and purple depict the standard approaches when conducting echocardiography. The images used for the left ventricular global longitudinal, radial and circumferential strain measurements that play a key role in this dissertation are acquired in the short axis and apical planes.

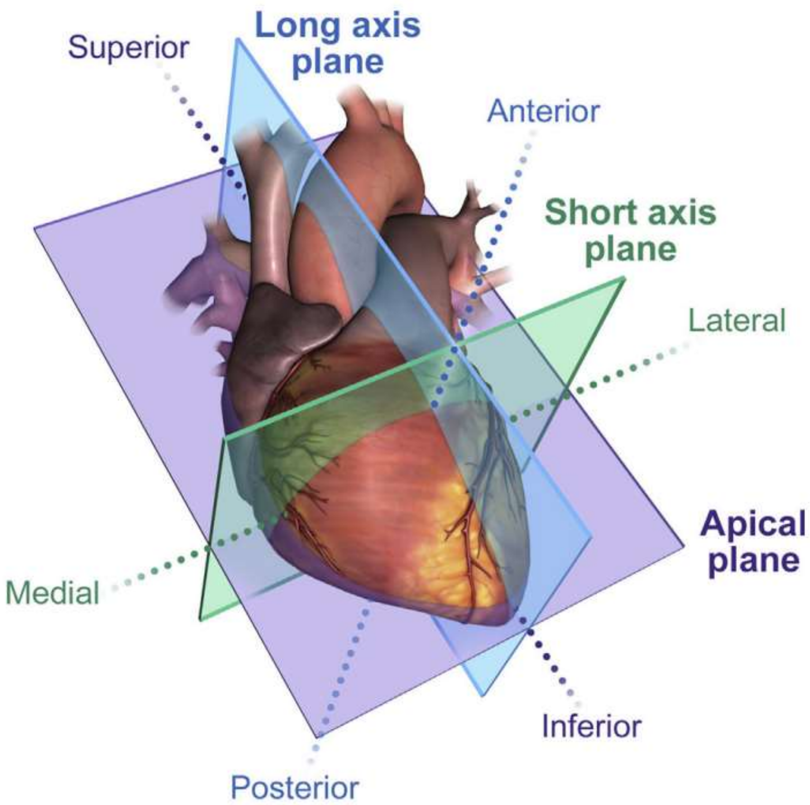

Image 1: Anatomical image of the heart with visualized planes of echocardiographic image acquisition. Source: Adapted with permission from [3].

Image 2 shows a so called 4-chamber view on the left, which is acquired from an apical perspective (the ultrasound probe rests on the torso directly above the apex of the left ventricle, i. e. the tip of the heart) and a transverse image of the left ventricle on the right obtained in the so called parasternal short axis; for this the ultrasound probe rests to the left of the sternum near its middle.

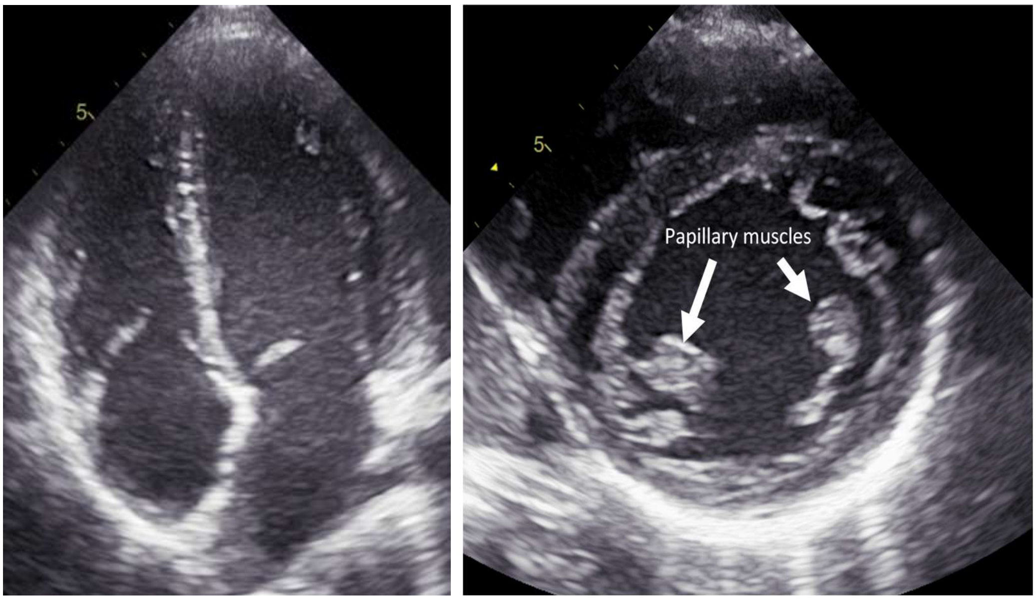

Image 2: Left: Apical 4-chamber view of the heart. Right: Transverse image of the left ventricle in the parasternal short axis at the level of the papillary muscles. Source: Own images.

The assessment of cardiac form and function includes valve function, measurements of pressures in and dimensions of cardiac chambers, as well as myocardial kinetics. Classically, the “ejection fraction” (EF) is the main parameter of assessing left ventricular systolic function: It is defined as the percentage of blood volume ejected from the left ventricle during one cardiac contraction; reference ranges are 52-72% (male) and 54-74% (female) [4]. It is usually acquired based on the changes of the endocardial border of the left ventricle between diastole and systole, thus allowing for the calculation of a delta regarding the left ventricular blood volume. Image 3 shows an apical 4-chamber view in diastole (left, with the area of the left ventricle marked in green) and in systole (right, with the area of the left ventricle marked in blue). Thus, a delta in the area can be calculated, which in turn can be used to calculate the ejection fraction. To achieve a higher degree of accuracy this can be done in two dimensions (2- and 4-chamber views) or in 3 dimensions (2-, 3- and 4-chamber views).

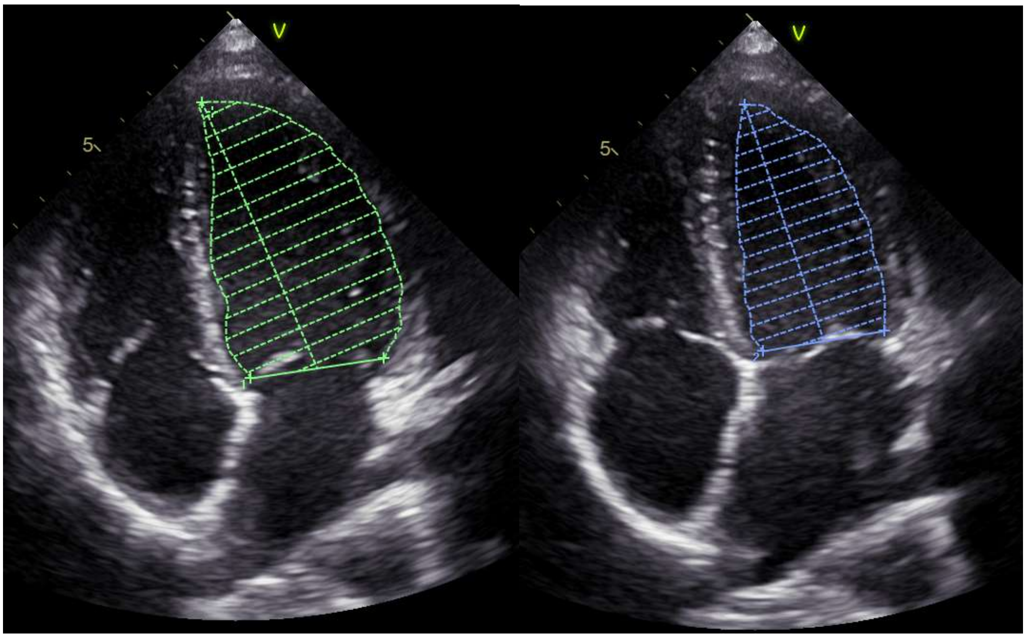

Image 3: Apical 4-chamber view with marked area of the interior of the left ventricle in diastole (left, green) and systole (right, blue). Source: Own images.

Speckle Tracking Echocardiography and Strain Analysis

Cardiac strain describes the deformation of the heart muscle while contracting and relaxing during systole and diastole. Left ventricular longitudinal strain is the “shortening” of the left ventricle measured from base to peak in percent, thus resulting in a negative value in a healthy heart, for example “-19.5%”. Circumferential strain describes myocardial “shortening” in percent in a circular manner in the short axis, while radial strain measures the “thickening” of the myocardium during contraction in the short axis. Longitudinal and circumferential strain values are stated as negative percent to portray a “shortening”, while radial strain is stated as a positive value, as it describes a “thickening” [5, 6] (see image 4). In this dissertation and the studies on which it is based strain values are documented and discussed as absolute values (e. g. |-19.5%|) to avoid misunderstandings. For example: A change from -19.5% to -20.5% would formally have to be described as a “reduction”; however, using absolute values a change in left ventricular longitudinal strain from |-19.5%| to |-20.5%| can correctly be described as an “increase” in left ventricular strain, which is the relevant information, as the delta -in this case the degree of “shortening”- is greater at “-20,5%” than at “-19.5%”.

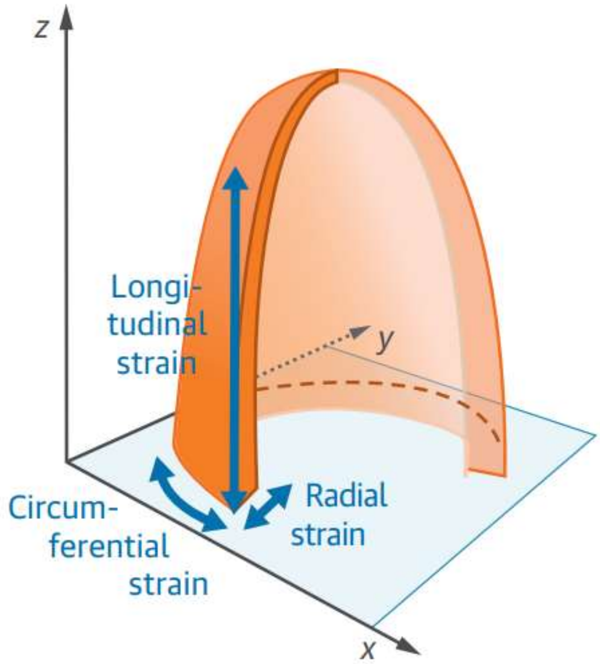

Image 4: A schematic depiction of a left ventricle, demonstrating the vectors of the three types of strain. Source: Adapted with permission from [7].

These strain values are calculated by computer programs that track individual speckles (or "dots") in the myocardium during a cardiac cycle and asses the changes of the distance between them (see image 5). Image 5 visualizes the technique of speckle tracking: The grainy image of the heart is the result of many small speckles, which are more clearly discernable in the smaller close-up images. The speckle tracking software logs onto many of these speckles at a certain point in the cardiac cycle and follows each throughout the cycle (i. e. from relaxation in the diastole through contraction in systole back to relaxation). Thus, the software can calculate changes in myocardial length and thickness based on changes in the locations of many of these speckles, enabling an assessment of cardiac activity in greater detail and more dimensions than classical ejection fraction via biplane area assessment.

