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Open Access Journal of Cardiology
ISSN: 2578-4633

Female Older t han Fifty Years Need a Different Regression Equation for Calculation of Age Predicted Maximal Heart Rate for Evaluation of Exercise Stress Test Using Bruce Protocol

Mittal SR[1]* and Mittal G[2]

[1]Department of Cardiology, Mittal Hospital & Research Centre, India

[2]MSc (Economics), City Bank, India

***Corresponding author:** Mittal SR, Department of Cardiology, Mittal Hospital & Research Centre, Pushkar Road, Ajmer(Raj)-305001, India, Email: drsrmittal@gmail.com

Research Article

Volume 7 Issue 1

Received Date: April 08, 2023

Published Date: April 25, 2023

DOI: 10.23880/oajc-16000177

Abstract

There is lack of consensus regarding regression equation to be used for calculation of age predicted maximal heart rate for evaluation of exercise stress test. We evaluated stage wise increase in heart rate during treadmill stress testing using Bruce protocol in seventy normal individual after excluding various confounding factors. We analyzed the data in two genders of different age groups and calculated the statistical significance of difference between different groups. Formula of 220-age was used for calculation of age predicted maximal heart rate. Females older than fifty years could not reach fourth stage. Total increase in heart rate and percentage of age predicted maximal heart rate were also lower in females older than fifty years. Our study shows that 80% of age predicted maximal heart rate is normal for females older than fifty years and should not be 'considered as chronotropic incompetence.' There is need for developing a different regression equation for calculation of age predicted maximal heart rate for females older than fifty years.

Keywords: Age Predicted Maximal Heart Rate; Chronotropic Incompetence; Coronary Artery Disease; Exercise Electrocardiography; Treadmill Stress Testing

Introduction

Heart rate response to exercise has been studied by several workers. Most of the studies have focused on failure to attain age predicted maximal heart rate (chronotropic incompetence) and it's relation with 'over all' or cardiovascular mortality [1-5]. These studies have, however, not excluded other confounding factors that could affect the heart rate response to exercise and outcome on long term follow up [6]. Further, there is no data on stage wise increase in heart rate and their significance. There is also disagreement regarding regression equation for calculation of age-predicted maximal heart rate [7]. Some authors have observed no difference in maximal heart rate between men and women [8,9]. These studies have resulted in recommendation of same regression equation for men and women for calculation of age predicted maximal heart rate [9]. Others have observed that age predicted maximal heart rate is lower in females [10,11]. This has resulted in recommendation of different regression equation for females [10,12]. Difference in opinion is probably because these studies combined individuals of different age or sex. There is no data on stage wise increase in heart rate in normal persons of different age and sex using Bruce protocol. We, therefore, studied stage wise increase in heart rate of normal individual of different age groups of two genders after strictly excluding various confounding factors.

Material and Methods

Inclusion Criteria

- Absence of any cardiovascular symptoms.
- Normal clinical examination.
- Normal resting twelve lead electrocardiogram.
- Normal 2-dimensional and colour Doppler echocardiographic examination.
- No evidence of myocardial ischemia during exercise electrocardiographic testing.

Exclusion Criteria

- Patients with contraindications for exercise stress testing [13].
- Conditions that could hamper exercise capacity e.g. Debility, orthopaedic problems, hemoglobin less than 10gm% [14], left or right ventricular dysfunction [15], chronic pulmonary disease, systemic or pulmonary artery hypertension.
- Conditions that could affect heart rate response to exercise e.g. autonomic neuropathy, patients with paced ventricular rhythm, patients taking betablockers, diltizem or verapamil.
- Resting heart rate less than 60 beats per minute. Such individual could have sinus node dysfunction or inherently increased parasympathetic. Activity. These factors could affect heart rate response to exercise.
- Conditions that could affect correct interpretation of the exercise electrocardiogram [16]. e.g. intraventricular conduction defects, ST-segment and/or T wave changes in the resting electrocardiogram, presence of preexcitation in the resting electrocardiogram, electrocardiographic evidence of left and/or right ventricular hypertrophy, ST-segment and/or T wave changes during standing and/or hyperventilation.
- Individual who could not perform adequate exercise form any cause
- Development of any of the following findings that could suggest possibility of myocardial ischemia e.g angina, ST-segment elevation of any magnitude during exercise, ST-segment depression of 1mm during exercise or recovery, increasing frequency of ventricular premature beats during exercise or new appearance of ventricular premature beats during recovery.
- Development of any bradyarrhythmia or tachyarrythmia during stress.
- When any possibility of myocardial ischemia could not be excluded with confidence e.g. development of ST-segment depression of less than 1 mm, ST-segment depression localized to inferior leads showing significantly downsloping P-q segment, new appearance of isolated shallow T wave inversion.

