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Exercise stress test in apparently healthy individuals – where to place the finish line? The Ferrari corporate wellness programme experience

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Abstract

Aims: The aim of our study was to assess the clinical significance of the exercise stress testing endpoints, namely 85% of maximal theoretical heart rate (MTHR), metabolic equivalent of task, and rating of perceived exertion (RPE), and their relation to electrocardiographic (ECG) changes in a healthy adult population.

Methods: A cross-sectional study was conducted on 408 males and 52 females (mean age 39.4 ± 8.6 years) who performed the maximal cycle ergometer exercise stress test until volitional exhaustion, reporting the RPE score at 85% of MTHR and at peak exercise. Metabolic equivalents of task were indirectly calculated from the maximum workload and compared with the predicted values. Sitting torso-lead ECG and blood pressure were recorded at rest, during exercise and during recovery.

Results: Of 460 participants, 73% exceeded 85% of MTHR. The RPE score represented the overall most significant endpoint of exercise stress testing, with the median value of 17 at peak exercise. ECG events were detected in 23/124 (18.5%) who reached $\leq 85\%$ of MTHR and in 61/336 (18.2%) who achieved $>85\%$ of MTHR ($p = 0.92$). In the latter group, 54% of ECG changes occurred at $< 85\%$ of MTHR and 46% at $> 85\%$ of MTHR ($p = 0.51$). If the exercise stress testing had been interrupted at $\leq 85\%$ of MTHR, almost half of the ECG events would have remained undetected and 35% of the cardiovascular abnormalities observed at the diagnostic follow-up would have remained undiagnosed.

Conclusion: Terminating exercise stress testing before volitional exhaustion and an RPE score of 17 limits the test accuracy and reduces the possibility to detect cardiovascular abnormalities in apparently healthy adult populations.

Keywords

Exercise test, physical exertion, metabolic equivalent, heart rate, electrocardiography, cardiovascular abnormalities

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Introduction

Exercise stress testing (EST) is a common tool in cardiology and sports medicine.[1] EST has been recently included in the cardiovascular screening programmes for sports eligibility in asymptomatic adults.[2] While the indications for termination of EST in pathologic conditions are well defined and widely accepted,[3] the

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finish line of the exercise test is difficult to place in the absence of abnormalities because of the lack of consistent data and a consensus among experts. The most common parameters used for decision making during EST include maximal theoretical heart rate (MTHR) predicted based on age, energy expenditure expressed in metabolic equivalent of task (MET) in proportion to body weight, and volitional fatigue measured by subjective rating of perceived exertion (RPE) on the Borg scale.[4] All these methods have been extensively evaluated and their limitations have been acknowledged and discussed. There is evidence that a strict cut-off at 85% of MTHR cannot be considered an effective measure of exertion level;[5] RPE is usually subjected to high inter-individual variability,[6,7] while MET values are highly influenced by the exercise modality[8] or body composition.[9] In view of the above limitations, the aim of our cross-sectional study was to assess the clinical significance of the common EST endpoints, namely 85% of MTHR, METs, and RPE score, and their relation to electrocardiographic (ECG) changes and cardiovascular abnormalities in a healthy adult population.

Methods

From April 2017 to July 2017, our study included 469 adult (>18 years old) males and females from the voluntary corporate Formula Benessere wellness programme organized by the Med-Ex company in the Ferrari factory in Maranello (Modena, Italy). Med-Ex is a private company that offers comprehensive wellness solutions aimed at improving the quality of life of employees through nutritional and exercise prescription counseling.[10] Since 2004, the Ferrari Formula Benessere wellness programme has provided an on-site yearly medical screening, including complete cardiovascular evaluation (family and personal history, physical examination, blood pressure measurements, resting and stress testing electrocardiogram), glucose measurement and lipid profile (triglycerides, high-density lipoprotein, low-density lipoprotein and total cholesterol). The participants of the Formula Benessere corporate programme follow a complimentary supervised exercise programme (2–3 sessions/week) at a fitness centre within the corporate facility headquarters, receive personalized dietary counselling and follow a strict tobacco cessation programme.

