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Determination of Morphological and Functional Adaptations in Top Level Female Handball Players Using Cardiac MR Imaging

Bestimmung morphologischer und funktioneller Adaptationsprozesse bei professionellen Handballspielerinnen mittels kardialer Magnetresonanztomographie

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Rationale and Objectives: Long-term physical training is associated with morphological and functional adaptations of the cardiovascular system. Aim of this prospective study was to assess physiologic adaptations and structural cardiac remodelling and to analyze the presence and distribution of myocardial Late Gadolinium Enhancement (LGE) by cardiac magnetic resonance imaging (MRI).
Materials and Methods: Thirteen female professional handball players (mean age 25.1 ± 4.7) and 13 age- and gender-matched non-athlete controls (mean age 25.5 ± 4.2) underwent cardiac MRI at 1.5T. Steady-state free-precession cine MRI was used to calculate left and right ventricular end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), ejection fraction (EF), myocardial mass (MM) and cardiac remodeling index (RI). Macroscopical structural alterations or myocardial scar were excluded by late gadolinium enhancement (LGE) imaging.
Results: Indexed LV-EDV and RV-EDV were significantly (P<.001) increased in athletes compared to controls. There was no difference in LV-EF of athletes (61.1 ± 3.3 %) and controls (62.5 ± 5.0 %). The LV-RI of athletes (0.65 ± 0.07 g/ml) was similar to those of the control subjects (0.64 ± 0.06 g/ml). Neither subendocardial nor midwall myocardial LGE, indicating replacement scarring or interstitial fibrosis, were observed.
Discussion and Conclusion: Physical exercise is associated with enlargement of LV and RV chamber size, MM and increased SV in comparison to healthy individuals. MRI enables direct, objective measurement of these features and therefore may allow differentiating them from hypertrophic cardiomyopathy. While no LGE was identified, study results confirm the existence of a balanced mild myocardial hypertrophy and ventricular dilatation in athletes. Based on our results, eccentric LVH in the absence of cardiovascular symptoms has to be judged as a benign phenomenon in these elite athletes, representing a physiologic adaptation to intense exercise training.

Key Words: cardiac function, cardiac hypertrophy, athlete's heart, Magnetic resonance imaging, late gadolinium enhancement.

SUMMARY

Problemstellung: Körperliches Ausdauertraining ist vergesellschaftet mit morphologischen und funktionellen Anpassungsvorgängen des kardiovaskulären Systems. Zielsetzung dieser Studie war die quantitative Bestimmung dieser Adaptationsvorgänge im Vergleich zu einem Normkollektiv sowie der Ausschluss einer myokardialen Fibrose mittels der kardialen Magnetresonanztomographie (MRT).
Methoden: 13 professionelle Handballspielerinnen (25,1 ± 4,7 Jahre) sowie 13 alters- und geschlechtsadaptierte, nicht sportlich aktive Probandinnen (25,5 ± 4,2 Jahre) unterzogen sich einer kardialen MRT bei 1,5 Tesla. Auf Basis der akquirierten steady-state free-precession (SSFP) Cine-Sequenzen wurden kardiale Funktionsparameter, die Myokardmasse (MM) sowie der kardiale Remodeling Index (RI) bestimmt. Ergebnisse: Auf Körperoberfläche normierte Indices für links- und rechtsventrikuläres EDV waren bei den Handballerinnen signifikant (P < 0,001) höher verglichen mit dem Normkollektiv. Demgegenüber konnte kein Unterschied der linksventrikulären EF bestimmt werden (61,1 ± 3,3 % gegenüber 62,5 ± 5,0 %). Der LV-RI zeigte mit 0,65 ± 0,07 g/ml bei den Athleten gegenüber 0,64 ± 0,06 g/ml bei den Probandinnen ebenfalls keine signifikante Differenz. Bei keiner Athletin wurde ein myokardiales LGE als möglicher Hinweis auf eine vermehrte myokardiale Fibrosierung nachgewiesen. Diskussion: Körperliches Ausdauertraining führt im Vergleich mit einem nicht-trainierten Kollektiv zu einer signifikanten Vergrößerung von rechts- und linksventrikulären enddiastolischen Ventrikelvolumina, einem vergrößerten Schlagvolumen sowie einer erhöhten Myokardmuskelmasse. Der fehlende Nachweis eines LGE bestätigt die Exsistenz einer ausgeglichenen milden Myokardhypertrophie bei Sportlern, die als benigner Adaptationsprozess als Folge des intensivierten körperlichen Trainings angesehen werden kann. Die kardiale MRT erlaubt eine präzise, objektive und quantitative Bestimmung dieser Adaptationsvorgänge und eignet sich daher, diese beim Sportlerherz nachweisbaren Veränderungen frühzeitig gegenüber der hypertrophen Kardiomyopathie zu differenzieren.

