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Relationship Between Exercise Heart Rate and Age in Men vs Women

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Abstract

Objective: To analyze a large cohort of patients who underwent exercise testing and also report sex differences in other exercise heart rate (HR) parameters to determine whether separate sex-based equations to predict peak HR are indicated.

Patients and Methods: Patients aged 40 to 89 years who performed treadmill exercise tests (Bruce protocol) from September 21, 1993, to December 20, 2010, were included. Patients with cardiovascular disease or taking HR-attenuating drugs were excluded. After analyses on preliminary cohort, peak HR—modifying factors were eliminated to obtain a pure data set. Analysis of variance was used to test difference in HR responses by sex with age adjustment.

Results: A total of 37,010 patients (67.3% men) were included in the preliminary cohort. Men had higher peak HR (166±17 vs 163±16 beats/min [bpm]; $P<.001$), HR reserve (90±19 vs 84±17 bpm; $P<.001$), and HR recovery (19±8 vs 18±9 bpm; $P<.03$). Poor exercise capacity, current smoking, diabetes, and obesity had significant peak HR—lowering effects (all $P<.001$). In a pure cohort of 19,013 patients (51.3% of full cohort) without these factors, regression lines approximated more closely the traditional line of $220 -$ age. For men, the regression line in our final cohort was peak HR $= 220 - 0.95 \times$ age. For women, both slope (0.79 bpm/y) and intercept (210 bpm) were still substantially different from those obtained with the traditional formula.

Conclusion: The HR responses to exercise are different in men and women. The HR response of men was close to that obtained with the traditional formula, but peak HR in women had a lower intercept and decreased more slowly with age. A separate formula for peak HR in women appears to be appropriate.

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Exercise heart rate (HR) responses have been studied for many years, without full agreement about differences in HR by age in men vs women. Peak exercise HR has been estimated as $220 -$ age for both men and women since an initial report in the 1970s by Fox et al,[1] though more recent studies question the accuracy of this formula, particularly in women.[2-6] The number of women undergoing exercise testing has increased in recent years, so laboratories have more experience testing women. Also, sports activities for women have increased, so women are more accustomed to high levels of exertion. Although these important facts are known, women have been underrepresented in most cardiovascular studies, including those involving exercise testing. A new formula for calculating peak HR in women has been proposed. The HR responses to exercise are used to identify higher risk patients, so it is important to have accurate, up-to-date norms.[3,7-11]

We analyzed a large cohort that underwent clinical exercise testing to determine factors that affect exercise HR. Then we performed an analysis of HR responses by sex and age in a subcohort without factors strongly affecting the HR response.

PATIENTS AND METHODS

This was a retrospective database study approved by the Institutional Review Board of Mayo Clinic, Rochester, Minnesota. Subjects who did not consent to have their data used in research under Minnesota Statute (§144.335) were excluded.[12]

Study Population

Patients who underwent exercise treadmill testing between September 21, 1993, and December 20, 2010, were identified retrospectively using

the Mayo Integrated Stress Center database in Rochester, MN. This computerized database contains prospectively collected demographic and clinical information about patients. The study included patients aged 40 to 89 years who had performed nonimaging treadmill tests according to the Bruce protocol. Exclusion criteria to define our preliminary cohort were (1) documented history of known cardiovascular disease, including ischemic heart diseases, heart failure, cardiac surgery, structural or valvular heart diseases, major arrhythmias, defibrillator or pacemaker, congenital heart diseases, cerebrovascular diseases, and peripheral vascular diseases; (2) use of any HR-attenuating or rhythm-modifying agents, including beta blockers, calcium channel blockers, sotalol, and amiodarone, at the time of the exercise test; (3) patients younger than 40 years—because reasons for exercise testing in younger patients were different and the number of younger patients was relatively small; (4) the test was not symptom limited but stopped because of ST changes, major arrhythmias, or abnormal blood pressure response; and (5) for patients who underwent multiple exercise tests during the study period, only the initial exercise test was included.