Each participant received a detailed explanation on the benefits and risks related to EST and provided written informed consent to participate in a research study and data collection. Participants with known cardiovascular and/or metabolic diseases were excluded. Likewise, those using agents that influence heart rate, for example, beta-blockers, and those unable to perform a cycle ergometer EST owing to an orthopaedic complaint or other reasons were excluded from the study. The clinical history of individual participants was recorded and thorough cardiovascular risk assessment was performed using the Systemic Coronary Risk Evaluation system, based on age, sex, blood pressure, blood cholesterol and smoking history.[11] Anthropometric measures, including height and weight, were collected and the body mass index was calculated. The physical activity level was determined according to World Health Organization recommendations for distinguishing between active and sedentary women and men.[12] In brief, participants who engaged in at least 150 min of moderate-intensity aerobic physical activity throughout the week or at least 75 min of vigorous-intensity aerobic physical activity throughout the week or an equivalent combination of moderate- and vigorous-intensity activity were considered to be active.

Each participant performed the maximal cycle ergometer EST (Daum Ergometer Premium 8i, Daum Electronic Gmbh, Fürth, Germany). The protocol consisted of 2 min of unloaded cycling, followed by increments of 50 W for men and 30 W for women every 2 min.[10] In the absence of ECG changes and/or other events that necessitated early termination, the test continued until volitional exhaustion. Sitting torso-lead electrocardiogram was recorded at rest, during the exercise and during recovery using Cardioline Cube PC software (Cardioline US, San Diego, CA, USA). Similarly, systolic and diastolic pressures were recorded at rest, during each phase of exercise and during the first 5 min of recovery. All tests were conducted under the supervision of a cardiologist or a sports medicine physician trained in cardiology, in compliance with the exercise standards for testing.[13]

For the scope of our study, the MTHR (beats/min) was calculated before the start of EST, based on the formula 220 − age and the 85% of MTHR value was established. Each participant reported the RPE on an ordinal self-administrated Borg scale, ranging from 6 (no exertion at all) to 20 (maximal exertion), based on the subjective judgment of effort at the end of EST. Additionally, in participants who continued EST over the 85% of MTHR, the RPE scores were recorded both at 85% of MTHR and at peak exercise. To determine the exercise intensity, METs were indirectly calculated from the maximum workload measured by the ergometer software during EST, according to the published guidelines.[3] The theoretical MET values, which each participant should achieve during EST, were predicted using a previously validated equation for healthy men[14] and women,[15] based on age and physical activity level. Then, the measured METs were compared with the theoretical METs predicted for each participant and the result was expressed as percentage of theoretical METs. All ECG changes occurring during EST were recorded, together with the exact heart rate and percentage of MTHR at the time of event. Particular attention was paid to arrhythmias and ST-T changes. Every participant who showed ECG changes during EST was followed with a diagnostic work-up, including colour-Doppler echocardiography.

Categorical variables were described as frequency with percentage, while continuous variables with normal distribution were reported as mean with standard deviation (SD). For continuous variables not normally distributed and ordinal variables, including RPE scores, values were reported as median with interquartile range (IQR). For continuous data with not normal distribution and for ordinal data, we applied a non-parametric Mann–Whitney U test for independent samples when comparing between two groups, a Kruskal–Wallis analysis when comparing between more than two groups and a non-parametric Wilcoxon test for paired samples when comparing within a group. If an overall significance level was reached in the Kruskal–Wallis analysis, the non-parametric pairwise comparison tests with Bonferroni adjustment were used to analyse differences among groups. The chi squared test and Fisher's exact test were used to compare the recorded frequencies of categorical variables.

The value of $p < 0.05$ was considered statistically significant. All analyses were performed by an author not involved in data collection and were conducted using Stata Software v.12 (StataCorp. 2011, Stata Statistical Software: Release 12. College Station, TX, USA: StataCorp LP).

Results

Of the 469 individuals who performed EST in our study, nine were excluded from analysis owing to an exaggerated systolic blood pressure response > 220 mmHg (four participants) or a painful orthopaedic condition (five participants: low back pain in three and knee pain in two), which necessitated early termination of the test. Hence, our sample consisted of 460 participants, 408 males (88.7%) and 52 females (11.3%). The mean age of the total population was 39.4 ± 8.6 years (range 24–62).

