Cardiac Troponin-T Release After Sport and Differences by Age, Sex, Training Type, Volume, and Intensity: A Critical Review

Massimiliano Cantinotti, MD,*† Aldo Clerico, MD,* Raffaele Giordano, MD, PhD,‡ Nadia Assanta, MD,* Eliana Franchi, MD,* Martin Koestenberger, MD,‡§ Pietro Marchese, MD,* Simona Storti, MD, PhD,* and Flavio D'Ascenzi, MD, PhD¶

Abstract

Background: Postexercise release of cardiac troponin (cTn) is a well-known phenomenon, although the influence of various confounders remains unclear. The aim of this critical review was to analyze the postexercise release of cTn according to age, sex, different types of sport, exercise intensity and duration, and training level. **Data Sources:** A literature search was performed within the National Library of Medicine using the following keywords: cTn, peak, release, and exercise. The search was further refined by adding the keywords athletes, children/adolescents, and sport. **Main Results:** For final analysis, 52 studies were included: 43 adult studies, 4 pediatric studies, and 5 with a mixed population of adults and children. Several studies have investigated the kinetics of cTn response after exercise with different biomarkers. The current evidence suggests that sport intensity and duration have significant effects on postexercise cTn elevation, whereas the influence of the type of sport, age, and sex have been not completely defined yet. Most data were obtained during endurance races, whereas evidence is limited (or almost absent), particularly for mixed sports. Data on young adults and professional athletes are limited. Finally, studies on women are extremely limited, and those for non-White are absent. **Conclusions:** Postexercise release of cTn can be observed both in young and master athletes and usually represents a physiological phenomenon; however, more rarely, it may unmask a subclinical cardiac disease. The influence of different confounders (age, sex, sport type/intensity/duration, and training level) should be better clarified to establish individualized ranges of normality for postexercise cTn elevation.

Key Words: cardiac troponin, athletes, athlete's heart

(*Clin J Sport Med* 2022;32:e230–e242)

INTRODUCTION

A postexercise release of cardiac troponin (cTn) has been observed commonly in healthy athletes of different ages.[1-7] In the last 20 years, few reviews[1-7] and several studies[8-65] tried to clarify the kinetic and factors underlying the exercise-induced release of cTn. Although some aspects have been defined, others still remain unclear. The cTn release usually happens in the first hours after exercise, with a recover within 24 to 48 hours.[1-7] In the last decade, the progressive improvement in analytical performance of immunometric assays has allowed the measurement of circulating levels of cardiac troponin I (cTnT) in apparently healthy adults.[66-73] These high-sensitivity methods demonstrated that both cTnI and cTnT concentrations increase after strenuous prolonged exercise in most athletes (ie, more than two-thirds in marathon runners), reaching values beyond the normal threshold (ie, the 99th percentile of cTn distribution value of the reference population), as recommended by international guidelines for myocardial injury and acute myocardial infarction (AMI).[70-73] This acute elevation of high-sensitivity cardiac troponin (hs-cTn) assay after exercise has been considered a physiological response without long-term adverse consequences for a long time[70,71] However, recent studies suggested that exercise-induced increase in hs-cTn are not always benign and should be considered as an early cardiovascular risk marker.[42,43] These recent data[42,43] raise the question whether some relevant confounders in cTn response after exercise, including analytical characteristics of cTn-assay methods (ie, high-sensitivity vs. non–high-sensitivity laboratory tests) and experimental study designs and populations (eg, different sports, exercise duration and intensity, age, body size, and sex), play a relevant role in influencing the large heterogeneity in the literature currently available. The aim of this review is to critically review the evidence on postexercise release of cTn in athletes with different age, sex, and sports disciplines, to underscore the current knowledge on this topic and the remaining gaps to be evaluated in future research.

Submitted for publication July 22, 2020; accepted March 28, 2021.

*From the *Pediatric Cardiology Unit, Fondazione CNR-Regione Toscana G. Monasterio, Massa, Italy; †Pediatric Cardiology Unit, Institute of Clinical Physiology (IFC) National Research Institute (CNR), Pisa, Italy; ‡Department Advanced Biomedica Sciences, University of Naples Federico II, Naples, Italy; §Division of Pediatric Cardiology, Department of Pediatrics, Medical University Graz, Austria; and ¶Department of Medical Biotechnologies, Division of Cardiology, University of Siena, Italy.*

The authors report no conflicts of interest.

Corresponding Author: Raffaele Giordano, MD, PhD, Department Advanced Biomedica Sciences, University of Naples Federico II, Naples, Via Pansini 5, 80131 Italy (r.giordano81@libero.it).

http://dx.doi.org/10.1097/JSM.0000000000000940

METHODS

Search Strategy

Potential publications were identified from a systematic search in the National Library of Medicine (PubMed access to MEDLINE citations; http://www.ncbi.nlm.nih.gov/PubMed/). The search strategy included a mix of Medical Subject Headings and free-text terms for the key concepts, starting from troponin, peak, raise, and exercise. The search was further refined by adding the keywords athletes, children, adolescent, and sport type. In addition, we identified other potentially relevant publications using a manual search of references from all eligible studies and review articles, as well as from the Science Citation Index Expanded on the Web of Science. Two reviewers (M.C. and M.K.) independently assessed all identified reports, and a consensus was reached for inclusion in the analysis. All articles identified by the above search strategy were evaluated. Studies were excluded if they (1) evaluated subjects with cardiovascular disorders, (2) were focused on other biomarkers rather than cTn, (3) have a sample size less than 20 subjects (unless they were retained to add unique information), and (4) were written in languages other than English.