Exercise test protocol

- Mason-Likar lead system was used [17]. All twelve leads were recorded simultaneously.
- All treadmill stress tests were performed using Bruce protocol [18].
- Exercise stress tests were symptom limited (exhaustive) rather than using age adjusted heart rate as the end point to assess maximal heart rate response and exclude any possibility of myocardial ischemia [19].
- Exercise was terminated if there was development of angina, any magnitude of ST-segment elevation, ST-segment depression of 1mm, any bundle branch block, increasing frequency of premature ventricular contractions or inability to continue exercise from any cause [20].
- Ten seconds of post-exercise cool down walk was practiced to avoid post exertional dizziness or syncope doe to sudden reduction in venous return or a vagal response due to sudden stopping of exercise [21].
- Recovery was usually recorded for six minutes. Recovery period was extended if indicated. Finally seventy patients qualified for analysis.

Evaluation of Heart Rate

Computer derived heart rate was used for analysis. Heart rate was calculated manually if it was fell that there was some error in computer evaluation of heart rate. Age predicted maximal heart rate (MPHR) was calculated by formula of Fox et al (200-age) [22].

Statistical Analysis

First we evaluated the effect of age on heart rate response during stress phase of treadmill testing. Individuals were dividing into three groups. Group A- Individuals whose age was less than thirty years. It included twelve males and five females. Group B- Individuals with age between 30 years and fifty years. This group included twenty nine males and seven females. Group C- Individual with age more than fifty years. This group included eleven males and six female.

Subsequently we analysed the heart rate response between males and females of different age groups. BMI does not affect maximal heart rate [23]. We therefore did not analyze the effect of this variable. Difference between different groups was evaluated using 'unpaired t test' [24]. Significance of changes in heart rate between different stages was evaluated using 'paired t test' [25].

Results

Effect of Age

All individuals attained age adjusted maximal heart rate irrespective of age. Demographic variables in different age groups and significance of difference between different groups are shown in Table 1. There was no significant difference in supine resting heart rate, supine resting systolic blood pressure and supine resting diastolic blood pressure between different age groups. Increase in heart rate from supine position to standing position and pre exercise heart rate were significantly lower (P < 0.05 and P < 0.01 respectively) in individuals older than fifty years. Heart rate (mean+SD) at the end of different stages and increase in heart rate over heart rate over previous stage of stress in different age groups and statistical significance of differences are shown in Table 2. Individuals alder than fifty years had relatively greater increase in heart rate during stage 2. Increase in heart rate during stage four was significantly lower in individuals of more than fifty years. Total increase in heart rate during stress was, however, not significantly different in different age groups.

Parameter	Age			P Value		
	A	B	C	A v/s B	B v/s C	A v/s C
	less than 30 years	30 to 50 years	more than 50 years			
Age (years)	26.8±2.96	38.68±5.70	57±4.49	<0.001	<0.001	<0.001
Resting supine HR/min	72.33±9.14	76.84±12.49	70.4±7.84	>0.10 (NS)	>0.10 (NS)	>0.10 (NS)
SBP (mm Hg)	125±9.04	123.06±11.84	122.72±11.03	>0.10 (NS)	>0.10 (NS)	>0.10 (NS)
DBP (mm Hg)	82.5±6.21	81.20±8.66	82.72±6.46	>0.10 (NS)	>0.10 (NS)	>0.10 (NS)
Increase in HR from supine to Standing position	34.33±15.68	24.5±14.93	18.7±8.96	>0.05	>0.10 (NS)	>0.01
Pre-exercise HR/min	106.66±17.83	99.85±18.05	91.45±13.82	>0.10 (NS)	>0.10 (NS)	>0.05

Table 1: Demographic parameters (Mean±SD).