All participants were divided into two groups based on the highest percentage of MTHR reached during EST: group 1 with ≤ 85% of MTHR and group 2 with > 85% of MTHR. Group 1 had 124 participants (27%; 102 males and 22 females) and group 2 had 336 participants (73%; 306 males and 30 females). Their demographic characteristics and EST parameters are reported in Table 1. The scatter plot in the Figure 1 shows the values of the heart rate (HR) recorded at peak exercise in relation to age. The maximal HR at peak exercise in the overall population followed normal distribution and was significantly higher than 85% of MTHR, which, based on the formula 220 − age, corresponded to 153.55 beats/min (SD 7.29). In fact, the mean per cent value of MTHR in the entire cohort was 90.5% (SD 6.9), equal to 163.87 beats/min (SD 13). This difference was not age-related and, for the same age, a wide distribution of HR was evident, showing great inter-individual variability. Considering the highest percentage of MTHR reached during EST, the median value was 85% (IQR 81%–85%, range 68%–85%) in group 1 and 93% (IQR 90%–96%, range 86%–111%) in group 2.

Table 1. Characteristics of the study population according to the achieved percentage of MTHR (≤ 85% or > 85%) and theoretical MET (<100% or ≥ 100%).

Characteristic	Group 1 ≤ 85% of MTHR		Group 2 > 85% of MTHR		
	<100% MET n = 37	≥100% MET n = 87	<100% MET n = 35	≥100% MET n = 301	p value
Sex, F/M	10/27	12/75	7/28	23/278	0.001
Age, years	36.3 ± 7.3	38.8 ± 9.1	34.3 ± 8.1	40.5 ± 8.4	0.0001
BMI, kg/m^2	26.8 ± 5.6	24.4 ± 3.3	27.4 ± 4	24.3 ± 3	0.0001
HR at rest, beats/min	78.7 ± 8.8	72.4 ± 10	85 ± 14.9	76 ± 12.2	0.0001
HR at peak, beats/min	149.8 ± 12	151.4 ± 9.7	170.8 ± 10.4	168.4 ± 10.3	0.0001
% of MTHR achieved	83 (80–85)	85 (82–85)	92 (89–94)	93 (90–96)	0.0001
% of predicted MET achieved	89 (83.1–94.8)	118.7 (108.6–129.3)	94.4 (88.3–98.4)	126 (113.9–141.8)	0.0001
RPE at peak	16 (15–18)	17 (16–18)	16 (15–18)	17 (16–19)	0.116

Normally distributed data are reported as mean ± SD. Not normally distributed data are reported as median (interquartile range).
MTHR: maximal theoretical heart rate; MET: metabolic equivalent of task; F: female; M: male; BMI: body mass index; HR: heart rate; RPE: rating of perceived exertion

The median value of the RPE score at peak exercise was 16.5 (IQR 16–18, range 12–20) in group 1 and 17 (IQR 16–19, range 9–20) in group 2 (Figure 2(a)). This difference was not statistically significant (p = 0.067). Additionally, in the participants who continued EST over 85% of MTHR (group 2), the RPE scores were recorded not only at peak exercise but also at 85% of MTHR and the median value was 14 (IQR 13–16, range 6–20). When compared with the RPE score at peak exercise in the same group, a statistically significant difference ($p < 0.001$) was observed (Figure 2(b)).

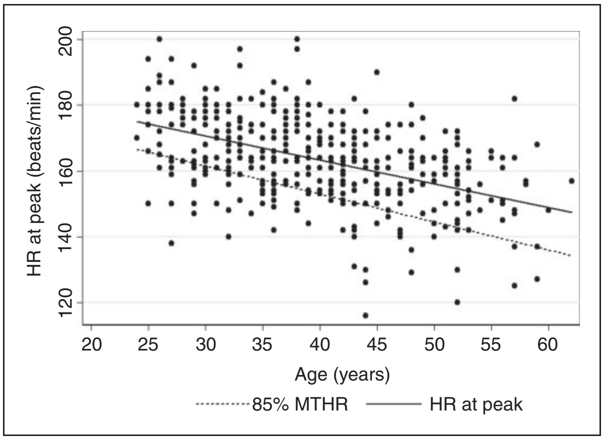

Figure 1. Heart rate at peak exercise in relation to age. The dashed line indicates 85% of MTHR predicted for age, while the continuous line is a regression line of the actual maximum heart rate reached during exercise stress testing.
HR: heart rate; MTHR: maximal theoretical heart rate

In both groups, the majority of participants (85%) reached the theoretical METs predicted before EST. Among those who terminated the test at ≤85% of MTHR (group 1), 37/124 participants (29.8%) did not equal the theoretical MET value. The same was observed in only 35/336 participants (10%) who reached > 85% of MTHR (group 2). The difference between groups was statistically significant ($p < 0.001$).