Schlüsselwörter: Herzfunktion, Myokardhypertrophie, Sportlerherz, Magnetresonanztomographie, Late Enhancement-Bildgebung

INTRODUCTION

Cardiac remodeling can be a physiological or pathological condition. Physiological remodeling can be seen in athletes and is characterized by a compensatory change in the proportion and function of the heart. Pathological remodeling may occur after conditions such as myocardial infarction (pressure overload), inflammatory myocardial disease, idiopathic dilated cardiomyopathy (DCM) or volume overload (10).

accepted: October 2013
published online: November 2013
DOI: 10.5960/dzsm.2013.099
Kramer U, Mangold S, Krumm P, Seeger A, Franzen E, Niess AM, Claussen CD, Burgstahler C: Determination of Morphological and Functional Adaptations in Top Level Female Handball Players Using Cardiac MR Imaging. Dtsch Z Sportmed 64 (2013) 333 - 338.

Table 1: Physical characteristics of Handball Players and Control Subjects. Data are given as means ± standard deviations. BSA=body surface area, BPM=beats per minute.
* Statistically significant

	Handball Players (n=13)	Control Subjects (n=13)	P Value
Age [y]	25.1 ± 4.7	25.5 ± 4.2	0.8332
Weight [kg]	70.6 ± 9.4	58.0 ± 5.8	* 0.0002
Height [cm]	172.7 ± 4.7	168.1 ± 6.1	* 0.0354
BMI [kg/m2]	23.3 ± 1.8	20.5 ± 1.3	0.06
BSA [m2]	1.84 ± 0.14	1.6 ± 0.1	* 0.0003
Resting Heart rate [bpm]	59.9 ± 4.0	73.6 ± 11.6	* 0.0078

The athlete's heart (AH) is a physiological condition that can be defined as a morphological consequence of systematic training in athletes with the following features: increase in maximal cardiac output (CO), increase in stroke volume (SV), decrease in resting heart rate (HR) and electrocardiographic (ECG) changes in conduction and repolarisation. A broad variety of cardiovascular adaptations can be achieved after either dynamic or isometric exercise, or a combination of both (14). In the past, a lively debate has been led concerning the existence of two different types of AH. Morganroth et al. was the first to uncover two morphologic types of AH: a strength-trained heart and an endurance-trained heart, depending on the type of exercise performed (11). In endurance training the volume load is a predominant factor; therefore, the endurance-trained heart develops eccentric myocardial hypertrophy, whereas the pressure load in resistance training will lead to an increase in myocardial wall thickness, so called concentric myocardial hypertrophy (21,22,23,24). However, more recent publications confirmed the thesis a concentric myocardial hypertrophy usually is associated with taking medication with known cardiovascular side effects (e.g. steroids) (13).

However, it is important to distinguish such normal physiological adaptations to training from pathologic conditions such as hypertrophic cardiomyopathy (HCM), the most common cardiovascular cause of sudden cardiac death (SCD) in young athletes (1,7,9). Identification of the latter in athletes can be difficult as some athletes develop substantial physiologic left ventricular hypertrophy (LVH) as a consequence of intense physical training. Therefore, the differentiation between physiologic and pathologic LVH may represent an important and difficult clinical issue. Newer imaging modalities may have an important role in addressing this important line of enquiry (6,17,26).

Cardiac magnetic resonance imaging (MRI) has emerged as a highly reproducible and accurate imaging methodology for determining LV mass (LVM) and cardiac dimensions. MRI can accurately measure these parameters with low inter-observer and inter-study variability (16). Additionally, using delayed gadolinium enhancement cardiac MRI can depict areas of overt scar or fibrosis (2,5,19). Myocardial late gadolinium enhancement (LGE) imaging has already been demonstrated to provide additional insights into conditions associated with deposition of fibrosis such as myocardial infarction, hypertrophic or dilated cardiomyopathy, as well as acute inflammatory myocarditis or other rarer cardiomyopathies. Hence LGE imaging can be used as a risk-stratification tool in ischemic as well as non-ischemic cardiac diseases.

