***Introduction: FEMALE ATHLETE´S HEART :***

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For a long time girls and women in general were discouraged from participating in sports, exhaustive training and competition. The underlying idea was that physical activity could harm the reproductive system diminishing fertility.
Time passed and the evolution of female performance in sports and mothers who became world champions persuaded sports scientists to question these concepts.
Another interesting myth in the past was that women had a weaker heart and were considered to be physiologically incapable of prolonged physical activity (1).
Women´s Olympic Marathon was run for the first time in Los Angeles 1984.
In the following 20 years, dramatic improvements in performance times, especially in endurance events has been achieved.
The participation of female athletes at the Olympic Games has increased from 23 % of all participants in Los Angeles 1984, to 38 .2 % in Sydney 2000 and the number will be higher in Athens 2004.
Do the differences in performance between female and male reflect biological differences, or are mainly the result of education , social and cultural restrictions placed on young girls?
Coronary heart disease is the leading cause of death in women in many countries, and claime more lives than all forms of cancer, accidents and diabetes combined. Exercise is one of the most effective tools for maintaining a healthy heart via modification of such risk factors as hypertension, elevated lipids and lipoproteins, obesity and diabetes (2). Exercise is also considered an independent factor in the prevention of coronary heart disease.
Is the commitment of the IOC Medical Commission to get the scientific evidence and medical support to give the female athlete equality and the best conditions in sports participation. Therefore, it is our aim to provide in this document a comprehensive overview of the physiologic and medical features of the cardiovascular evaluation of the women athletes, as described by a panel of scientists of specific expertise.

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***Female Athlete Heart : IOC Medical Commission Position Stand***

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# CARDIAC REMODELING IN WOMEN ATHLETES and IMPLICATIONS FOR CARDIOVASCULAR SCREENING

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Long-term athletic training is associated with left ventricular (LV) remodeling, including increased dimensions in cavity size, wall thickness and mass, which are regarded as a physiologic adaptation to increased hemodynamic load induced by chronic and intensive exercise training and described as "athlete's heart" [1-5]. Although numerous studies have extensively described the athlete's heart, most were limited to males and information regarding female athletes has remained incomplete.

In the last decade, however, the increasing participation of women at the highest levels of competitive sports, while exposing athletes to a more substantial alterations in cardiac morphology, has offered the opportunity to investigate the characteristics of cardiac remodeling in elite female athletes, as well as the gender-specific differences.

We had the possibility to explore this issue, by evaluating a large population of highly trained and elite female athletes, in comparison with male elite athletes [6]. We took advantage of the large data-base of the institute of Sports Science, where a large population of competitive athletes, of both sexes, have been consecutively examined with echocardiography as a part of the medical program for elite Italian athletes [7]. Our study included a group of 600 female athletes, free of structural cardiovascular disease, who were engaged in a wide range of 27 different sports, with long participation in competitions, including about one-third of elite athletes, who had achieved recognition in international and Olympic events.

*Cardiac dimensions in female athletes.*

In the overall group of female athletes, LV end-diastolic cavity dimension ranged from 40 to 66 mm (mean 49±4) (Figure 1). While the vast majority of athletes showed absolute values within the normal limits (i.e., end-diastolic diameter ≤ 54 mm) [8], a substantial minority (about 8%), had LV cavity size enlarged, and occasionally markedly dilated (i.e., ≥

60 mm). Maximal LV thickness (usually corresponding to the anterior ventricular septum) ranged 6 to 12 mm (mean 8.2±0.9). Maximum LV wall thickness was > 10 mm in a minority of female athletes (only 9 subjects) and did not exceed the upper normal limits (i.e., 12 mm) [8] in any of the 600 athletes. Relative wall thickness was 0.34±0.03, with a wide range from 0.24 to 0.50. Finally, LV mass (normalized to body surface) area was 80±16 $g/m^2$ and was above the accepted normal limits (i.e., 110 $g/m^2$) [9] in a 6 %.

*Comparison of female athletes with sedentary controls.*

When female athletes and sedentary controls (of comparable age, body size and racial composition) were compared, athletes showed enlarged LV cavity dimension (average, +6%), increased wall thickness (average, +14%), relative wall thickness (average, +9%), and mass normalized to body size (average, +25%). Compared to sedentary controls, athletes also showed mildly enlarged left atrial dimension (average, +4%) [6].

Despite morphologic differences, athletes did not show alterations of the indexes of LV systolic function (ejection fraction was > 50% in each); also, diastolic filling pattern as assessed by Doppler echocardiography was normal, including early diastolic peak flow velocity (73±13 vs. 72±11 cm/sec in controls; ns) and deceleration of early peak flow velocity (521±133 vs. 515±120 $cm/sec^2$ in controls; ns); however, late (atrial) peak flow velocity was lower in athletes than controls (30±8 vs. 35±8; $p<0.001$) as a consequence of the bradycardia typical of trained subjects. Consequently, athletes also showed increased ratio of the early to late peak flow velocities (2.6±0.9 vs. 2.2±0.6 of controls; $p<0.001$) [6].

*Comparison of female with male athletes.*

A group of 738 male athletes (previously reported as part of previous analysis [10]) of similar age, ethnic origin, sporting disciplines and intensity of training participated, were used for comparison with the group of 600 female athletes. Women showed smaller LV cavity

dimension (-11%), maximum wall thickness (-23%), relative wall thickness (-9%) and mass normalized to body size (-31%) compared to male athletes. Also, aortic root (-9%) and left atrial dimension (-14%) were smaller in female athletes.

LV cavity size in male athlete population showed a wide range of values, from 44 to 66 mm, which was similar to that observed in female athletes, from 40 to 66 mm (Figure 1). In contrast, LV wall thickness showed a broader range of values in male (7 to 16 mm) than in female (6 to 12 mm) athletes [10]. Indeed, LV wall thickness exceeded the upper limits of normal in a small subset of elite male athletes (2%), while it remained within the accepted normal limits in all female athletes. (Figure 2). The gender-related differences in LV wall thickness are not related to the different body size (or composition) of the female athletes, because normalization of LV wall thickness for body surface area or height did not abolish differences among sexes, and men continued to significantly exceed women [6].

*Determinants of LV remodeling in female athletes.*

In the overall group of 600 athletes, the impact of different determinants on LV dimensions was assessed by stepwise regression analysis [6]; which showed that about 50% of the variability in LV cavity dimension was associated with body size, greater chronological age and lower resting heart rate (which in our population also reflect the intensity and duration of athletic conditioning). Analysis of covariance also confirmed the significant impact of type of sport, and showed that endurance disciplines (such as cycling, cross country skiing, rowing/canoeing) had the greatest effect on LV cavity dimensions. Other disciplines, such as team ball (which include aerobic and anaerobic exercise training) showed a moderate impact on LV cavity dimension; finally, technical disciplines (such as equestrian or yachting) had only a minimal effect, as shown in Figure 3. These findings are consistent with previous investigations in male athletes, in which different training profiles have shown

to alter cardiac dimensions in different way, with endurance disciplines demonstrating the greatest impact on LV cavity dimension and wall thickness [10].

