Skeletal troponin I as a marker of exercise-induced muscle damage

STEPHAN SORICHTER, WALTER GEBERT, DANIEL RAMA, CHARLES CALZOLARI, ERIKA ARTNER-DWORZAK, and BERND PUSCHENDORF. Departments of *1* Medical Chemistry and Biochemistry and of *2* Sports Medicine, University of Innsbruck Medical School, A-6020 Innsbruck, Austria; and *3* Sanofi Research Centre Montpellier, F-34184 Montpellier, France

Sorichter, Stephan, Johannes Mair, Arnold Koller, Walter Gebert, Daniel Rama, Charles Calzolari, Erika Artner-Dworzak, and Bernd Puschendorf. Skeletal troponin I as a marker of exercise-induced muscle damage. J. Appl. Physiol. 83(4): 1076–1082, 1997.—The utility of skeletal troponin I (sTnI) as a plasma marker of skeletal muscle damage after exercise was compared against creatine kinase (CK), myoglobin (Mb), and myosin heavy chain (MHC) fragments. These markers were serially measured in normal physical education teacher trainees after four different exercise regimens: 20 min of level or downhill (16% decline) running (intensity: 70% maximal O2 uptake), high-force eccentric contractions (70 repetitions), or high-force isokinetic concentric contractions of the quadriceps (40 repetitions). Eccentrically biased exercise (downhill running and eccentric contractions) promoted greater increases in all parameters. The highest plasma concentration was found after downhill running (median peaks: 309 U/l CK concentration ([CK]), 466 µg/l Mb concentration ([Mb]), 1,021 µU/l MHC concentration ([MHC]), and 27.3 µg/l sTnI concentration ([sTnI]). Level running produced a moderate response (median peaks: 178 U/l [CK], 98 µg/l [Mb], 501 µU/l [MHC], and 6.6 µg/l [sTnI]), whereas the concentric contraction protocol did not elicit significant changes in any of the markers assayed. sTnI increased and peaked in parallel to CK and stayed elevated (>2.2 µg/l) for at least 1–2 days after exercise. In contrast to MHC, sTnI is an initial, specific marker of exercise-induced muscle injury, which may be partly explained by their different intracellular compartmentation with essentially no (MHC <0.1%) or a small soluble pool (sTnI: median 3.4%).

myosin heavy chain; creatine kinase; myoglobin

UNACCUSTOMED PHYSICAL EXERCISE results in protein leakage from injured skeletal muscle fibers (15), which is more pronounced after eccentrically than after concentrically biased exercise (19). Plasma activities or concentrations of certain myofibrillar proteins have been used in addition to direct muscle biopsy studies to estimate skeletal muscle damage and its magnitude (6). After exercise the muscle-injury markers increase in plasma with a varying delay after exertion (6, 15), and the increase seems to be also related to the type and the intensity of exercise (22) and to the previous activity level of the subjects (8).

Measurements of plasma creatine kinase (CK) activity and of myoglobin (Mb) and myosin heavy chain (MHC) fragment concentrations have been proposed for determining muscle injury (15, 21), but all presently available markers have limitations. None of them is a skeletal muscle-specific marker. Plasma CK activity is most frequently used. However, there are several observations on the variability of CK activity responses after comparable, histologically quantified exercise-induced muscle damage in humans (9) and animals (10), which preclude a simple interpretation of increased CK activity, especially with regard to the magnitude of injury. An explanation could be that the exercise-induced release of the predominantly cytoplasmic proteins, such as CK and Mb, can, in principle, be caused by either temporary muscle fiber damage accompanied by membrane leakage with subsequent resealing of the membrane or caused by a final death of the muscle fiber (18). Therefore, more recent research interests have been focused on contractile proteins, such as MHC (15). MHC is a structurally bound contractile protein of the thick filaments, and an increase in plasma MHC concentrations after exercise, therefore, indicates both membrane leakage and degradation of the contractile apparatus (15). However, MHC shows a delayed increase after exercise-induced muscle injury (16). It is therefore not suitable for early diagnosis. In contrast to MHC, skeletal muscle troponin subunits may be early markers for skeletal muscle damage; it has already been demonstrated that the predominantly structurally bound cardiac isoform of troponin I (TnI; [CTnI]; cytosolic pool of only 3–4% of total CTnI content (10)) is an early, highly specific, and sensitive marker for myocardial injury (17). Similarly, the features of an ideal marker of skeletal muscle injury are 1) absolute skeletal muscle specificity, 2) broad diagnostic window that allows early (within 2–6 h after the onset) and late (after 24–48 h) diagnosis, and 3) high sensitivity with a great magnitude of response. On the basis of our experience with cTnI as a cardiac marker, we hypothesized that skeletal troponin I (sTnI) is a promising marker to assess exercise-induced skeletal muscle damage. TnI is a regulatory protein that is only expressed in striated muscle fibers (24). There are different isoforms in skeletal and cardiac muscle fibers (24). Our laboratory has recently developed an immunoenzymometric assay for the measurement of sTnI (20). The purposes of the present study were 1) to test the utility of sTnI as a marker of skeletal muscle damage after different exercise regimens and to compare the time courses of this new parameter with CK, Mb, and MHC and 2) to quantify the soluble pool of sTnI in skeletal muscle.
MATERIALS AND METHODS

