The Impact of Endurance Training on the Cardiac Health of Women

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At the Paris Olympics in 1900, endurance sports were exclusively dominated by men; a mere 22 women participated, competing in the five “gentrified” events of croquet, equestrian, golf, tennis, and sailing. It took until the latter half of the twentieth century for the world to witness women competing in major Olympic endurance sports such as cycling (Los Angeles, 1984) and triathlon (Sydney, 2000).

Wider women’s participation in the Olympics roughly coincided with the establishment of Title IX of the United States’ Educational Amendments of 1972, which mandated equal access for women in any program that received Federal funding – including sports in public schools and universities. These two major developments fueled an explosion of female participation in a variety of events at all skill levels. The **percentage** of women finishers in marathons in the U.S. rose from only 10% in 1980 to a robust 45% by 2015. Women set a new record for **Olympic participation** at the 2016 Rio Olympics, with nearly equal numbers (5,176 athletes, or 45% of total), and with representation in all events included in the games.

Paradoxically, women have generally been under-represented in medical research studies looking at cardiac health, adaptation to endurance training and its potential consequences. Despite this surge of female athletic participation, we still haven’t achieved gender equality when it comes to understanding and caring for the female athlete’s heart. And recent small-scale studies suggest that there are in fact important cardiac differences between the sexes.

Some of the key questions are: to what extent do underlying genetic and hormonal factors impact normal changes in a woman’s heart related to exercise? How do these influences alter her risk for developing chronic heart problems or sudden cardiac death during competition? Are women better equipped to handle endurance training by design? Some recent research suggests that **pregnancy** subjects the female body to **cardiac stresses** similar to those that male athletes experience in even the most competitive events, including events like the Tour de France.

Below we examine the current understanding of cardiac development and risks in women endurance athletes, how and why women may differ from men in this regard, and recommended precautions that should be taken in training and competition by elite female endurance athletes.

Sudden Cardiac Death in Female Endurance Athletes

Sudden cardiac death (SCD) during athletic competition is fortunately a rare occurrence, and it tends to affect men more commonly than women. In fact, a woman’s risk of SCD during endurance sports is estimated to be some 10 times lower than for her male colleagues. Professional cycling, during the past 3 seasons, has seen a total of 6 elite men tragically die directly from heart problems during races (5 in road racing, 1 on the track), with the most recent being **Robbert de Greef** in March 2019. During the same time period, there were zero incidents involving women, and indeed there are no known reports of SCD during elite women’s cycling events for the past 20 years. Professional female cyclists are far more likely to die from training accidents (usually involving automobile collisions) than from heart problems.

Interestingly, these observations regarding SCD in cycling seem not to be true for other endurance sports. Marathon running has a huge participant base – much larger than the women’s pro peloton – with nearly

a half-million **participants in 2019** alone. This huge statistical sampling clarifies **the measure of SCD risk** : 1 incident per 150,000 participants overall, but more commonly occurring in men (1/ 100,000), and much less likely to occur in women (1/243,000).

Despite this fairly low risk of SCD in women, the sheer volume of running participants makes it easier to find reports of SCD. For example, **Taylor Ceepo**, age 22, died in May 2019 – less than 1 mile from the finish line at the Rite-Aid Cleveland Marathon. The medical examiner's report indicated that Ceepo experienced "sudden cardiac death in association with physical exertion, pseudoephedrine use (a fairly benign over-the-counter decongestant) and cardiomyopathy." Her tragedy should remind us that even in very young and apparently healthy women, undiagnosed heart disease is still a common killer (3rd behind unintentional injuries and cancer in her age group), and her autopsy findings highlight the importance of screening women for underlying heart problems.

The most common **causes of SCD** are generally driven by age rather than sex. Athletes under age 35 – both men and women alike – are susceptible to genetically inherited structural heart problems including hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC), as well as potentially lethal heart rhythm problems called "channelopathies." Above age 35, coronary artery disease predominates, with women being preferentially protected by their higher estrogen levels, until they reach menopause. Initially, the ten-fold higher incidence of SCD in men was thought to be simply due to the much larger numbers of men participating in endurance sports. But now that participation rates are becoming nearly equal, women's risk of SCD is still not as high as that experienced in the male population.

Several theories exist that might explain why women appear to be more "protected" from SCD during intense competition. One explanation may lie in the sympathetic nervous system, which is responsible for the body's "fight or flight" response. Male physiology is observed to be "wound more tightly," meaning that their arteries and blood vessels tend to constrict more during intense activity than women. The increased blood pressure adds resistance to blood the heart is pumping out. When this increased pressure load is coupled with an outpouring of adrenaline during competition, the strains placed on the heart may trigger lethal rhythm problems in susceptible individuals – generally those with underlying inherited cardiac problems or acquired fibrosis (scarring) from long-term training. For unclear reasons, even in the context of equal training volumes, men more commonly develop potentially lethal fibrosis substrate, placing them at higher risk of SCD than women.