Clinical Data

Demographic and relevant clinical characteristics extracted from the database included hypertension (defined by previous diagnosis or receiving antihypertension medication), diabetes mellitus (defined by previous diagnosis), obesity (defined as body mass index of ≥ 30 kg/m^2), and current smoking. We also identified patients who were grossly unfit or unable to exercise adequately as having a functional aerobic capacity (FAC) of <80%.

Exercise Treadmill Test Protocol

Symptom-limited treadmill exercise testing was performed using the standard Bruce protocol according to the American College of Cardiology/American Heart Association guidelines.[13-15] Symptoms, blood pressure, HR, rating of perceived exertion, and workload were electronically entered into the database during the final minute of each stage of exercise, peak exercise, 1 and 3 minutes of active recovery, and 6 minutes after peak exercise in passive recovery. Tests were supervised by a certified exercise specialist or cardiac nurse and interpreted by a cardiologist who was immediately available for emergencies.

Exercise Treadmill Test Variables

Exercise data used in analyses included percentage of predicted FAC calculated from published equations from our laboratory with adjustment for age and sex.[5] Patients with an FAC of ≤80% were considered either grossly unfit or unable to exercise adequately to achieve peak HR. A positive exercise electrocardiogram (ECG) was defined by standard criteria. An abnormal exercise ECG was defined as any test with ≥1.0 mm ST deviation irrespective of whether the resting ST segments were normal. Resting HR—obtained in the standing position—and peak HR were identified and used to calculate the HR reserve (difference between peak and resting HR). The HR recovery was defined as peak HR minus HR at 1 minute of active recovery (1.7 miles per hour/0% grade) and was considered abnormal if it was ≤12 beats/min.[16]

Statistical Analyses

Statistical analyses proceeded in 2 parts: (1) create a preliminary cohort of patients without cardiovascular disease or drugs affecting HR and identify the comorbidities that influence peak HR and (2) determine the relationship between exercise HR and sex in a pure cohort with those comorbidities eliminated. Baseline characteristics and exercise test variables in the preliminary cohort were compared by sex using 2-sided t tests for continuous variables and the chi-square test of continuity for categorical variables. Analysis of variance using the general linear model was used to identify factors affecting peak HR with adjustment for sex and age. Factors included in the model were diabetes, hypertension, hyperlipidemia, obesity, and unfit status (FAC<80%), current smoking, and abnormal exercise ECG. We then developed the pure cohort in which patients with affecting factors were eliminated. General linear model was used to determine the effect of sex and age on peak HR and other HR parameters in the pure cohort. SAS (version 9.2; SAS Institute, Cary, NC) was used for all statistical procedures. Significance was set at $P<.05$.

RESULTS

Study Population

Our cohort was derived from adults consecutively referred for exercise stress testing at

Mayo Clinic, Rochester, between September 21, 1993, and December 20, 2010. We initially reviewed 105,220 exercise tests on 79,769 unique patients. Of these, 37,010 met preliminary inclusion and exclusion criteria as described in Figure 1.

Clinical characteristics of the preliminary cohort are presented according to sex in Table 1. Approximately 90% were white, 3% African American, and 7% another race. The low prevalence of hypertension was likely explained by the exclusion for HR-attenuating drugs. In general, the risk factor burden was low, consistent with the sociodemographic characteristics of the cohort and the exclusion for cardiovascular disease.

