Cardiac troponin elevation in athletes: blame the musician and not the instrument

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Cardiac troponins (cTn) are a heterogeneous family of intracellular structural proteins that are typically absent from the circulating blood pool in the absence of recent or on-going myocardial injury. The development and wide-spread dissemination of cTn testing revolutionised clinical medicine. Replacing historically useful but non-specific markers of tissue injury including creatine kinase, lactate dehydrogenase and aspartate transaminase, cTn testing enabled prompt and accurate diagnosis of myocardial injury. Prompt cTn testing, when coupled with the appropriate clinical scenario, represents the gold-standard method of documenting acute myocardial injury and, thus, plays an essential role in the diagnosis of acute coronary syndromes and other cardiovascular disease processes. However, not all elevated cTn is created equal and as with any diagnostic tool, pitfalls of clinical application deserve consideration.

A wide body of literature documents the presence of detectable cTn in the blood following moderate to strenuous exercise in people without underlying heart disease.[1] An elegant landmark physiology study documented cTn release among healthy young men and women participating in a treadmill-based marathon run.[2] Subsequently, a study of recreational Boston marathon runners documented near ubiquitous cTn elevation following race completion.[3] Similar findings have now been reproduced across athletes representing numerous endurance and team-sport disciplines. The purpose of this commentary is to examine the potential clinical role and limitations of post-exercise cTn testing in athletes.

MECHANISMS OF CTN RELEASE

Explanatory mechanisms underlying exercise-induced cTn remain incompletely understood. Proposals include increased cardiomyocyte membrane permeability, adaptive myocyte apoptosis and/or turnover and overt myocyte necrosis perhaps coupled with hemoconcentration (ie, dehydration) and transient relative reductions in renal clearance.[1] Among patients with neuromuscular disease, cross-reactivity with skeletal troponin has been reported for several specific cTn assays that measure the troponin T isoform rather than the troponin I isoform. However, skeletal muscle sources of neither cTn isoform have been associated with exercise-induced cTn elevation. The degree to which each of these mechanisms contribute to postexercise cTn elevations remains unknown but likely apply differentially as a function of athlete age, environmental conditions and baseline cardiovascular health. Many authors have examined hypothetical correlations among athletes between exercise-induced cTn release and both non-invasive imaging markers of cardiac fatigue and subclinical cardiac abnormalities including coronary artery calcification and non-ischaemic myocardial fibrosis.[1] The results of these efforts have been mixed and there is currently insufficient data to support a definitive relationship between exercise-induced cTn elevation and these phenotypes.

However, it must be underscored that established and *clinically relevant* diseases of the cardiovascular system contribute to the incidence and magnitude of postexercisel cTn.[4] This important lesson was perhaps best illustrated in the context of 'sport' in a study of older men and women (median age ~61 years), a population enriched for acquired age-related heart disease, participating in the famous Nijmegen marches in the Netherlands.[5] In this study, cTn exceeding assay-specific upper limits of normal was both common and associated with an approximate three-fold increase in major adverse cardiac events during a median follow-up of 43 months. While this study represents an important addition to the literature and aligns with those that have examined the prognostic value of cTn among clinical populations, it should be linked with caution, if at all, to the story of cTn release among truly healthy exercisers.

CTN TESTING IN ATHLETES: CLINICAL STRATEGIES

When and in whom should cTn be measured after exercise? Beyond the scope of future physiology studies aimed at clarifying the mechanisms underlying this intriguing phenomenon, the answer is rarely. In clinical practice, biomarker testing is only of value when it informs 'next step' action items and/or informs the prognosis. The use of cTn after exercise among asymptomatic, otherwise healthy athletic people, fulfils neither criterion. More than a decade ago, a clinical algorithm highlighting the limited role of cTn testing following exercise was proposed.[6] Despite hundreds of subsequent papers examining exercise-induced cTn characteristics and clinical correlates, the basic tenants of this algorithm are unchanged and remain actionable as summarised. First, most if not all endurance athletes who participate in a race or a strenuous training session will have detectable levels of cTn that may exceed clinical cut points for the diagnosis of myocardial infarction. Thus, the use of routine 'finish line' cTn testing is strongly discouraged as it provides limited information to guide triage decisions or the initial provision of care among most athletes who seek medical attention during or after endurance events and may generate unnecessary downstream evaluations and distract clinicians from considering alternative diagnoses.[7] However, cTn remains a valuable component of the evaluation of the athlete who presents with clinical features suggestive of an acute coronary syndrome (ie, typical anginal chest pain or acute ischaemic electrocardiographic changes). Here, the magnitude and temporal nature of serial cTn levels can be useful to determine the role and timing of an invasive angiographic strategy as suggested by contemporary clinical guidelines.[8]

The last two decades have witnessed the triumphant rise of cTn testing. This simple and readily available biomarker has singlehandedly revolutionised the evaluation of patients presenting with acute chest pain. During this time, cTn assays have become increasingly more sensitive and thus capable of excluding myocardial injury with exquisite accuracy. However, increased sensitivity has come with decreased specificity.

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Key points

- ⇒ Cardiac troponin (cTn) elevation after exercise, often exceeding levels used for the clinical diagnosis of acute myocardial infarction, is common among athletes without underlying cardiovascular disease.
- ⇒ The precise mechanism(s) underlying exercise-induced cTn elevation remain incompletely defined but may include increased permeability of cardiomyocyte membranes, elevated adaptive cardiomyocyte apoptosis and turnover, myocyte necrosis, haemoconcentration and transient impairment of renal function.
- ⇒ At present, there is no evidence that post-exercise cTn elevation among young competitive athletes carries adverse prognostic implications. In contrast, an association between postexercise cTn elevation and major adverse cardiac events has been reported in ageing exercisers with pre-existing cardiovascular risk factors.
- ⇒ Post-exercise cTn testing (<24 hours) in asymptomatic athletes or in athletes presenting with clinical features that are not suggestive with an acute coronary syndrome is not recommended.

Contemporary-generation cTn assays are commonly and appropriately referred to as 'high sensitivity', but their inherently low specificity is often forgotten. In no setting is this fundamental trade-off more important than in the consideration of postexercise cTn testing. What began as a non-specific finding without clinical relevance has become increasingly complex and imprecise as time has passed. However, let us not blame cTn testing, which has proven to be one pioneering instrument when applied for its intended use. Rather, let us remind the musician to play this instrument only in the right venue and to the right audience.

Contributors Both authors contributed to the writing and revision of this invited editorial.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Commissioned; externally peer reviewed.

To cite Jean-Gilles M, Baggish A. *Br J Sports Med* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/bjsports-2023-107341

Accepted 11 October 2023

Br J Sports Med 2023;**0**:1–2. doi:10.1136/bjsports-2023-107341

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