Another possible explanation relates to obvious hormonal differences between men and women. In some animal models, testosterone has been shown to affect the way the heart conducts impulses – making men, at least in theory – more susceptible than women to developing "electrical instability" resulting in malignant heart arrhythmias. Clinically, testosterone promotes thickening of the heart muscle, which may explain why men are more susceptible than women in developing complications from diseases like HCM and ARVC. Estrogens, on the other hand, are protective in this regard, and delay that same process of heart muscle thickening. Despite equal patterns of genetic transmission of HCM and ARVC between both sexes, hormonal differences may explain why these maladies tend to remain latent for a longer period of time in women, presumably translating to a survival advantage and lower risk of SCD.

Potential Cardiac Problems for the Female Endurance Athlete – And How to Screen For Them

Sports medicine screening programs are designed to identify potential cardiac risks in individuals who exhibit no outward symptoms of heart problems. Such programs aim to increase participation but to do so with a reasonable level of caution, to ensure the safety of the athlete. Despite the lower risk of SCD in women, screening is still important.

Pre-participation screening typically involves a comprehensive medical history review, focused physical examination, and in some cases an electrocardiogram (EKG). EKG tests are proven to be more sensitive

than history and physical examination alone in detecting pathology, especially regarding heart rhythm issues. EKG interpretation should always be completed by a skilled reader able to distinguish the fine line between normal adaptation to exercise and pathology. Guidelines like the **International Recommendations for EKG Interpretation in Athletes** will increase reading accuracy and reduce the number of false findings, which often lead to expensive and unnecessary longitudinal testing. Men exhibit changes in their EKG patterns more often than women, and these variations in many instances are considered normal purely as the result of physiologic adaptation to training. On the other hand, women are less likely to stray from normal parameters, so most EKG changes are concerning and more likely represent a real problem.

Consistent endurance training induces **physiologic remodeling**, or normal adaptations to the heart resulting in improved efficiency of an athlete's engine. Cyclists are unique because they typically perform the most prolonged exercise pattern – more hours per day and more days per year than nearly any other athletes. Cyclists often sustain markedly elevated heart rates for extended periods of time during two distinct types of high cardiac output workouts. First, high intensity aerobic workouts at near peak efficiency, coupled with sustained elevations in heart rate, create a dynamic stress, or a "volume load" on the heart. And second, long tempo efforts punctuated by intense anaerobic dashes create static stress, exposing the heart to a "pressure load" because of sustained increases in blood pressure.

Cyclists therefore typically exhibit prominent changes in heart structure due to a combination of dynamic stress (volume overload) and static stress (pressure overload) resulting in generally increased cardiac mass, with mildly enlarged hearts and mildly increased heart wall thickness – at least in men. Statistically, women are generally smaller than men with lower lean body mass. Due to their higher estrogen levels, women tend to adapt to exercise in a qualitatively similar manner, but quantitatively different than men – showing only minimal heart enlargement and virtually no heart wall thickening. In fact, only about 7% of healthy women show any significant increase in their heart size due to habitual exercise, whereas 47% of men show cardiac enlargement.

Symptoms of heart problems in women are often different to those reported by men. For example, women are less likely to experience classic chest pain due to a heart problem, but may report more subtle symptoms like indigestion, heartburn, fatigue, or poor exercise performance. Misinterpretation of these sometimes confusing symptoms often leads to a delay in diagnosis and poorer long-term outcomes for women. An unexplained decline in athletic performance is obviously concerning to any elite athlete – whether male or female – because this may be the only clue to a serious underlying heart problem.

However, in young women, such nonspecific symptoms are often incorrectly blamed on things like menstrual problems, eating disorders, iron deficiency anemia, pregnancy, or thyroid disease. In many cases it is the woman's primary care provider who must be savvy enough to exclude these other diagnoses, realizing there is a potential heart problem and then making an appropriate referral to a cardiologist.

Estrogen generally protects women from developing CAD at young ages, but the risk rises as they reach menopause. And paradoxically, some young women may actually be at increased risk for CAD because of a syndrome called **Relative Energy Deficiency in Sports** (RED-S). Sports which favor lean body mass are often associated with heavy training loads and dieting to achieve optimal body weight. In some women this results in the **Female Athlete Triad** of menstrual dysfunction, unexplained decline in performance (with or without an eating disorder), and decreased bone density, leading to increased probability of fractures.