General Exercise Test Results

Exercise test results are given in Table 2. Performance time was greater for men than for women, as expected. The FAC was near 100% for both sexes because we used our own laboratory standards for the FAC.[5] All tests were symptom limited; peak rating of perceived exertion averaged approximately 18 on the 6-20 Borg Scale.[17] Resting HR was higher for women than for men, but other HR parameters and blood pressure parameters were higher for men than for women. Positive exercise ECG was slightly more common in men than in women, with no difference in the frequency of abnormal exercise ECG (includes all tests with ≥1 mm ST depression regardless of resting

FIGURE 1. Flowchart of the study population (between September 1993 and December 2010).
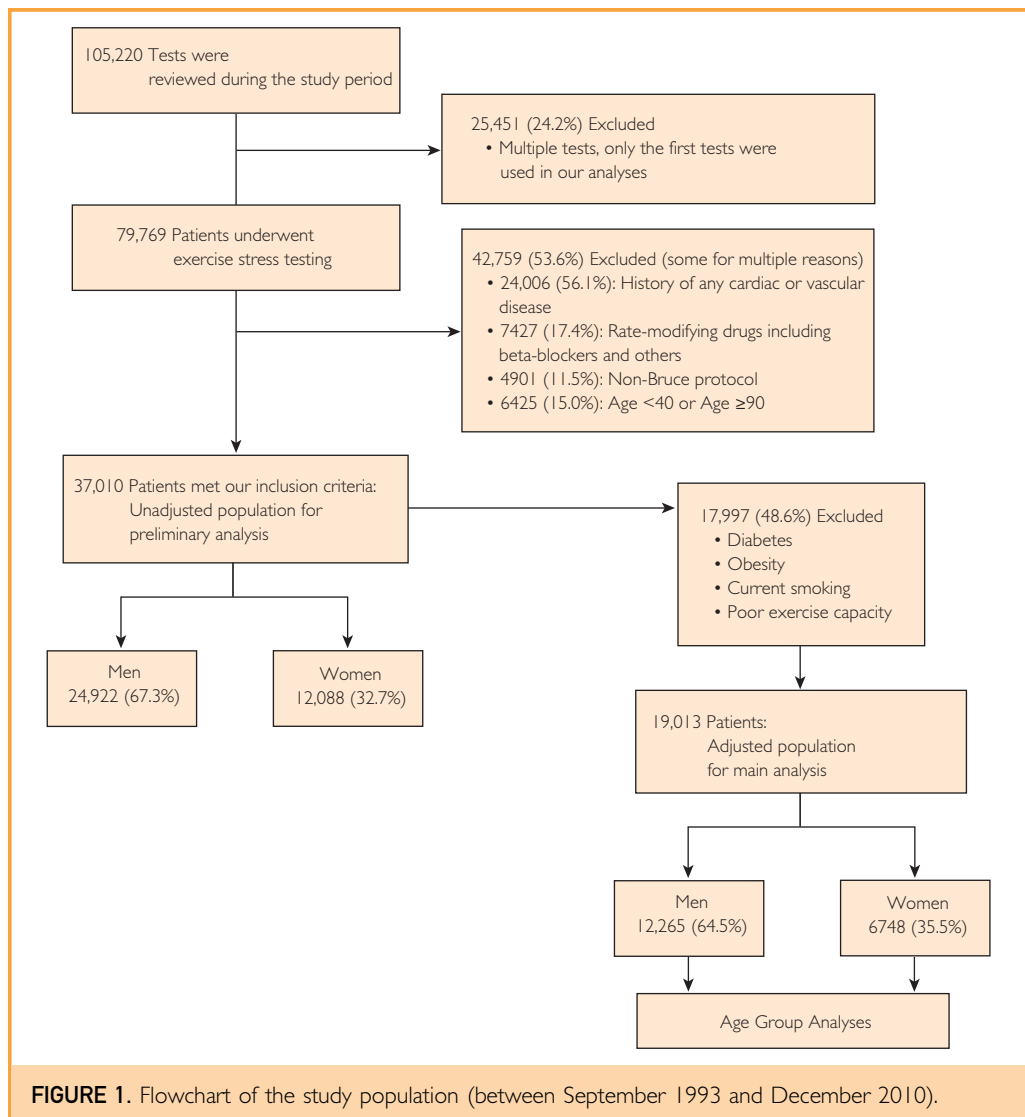
ST-T abnormalities). Note that the large sample size meant that very small, probably nonphysiological differences were nonetheless statistically significant.

