Chronotropic Incompetence

Ready for Prime Time*

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In this issue of the Journal, Azarbal et al. (1) report on the prognostic value of the heart rate (HR) response to exercise among a large cohort of patients undergoing exercise myocardial perfusion testing. Although previous groups have reported that an impaired HR response to exercise, or chronotropic incompetence, is an independent predictor of risk (2–6), this very well done observational study represents the first attempt to show its prognostic value over and above detailed findings of myocardial perfusion scintigraphy. In a sense, this report represents a different type of clinical thinking, whereby the exercise test provides additional useful clinical information after myocardial perfusion findings are known.

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Chronotropic incompetence has proved to be a predictor of outcome in numerous cohorts that have included tens of thousands of patients (1,2,4–9), yet its clinical, or what I will call prime-time, value has been questioned (10). With the addition of the current study by Azarbal et al. (1), the time has come to consider the chronotropic response to exercise as part of the routine interpretation of exercise testing. Yet, this study provides much more than just confirmatory findings; it provides important insights as to how best to measure chronotropic response and how to incorporate it into clinical decision-making.

The HR response to exercise reflects complex physiologic processes that are closely related to age, functional capacity, resting HR, coronary disease severity, and autonomic nervous system balance (3,5,6,11–14). Because peak exercise HR is correlated with age, the traditional approach has been to consider a patient as chronotropically incompetent when <85% of the age-predicted HR is achieved. This measure is still confounded (5,14), however, by resting HR and functional capacity, and therefore another approach has been proposed (4,5,14). This involves invoking the concept of HR reserve (14), which is the difference between maximal predicted HR (or 220 beats/min minus the patient’s age) and resting HR. Failure to use 80% of HR reserve constitutes chronotropic incompetence (4,14). Thus, a 60-year-old patient with a resting HR of 70 beats/min would need to reach a HR of 142 beats/min to be chronotropically competent.

Azarbal et al. (1) found that failure to reach 85% of the age-predicted maximum HR was independently predictive of death but that failure to use 80% of HR reserve was a substantially stronger predictor of risk and captured a greater number of at-risk subjects. Patients who either had no perfusion defects or mild-to-moderate defects but manifested a normal chronotropic response (as assessed by the HR reserve method) were at very low risk for cardiac death. Patients with chronotropic incompetence but a normal myocardial perfusion scan had just as high a risk of all-cause death as patients with an abnormal scan but a normal chronotropic response (refer to Fig. 1B in Azarbal et al. [1]).

What are the practical implications of these findings? First, when assessing HR response to exercise, the HR reserve approach should be used and should replace the traditional percent of age-predicted HR achieved. Second, many clinicians consider exercise nuclear studies that show chronotropic incompetence but normal myocardial perfusion imaging as being non-diagnostic or submaximal. In other words, the test may be problematic, but the patient is fine. The evidence clearly shows that this is not so—the patient is at substantially increased risk. Third, the chronotropic response to exercise can help clinicians decide what to do with patients who have mild-to-moderate perfusion abnormalities. Those with a preserved chronotropic response are at such low risk that a conservative, non-invasive approach is wholly appropriate. Finally, and arguably most importantly, these findings demonstrate that the exercise test provides critical prognostic information beyond that provided by nuclear imaging. Thus, patients referred for nuclear imaging should be specifically referred for treadmill stress if they are capable of exercise. The temptation to order pharmacological imaging should be resisted.

Azarbal et al. (1) also found that chronotropic response predicts outcome over and above functional capacity, one of the most powerful predictors of all-cause and cardiac death (15,16). Combining chronotropic response with functional capacity enables clinicians to confidently identify patients who are at very low risk and who can be spared needless tests, procedures, and anxiety.

There are some important limitations of the study by Azarbal et al. (1). The follow-up period of two years was relatively short. Information regarding HR recovery (17–19) and ventricular ectopy during recovery (9) was not reported; both of these have been shown to be powerful predictors of risk. Ejection fraction was not directly measured. We do not know how to interpret chronotropic response among patients receiving beta-blockers. Finally, this study does not inform us as to how best to treat chronotropic incompetence. Future work will be needed to determine the precise underlying biological mechanisms (3,13); this will hopefully lead to candidate strategies for treatment trials.

Nonetheless, despite these limitations and uncertainties,
the study by Azarbal et al. (1) is an important reminder that the exercise stress test should play a pivotal role in the evaluation of patients with known or suspected coronary disease and is not merely a gateway to imaging or coronary angiography. By taking into account those exercise test predictors that strongly predict risk, including chronotropic response, functional capacity, HR recovery, and ventricular ectopy in recovery, the clinician has the ability to confidently identify low-, intermediate-, and high-risk patients in an easy, safe, and inexpensive way. Given the extensive work that has been performed during the past five years by a number of groups (1,2,9,16,20), the evidence is now overwhelming that the exercise test, when properly interpreted, is hardly a dying technology but is rather among the most powerful cardiovascular prognostic tools available. With the Azarbal et al. (1) study, one of the key components of exercise test interpretation, the chronotropic response as measured by proportion of HR reserve achieved, has made it to prime time.

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REFERENCES