Other factors may likely explain part of the gender-related LV dimensional differences. Gender itself is an independent determinant and, although large proportion of the differences between males and females are due to different average body size, other mechanisms possibly implicated are the lower absolute blood pressure response to exercise [11], and lower availability of anabolic androgenic hormones (which stimulates cardiac protein synthesis [12]) in female vs. male athletes. Finally, genetic factors have recently achieved major recognition and have stimulated several investigations which support their role in the cardiac remodeling induced by exercise training [13,14].

*Outer limits of LV remodeling in female athletes and implications for cardiovascular screening*

The upper limits to which absolute LV dimensions are increased with athletic conditioning in women have particular relevance to the differential diagnosis between athlete's heart and structural cardiovascular disease. In fact, female athletes not uncommonly show enlarged LV cavity dimension (i.e., end-diastolic dimension ≥ 54 mm) and, occasionally, markedly dilated (≥ 60 mm) that overlap into a distinctively pathologic range observed in patients with dilated cardiomyopathy (DCM) [15,16]. This morphologic finding raises differential diagnosis between an extreme cardiac adaptation to intensive exercise training and a pathologic cardiac condition with the potential for adverse clinical consequences. The correct identification of physiologic LV dilatation may avoid an unnecessary withdrawal of the athlete from competitions, and the unjustified loss of the varied benefits (including economic) derived from sport [17].

In DCM patients LV cavity is disproportionately enlarged and modifies to a more spherical shape [16]; in trained athletes LV cavity enlargement is associated with mild

enlargement of the right ventricle and the physiologically dilated LV cavity maintains the normal ellipsoid shape, with the mitral valve normally positioned, and without mitral regurgitation [18,19]. The most definitive evidence for DCM is the presence of global systolic dysfunction (i.e., ejection fraction < 50%), and/or evidence of segmental wall motion abnormalities. Instead, athletes with physiologic LV cavity enlargement do not show global systolic dysfunction, segmental wall motion abnormalities, or abnormal diastolic filling pattern [18]. Finally, LV cavity enlargement is common in athletes training in largely aerobic disciplines, such as cycling, cross-country skiing, rowing, long-distance running, and is associated with superior physical performance [18].

The upper limits of absolute LV wall thickness in female athletes rarely exceed 11 mm, and never overlapped into the abnormal range (i.e., ≥ 13 mm) compatible with hypertrophic cardiomyopathy (HCM) [20]. This observation appears to differ importantly from that found in male athletes, in whom LV wall thicknesses may exceed upper normal limits (i.e., 12 mm) in a important minority [10]. Therefore, intense athletic conditioning apparently does not represent a sufficient stimulus to increase LV wall thicknesses in women up to the gray zone of borderline LV hypertrophy, and such athletes do not show morphologic changes that resemble HCM [6]. Considering that male and female patients with HCM show a similar magnitude of LV wall thickening [21], the presence of LV wall thickness of ≥ 13 mm in a female athlete is unlikely to represent a physiologic consequence of athletic conditioning and more likely is expression of a primary pathologic hypertrophy, such as HCM.

LEGENDS

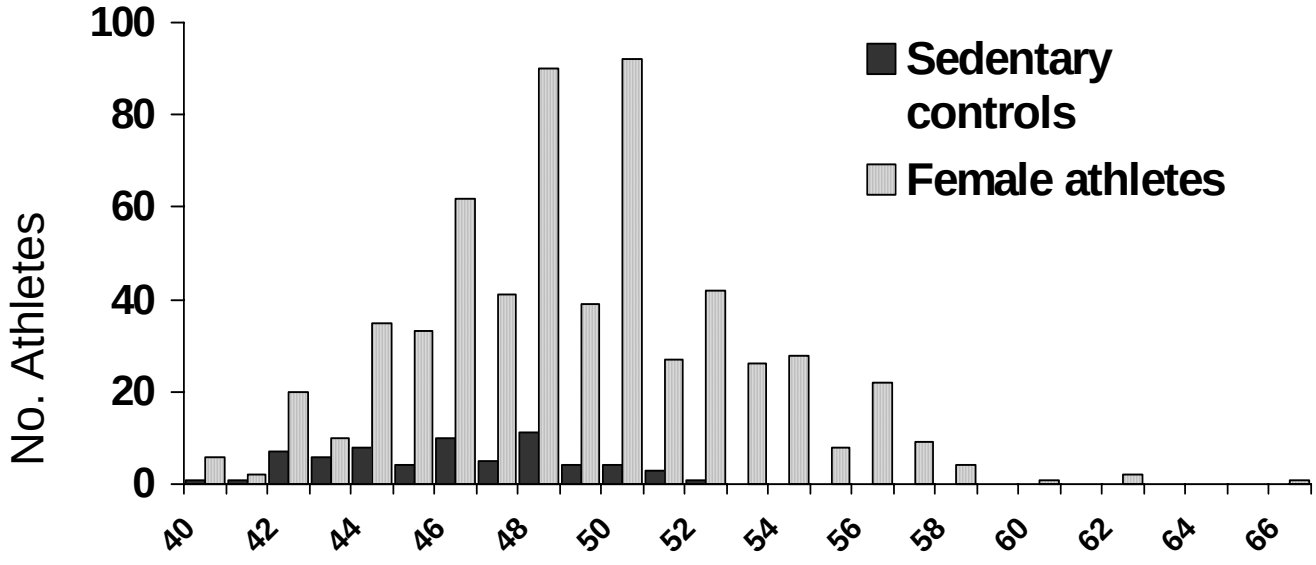


Figure 1. Distribution of left ventricular end-diastolic cavity dimensions in a large population of 600 consecutive female athletes, white Italians, engaged in a spectrum of 27 different disciplines, routinely examined with echocardiography at Institute of Sports Science *(black bars)*. A substantial minority (8%) of these athletes showed cavity dimension that exceeded the upper normal limits. For comparison, distribution of cavity dimension in a group of 65 sedentary female controls, of the same age and body size, is shown *(gray bars)*.

