

Cardiac Troponin Release After Endurance Exercise: Still Much to Learn

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The use of high-sensitivity troponin assays enables safe, robust, and early exclusion of acute myocardial infarction in the emergency department. Temporary elevation of troponins is, however, a common finding in a wide variety of medical conditions (eg, systemic infections, renal failure, cerebrovascular accident, and atrial fibrillation).¹ Since 1987, numerous studies have demonstrated that troponin levels above the rule-in criteria for the diagnosis of acute myocardial infarction are common also after strenuous exercise in presumably healthy individuals.² The pathophysiological characteristics of exercise-induced elevations in cardiac troponins remain unclear. Proposed mechanisms include the concept that a small proportion of free troponin molecules circulate in the cytosol of the cardiomyocyte. These molecules may be released into the extracellular space after an exercise-induced reversible cell injury, which causes a temporary increase in membrane permeability. This, in turn, allows intact or degraded troponin fragments to enter the bloodstream.³ Other potential candidates suggested include cardiomyocyte necrosis or apoptosis.

Exercise intensity and duration, together with exercise-induced high heart rate, have been the most consistent predictors for the exercise-induced cardiac troponin elevations.^{2,4} Other more inconsistent predictors include young age, as well as training and hydration status. Recent studies have suggested that high levels of physical activity are associated with higher prevalence of coronary calcium.⁵ Minor exercise-induced troponin elevations are, however,

unlikely to be caused by coronary atherosclerosis or myocardial ischemia in asymptomatic healthy individuals.⁴

In this issue of the *Journal of the American Heart Association (JAHA)*, Bjørkavoll-Bergseth and coworkers report the NEEDED (North Sea Race Endurance Exercise Study) 2014 study heart rate analyses on 177 presumably healthy recreational athletes completing a 91-km recreational mountain-bike race.⁶ The analyses were based on heart rate recordings with several different sport watch producers, causing challenges in data acquisition and analysis. The present study is, however, the largest and most comprehensive study to date to investigate the relationship between heart rate and exercise-induced troponin release. The main finding was that the duration of exercise with heart rate >150 beats per minute was the best predictor of postexercise troponin increase, but the simple chronotropic measures (ie, mean or maximum heart rate during the race) did not reach independent predictive power. These findings support the view that the exercise-induced troponin release is dependent on a minimum heart rate/exercise intensity and the duration of exercise above a critical threshold is crucial for the magnitude of the troponin elevation. It is, however, noteworthy that adding these heart rate features in the predictive model increased the R^2 only by a maximum of 5 percentage points.

Taken together, exercise intensity coupled with exercise duration reflected in heart rate dynamics during exercise seems to be the most consistent and significant predictor of troponin release in presumably healthy individuals.⁷ These features explain only a small proportion of the wide interindividual variation in troponin response to exercise. The exercise type seems also to have an effect on troponin release. Exercise-induced troponin elevations are common after long-distance running, but occur rarely (9%) after long-distance walking, supporting the crucial role of high heart rate in this process.^{4,8}

Chronically elevated troponin concentrations, even those <99th percentile, predict cardiovascular events in various patient groups and in the apparently healthy general population.⁹ Interestingly, troponin levels increase with age and high physical activity seems to reduce this age-related troponin increase in elderly subjects.¹⁰ Transient minor

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elevation of cardiac troponins after exercise has been regarded as a normal physiological phenomenon, considering the known cardiovascular health benefits of physical exercise.⁵ This conception has been challenged by recent observations. Transient postexercise ventricular dysfunction has been shown to correlate with troponin increase after intense endurance exercise.¹¹ Second, more marked troponin release has been observed among marathon runners with evidence of myocardial scarring,¹² and a pronounced and prolonged troponin increase may be related to obstructive atherosclerotic coronary artery disease.¹³ More important, a recent report showed that minor troponin I elevations after long-distance walking independently predicted higher mortality and cardiovascular events in a cohort of 725 older subjects, many of whom had either cardiovascular disease or risk factors.⁸ On the other hand, Möhlenkamp and coworkers evaluated 6-year coronary event rates in marathon runners with postexercise cardiac troponin I above and below the median and found no differences in a small cohort of 74 runners.¹² These findings suggest that exaggerated and prolonged release of cardiac troponins after physical exercise may be an early marker of cardiovascular events, especially in older subjects, but this association is difficult to ascertain. Myocardial ischemia may cause troponin release during prolonged exercise in patients with obstructive coronary artery disease, although the changes during conventional exercise testing seem to be nondiagnostic.¹⁴

Cardiac troponins are a cornerstone in the diagnosis of acute coronary syndromes. Problems arise when subjects undertaking endurance exercise present with chest pain to the emergency department shortly after training or racing. Rigorous exercise may cause plaque erosion or silent ruptures and is associated with transient risk of sudden cardiac death and myocardial infarction. The overall risk of cardiac arrest is, however, small (eg, only $\approx 1/100\,000$ marathon runners).¹⁵ In view of the present and earlier findings, clinicians should be cautious when interpreting elevated postexercise troponin levels without clinical symptoms and signs of myocardial ischemia or myocarditis. The wide interindividual predisposition to exercise-induced troponin elevation, together with the variation in the type, strength, and duration of exercise, renders the clinical judgment of troponin values difficult. The benign troponin release pattern is characterized by relatively low peak concentrations that occur within a few hours after exercise and normalize within 24 hours compared with a more prolonged elevation in myocardial infarction or myocarditis.¹⁶ Recent data suggest that the reversible myocardial injury is preferentially characterized by the release of small troponin fragments to the circulation rather than intact troponin molecules found in myocardial necrosis.¹⁷ It remains to be seen whether future developments in the measurement of specific troponin fragments could help in the clinical differential diagnosis.

Our current understanding on the causes and clinical implications of transient troponin elevation after endurance exercise is still incomplete. It is not known whether repetitive exercise-induced troponin releases are benign or whether these signals of minor injuries predict future cardiovascular abnormalities. Heavy endurance training has been shown to increase the prevalence of atrial fibrillation and may be associated with adverse remodeling of the right ventricle.^{18,19} The findings of the CCHS (Copenhagen City Heart Study) on U-shaped association between all-cause mortality and dose of jogging, as calibrated by pace, quantity, and frequency of jogging, are also of interest in this respect.²⁰ Light and moderate joggers had lower mortality than sedentary nonjoggers, whereas strenuous joggers had a mortality rate not statistically different from that of the sedentary group.

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