RESULTS

Among 98 studies initially selected, 46 were excluded for the above-mentioned criteria (3 evaluated subjects with cardiovascular disorders, 5 evaluated other biomarkers rather than cTn, and 38 had a sample size less than 20 subjects) and 52 studies were included in the final analysis. Forty-three adult studies,[10-15,17-20,22-24,26-33,35-40,42-51,53,60-63,65] 4 pediatric studies,[31,36,37,52] and 5 with a mixed population of adults and children[8,9,16,25,64] were included. Table 1.

Studies in Different Types of Sport, Sex, Age, and Ethnicity

Most of the studies were conducted on endurance athletes[1,12,13,15,17-24,26-30,33,34,40,42-44,47,49,51,53,54,57,58,60,65] and evaluated the release of cTnT after marathon,[12-13,18-20,22,23,26-29,32-34,40,43,51,54] half-marathon,[57,58] ultramarathon,[10,44,47,53] long-running,[21-22,49] triathlon,[15,24,30,45-46,56] or cycling[28,31,42,60,65] races. Data were relatively limited in some sport disciplines, such as soccer, rugby basket, raw, and table tennis,[8-9,16,35,36,52,63-64] and almost absent in other disciplines (eg, tennis, skiing, dance, rugby, and boxes). Most of the data were collected on amateur athletes,[10,14-15,17-20,22-24,26-29,32-34,37-38,40,42-51,53-54,56-58,63] whereas only 6 articles were conducted in professional athletes[16,35,51,60,64-65]; 4 studies enrolled a mixed population of amateur and elite athletes.[30,35,51,55]

Nineteen studies[10,12,20,29,32,33,38,40,42-45,47-49,51,53-54,58] were conducted in athletes with a mean age older than or equal to 40 years and 8 studies[4,13,22-24,26,27,50,54] in athletes with a mean age older than or equal to 35 years. Only 11 articles included young adults.[16-17,19,30,35,51-52,59,63-65] In most of the studies, the population was mainly[10,19,22,26,29,30,32-33,43,47-48,53-57] or entirely[9,12,15,17-18,24,28,31,35,38,40,44,48,49,51-52,59-60,64,65] constituted by men, whereas data on women are very limited.[8,27,42,45,50,58,64] Data on children and adolescents were also relatively limited.[1,8,9,16,25,31,36,52,64] Most of the studies were performed in White, whereas the impact of ethnicity has been rarely investigated.[23,27,52]

Kinetics of Different Cardiac Troponin Biomarkers

Percentages of athletes above the upper reference limit (URL) after exercise were higher for hs-cTnT (from 62% to 100%)[2,5,8-9,13,15,17-20,25-26,32,38,54,64] than for cTnT (from 18% to 86%)[12,18,23-24,27,29,33,40,48,51-53] and for cTnI (from 33% to 100%)[23,27-30,32] (Table 1). For non–high-sensitivity methods, some authors also reported the percentage of subjects above the cut-off for the suspicion of AMI for cTnT,[9,23,24,27,29,30,33,44,48,60] ranging from 8% to 44% for cTnT[9,23-24,27,29,33,44,48,60] and from 60% to 64% for cTnI.[23,29-30] The recovery was different according to the different biomarkers. Indeed, cTn-T values usually recovered faster within 24 hours[22,27,29,52] whereas recovery of troponin I[27,29,42,52] and hs-cTnT[8,15,17,22,26,32] required up to 3 days (Tables 2-4).

Data on children and adolescents[8,9,16,25,31,36-37,52,64] confirm the findings observed in adults. A systematic review[1] and meta-analysis including 336 adolescents (mean age 15.1 ± 2.3 years) demonstrated that cTnT and cTnI had a similar kinetic of postexercise peaks (at 2-5 hours for cTnT and 3-6 hours for cTnI). cTnT values reduced significantly at 24 hours (although it remained higher as compared with baseline values, $P = 0.01$), whereas cTnI values at 24 hours did not significantly decrease ($P = 0.6$). Participants who had postrace values above the URL were 76% for cTnT (range 66%-87%) and 39% for cTnI (range 26%-60%). Adolescents exceeding the cut-off for AMI were 51% (range 32%-81%) for cTnT and 11% (range 5%-24%) for cTnI.[1] As stated above, data on women[8,22,27,42,44,50] are limited, and only one study[8] performed a comparison between men and women, demonstrating differences in the kinetic of troponin elevation. In 50 adolescent and 16 adult swimmers,[8] postexercise hs-cTnT peak values were reached from 5 minutes to 12 hours; notably, females had a delayed peak (1 hour in females vs 5 minutes in males, $P < 0.0001$) and a delayed return to baseline values (24 hours in females vs 12 hours in males, $P < 0.0001$).[8]

Differences According to the Type of Sport

Data on differences in cTn release among various types of sport are relatively scarce.[1,4,9,15,41,47,61-62] A meta-analysis including 26 studies and 1,120 athletes[4] reveled higher cTnT elevation after running races than after cycling or triathlon events ($P = 0.059$).[4] The postrace release of cTnT was more common in shorter than in longer competitions (eg, marathon vs ultramarathon), and the higher exercise intensity of shorter races has been hypothesized as a potential cause of this difference.[4,41,47] However, the percentage of subjects with positive troponin levels was similar after the downhill or flat course marathon.[61-62] Another metanalysis,[1] including 336 adolescent athletes, demonstrated that among 4 types of sport, cTnT increase was higher in marathon and treadmill run compared with intermittent table tennis ($P < 0.01$) and swimming ($P = 0.004$). Conversely, no significant differences were found among different types of training for cTnI.[63] In 18 young athletes,[63] heavy resistance training session did not cause a raise in cTnI or cTnT levels, whereas in 24 age-matched indoor soccer players, the authors observed an increase in cTnI (pre-0.026 ± 0.047 ng/Lpeak and post-0.033 ± 0.051 ng/L, $P = 0.008$) but not in cTnT.