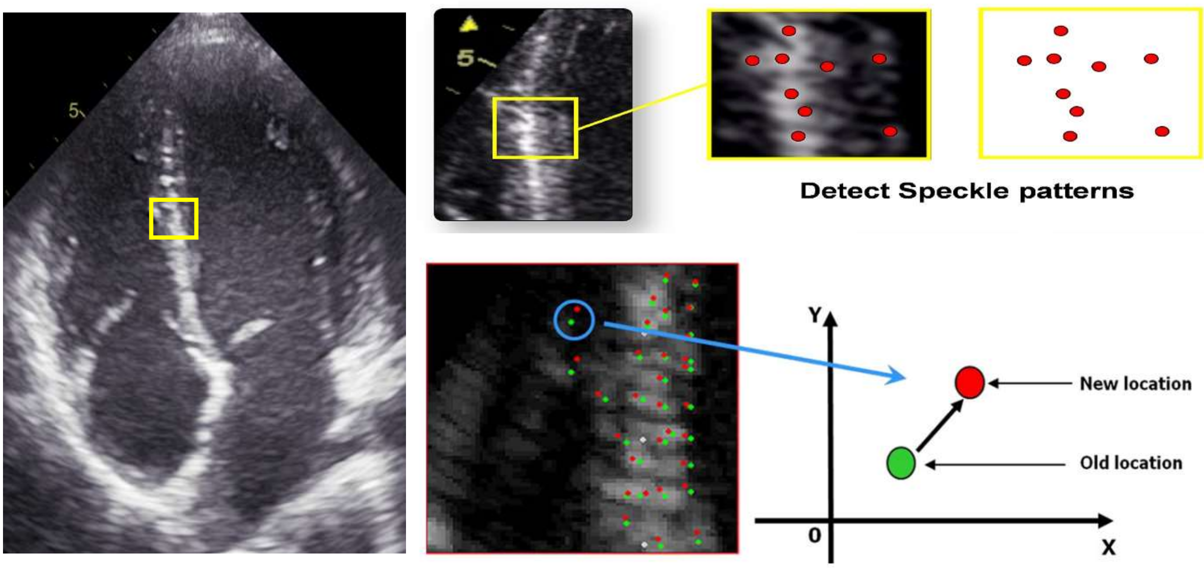

Image 5: Left: Apical 4 chamber view with selected myocardium of the septum (yellow box). Source: Own image. Right top: Visualization of automated speckle selection in area of myocardium. Right bottom: Visualization of automated tracking of change in location of each speckle. Source: Images adapted with permission from [8, 9].

Echocardiographic images are acquired in apical 3-chamber, 2-chamber and 4-chamber views for longitudinal strain values and in the parasternal short axis at the level of papillary muscles for circumferential and radial strain values. Automated speckle tracking with strain analysis is performed for different segments. This is demonstrated in image 6 for the longitudinal strain of the left ventricle in a 4-chamber view (see image 6) and in image 7 for a parasternal short axis view of the left ventricle (see image 7).

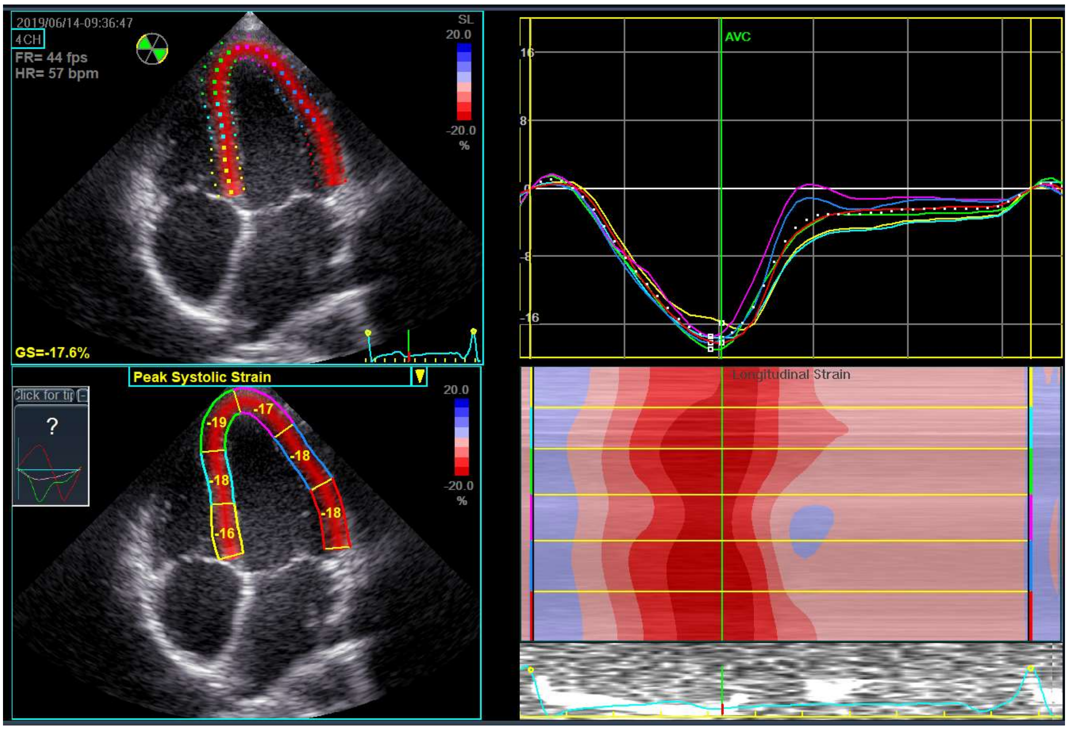

Image 6: Measurement of left ventricular longitudinal strain in a 4-chamber view. The image at the bottom left depicts the peak systolic strain per segment of myocardium. The image at the top right depicts the systolic strain over time; note the high level of synchronicity of the colored lines (each representing one myocardial segment) with a synchronous strain peak at the moment of aortic valve closure (AVC). Bottom right: Color-coded strain values over time. Source: Own image.

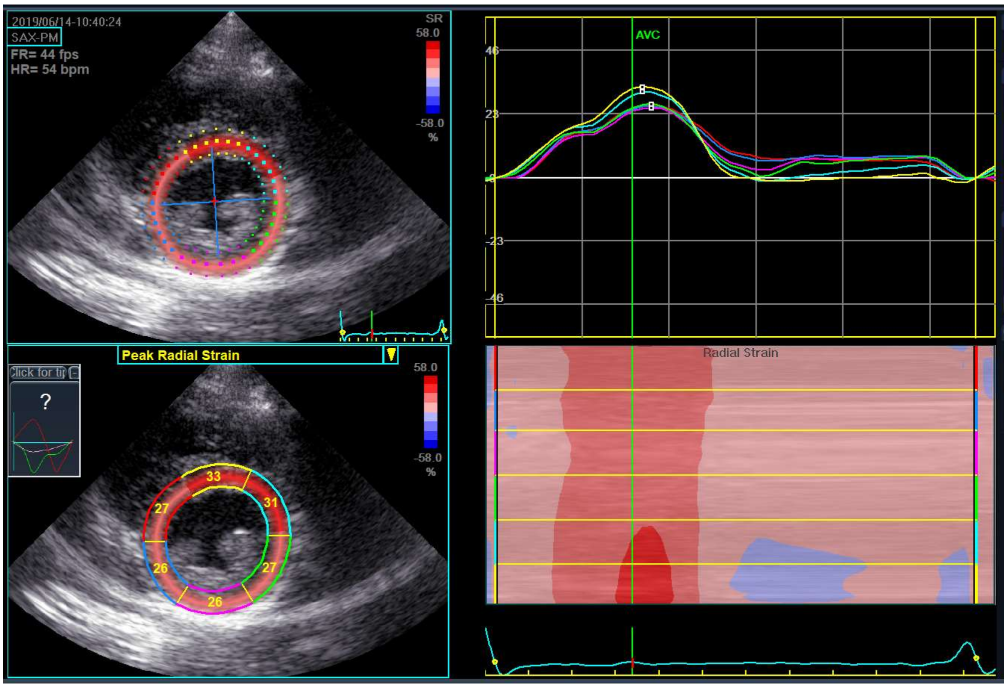

Image 7: Parasternal short axis transverse view of the left ventricle at the level of the papillary muscles. The strain analysis depicts regional peak radial strain values per segment (bottom left); radial strain throughout the selected cardiac cycle for each segment (line graph, top right; color-coded, bottom right). Source: Own image.

The measurements for the separate segments can be combined and expressed as "global strain", which can represent the entire left ventricle in the form of the "left ventricular global longitudinal strain" (LVGLS). All segments of the left ventricular longitudinal strain are summarized in the so called "bull's eye". This is demonstrated in image 8: In the two top and bottom left images the change in length of the left ventricle as calculated by changes in speckle positions is shown in "%" on the y-axes, while the x-axes represent the timeline of the cardiac cycle. The different colors of the lines represent different myocardial segments. Thus, the high degree of synchronicity between the different myocardial segments is evident based on the high level of synchronicity of the different colored lines throughout the cardiac cycle; it is the synchronous pattern of contraction and relaxation of a healthy left ventricle. The red disc in the bottom right image is the afore-mentioned "bull's eye", which shows the peak systolic strain (highest degree of "shortening" in "%") of all myocardial segments throughout the cardiac cycle, the center representing the apical segments, the border the basal segments and the fields in between the medial segments.

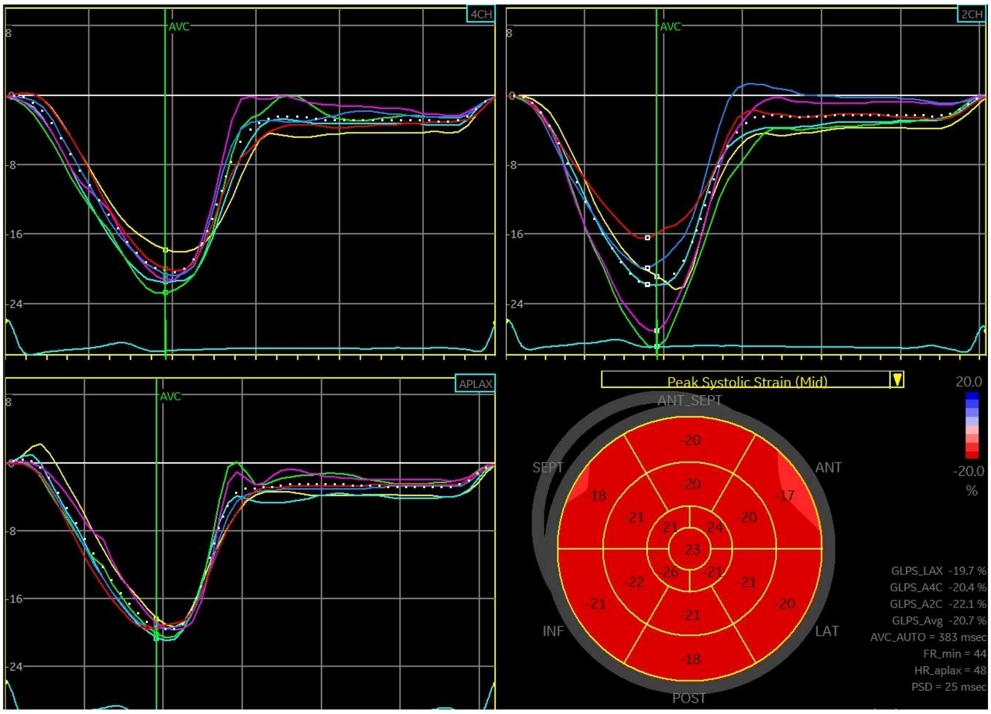

Image 8: Bull's eye view (bottom right) of left ventricular longitudinal strain, depicted for each segment (LV-apex in the center, LV-base in the periphery), derived by averaging all apical peak longitudinal strain measurements as shown in the three line graphs representing the 4-chamber (top left), 2-chamber (top right) and 3-chamber (bottom left) view measurements. Source: Own image.