	(mean±SD)			P value		
Hear rate response	**(A) Age less than 30 years**	**(B) Age 30 to 50 years**	**(C) Age more than 50 years**	**A v/s B**	**B v/s C**	**A v/s C**
HR at end of stage 1	119.41±17.81	115.51±26.48	109±12.75	>0.10 (NS)	>0.10 (NS)	>0.10 (NS)
Increase in HR during stage 1	11.91±21.41	22.46±13.97	17.54±7.41	>0.10 (NS)	>0.10 (NS)	>0.10 (NS)
HR at end of stage 2	136.91±20.74	138.06±18.69	131.09±16.56	>0.10 (NS)	>0.10 (NS)	>0.10 (NS)
Increase in HR during stage 2	17.5±12.44	17.24±8.57	22.09±8.59	>0.10 (NS)	0.1	>0.10 (NS)
HR at end of stage 3	164.08±27.31	159.72±19.08	152.72±23.57	>0.10 (NS)	>0.10 (NS)	>0.10 (NS)
Increase in HR during stage 3	27.08±17.23	20.17±8.55	21.64±9.61	>0.10 (NS)	>0.10 (NS)	>0.10 (NS)
HR at end of stage 4	180.90±15.75	173.13±14.89	156.2±20.77	>0.10 (NS)	0.1	<0.05
Increase in HR during stage 4	18.92±16	13.95±10.78	6.6±8.76	>0.10 (NS)	>0.10 (NS)	>0.05
Total increase in HR	69.91±22.16	71.32±15.40	64.63±17.25	>0.10 (NS)	>0.10 (NS)	>0.10 (NS)

Table 2: Heart rate response during stress.

Effect of Sex in Different Age Groups

We then tried genderwise analysis of different age groups to see if the gender had any influence on our findings observed during agewise analysis of heart rate response. On gender wise analysis of data in different age groups, we observed that in the age group of less than thirty years, females had relatively lower supine systolic blood pressure and relatively less increase in heart rate on standing from supine position (P< 0.05, (Table 3)). In the age group of 30 to 50 years also, females had relatively lower supine resting systolic blood pressure than their male counterparts (P<0.05, (Table 4)).

Variable	Less than 30 years		
	M	F	P
Age (years)	26.08±2.96	26.0±2.54	>0.10 (NS)
Resting supine heart rate /minute	72.33±9.14	74.8±2.48	>0.10 (NS)
SBP (mm Hg)	125±9.04	114.0±8.94	<0.05
DBP (mm Hg)	82.5±6.21	79.8±7.91	>0.10 (NS)
Increase in HR from supine to pre-exercise	34.33±15.68	20.4±8.38	<0.05
Pre-exercise (HR/minute)	106.66±17.83	95.2±10.54	>0.10 (NS)

Table 3: Demographic variables (mean+SD) of patients less than 30 years.

Variable	M	F	P
Age (years)	38.68±5.70	39.0±7.89	>0.10 (NS)
Resting supine heart rate /minute	76.84±12.49	74.66±14.81	>0.10 (NS)
SBP (mm Hg)	123.06±11.84	116.66±5.16	<0.05
DBP (mm Hg)	81.20±8.66	81.66±9.83	>0.10 (NS)
Increase in HR from supine to pre-exercise	24.5±14.93	24.6±5.44	>0.10 (NS)
Pre-exercise (HR/minute)	99.85±18.05	99.33±18.21	>0.10 (NS)

Table 4: Demographic variables (mean + SD) of patients between 30 years.

In the age group of above fifty years, females had relatively higher resting, supine heart rate than their male counterparts (P< 0.01, (Table 5)). There was no significant defence in other variables.