For hs-cTnT, data on the impact of different types of sport are extremely limited.[17] In a small study[17] including 15 amateur triathletes (35 ± 9 years), who underwent trial of 60 minutes of swimming, running, or cycling, the type of exercise did not influence postexercise hs-cTnT release ($P = 0.102$).

Influence of Sport Intensity and Duration

The effect of sport intensity and duration has been evaluated by several authors.[4-5,13,17,22,24,26-28] The intensity of exercise

TABLE 1. Studies on Postexercise cTn Rise Included in the Present Review Divided According to Biomarker Type, Type of Sport, Training Level, and Age

Author	Biomarker	Method	Sport Type	Training Level	Sex, Age, yrs
Sherr et al,[20] 2011, Germany	Hs-cTnT	Roche Diagnostic, Penzberg, Germany	Marathon (Munich marathon)	Amateur well trained; km/wk: 54.1 ± 21.8 km	102 M; age **42 ± 9.5** yrs
Roca et al,[26] 2017, Spain	Hs-cTnT	NR	Marathon (Barcelona marathon)	Amateur well trained; years of training: mean 7, range 5-11	57 M, 22 F; age 39 ± 6 yrs
Baker et al,[2,19] 2019, United Kingdom	Hs-cTnT	Roche Modular E170, 5th Generation, Basel, Switzerland	Marathon (Brighton marathon)	NR	18 M, 8 F; age 26 yrs
Richardson et al,[13] 2018, United Kingdom	Hs-cTnT	Roche Modular E170, 5th Generation, Basel, Switzerland	Marathon (Brighton marathon)	Amateur, trained and not trained	39 M, 13 F; age 39 ± 11
Hermann et al,[29] 2003, Germany	cTnT cTnI	cTnT Roche Diagnostics, automated analyzer (Elecsys 2010), Mannheim, Germany cTnI Accu TnI method (Beckam Coluter) on access analyzer	Marathon (Mainz marathon)	Amateur, level of training NWR	40 M, 6 F; age 40 ± 7 yrs
Frassl et al,[27] 2008, Germany	cTnT cTnI	cTnT Roche Diagnostics, automated analyzer (Elecsys 2010), Mannheim, Germany cTnI Advia Centaur Assay (Bayer Healthcare, Leverkusen, Germany)	Marathon (Berlin marathon)	Amateur well trained, training history NWR	15 F; age 36 ± 6 yrs
Serrano Ostariz et al,[22] 2011, Spain	cTnI	Access, Beckam Coulter, Krefeld, Germany	Marathon (Zaragoza marathon)	Amateur well trained, years of training 8 ± 4	19 M, 2 F; age 38 ± 8 yrs
Mingles et al,[32] 2009, Netherlands	Hs-cTnT cTnI	Hs-cTnT Roche Diagnostic cTnI-Architect Abbot Diagnostic	Marathon (Maastrichts Mooiste)	Amateur well trained, mean previous marathon = 8	70 M, 15 F; age 47 (45-49) yrs
Fortescue et al,[23] 2006, USA	cTnT cTnI	cTnT Bayer Labs ACS Centaur immunoassay cTnI Elecsys STAT immunoassay Roche Diagnostic	Marathon (Boston marathon)	Amateur, trained and not trained	319 M, 163 F; age 38.8 ± 10.2 yrs
Hubble et al,[43] 2007, Australia	cTnI	Ultratroponin assay, Siemens Healthcare Diagnostics, Tarrytown, NY	Marathon (Perth marathon)	Amateur: previous marathon = 3 (1-8); km/wk 60.1 (20.5)	65 M, 27 F; age 43.1 ± 9.8 yrs
Leers et al,[54] 2006, The Netherlands	cTnT	Roche Diagnostics, Hoffmann-La Roche, Inc., Basel, Switzerland	Marathon: Visé-Maastricht-Visé marathon	Amateur, training history NWR	25 M, 2 F; age 48 ± 8 (34-64) yrs
Saravia et al,[18] 2010, Germany	Hs-cTnT cTnT	Roche Diagnostics, Hoffmann-La Roche, Inc., Basel, Switzerland	Marathon (Berlin marathon)	Amateur, training history NWR	78 M; age NR
Jassal et al,[40] 2009, Canada	cTnT	3rd generation Roche Elecsys assay	Marathon (Manitoba marathon)	Amateur, trained and not trained	61 half marathons: 40 M, 21 F, 40 ± 12 yrs; 68 marathons: 44 M, 24 F, 42 ± 14 yrs
Neilan et al,[33] 2006, USA	cTnT	cTnT STATT, Roche Diagnostics, Indianapolis, Ind, Roche Elecsys 1010	Marathon (Boston marathon)	Amateur well trained, 42 ± 9 miles/wk	41 M, 19 F; age 41 (21-65) yrs
Siegel et al,[50] 2008, Boston, USA	cTnT	cTnT Roche Diagnostics, Indianapolis, Ind, Roche Elecsys	Marathon (Boston marathon)	Amateur	99 collapsed runner: 61 M, 38 F; 39.1 ± 10.4 yrs

TABLE 1. Studies on Postexercise cTn Rise Included in the Present Review Divided According to Biomarker Type, Type of Sport, Training Level, and Age *(Continued)*

