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Research paper

Cardiodiagnostic sex-specific differences of the female athlete in sports cardiology

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ABSTRACT

The cardiovascular care of highly active individuals and competitive athletes has developed into an important focus within the field of sports medicine. An evolving understanding of exercise-induced cardiovascular remodeling in athletes has led to a more robust characterization of physiologic adaptation versus pathological dysfunction, but this distinction is often challenging due to diagnostic commonalities. Current data reflects sporting-focused analyses of mainly male athletes, which may not be easily applicable to the female athletic heart. Increasingly female-specific cardiac dimensional and physiologic data are starting to emerge from comparative studies that may be utilized to address this growing need, and further guide individualized care. Here, we review current literature evaluating female-specific cardiovascular adaptations of the athletic heart, and formulate a discussion on cardiac remodeling, cardiodiagnostic findings, etiologic mechanisms, limitations of currently available data, and direction for future research in the cardiovascular care of female athletes.

1. Introduction

Over the past two decades, the proportion of the adult population in the United States engaging in physical activity has steadily increased from approximately 60 % to over 75 %, reflecting a global trend towards incorporation of fitness in cardiovascular disease mitigation strategies [1]. In turn, a growing proportion of highly active individuals and athletes involved in competitive sport has led to the development of sports cardiology; an evolving entity within cardiovascular medicine aimed at addressing the unique needs of this specialized population [2]. The improved understanding of physiologic demands and anticipated exercise-induced cardiovascular adaptations of different sporting disciplines has led to the better stratification of the electrical and structural changes associated with what is colloquially referred to as the *athletic heart* [3–5]. Much of the current understanding of athletic cardiac function and adaptation, however, stems from analyses of male athletic data, creating significant challenges when translating this understanding to care of the female athlete [4]. Female cardiac remodeling data is crucial to differentiating benign exercise-associated physiologic changes from more deleterious pathologic findings, a distinction that is often difficult due to the subtle sex-specific differences in cardiovascular structural physiology. The purpose of this review is to discuss cardiovascular changes associated with exercise, distill and categorize female-specific cardiodiagnostic data, and explore potential underlying mechanisms for these observations. The aim, therefore, is to summarize the most recent and emerging data within the field of female sports cardiology diagnostics, assess gaps in evidence, and provide specific summarized guidance for clinicians providing care for the female athlete.

2. Background

The term exercise-induced cardiac remodeling (EICR) describes the specific hemodynamic effects of sport training on cardiac physiology

Abbreviations: ARVC, arrhythmogenic right ventricular cardiomyopathy; BSA, body surface area; CAC, coronary artery calcium; CMR, cardiac magnetic resonance; CT, computed tomography; ECG, electrocardiogram; EICR, exercise-induced cardiac remodeling; HCM, hypertrophic cardiomyopathy; LV, left ventricle/ventricular; LVOT, left ventricular outflow tract; RV, right ventricle/ventricular; TWI, T-wave inversions.

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and anatomy. Evidence of cardiac remodeling dates to observations from the late 1800s on skiers and rowers who were noted to have cardiac chamber enlargement linked temporally to competitive exercise [5]. Cardiac adaptations are greatly correlated to the type of sport, often characterized by the relative proportions of the two main types of exercise: (1) static activities, incorporating overcoming resistance with sustained muscular contractions, and (2) dynamic activities, requiring regular contraction of large muscle groups [6]. For example, endurance running has a high dynamic component, whereas weightlifting has a high static component. Moreover, sport intensity is also an important consideration for cardiac remodeling. Although various classification schemas have been developed, the broad categories of low, moderate, or high intensity are commonly described. These groupings are often characterized by the percentage of maximum oxygen consumption (VO_2 max), maximal heart rate, heart rate reserve, rate of perceived exertion scale, and degree of aerobic versus anaerobic training [3].

Longitudinal studies from as early as the 1980s have described the causal relationship between exercise and myocardial changes, including changes in cardiac structure and function [7]. The interplay between the static and dynamic components, as well as the intensity of sport, creates a unique spectrum of physiologic stress and subsequent cardiac adaptation. EICR takes this into account and has been postulated to be the result of summative adaptive structural, functional, and molecular changes [8]. More specifically, EICR incorporates changes in cardiac chamber dimensions, myocardial mass, diastology, electrical conduction, coronary artery architecture, and vascular hemodynamics [7,9,10]. For instance, endurance sport may lead to volume-provoked dilation of all four cardiac chambers, whereas strength-based sport may lead to ventricular wall thickening without dilation [5]. The intricacies of EICR are highly individualized and dependent on additional factors including age, ethnicity, and sex [11]; the latter of which is the focus of this discussion.