Variable	M	F	P
Age (years)	57.0±4.99	65.0±8.54	>0.10 (NS)
Resting supine heart rate /minute	70.4±7.84	81.0±3.60	<0.01
SBP (mm Hg)	122.72±11.03	133.32±11.54	>0.10 (NS)
DBP (mm Hg)	82.72±6.46	80.0±10.0	>0.10 (NS)
Increase in HR from supine to standing	18.7±8.96	19.33±2.07	>0.10 (NS)
Pre-exercise (HR/minute)	91.45±13.82	100.33±5.50	>0.10 (NS)

Table 5: Demographic variables (mean + SD) of patients above 50 years.

On analysis of heart rate at different stages of stress and increase in heart rate over the previous stage, females younger than thirty years had significantly greater increase (P 0.01) during stage one than their male counterparts (Table 6). Total increase in heart rate during stress s was similar in both genders. Both genders achieved more than 90% of age predicted maximal heart rate. In the age group of 30 to 50 years, there was no significant difference in heart rate attained at the end of each stage, increase in heart rate over the previous stage and total increase in heart rate during stress in the two genders (Table 7). Both genders attained more than 90% of their age predicted maximal heart rate (Table 7). Amongst the individuals of more than 50 years, increase in heart rate during stage three was significantly lower in females (P< 0.001, (Table 8)); none of the females reached stage four of Bruce protocol. Total increase in heart rate and percentage of age predicted maximal heart rate attained were also relatively lower in females.

Hear rate response	M	F	P
HR at end of stage 1	115.51±26.48	128.57±26.43	>0.10 (NS)
Increase in HR during stage 1	22.46±13.97	26.71±13.81	>0.10 (NS)
HR at end of stage 2	138.06±18.69	148±30.69	>0.10 (NS)
Increase in HR during stage 2	17.24±8.57	19.42±9.39	>0.10 (NS)
HR at end of stage 3	159.72±19.08	162.71±21.58	>0.10 (NS)
Increase in HR during stage 3	20.17±8.55	15.85±13.94	>0.10 (NS)
HR at end of stage 4	173.13±14.89	166.66±11.14	>0.10 (NS)
Increase in HR during stage 4	13.95±10.70	15.66±15.30	>0.10 (NS)
Total increase in HR	71.32±15.40	56.5±22.73	>0.10 (NS)
% of age predicted MHR attained	95.31±7.06	94±8.46	>0.10 (NS)

Table 7: Heart rate response during stress (Bruce protocol) (Age group 30 to 50 years).

Hear rate response	M	F	P
HR at end of stage 1	109±12.5	121.33±24.37	>0.1 (NS)
Increase in HR during stage 1	17.54±7.14	21±19.15	>0.1 (NS)
HR at end of stage 2	131.09±16.36	138.33±29.39	>0.1 (NS)
Increase in HR during stage 2	22.09±8.50	17±13.22	>0.1 (NS)
HR at end of stage 3	152.72±23.57	146.33±32.95	>0.1 (NS)
Increase in HR during stage 3	21.63±9.61	8±4.35	<0.001 (NS) V.siginificant
HR at end of stage 4	156.2±20.77	------	--------
Increase in HR during stage 4	6.6±8.78	-------	----------
Total increase in HR	64.63±17.25	46±29.51	>0.1 (NS)
% of age predicted MHR attained	94.37±14.41	82.5±3.52	>0.1 (NS)

Table 8: Heart rate response during stress (Bruce protocol) (Age group more than 50 years).

Discussion

We observed that there was no significant difference in resting supine heart rate, resting supine systolic and diastolic blood pressure in different age groups. This shows that the different age groups were comparable regarding these parameters. Increase in heart rate from supine position to standing position and pre-exercise heart rate in standing position were significantly lower in individuals older than fifty years as compared to individuals younger than thirty years. ((Table 1), A versus C, highlighted). Difference was not significant when compared to age group between thirty to fifty years ((Table 1), B vs C). Increase in heart rate on standing from supine position is secondary to gravity induced pooling of blood in the lower limbs and inferior mesenteric area. Reduced venous return and resultant low cardiac output cause reflex sympathetic stimulation and increase in heart rate [26]. With advancing age, there is reduced cardiac responsiveness to sympathetic stimulation [27]. This could be responsible for relatively less increase in heart rate on standing from supine position in individuals older than fifty years. We also observed that the heart rate during fourth stage and increase in heart rate during the fourth stage over the heart rate at the end of the third stage were also significantly lower in individuals older than fifty years as compared to individuals younger than thirty years ((Table 2), A vs C highlighted) . Heart rate during stage four was also lower as compared to individuals aged thirty to fifty years ((Table 2), B vs C highlighted). However, the difference was non significante (p=0.10).Previous workers have also observed significant decline in maximal heart rate with increasing age [28-31]. During exercise, initial increase in heart rate is due to withdrawal of parasympathetic lane [28]. Subsequent increase is due to increased sympathetic activity [28]. Responsiveness of the sinoatrial node to sympathetic stimulation declines with advancing age. Apoptosis of sinoatrial node pacemaker cell [32] and less calcium influx [23] are considered responsible for lower maximal heart rate with advancing age.