Author	Biomarker	Method	Sport Type	Training Level	Sex, Age, yrs
Siegel et al,[51] 1997, Boston, USA	cTnT	cTnT ELISA Boeheringer Mannheim, Diagnostics, Lewes, United Kingdom	Marathon (Boston marathon)	Amateur, well trained, years of training: 15 ± 9. Previous marathons: 16 ± 6, miles/wk 37 ± 14	45 M; age 50 ± 6 yrs
Martinez Navarro et al,[44] 2019, Spain	Hs-cTnT	ECLIA Cobas e411 analyzer (Roche Diagnostics, Penzberg, Germany)	Ultramarathon (Spanish Ultra-Endurance Championship)	Amateur, trained: years since previous marathon: 4.63 ± 3.97. Average weekly session 4.37 ± 1.45	46 M; age 42 ± 7.49 yrs
Dalla Vecchia et al,[57] 2013, Italy	cTnI	Roche Diagnostic (Mannheim, Germany)	Half-marathon (corri Pavia)	Amateur, trained	35 31 M, 4 F; age 42 ± 7 yrs
Vidotto et al,[58] 2005, Vienna, Austria	cTnI	Dimension/Dade Behring Limited, United Kingdom	Half-marathon (Wachau half-marathon)	Amateur, trained; M 50 ± 15.6 km/wk; F 33.1 ± 17.1 km/wk	12 M; age 42.8 ± 7.3: 13 F; age 39.0 ± 6.5
Have et al,[12] 2002, United Kingdom	cTnT	Elecsys 1010 automated batch analyzer (Roche Diagnostics, Mannheim, Germany)	Ultramarathon (2-d Lowe Alpine Mountain Marathon 2000)	Amateur, trained	26 M; age 41 ± 10 yrs
Scott et al,[53] 2008, London, United Kingdom	cTnT	cTnT STATT, Roche Diagnostics, Indianapolis, Ind) Roche Elecsys 1010	Ultramarathon (Western States 100 miles endurance run) California	Amateur, trained	20 M, 5 F; age 41.2 ± 4.7 yrs
Aagard et al,[38] 2014, Sweden	Hs-cTnT	NWR	Long running (30 km) (Lidingöloppet, 30 km cross country race)	Amateur first marathon, training 2.4 ± 1.9 h/wk	42 M; age >45 (50.5 ± 5) yrs
Sahlen et al,[48] 2008, Sweden	cTnT	Roche Diagnostics Scandinavia AB, Bromma, Sweden	Long running (Lidingöloppet, 30 km cross country race)	Amateur well trained, previous races 11.9 ± 10.8, weekly exercise 4.6 ± 2.3 h	37 M, 6 F; age >55 (60.9 ± 3.6) yrs
Sahlen et al,[49] 2010, Sweden	cTnT	Roche Diagnostics Scandinavia AB, Bromma, Sweden	Long running (Lidingöloppet, 30 km cross country race)	Amateur well trained, 20 new runners, endurance event years 2 (0-3); km/week 20 (10-35), 23 repeat runners, endurance event years 3 (23.5); km/week 30 (18.5-32.5)	20 M new runners: age 46 ± 8 yrs; 23 M repeat runners: age 46 ± 6 yrs
Ashley et al,[55] 2006, Toronto, Canada	cTnI	AccuTnI Assay, Beckman Coulter, Fullerton, California	Endurance training (Adrenalin Rush Adventure race)	Elite and Amateurs	62 M, 23 F; age 34 ± 5 yrs
Legaz Arrese et al,[17] 2015	Hs-cTnT	STAT immunoassay, Cobas E 601 analyzer (Roche Diagnostic, Penzberg, Germany)	Endurance training	Untrained	58 M; age 30.6 ± 8.7 yrs
Scharhag et al,[47] 2005, Germany	cTnT and cTnI	cTnT Roche Diagnostics, Automated Analyzer (Elecsys 2010), Mannheim, Germany cTnI AccuTnI Assay, Beckman Coulter, Krefeld, Germany	Endurance training: Mainz Marathon, 100-km ultramarathon (German Championship), and St wendel MTB-Marathon, distance (110 km, altitude difference 2800 m)	46 marathons: years of training 7 ± 6; 100 km run; years of training 12 ± 4. Mountain bike marathon: years of training 10 ± 6	40 M, 6 F marathons: age 40 ± 7 yrs; 14 (4 F) 100 km run: age 44 ± 8 yrs; 42 M, 3 F mountain bike marathon: age 36 ± 6 yrs
Tulloh et al,[24] 2006, Australia	cTnT	Roche chemiluminescence assay	Triathlon (Australian Ironman Triathlon)	Amateur well trained, years of training 9.7 ± 4.2	32 M; age 38 ± 5.2 yrs
Danielson et al,[45] 2017	cTnT	Cobas e411, Roche Diagnostics GmbH, Mannheim, Germany	Triathlon: Ironman triathlon (3.8 km swim, 180 km cycle followed by a 42 km run)	Amateur well trained (training history NWR)	15 M, 15 F; age 42.5 ± 6.5 yrs
Denvir et al,[56] 1999, Glasow	cTnI	Beckam Access Analyzer (Sanofi Diagnostics)	Triathlon: Scottish Coast to coast 300 km cycling/ running/canoe triathlon	Amateur well trained	25 M, 6 F; age 34.1 ± 7.9 yrs
Cleave et al,[46] 1998, USA	cTnT cTnI	cTnT Boehringer Elecsys1010 cTnI	Triathlon: New Zealand Ironman (3.8 km, cycles 180 km, and runs 42.2 km)	Amateur	64 (age and sex not reported)

