Editorial / *Editöryal Yorum*

Standing the test of time: exercise testing for heart failure prognosis in the beta-blocker era

Beta-bloker çagında kalp yetersizliği prognozunun belirlenmesinde egzersiz testi: Zamana meydan okumak

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Heart failure is a major world health problem. Despite many treatments, mortality and hospitalizations remain high. Prognosis can be quite difficult, particularly regarding the interaction of multiple therapies on our diagnostic tools. Therefore, it is imperative that we periodically revisit the utility of prognostic markers to ensure that our interpretation of testing results remains clinically relevant. Cardiopulmonary exercise testing is a prime example of this conundrum. Originally popularized for the prediction of outcomes in systolic heart failure prior to the beta-blocker era, it remains widely utilized, particularly in assessing the severity of heart failure in patients considered for heart transplant.[1] Since that time, beta-blockers have been shown to significantly improve outcomes in heart failure, as have other treatments, including angiotensin receptor blockers, aldosterone receptor blockers, implantable defibrillators for primary prevention of sudden death, and cardiac resynchronization devices.

In this issue of *Archives of the Turkish Society of Cardiology*, Dufay-Bougon et al.[2] evaluated the prognostic value of cardiopulmonary exercise testing in systolic heart failure patients on chronic beta-blocker therapy in a large retrospective study. Three hundred and ninety patients with left ventricular ejection fraction (LVEF) <45% (mostly New York Heart Association [NYHA] functional class II) underwent exercise testing and were followed for clinical outcomes over a mean period of two years. Maximal oxygen uptake (peak VO_2), the slope of minute ventilation relative to carbon dioxide production (VE/VCO_2), and circulatory power were predictive of both all-cause mortality and major cardiovascular events.

Abbreviations:

LVEF *Left ventricular ejection fraction*
NYHA *New York Heart Association*

Of note, all patients were tested after a three-week inpatient cardiac rehabilitation that included exercise training five times per week. This raises the question of a training effect on testing results, which would be expected to improve testing parameters relative to outcomes, and may make the results less applicable to a non-trained population. The ability of these patients to tolerate intensive cardiac rehabilitation also suggests that the patient population studied was relatively healthy for a systolic heart failure cohort. Indeed, these patients were mostly functional class II, and close to half were not on diuretics. The relatively good functional status of this cohort is reflected in the cardiopulmonary testing results (mean peak VO_2 of 19.5 ml/kg/min, mean VE/VCO_2 of 32.3). It is also important to note that testing was solely via bicycle ergometer, and thus results may not be comparable

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to treadmill testing, which generally yields higher peak VO_2.[3] As a final note regarding the population tested, patients were enrolled about 10 years ago (2000-2004), which may affect the treatments patients received. While the medical therapy seems generally comparable to today's standards, the authors do not provide information on implantable defibrillators or cardiac resynchronization devices. This further emphasizes the constantly evolving nature of medical treatment and testing that this study tries to address.

Cardiopulmonary exercise testing yields a large amount of data. This study provides some exciting prognostic value to many of these variables. It is interesting that there was not a firm cut-off value for peak VO_2, but at least by univariate analysis, lower values were associated with worse prognosis. This would seem to indicate that peak VO_2 still has prognostic value in systolic heart failure patients treated with beta-blockers, confirming other reports, but the question remains regarding at what values clinicians should be concerned for their patients, again consistent with prior reports. Therefore, peak VO_2 must be taken in context with other cardiopulmonary exercise testing variables and/or clinical variables of prognostic significance to yield a risk profile for any given patient. Other cardiopulmonary exercise testing variables of prognostic value are highlighted in the present study, including VE/VCO_2, calculated in two different ways, circulatory power, and maximum workload. Elevated VE/VCO_2 reflects increased ventilatory drive or work of breathing that can limit functional capacity in heart failure and has been shown to be predictive of outcomes, yet data on beta-blocker-treated patients have been limited; therefore, the present study confirms its prognostic utility in such patients. Circulatory power is more recently described and is the product of the peak VO_2 and either the maximal arterial systolic blood pressure or the mean arterial blood pressure (both methods seem to be predictive of outcomes). Since peak VO_2 is highly predictive, it is no surprise that circulatory power is as well.

Thus, as treatments for systolic heart failure evolve, so too must our prognostic measures. It is good to see that in the era of chronic beta blockade, cardiopulmonary exercise testing continues to have a valuable place in our testing repertoire.

Conflict-of-interest issues regarding the authorship or article: None declared

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Key words: Adrenergic beta-antagonists/therapeutic use; heart failure/drug therapy; prognosis.

Anahtar sözcükler: Adrenerjik beta-antagonist/terapötik kullanım; kalp yetersizliği/ilaç tedavisi; prognoz.