Although exercise related adaptations of the LV in AH have been examined by a number of preferably echocardiographic studies, there are no data existing regarding the (dedicated) assessment of the effects of this specific type of training on cardiac morphology and function in professional female handball players by cardiac MRI. Therefore, purposes of this prospective study were as follows: (1) to assess physiologic adaptations and structural cardiac remodelling and (2) to determine biventricular functional parameters and myocardial mass as well as (3) to analyze the presence and distribution of myocardial LGE by cardiac MRI and (4) to compare findings to those of healthy non-athlete controls. It was hypothesized that the ratios between LV and RV mass and volume of the athlete's heart and hearts of the control group would be similar.

MATERIALS AND METHODS

This study was approved by the local ethics committees, and all participants provided written informed consent before study enrollment. The investigation was conducted in accordance with the Declaration of Helsinki.

Study population

Thirteen consecutive professional female handball players (mean age 25.1 ± 4.7) and 13 age and gender matched non-athlete controls (mean age 25.5 ± 4.2) volunteered for the study. Athletes were top national handball players (national first league) with a mean training volume of 12 ± 2 h/week and more than 6 years of continuous training, who competed at national and international levels.

To exclude cardiovascular and other relevant diseases, each participant underwent a physical examination, including a determination of standard blood parameters, resting heart rate, blood pressure at rest, ECG and color Doppler echocardiography. Furthermore, all participants were screened for history of myocarditis and were asked to complete a medical history questionnaire; all subjects denied the use of drugs (e.g steroids) and had normal findings at physical examination and rest echocardiography. Training experience, weekly training volume averaged over the preceding 6 months as well as periods of rest was documented. Control subjects were included if they had normal clinical history and were active in recreational sports but did not engage in any routine physical training (> 3h/wk), which serves as an accepted cutoff threshold in previous studies (8); none of them was routinely active in competition sports or reported previous cardiovascular disease.

Exclusion criteria for study participation included any history of cardiopulmonary disease as well as standard contraindications for MR imaging. None of the subjects were taking any cardiovascular medication or medication with known cardiovascular side effects; all the test subjects were non-smokers.

Resting heart rate (HR), weight and height were measured for all subjects. Body mass index (BMI) as well as body surface area (BSA) was calculated (square meters) for each of them using the Mosteller standard equitation (12). Clinical and anthropometric data of study population are shown in detail in Table 1.

Magnetic resonance imaging

MRI was performed on a 1.5 Tesla (T) scanner (Magnetom Avan-

to, Siemens Medical Systems, Germany). To evaluate functional parameters, the protocol included a breath-hold Steady-State Free-Precession (SSFP) pulse sequence (repetition time/echo time 3.0/1.5 ms; flip angle 60°) used to acquire cine images in 2-chamber, 4-chamber, short-axis, as well as outflow tract orientation of the right (RV) and left ventricle (LV). A stack of contiguous short-axis slices from ventricular apex to base (slice thickness 5mm, gap 5mm) was obtained, parallel to the atrioventricular groove, covering the entire left and right ventricle.

For LGE imaging an inversion-recovery (IR) segmented k-space gradient-echo MR sequence were performed. For all examinations, the optimal inversion time to suppress the signal of normal myocardium was determined with an inversion recovery prepared SSFP sequence with incrementally increasing inversion times. MR images were acquired in short- and long-axis views 10 minutes after intravenous injection of 0.15 mmol per kilogram of body weight gadobutrol (Gadovist, Bayer Healthcare, Germany). LGE imaging was only performed in athletes. Total examination time was between 25-35 minutes.

Image Analysis

Two experienced observers with more than 3 (S.M.) and more than 10 (U.K.) years of experience in the interpretation of cardiac MR imaging independently reviewed the image loops of each subject in a random fashion. Readers were blinded for subject details. For LGE image analysis both readers visually judged the occurrence (absence versus presence), localization, and pattern of LGE.

Cardiac function: Quantitative analysis was performed off-line using dedicated software (ARGUS, Siemens Medical Systems, Germany). LV and RV wall-mass and volumes were measured by tracing endocardial and epicardial contours on the short-axis views. Papillary muscles and trabeculae were included in the ventricular volumes (and excluded from the wall-mass) for efficiency and reproducibility. For mass calculation, the interventricular septum was included as part of the left ventricle.