TABLE 1. Studies on Postexercise cTn Rise Included in the Present Review Divided According to Biomarker Type, Type of Sport, Training Level, and Age *(Continued)*

Author	Biomarker	Method	Sport Type	Training Level	Sex, Age, yrs
		Abbot AxSym analyzer			
Christou et al,[10] 2019, Greece	Hs-cTnI	Siemens Advia centaur immunoassay	Ultraendurance running (The Spartathlon race, ultraendurance 246 km running race with 1053 m maximum elevation)	Amateurs well trained, (training history NWR)	19 M, 8 F; age 45 ± 7 yrs
La Gerche et al,[30] 2008, Australia	cTnI	Abbot AxSYM, Illinois	Ultraendurance triathlon (Australian Ironman 3.8 km swim, 180 km cycle, and 42.2 km)	Professionals and Amateurs. Competing years 8.0 ± 7	20 M, 7 F; age 32 (22-54) yrs
Neumayr et al,[28] 2001, Austria	cTnI cTnT	Assym analyzer, Abbot Diagnostika, Wiesbaden, Germany	230 km, Mountain cycle (Tyrolean O¨tztaler Radmarathon)	Amateurs well trained, training distance before the race 5.300-8000 km	38 M; age 32-37 yrs
Legaz Arrese et al,[15] 2015, Spain	Hs-cTnT	STAT immunoassay, Cobas E 601 analyzer (Roche Diagnostics, Penzberg, Germany)	Triathletes: maximal stress test	Amateurs well trained, years of training 7 ± 3	15 M; age 35 ± 9 yrs
Legaz Arrese et al,[35] 2015, Spain	cTnI	EDTA plasma with the Access AccuTnI assay (Beckman Coulter, Fullerton, California)	Rowing: 30-minute rowing test	Elite year of training 8.2 ± 5.4, amateurs year of training 3.7 ± 1.5	Males: 18 elite, age 21.0 ± 4.1 yrs; 13 amateurs, age 21.2 ± 2.0 yrs
Romagnoli et al,[59] 2014, Italy	Hs-cTnT	Roche Diagnostics, Penzberg, Germany; Roche Elecsys 2010	Maximal exercise test	Sedentary and trained	10 M sedentary: age 30 ± 6 yrs; 13 M trained: age 34 ± 7 yrs
Carranza-Garcia et al,[63] 2010, Spain	cTnI and cTnT	cTnT Roche Diagnostics, Lewes, United Kingdom, Roche Elecsys 2010 cTnI Beckman Coulter, Fullerton, California	Strength training: indoor soccer	18 strength training history 5 ± 4 yrs, 3 ± 1 session/wk; 12 M indoor soccer training history 18 ± 3 yrs, 4 ± 0 session/wk; 12 F indoor soccer training history 11 ± 5 yrs, 3 ± 0 session/wk	18 strength training: age 24 ± 3 yrs; 12 M indoor soccer: age 24 ± 4 yrs; 12 F indoor soccer: age 22 ± 4 yrs
Skadberg et al,[42] 2017, Norway	Hs-cTnI	Hs-cTnI STAT assay from Abbott Diagnostics, analyzed on an architect i2000SR (Abbott Diagnostics, Illinois) (immunochemistry) w	Cyclist (North Sea Race, mountain bike)	Amateurs: training history: 5.0 (3-13.5) yrs; training 6.5 (3.5-9) h/wk	74 M, 43 F; age 43 ± 10 yrs
Bonetti et al,[65] 1996, Italy	cTnT	Boehringer Mannheim immunometric assay	Cyclist (Giro d' Italia)	Professionals	25 M; age 29.0 ± 3.5 yrs
Klinkenberger et al,[60] 2012	Hs-cTnT	Roche Diagnostics, Penzberg, Germany: Roche Elecsys 2010	Cyclist: 60-minute exercise trials	Professionals: training 11 ± 4 h/wk	31 M; age 25 ± 5 yrs
Children and adolescents					
Legaz Arrese et al,[8] 2017, Spain	Hs-cTnT	STAT Immunoassay, Cobas E 601 Analyzer (Roche Diagnostics, Penzberg, Germany)	Swimming	Amateurs, well trained years of training: adults 7.1 ± 6.4; adolescent tunner-3 2.3 ± 1.6; tunner-4 2.7 ± 20; tunner-5 4.8 ± 3.6	16 adults: 7 M, 9 F; age 35 yrs, 50 adolescents: 25 M 25 F; age 15 yrs
Cires-Sastre et al,[9] 2020, Spain	Hs-cTnT	STAT Immunoassay, Cobas E 601 Analyzer (Roche Diagnostics, Penzberg, Germany)	Soccer 7	Amateurs (well trained, years of training children 4.6 ± 1.7, adults 23.6 ± 14.5)	All M: 24 children; age 10.7 ± 1.6 yrs, 12 adults: age 37.5 ± 12.7 yrs
Cires-Sastre et al,[36] 2020, Spain	Hs-cTnT	STAT Immunoassay, Cobas E 601 Analyzer (Roche Diagnostic, Penzberg, Germany)	Soccer	Amateurs (well trained, years of training 5.9 ± 1.7)	20 M; age 11.9 ± 2 yrs
Wedin et al,[64] 2014, Sweden	Hs-cTnT	Elecsys 2010 automated batch analyzer (Roche Diagnostics, Mannheim, Germany)	Football	Elite	23 M; 16-34 yrs

TABLE 1. Studies on Postexercise cTn Rise Included in the Present Review Divided According to Biomarker Type, Type of Sport, Training Level, and Age *(Continued)*