Speckle tracking echocardiography has been demonstrated to be a reliable tool for detecting subclinical myocardial changes in several pathologies ([10, 11]) and LVGLS is a better reproducible measure of left ventricular function than ejection fraction [12]. Inter- and intra-observer variability of LVGLS is comparable to the classical planimetric measurement of ejection fraction, while variability is somewhat higher for radial and circumferential strain measurements [5]. Cardiac strain analysis is also more sensitive to changes in heart function than classical parameters like ejection fraction. While reference ranges for "normal" strain values in the general (and athlete) population remain to be defined (due to many influencing factors), past publications tend to agree that a healthy left ventricle should produce global longitudinal strain values of > |-18%| ± 2% [6, 13–15].

Cardiac Adaptations to Exercise: The "Athlete's Heart"

Structural and functional cardiac adaptations to physical activity as performed by elite athletes are a well-studied phenomenon. Athlete's heart (AH), an enlargement of cardiac chambers and dimensions, usually accompanied by physiological myocardial hypertrophy, as a reaction to high training volumes has been the focus of intense research [16–18]. Especially high volumes and intensities of endurance training, associated with high levels of transported blood volumes and elevated intracardiac pressures, appear to be the stimulus for the development of athlete's heart. The described adaptations allow for a larger stroke volume and thus – as maximal heart rates are not reduced in athletes in comparison to non-athletes – to a significantly larger cardiac output when exercising [17]. While these adaptations are well studied and largely well understood (even though many gaps in knowledge remain), the hearts of female athletes have been somewhat neglected in research in comparison to the large number of studies focusing on the hearts on male athletes. Thus, when Morganroth et. al described the athlete's heart in different types of sports 50 years ago, only male athletes were included in the analysis [18]. While women make up roughly 50% of the participants in sports in the United States of America today

([17]), their underrepresentation in the scientific research in sports cardiology remains a phenomenon [19]. Despite this, understanding of the female athlete's heart has increased in the last decades, resulting in the insight that similar adaptations take place in the hearts of female athletes with high training volumes, but some of these adaptations are less frequent and less pronounced (e. g. significant hypertrophy) [19].

Echocardiographic Strain Analysis in Athletes

The effects of exercise on a recreational and competitive level on myocardial strain patterns have been the focus of several studies. Global strain values generally did not change in physiological adaptations to exercise but were reduced in pathological hypertrophy [6, 20, 21]. Even though results vary between studies, large reviews and meta-analyses reach the conclusion that LVGLS should not normally be reduced in athletes compared to controls, even when physiological hypertrophy is present [6, 22]. Thus, strain analysis is a helpful tool for differentiating between physiological adaptations to exercise and pathological entities with an increased potential for sudden cardiac death such as hypertrophic cardiomyopathy [23]. Regarding global circumferential strain (GCS) and global radial strain (GRS) studies are even fewer but may indicate differences between certain athletic populations and controls [22].

However, these insights are derived almost solely from data of male athletes. The few studies including female athletes usually analyze the whole athlete cohort without sub-analysis by sex, fail to specify sporting disciplines or include very few female athletes. The largest cohort of female athletes at the time of the first publication of this dissertation (*Publication 1*) was included by Caselli et al. (n=78/200), who found that the LVGLS was slightly higher in females (athletes and controls) compared to males [24]. Sporting disciplines were not specified exactly. In the same year D'Ascenzi et al. reported no difference in LVGLS when analyzing 36 female and 55 male athletes from different sporting disciplines [14]. D'Ascenzi et al. also published left ventricular strain data of 24 female volleyball players in a study focused on atrial and right ventricular strain [25]. To the author's knowledge at the time of *Publication 1* less than 150 cases of 2D-STE (2-dimensional speckle tracking echocardiography) derived left ventricular strain of female athletes have been published from controlled studies collectively. Also, regarding female athletes most athletic disciplines have been left untouched or not been specifically reported.

Echocardiographic Strain Analysis and Covid-19

During the Covid-19 pandemic most people, including elite athletes, suffered an infection with the novel Severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). While the primary symptoms of the disease and thus the diagnostic and therapeutic focus initially lay on the respiratory tract, the potentially systemic nature of Covid-19 quickly became apparent [26]. Though most patients recover fully, a subgroup presents with a wide variety of prolonged symptoms, often including reduced exercise capacity. The mechanisms as well as the role of exercise in the recovery after Covid-19 remain unclear and thus the focus of recent research [27].

Myocardial Involvement of Covid-19 in the General Population

Early data mainly from hospitalized patients from the general population demonstrated often severe systemic disease including myocardial injury in Covid-19 patients [28]. Echocardiographic assessment soon showed that left ventricular global longitudinal strain (LVGLS) was reduced in many of these patients [29, 30]. An MRI (magnetic resonance imaging) meta-analysis including almost 3000 adult individuals after contracting Covid-19 found greatly varying documentation of inflammatory and post-inflammatory signs; overall the findings differed greatly from healthy controls without prior Covid-19 infection, where hardly any such signs were detected [31].

Myocardial Involvement of Covid-19 in Athletes

While LVGLS data measured by speckle tracking echocardiography in athletes after a SARS-CoV-2 infection is still relatively scarce at the time of the second publication of this dissertation (*Publication 2*), the host of MRI-data is somewhat more abundant. First studies assessing myocardial involvement in athletes suggested higher rates of myocardial inflammation than generally expected from known viral agents: An early MRI-study detected signs of myocardial inflammatory involvement in roughly 1/3rd of a cohort of 54 student athletes after SARS-CoV-2 infection [32]. A multicenter analysis of ~ 1600 college athletes after Covid-19 disease diagnosed clinical or subclinical myocarditis in 37 athletes (2,3%) including the diagnostic tool of MRI, but not strain analysis [33]. An MRI-study of 147 highly trained athletes after Covid-19 infection found signs of myocarditis in 1.4% of cases. No significant differences regarding MRI-derived GLS were detected in the whole cohort in comparison to an athletic control group [34]. In a cohort of 107 college athletes assessed by speckle tracking echocardiography after a SARS-CoV-2 infection no differences in GLS, GCS or GRS were reported [35].

Prolonged data collection in the later stages of the pandemic and larger trials did, however, indicate milder symptomatic disease with very little relevant myocardial injury and with good recovery in athletes. In the largest study to date at the time of *Publication 2* assessing 789 professional athletes after a Covid-19 infection only 20 demonstrated echocardiographic abnormalities and only 5 athletes ended up presenting with inflammatory aspects in cardiac MRI. However, even though screening included echocardiography in many cases, this data was only reported in athletes with any abnormal findings [36]. Casasco et al. observed 4143 Italian athletes after a Covid-19 infection and found myocarditis in only 0.12%; myocardial strain data was not reported [37].

Most recently, Schellenberg et al. reported lower LVGLS values in athletes after Covid-19 when compared in a cross-sectional fashion to healthy controls; despite the difference all values were within the range currently defined as normal [38].

Aims of the Dissertation

1. To further the understanding of speckle tracking echocardiography-derived strain analysis of the left ventricle as a diagnostic tool in female athletes. Data prior to this publication was focused almost exclusively on male athletes. By analyzing strain data in elite female football- and volleyball-athletes and comparing results to non-trained controls the included study aimed to assess whether exercise induced cardiac adaptations influence left ventricular strain values in healthy female athletes.

2. To apply the highly sensitive diagnostic tool of speckle tracking echocardiography-derived strain analysis in sports cardiology to detect potential myocardial effects of a SARS-CoV-2 infection in elite athletes. To attain a comprehensive understanding of the subacute and longer-term cardiac health of elite athletes after Covid-19 a baseline comparison to healthy control athletes was conducted as well as a longitudinal assessment up to eight months after the infection.

Publications of the Dissertation

Cardiac adaptations in elite female football- and volleyball-athletes do not impact left ventricular global strain values: a speckle tracking echocardiography study

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ORIGINAL PAPER

Cardiac adaptations in elite female football- and volleyball-athletes do not impact left ventricular global strain values: a speckle tracking echocardiography study

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Abstract

Cardiac adaptations to exercise on an elite level have been well studied. Strain analysis by speckle tracking echocardiography has emerged as a tool for sports cardiologists to assess the nature of hypertrophy in athletes' hearts. In prior studies, strain values generally did not change in physiological adaptations to exercise but were reduced in pathological hypertrophy. However, research in this field has focused almost solely on male athletes. Purpose of the present study is to investigate strain values in the hearts of female elite athletes in football and volleyball. In this cross-sectional study echocardiography was performed on 19 female elite football-players, 16 female elite volleyball-players and 16 physically inactive controls. Conventional echocardiographic data was documented as well as left ventricular longitudinal, radial and circumferential strain values gained by speckle tracking echocardiography. The hearts of the female athletes had a thicker septal wall, a larger overall mass and larger atria than the hearts in the control group. Global longitudinal, radial and circumferential strain values did not differ between the athletes and controls or between sporting disciplines. No correlation between septal wall thickness and global strain values could be documented. Cardiac adaptations to elite level exercise in female volleyball and football players do not influence global strain values. This has been documented for male athletes of several disciplines. The present study adds to the very limited control-group comparisons of left ventricular strain values in elite female athletes. The findings indicate that global strain values can be used when assessing the cardiac health in female athletes.

Keywords Speckle tracking echocardiography · Strain analysis · Athlete's heart · Exercise · Sports cardiology

See *Appendix* for full publication.

Subacute and long-term effects of COVID-19 on cardiac health and function in German elite athletes assessed by strain analysis: a speckle tracking echocardiography observational trial

Sport Sciences for Health
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RESEARCH

Subacute and long-term effects of COVID-19 on cardiac health and function in German elite athletes assessed by strain analysis: a speckle tracking echocardiography observational trial

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Abstract

Introduction During the COVID-19-pandemic, most elite athletes were infected with the novel severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2). Initial worries of high rates of multi-organ complications including the heart and ending sporting careers were disproved by large studies. However, the effects of COVID-19 on the heart and its function in elite athletes remains unclear, especially in the prolonged post-infection follow-up and during and after return to competition.