On genderwise subanalyse of different age groups, we observed that females less than fifty years had relatively lower resting supine systolic blood presser. (P<0.05) than their male counterparts. In the age group of individuals above fifty years, females had higher difference in resting supine systolic blood pressure but it did not reach statistical significance. It is known that incidence of hypertension is lower in females of premenopausal age than age matched males [33]. After the age of menopause, the incidence of hypertension increases in females [34]. In the age group of individuals above fifty years females had relatively higher supine resting heart rate (P<0.01) than their male counterparts. Anxiety about the stress test can cause overreaction of heart rate [35].

Analysis of heart rate response to stress in individuals younger than thirty years revealed significantly greater increase in heart rate during the first stage in females. Anxiety about the exercise test may result in overreaction of heart rate of the beginning of the exercise which stabilizes after some time [35]. There was, however, no significant difference in heart rate at the end of second and third stage. Both groups could attain more than 90% of the age predicted maximal heart rate. However, only one female could reach fourth stage. In the age group of 30 to 50 years, there was no difference in heart rate response during different stages of stress. Both genders attained more than 90% of the age predicted maximal heart rate. In the age group of more than 50 years, no females reached the fourth stage. Up to second stage there was no significant difference in the heart rate response of males vs females. Increase in heart rate during third stage was significantly lower in females. Females also attained relatively less percent of age predicted maximal heart rate than males; however, the difference was not statistically significant. Overall, we observed that females over 50 years of age could perform less exertion and attained relatively less percentage of the age predicted maximal heart rate. Males have greater work capacity as well as aerobic capacity as compared to women. Males, therefore, can take greater work load and attain greater maximal heart rate [14,36-38].

Our study clearly shows that inclusion of females contributed significantly to the decreased maximal heart rate in individuals older than fifty years. However, during the treadmill stress test women failed to reach the fourth Stage as compared to men. For this reason, the difference might not be a lower peak maximal heart rate, but a lower exercise capacity in women. Other workers have also observed that, in women, maximal heart rate remains fairly steady across the middle age [39] but decreases rapidly after the age of 60 years [40]. It is, therefore, clear that a relatively low maximal heart rate in women above fifty years should be considered normal and should not be labelled as ‘chronotropic incompetence’. We also fell that a separate regression equation should be developed for calculation of age predicted maximal heart rate for females above the age of fifty years. A different exercise protocol should also be considered in women older than 50 years. It is also possible as the population reviewed in this report consisted of women with a low exercise capacity.

Conclusion

Our study showed that there can be genderwise difference in the heart rate attained at the end of different stages of stress during treadmill stress testing using Bruce protocol. These differences were, however, not very significant. Individuals below the age of fifty years were able to attain more than 90% of their age predicted maximal heart rate irrespective of gender. Females had relatively less exercise capacity and infrequently reached the fourth stage. The difference was very significant in individuals above the age of fifty years. No female reached stage four in the age group of more than fifty years. Total increase in heart rate and percent of age predicted maximal heart rate attained by the end of exercise were also lower in females. We feel that 80% of age predicted maximal heart rate should be considered adequate in females older than fifty years. Such valves should not be labelled as ‘chronotropic incompetence’ in females older than fifty years. There should be separate regression equations for the two genders older than fifty years, for calculation of the age predicted maximal heart rate.

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