Exercise Analysis

Subjects. All 61 physical education teacher trainees (mean age 25 yr; range 21–29 yr) had no physical limitations to exercise and were not involved in any specific training. After approval was obtained from the local ethical committee, the risks and benefits of the study were explained and written informed consent was obtained from each participant. All subjects were instructed to refrain from unaccustomed exercise during the course of the study, beginning 48 h before the exercise session.

Warm-up protocol. All subjects performed an ~15 min warm-up before each exercise bout. It consisted of 5 min of level running on a treadmill at a running speed of 8 km/h and a 0% incline, which was followed by 5 min of stretching the leg muscles, and it ended with three series of eight knee bends.

Level-running regimen. Six subjects successfully performed an incremental load exercise test of their maximal oxygen uptake (VO2max) on a treadmill ergometer (Saturn, HP-Cosmos, Nussdorf, Germany). After baseline measurements at rest were completed, the treadmill test was started at a velocity of 8 km/h and a 0% incline. The running speed was increased by 2 km/h every 3 min until exhaustion. Oxygen uptake (VO2) was measured every 30 s via an open-chest sampling system (EOS-Sprint, Jaeger, Würzburg, Germany), and the highest level of VO2 was defined as VO2max. Heart rate (HR) was calculated from a continuously monitored electrocardiogram. Capillary blood lactate concentrations were measured at the end of each 3-min period. The exercise session was done 2 wk after the VO2max test and consisted of 20-min level treadmill running (0% incline). The exercise intensity was set at 70% of each subject’s VO2max. Running speed HR was monitored. The target HR was that achieved at 70% VO2max, which was determined in the preexercise VO2max test. Capillary blood lactate concentrations were measured every 5 min. Venous blood samples for the determination of muscle proteins were collected before exercise, 5 and 30 min after exercise, and 1, 2, 3, 6, and 9 days after exercise.

Downhill-running regimen. Thirteen subjects successfully performed an incremental-load exercise test of their VO2max on a treadmill ergometer (Saturn, HP-Cosmos) as described for the level-running regimen. The exercise session was done 2 wk later and consisted of 20-min downhill treadmill running (16% incline). The exercise intensity was set at 70% of each subject’s VO2max. Running speed was HR monitored. The target HR was that achieved at 70% VO2max, which was determined in the preexercise VO2max test. Capillary blood lactate concentrations and venous blood samples for the determination of muscle proteins were measured and collected as described for level-running regimen.

Eccentric exercise regimen. Exercise was conducted with subjects in a sitting posture on an exercise rack specially designed to elicit the required eccentric action of the quadriceps femoris (15). After warming up, all 30 subjects were tested for their maximal voluntary force generation of the investigated leg, with the knee held at an angle of 1.745 rad (3.14 rad correspond to full extension of the knee). Subjects then had to hold their knees at an angle of 2.62 rad, when a special trigger mechanism suddenly released 150% of the maximal voluntarily generated force. Subjects were instructed to straighten their knee against the pressure of this weight. However, given the arrangement, they could not help flexing their knee, although they tried to resist. A pulley system allowed the researcher to bring the weight to the starting position without any loading concentric exercise of the investigated leg. Each subject performed a single bout of eccentric exercise by using only one leg. The exercise bout consisted of 7 sets of 10 eccentric contractions of the quadriceps femoris muscle group. Each contraction lasted 1–2 s, with 15 s of rest between contractions. The seven sets were each separated by 3 min of rest. The schedule has been described in detail elsewhere (15, 23). Blood samples for the determination of muscle proteins were collected before exercise and 1, 4, and 7 days after exercise.