End-diastolic volumes (EDV) and end-systolic volumes (ESV) were used to determine stroke volume (SV: EDV-ESV) and ejection fraction (EF: EDV-ESV/EDV x 100). The LV and RV mass was determined by summation of EDVs within the epicardial and endocardial borders of the short-axis slices and multiplying the myocardial tissue volume by its specific density of 1.05 g/cm^3. Additionally, all parameters were indexed to BSA for comparative analysis. LV hypertrophy was considered when LV mass index (LVMI) was greater than two standard deviations above the mean of the respective gender group, i.e. equal or greater 105 g/m body surface area in women. Finally, the LV remodeling index (MM/LV-EDV) was calculated to determine the pattern of ventricular remodeling in the two cohorts. An increased remodeling index is consistent with concentric LVH, whereas a reduced remodeling index is indicative of isolated cavity dilatation.

Second, regional wall motion assessment was done qualitatively by both observers in consensus. Regional wall motion abnormalities were allocated to the American Heart Association 17-segment model (3).

Third, maximum left atrial size (cm^2) was measured at end-systole just before the opening of the mitral valve as determined on a four-chamber view of the left ventricle. Finally, left ventricular end-diastolic short-axis diameter (midcavity slice position) was measured in athletes and controls.

Cardiac morphology: Morphological aspects were evaluated as well. Septal and inferior LV wall thickness more than 13 mm was suspicious of a moderate form of HCM. Moreover, presence and type of LVH were recorded. Criteria indicating an arhythmogenic right ventricular cardiomyopathy (ARVC) like isolated RV enlargement, wall motion abnormalities, or aneurysm formation were noted.

Late Gadolinium Enhancement: Macroscopical myocardial fibrosis was documented as indicated by the presence of LGE with each image reviewed by both observers. Images were assessed for the presence, location (described as subendocardial, midwall or subepicardial), the pattern (patchy, spotty or linear), and volume (ml^3) of myocardial enhancement. Patients were classed as having positive LGE, if LGE was detectable on at least two orthogonal planes.

Areas of LGE were identified visually. LGE was defined as an area of visually identified contrast enhancement with a mean signal intensity that was greater than five standard deviations higher than the mean signal intensity of an adjacent area of reference ventricular myocardium, which although nulled had a mean signal intensity significantly above zero.

On the basis of previous experience from clinical and experimental studies, the damaged regions were defined as indicative of myocardial infarction if they were located predominantly in subendocardial areas and attributable to coronary perfusion territories. Midmyocardial or subepicardial LGE with a patchy or spotty distribution was defined as a non-ischemic pattern.

We subsequently analyzed patterns of LGE both subjectively and objectively based on mean signal intensity (SI). No quantitative analysis based on signal-to-noise ratio (SNR) or contrast-to-noise ratio (CNR) measurements were performed.

Statistical analysis

Normality was tested by the Kolmogorov-Smirnov test, and differences between endurance athletes and control subjects were measured by the Student`s t-test for independent samples. Mann-Whitney non-parametric test was used to compare body habitus parameters, heart rate between groups, as well as cardiac dimensions and functional parameters. Data are expressed as the mean value ± standard deviation (SD). The level for a statistically significant difference was set at a p-value less than 0.05. Statistical tests were performed using JMP (JMP Discovery Software 4.0.5; Cary, NC, USA).

RESULTS

For Cine SSFP-images and LGE imaging a satisfactory image quality was obtained in all MR examinations.

Physical characteristics

All athletes were asymptomatic in terms of cardiovascular or pulmonary symptoms. ECG at rest and stress was without any abnormal findings in 7 athletes; 2 subjects were presenting with an incomplete right bundle branch block, in 2 subjects a biphasic T-wave was found as well as a negative T-wave in another 2 subjects. Within the study population there was a good correlation in terms of age (25.1 ± 4.7 yrs. vs. 25.5 ± 4.2 yrs.; k = 0.67). Athletes showed a significantly higher weight and height in comparison with non-athlete controls. BMI did not differ significantly (p = 0.056) between athletes

Table 2: Cardiac LV and RV functional parameters. Data are given as means ± standard deviations. Indexed cardiac parameters are normalized to body surface area (BSA).
* Statistically significant