Prolonged endurance training in young women can lead to menstrual irregularities resulting in the same kind of reduced estrogen levels typically seen in older postmenopausal women. These athletes should be evaluated for the more traditional cardiac risk factors such as high blood pressure, cholesterol problems,

and diabetes, with appropriate intervention to modify their risk. Treatment of the Female Athlete Triad is challenging and may require a multidisciplinary approach to improve an athlete's overall "energy balance." Strategies include decreasing training volume, modifying dietary habits, medically replacing estrogen levels, promoting bone health with dietary supplements, and seeking appropriate professional help to correct eating disorders if present. Due to the focused and highly competitive nature of many endurance athletes, this is often a tall order to fill since they may resist decreasing their training volume.

Long-Term Effects of Endurance Training in Women

Regular exercise is the cornerstone of prevention and treatment of many cardiac and non-cardiac diseases. But some researchers suggest that the benefits of exercise are like a "drug"– the benefits of moderate training reach a plateau and exceeding that plateau, or "overdosing," may be detrimental to the athlete's health. Several studies have reported unexpected abnormalities in endurance athletes – primarily in men – suggesting either transient or permanent heart damage which puts them at risk for chronic heart issues. Findings have included a five-fold increased risk of atrial fibrillation (AFIB), increased coronary artery calcium deposits (which indicate clinically silent CAD), and scarring of the heart muscle. However, there are several general guidelines that all athletes should be aware of:

- Moderate exercise is beneficial for both men and women in terms of improving overall cardiovascular health. When adjusted for gender, habitual endurance training does not result in increased cardiac risk for women, but some studies suggest otherwise for men.
- Development of AFIB in athletes is related to the remodeling, or enlargement of the left atrium (left upper heart chamber receiving blood from the lungs), as well as increased sympathetic tone (the involuntary "fight or flight response" triggered by the sympathetic nervous system, rather than voluntary movement). Women have generally lower sympathetic tone than men, and they also exhibit less remodeling of the left atrium related to exercise, suggesting a smaller risk of developing AFIB. One large **study** including data from 150,000 female athletes showed that fit women were at higher risk of developing AFIB than their sedentary peers most likely because of remodeling of the atrium. But their risk was still lower than what occurs in men.
- Contrary to their male counterparts, veteran female athletes exhibit less coronary calcium deposition. Coupled with the protective influence of estrogen, the long-term effects of habitual exercise do not appear to negatively impact a woman's CAD risk as she ages.
- Endurance athletes may develop varying degrees of heart fibrosis which is related to the number of years training and the number of endurance events completed. A **recent study** comparing male and female triathletes showed 17% of men with evidence of fibrosis "scarring" on MRI scans, but no women in the population had the same tell-tale signs. This is an important finding for researchers since heart scarring is felt to be the precursor to significant heart rhythm problems which could result in SCD. Scarring seems to be related to elevated blood pressure during exercise and increased heart thickness. Women generally have smaller overall cardiac mass and less fibrosis compared to men, and the protective effects of estrogen lowers the risk of SCD.

The biological adaptation to handle the stress of pregnancy may be a key reason for the apparently better female adaptation to endurance training. Recent research has highlighted that during pregnancy, the body functions at a basal metabolic rate of 2.2 times the normal – burning up to 4000 calories a day. Extended over a period of 40 weeks, pregnancy can essentially be considered the ultimate endurance event – a true test on the limits of human performance. Under typical circumstances, a body functioning above 2.5 times the normal metabolic rate over a prolonged period will begin to break down. But most women emerge from pregnancy and go on to live healthy lives, having tolerated a level of metabolic strain considered by some to be similar to that experienced by athletes participating in some of the most competitive endurance events.

There are also massive changes in the amount of fluid in a woman's body during pregnancy, creating cardiac stresses similar to endurance training. In order to support the developing fetus, she must increase

her blood volume by a massive 50%, and her cardiac output by 40-50% constituting the ultimate dynamic stress on the heart. The female body appears to require less adaptation by the heart muscle and chambers to accommodate these changes.

More overlap in research examining the similarities between the effects of endurance training in women and the cardiac demands placed on them during pregnancy may help to explain these gender-based differences in adaptation to exercise and related cardiac risk. Additional research specifically devoted to women is critical to a better understanding of how gender influences normal cardiac adaptation to exercise, as well as to more accurately identify pathologic conditions which sometimes seem to overlap with normal physiology.

Despite the substantially lower risk of SCD in women, cardiac risk screening of female endurance athletes and at-risk pregnant women is still important, and should be carried out by clinicians familiar with the differences in adaptive physiology between men and women. Women often experience challenging and atypical cardiac symptoms, requiring a high index of suspicion on the part of their doctors – often at the primary care level – to identify these underlying problems. As the current generation of elite female athletes matures into tomorrow's Master's champions, we will undoubtedly learn a great deal more about the long-term cardiac implications of endurance training in women.

By Dr. Mehreen Quershi, Dr. William Apollo, and Steve Maxwell, December 11th, 2019.