Taking into account the percentage of MTHR (≤85% or >85%) and the percentage of theoretical METs (<100% or >100%) recorded at peak exercise, the entire cohort was stratified into four subgroups (Figure 3). Interestingly, there was no difference in RPE score between the subgroups ($p = 0.116$), indicating a similarly perceived effort despite the difference in the percentage of MTHR and theoretical METs achieved during EST. These findings indicate that the RPE score is the most consistent parameter for terminating EST. In fact, independent of the achievement of the specific percentage of MTHR or theoretical METs,

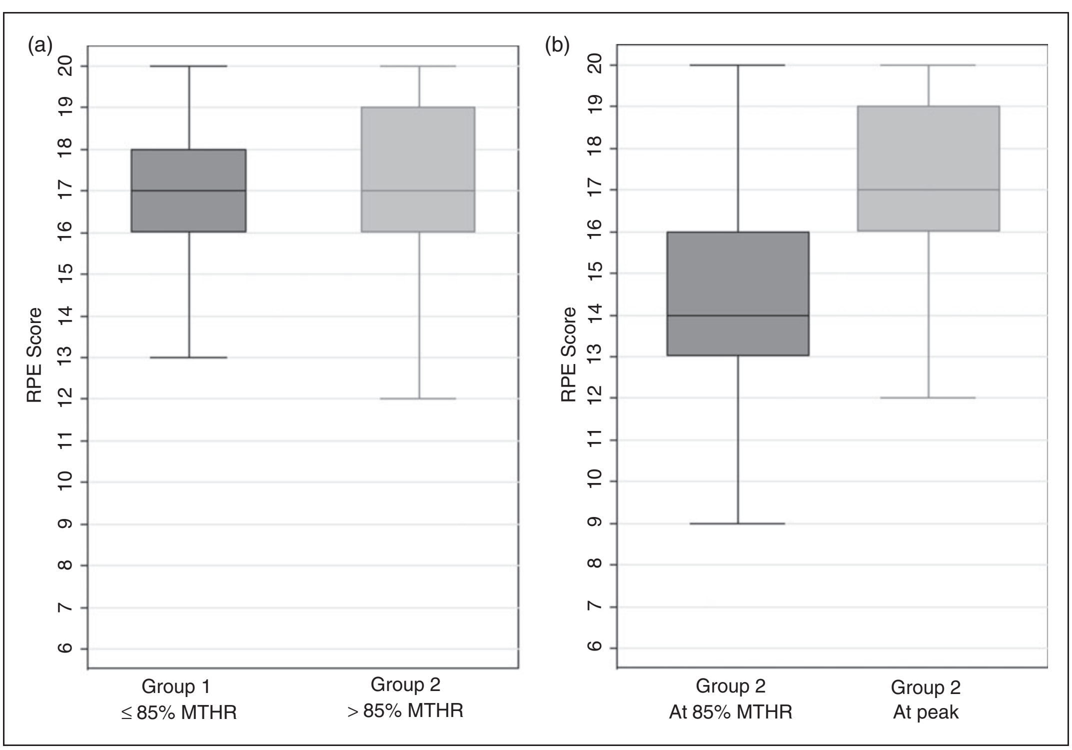

Figure 2. The RPE scores reported (a) at peak exercise in participants who terminated the test at ≤ 85% of MTHR and those who reached > 85% of MTHR and (b) at both 85% of MTHR and peak exercise in participants who reached > 85% MTHR.
MTHR: maximal theoretical heart rate; RPE: rating of perceived exertion.