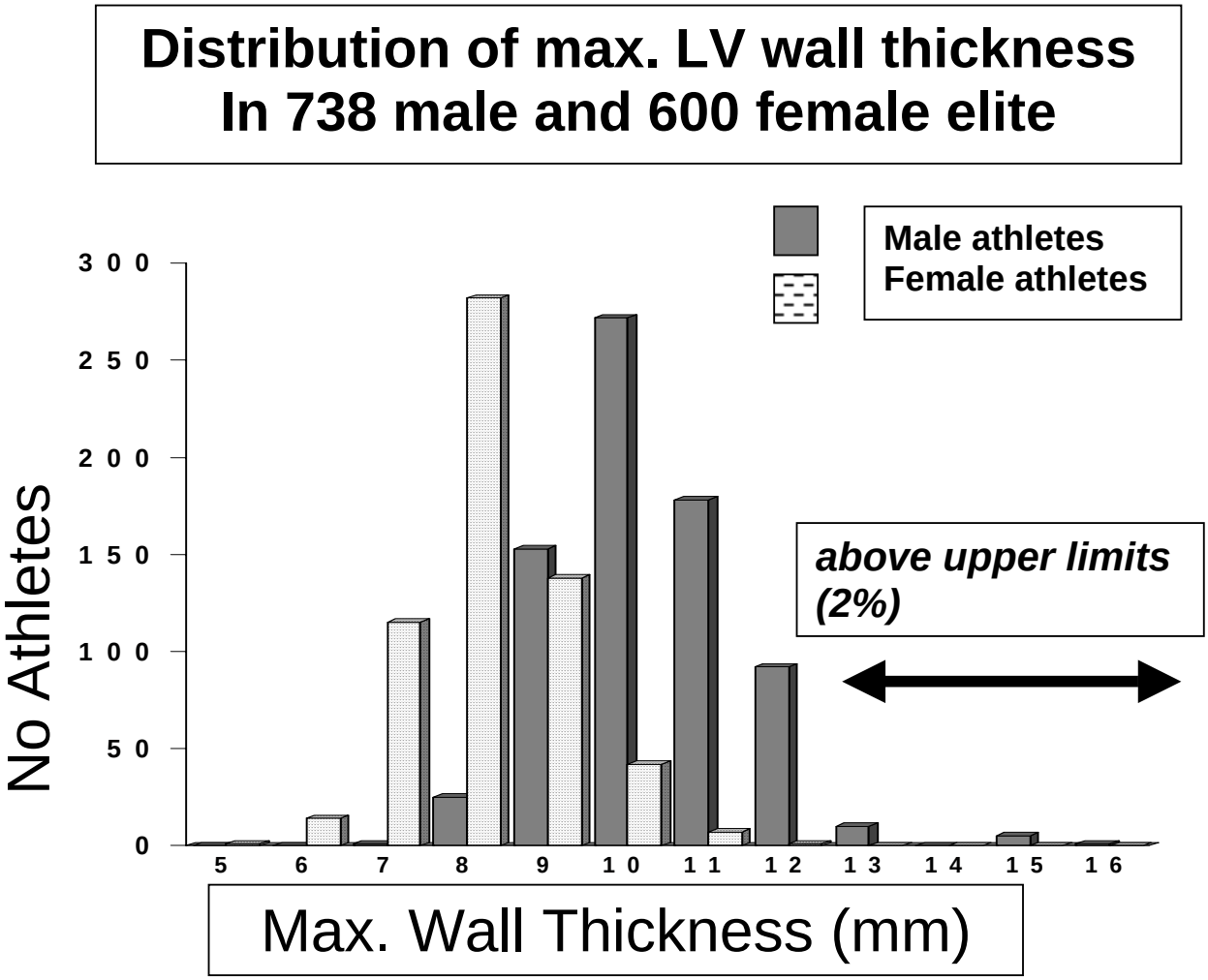


Figure 2. Distribution of maximum left ventricular wall thickness in the 600 female athletes *(black bars)*. For comparison, distribution of maximum wall thickness in a group of 738 male athletes, of the same ethnic origin, age range and spectrum of sport disciplines participated, is shown *(gray bars)*. While 2% of these athletes exceed upper normal limits (i.e., 12 mm), women rarely have wall thickness greater than 11 mm and none exceeds the normal limit.

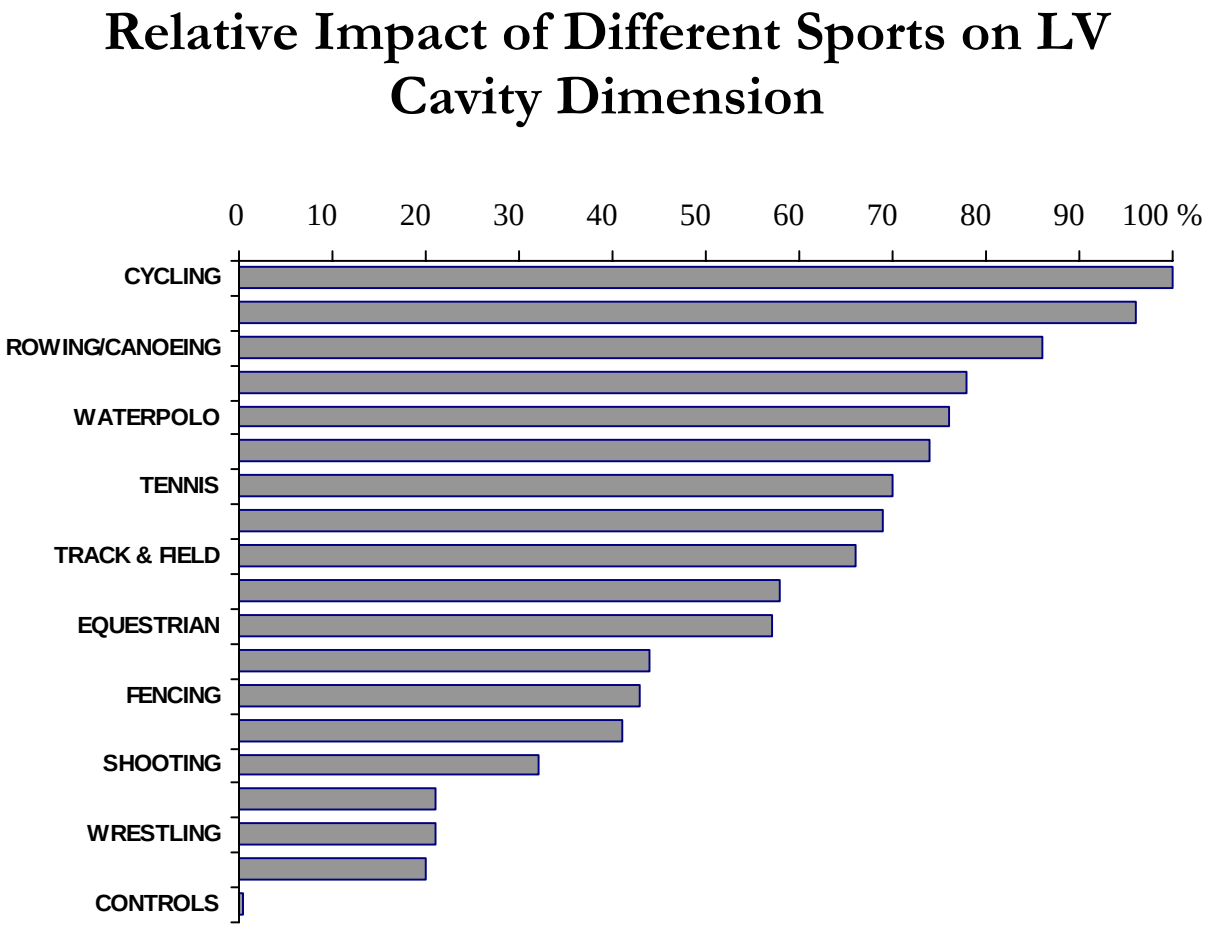


Figure 3. Representation of the impact of different sport disciplines on left ventricular cavity dimension assessed by stepwise and covariance analysis in our population of 600 competitive female athletes [6].