Methods In the year 2020, a cohort of 127 elite athletes (boasting an accumulated 58 Olympic and world championship medals) was recruited, 76 of them recently having undergone a SARS-CoV-2 infection. Echocardiography was conducted 1 (T0), 5 (T1) and 9 (T2) months after the infection in the infected cohort and at baseline for the control cohort. Left-ventricular global longitudinal, circumferential, and radial strain was compared cross-sectionally at baseline between athletes after a COVID-19-infection and control athletes, as well as longitudinally in the COVID-19-cohort.

Results At baseline, global longitudinal strain (reported as absolute %-values) was significantly higher in the COVID-19-cohort in comparison to control-cohort (20.37 ± 1.98% vs. 19.41 ± 2.11%, respectively, $p = 0.042$). In the longitudinal assessment within the COVID-19-cohort the global longitudinal strain was significantly higher shortly after the infection (T0) than at the two follow-up measurements (T0: 20.37 ± 1.98%; T1: 19.34 ± 1.65%; T2: 19.30 ± 1.68% ($p = 0.0052$ and $p = 0.0044$, respectively)). No significant differences for any of the comparisons were found for circumferential or radial strain.

Discussion The significantly elevated values in the COVID-19-cohort at T0 may be due to an affectation of the autonomic nervous system, which has previously been documented as a result of COVID-19-disease. No cardiac injury after COVID-19 was detected using strain analysis. All documented global longitudinal strain values were within the normal range for athletes. A return to training and competition had no deleterious effect on cardiac health in athletes after a COVID-19-infection in this trial.

Keywords Athletes · Echocardiography · Heart · COVID-19 · Strain analysis · Speckle tracking

See *Appendix* for full publication.

Complete List of (Co-)Authored Medline-Indexed Publications

1: Feuerbacher JF, Jacobs MW, Heumann P, Pareja-Blanco F, Hackney AC, **Zacher** J, Schumann M. Neuromuscular Adaptations to Same Versus Separate Muscle-Group Concurrent Aerobic and Strength Training in Recreationally Active Males and Females. Scand J Med Sci Sports. 2025 Feb;35(2):e70025. doi: 10.1111/sms.70025. PMID: 39921365; PMCID: PMC11806282.

2: Jacko D, Schaaf K, Aussieker T, Masur L, **Zacher** J, Bersiner K, Bloch W, Gehlert S. Acute resistance exercise and training reduce desmin phosphorylation at serine 31 in human skeletal muscle, making the protein less prone to cleavage. Sci Rep. 2024 Nov 14;14(1):28079. doi: 10.1038/s41598-024-79385-0. PMID: 39543356; PMCID: PMC11564833.

3: Schneeweis C, Diebold K, Schramm T, Syrek C, Predel HG, Manka R, **Zacher** J. Mid- to long-term cardiac magnetic resonance findings in elite athletes recovered from COVID-19: results from an ongoing observational COVID-19 study at a German Olympic medical centre. Swiss Med Wkly. 2023 Dec 15;153:3534. doi: 10.57187/s.3534. PMID: 38579332.

4: Jacko D, Masur L, Schaaf K, **Zacher** J, Bersiner K, de Marées M, Bloch W, Gehlert S. Resistance training does not increase myocellular garbage dumps: A pilot study on lipofuscin in skeletal muscle fibers of resistance trained young men. Physiol Rep. 2024 Feb;12(3):e15922. doi: 10.14814/phy2.15922. PMID: 38296333; PMCID: PMC10830392.

5: Widmann M, Gaidai R, Schubert I, Grummt M, Bensen L, Kerling A, Quermann A, **Zacher** J, Vollrath S, Bizjak DA, Beckendorf C, Egger F, Hasler E, Mellwig KP, Fütterer C, Wimbauer F, Vogel A, Schoenfeld J, Wüstenfeld JC, Kastner T, Barsch F, Friedmann-Bette B, Bloch W, Meyer T, Mayer F, Wolfarth B, Roecker K, Reinsberger C, Haller B, Niess AM; CoSmo-S Consortium. COVID-19 in Female and Male Athletes: Symptoms, Clinical Findings, Outcome, and Prolonged Exercise Intolerance-A Prospective, Observational, Multicenter Cohort Study (CoSmo-S). Sports Med. 2024 Apr;54(4):1033-1049. doi: 10.1007/s40279-023-01976-0. Epub 2024 Jan 11. PMID: 38206445; PMCID: PMC11052799.

6: Lichtenstein E, Held S, Rappelt L, **Zacher** J, Eibl A, Ludyga S, Faude O, Donath L. Agility training to integratively promote neuromuscular, cardiorespiratory and cognitive function in healthy older adults: a one-year randomized-controlled trial. Eur Rev Aging Phys Act. 2023 Nov 11;20(1):21. doi: 10.1186/s11556-023-00331-6. PMID: 37951885; PMCID: PMC10638759.

7: Bros J, Ibershoff L, Zollmann E, **Zacher** J, Tomschi F, Predel HG, Bloch W, Grau M. Changes in Hematological and Hemorheological Parameters Following Mild COVID-19: A 4-Month Follow-Up Study. Hematol Rep. 2023 Oct 10;15(4):543-554. doi: 10.3390/hematolrep15040057. PMID: 37873792; PMCID: PMC10594454.

8: **Zacher** J, Filipovic K, Predel G, Schmidt T. Exercise and Atrial Fibrillation: The Dose Makes the Poison? A Narrative Review. Int J Sports Med. 2024 Jan;45(1):17-22. doi: 10.1055/a-2152-7628. Epub 2023 Oct 6. PMID: 37802082; PMCID: PMC10776210.

9: **Zacher** J, Branahl A, Predel HG, Laborde S. Effects of Covid-19 on the autonomic nervous system in elite athletes assessed by heart rate variability. Sport Sci Health. 2023 May 18:1-12. doi: 10.1007/s11332-023-01067-7. Epub ahead of print. PMID: 37360977; PMCID: PMC10191822.

10: **Zacher** J, Wesemann F, Joisten N, Walzik D, Bloch W, Predel G. Cellular Integrative Immune Markers in Elite Athletes. Int J Sports Med. 2023 Apr;44(4):298-308. doi: 10.1055/a-1976-6069. Epub 2022 Nov 10. PMID: 36356591; PMCID: PMC10072930.

11: Jacko D, Schaaf K, Masur L, Windoffer H, Aussieker T, Schiffer T, **Zacher** J, Bloch W, Gehlert S. Repeated and Interrupted Resistance Exercise Induces the Desensitization and Re-Sensitization of mTOR-Related Signaling in Human Skeletal Muscle Fibers. Int J Mol Sci. 2022 May 12;23(10):5431. doi: 10.3390/ijms23105431. PMID: 35628242; PMCID: PMC9141560.

12: Grau M, Zollmann E, Bros J, Seeger B, Dietz T, Noriega Ureña JA, Grolle A, **Zacher** J, Notbohm HL, Suck G, Bloch W, Schumann M. Autologous Blood Doping Induced Changes in Red Blood Cell Rheologic Parameters, RBC Age Distribution, and Performance. Biology (Basel). 2022 Apr 23;11(5):647. doi: 10.3390/biology11050647. PMID: 35625375; PMCID: PMC9137932.

13: Grau M, Ibershoff L, **Zacher** J, Bros J, Tomschi F, Diebold KF, Predel HG, Bloch W. Even patients with mild COVID-19 symptoms after SARS-CoV-2 infection show prolonged altered red blood cell morphology and rheological parameters. J Cell Mol Med. 2022 May;26(10):3022-3030. doi: 10.1111/jcmm.17320. Epub 2022 Apr 13. PMID: 35419946; PMCID: PMC9097836.

14: Schmidt T, Bjarnason-Wehrens B, **Zacher** J, Predel HG, Reiss N. Sports, Myocarditis and COVID-19: Diagnostics, Prevention and Return-to-play Strategies. Int J Sports Med. 2022 Dec;43(13):1097-1105. doi: 10.1055/a-1810-5314. Epub 2022 Mar 28. PMID: 35345017; PMCID: PMC9713464.

15: Schams P, Feodoroff B, **Zacher** J, Eibl A, Froböse I. Validation of a smart shirt for heart rate variability measurements at rest and during exercise. Clin Physiol Funct Imaging. 2022 May;42(3):190-199. doi: 10.1111/cpf.12746. Epub 2022 Mar 28. PMID: 35274441.

16: Niess AM, Widmann M, Gaidai R, Gölz C, Schubert I, Castillo K, Sachs JP, Bizjak D, Vollrath S, Wimbauer F, Vogel A, Keller K, Burgstahler C, Quermann A, Kerling A, Schneider G, **Zacher** J, Diebold K, Grummt M, Beckendorf C, Buitenhuis J, Egger F, Venhorst A, Morath O, Barsch F, Mellwig KP, Oesterschlink J, Wüstenfeld J, Predel HG, Deibert P, Friedmann-Bette B, Mayer F, Hirschmüller A, Halle M, Steinacker JM, Wolfarth B, Meyer T, Böttinger E, Flechtner-Mors M, Bloch W, Haller B, Roecker K, Reinsberger C. COVID-19 in German Competitive Sports: Protocol for a Prospective Multicenter Cohort Study (CoSmo-S). Int J Public Health. 2022 Feb 7;67:1604414. doi: 10.3389/ijph.2022.1604414. PMID: 35197815; PMCID: PMC8859834.

17: Notbohm HL, Feuerbacher JF, Papendorf F, Friese N, Jacobs MW, Predel HG, **Zacher** J, Bloch W, Schumann M. Metabolic, hormonal and performance effects of isomaltulose ingestion before prolonged aerobic exercise: a double-blind, randomised, cross-over trial. J Int Soc Sports Nutr. 2021 May 17;18(1):38. doi: 10.1186/s12970-021-00439-z. PMID: 34001166; PMCID: PMC8130436.

18: Bloch W, Diel P, **Zacher** J. Ion channel regulation in endothelial function: the key role of dietary polyunsaturated fatty acids for TRPV4 activity. Cardiovasc Res. 2021 Nov 1;117(12):2409-2410. doi: 10.1093/cvr/cvab097. PMID: 33878153.

19: Walzik D, Joisten N, **Zacher** J, Zimmer P. Transferring clinically established immune inflammation markers into exercise physiology: focus on neutrophil-to- lymphocyte ratio, platelet-to-lymphocyte ratio and systemic immune-inflammation index. Eur J Appl Physiol. 2021 Jul;121(7):1803-1814. doi: 10.1007/s00421-021-04668-7. Epub 2021 Mar 31. PMID: 33787989; PMCID: PMC8192383.

20: **Zacher** J, Dillschnitter K, Freitag N, Kreutz T, Bjarnason-Wehrens B, Bloch W, Predel HG, Schumann M. Exercise training in the treatment of paroxysmal atrial fibrillation: study protocol of the Cologne ExAfib Trial. BMJ Open. 2020 Oct 31;10(10):e040054. doi: 10.1136/bmjopen-2020-040054. PMID: 33130570; PMCID: PMC7783621.

21: Morat M, Faude O, Hanssen H, Ludyga S, **Zacher** J, Eibl A, Albracht K, Donath L. Agility Training to Integratively Promote Neuromuscular, Cognitive, Cardiovascular and Psychosocial Function in Healthy

Older Adults: A Study Protocol of a One-Year Randomized-Controlled Trial. Int J Environ Res Public Health. 2020 Mar 12;17(6):1853. doi: 10.3390/ijerph17061853. PMID: 32178430; PMCID: PMC7143005.