Peak HR by Age in Men vs Women in the Preliminary Clinical Cohort

To further examine the relationship between peak HR and age in men vs women, we separately plotted peak HR by age for men and women in the preliminary cohort of 37,010 patients (Figures 2, A and B). Using linear regression, lines predicting peak HR by age are shown in Figure 2, along with 90% CIs and the traditional line depicting 220 − age. Note a large variance around the regression line in both sexes. The regression line more closely approximated 220 − age in terms of both intercept and slope for men vs women.

Analysis of Factors Affecting Peak HR

Using multivariate regression on the preliminary cohort, comorbidities significantly affecting peak HR included poor exercise capacity ($\beta=-11$ beats/min [bpm]), current smoking (−6 bpm), diabetes (−3 bpm), and obesity (−2 bpm). We excluded patients with these comorbidities to form the pure cohort of 19,013 patients (51.3% of full cohort). Peak HR was again plotted against age for men and women separately in Figures 2, C and D. The distribution of peak HR by age became tighter (with improved R^2) after eliminating patients with modifying risk factors, and the regression lines more closely approximated the traditional 220 − age formula. For men, the regression line in our pure cohort was peak HR = 221 − 0.95 × age. For women, it was peak HR = 210 − 0.79 × age, which was still substantially different from the traditional 220 − age formula. Comparing the relationship of peak HR to age between men with women in our pure cohort, both the regression slopes and intercepts were different at $P<.001$.

Exercise Test Parameters by Age in Men vs Women in the Pure Clinical Cohort

We divided the final data set into 5 age groups to analyze the effect of aging on HR parameters in men and women. All exercise HR parameters showed an inverse linear relationship to age in both sexes (Figure 3). Resting HR was higher in women than in men in all age groups. The HR reserve was lower in women than in men

TABLE 1. Baseline Characteristics in Men vs Women in the Preliminary Clinical Cohort			
Characteristic	Men (n=24,922)	Women (n=12,088)	P
Age (y)	54±9	55±9	<.001
Hypertension	18	16	<.001
Diabetes	6	4	<.001
Body mass index (kg/m²)	29±5	27±6	<.001
Obesity	35	28	<.001
Current smoking	10	9	.002
Unfit physical status	19	21	.002

Continuous data are presented as mean ± SD, and categorical data are presented as percentage of sample.

and showed continuously decreasing differences by successive age groups. In the 40 to 49 and 50 to 59 years age groups, significant differences were found in peak HR, but the curves crossed at the 60 to 69 years age group, and so older women had slightly higher peak HR than did men. Differences in HR recovery were small on comparing men and women, with a significant difference only in the age group 50 to 59 years.

DISCUSSION

This study was designed to evaluate the sex differences in HR responses and determine whether a separate equation for predicting peak HR for women is justified. After first eliminating patients with cardiovascular disease or taking drugs affecting HR and then eliminating those with comorbidities affecting peak HR, we show that most HR responses to exercise are significantly different in men vs women. Women have a higher resting HR at all ages. The HR reserve is higher in men at all ages, principally due to lower resting HR. The HR recovery, however, is statistically significantly different between men and women only in the age group 50 to 59 years. Peak HR is significantly lower in younger women than in men, but it declines more slowly with age such that peak HR at ages 70 to 79 and 80 to 89 years is not significantly different between men and women. Although the HR response of men in our cohort was almost identical to that with the traditional 220 − age formula, a lower intercept (210 bpm) and slope (0.79 bpm/y) are required to predict peak HR in women. All exercise HR parameters have an inverse linear relationship to age in both men and women.