Abbreviations: Hockey = Field hockey.

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**Cardiovascular Response to Exercise in Women**

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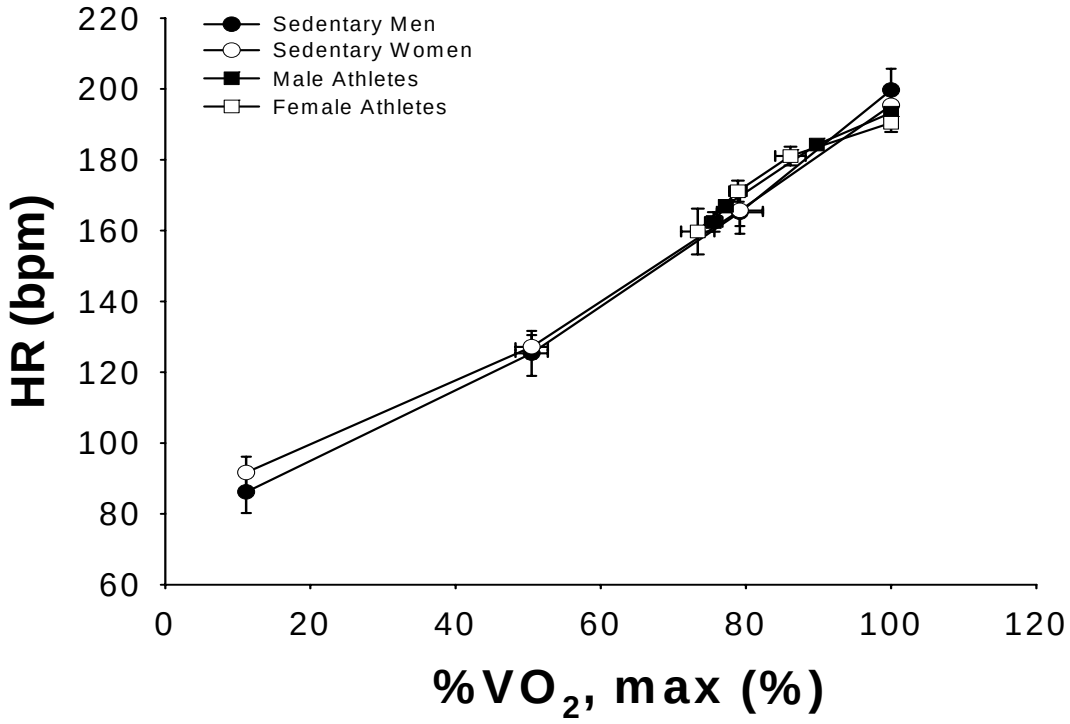
There are physiological and morphological gender differences in humans. It is likely that certain gender-specific factors such as differences in hormonal levels, menstrual cycle variability, and physical characteristics (primarily cardiac size and function) may influence the cardiovascular response to exercise in women.

The most consistent gender difference in cardiovascular responses during submaximal exercise and at peak effort is the lower stroke volume (SV) of women and the smaller increase in SV from rest to exercise. It has been proposed that the smaller SV response during exercise in women is due mainly to a smaller cardiac size, particularly left ventricular (LV) volume and mass [1,2]. Additionally, the difference in cardiac size has also been assumed to account for a majority of the difference in maximal oxygen uptake ($VO_{2,}$ max) during exercise in genders, which is usually reported to be higher in men than in women, whether it is expressed in absolute value or relative to body mass [2].

Previous studies demonstrated that in normal men during upright exercise, SV was augmented through both an increase in LV end-diastolic volume and a decrease in LV end-systolic volume, resulting in an increase in LV ejection fraction [3-5]. However, it has also been suggested that LV ejection fraction did not increase or even decreased from rest to peak exercise in women [6-8]. This notion was supported by the findings that during treadmill exercise, stroke index (SV normalized by body surface area) was lower in women than in men, and did not increase from rest to peak exercise in women [9, 10]. In contrast, Sullivan et al. [11] observed no differences between men and women in cardiac index, stroke index, LV end-diastolic and end-systolic volume indexes in the time course, or magnitude of changes with respect to oxygen uptake ($VO_2$), expressed as percentage of $VO_{2,}$ max.

Our unpublished data on heart rate (HR) responses to exercise in untrained and highly trained young individuals is consistent with the findings of Sullivan et al. [11]. In

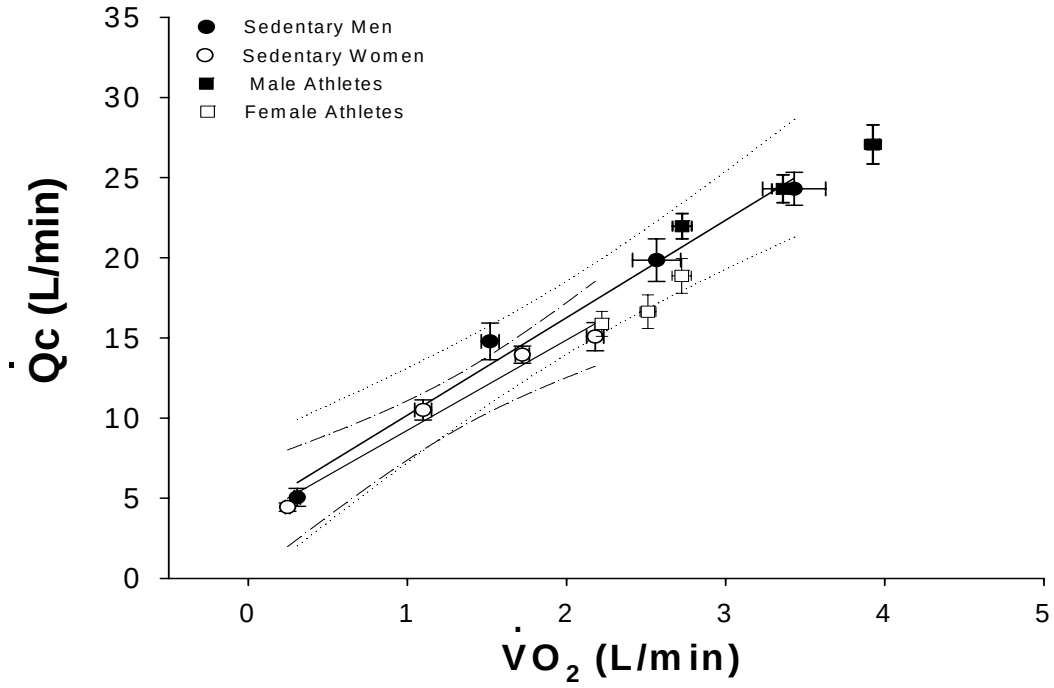
accordance with previous studies, we found that HR increased progressively during submaximal exercise and reached a maximal value (HR, max) at peak exercise effort in all subjects. The increase in HR was greatest in untrained women and smallest in highly trained men at the same absolute work rate which was expressed as $VO_2$ (ml/kg/min), while highly trained women had a smaller increase in HR than untrained men. However, HR max was not different between genders. Interestingly, when we compared the HR responses at the same relative work rate, namely, the percentage of $VO_2$ max (%$VO_2$ max), we found no difference among groups (Figure 1).