	Handball Players (n=13)	Control Subjects (n=13)	Difference [%]	P Value
LV-EDV [ml]	175.7 ± 19.2	121.5 ± 14.0	45	* <0.0001
LV-EDV Index [ml/m2]	95.5 ± 6.1	73.8 ± 6.7	29	* <0.0001
LV-ESV [ml]	68.3 ±8.9	46.3 ± 9.8	48	* <0.0001
LV-ESV Index [ml/m2]	37.1 ± 3.5	28.1 ± 5.5	32	* <0.0001
LV-SV [ml]	107.4 ± 13.6	75.3 ± 8.3	43	* <0.0001
LV-SV Index [ml/m2]	58.4 ± 5.3	45.8 ± 3.9	28	* <0.0001
LV-EF [%]	61.1 ± 3.3	62.5 ± 5.0	-2	0.3918
RV-EDV [ml]	188.1 ± 21.6	126.8 ± 18.3	48	* <0.0001
RV-EDV Index [ml/m2]	102.2 ± 7.4	76.1 ± 9.2	34	* <0.0001
RV -ESV [ml]	84.8 ± 15.3	54.5 ± 11.8	56	* <0.0001
RV-ESV Index [ml/m2]	46.0 ± 6.3	33.2 ± 7.1	39	* <0.0001
RV-SV [ml]	104.0 ± 13.2	72.3 ± 10.5	44	* <0.0001
RV-SV Index [ml/m2]	56.6 ± 5.9	43.9 ± 5.2	29	* <0.0001
RV-EF [%]	55.5 ± 4.5	57.2 ± 4.9	-3	0.3547
MM [gr]	114.0 ± 11.2	77.4 ± 9.0	47	* <0.0001
LVMI [gr/m2]	62.2 ± 5.9	47.3 ± 5.4	31	* <0.0001
Remodeling Index [gr/ml]	0.65 ± 0.07	0.64 ± 0.06	2	0,43

(23.3 ± 1.8 kg/m^2) and controls (20.5 ± 1.3 kg/m^2). BSA was significantly increased in athletes (1.84 ± 0.14 m^2 vs. 1.6 ± 0.1 m^2, p = 0.0003). The resting heart rate was significantly lower in athletes than in control subjects (60 ± 4/min vs. 74 ± 12/min, respectively, p = 0.0078).

Cardiac morphological and functional parameters

Total left and right ventricular volume and ventricular mass were considerably larger in the athletes, as expected, than in the control subjects, and the differences persisted when these values were corrected for body surface area.

When compared to controls, athletes had significantly increased LV and RV end-diastolic, end-systolic, and stroke volumes and mass indices (myocardial mass/BSA). In contrast, LV and RV ejection fractions did not differ between the two groups.

The indexed LV-EDV and LV-ESV were significantly (p < 0.0001) higher in athletes than in control subjects. As a consequence, the LV-SV of athletes were increased compared with non-athlete controls. There was no difference in LV-EF of athletes compared with controls (61.1 ± 3.3 % vs. 62.5 ± 5.0 %); LV-EF was within the normal range (57-66 %) in all individuals according to published MRI data for healthy persons (22) and did not differ from those in control subjects (p = 0.392). The LV remodeling index of athletes were similar to those of the control subjects (0.65 ± 0.07 g/ml vs. 0.64 ± 0.06 g/ml; p = 0.43). (Fig. 1). Results of the morphological and functional analysis are given in detail in Table 2.

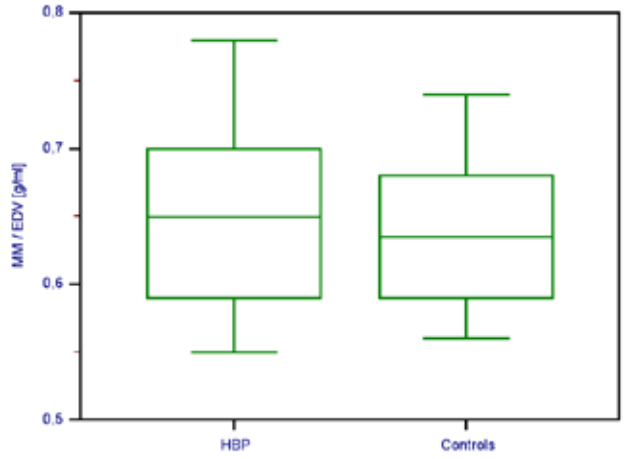

Figure 1: Box plot of left ventricular remodeling index (left ventricular myocardial mass divided by end-diastolic volume) in professional handball players (HBP) and untrained control subjects. No significant differences (p=0.43) were obtained.