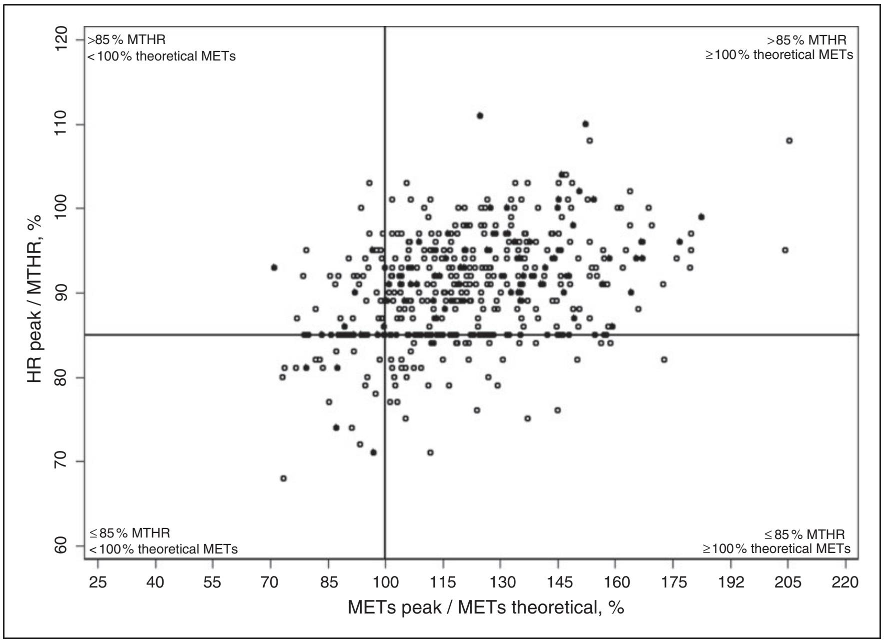

Figure 3. Distribution of participants based on the actual percentage of MTHR and theoretical METs reached during exercise stress testing. Hollow circles indicate individuals without electrocardiographic events and solid circles indicate individuals with electrocardiographic events.
HR: heart rate; MET: metabolic equivalent of task; MTHR: maximal theoretical heart rate

Table 2. Incidence of electrocardiographic events recorded during exercise stress training and of cardiovascular abnormalities detected in the diagnostic follow-up.

	Group 1 $\leq$ 85% of MTHR $n = 124$	Group 2 > 85% of MTHR $n = 336$		
		Events at $\leq$ 85% of MTHR	Events at > 85% of MTHR	p value
ECG events, $n = 84$	23 (18.5%)	61 (18.2%)		0.92
		33 (54%)	28 (46%)	0.51
Atrial arrhythmias, $n = 8$	3 (2.4%)	5 (1.5%)	0 (0%)	0.14
Ventricular arrhythmias, $n = 63$	18 (14.5%)	22 (6.6%)	23 (6.8%)	0.76
Atrial and ventricular arrhythmias, $n = 9$	1 (0.8%)	5 (1.5%)	3 (0.9%)	0.45
ST-T changes, $n = 4$	1 (0.8%)	1 (0.3%)	2 (0.6%)	1.0
Cardiovascular abnormalities, $n = 20$	5 (22%) AoR (1), LAD (2), TrR (1), MVP + MR (1)	8 (24%) LAD (2), AoD (2), LVH (2), MVP + MR (1), ablation (1)	7 (25%) MR (2), AoR (2), LVH (1), HC (1), MVP + MR (1)	1.00

MTHR: maximal theoretical heart rate; ECG: electrocardiographic; AoR: aortic regurgitation; LAD: left atrial dilatation > 40 mm; AoD: aortic dilatation > 40 mm; TrR: tricuspid regurgitation; MVP: mitral valve prolapse; MR: mitral regurgitation; LVH: left ventricular hypertrophy; HC: hypertensive cardiomyopathy

participants from all subgroups terminated EST at a similar RPE score.

Finally, the performance data from our study were matched to the presence of ECG changes during EST and the incidence of cardiovascular abnormalities in our sample of apparently healthy individuals (Table 2 and Figure 3). Overall, ECG events, including atrial arrhythmias, ventricular arrhythmias, both atrial and ventricular arrhythmias and ST-T changes, were detected in 84/460 participants (18.3%); in particular, in 23/124 participants from group 1 (18.5%) and in 61/336 participants from group 2 (18.2%; $p = 0.92$). Among the latter, 33/61 participants (54%) presented ECG changes at < 85% of MTHR and 28 (46%) at > 85% of MTHR ($p = 0.51$). Thus, if the test had been interrupted at 85% of MTHR, nearly half of the

ECG abnormalities would have remained undetected, determining a significant reduction ($p = 0.028$) in the recorded events in group 2. In particular, 23/45 of all ventricular arrhythmias (50%) would have been missed; among those, four cases with > 10 premature ventricular complexes and two cases with ventricular couplets and triplets. Importantly, the diagnostic work-up with colour-Doppler echocardiogram showed the presence of structural heart disease in 6/23 cases of ventricular arrhythmias in participants who were allowed to continue their EST > 85% of MTHR, including two cases of mitral regurgitation, two cases of aortic regurgitation, one case of left ventricular hypertrophy and one case of hypertensive cardiomyopathy. In 1/2 of the cases of ST-T abnormalities documented at > 85% of MTHR, a mitral valve prolapse with valvular regurgitation was present. Again, if EST had been terminated at 85% of the MTHR, as is commonly practised in the cardiovascular screening for sports eligibility in asymptomatic adults using EST, 7/20 structural cardiovascular abnormalities documented in the study (35%) would have remained undiagnosed (Table 2).