Therefore, results from our study and Sullivan et al.'s may suggest that cardiovascular control during dynamic exercise is similar in men and women, no matter whether they are trained or untrained.

One of the key principles in exercise physiology in humans is the remarkably constant relationship between the increase in $VO_2$ and the corresponding increase in cardiac

output [12]. In general, about 6 L of cardiac output are required for every liter of $VO_2$ above rest, regardless of age, gender, or fitness level [13]. In numerous studies from our laboratory, we observed that the relationship between the increase in $VO_2$ and the corresponding increase in cardiac output during exercise was entirely overlapped, and the slope of the line was exactly the same between men and women as well as between untrained and highly trained individuals (Figure 2).




This observation confirms that cardiovascular control during exercise is constant in normal individuals, independent of age, gender, and physical condition.

Indeed, in the late 1970's Wilmore [14] found that there were rather substantial physiological and morphological gender differences between the average male and the average female, however, these differences seemed to be reduced considerably when

comparisons were made between the highly trained male and female athletes who were competing in the same event or sport. Later, Zwiren et al. [15] investigated cardiovascular responses to submaximal bicycle ergometry exercise in equally trained men and women, and found that the magnitude of gender-related differences in cardiovascular responses during exercise appears to be smaller than previously thought. They thereby concluded that gender difference in certain cardiovascular responses to submaximal exercise was a consequence of different levels of physical condition of men and women. Similarly, O'Toole [16] reported that the overall response of the cardiovascular system to exercise was similar in men and women. In 1990's, Pivarnik and Sherman [17] also found that gender differences appear to be negligible when comparing aerobically trained men and women. Mitchell et al. [18] demonstrated that the overall response to acute and chronic exercise in women appears to be similar to the response in men. In addition, it has been shown that although highly trained women runners have much higher $VO_2$ max, submaximal as well as maximal SV, while lower HR than those untrained women of comparable age, they have similar cardiovascular endurance capacity compared to highly trained men [19].

It is well known that $VO_2$ max decreases with advancing age [12,20]. A lower SV, HR, and arterio-venous oxygen difference at maximal exercise contribute to the age-related decline in $VO_2$ max not only in the untrained individuals, but also in the endurance exercise trained men and women [21]. Fleg et al. [22] found that age and gender each had a significant impact on the cardiac response to exhaustive upright cycle exercise. It was demonstrated by Hossack and Bruce [9] that the normal range of maximal values for $VO_2$, HR, cardiac index, and stroke index during treadmill exercise testing decreased with age in both genders, but men showed a significantly greater reduction than women. On the other hand, FitzGerald et al. [23] reported that the absolute (ml/kg/min per year) rate of decline in $VO_2$ max with

increasing age was greatest in highly trained women, next greatest in active women, and lowest in sedentary women; however, when expressed as percent or relative decrease from mean levels at ~25 yr of age, the rate of decline in $VO_2$ max was similar in the three groups. Similar to the previous findings in untrained women [24-26], it was found that menopausal status did not affect cardiovascular fitness in masters women runners [19].

In summary, it seems to us that gender does not affect significantly cardiovascular responses to exercise in both untrained and highly trained individuals. For any task requiring a given absolute oxygen uptake, women are working at a higher percentage of their exercise capacity than men. This would result in a higher HR, greater stress, and a quicker onset of fatigue during the exercise. If allowed to work at a similar percentage of their maximal exercise capacity, men and women would have similar cardiovascular responses. Though cardiovascular endurance capacity declines with advancing age without obvious gender differences, the menopausal status does not seem to influence cardiovascular fitness in sedentary women and in masters women athletes.

*Acknowledgement:* We would like to thank Jere Mitchell, M.D. for his review of the manuscript and thoughtful suggestions.

## Figure Legends

**Figure 1.** Comparisons of heart rate (HR) responses during submaximal and maximal exercise in sedentary men and women, compared with HR response during submaximal exercise in highly trained male and female athletes at the same relative work rate, expressed as the percentage of maximal oxygen uptake (%$VO_2$, max).

**Figure 2.** Relationship between the increase in oxygen uptake ($VO_2$) and the corresponding increase in cardiac output (Qc) during submaximal and maximal exercise in sedentary men and women, compared with $VO_2$ during submaximal exercise in highly trained male and female athletes.

Data refer to 6 sedentary men and 6 sedentary women at rest, during 2 submaximal steady-state work rates, and an incremental test to maximal. Athlete data refer to 39 (27 men and 12 women, aged 18-31 yr) competitive collegiate athletes performing 3 steady-state work rates up to 10 mph for women and 12 mph for men. All studies done on treadmill, using the same acetylene rebreathing system for cardiac output, and Polar HR monitor. Regression lines drawn through data from sedentary men and women only.

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**Prevention of Heart Disease in Female Athletes**

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**Prevention of Atherosclerotic Cardiovascular Disease.**

Studies over the last two decades have documented marked differences between men and women in the presentation, management, and prognosis of atherosclerotic coronary artery disease (CAD). Women present with CAD 10 -- 15 years later than men [1]. This apparent protection was presumably mediated by endogenous estrogen, but the increased risk of cardiac disease with hormonal therapy demonstrated by the Heart and Estrogen/progestin Replacement Study (HERS) [2] and the Women's Health Initiative [3] question this mechanism. Women are also more likely to present with atypical chest pain whereas men are more likely to present with a first myocardial infarction [4], although recent data suggest that unstable angina may be coming a more frequent initial symptom in men [5]. Physicians' treatment of women with possible heart disease may also differ from their treatment of men. Some studies suggest that primary care physicians refer women, especially African-American women, less frequently for coronary angiography [6], whereas among academic cardiologists, the lower physician referral rate appears appropriate given the women's lower risk of atherosclerotic disease [7]. Prognosis following acute myocardial infarction, angioplasty or bypass surgery is also worse in women than in men, probably because of the women's older age at presentation and a higher incidence of other co-morbidities such as diabetes, hypertension and hyperlipidemia. [8-11]. Women have smaller sized vessels which may be more difficult to treat with revascularization techniques. Indeed, gender based differences in outcomes are eliminated when adjusted for body surface area, as a possible surrogate for coronary vessel size [10,11].

Because of the later in life presentation of atherosclerotic CAD in women, coronary disease is extremely unusual in female athletes since these athletes are generally very young women. The diagnosis of atherosclerotic CAD in a female athlete who does not smoke or

have diabetes suggests a congenital defect in lipoprotein metabolism, such as a defect in the low density lipoprotein receptor or familial dysbetalipoproteinemia [12]. Indeed, if CAD is diagnosed in a woman, the clinician should consider non-atherosclerotic causes of CAD, including vasculitis, spontaneous coronary artery spasm or spasm secondary to such sympathomimetics as cocaine, coronary artery dissection especially if the event occurs during or soon after pregnancy, systemic emboli from such conditions as mitral stenosis, paradoxical emboli from an atrial septal defect or patent foramen ovale, or even cardiac tumors or vegetations.