22: **Zacher** J, Blome I, Schenk A, Gorr E. Cardiac adaptations in elite female football- and volleyball-athletes do not impact left ventricular global strain values: a speckle tracking echocardiography study. Int J Cardiovasc Imaging. 2020 Jun;36(6):1085-1096. doi: 10.1007/s10554-020-01809-5. Epub 2020 Mar 13. PMID: 32170496.

23: Eibl AD, Predel HG, Sanders T, **Zacher** J. Neuronale Kontrolle des Blutdrucks [Neuronal Blood Pressure Regulation]. Klin Monbl Augenheilkd. 2019 Feb;236(2):145-149. German. doi: 10.1055/a-0808-4843. Epub 2019 Feb 14. PMID: 30763971.

24: **Zacher** J, May E, Horlitz M, Pingel S. Binge drinking alcohol with caffeinated "energy drinks", prolonged emesis and spontaneous coronary artery dissection: a case report, review of the literature and postulation of a pathomechanism. Clin Res Cardiol. 2018 Oct;107(10):975-979. doi: 10.1007/s00392-018-1262-y. Epub 2018 May 4. PMID: 29728830.

25: **Zacher** J, Kasenda B, Engert A, Skoetz N. The role of additional radiotherapy for primary central nervous system lymphoma. Cochrane Database Syst Rev. 2014 Jun 16;2014(6):CD009211. doi: 10.1002/14651858.CD009211.pub2. PMID: 24931518; PMCID: PMC6524751.

Short Summary of Main Results and Conclusions of the Publications

The following results and consecutive conclusions were obtained in the included trials and are briefly summarized here:

Publication 1 (Strain Analysis in Female Athletes):

The hearts of the included female athletes differed from the non-athletic control subjects in aspects that are typical adaptations to regular exercise. The interventricular septum diameter in diastole (IVSd) was larger in both female elite athlete populations compared to non-athletic controls, but not different between sporting disciplines. Only five athletes (4 football players and 1 volleyball player) and no controls had IVSd ≥ 1 cm as a sign of left ventricular hypertrophy. The volleyball players generally had larger hearts than the football players and the control group. The left ventricular posterior wall in diastole (LVPWd) was thicker in athletes than controls and in football players than volleyball players. Athletes had larger atria than controls, larger right ventricles and larger left ventricular end diastolic volume (LVVED) and a larger stroke volume (LVSV). No differences were observed between sporting disciplines when indexed for body surface area (BSA). Ejection fraction (EF) was without significant difference between all groups, as were parameters of diastolic function. The hearts of the volleyball-athletes were longer than those of the football players and control subjects as seen in the increased length of the right ventricle in diastole (RVDl).

No significant differences were documented in global longitudinal strain (GLS), global circumferential strain (GCS) or global radial strain (GRS) between the athletes and controls or between sporting disciplines. A detailed analysis of the individual segments did not reveal any relevant differences in any strain type when comparing the different groups of participants. When pooling segmental values into the three categories *basal*, *mid-ventricular* and *apical* the volleyball players (VP) showed a significantly lower apical longitudinal strain compared to football players (FP) and controls (C) that was still, however, in the expected physiological reference range. No correlation between septal wall thickness (IVSd) and any of the global strain parameters could be documented. A comparison of global longitudinal strain values between participants with septal wall thickness ≥ 1 cm and < 1 cm yielded no significant differences (p=0.81).

This illustrates that global strain values do not seem to differ significantly between healthy female athletes and healthy female non-athletic controls. Cardiac adaptations to exercise like increase of left ventricular dimensions or hypertrophy do not seem to influence cardiac strain values significantly.

Publication 2 (Strain Analysis in Elite Athletes After Covid-19):

Classic echocardiographic parameters including ejection fraction did not differ between COV (elite athletes with prior SARS-CoV-2 infection) and CON (elite athletes in the control group without prior SARS-CoV-2 infection). All strain value assessments lay within the physiological reference ranges. At baseline at the measurement time-point one month after the SARS-CoV-2 infection (T0) left ventricular global longitudinal strain was slightly but significantly greater in the Covid-19 cohort in comparison to the control cohort (|-20.37|±1.98% vs. |-19.41|±2.11%, respectively, p= 0.042). In the longitudinal assessment within the Covid-19 cohort the global longitudinal strain was significantly higher shortly after the infection (T0) than at the two follow-up measurements four (T1) and eight (T2) months after the infection (T0: |-20.37|±1.98%; T1: |-19.34|±1.65%; T2: |-19.30|±1.68% (p=0.0052 and p=0.0044, respectively)). No significant differences for any of the comparisons were found for global circumferential or global radial strain.

These findings based on highly sensitive strain analyses underline the growing consensus that elite athletes generally recover well from a SARS-CoV-2 infection without cardiac injury. The slight increase in contractility measured shortly after the infection could be attributed to temporary infection-associated modulations of the autonomic nervous system as described by this candidate in another trial [39].

Discussion

Cardiac Adaptations and Left Ventricular Strain Values in Female Athletes

As anticipated, the elite female athletes demonstrated a cardiac anatomy that has been described in many prior investigations as an adaptation to high levels of physical exercise [16]. While the study comparing cardiac anatomy of female athletes to non-athletic controls lacks the longitudinal design to investigate the effect of the specific sporting discipline on cardiac adaptations, the observed differences between the athletes and control group regarding conventional echocardiographic parameters can safely be assumed to be exercise-related. Thus, the hearts of the athletes had a larger mass (absolute and indexed to body surface area), a thicker septum, larger atrial volumes and a wider right ventricle than the hearts in the control group. The heart rate of the athletes was lower and in the sub-group analysis the volleyball players had a higher fat-free mass and less visceral fat than the control group.

The three left ventricular strain parameters GLS, GRS and GCS did not differ between the sporting disciplines or between athletes and controls. Especially the lack of difference in the global longitudinal strain values -the to date most thoroughly evaluated strain parameter- is in accordance with prior studies focusing on strain values in female athletes. D'Ascenzi et al. published the left ventricular global longitudinal strain values of 24 female volleyball-athletes measured with the same vendor and software as used for *Publication 1* at -19.7±1.8% after detraining for 3 months and at -20.5±2.1% after 4 months of intense training; no LVGLS data was published for the control group as the study focused on the atria and the right ventricle [25]. Caselli et al. published LVGLS data from a large athlete cohort (n = 200, including 78 female athletes) finding LVGLS values in athletes within the expected reference range for healthy adults, but with slightly lower values when compared to the control group; LVGLS was lower in females than males across the whole cohort. Similar LVGLS values as in *Publication 1* were presented for the athletes overall, albeit using hard- and software of a different vendor [24]. Vendor differences regarding the measurement and calculation of strain analyses pose a difficulty in the transfer of strain analysis into the day-to-day clinical use [40]. Reference values have been described for different cardiac strain measurements of the largest vendors; the growing number of vendors offering forms of cardiac strain analyses and the differences of vendor specific reference ranges complicate the realization of large multicenter trials as well as the clinical cooperation amongst sports-medical settings with echocardiography machines from different vendors. Cappelli et al. included 9 female endurance athletes in their comparison of 50 endurance athletes with hypertensive patients and healthy controls: LVGLS did not differ between the athletes and the control group; results were not specified by sex. The GLS values were comparable to the results of *Publication 1* [41]. A position statement by Pelliccia et al. and a review by D'Ascenzi et al. present similar LVGLS values as found in *Publication 1* and conclude that even high training volumes in elite athletes do not normally reduce LVGLS values [6, 21]. A meta-analysis published by Beaumont et al. in 2017 included only male athletes but thoroughly analyzed all available data, concluding that GLS values do not differ between athletes of varying disciplines and controls; LVGLS values were comparable to the data of *Publication 1*. The authors did, however, find a correlation between LVGLS and left ventricular mass index, suggesting a small LVGLS reduction associated with increasing physiological exercise-associated hypertrophy, interpreted by the authors as indicative of an increased functional reserve in the highly trained heart [22]. Possibly due to the fact that hypertrophy is more pronounced in male athletes *Publication 1* did not show this association between hypertrophy and LVGLS reduction, even in the detailed regional analysis: To probe in more detail for an influence of physiological hypertrophy on strain values the anteroseptal and septal (3-chamber view and 4-chamber view respectively) longitudinal strain values and the septal segments in the short axis strain values were analyzed regarding possible correlations between strain values and septal thickness; no significant correlations were observed.

The detailed comparison of segmental strain values between the groups did not reveal differences between individual segments, supporting the credibility of the similarity between the global values. The only deviation from the overall similar values between the groups was a slightly lower longitudinal strain in the combined apical segments in the elite volleyball players compared to both elite football players and controls. Whether this finding is connected to differences in cardiac architecture and resulting contraction patterns or is a coincidental aberration remains unclear. The differences in height between the taller volleyball athletes (logically a result of sport specific advantages) compared to the shorter football athletes and controls may be associated with the finding of “longer” hearts as documented in the higher lengths of the right ventricle. This difference in heart architecture may well result in small differences in contractile patterns at rest or during exercise. This does, however, remain conjecture and should be elucidated in further larger studies including detailed segmental strain findings in athletes of different sexes and sporting disciplines. To date the factors influencing regional longitudinal strain in different athlete populations and experimental settings are not fully explored. Stefani et al. demonstrated a basal-apical gradient with an increase in mid-apical left ventricular longitudinal strain in male football players after an acute three minute physical exertion (compared to the resting state beforehand) [42]. In their meta-analysis on cardiac strain in athletes Beaumont et al. describe a higher apical dynamic in athletes, demonstrated by a reduced apical circumferential strain at rest, which increases during exercise [22]. Cappelli et al. report an increase in apical circumferential strain in hypertensive patients compared to athletes and controls, suggesting a compensatory mechanism for a beginning reduction of contractile function. Based on these observations, the reduction in apical strain in the volleyball-athletes may be a sign of an apical contractile reserve that may differ from the football and control cohort due to the elongated left ventricular structure. This, too, remains conjecture and should be investigated by regional strain analyses comparing pre- and post-exercise settings. Several trials have investigated cardiac function and left ventricular architecture in tall athletes and documented increased septal wall thickness and ventricular mass and dimensions [43–46]. Regarding strain analysis by speckle tracking echocardiography Butz et al. found no correlations between strain values and height in athletes, patients with hypertrophic cardiomyopathy and control subjects [20]. However, the influence of left ventricular architecture has been demonstrated to affect strain values [7]. Thus, future studies including tall athletes should aim to recruit a non-athletic control cohort of similar height to reduce the chance of distorted comparisons due to this physical characteristic. Ventricular loading conditions, too, have been shown to influence cardiac strain values [7]; the loading conditions of all participants assessed for *Publication 1* were similar, lacking load-influencing co-morbidities and resting in a semi-supine position during echocardiography with no prior physical exertion. A potential error source when assessing apical strain values is apical foreshortening [47]; however, great care was applied during image acquisition and analysis to avoid this phenomenon.