Short concentric exercise regimen. After a warm-up, standardized loading of the thigh muscles of one leg was performed in 12 subjects on a computer-interfaced dynamometer (Cybex 6000, Ronkonkoma, NY) at an angular velocity of 3.14 rad/s with 40 repetitions without rest. The subjects performed maximum voluntary knee extension from 1.57-rad flexion over a range of 1.57 rad to full extension of the knee. Peak torques [in Newton meters (N/m²)] were recorded throughout the exercise regimen. Maximal HR (HRmax) during the exercise was determined from a continuously monitored electrocardiogram. Capillary blood lactate concentrations were measured directly 1, 3, and 5 min after exercise was completed. Venous blood samples for the determination of muscle proteins were collected before exercise, 5 and 30 min after exercise, and 1, 2, 4, 6, 10, and 24 h after exercise.

Laboratory Analysis

Determination of sTnI and MHC pools of human skeletal muscle. Human skeletal muscle specimens (m. psoas major, m. gastrocnemius) were obtained from three different subjects at autopsy within 24 h after death. Cytosolic and myofibrillar fractions were prepared according to previously described protocols for the quantification of the soluble cTnI pool (1). Small pieces of skeletal muscle (~0.25 g) were homogenized in 10 volumes of cytosolic buffer ([in mM] 1 KH2PO4, 1 ethylene glycol-bis-(β-aminoethyl ether)-N,N,N’,N’-tetraacetic acid (EGTA), and 20 KCl, pH = 6.8, and 20 tablets/l of a protease-inhibitor mixture, Complete protease-inhibitor cocktail no. 1697498, Boehringer Mannheim, Mannheim, Germany). After the homogenate was centrifuged at 20,000 g for 15 min, the pellet was resuspended in 10 volumes of cytosolic buffer, and the centrifugation was repeated. The supernatants of each centrifugation were assayed separately, and the data were combined to calculate the soluble, cytosolic fractions of proteins.

The final pellet was resuspended in 10 volumes of extraction buffer ([in mM] 40 sodium pyrophosphate, 1 EGTA, and 1 MgCl2, pH = 9.0, and 20 tablets/l of Complete protease-inhibitor cocktail no. 1697498, Boehringer Mannheim). After being stirred for 30 min at 4°C, the extract was centrifuged at 20,000 g for 15 min. The pellet was reextracted twice. The supernatants of each centrifugation were assayed separately, and the data were combined to calculate the myofibrillar fractions of proteins.

Lactate dehydrogenase (LDH), CK, Mb, sTnI, cTnI, and MHC were measured in each fraction as described below. The cytosolic fraction was divided by the total fraction (cytosolic plus myofibrillar) to obtain the percentage of the measured markers in the cytosolic fractions.

The remaining pellet with actin-myosin filaments was resuspended in 50 mM sodium pyrophosphate (pH = 7.4) for MHC measurements.

Quantification. LDH, a soluble, cytosolic enzyme, was used to check the quality of fraction separation by the centrifugation protocol used. As expected, LDH activity was only found in the cytosolic fractions. The median amounts of the soluble precursor TnI pool were 42.4 μg/L wet weight and 832 μU/g.
wet weight for MHC. The soluble TnI was 3.4% (median) of the total TnI content. MHC concentrations in all cytosolic fractions were much lower than 0.1% of total MHC. The percentages of CK, Mb, and sTnI in the cytosolic fractions of skeletal muscle are shown in Table 1.

Lactate. Capillary blood samples for the determination of lactate concentration were collected from a prewarmed earlobe. One hundred microliters of the sample were immediately mixed with 200 µl of a cold 8% perchloric acid solution and refrigerated for subsequent lactate determination. Lactate was determined by using an enzymatic method (LACT, Boehringer Mannheim).

Blood collection. Blood was collected in EDTA-coated tubes (Sarstedt, Nümbrecht, Germany) from a superficial forearm vein. It was immediately centrifuged. Plasma CK activity was assayed on the same day; aliquots of plasma samples for sTnI, cTnI, MHC, and Mb measurements, respectively, were subsequently frozen and stored at −20°C until assayed.