Women were often excluded from many early CAD prevention trials [13]. This limits the data which can be used for designing evidenced based prevention strategies in women. The experience with hormonal replacement therapy discussed above highlights the critical importance of using evidenced based preventive approaches. Strategies to prevent atherosclerotic coronary disease in older female athletes should be directed toward management of the basic atherosclerotic risk factors including cigarette smoking, hyperlipidemia, hypertension, glucose intolerance, obesity, and physical inactivity.

Evidenced based guidelines for the prevention of cardiovascular disease in women have recently been presented [14]. This is an extremely useful document for the following reasons:

1. It provides clinical guidelines for dividing women into 4 categories of risk based on estimated 10 year risk of CAD: low (<10%), intermediate (10-20%), and high (>20%). The high risk group is comprised of women with established atherosclerotic disease, renal disease, diabetes or whose calculated risk using the Framingham Risk Equations exceeds 20%. In addition, the document includes an appendix that can be used in the office with individual patients to calculate their ten year CAD risk.

2. The Women's Guidelines summarize in tabular form the recommended prevention strategies for women for easy access (Table 1)
3. These Guidelines It also includes website listings for other guideline documents such as Third National Cholesterol Education Program Adult Treatment Panel III Guidelines (http://circ.ahajournals.org/ctgi/reprint/106/f25/3143.pdf), the Seventh Report for the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood pressure (JUC7) (http://hyper.ahajournals.org/cgi/content/full/42/6/1205), and recommendations from the American Diabetes Association (http://www/diabetes.org/home.jsp)

The treatment plan for both hyperlipidemia [15] and hypertension [16] is based on the patients estimated total cardiovascular risk. All guidelines advocate lifestyle changes including weight reduction, dietary modification, and increased physical activity before pharmacological therapy. Because the risk of atherosclerotic disease is markedly reduced in young women, most female athletes will not qualify for pharmacological management. Secondary causes of hyperlipidemia and hypertension must be excluded in young athletes so that therapy can be directed at the underlying cause and to avoid unnecessary, prolonged pharmacological therapy. For hyperlipidemia, secondary causes include hypothyroidism, undiagnosed diabetes and insulin resistance, nephrotic syndrome, and other pharmacologic therapy. Medications capable of increasing lipid levels include such agents as alcohol, oral estrogen, and the retinoic acid derivatives used to treat acne in young subjects. For hypertension, secondary causes include medications containing sympathomimetics, hyperthyroidism, aortic coarctation, hyperaldosteronism, renal disease and renal artery

stenosis from fibromuscular dysplasia. Smoking cessation and diabetes management should be aggressively pursued in young female athletes. Hypertension in young athletes should also be aggressively treated to prevent marked hypertension during exertion and its attendant cerebrovascular risks as well as the late sequelae of long standing, untreated hypertension. Pharmacological treatment of hyperlipidemia in many young female athletes, however, can often be deferred until they have completed childbearing unless the hyperlipidemia is severe.

**Prevention of Bacterial Endocarditis.**

Many athletes are capable of athletic competition despite mild to moderate valvular heart disease. These women are potentially at risk for subacute bacterial endocarditis from dental, vaginal, and gastrointestinal procedures and for acute endocarditis from infected skin lesions acquired during competition. Subacute bacterial endocarditis is most frequent in valvular lesions where high velocity blood flow enters a lower pressure chamber; high velocity flow into a lower pressure chamber disrupts laminar blood flow and creates areas of platelet, fibrin, and bacterial deposition. This physiologic profile applies to all left-side of the heart valvular lesions with the exception of pure mitral stenosis. Mitral stenosis alone is an unusual substrate for subacute bacterial endocarditis.

Antibiotic endocarditis prophylaxis prior to procedure likely to produce bacteremia such as dental cleanings should be prescribed for all female athletes with valvular heart disease. The only exception is an athletes with tricuspid or pulmonary regurgitation when a murmur is not detected. Right-sided pressures are lower than left sided pressures, which reduces the risk of bacterial deposition. Furthermore, trivial tricuspid and pulmonary regurgitation detected only by Doppler is common in athletes and not necessarily represent a risk factor for endocarditis. Athletes should be provided with the wallet sized instruction cards available in bulk at minimal cost from the Heart Association, 7272 Greenville Avenue,

Dallas, TX 75231-4596.

The role of subacute endocarditis prophylaxis in mitral valve prolapse (MVP) is controversial. Antibiotic prophylaxis is generally recommended only if a murmur is present [17]. In patients with only a mid-systolic click, the general recommendation is to use endocarditis prophylaxis only in the presence of signs of severe valvular pathology [17]. We place all patients with definite MVP on endocarditis prophylaxis before procedures associated with potential bacteremia. Mitral regurgitation (MR) is often intermittent in patients with MVP and can be missed on a single examination. Also as many as 33% of patients with MVP, but without MR at rest, can induce MR with exercise [18]. The cost and risk of endocarditis prophylaxis in MVP patients is small and the potential benefit, if endocarditis is prevented, great. In addition to these steps to prevent subacute bacterial endocarditis, skin lesions acquired in competition should be promptly cleaned, observed and treated with appropriate antibiotics if infected to prevent bacteremia with the attendant risk of acute endocarditis.

**Rheumatic Fever Prophylaxis.**

Guidelines for the prevention of rheumatic fever have been published [19]. Rheumatic fever prophylaxis is extremely important in female athletes who have had prior rheumatic carditis. Recurrent episodes of rheumatic carditis exacerbate the valvular injury, increase the severity of the valvular lesion and may accelerate the need for valvular surgery. Patients with prior rheumatic fever who develop streptococcal pharyngitis are at high risk for recurrent rheumatic fever, and the infection need not be symptomatic to reactivate the carditis. Also, rheumatic fever can occur after a streptococcal infection even when the infection is treated promptly and correctly. Individuals exposed to groups, such as athletes on athletic teams and their coaches, are more likely to acquire a streptococcal infection. For all of these

reasons, any female athlete or coach with documented rheumatic valvular disease should receive antibiotic prophylaxis until at least age 40 (and probably for life) if the athlete continues to be exposed to groups of athletes.

The best prophylactic treatment is 1.2 million units of benzathine penicillin G intramuscularly every 3 weeks [19]. Oral treatment with 250 mg of penicillin V twice a day is acceptable, but much less dependable since prophylaxis is reduced because of reduced compliance. Patients allergic to penicillin can be treated with sulfadiazine 1 gm daily or erythromycin 250 mg twice daily or clindamycin 300 mg twice daily. Erythromycin or clincamycin is usually a better choice in athletes because of the photosensitivity that can occur with sulfur containing compounds.