Risk factors such as diabetes, smoking, obesity, and poor exercise performance are associated with lower peak HR, perhaps secondary

TABLE 2. Exercise Test Parameters in Men vs Women in the Preliminary Clinical Cohort[a,b]

Parameter	Men (n=24,922)	Women (n=12,088)	P
Exercise time (min)	9.8±2.3	7.6±2.0	<.001
FAC (%)	97±21	99±24	<.001
Resting HR (bpm)	76±13	80±12	<.001
Percent predicted peak HR traditional (%)	100±9	99±9	<.001
Peak HR (bpm)	166±17	163±16	<.001
HR recovery (bpm)	19±8	18±9	.03
HR reserve (bpm)	90±19	84±17	<.001
Resting systolic BP (mmHg)	125±17	120±18	<.001
Resting diastolic BP (mmHg)	81±11	77±11	<.001
Peak systolic BP (mmHg)	184±24	168±24	<.001
Peak diastolic BP (mmHg)	78±16	75±16	.001
Peak RPE	18±1	18±1	.03
Abnormal ECG (%)	9	8	.07
Positive ECG (%)	5	4	<.001

[a]BP = blood pressure; RPE = rating of perceived exertion.
[b]Continuous data are presented as mean ± SD, and categorical data are presented as percentage of sample.

to less than maximal physiologic vs perceived effort. Respiratory distress, for example, may cause a smoker to stop exercising before cardiac output has reached its limit. We eliminated all these risk factors to get a pure cohort and determined that a separate formula for peak HR in women seems appropriate because the traditional formula of 220 − age overestimates peak HR in younger women (age, 40-50 years) and underestimates in elderly women (age, 50-90 years).

The HR responses to exercise have been studied for many years in various populations. All studies report a strong inverse relationship between peak HR and age. The traditional equation to predict peak HR (220 − age) for both men and women was established by Fox et al[1] in a small cohort of 220 subjects, mostly men younger than 55 years.

Subsequently, a meta-analysis on 18,712 subjects performed by Tanaka et al[2] showed a different regression equation to predict peak HR but the regression lines were not different for men and women (men: peak HR = 209 − 0.73 × age; women: peak HR = 208 − 0.77 × age).[2] In Tanaka et al's meta-analysis, only healthy (defined by nonischemic ECG response), nonmedicated, nonsmoking subjects were involved, although we have no exact information about exclusions for cardiovascular diseases, diabetes, and hypertension. Tanaka et al also performed a complementary laboratory study in a healthy population using nonmedicated and nonsmoking adults

without coronary artery disease to verify the maximal level of effort by Vo2 testing (using a respiratory exchange ratio of ≥1.15 as indicative of maximal effort). The regression lines derived (men: peak HR = [210 − 0.72 × age] vs women: peak HR = [207 − 0.65 × age]) were very similar to the meta-analysis findings, again without significant differences by sex. In Tanaka et al's 2 studies, men more so than women show HR responses that differ from those in our data. Although we generally take the traditional formula for peak HR in men for granted, our confirmation that 220 − age is an appropriate formula for predicted peak HR in men is an important finding in the present study.

We have previously published findings from our laboratory[5] on exercise HR in a study that focused on exercise blood pressure response in 7863 men and 2406 women without cardiovascular disease or hypertension. That cohort was tested in an earlier time frame (1988-1992), and we did not restrict the cohort according to diabetes, smoking, or poor test performance. Regression equations for peak HR were 213 − 0.90 × age for men and 203 − 0.76 × age for women with lower intercepts observed vs the present study, likely because of the less restricted nature of the earlier cohort.