Author	Biomarker	Method	Sport Type	Training Level	Sex, Age, yrs
Lopez-Laval et al,[16] 2015, Spain	cTnI	Access AccuTnI assay, Beckam Coulter, Fullerton, California	Basket	Professionals: years of training 17 ± 5. Elite junior: years of training 4 ± 0. Amateurs: years of training 8 ± 4	All males: 12 professionals; age 27 ± 34.1 yrs: 12 amateurs; age 26.9 ± 29 yrs: 12 elite juniors; age 16.6 ± 0.9
Fu et al,[37] 2009, China	cTnT	Elecsys 2010 automated batch analyzer (Roche Diagnostics, Basel, Switzerland)	Runners: treadmill test	Amateurs, well trained, years of training 3.4 ± 1.5	13 M; age 14.8 ± 1.6 yrs
Tian et al,[25] 2012, United Kingdom	Hs-cTnT	Modular Analytics E 170, Roche Diagnostic, Mannheim, Germany	Runners: treadmill test	Amateurs, well trained year of training; adults 2.5 ± 1.1; adolescents 2.7 ± 1.3	All males: 13 adults, age 24 ± 3.6 yrs; 13 adolescents, age 12 ± 1.1 yrs
Peretti et al,[31] 2020, Italy	Hs-cTnT	Modular analytics E 170, Roche Diagnostic, Mannheim, Germany	Cyclist	Trained (at least from 1 yr)	21 M; age 9.2 ± 1.7
Ma et al,[52] 2013, China	cTnT and cTnI	cTnT Elecsys 2010 automated batch analyzer (Roche Diagnostics, Basel, Switzerland) cTnI Access AccuTnI assay, Beckman Coulter, Fullerton, CA	Table tennis	Amateur	28 M; age 7.21 ± 1.11 yrs

cTnI, cardiac troponin I; cTnT, cardiac troponin T; EDTA, ethylenediaminetetraacetic acid; F, females; Hs-cTnI, high-sensitivity cardiac troponin I; Hs-cTnT, high-sensitivity cardiac troponin T; M, males; NWR, not well reported.

was defined according to different methods, including mean heart rate (HR),[9,13] peak HR,[4,9] and percentage of maximal HR.[5,22] Results of a recent (2019) metanalysis,[5] including 22 studies on adults analyzing different sports, showed that postexercise cTn release was positively correlated with exercise intensity (evaluated by the mean HR). Average[13,17] and peak HR[13] and race time[26,44] were positively associated with cTn postexercise rise,[14] regardless of the biomarker used. However, data are not univocal. For instance, in 102 marathon men (42 ± 9.5 years),[20] arrival time and exercise intensity (measured as percentage of the maximal HR) were not associated with hs-cTnT peak. A few studies evaluated the effects of exercise intensity and duration also in adolescents[1,4-5,9]. (1) The type of sports and exercise intensity and duration were positively associated with cTnT increase ($P < 0.001$ and $P = 0.003$, respectively), whereas no significant association was found for cTnI. However, the methods used to quantify exercise intensity were not reported by the authors.[1] In 20 male adolescent's soccer players (age 11.9 ± 2 years), the magnitude of hs-cTnT elevation at 3 hours after exercise was mainly explained by the exercise duration in the maximal HR zone (maximum probability of effect—MPE = 92.5%), time in the high-speed zone (MPE = 90.4%), and distance in the high-speed zone (MPE = 90.45%).[5] In 24 adolescents (10.7 ± 1.6 years)[9] playing football—7 training experience was associated with baseline cTnT values ($P < 0.001$), whereas distance, mean speed, peak, and mean HR were associated to the elevation of cTnT ($P < 0.001$, $P < 0.001$, $P = 0.013$, $P = 0.016$).

The cTn response in different sports disciplines has been studied also after stress testing.[22,25,37,59-60,63] However, data are quite controversial. In 31 competitive cyclists[60] (age 25 ± 5 years), 60 minutes of steady-state exercise induced cTnT elevation in 53% of the study population, a time trail of 60 minutes in 61%, and both the exercises (ie, 120 minutes) in 71% of the subjects. A maximal intensity treadmill stress testing did not induce significant changes in hs-cTnT,[59] either in sedentary subjects or in trained (<12 h/wk) athletes. Similarly, in 18 males (24 ± 4 years), intermittent bouts of exercise (eg, heavy strength-training session lasting 1.5 hours, with 12 exercises repeated 3 times) did not induce significant changes in pre-exercise and postexercise cTnT and cTnT levels.[63] A few studies evaluated the ventilatory threshold (VT) at treadmill as an indicator of sports intensity[22,25,37] and demonstrated a significant association among sports intensity, its duration, and cTn release. In 13 male adolescent (14.1 ± 1.1 years) and 13 adult (24.0 ± 3.6 years) recreational runners,[25] performing a 90-minute constant-load treadmill run at 95% of ventilatory threshold, hs-cTnT peaked in all runners, although the peak was higher in adolescents as compared with adults ($P < 0.05$). Fu et al evaluated the effects of 2 45-minute and 90-minute constant-load treadmill run with intensities set at the running speeds that corresponded to either 80% or 100% ventilatory threshold in adolescent male runners[37]; they demonstrated that exercise duration and intensity are essential factors in eliciting cTnT release interactively after an endurance exercise and that exercise intensity compared with duration seems to cause a more pronounced increase in cTnT levels.[37] In 21 subjects (age 38 ± 8 years) running 45, 90, and 180 minutes at 85% and 95%, respectively, of their individual anaerobic threshold, cTnI was always elevated and was associated both with the exercise duration ($P = 0.003$) and its intensity ($P = 0.037$); conversely, NT-pro-BNP was associated with exercise duration ($P =$

0.049), but not exercise intensity ($P = 0.451$).[22] Data on females are very limited.[14] In 17 sedentary females (18-25 years),[14] no significant differences were noted in peak postexercise cTnT in trials conducted either at moderate-intensity continuous (at 60% of $\dot{V}O_2max$) or high-intensity interval (at 90% of $\dot{V}O_2max$).