**Table 1: Summary of Clinical Recommendations from "Evidence -- Based Guidelines for Cardiovascular Disease Prevention in Women" [14]**

***Lifestyle Interventions***

**Cigarette Smoking:** Women should avoid smoking and environmental tobacco smoke.

**Physical Activity:** Women should engage in a minimum of 30 minutes a day of moderate physical activity on most, preferably all, days of the week.

**Heart -- Healthy Diet:** Women should consume a diet with saturated fat <10% of calories, cholesterol <300 mg a day, and limited transfatty acid intake.

**Weight Maintenance/Reduction:** Women should maintain a BMI between 18.5 and 24.9 kg/m2 and a waist circumference < 35 inches.

**Omega-3 Fatty Acids:** High risk women may consider omega-3 fatty acid supplementation.

**Folic Acid:** High risk women with higher than normal homocysteine levels may consider using folic acid supplementation.

***Major Risk Factor Interventions***

**Blood Pressure:** Women should receive pharmacotherapy if the blood pressures ≥ 140/90 mm Hg despite hygienic intervention. Lower blood pressures may require pharmacotherapy in the presence of target organ damage or diabetes.

**Lipids: High risk** women should receive pharmacotherapy if the LDL-C ≥ 100 mg/dl.
High risk women with and LDL-C < 100 mg/DL should receive statin therapy.
High risk women with a low HDL-C or triglycerides (TG) >200 mg/dl should receive niacin or fibrate therapy.

**Intermediate risk** women should receive LDL-C lowering therapy if the LDL is ≥ 130 mg/dl. Once at the LDL-C goal of <130 mg/dl, intermediate risk women should receive niacin or fibrate therapy if the HDL-C is low or TG ≥ 200 mg/dl.

**Lower risk** women <2 risk factors should receive LDL -- C lowering pharmacotherapy if LDL-C ≥ 190 mg/dl. Their LDL -- C goal is < 160 mg/dl. Lower risk women with ≥2 risk factors should receive LDL -- see lowering pharmacotherapy if the LDL-C >160 mg/dl. Their LDL goal is < 130 mg/dl. Lower risk women should receive niacin or fibrate therapy if the HDL is low or TG ≥ 200 mg/dlNG/DL

**Diabetes:** Diabetics should use lifestyle and pharmacotherapy to achieve Hb A1c < 7 percent.

**Aspirin:** Aspirin and 75 -- 162 mg should be used in high-risk women unless contraindicated. Aspirin can be considered for use in intermediate risk women. Routine aspirin use is not recommended in lower risk women.

**ACE inhibitors:** Ace inhibitors should be used unless contraindicated in high-risk women.

**Warfarin therapy**: Warfarin is recommended in women with chronic or paroxysmal atrial fibrillation to maintain an INR of 2 -- 3 unless the woman is considered to have a stroke risk of < 1% per year or there is a high risk of bleeding. Aspirin should be used when warfarin is contraindicated or the woman is at low risk for stroke.

**Hormonal Therapy:** Combined estrogen and progesterone hormonal therapy and unopposed estrogen should not be initiated to prevent cardiovascular disease.

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# THE MASTER FEMALE ATHLETE

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The natural course of aging brings an increased likelihood of cardiovascular disease, such that it is the most common cause of death in both men and women in the developed world. In addition, recent dietary and lifestyle changes have resulted in rising rates of cardiac disease and its complications in women across the globe. Recently, society and medical professionals have become more aware of the benefits of exercise in reducing the risks of diseases, including heart disease and cancer, as well as improving physical well-being, slowing the physical effects of aging, and improving mental health. For women especially, who live longer than their male counterparts, exercise is not only a way of improving the quality of life but also likely prolonging it.

As exercise has become recognized as a way of improving health and not solely as a means to being victorious during a sporting event, the numbers of both female and master athletes have increased. There has been far more research on the male athlete than female, and virtually all research regarding the risks and benefits of elite and master athleticism involve male athletes. Master athletes are generally considered those over 35 years of age, even more frequently those in the $4^{th}$ and $5^{th}$ decade.

In contrast to the lack of data on elite master female athletes, recent studies regarding the female recreational athlete have demonstrated the benefits of exercise. One such article finds significant correlations between cardiac disease and smoking, diet, obesity, and exercise [1]. There was a linear decrease in cardiovascular events with increasing hours per week of exercise. Those women who exercised (including brisk walking) over 5 hours per week had a 40% reduction of relative risk of a cardiac event [1]. As exercise becomes more popular, it becomes increasingly important to understand not only the risks and benefits of exercise in this population, but also how to properly evaluate the female master athlete prior to initiation of a strenuous exercise regimen. With this knowledge, we can more

safely encourage those who are at low risk and counsel those at higher risk, or teach those with established heart disease how to participate in an adjusted exercise regimen.

*Cardiovascular changes associated with aging.*

As men and women age, the cardiovascular system becomes less efficient. Maximum oxygen consumption declines with age at the rate of 10% per decade after the age of 25 [2]. It is not clear if exercise can slow this rate of decline. Studies have shown that athletes have greater retention of aerobic abilities than sedentary individuals [3]. In addition, with aging comes a less compliant vascular bed, increased likelihood of hypertension and dysfunction in lipid metabolism. The later two effects are known risk factors for cardiovascular disease. Exercise creates a healthier vascular bed through weight loss and by directly decreasing blood pressure. Exercise also lowers both LDL cholesterol and triglycerides, and increases protective HDL cholesterol [4]. In addition, exercise improves glucose tolerance and insulin responsiveness [5]. The short-term effects of weight loss and increased fitness are therefore coupled with a decreasing long-term risk of a cardiovascular event [6].

*How much exercise is needed to achieve benefits in healthy women?*

In 1995, the US Centers for Disease Control (CDC) and the American College of Sports Medicine (ACSM) recommended that adults participate in 30 minutes of moderately intense exercise most days of the week. In 2002, the US Institute of Medicine (IOM) increased the exercise goal to 60 minutes of moderately intense, daily activity, citing research that suggests that additional benefit is gained from additional exercise. Similarly studies have also shown a proportional improvement in cardiovascular health when intensity of exercise is increased[7]. However, other research has shown that moderate exercise is as or more effective in lowering blood pressure than high intensity exercise, and that the benefits of exercise are more closely correlated with the duration of exercise instead of level of intensity

[5]. In particular, data from the Nurses Health Study (NHS) indicate a mortality benefit from day from even a very low level activity in women-- as little as one hour brisk walking per week [6].

In addition to physiological benefits, there are significant psychological benefits of exercise, both indirectly through weight loss and improvement in self-esteem and directly through release of endorphins. When exercise replaces risky habits such as smoking, or is part of healthy life style modification including diet and stress reduction, the benefits can be exponential.

In the female population with overt cardiovascular disease (CVD), the benefits of exercise are equally apparent and play a key role in the rehabilitation process after a cardiovascular event, such as a heart attack or stroke, as well as the treatment of cardiac risk factors. In the setting of a safe, monitored environment, exercise improves quality, and likely quantity, of life. As with healthy women, exercise in the female with cardiovascular disease also promotes psychological well being as well as impairing strength and ability to complete activities of daily life.