An analysis of exercise tests in the St. James Women Take Heart Project performed by Gulati et al[3] proposed a women's formula for age-predicted peak HR = 206 − 0.88 × age. This was a volunteer cohort of 5437 asymptomatic
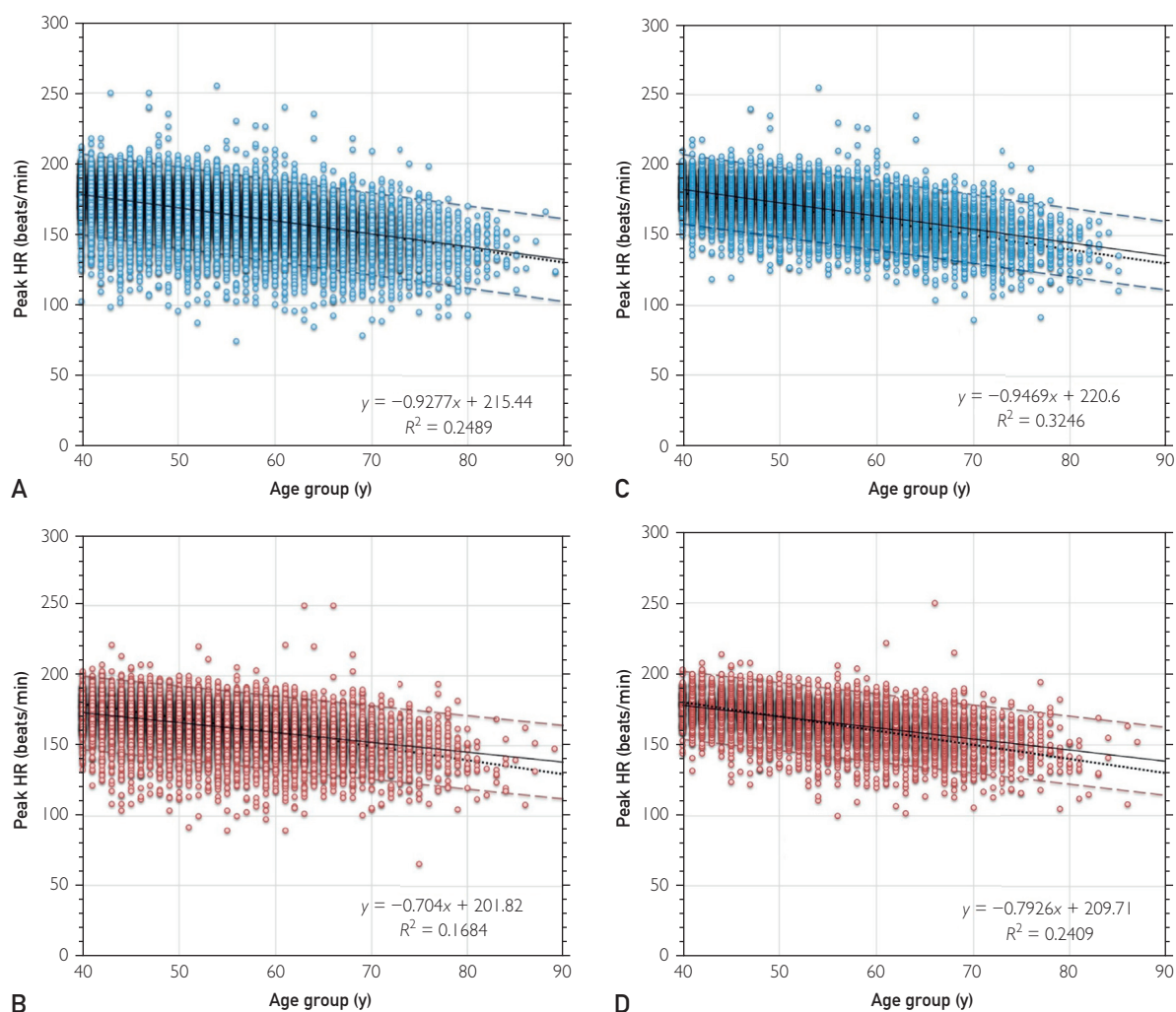
FIGURE 2. Scatter plot diagrams of the peak HR on the preliminary, unadjusted clinical cohort by age in men (A) and women (B), and on the final, adjusted clinical cohort in men (C) and women (D). Results of linear regression are shown as continuous lines, with 90% CIs shown as broken lines, whereas the traditional formula of 220 − age is shown as dotted lines.

women, but no men were tested identically for comparison. Women included were 35 years or older, had no active cardiovascular disease, and were able to walk on a treadmill at a moderate pace, but diabetic women and smokers were not excluded.