TnI. TnI is the inhibitory protein of the troponin-tropomyosin regulatory complex, which regulates the interaction of actin and myosin in striated muscles. sTnI has a molecular mass of about 18.5 kDa; cTnI has an extra 30 residues at the NH₂-terminus, resulting in a molecular mass of 24 kDa (5). By lymphocyte hybridization, high-affinity monoclonal antibodies (MAbs) directed against the non-cardiac-specific part of TnI and other high-affinity MAbs directed against the cardiac-specific part of TnI were obtained. Eighteen of these MAbs were specifically directed against the cTnI, whereas 10 MAbs recognized also the sTnI. Screening of all MAbs by pairs (one coated MAb on NUNC Maxisorb immunotubes, the other as peroxidase-labeled conjugate) was used to construct the antigenic map. This epitopic map has permitted identification of some pairs of MAbs capable of measuring TnI concentrations. Two optimal pairs of MAbs were selected to determine both sTnI and cTnI concentrations by using two independent immunoenzymometric assays. One assay detects all TnI isoforms; the other assay is specific for cTnI. The production and characterization of MAbs as well as the assay characteristics have been described in detail elsewhere (11, 20).

The assay for measurement of sTnI enables a sensitive estimation of TnI in the range of 0.1 to 1.5 µg/l in EDTA-plasma. The lower detection limit of the assay was 0.05 µg/l (3 SD above the mean nonspecific binding of the reagent blank). The within-run and between-run variations of the assay were calculated nonparametrically as the 95th percentile of sTnI concentrations in 79 apparently healthy subjects (blood donors), was 2.2 µg/l. The median was 0.5 µg/l, and the interquartile range was 0.3 to 0.9 µg/l. cTnI could not be detected in any sample.

MHC. Concentrations of MHC fragments were measured by an immunoradiometric assay (ERIA Diagnostics Pasteur, Marnes la Coquette, France). This sandwich assay uses a pair of MAbs primarily raised against two different epitopes on subfragment 2 in the rod of human ventricular beta-type heavy meromyosin. Owing to the strong structural similarity of beta-type cardiac MHC and MHC of slow-twitch skeletal muscle fibers, both antibodies react strongly with human slow-twitch skeletal muscle but not with fast-twitch skeletal MHC or any other MHC isoform (13). The affinities of the antibodies to slow skeletal muscle myosin were identical to those to beta-type cardiac MHC (13). The URL of MHC in plasma is 300 µU/l. The detection limit of the assay is 10 µU/l (1 µU/l corresponds to 1 µg/l) (12). The intra- and interassay CVs were 3.9 and 6.8%, respectively.

CK. CK was measured by a standardized commercially available enzymatic assay (Granunest 15, Merck, Darmstadt, Germany). The URL for men is 80 U/l (25°C). The intra- and interassay CVs were 8.4 and 10.1%, respectively.

Mb. Mb was measured by a commercially available enzyme immunoassay (Myoglobin-Access, Sanofi-Diagnostics-Pasteur, Marnes-la-Coquette, France). The URL is 70 µg/l. The intra- and interassay CVs were 4 and 7%, respectively.

Statistics

All variables were tested for normal distribution and equal variance. Mean and SDs, median, interquartile range (IQR), and percentiles were calculated to describe continuous variables. The Wilcoxon signed-rank and Mann-Whitney rank-sum test and one-way analysis of variance for repeated measurements with post hoc comparisons by using the Student-Newman-Keuls method were used for intra- and intergroup comparisons. A P value of <0.05 was considered to indicate statistical significance.

RESULTS

Level and Downhill-Running Exercise

During exercise, lactate levels rose to ~4 mM in both downhill and level runners, respectively. Plasma CK was significantly elevated after exercise in both downhill and level runners, with peak values within 24 h after finishing. Interestingly, peak values did not differ between both groups [median (IQR): 309 (154–570) vs. 178 (131–291) U/l; P = 0.27]. Mb increased most rapidly after exercise with peak values within 6 h after subjects finished. Peak values were significantly higher in downhill vs. level runners [median (IQR): 466 (286–764) vs. 98 (57–137) µg/l]. MHC increased after exercise, with peak values 48 h after subjects finished. Peak values were significantly higher in downhill vs. level runners [median (IQR): 1,021 (457–1,540) vs. 501 (290–773) µg/l]. cTnI was not detectable in any sample. sTnI increased rapidly after exercise, with peak values within 6 h after subjects finished. Peak values were significantly higher in downhill vs. level runners [median (IQR): 27.3 (8.5–43) vs. 6.6 (3.7–9.0) µg/l] (see Figs. 1 and 2).