Influence of the Training Status

Several studies on adult marathon runners[20,23,29,32] demonstrated that a low training status correlates with high postexercise cTn elevation. Different methods have been used to define the training level, including the number of previous marathons/races,[20,23,29,32,43,44,48-49,51] the years of training,[8,9,15,18,22,24-26,28,30,31,35-37,40,42,44,47,51,63] the distance performed in the weeks/months before the race,[20,28,33,44,48,51] and training hours/km/week.[9,18,20,33,35,38,40,42-44,48-49,51,58,63] The number of previous marathons[20,23,28,32] was highly negatively correlated with postrace cTn values, including hs-TnT,[20,32] cTnT,[23,32] and cTnI ($P = 0.001$).[23,29,32] Among 482 marathon runners (female = 163, age 38.8 ± 10.2 years, 9% non-White athletes),[23] runners with no previous marathon experience had 3 times more likely the probability to have a troponin increase after the marathon as compared with experienced runners. In 60 marathon runners (41 men and 19 women, average age: 41 years, range 21-65 years),[33] training ≤35 miles/week had the greatest increase in cTnT, with 50% over 0.10 ng/L, whereas participants training ≥35 miles/week had lower release of cTnT, and none was over 0.10 ng/L (overall $P < 0.001$). Notably, the median change in cTnT values between prerace and postrace was not significant in runners training >45 miles/week. Similarly, in 38 well-trained male amateur cyclists (age range: 33-42 years), there were significant differences in race time and total training distance ($P < 0.05$) between those with and without postrace cTnI increase[28]; indeed, those with lower race time and higher training distance had a lower release of cTnI.

Although postexercise release of cTn is lower, baseline cTn values tend to be higher in trained athletes[9,16-17,35,60] as compared with less trained subjects. In a study enrolling 46 subjects from 18 to 45 years, 28 were assigned to an endurance training program and 18 to a control group[17]; after a 14-week training program, both baseline and postexercise hs-cTnT values were higher compared with pretraining values and to controls ($P = 0.008$).[17] Furthermore, a few studies have demonstrated that baseline values were predictors of postexercise cTn.[9,16-17,21-22,60] Limited data are available on the influence of training status and troponin release in adolescent athletes.[8,16,31] A study on paired groups of professional and junior basketball players showed higher baseline and postexercise cTnI values in professional than in amateur athletes ($P < 0.005$).[16] In 24 adolescents (10.7 ± 1.6 years)[9] playing football—7, training experience was associated with baseline cTnT values ($P < 0.001$).

Effects of Age and Other Confounders

Results on the effects of age on cTn response after exercise were quite controversial. Indeed, although some authors demonstrated that age was positively associated with postexercise cTn elevation,[16,23,25,28,32] others reported either no correlation[8,12,24,40,43,48] or inverse correlation[5,23] with age. Data on cTn response in younger athletes are quite variable.[8,16,25] Tian et al found higher cTn values in adolescents than in adults,[25] whereas other authors did not find differences between adolescents and adults.[8,9,16] Tian et al also demonstrated that[25] peak hs-cTnT was correlated with age ($R = 0.685$, $P < 0.05$). No significant effects of age and Tanner stage on hs-cTnT values were reported also in a study on 50 adolescent swimmers.[8] In a meta-analysis including 14 studies and 336 adolescents,[1] age had a negative correlation with cTnT postexercise increase ($P < 0.01$) and no correlation with cTnI ($P = 0.33$). In a study[9] on 12 adults (37.5 ± 12.7 years) and 24 adolescents (10.7 ± 1.6 years) after football-7, age ($P < 0.01$), body mass ($P = 0.001$), and height ($P < 0.001$) were associated with baseline cTnT values, but not with postexercise peaks values. The effects of sex have been poorly investigated,[8,23,26,32,45,63] and female athletes are usually underrepresented in studies on athletes.

In a large study evaluating 482 marathon runners (age 38.8 ± 10.2 years, 9% non-White) and including 163 females,[23] athletes with higher troponin increase were younger (age <30 years) and more likely women. However, a study with a small sample size (85 marathon runners, age 26-71 years, including 15 females)[32] revealed no association between sex, body mass, and cTn concentrations. Furthermore, in adolescent athletes,[8] higher levels of hs-cTnT were found in males compared with females ($P < 0.001$).