Discussion

Several international position statements[16–19] recommend EST for cardiovascular screening in over 35-year-old people practising leisure and/or competitive sports activities, in particular in those individuals with high cardiovascular risk; however, the finish line or a cut-off for test termination has not been unequivocally established. Our study indicates that without an appropriate and standardized criterion for test termination, EST cannot reliably evaluate exercise-related cardiovascular problems in a healthy active population. These observations possibly increase in clinical significance when applied to the cardiovascular screening for preventing sudden cardiac death in athletes.

The results of the present study demonstrated that the most common parameter for EST termination, that is, 85% of MTHR, did not correspond to the maximal exertion on the RPE scale in the majority of healthy individuals. Indeed, when EST continued until volitional fatigue, the majority of participants was able to achieve > 85% of MTHR. Accordingly, the RPE score recorded at 85% of MTHR was significantly lower than the RPE score recorded at peak exercise in those participants. Hence, we suggest that, in healthy individuals, the choice of the 85% of MTHR as a threshold to terminate EST may not be adequate. This is confirmed when considering that almost 50% of the ECG abnormalities occurring during EST, including complex ventricular arrhythmias and ST-T changes, and 35% of cardiovascular abnormalities would have been undetected if the cut-off of 85% of MTHR had been applied. This observation agrees with conclusions from other studies,[20,21] in which the choice of 85% of MTHR as the primary exercise endpoint led to the underestimation of exercise capacity and inducible ischaemia events. Of note, the MTHR and, accordingly, its 85% value, are predicted based on age. Our data demonstrated a high maximal heart rate variability at all ages, proving this age-related criterion to be less individual and reliable than the RPE score. Similar observations on age variability were made when the criterion for EST termination was the peak respiratory exchange ratio.[22]

The METs are commonly used to indicate exercise intensity and energy expenditure during exercise. It was suggested that reaching ≥ 10 METs during EST could allow one to avoid the cardiac perfusion study,[23] while ≥ 11 METs could be an indicator of higher survival.[24] In our opinion, a fixed METs threshold is not an appropriate reference for the evaluation of the intensity of exercise in the general population. The estimation of METs is indirect and uses the standard resting metabolic rate expressed by 1 MET value of 3.5 ml of $O_2 \times kg^{-1} \times min^{-1}$. This value is lower in obese individuals[9,25] and it was found that this standard underestimates the true MET level in over 80% of cases.[26] The present results indicate that using theoretical METs as an endpoint in EST leads to inaccurate conclusions and is less reliable than the RPE score.

Even if subjective in nature, the RPE score emerges as the most robust parameter for defining a complete EST. In fact, considering the percentage of MTHR alone or in combination with METs, RPE scores recorded at the end of EST remained constant without significant differences between groups. Based on data from our study population, an RPE score < 16 lies below the 25th percentile, while a score of 17 corresponds to the 50th percentile. The latter value should be considered as an endpoint in EST.

In conclusion, the results of our cross-sectional study indicate that the majority of an apparently healthy population can exceed 85% of MTHR when termination of EST is based on physical exhaustion (an RPE score of 17). Termination of EST below this level limits the accuracy of the test and reduces the possibility of detecting cardiac abnormalities in apparently healthy active populations.

Author contribution

SF, FF, MS and BA contributed to the conception or design of the work. SF, FF, DPF, APE, SMG, SG, BA, CA, BV, FN, FU, TM, ND, DMF, CC, DAF, MS and BA contributed to the acquisition, analysis or interpretation of data for the work. SF, ND and BA drafted the manuscript. SF, FF, DPF, APE, SMG, SG, BA, CA, BV, FN, FU, TM, ND, DMF, CC, DAF, MS and BA critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of conflicting interests

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