Comparison of the time needed to reach peak values in downhill runners revealed significant differences
among all four measured parameters. The median time-to-peak values for Mb, sTnI, CK, and MHC were 120 min, 360 min, 1 day and 2 days, respectively.

High-Force Eccentric Exercise

cTnI was not detectable in any sample. CK [median (IQR): 201 (111–299) U/l], Mb [median (IQR): 125 (89–142) µg/l], MHC [median (IQR): 330 (168–454) µU/l], and sTnI [median (IQR): 6.8 (3.1–14.9) µg/l] increased significantly in response to the high-force eccentric exercise bout (see Fig. 3).

Short Concentric Exercise

The most prominent change observed after 40 isokinetic contractions of the thigh muscles at 3.14 rad/s on an isokinetic dynamometer was an increase in
lactate, even though the muscle fibers maintained their contractile proteins and enzymes.

Total work for extension and flexion amounted to 8,041 J (median; IQR: 7,787–9,372 J). Capillary lactate accumulated maximally 1 min after exercise to 14 mM (median; IQR: 12.5–14.4 mM), the median HR increased from 94 to 175 beats/min and decreased 5 min after exercise to 95 beats/min. Before exercise, plasma concentrations of all myofibrillar proteins were within normal ranges. cTnI was not detectable in any sample. There were no significant changes of sTnI, Mb, CK, or MHC plasma values, respectively (see Fig. 4).

DISCUSSION

The rationale underlying this study was that the present commonly used markers (CK, Mb) of exercise-
induced muscle injury have several limitations, as outlined at the beginning of this study, and they are therefore not ideal indicators of skeletal muscle damage. Contractile and regulatory proteins are abundant in muscle fibers, and the premise was that skeletal muscle-specific proteins leaking into the circulation may be useful markers for detecting exercise-induced muscle injury. Our laboratory previously reported that one of these proteins, MHC, shows a delayed increase, with late peak values in plasma after exercise-induced muscle injury (15, 16), and this study confirms these earlier observations. Therefore, MHC is not suitable for early diagnosis, and additionally the complexity of MHC isoforms and their expression patterns in striated muscles (12, 13, 15) make it difficult to develop an assay that specifically identifies skeletal muscle damage. From our previous investigations of cTnI, we knew that this marker rapidly increases after myocardial injury (11, 17). In contrast to MHC, there are only three TnI isoforms, one for slow-twitch skeletal muscle, one for fast-twitch skeletal muscle, and one for myocardium (24), and TnI is only expressed in striated muscles. We succeeded in developing an enzyme immunoassay that detects all three TnI isoforms (20), and we used an already commercially available assay (11) to measure cTnI for exclusion of myocardial damage. Undetectable cTnI in all measured samples made it possible to attribute all measured TnI to sTnI being released into the circulation after exercise-induced muscle injury.

We evaluated the response of sTnI and compared its concentration time courses against CK, Mb, and MHC in serially collected blood samples of different groups of athletes. These individuals underwent four different exercise regimens: 20 min of level or downhill (16% decline) running (intensity: 70% V̇O₂max), high-force eccentric contractions of the quadriceps group (70% maximal contractions), and high-force isokinetic contractions of the quadriceps group (40 contractions). Eccentrically biased exercise (downhill running and eccentric contractions) promoted greater increases in all parameters. However, in contrast to sTnI, MHC, and Mb, CK peaks did not differ significantly between downhill and level runners, although delayed-onset muscle soreness was much more pronounced in downhill runners. This is in good agreement with previous observations that plasma CK activity may not be a reliable index of microscopic injuries that occur to muscle fibers that are not conditioned for eccentric activity (9). Pure high-intensity concentric contractions of the quadriceps femoris muscle group on a dynamometer (median workload 8,041 J) did not elicit significant changes in any of the markers assessed, although the capillary lactate rose on average to 14 mM. Intramuscular acidosis may result in lowered muscle performance associated with the feeling of fatigue (3), but our results demonstrate that acidosis and lactate accumulation alone do not necessarily lead to protein leakage from exercised muscles. After exercise-induced muscle injury, sTnI increased in parallel to CK, peaked within 24 h, and stayed elevated for at least 1–2 days after exercise. In general, there was a greater relative increase in sTnI over baseline values compared with the other tested markers. Because of the pronounced increases in all tested markers and frequent blood sampling, time-to-peak values of markers were calculated and compared in downhill runners. Mb peaked earliest (median 2 h), followed by sTnI (median 6 h), CK (median 1 day), and MHC (median 2 days). Time-to-peak values observed for Mb, CK, and MHC agree with previous observations (15, 21). Confirming previous results (15, 21), we observed delayed peaks of CK and MHC after high-force pure eccentric exercise; however, no delayed sTnI peaks were found in these individuals.