3. Cardiodiagnostics of female athletes

3.1. Electrocardiography

A resting 12-lead electrocardiogram (ECG) is a common component in the screening and diagnostic cardiovascular evaluation of athletes [3]. Contemporary recommendations for ECG interpretation in athletes were updated in 2017 to aid in distinguishing physiologic adaptations from pathological findings [12]. Even though sex-specific criteria are limited, some well-described ECG patterns may be utilized to guide clinical decision-making (Table 1).

Table 1
Electrocardiographic findings.

Parameter	Common in female athletes[a]	Rare in female athletes[a]
Ventricular repolarization	Anterior TWI in leads V1-V2 [13–16]	Combination of Anterior TWI and J-point elevation > 0.1 mV in leads V1-V2 [17] Deep TWI > 0.2 mV [15] Lateral TWI [18]
Conduction	Shortened conduction times, including PR interval, ventricular activation time, and QRS duration [19]	QRS duration > 100 ms [14] First degree atrio-ventricular block [16,19] Incomplete right bundle branch block [16,19]
Structural		Isolated voltage criteria for LV hypertrophy [14,20] Early repolarization pattern [16,20–22]

TWI: T-wave inversions, LV: left ventricular.
[a] Compared to male athletes.

3.2. Echocardiography

The incorporation of two-dimensional echocardiography in cardiovascular evaluation has led to detailed characterization of atrial and ventricular volumetric data, diastology, and myocardial remodeling, adding to the more complete understanding of structural adaptations of the athletic heart [23]. Many of these measurements are clinically relevant in athletic populations as they are used in the delineation of anticipated exercise-induced changes from pathologic changes seen in hypertrophic cardiomyopathy (HCM) [24] and arrhythmogenic right ventricular cardiomyopathy (ARVC) [25]. Findings suggestive of EICR include ventricular wall thickening and chamber dilation consistent with sport-specific cardiovascular demand, normal or enhanced diastology, and modest aortic dilation [5]. Comparative studies have highlighted that even within EICR, female-specific echocardiographic patterns arise that are particularly noteworthy (Table 2).

3.3. Advanced cardiac imaging

Advanced cardiac imaging, including cardiac magnetic resonance (CMR) and cardiac computed tomography (CT), support the noninvasive evaluation of the athletic population for relevant conditions such as cardiomyopathies, myocarditis, coronary anomalies, coronary atherosclerosis, and arrhythmogenic substrates [34]. CMR has become the imaging of choice for characterization of RV structure and function, and has the added benefit of assessing tissue architecture and ventricular hypertrophic changes [5]. Cardiac CT, and particularly cardiac CT angiography, may be most appropriate for evaluation of proximal coronary and aortic root anatomy [5]. Cost, accessibility, and ability to characterize ventricular morphology all play important roles in choice of advanced imaging modality [5]. Normative data in the athletic population may be limited, however some general trends have emerged that are supplementary to echocardiography (Table 3).

4. Underlying mechanisms

Sex-specific differences in cardiac remodeling are thought to be multifactorial, including hormonal, molecular, and genetic influences [4]. As EICR incorporates some degree of adaptive hypertrophy, many investigators have focused on elucidating underlying mechanisms of cardiomyocyte turnover. Estrogen has a protective effect on the preservation of cardiomyocytes, combating age-related degradation [39,40], and attenuating pathologic hypertrophy [41]. Antihypertrophic effects of estrogen may also relate to molecular mechanisms including the inhibition of protein expression, such as calcineurin, involved in signaling pathways responsible for pathological cardiac hypertrophy [42]. Conversely, testosterone has been associated with inflammation and

Table 2
Echocardiographic findings.

Parameter	Common in female athletes[a]	Rare in female athletes[a]
Chamber dimensions	Larger absolute cardiac dimensions [18] Larger LV end-diastolic diameter[b] [14,16,18,29] Larger RV end-diastolic area[b] [16,29–31] Larger RV outflow tract[b] [16,29–31]	LV wall thickness >12 mm [14,26–28]
Chamber structure	Eccentric LV hypertrophy [14]	
Aortic apparatus	Smaller aortic root dimensions [32]	Aortic root >34 mm [33]
LVOT	Higher LVOT velocity [29]	

LV: left ventricular, RV: right ventricular, LVOT: left ventricular outflow tract.
[a] Compared to male athletes.
[b] Indexed to body-surface area (BSA).