## ***Exercising safely***

As the older female considers involvement in a sport or training program, the wide variety of benefits previously discussed can be anticipated. However, the challenge of exercising safely is increased in older athletes because of a high prevalence of heart disease, as well as concomitant non-cardiac diseases. In a minority of athletes, participation in athletics can even be harmful. While event rates of sudden death during masters athletic events are not available for women, those in men range from 1:15,000 to 1:50,000 athletes. Events are more frequent in those who are beginning a training program or who exercise irregularly ("weekend warriors") [8].[8]

Cardiac morbidity and mortality in master athletes largely results from coronary heart disease, with or without arrhythmias. It is therefore important to recognize and screen for signs or symptoms that may be indicators of future events. This is complicated by the more atypical presentation of coronary artery disease in women, including such vague complaints as nausea and fatigue, making it more difficult for physicians, trainers, and patients to detect a cardiac problem. Master female diabetic athletes are even more likely to manifest CVD with atypical, vague, or silent events. In addition, diabetic athletes require close monitoring of glucose and almost always require a decrease in their diabetic medication to avoid a spectrum of possible negative consequences, including hypoglycemia, seizures, and even coma.

Other cardiac pathology increasing the risk of exercise-related events are more likely to be seen in the master population, including abnormalities of the native electrical pathway, valvular heart disease, and dilated or hypertrophied cardiomyopathies. Hypertrophied myocardium can result from years of hypertension or inherited hypertrophic cardiomyopathy (HCM). Incidence of HCM is similar in males and female, however the higher number of female deaths from HCM makes it an important consideration for the female master athlete.

## Exercise prescription for the older woman

A recent expert consensus document regarding the screening and assessment of older athletes recommends that the first and most important step of preparticipation evaluation is a careful history and physical examination [2]. The history should focus on uncovering previously undiagnosed CVD by inquiring about risk factors for and symptoms consistent with CVD. Symptoms of chest discomfort, shortness of breath, fatigue, or diminishing abilities to carry out a training regimen is of particular concern. The athletes should also be

asked about family history of heart disease or sudden death in the family (including children). The physical exam checks a wide range of respiratory and cardiovascular function, including blood pressure, listening for murmur or bruits, and physical findings consistent with severe dyslipidemia, such as xanthalasmas or corneous arcus.

***Estimating cardiovascular risk***

A general prediction of risk can be made using algorithms obtained from the Framingham Heart Study [9]. In an older woman, a more accurate estimate is often desirable. A resting ECG can be useful in identifying those with significant previous myocardial injury, electrical abnormalities such as bundle branch block and pre-excitation, or left ventricular hypertrophy. American Heart Association (AHA) guidelines recommend an ECG exercise stress test in 3 groups of master athletes: 1) women older than 50-55 years of age with at least one cardiovascular risk factor, 2) patients with symptoms or signs of CVD, and 3) all patients >65 years of age, regardless of risk or symptoms [2].

A great deal of information can be obtained from a properly performed exercise stress test. Blood pressure response, time to maximum heart rate, and time to return to baseline indicates not only the level of conditioning, but also quick to rise and slow to normalize (delayed heart rate recovery) may be indicators of occult CVD and predict a poorer prognosis. Maximum exercise capacity (METS) also correlate with prognosis in both asymptomatic and symptomatic female CVD patients [10-12]. The Coronary Artery Surgery Study [13] found that exercising at 10 METS is associated with an excellent outcome, even for women with known CVD. The sensitivity of exercise stress testing is approximately 75%, and therefore a negative test may not be reassuring to those with multiple risk factors or symptoms of heart disease. Those with intermediate or high pre-test probability would

benefit from concurrent imaging to increase sensitivity and specificity and improve cost effectiveness, using either echocardiography or nuclear scanning.

***Exercise proscription***

If a pre-exercise evaluation offers proof of cardiovascular disease, that information may be used to guide and protect those individuals. The AHA guidelines suggest that those with discovered CVD (>50% stenosis in one or more coronary arteries), whether symptomatic or not, should not participate in high intensity sport. In addition, those with mild CVD, but with left ventricular dysfunction, hypotension, or dysrrhythmias with exercise, also should not be encouraged to participate in high intensity exercise. Women with blood pressures over 160/100 mmHg should be encouraged to delay highly intensive training until blood pressure is under control. Static exercise, such as high resistance weight lifting, increases blood pressure and may stiffen the left ventricle, and is therefore not recommended for those with moderate to severe hypertension, even if it is well controlled at rest.

While there are few data specific to women or to older athletes, the presence of other cardiovascular diseases should limit participation in certain competitive sports [8]. Master athletes with documented hypertrophic cardiomyopathy, dilated cardiomyopathy, or aortic or mitral stenosis should be counseled not to participate in high intensity or competitive exercise. However, such individuals may benefit from low intensity, supervised exercise programs. Athletes with asymptomatic mitral valve prolapse can enjoy unrestricted participation in sports, however those with moderate or greater regurgitation, syncope, family history of sudden death, or previous emboli should be restricted to low intensity sports.

*Final Recommendations:*

While the benefits of exercise in the master female athletes are substantial and may be

life changing for some individuals, the risks can also be serious and life threatening. Therefore appropriate evaluation and guidance of master female athletes is crucial. The following is a brief overview of some of the recommendations discussed above.

- *How much exercise is recommended for the master female?*

Between thirty to sixty minutes of moderately intense exercise, at least five times per week and preferably six to seven days per week.

- *When is a pre-participation evaluation indicated, and what should it consist of?*

It is crucial that all older women undergo a thorough medical evaluation prior to beginning an exercise regimen. In addition to those with any cardiac symptoms who require a full clinical evaluation, a formal determination of risk should be performed in all master athletes, and those deemed at moderate or greater risk should undergo stress testing before undertaking intensive training or any new exercise regimen in a previously sedentary individual.

During the pre-participation evaluation it is important to educate the athlete or those considering initiating an exercise regimen, regarding both the benefits and risks of the planned exercise. Education regarding the risks and signs of danger of CVD is also an important component of pre-participation counseling, as it equips the athlete with valuable tools for her on-going health.

Once the evaluation is completed, health care providers, exercise physiologists, and trainers assisting such women can confidently encourage those at low risk to participate in even high intensity sports and counsel those who are at increased risk to either limit activity to low intensity or not to participate in competitive sports. As we advocate exercise for the older woman, our own participation in physical conditioning can serve as a persuasive example.

- *Can women with cardiac disease exercise?*

Women with known stable coronary disease can benefit from an exercise program, with some limitations. Both improvement in cardiovascular physiology and prevention of future events occur with regular exercise.

- *Are there limits to exercise for women with cardiac disease?*

Those with significant, untreated CAD (> 50% stenosis), documented hypertrophic cardiomyopathy, and those with mild CVD in combination with reduced left ventricular function, dysrhythmia, or hypotension should limit activity to low intensity sports, or recreational exercise with slowly increasing duration. Those with moderate hypertension should not participate in highly intensive exercise until blood pressures are better controlled.

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