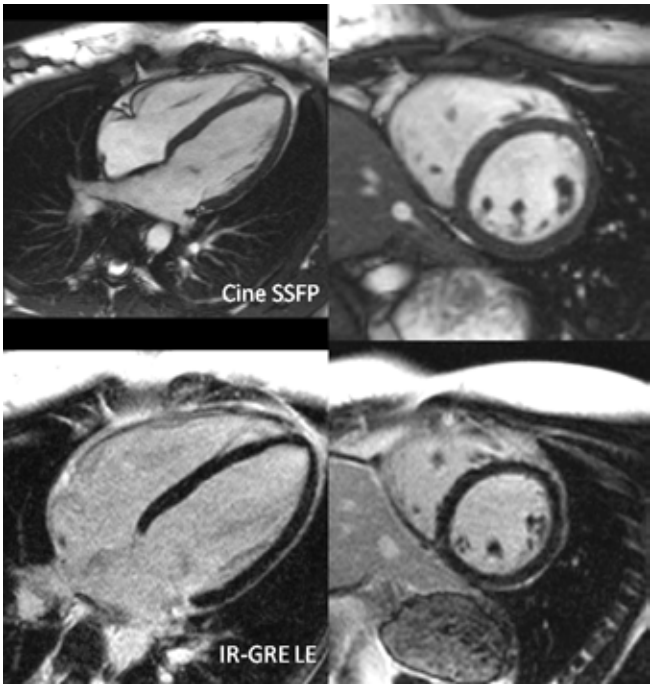

Figure 2: Corresponding steady-state free-precession cine images at end-diastole (upper row) and late enhancement images (lower row) in four-chamber view orientation (left) and a midventricular short-axis view (right). No late gadolinium enhancement can be found.
SSFP=steady-state free-precession, IR-GRE LE=inversion-recovery gradient-echo late enhancement

All indexed myocardial masses in athletes were within normal ranges (53.0-71.6 gr/m^2). There was a moderate correlation between indexed LV-EDV and body size (Pearson correlation, 0.61). Neither a significant correlation between athletes age (p = 0.58) nor training volume and MM index (p = 0.39) was observed.

No regional wall motion abnormalities were found. End-diastolic midventricular short-axis diameter was 5.2 ± 0.5 cm in athletes and 4.7 ± 0.4 cm in controls. Left atrial size was significantly enlarged (22.2 ± 2.6 cm^2) in athletes when compared to controls (11.5 ± 1.1

cm^2). End-diastolic septal thickness in athletes (8.6±0.9 mm) did not differ from those in controls (7.7±0.8 mm). There was no evidence of HCM or ARVD in all subjects.

Myocardial late gadolinium enhancement

LGE imaging was only available in athletes. None of thirteen handball players demonstrated LGE lesions. Neither subendocardial nor midwall macroscopical structural myocardial alterations were identified by visually reading or quantitative SI measurements.
There was no evidence for ischemic myocardial damage. (Fig.2)

DISCUSSION

The main findings of the present study are as follows: highly trained, asymptomatic female handball players have increased cardiac dimensions and muscle mass compared to a healthy age and sex-matched population with recreational sports activities. The increase in SV is attributable only to the larger EDV of hypertrophied ventricles and not to a higher EF. There were no differences in the LV-to-RV ratios of volume indexes. Moreover, to our knowledge there are no previous investigations available, to evaluate the prevalence and pattern of myocardial LGE in a cohort of asymptomatic female handball players. The absence of myocardial LGE combined with normal, but improved functional parameters argues for physiological, benign adaptive structural and functional changes which has been typically attributed to endurance training, representing a balanced cardiac hypertrophy with regulative enlargement of all chambers.

Definition of the term "Athlete`s heart"

The term AH was first described in 1899 by Henschen et al. (20). Today, it is used for the physiological cardiac adaptation to intensive training. In contrast to HCM the left and right heart is harmonically affected. The degree of cardiac enlargement depends on the duration, intensity and the character of physical activity (7,10,23,24,26) and is described to be highest in triathletes, long-distance runners, cyclists and cross-country skiers (26,27).

Up to now, there are only limited data about the effect of sports disciplines that incorporate a combination of both, dynamic as well as static training (e.g. handball) on myocardial remodeling as assessed by cardiac MR imaging. Moreover, only few studies are available with regard to cardiac adaptation in female athletes. Available data from echocardiographic studies reflect that the magnitude of morphological adaptation of the heart is lower in females compared to men (14,25). To the best of our knowledge, the present study is the first to specifically examine the adaptive changes - namely the significantly elevated LV mass and increased chamber sizes - in response to exercise in professional female handball athletes.