Table 3
Advanced imaging findings.

Parameter	Common in female athletes[a]	Rare in female athletes[a]
Volumetric analysis	Smaller LV and RV end-diastolic volume[b] [35] Smaller LV and RV end-systolic volume[b] [35] Smaller LV and RV ventricular volumes and ventricular masses [37]	Pronounced LA and RA remodeling [36]
CAC		Correlation between level of fitness and CAC score [38]

LV: left ventricular, RV: right ventricular, CAC: coronary artery calcium.
[a] Compared to male athletes.
[b] Indexed to body-surface area (BSA).

hypertrophy in post-ischemic myocardial remodeling in mice, which is worsened when circulating estrogen is low, suggesting additional indirect protective effects of estrogen [43]. Testosterone deficiency in a rat model demonstrated reduced cardiac hypertrophy, LV dilation, and expression of genes involved in pathologic LV remodeling [44]. Additionally, multiple studies on energy metabolism have demonstrated the preferential oxidation of fatty acid and high lipolytic activity in female athletes, a process that is linked to physiological, rather than pathological, cardiac hypertrophy [8,31,45]. Observations that athletes that train similarly have differences in the development of LV hypertrophy led to the further understanding of genetic influences, including polymorphisms in genes involved in the renin-angiotensin-aldosterone system; some of which are sex-specific [46,47]. Certainly, some of the hormone-influenced cardiac remodeling may be adaptive and advantageous, however, more is yet to be understood about the applicability of these data in larger scale clinical settings when advising athletes. Female-specific influences on cardiac physiology and related remodeling remain incompletely understood and are the topic of ongoing investigation.

5. Discussion and summary

Based on these comparative studies and observations, some guiding principles can be formulated that may be of utility for informing the cardiovascular evaluation of female athletes. First, LV remodeling in female athletes is typically eccentric, with overall larger BSA-indexed LV end-diastolic dimensions, prompting consideration of pathology if concentric hypertrophy or smaller BSA-indexed LV end-diastolic dimensions are encountered. Volumetric analysis from advanced imaging, however, demonstrates smaller ventricular BSA-indexed end-systolic and end-diastolic volumes, suggesting that perhaps contractile directionality differs between sexes, with a more elliptical rather than spherical shortening in females. Second, LV wall thickness is typically <12 mm in female athletes and higher values should prompt consideration of pathology, including HCM. Third, BSA-indexed RV dimensions are larger in female athletes, possibly overlapping with criteria for ARVC, thus requiring special attention when present. Fourth, TWI in female athletes are common anteriorly, however if deep and >0.2 mV, associated with J-point elevation >0.1 mV, or located laterally, these findings should prompt consideration of pathology, including conduction disease and ischemia, particularly in the presence of symptoms. Fifth, early repolarization patterns and voltage criteria for LV hypertrophy are rare in female athletes, thus their presence may warrant further investigation. Sixth, there is no clear association between degree of fitness and CAC in female athletes when adjusted for traditional risk factors, suggesting coronary atherosclerotic evaluation should mirror that of the general population when suspected.

6. Limitations and future direction

The paucity of data on sex-specific differences may be attributed to underrepresentation and the inherent difficulty in developing large prospective studies. This may be because matched controls are difficult to establish, mainly due to the variability encountered in age, type of sport, duration of sport, cumulative intensity of conditioning, race, and genetic determinants. Adding another layer of complexity, specific to female athletes, is menopausal status, time of menarche, time since menopause, and obstetric history. Normative electrocardiographic and echocardiography data of female athletes is also sparse, further limiting the development of sex-specific guidance on interpretation. Addressing these major limitations in future investigation is crucial to a more complete understanding of female cardiac physiologic adaptations, pathologic changes, risk stratification, and screening guidelines.

7. Conclusion

The number of female athletic competitors continues to increase steadily. The Olympic Summer Games is reflective of this trend, with 38.2 % female athletes in the Sydney 2000 games, increasing to 48.8 % at the Tokyo 2020 games [48]. This change shines light on the need for an increased proportion of female athletes in future research. The sports cardiology community is urged to expand upon the known data with diverse and robust longitudinal studies focusing on sex-specific cardiac adaptations to exercise. This guidance is not only crucial to combat cardiovascular disease through a more complete understanding of exercise physiology, but also to support the uniquely multidimensional cardiovascular care of female athletes.

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Declaration of competing interest

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