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## Post-Exercise Release of Cardiac Troponins

Post-exercise release of cardiac troponin (cTn)T and cTnI has been previously reported after prolonged strenuous exercise (1). Up to now, it has been unclear whether post-exercise release of cTn represents necrosis of cardiac myocytes and thus irreversible damage or a transient and reversible change in membrane permeability of the myocyte (1). Similarly, whether the substrate for post-exercise release of cTn is physiologic or pathologic has not been determined (1).

Middleton et al. (2) examined the kinetics of cTnT during and after completion of a marathon on a motorized treadmill. They suggest that the consistent elevation and pattern of cTnT observed in all participants during and after exercise likely reflects a physiologic as opposed to pathologic substrate. It seems unlikely that minor elevations in cTnT subsequent to endurance exercise are due to myocardial necrosis (2). Rather, it is possible that post-exercise cTn release represents reversible cardiomyocyte membrane damage that might reflect part of a remodeling process (2).

To test the effects of reversible myocardial ischemia, Kurz et al. (3) used a pre-commercial high-sensitivity cardiac troponin T (hsTnT) assay with a 5-fold lower detection limit than the standard assay. Single-photon emission computed tomography was performed to objectively document transient reversible ischemia. The finding that hsTnT does not increase after reversible myocardial ischemia supports the experimental results of Fishbein et al. (4), demonstrating that troponin release was restricted to irreversible myocyte necrosis. Moreover, intact cTnI and degradation products were detectable by Western blot-direct serum assay (WB-DSA) in patients with acute ST-segment elevation myocardial infarction (5). Metabolic inhibition of cardiomyocytes induces parallel release of intact cTnT and cTnI and their degradation products, starting only after onset of irreversible cardiomyocyte damage (6). By contrast a recent study demonstrates that viable cardiomyocytes release cTnI as an intact protein by a stretch-related mechanism mediated by integrins (7). Integrin stimulation in cardiomyocytes does not result in degradation of cTnI into its fragments (7). Accordingly, if post-exercise release of cTn represents reversible cardiomyocyte membrane damage, it is due to a stretch-related mechanism (7) as opposed to metabolic stress or ischemia (3,4,6). However, it has been previously demonstrated that no relationship exists between post-exercise cTn release and a stretch-related mechanism (8).

Therefore, it is possible that release of cTn represents irreversible damage that has been proposed either as pathognomic of cardiac necrosis or might reflect part of a remodeling process (physiologic substrate) (1,9). To further understand exercise-induced cTn release, future work should use WB-DSA (5) to

demonstrate degradation products representing irreversible cardiomyocyte damage (3,4,6,7).

\*Arnold Koller, PhD  
Wolfgang Schobersberger, MD

\*Institute for Sportsmedicine  
Alpine Medicine and Health Tourism  
LKH Innsbruck  
Anichstrasse 35  
A-6020 Innsbruck  
Austria  
E-mail: [arnold.koller@uki.at](mailto:arnold.koller@uki.at)

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## Reply

We thank Drs. Koller and Schobersberger for their interest in our study (1). The mechanism of release of cardiac troponin (cTn) in apparently healthy individuals remains unclear (2). Our data demonstrate that cTn might be released in all individuals after prolonged exercise and have been confirmed by others (2). Recent studies using highly sensitive developmental assays demonstrate a normal distribution of cTn in apparently healthy populations (2,3). Therefore, it is likely that post-exercise release of cTn is due to a physiologic as opposed to a pathologic substrate. Conversely, elevations of cTnT above the 99th percentile of currently available commercial assays confer poor prognosis in general clinical populations (4).

Koller and Schobersberger suggest, on the basis of the work of Hessel et al. (5), a potential physiologic mechanism responsible for post-exercise cTn release. Ventricular stretch induced by prolonged exercise might stimulate integrins located in the cellular membrane that link the cytoskeleton to the extracellular matrix. Integrins could facilitate transport of the small (3% to 8%) cytosolic fraction of cTn out of healthy cardiomyocytes (6). However, the careful interpretation of Western blotting performed