Cardiac MRI has validated these findings, with smaller cohorts being required given the improved accuracy of this modality in measuring MM or ventricular volumes when compared to echocardiography (6,24). An MRI study of 21 male endurance athletes by Scharhag et al has shown that the typical response to intensive endurance training is a balanced hypertrophy of the heart, with an increase of LV volumes but with a preserved EF (7). Similar results have been confirmed by Scharf et al in 26 elite male triathletes (21). A recent study by Scharf has been focused on 29 male professional soccer players (22). By comparing these study results in closer detail, especially MM, it has to be taken in account, there are different rules existing about how much papillary muscle or trabeculae should be included. This will result in substantial differences in measured MM. We excluded papillary muscles for wall mass and include them in the endovascular volumes for reproducibility and efficiency.

Clinical implications

Although both pathological and physiological cardiac hypertrophy is associated with an increase in heart mass, pathological hypertrophy is associated with a complex array of events. In general, fibrotic changes in hearts of patients suffering from HCM have been recognized in histopathology for decades and can be classified into diffuse (interstitial) or segmental (replacement) fibrosis (1,7,9). While a limited spatial resolution of LGE imaging does not permit the visualization of interstitial fibrosis, only macroscopic areas of replacement fibrosis can be reliably detected.

In our population, using LGE imaging, macroscopical structural myocardial abnormalities were excluded. The major clinical relevance of this finding is that the presence of subclinical myocardial damage (1) may place these athletes at higher-than-anticipated risk for a coronary event and (2) the absence of LGE might provide further evidence for the benign nature of the hypertrophy associated with AH.

As a consequence, enlargement of camber sizes and mild hypertrophy of LV mass are recognized features of professional athletes, and our data are in line with previous data. However, in contrast to the above mentioned studies, we were able to demonstrate this phenomenon even in female athletes that do not practice systematic endurance training. Moreover, we performed LGE to rule out myocardial fibrosis in the context of AH, which has not been done previously.

Nevertheless, it remains unclear whether our results are transferable to other sport disciplines; moreover, it is impossible to distinguish if these cardiac adaptations seen in our study are a consequence of a specific type of sport or related to the similarity of modern comprehensive training methods.

Study limitations

The study exhibits some limitations that warrant mention when interpreting our data. First, although a substantial number of female athletes were studied, it is still a relatively limited number of subjects compared with previous studies in endurance athletes. Furthermore, this cohort of athletes is still heterogeneous with regard to duration of regular physical exercise. Second, the technique of LGE imaging is an established tool to depict focal macroscopic fibrosis, but it might fail to detect diffuse interstitial fibrosis. This is a known, but critical drawback of LGE imaging, because it is qualitative, not quantitative, and it relies on the difference in SI between damaged and normal adjacent myocardium to generate image contrast. Third, the control group could only be matched in terms of gender and age, as professional handball players are typically taller and more athletic than inactive individuals. This might a major issue, because it is known that correction for body composition is mandatory for appropriate interpretation of equivocally altered cardiac dimensions; moreover, several other parameters like fat-free mass (FFM), septal wall thickness (SWT) or end-diastolic diameter (LVEDD) have to be considered. (17) Nevertheless, adipose tissue in athletes was significantly reduced (mean 15.6±4.2%) when compared to sedentary controls. Fourth, we were focusing on female handball players and did no direct comparison to other sports disciplines.

CONCLUSION

Systematic physical exercise in female handball players is associated with an increased cardiac output and volume load of LV and RV, causing the AH to generate a mild to moderate dilatation and an increased SV in comparison to healthy individuals. While no myocardial LGE was identified, these study results confirm our hypothesis of the existence of a balanced mild myocardial hypertrophy and balanced ventricular dilatation in athletes. Based on our results, eccentric LVH in the absence of cardiovascular symptoms has to be judged as a benign phenomenon in these elite athletes, representing a physiologic adaptation to intense exercise training.

Acknowledgments

The authors would like to thank the participants for study participation. Furthermore, we would also like to acknowledge the dedicated personnel in the MR imaging facilities of the Department of Diagnostic and Interventional Radiology, who assisted in collection of data.

Conflict of interest

The author has no conflicts of interest.

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