The present study not only is the largest clinical cohort analyzed to compare peak HR vs age in men and women but also presents important normative data for other HR parameters including resting HR, HR reserve, and HR recovery. We also show the impact of selected risk factors in attenuating the peak exercise HR, potentially allowing us to reconcile

differences in peak HR response among the various published studies.

Peak HR is one of the most commonly used parameters in clinical cardiovascular medicine, so correct determination is important. On the one hand, peak HR can be used to determine the adequacy of exercise testing with a target of at least 85% of predicted maximal HR.[11] Using the wrong target HR for women may theoretically result in unnecessary repeat testing, though we project that <1% of tests would be reclassified as adequate vs inadequate, with most of those being in older women in whom traditional vs new predicted HR differences
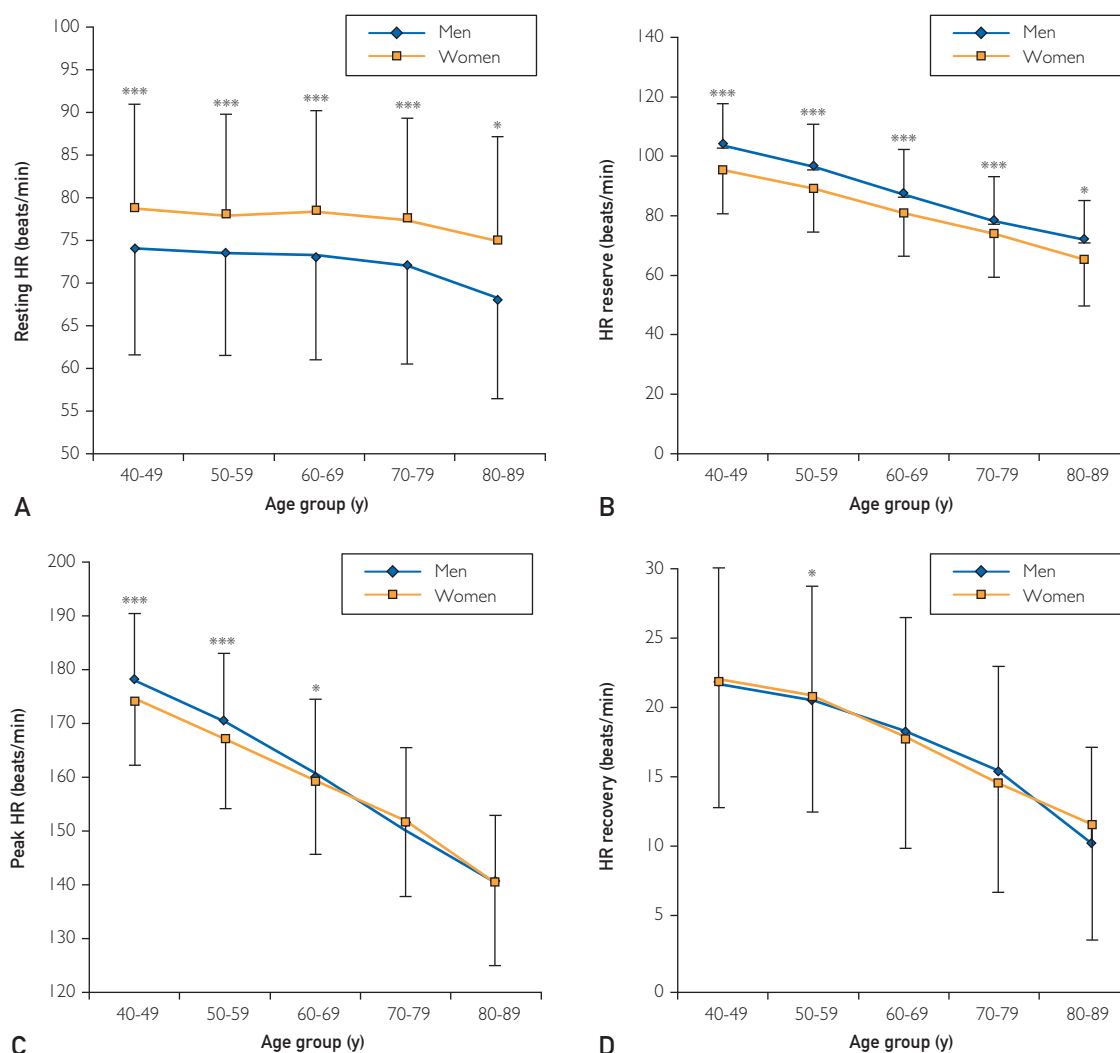
FIGURE 3. Resting HR (A), HR reserve (B), peak HR (C), and HR recovery (D) by age in men vs women in the final cohort. Data points represent mean ± SD. Significance levels: ***P<.001, *P<.05.

