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EDITORIAL COMMENT

Chronotropism during exercise. Methodological and conceptual inconsistencies☆

Cronotropismo no esforço. Inconsistências metodológicas e conceptuais

Miguel Mendes

Serviço de Cardiologia, CHLO, Hospital de Santa Cruz, Carnaxide, Portugal

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The authors of the article[1] to which this editorial refers assessed the effect of a cardiac rehabilitation program (CRP) on the chronotropic index (CIx) of patients after acute coronary syndrome (ACS), most of whom had been treated with several beta-blockers (BB) at different doses.

The study of the chronotropic response to exercise is of the utmost importance because, although it is well established that the presence of chronotropic incompetence (CI) has a negative impact on patient progress, little is known about this undervalued topic, particularly because possible improvement is not acknowledged.

The diagnosis of CI is complicated by the existence of several formulas for calculating the maximum predicted heart rate (MPHR), different criteria for defining HF, particularly in the context of BB.

The authors retrospectively assessed a population of CRP participants, consisting of 543 consecutive patients after ACS, mostly male (14.9% female), asymptomatic (89% in New York Heart Association (NYHA) class I, who did not have significant impairment of left ventricular function (LVF). At admission and 12 months after ACS, about 86% and 87% of the cases were under BB, respectively.

Chronotropism and functional capacity (FC) were studied using conventional exercise testing (ET) performed at three time points: before CRP, at the end of phase II, and 12 months after ACS. BB doses were converted into equivalents and the population was divided into three groups according to whether the dosage had been reduced, remained unchanged, or increased.

Maximum predicted heart rate was calculated using the 220-age formula and Brawner's formula, and CI was diagnosed if the maximum heart rate (HRM) was less than 80% of the MPHR determined by the two formulas. Patients underwent eight to 24 sessions of aerobic and muscle strength training according to current international guidelines. After finishing the CRP there was an average reduction of 3 ppm at rest and an average increase of 5 ppm at peak exertion in the entire study population.

Similarly, the CIx increased both when it was calculated using the 220-age formula or Brawner's formula. FC increased by about 2 METs after the program, and the gain was maintained 12 months after ACS, with a positive correlation between the increase in chronotopism and FC, which increased by about 0.37 estimated METs for each 1% of CIx calculated based on the 220-age formula, independent of age, gender, and BB dose.

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E-mail address: miguel.mendes.md@gmail.com

The authors correctly identify several limitations of their study. However, they did not consider the fact that CRP duration varied between eight and 24 sessions, which could have an impact on both FC and CI improvement, and that FC was assessed by conventional ET and not by cardiorespiratory ET, which would provide a more accurate measurement. It should be emphasized that cardiorespiratory ET, although recommended, is not considered mandatory in international recommendations in CRPs for patients with good LVF.

They concluded that HF is improved by physical training in CRPs for patients after mildly symptomatic ACS, without compromised normal LVF, mostly on BB medication, regardless of the dose.

The authors found that the classic (220-age) formula for calculating MPHR had a higher correlation with increasing FC relative to Brawner's formula.

The calculation of CIx can be performed at submaximal[2] or maximal effort[3,4] levels.

Wilkoff[2] defined CIx as the quotient between the chronotropic reserve and the metabolic reserve at submaximal effort. CIx has the advantage of being adjusted to the age and FC of the individual and of being independent of the ergometer or protocol used. In normal adults, the percentage of chronotropic reserve is equal to the percentage of metabolic reserve. This concept means chronotropism can be assessed at any point in an ET using the formula: HR at staging is equal to (220-age HR at rest) multiplied by (METs at staging-1 dividing by METs reached at peak effort). The normal CIx is 1.0, accepting a range between 0.8 and 1.3. If it is $\leq$0.8 at a given point, CI is considered to exist.

It can also be determined at maximal effort level, considering the value of MPHR based on age and one of several equations; calculating the respective percentage that was reached by the highest HR reached in ET interrupted by exhaustion. In this case, there are two difficulties: choosing the equation that best applies to the individual under study and ensuring that the degree of exhaustion has been reached.

Regarding formulas, there is no consensus among experts and no univocal guidelines in international recommendations[3,4]. Most exercise physiology laboratories continue to use the classical formula (HRM=220-age), although some studies have suggested that Brawner's formula (HRM=164-age $\times$ 0.7) would be the most appropriate for individuals with suspected or confirmed[5] coronary heart disease, particularly for those who are undergoing BB therapy, and Tanaka's formula[6] (HRM=206-age $\times$ 0.88) for healthy individuals. Any of the proposed equations have an underlying standard deviation around 10-20 beats, which has led most centers to continue to use the equation HRM=220-age because it is easier to use, and they do not see significant usefulness in the alternatives.

The second difficulty has to do with the certainty that the maximum HR has been reached. Usually this is performed subjectively when the patient or the ET performers consider that physical exhaustion has been reached. If we want to be rigorous, we have to perform a cardiorespiratory ET in which the intensity of effort that conditions the achievement of a respiratory quotient value greater than 1.10[4] must be reached. It is a gross error to consider reaching 85% of MPHR as a criterion to define a maximum effort test and decide upon its suspension.

In fact, the best methodology for calculating CIx involves selecting a specific protocol to study chronotropism such as CAEP[7] and performing a cardiorespiratory exercise test in which a QR greater than 1.10 is achieved.

After performing the ET, if we intend to assess CI by the HRM achieved, we need to choose one of its definitions. The definition of CI in medical literature is not agreed upon, and criteria for CI have been found based on percentages ranging from 70, 80 and 85% of MPHR, although most agree on the inability to reach 85% of MPH or 80% of chronotropic reserve (the difference between HR at rest and HR achieved during maximum effort) in individuals not on BB medication, and 62% of MPHR in patients on BB based on the formula HRM=220-age. Brawner's formula and others significantly underestimate the HRM, as can be seen in the work of Tiago Pimenta et al.

The methodological difficulties and current inconsistencies in the definition of HF should encourage the conduct of prospective studies to establish an evaluation methodology and a more precise and clear definition, since the evaluation of chronotropism during exercise has already proven to have a high prognostic value for cardiovascular morbidity and mortality.

In the context of cardiovascular disease, particularly in HF[8], both CIx and HR reduction in the first and third minutes of recovery, as well as HR variability are also predictors of poor prognosis, but are modifiable by aerobic exercise[9]. The study of HR variability during exertion requires the use of specific software not usually made available by exercise text equipment.

Conflicts of interest

The authors have no conflicts of interest to declare.

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