Should the attainment of predicted heart rate maximum be used as an exercise test end point?

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Abstract
Age predicted maximum heart rates based on the formula 220-age have long been used in fitness and clinical settings to gauge exercise intensity and predict exercise test end points. Exercise stress tests have in some cases been routinely terminated based on the attainment of this equation, despite recommendations that age predicted maximum heart rates should not be used as an exercise test endpoint when screening for myocardial ischemia. Here we describe two cases that challenge the practice of terminating exercise stress tests based on predicted maximum heart rates during screening for myocardial ischemia.

INTRODUCTION
The history of the 220-age equation dates back to 1971 and was derived by a linear best fit to a series of data taken from 10 studies examining the relationship between age and exercise maximum heart rate (HR_max)\(^{(1)}\). The data was only intended to be an estimation based on the apparent linear decline of HR_max with age observed in those studies. However, the participants in these studies were all male and under the age of 55 and therefore not representative of the entire population. Nevertheless the use of this equation has become widespread in many fitness centres and diagnostic testing laboratories throughout the world, probably due to its ease of calculation\(^{(2,3,4)}\). Recent research suggests that using the 220-age equation as a termination end point significantly underestimates HR_max in adults older than forty years of age\(^{(5)}\). This may lead to underestimating the true level of stress imposed on the heart, therefore hindering the detection of significant coronary artery disease (CAD) and decreasing the diagnostic ability of the test\(^{(6)}\). This could lead to increased rates of false negative results, placing patients at unnecessary risk.

CASE 1
Patient X was a 67 year old male presenting with left sided chest pain. He had a family history of ischemic heart disease (father died at age 60) and no other known risk factors. An exercise stress test (EST) was performed using the standard Bruce protocol. During stage 3 (7:50 minutes) target heart rate according to the equation 220-age was attained (153 bpm). The stress electrocardiogram (ECG) displayed sinus tachycardia with no diagnostic ST segment changes evident (Figure 1). The test continued until volitional fatigue was reached at 9:50 minutes. Maximum heart rate was 176 bpm (115% of 220-age) and the ECG displayed horizontal/downsloping ST segment depression of up to 2mm (Figure 2a) in the inferolateral leads that is resolved in the first minute of recovery (Figure 2b). Our facility considers horizontal or downsloping ST segment depression of greater than 1 mm at 80 milliseconds beyond the J point positive for myocardial ischemia\(^{(7)}\). Patients demonstrating this diagnostic criterion are sent for further investigation, most commonly coronary angiography. Subsequent angiography in this patient revealed a 70% eccentric mid-occlusion in the right coronary artery that was stented.
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CASE 2

Patient Y was a 66 year old female presenting with chest pain that responded well to nitrates. Her medical history and risk factors included hypertension, dyslipidemia, asthma and a strong family history of ischemic heart disease. Resting standing blood pressure was 135/65 mmHg and the ECG was normal with postural T wave changes noted in the inferior leads II, III and aVF upon standing (Figure 3a). The patient exercised to fatigue using the Bruce protocol for 6:44 minutes, reaching a maximum heart rate of 176bpm. No chest pain or significant arrhythmias were noted throughout the test. During stage 2 (4:47 minutes) heart rate reached 169 bpm (109% of 220-age) and up-sloping/horizontal ST segment depression of up to 1.5mm diagnostic of ischemia, was noted in V4-V6 (Figure 3b). The patient exercised for a further 2 minutes until fatigue at 6:44 minutes, with no changes to the level of ST segment depression during this time. The ST segment depression resolved within the first minute of recovery (Figure 3c). Angiography revealed a 30% proximal lesion in the LAD and 90% stenosis of the first diagonal branch subsequently stented.

DISCUSSION

The cases presented here demonstrate the development of diagnostic ST segment depression at heart rates greater than age predicted maximum calculated by the 220-age equation. Interestingly no diagnostic ECG changes occurred before the attainment of predicted heart rate and in all cases ST segments were normalised within one minute into recovery. No other signs of ischemia were noted in all three tests. This raises the question whether diagnostic ECG changes would have occurred if the tests were terminated on attainment of 100%, or worse still, 85% of 220-age? Due to the nature and time course of the changes, specifically the normalisation of ST segments within one minute of recovery and the fact that no other signs of ischemia were present; it is possible that the lesion may have gone undetected.
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There is much debate over what constitutes $HR_{\text{max}}$, and more importantly over what percentage of $HR_{\text{max}}$ is required to detect ischemic changes. Esquivel et al., showed that during exercise thallium-201 testing the amount of perfusion defect was independent of heart rate and exercise intensity. Stratmann et al., found no significant difference in the sensitivity of exercise technetium-99m irrespective of $HR_{\text{max}}$ in patients with angiographically confirmed CAD. More recently, various studies have found ischemia to be more common in patients with sub-maximal (<85% 220-age) heart rates. These studies however concluded that patients with CAD are often unable to complete exercise testing due to early termination owing to symptoms and therefore never attain a true $HR_{\text{max}}$.

In previous years, the Scandinavian Committee on Electrocardiogram Classification recommended a target heart rate of 85% of $HR_{\text{max}}$ as a suitable termination point. There is now substantial evidence demonstrating significant variation in individual subject values for $HR_{\text{max}}$, and therefore current guidelines recommend other end points be used for termination. However heart rate is still commonly used as an exercise test end point in many research and diagnostic facilities. Supporters of sub-maximal testing claim ST segment changes occurring at higher heart rates have less significance and a tendency to produce an increased rate of false-positive results. More recently, Lewis and Amsterdam confirmed this finding showing that higher heart rates (>90% of 220-age) did indeed have a greater tendency to generate more false positive results than at lower heart rates (<85% of 220-age). In contrast however, a study of middle aged men by Lester et al. displayed only one positive test using sub-maximal stress. When maximal stress testing was performed in the same patients five more tests were found to be positive. In more recent times, Garber et al. tested a group of patients with known CAD using a maximum fatigue protocol. The test was repeated several days later at 70% of $HR_{\text{max}}$ for at least 20 minutes. Eighty-five percent of the patients developed ST segment depression using the sub-maximal test compared to 100% on the maximal test.

There appears to be evidence supporting the use of either heart rate or maximal fatigue as termination end points for EST. Our laboratory no longer uses heart rate as a termination endpoint when screening for inducible ischemia and consequently we have found no difference in the number of false positive results. This is due in part to concomitant increases in the detection of non significant lesions (20-50%) and significant lesions (>50%) when maximal fatigue is applied as the test end point. The patient data presented here displayed significant single vessel disease only. Perhaps ischemic changes during stress testing may have occurred earlier had considerable disease been present in other vessels. Nevertheless, a single vessel lesion is still considered CAD and patients need to be managed accordingly.

CONCLUSION

This study only represents two cases, however the potential clinical sequelae of increased false negative results suggests that further standardisation of termination endpoints particularly in relation to heart rate need to be addressed. In line with American College of Cardiology and American Heart Association recommendations described elsewhere, our laboratory suggests that exercise test endpoints other than heart rate be used when screening for myocardial ischemia, in order to provide safe and acceptable care to patients suspected of having CAD.

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