The average septal thickness in the elite athletes in *Publication 1* was 0.83 cm ± 0.12 cm and thus within the range of previous observations [48, 49]. As observed in these large athlete cohort studies, septal hypertrophy is generally less pronounced in female elite athletes than in male elite athletes. However, hypertrophy does occur in female athletes, as do pathological conditions such as hypertension or hypertrophic cardiomyopathy. Still, while the critical question for the sports cardiologist regarding the physiological or pathological nature of borderline septal hypertrophy is a lot more common in male athletes, investigations into the effects on cardiac strain in female athletes with pronounced cardiac adaptations must not be neglected. Also, strain analysis by speckle tracking echocardiography has been demonstrated as a useful tool in the detection of inflammatory cardiac processes [5]. In the day-to-day care of elite athletes the question of myocarditis arises regularly, thus adding to the necessity to establish reference ranges of LVGLS for all athlete cohorts to allow for strain analysis to be effectively used regarding the diagnosis of this pathology.

Cardiac Effects of Covid-19 Disease in Athletes Assessed by Strain Analysis

To the candidate's knowledge at the time of submission *Publication 2* was the first and then only subacute to long-term longitudinal assessment of cardiac function via speckle tracking echocardiography in elite athletes after contracting Covid-19. All included athletes were without signs of myocarditis and demonstrated cardiac function within the normal spectrum previously documented for athletes [6, 15]. Thus, fortunately, the results add to the growing pool of data demonstrating that athletes generally recover well after Covid-19 and that myocardial injury is rare. Our research group had previously demonstrated good cardiac health in an MRI-trial in a subgroup of our elite athlete population [50]. In a large multicenter assessment of > 3000 college athletes after Covid-19 cardiac involvement was reported in 0.7% of cases; cardiac strain data was not reported [51]. A narrative review assessing 24 studies of Covid-19 effects on athletes draws the conclusion that the initial fear of large numbers of cardiac injuries through a SARS-CoV-2 infection in athletes could not be confirmed. On the contrary, cardiac involvement was rare in the young and healthy athlete cohort [52]. In the largest study to date at the time of *Publication 2* assessing 789 professional athletes after contracting Covid-19 only 20 demonstrated echocardiographic abnormalities [36]. Almost all of these 20 "abnormalities" were a mildly reduced left ventricular ejection fraction (LVEF), which is a recognized non-pathological adaptation in some highly trained athletes [44, 53]. Only 5 of the 789 athletes had inflammatory aspects in cardiac MRI; albeit not all athletes received cardiac MRI, but based on a diagnostic cascade where deemed necessary (e. g. in case of abnormal findings during echocardiography) [36].

The novel finding of *Publication 2* is the significantly elevated longitudinal myocardial contractility in the COV cohort at T0 when compared to the CON cohort and when compared to the follow-up measurements at T1 and T2. Similarly, a retrospective MRI-Study assessing 122 College athletes after Covid-19 found intact cardiac function with slightly higher global radial and circumferential strain values compared to healthy non-athletic controls [54]. This data is, however, limited by the control group being non-athletes and on average 15 years older than the athletes. A meta-analysis including 21 studies and > 2300 patients found reduced ejection fractions and reduced LVGLS in non-athletic Covid-19 survivors in analyses up to 1 year after the infection [55]. This trial did, however, include studies with hospitalized patients, some receiving intensive care treatment, and is thus not a good comparator to our athlete cohort with no hospitalizations.

Slight changes of LVGLS throughout a sporting season have been documented in elite athletes, showing mildly increased strain after weeks of intense training (correlating with reduced resting heart rates while blood pressure remained stable) [14]. Based on these data the LVGLS may have been lower -not higher- in the COV cohort if training cessation were the cause. The discrepancy of a slight LVGLS increase in COV compared to CON may be blood pressure associated, as systolic blood pressure was slightly higher in CON than COV. Cardiac strain is load dependent, showing a reduction when after-load is reduced [7, 56]. Thus, a slightly lower blood pressure may lead to slightly elevated LVGLS values when comparing COV and CON. However, no significant longitudinal blood pressure changes were observed in COV (albeit with reduced numbers due to drop-outs during follow up), even though LVGLS values changed. If the slight difference in blood pressure between the groups were Covid-19-associated, a change in blood pressure in COV should be observed in the long-term follow up. Since this was not the case the small difference between CON and COV may be due to the slightly higher percentage of male athletes in CON; this however, remains conjecture until elucidated in future studies.

Baruch et al. found an impairment in LVGLS in 25% of hospitalized Covid-19 patients three months after discharge [57], while Oikonoumou et al. documented not only slightly lower LVGLS values in patients one month after hospitalization, but also a correlation with autonomic nervous system dysfunction measured by heart rate variability (HRV) [58]. Larger longitudinal assessments of athletes after Covid-19 showed no relevant increases in cardiac injury: Petek et al. observed > 3500 college athletes for an average of 1.12 years. Initially myocardial involvement was documented in 0,6%. During follow-up two adverse events (one sudden cardiac death due to prior known structural heart disease and one case of atrial fibrillation) were reported, both in athletes without initially documented cardiac involvement [59].

A potential cause for the somewhat paradox LVGLS elevation in the COV cohort at T0 may be a temporary modulation of the function of the autonomic nervous system in this young and healthy cohort. Clinical experience as well as empirical observations have demonstrated often prolonged cases of Covid-19 with very mild cardiovascular symptoms weeks after the infection: Many athletes complained of elevated heart rates at rest and during only mild exercise (faster increases of heart rate than prior to the infection), as well as experiencing Postural Orthostatic Tachycardia Syndrome (POTS) or orthostatic hypotension [60]. Our research group previously demonstrated autonomic impairment in recovered elite athletes from this cohort using heart rate variability (HRV) and an orthostatic challenge [39]. Nemes et. al found a general associations between cardiac strain parameters and autonomic nervous function [61]. A small trial documented diminished LVGLS values correlating with reduced HRV in patients with prolonged symptoms after Covid-19 [62]. In summary, these observations suggest that indeed infection-associated changes in the autonomic nervous system may be the cause for the slight LVGLS elevation at T0 in COV.

Strengths and Limitations

One strength of both studies included in this dissertation is the novelty of the data at the time of publication: We gain specific insights into the cardiac structure of elite female athletes from selected disciplines and learn about the effects of Covid-19 on cardiac health and strain values in elite athletes in the mid- to long term. Another strength is the level of elitism of the included athletic population (many Olympic and national medalists). Thus, too, the cohorts are very homogenous. One limitation is the relatively small sample size in both studies, aggravated by drop-outs in the longitudinal strain assessments; albeit many trials in the sports sciences include even fewer participants and numbers were large enough in the included studies to achieve statistically significant results. Another limitation is the inability to translate the results to the general population due to the specific selection of the cohorts. The lack of symptom documentation in the Covid-19 trial is another limitation, as it disallows for assessing potential correlations between heart health, strain values and symptom severity.

Conclusions and Outlook

In the study focusing on female elite athletes (*Publication 1*) exercise-specific cardiac adaptations were documented in football and volleyball players, while left ventricular strain values were unchanged by these adaptations and in comparison to unathletic controls. The female athlete has been somewhat neglected regarding research of cardiac strain values, their possible alterations due to high training volumes and their utility as a diagnostic tool. Our findings add to the very limited data available at the time of publication regarding speckle tracking echocardiography derived left ventricular strain values in female athletes: By demonstrating no significant differences in cardiac strain values between healthy female athletes and unathletic controls, these data help to establish strain analysis as a useful tool in sports cardiology. Further research focusing on cardiac strain in female athletes of different ages and sporting disciplines is needed to establish reference values and further improve the utility of strain analysis by speckle tracking echocardiography as a diagnostic tool across many disciplines of female elite athleticism.

The study assessing cardiac strain in athletes after Covid-19 (*Publication 2*) was the first at the time of publication to document mid- to long-term cardiac effects of Covid-19 in elite athletes assessed by speckle tracking echocardiography. The trial showed short term changes in cardiac strain after Covid-19, most likely as a result of temporary post-infection changes in the autonomic nervous system, while also documenting healthy hearts and strain values within expected reference ranges. It thus strengthens the understanding that elite athletes usually recover well after Covid-19 without cardiac damage. Further trials in larger cohorts including symptom documentation and longer-term follow up are needed to build on these results.

Both included studies underscore the insight that strain analysis by speckle tracking echocardiography is a useful tool in sports cardiology and should be a standard component in sports-cardiological athlete care. Experienced sports cardiologists should not only apply the technique in their day to day practice, but promote its use and expertise therein amongst younger generations of sports physicians and sports cardiologists.

While LVGLS is well established and -as just stated- ready to be fully integrated into the everyday athlete care, other derivatives of speckle tracking echocardiography like radial and circumferential strain, strain rate or ventricular twist are far less well established, but are diagnostic methods with potentially highly relevant practical applications. Their better understanding and that of other techniques should be a goal of sports cardiologists and sports physicians with an affinity for echocardiography and future studies they conduct. Due to differences between vendors of echocardiography machines, experiences should be compared between users of different brands and studies conducted specifically in the athlete population to allow the use of strain analysis across the board in everyday athlete care. Also, comparative analyses with MRI-derived strain analysis should be placed on the agenda of sports-cardiological research, as MRI is a widely used technique, especially to rule out or detect myocarditis. The candidate’s research team used MRI-derived strain in one such study assessing athletes’ cardiac function after Covid-19 [50].

While interdisciplinary cardiac assessment between echocardiography- and MRI-specialists seems relatively easily achievable under the common umbrella of cardiology (broadly) and sports cardiology (more specifically), a transfer of the technique of speckle tracking-derived strain analysis to other fields of sports medicine could be considered. While ultrasound is well established in sports orthopaedics and traumatology including functional assessments like shear wave elastography (SWE) [63], to the candidate’s knowledge ultrasound assessment of the moving muscle in a standardized fashion is not yet established in sports orthopaedics. Potentially, speckle tracking ultrasound in skeletal muscle like the quadriceps femoris during contraction and relaxation could aid in the differentiation between different types of sports-related muscle injury and assessment of muscle function.

Other interesting perspectives of cardiac strain analysis are the focus on different athletic disciplines and on measurement time points in the micro- and macro-cycles of professional training. As different athletic disciplines vary vastly regarding types and volumes of training, some are more prone to the development of cardiac adaptations in the sense of athlete's heart. Even though this dissertation has established in small cohorts of two disciplines of female athletes that cardiac adaptations to exercise do not seem to impact left ventricular strain values, large prospective and ideally multicenter studies should document potential effects of cardiac adaptations on strain values in male and female athletes of different sporting disciplines. These studies should include a focus on macro-cycle training phases (i. e. pre-season, competition, regeneration, etc.); as mentioned above the effects of seasonal time points have been assessed in female volleyball players [14] – this needs to be expanded for both sexes and multiple disciplines to optimize the use of strain analysis for the sports cardiologist in the long run. Once these data are broadly available the sports cardiologist would apply training-cycle specific reference ranges in the day-to-day athlete care. To make things more complicated, the described future studies should also include an assessment of potential changes in cardiac strain during micro-cycle training phases (i. e. shortly before and after training sessions and resting periods). As elite athletes usually train many hours of every day, it is likely that the sports cardiologist performs an acute or routine echocardiographic assessment in close chronological proximity to a training session, which may affect strain values. Thus, to further optimize this tool, studies will need to decipher in detail the acute and subacute effects of different types of training and regeneration (i. e. strength, endurance, high-intensity, yoga, autogenic training, etc.) on the different forms of cardiac strain values. Only then will this already very useful tool be fully optimized for the sports cardiologist.