In contrast to MHC, sTnI is an initial marker of exercise-induced muscle injury. Both markers are subunits of the thick and thin filaments in striated muscle fibers, respectively. Therefore, the early increase in sTnI after exercise-induced muscle damage raises questions about its release mechanisms. The presence of a soluble TnI precursor pool in the sarcoplasm of skeletal muscle fibers could be responsible for this rapid release. Because this issue has not been investigated so far, we quantified the cytoplasmic pools of human skeletal muscle MHC and TnI in autopsy specimens obtained from three different subjects. We found no evidence for a significant soluble MHC pool, whereas a small cytosolic sTnI pool of ~3–4% of the total sTnI content of skeletal muscle fibers was found. The amount of this sTnI pool is comparable to the soluble cytosolic pool reported for cTnI in the human myocardium (11). A relatively small soluble sTnI pool may explain the early release of sTnI but can be hardly the only reason for the rapidly occurring sTnI peak values after muscle damage. sTnI peak values were observed within 24 h after exercise-induced muscle damage, only with a small delay compared with Mb peaks. This suggests that other mechanisms must also be involved in its early release in high amounts. Armstrong (2) reported raised intracellular Ca²⁺ concentrations after unaccustomed eccentric exercise, which could promote muscle injury with its characteristic histological changes. This inability of the muscle fiber to regulate the influx of extracellular Ca²⁺ could be the primary factor underlying the activation of calpains (4), which are nonlysosomal Ca²⁺-activated neutral proteases present in striated muscle fibers. A selective degradation of the myofibrillar complex by calpains may contribute to the early increase in sTnI plasma levels after unaccustomed exercise (7). In contrast to MHC, sTnI is particularly susceptible to calpain digestion (4, 7). The two MAbs of the MHC assay recognize epitopes on subfragment 2 in the rod of cardiac beta-type or slow-twitch skeletal muscle heavy meromyosin. This fragment is very resistant to proteolysis because of its central location in the rod of MHC/myosin molecule and the thick filament, respectively (12). This and the absence of a soluble MHC precursor pool are probably responsible for the late increase in plasma MHC and its delayed peak values, which reflect a final stage of dissociation and/or degradation of the contractile apparatus.
Our results provide evidence that the high muscle force associated with eccentric contraction or the length change occurring during eccentric contraction causes a rapid dissociation and/or degradation with rapid removal of sTnI. These findings support the concept that eccentric exercise initiates a series of events that result in rapid disruption of the cytoskeletal network and contractile apparatus, which could be the mechanism for deterioration of the contractile response and loss in force generation (16). Lieber et al. (14) demonstrated a rapid loss of desmin labeling of the extensor digitorum longus muscles after cyclic eccentric exercise in rabbits. Cytoskeletal disruption may predispose the contractile apparatus to structural damage. Belcastro (4) reported an early degradation of the thin-filament troponin-tropomyosin complex after prolonged running in rats. It is certainly of benefit for a plasma marker of muscle injury, with greater responses occurring for eccentric exercise. sTnI has a broad diagnostic window, recognized within 2–6 h from the onset of exercise-induced muscle injury, such as sTnI, if it is able to reflect the rapid derangement of the contractile apparatus.

In summary, marked increases in sTnI can be detected within 2–6 h from the onset of exercise-induced muscle injury, with greater responses occurring for eccentric exercise. sTnI has a broad diagnostic window, is an initial marker, peaks within 24 h, and stays elevated for at least 1–2 days. In contrast to all other available markers, sTnI is a protein unique to skeletal muscle. Its early increase in plasma and, particularly, its short time-to-peak values indicate rapidly occurring alterations of the thin-filament troponin complex after exercise-induced muscle injury.

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Address for reprint requests: B. Puschendorf, Institut für Medizinische Chemie und Biochemie, Fritz-Preglstrasse 3, A-6020 Innsbruck, Austria (E-mail: johannes.Mair@uibk.ac.at).

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REFERENCES