become progressively larger. On the other hand, because poor HR response to exercise signals an adverse prognosis, an inappropriate target may again result in incorrect interpretation in selected patients.[7,8,10,11,18] Estimated peak HR is also used to prescribe exercise intensity for various types of patients when no exercise test was performed.[19] Our study both confirms the use of the traditional 220 — age formula for men and provides further evidence that a different formula should be used for women.

Younger patients were excluded from this study because we felt that there was a substantial referral bias. Syncope, chronic fatigue, congenital cardiac disorders, tachyarrhythmias, morbid obesity, and screening for sports participation are among the common referral diagnoses in younger subjects. Thus, we felt that their HR would significantly deviate from the regression line vs age derived in older patients. An analysis of the patients aged 20 to 39 years in our database confirmed these suspicions. Both peak HR and its decline with age were less vigorous in this younger population (men: peak HR = 193 − 0.40 × age; women: peak HR = 196 − 0.61 × age).

This study was not designed to specifically determine why the HR responses are different by sex. Since Title IX, it is unlikely that sex

differences in attitudes toward physical activity play a role, and the large number of women being tested obviates biases that test personnel might have against pushing women to high levels of effort. We might speculate that sex hormones are involved. High testosterone levels promote increased muscle mass in men at young ages, allowing them to push to higher exercise intensities and higher peak HRs during exercise compared with women, but declining testosterone levels gradually attenuate exercise intensity and HR in older men. Muscle mass and exercise performance may follow a less rapid decline in relatively testosterone-poor women. Further research of a more physiologic nature is obviously indicated.

Limitations

This is a cross-sectional analysis with single tests from different individuals. A longitudinal study with regularly repeated tests on a fixed population of healthy individuals would be more appropriate for determining the true physiologic effect of aging on exercise HR, but such a study would be much more difficult to conduct.

These exercise tests were conducted in a clinical environment in which patients were instructed to exercise to subjective fatigue. Patients were not specifically "pushed" to continue exercise until a definite plateau in HR was observed, nor did patients undergo repeat testing to be certain that a higher exercise HR could not be achieved on a second or third try. Gas exchange was not measured during exercise to confirm effort by respiratory exchange ratio.

We had a limited number of patients older than 80 years in our clinical cohort, and survival bias may have affected the HR responses of these older patients. Older individuals are also more likely to have orthopedic complaints that could represent a potential limitation of exercise HR.

The differences that we have noted in peak HR between men and women are not nearly as high as the variation in peak HR at any given age (SD ∼ 11-15 bpm depending on the age group). Thus, slightly adjusting the equation for predicting peak HR will not greatly improve the estimate of peak exercise HR for an individual female patient. Rather, the male-female differences in HR response to exercise shown here may lead us to an additional understanding of sex differences in aging.

CONCLUSION

HR responses to exercise are different in men and women. In this large cohort of patients with factors negatively affecting peak HR eliminated, the equation predicting peak HR in men was nearly identical to the traditional formula but peak HR in women had a lower intercept and decreased more slowly with age. A separate formula for peak HR in women seems to be appropriate.

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