Thus, while speckle tracking echocardiography-derived left ventricular global longitudinal strain is well established and should be used in daily athlete care, further refinement of the technique and understanding of its influencing factors will make it even more valuable in the everyday practice of sports cardiology.

References

1. Edler I, Hertz CH (2004) The use of ultrasonic reflectoscope for the continuous recording of the movements of heart walls. 1954. Clin Physiol Funct Imaging 24:118–136. doi: 10.1111/j.1475-097X.2004.00539.x
2. Flachskampf FA (ed) (2022) Kursbuch Echokardiografie: Unter Berücksichtigung nationaler und internationaler Leitlinien, 7., unveränderte Auflage. Georg Thieme Verlag KG, Stuttgart
3. Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, Horton K, Ogunyankin KO, Palma RA, Velazquez EJ (2019) Guidelines for Performing a Comprehensive Transthoracic Echocardiographic Examination in Adults: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr 32:1–64. doi: 10.1016/j.echo.2018.06.004
4. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt J-U (2015) Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 28:1-39.e14. doi: 10.1016/j.echo.2014.10.003
5. Collier P, Phelan D, Klein A (2017) A Test in Context: Myocardial Strain Measured by Speckle-Tracking Echocardiography. J Am Coll Cardiol 69:1043–1056. doi: 10.1016/j.jacc.2016.12.012
6. D'Ascenzi F, Caselli S, Solari M, Pelliccia A, Cameli M, Focardi M, Padeletti M, Corrado D, Bonifazi M, Mondillo S (2016) Novel echocardiographic techniques for the evaluation of athletes' heart: A focus on speckle-tracking echocardiography. Eur. J. Prev. Cardiol. 23:437–446. doi: 10.1177/2047487315586095
7. Voigt J-U, Cvijic M (2019) 2- and 3-Dimensional Myocardial Strain in Cardiac Health and Disease. JACC Cardiovasc Imaging 12:1849–1863. doi: 10.1016/j.jcmg.2019.01.044
8. Bansal M, Kasliwal RR (2013) How do I do it? Speckle-tracking echocardiography. Indian Heart J 65:117–123. doi: 10.1016/j.ihj.2012.12.004
9. Murtaza G, Virk HUH, Khalid M, Rahman Z, Sitwala P, Schoondyke J, Al-Balbissi K (2017) Role of Speckle Tracking Echocardiography in Dilated Cardiomyopathy: A Review. Cureus 9:e1372. doi: 10.7759/cureus.1372
10. Ancedy Y, Ederhy S, Jean M-L, Nhan P, Soulat-Dufour L, Adavane-Scheuble S, Chauvet-Droit M, Boccara F, Cohen A (2020) Does layer-specific strain using speckle tracking echocardiography improve the assessment of left ventricular myocardial deformation? A review. Arch Cardiovasc Dis 113:721–735. doi: 10.1016/j.acvd.2020.05.007
11. Minciună I-A, Hilda Orășan O, Minciună I, Lazar A-L, Sitar-Tăut AV, Oltean M, Tomoaia R, Puiu M, Sitar-Tăut D-A, Pop D, Cozma A (2021) Assessment of subclinical diabetic cardiomyopathy by speckle-tracking imaging. Eur J Clin Invest 51:e13475. doi: 10.1111/eci.13475
12. Karlsen S, Dahlslett T, Grenne B, Sjøli B, Smiseth O, Edvardsen T, Brunvand H (2019) Global longitudinal strain is a more reproducible measure of left ventricular function than ejection fraction regardless of echocardiographic training. Cardiovasc Ultrasound 17:18. doi: 10.1186/s12947-019-0168-9
13. Caselli S, Montesanti D, Autore C, Di Paolo FM, Pisicchio C, Squeo MR, Musumeci B, Spataro A, Pandian NG, Pelliccia A (2015) Patterns of left ventricular longitudinal strain and strain rate in Olympic athletes. J Am Soc Echocardiogr 28:245–253. doi: 10.1016/j.echo.2014.10.010
14. D'Ascenzi F, Pelliccia A, Alvino F, Solari M, Loffreno A, Cameli M, Focardi M, Bonifazi M, Mondillo S (2015) Effects of training on LV strain in competitive athletes. Heart 101:1834–1839. doi: 10.1136/heartjnl-2015-308189
15. Zacher J, Blome I, Schenk A, Gorr E (2020) Cardiac adaptations in elite female football- and volleyball-athletes do not impact left ventricular global strain values: a speckle tracking

echocardiography study. Int J Cardiovasc Imaging 36:1085–1096. doi: 10.1007/s10554-020-01809-5
16. Prior DL, La Gerche A (2012) The athlete's heart. Heart 98:947–955. doi: 10.1136/heartjnl-2011-301329
17. La Gerche A, Wasfy MM, Brosnan MJ, Claessen G, Fatkin D, Heidbuchel H, Baggish AL, Kovacic JC (2022) The Athlete's Heart-Challenges and Controversies: JACC Focus Seminar 4/4. J Am Coll Cardiol 80:1346–1362. doi: 10.1016/j.jacc.2022.07.014
18. Morganroth J, Maron BJ, Henry WL, Epstein SE (1975) Comparative left ventricular dimensions in trained athletes. Ann Intern Med 82:521–524. doi: 10.7326/0003-4819-82-4-521
19. Pelliccia A, Adami PE (2017) The Female Side of the Heart: Sex Differences in Athlete's Heart. JACC Cardiovasc Imaging 10:973–975. doi: 10.1016/j.jcmg.2016.08.010
20. Butz T, van Buuren F, Mellwig KP, Langer C, Plehn G, Meissner A, Trappe HJ, Horstkotte D, Faber L (2011) Two-dimensional strain analysis of the global and regional myocardial function for the differentiation of pathologic and physiologic left ventricular hypertrophy: a study in athletes and in patients with hypertrophic cardiomyopathy. The International Journal of Cardiovascular Imaging 27:91–100. doi: 10.1007/s10554-010-9665-5
21. Pelliccia A, Caselli S, Sharma S, Basso C, Bax JJ, Corrado D, D'Andrea A, D'Ascenzi F, Di Paolo FM, Edvardsen T, Gati S, Galderisi M, Heidbuchel H, Nchimi A, Nieman K, Papadakis M, Pisicchio C, Schmied C, Popescu BA, Habib G, Grobbee D, Lancellotti P (2018) European Association of Preventive Cardiology (EAPC) and European Association of Cardiovascular Imaging (EACVI) joint position statement: recommendations for the indication and interpretation of cardiovascular imaging in the evaluation of the athlete's heart. Eur Heart J 39:1949–1969. doi: 10.1093/eurheartj/ehx532
22. Beaumont A, Grace F, Richards J, Hough J, Oxborough D, Sculthorpe N (2017) Left Ventricular Speckle Tracking-Derived Cardiac Strain and Cardiac Twist Mechanics in Athletes: A Systematic Review and Meta-Analysis of Controlled Studies. Sports Medicine 47:1145–1170. doi: 10.1007/s40279-016-0644-4
23. Richand V, Lafitte S, Reant P, Serri K, Lafitte M, Brette S, Kerouani A, Chalabi H, Dos Santos P, Douard H, Roudaut R (2007) An Ultrasound Speckle Tracking (Two-Dimensional Strain) Analysis of Myocardial Deformation in Professional Soccer Players Compared With Healthy Subjects and Hypertrophic Cardiomyopathy. The American Journal of Cardiology 100:128–132. doi: 10.1016/j.amjcard.2007.02.063
24. Caselli S, Montesanti D, Autore C, Di Paolo FM, Pisicchio C, Squeo MR, Musumeci B, Spataro A, Pandian NG, Pelliccia A (2015) Patterns of Left Ventricular Longitudinal Strain and Strain Rate in Olympic Athletes. Journal of the American Society of Echocardiography 28:245–253. doi: 10.1016/j.echo.2014.10.010
25. D'Ascenzi F, Pelliccia A, Natali BM, Zaca V, Cameli M, Alvino F, Malandrino A, Palmitesta P, Zorzi A, Corrado D, Bonifazi M, Mondillo S (2014) Morphological and functional adaptation of left and right atria induced by training in highly trained female athletes. Circ Cardiovasc Imaging 7:222–229. doi: 10.1161/CIRCIMAGING.113.001345
26. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395:497–506. doi: 10.1016/S0140-6736(20)30183-5
27. Appelman B, Charlton BT, Goulding RP, Kerkhoff TJ, Breedveld EA, Noort W, Offringa C, Bloemers FW, van Weeghel M, Schomakers BV, Coelho P, Posthuma JJ, Aronica E, Joost Wiersinga W, van Vugt M, Wüst RCI (2024) Muscle abnormalities worsen after post-exertional malaise in long COVID. Nat Commun 15:17. doi: 10.1038/s41467-023-44432-3

28. Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, Jain SS, Burkhoff D, Kumaraiah D, Rabbani L, Schwartz A, Uriel N (2020) COVID-19 and Cardiovascular Disease. Circulation 141:1648–1655. doi: 10.1161/CIRCULATIONAHA.120.046941
29. Croft LB, Krishnamoorthy P, Ro R, Anastasius M, Zhao W, Buckley S, Goldman M, Argulian E, Sharma SK, Kini A, Lerakis S (2020) Abnormal left ventricular global longitudinal strain by speckle tracking echocardiography in COVID-19 patients. Future Cardiol. doi: 10.2217/fca-2020-0121
30. Goerlich E, Gilotra NA, Minhas AS, Bavaro N, Hays AG, Cingolani OH (2021) Prominent Longitudinal Strain Reduction of Basal Left Ventricular Segments in Patients With Coronavirus Disease-19. Journal of Cardiac Failure 27:100–104. doi: 10.1016/j.cardfail.2020.09.469
31. Shafiabadi Hassani N, Talakoob H, Karim H, Mozafari Bazargany MH, Rastad H (2021) Cardiac Magnetic Resonance Imaging Findings in 2954 COVID-19 Adult Survivors: A Comprehensive Systematic Review. J Magn Reson Imaging. doi: 10.1002/jmri.27852
32. Brito D, Meester S, Yanamala N, Patel HB, Balcik BJ, Casaclang-Verzosa G, Seetharam K, Riveros D, Beto RJ, Balla S, Monseau AJ, Sengupta PP (2021) High Prevalence of Pericardial Involvement in College Student Athletes Recovering From COVID-19. JACC Cardiovasc Imaging 14:541–555. doi: 10.1016/j.jcmg.2020.10.023
33. Daniels CJ, Rajpal S, Greenshields JT, Rosenthal GL, Chung EH, Terrin M, Jeudy J, Mattson SE, Law IH, Borchers J, Kovacs R, Kovan J, Rifat SF, Albrecht J, Bento AI, Albers L, Bernhardt D, Day C, Hecht S, Hipskind A, Mjaanes J, Olson D, Rooks YL, Somers EC, Tong MS, Wisinski J, Womack J, Esopenko C, Kratochvil CJ, Rink LD (2021) Prevalence of Clinical and Subclinical Myocarditis in Competitive Athletes With Recent SARS-CoV-2 Infection: Results From the Big Ten COVID-19 Cardiac Registry. JAMA Cardiol 6:1078–1087. doi: 10.1001/jamacardio.2021.2065
34. Szabó L, Juhász V, Dohy Z, Fogarasi C, Kovács A, Lakatos BK, Kiss O, Sydó N, Csulak E, Suhai FI, Hirschberg K, Becker D, Merkely B, Vágó H (2021) Is cardiac involvement prevalent in highly trained athletes after SARS-CoV-2 infection? A cardiac magnetic resonance study using sex-matched and age-matched controls. Br J Sports Med. doi: 10.1136/bjsports-2021-104576
35. Lakatos BK, Tokodi M, Fábián A, Ladányi Z, Vágó H, Szabó L, Sydó N, Csulak E, Kiss O, Babity M, Kiss AR, Gregor Z, Szűcs A, Merkely B, Kovács A (2021) Frequent Constriction-Like Echocardiographic Findings in Elite Athletes Following Mild COVID-19: A Propensity Score-Matched Analysis. Front. Cardiovasc. Med. 8:760651. doi: 10.3389/fcvm.2021.760651
36. Martinez MW, Tucker AM, Bloom OJ, Green G, DiFiori JP, Solomon G, Phelan D, Kim JH, Meeuwisse W, Sills AK, Rowe D, Bogoch II, Smith PT, Baggish AL, Putukian M, Engel DJ (2021) Prevalence of Inflammatory Heart Disease Among Professional Athletes With Prior COVID-19 Infection Who Received Systematic Return-to-Play Cardiac Screening. JAMA Cardiol 6:745–752. doi: 10.1001/jamacardio.2021.0565
37. Casasco M, Iellamo F, Scorcu M, Parisi A, Tavcar I, Brugin E, Martini B, Fossati C, Pigozzi F (2022) Return to Play after SARS-CoV-2 Infection in Competitive Athletes of Distinct Sport Disciplines in Italy: A FMSI (Italian Federation of Sports Medicine) Study. Journal of Cardiovascular Development and Disease 9. doi: 10.3390/jcdd9020059
38. Schellenberg J, Ahathaller M, Matits L, Kirsten J, Kersten J, Steinacker JM (2023) Left Ventricular Global Longitudinal Strain as a Parameter of Mild Myocardial Dysfunction in Athletes after COVID-19. Journal of Cardiovascular Development and Disease 10. doi: 10.3390/jcdd10050189
39. Zacher J, Branahl A, Predel H-G, Laborde S (2023) Effects of Covid-19 on the autonomic nervous system in elite athletes assessed by heart rate variability. Sport Sci Health 19:1–12. doi: 10.1007/s11332-023-01067-7
40. Voigt J-U, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann R, Pedri S, Ito Y, Abe Y, Metz S, Song JH, Hamilton J, Sengupta PP, Kolias TJ, d'Hooge J, Aurigemma GP, Thomas JD, Badano LP (2015) Definitions for a common standard for 2D speckle tracking echocardiography: consensus

document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. Eur Heart J Cardiovasc Imaging 16:1–11. doi: 10.1093/ehjci/jeu184

41. Cappelli F, Toncelli L, Cappelli B, Luca AD, Stefani L, Maffulli N, Galanti G (2010) Adaptative or maladaptative hypertrophy, different spatial distribution of myocardial contraction. Clin Physiol Funct Imaging 30:6–12. doi: 10.1111/j.1475-097X.2009.00896.x
42. Stefani L, Toncelli L, Di Tante V, Vono MCR, Cappelli B, Pedrizzetti G, Galanti G (2008) Supernormal functional reserve of apical segments in elite soccer players: an ultrasound speckle tracking handgrip stress study. Cardiovasc Ultrasound 6:14. doi: 10.1186/1476-7120-6-14
43. Malmgren A, Dencker M, Stagmo M, Gudmundsson P (2015) Cardiac dimensions and function in female handball players. J Sports Med Phys Fitness 55:320–328
44. Engel DJ, Schwartz A, Homma S (2016) Athletic Cardiac Remodeling in US Professional Basketball Players. JAMA Cardiol 1:80–87. doi: 10.1001/jamacardio.2015.0252
45. Butz T, van Buuren F, Mellwig KP, Langer C, Oldenburg O, Treusch KA, Meissner A, Plehn G, Trappe H-J, Horstkotte D, Faber L (2010) Systolic and early diastolic left ventricular velocities assessed by tissue Doppler imaging in 100 top-level handball players. Eur J Cardiovasc Prev Rehabil 17:342–348. doi: 10.1097/HJR.0b013e32833333de
46. Crouse SF, Rohack JJ, Jacobsen DJ (1992) Cardiac structure and function in women basketball athletes: seasonal variation and comparisons with nonathletic controls. Res Q Exerc Sport 63:393–401. doi: 10.1080/02701367.1992.10608761
47. Ünlü S, Duchenne J, Mirea O, Pagourelias ED, Bézy S, Cvijic M, Beela AS, Thomas JD, Badano LP, Voigt J-U, Hamilton J, Pedri S, Lysyansky P, Hansen G, Ito Y, Chono T, Vogel J, Prater D, Song JH, Lee JY, Houle H, Georgescu B, Baumann R, Mumm B, Abe Y, Gorissen W Impact of apical foreshortening on deformation measurements: a report from the EACVI-ASE Strain Standardization Task Force. Eur Heart J Cardiovasc Imaging. doi: 10.1093/ehjci/jez189
48. Finocchiaro G, Dhutia H, D’Silva A, Malhotra A, Steriotis A, Millar L, Prakash K, Narain R, Papadakis M, Sharma R, Sharma S (2017) Effect of Sex and Sporting Discipline on LV Adaptation to Exercise. JACC: Cardiovascular Imaging 10:965–972. doi: 10.1016/j.jcmg.2016.08.011
49. Pelliccia A (1996) Athlete's Heart in Women. JAMA 276:211. doi: 10.1001/jama.1996.03540030045030
50. Schneeweis C, Diebold K, Schramm T, Syrek C, Predel H-G, Manka R, Zacher J (2023) Mid- to long-term cardiac magnetic resonance findings in elite athletes recovered from COVID-19: results from an ongoing observational COVID-19 study at a German Olympic medical centre. Swiss Med Wkly 153:3534. doi: 10.57187/s.3534
51. Moulson N, Petek BJ, Drezner JA, Harmon KG, Kliethermes SA, Patel MR, Baggish AL (2021) SARS-CoV-2 Cardiac Involvement in Young Competitive Athletes. Circulation 144:256–266. doi: 10.1161/CIRCULATIONAHA.121.054824
52. Monosilio S, Prosperi S, Squeo MR, Spataro S, Spataro A, Maestrini V (2023) Short and Long-Term Cardiovascular Sequelae after SARS-CoV-2 Infection: A Narrative Review Focusing on Athletes. Viruses 15:493. doi: 10.3390/v15020493
53. Abergel E, Chatellier G, Hagege AA, Oblak A, Linhart A, Ducardonnet A, Menard J (2004) Serial left ventricular adaptations in world-class professional cyclists: implications for disease screening and follow-up. J Am Coll Cardiol 44:144–149. doi: 10.1016/j.jacc.2004.02.057
54. Priya S, Narayanasamy S, Walling A, Ashwath RC (2023) Subclinical cardiac involvement in student athletes after COVID-19 infection - Evaluation using feature tracking cardiac MRI strain analysis. Clinical Imaging 95:1–6. doi: 10.1016/j.clinimag.2022.12.004
55. Rahmati M, Koyanagi A, Banitalebi E, Yon DK, Lee SW, Il Shin J, Smith L (2023) The effect of SARS-CoV-2 infection on cardiac function in post-COVID-19 survivors: A systematic review and meta-analysis. Journal of Medical Virology 95:e28325. doi: 10.1002/jmv.28325

56. Burns AT, La Gerche A, d'Hooge J, MacIsaac AI, Prior DL (2010) Left ventricular strain and strain rate: characterization of the effect of load in human subjects. Eur J Echocardiogr 11:283–289. doi: 10.1093/ejechocard/jep214
57. Baruch G, Rothschild E, Sadon S, Szekely Y, Lichter Y, Kaplan A, Taieb P, Banai A, Hochstadt A, Merdler I, Arbel Y, Laufer-Perl M, Beer G, Kapusta L, Topilsky Y (2021) Evolution of right and left ventricle routine and speckle-tracking echocardiography in patients recovering from coronavirus disease 2019: a longitudinal study. Eur Heart J Cardiovasc Imaging. doi: 10.1093/ehjci/jeab190
58. Oikonomou E, Lampsas S, Theofilis P, Souvaliotis N, Papamikroulis GA, Katsarou O, Kalogeras K, Pantelidis P, Papaioannou TG, Tsatsaragkou A, Marinos G, Siasos G, Tousoulis D, Vavuranakis M (2023) Impaired left ventricular deformation and ventricular-arterial coupling in post-COVID-19: association with autonomic dysregulation. Heart Vessels 38:381–393. doi: 10.1007/s00380-022-02180-2
59. Petek BJ, Moulson N, Drezner JA, Harmon KG, Kliethermes SA, Churchill TW, Patel MR, Baggish AL (2022) Cardiovascular Outcomes in Collegiate Athletes After SARS-CoV-2 Infection: 1-Year Follow-Up From the Outcomes Registry for Cardiac Conditions in Athletes. Circulation 145:1690–1692. doi: 10.1161/CIRCULATIONAHA.121.058272
60. Luck JC, Blaha C, Cauffman A, Gao Z, Arnold AC, Cui J, Sinoway LI (2023) Autonomic and vascular function testing in collegiate athletes following SARS-CoV-2 infection: an exploratory study. Front Physiol 14:1225814. doi: 10.3389/fphys.2023.1225814
61. Nemes A, Kormányos Á, Orosz A, Ambrus N, Várkonyi TT, Lengyel C (2023) Correlations between vegetative autonomic function and specific left atrial functions in healthy adults: Insights from the three-dimensional speckle-tracking echocardiographic MAGYAR-Healthy Study. Journal of Clinical Ultrasound. doi: 10.1002/jcu.23603
62. Nour A, Fouad M, Salam ZA (2023) Evaluation of cardiovascular autonomic dysfunction in symptomatic post-COVID-19 patients using the heart rate variability (HRV) and detection of subtle LV dysfunction using 2D global longitudinal strain (GLS). Int J Cardiovasc Imaging 39:2107–2118. doi: 10.1007/s10554-023-02915-w
63. Sarto F, Spörri J, Fitze DP, Quinlan JI, Narici MV, Franchi MV (2021) Implementing Ultrasound Imaging for the Assessment of Muscle and Tendon Properties in Elite Sports: Practical Aspects, Methodological Considerations and Future Directions. Sports Med 51:1151–1170. doi: 10.1007/s40279-021-01436-7