DISCUSSION

Critical Analysis of Data

We performed a critical review of studies evaluating postexercise release of cardiac biomarkers in different types of sport, different intensity, duration, and different groups of age, sex, and training level. We identified agreement among different studies regarding the kinetics of postexercise cTn release and its recovery.[8,10,15,20,22-33,35-40,42-53,60,62-65] Trend of postexercise response have been defined for different biomarkers, including the historical cTnT[12,18,23-24,27-29,33,37,40,45-54,63,65] and cTnI[16,23,27-30,32,35,43,47,52,55-58,63] and the newer biomarker hs-cTnT,[8-9,13,18,15,17,20,25,26,31-32,38,42,44,59,64] whereas data on hs-cTnI are extremely limited.[10,42] However, discrepancies and lack of knowledge regarding the influence of some major confounders (sport intensity, its duration, age, sex, and training level) have been highlighted. There is a general good agreement among the studies about the positive correlation between sport intensity and its duration and the degree of cTn rise,[4,5,13,17,24,26-28,60,63] whereas the influence of the type of sport has been not completely defined.[1,4,9,15,41,47,61,62] Most of the current knowledge is derived from endurance sports[1,12-13,15,17-24,26-30,33-34,40,42-44,47,49,51,53-54,57-58,60,65] and particularly marathons.[12-13,18-20,22,23,26-29,32-34,40,43,51,54] Conversely, for other widely practiced sports, such as soccer and basketball, data are relatively limited,[8-9,16,35-36,52,63-64] whereas they are almost absent for other disciplines such as tennis, skiing, dance, rugby, and boxes. The lack of data from nonendurance sports hampers the possibility to clearly identify differences related to the type of sport. Therefore, current results are inconclusive, with limited differences among running versus cycling[4] or swimming.[1,4] The influence of the training status on postexercise release of cardiac biomarkers has been investigated by several authors; however, different estimates

TABLE 2. Main Studies on Hs-cTnT Rise After Sport

Authors	Population	Type of Sport	Timing of Sample Collection	Highest Hs-cTnT Increase	Hs-cTnT-Values		
Legaz-Arrese et al,[8] 2017, Spain	16 adults (7 M, 9 F), age 35 yrs; 50 adolescents: 25 M, 25 F, age 15 yrs	Swimming	Baseline, immediately after the race, at 1, 3, 6, 12, and 24 h	62% above URL of 14 ng/L	Tunner 1 Pre: 3.0 (3.0-8.6) 5 min: 3.6 (3.09.6) 1 h: **8.1** (3.0-40.4) 3 h: 11.9 (3.0-168.3) 6 h: 7.9 (3.0-95.9) 12 h: 4.3 (3.0-40) 24 h: 3.0 (3.0-18.5)	Tunner 2 Pre: 3.0 (3.0-7.5) 5 min: 4.3 (3.0-36.7) 1 h: 13.1 (3.0-145.5) 3 h: 21 (3.0-335.0) 6 h: 13.9 (3.0-171) 12 h: 6.2 (3.0-62.5) 24 h: 3.0 (3.0-26.7)	Tunner 3 Pre: 3.0 (3.0-10.0) 5 min: 8.7 (3.0-32.5) 1 h: 14.2 (3.0-70) 3 h: 22.7 (3.0-135.6) 6 h: 16.3 (3.0-162) 12 h: 7.0 (3.0-143.9) 24 h: 4.3 (3.0-86.4)
Legaz-Arrese et al,[15] 2015, Spain	15 M, age 35 ± 9	Swimming, cycling, and running	Baseline, 5 min, 1, 2, 6, 12, 24 h	Swimming (64%), cycling (71%), running (71%), above the URL of 14 ng/L	Swimming Pre: 4.21 ± 1.27 5 min: 7.23 ± 1.92 1 h: 11.13 ± 4.11 3 h: 18.91 ± 10.17 6 h: 16.5 ± 8.03 12 h: 9.7 ± 2.99 24 h: 5.99 ± 1.66	Cycling Pre: 4.31 ± 1.28 5 min: 5.97 ± 1.46 1 h: 10.08 ± 3.71 3 h: 16.75 ± 80.6 6 h: 10.61 ± 4.5 12 h: 8.21 ± 2.76 24 h: 5.75 ± 2.17	Running Pre: 4.31 ± 1.28 5 5 min: 6.91 ± 2.07 1 h: 10.44 ± 2.33 3 h: 19.09 ± 9.66 6 h: 16.7 ± 7.51 12 h: 9.5 ± 3.2 24 h: 6.33 ± 2.14
Legaz-Arrese et al,[17] 2015, Spain	58 M, age 30.6 ± 8.7 yrs	Endurance training	Baseline, 5 min, 1, 3, 6, 12, 24	80% above URL of 14 ng/L	Pre-training Pre: 3.6 (3.0-16.2) 5 min: 6.8 (3.0-39.4) 1 h: 10.0 (3.0-36.5) 3 h: 16.1 (4.9-140.7) 6 h: 15.2 (3.5-97.7) 12 h: 9.2 (3.0-39.1) 24 h: 6.3 (3.0-13.9)	Post training Pre: 5.1 (3.0-18.6) 5 min: 9.8 (3.0-28.7) 1 h: 13.6 (6.1-67.9) 3 h: 26.3 (6.6-171) 6 h: 18.9 (6.4-156.0) 12 h: 11.0 (4.6-68.5) 24 h: 6.7 (3.0-36.2)	
Scherr et al,[20] 2011, Germany	102 M, age 42 yrs	Marathon	Baseline, at 1, 24, and 72 h	89% above URL of 14 ng/L			
Tian,[25] 2012, United Kingdom	13 M adults, age 24 ± 3.6 yrs; 13 M adolescents, age 12 ± 1.1 yrs	90 minutes treadmill	Baseline, at 1, 2, 3, 4, 5, 6, and 24 h	Adult 85% above URL of 14 ng/L; adolescents 92% above URL of 14 ng/L	Adults Pre: 5.0 (3.0-14) 0 h: 9.3 (82.9-15.6) 1 h: 13.3 (5.3-54.9) 2 h: 16.3 (6.4-171) 3 h: 19.1 (9.7-305.6)	Children Pre: 3.0 (3.0-0.0-8.0) 0 h: 18.4 (83.0-69.9) 1 h: 81 (87.5-280) 2 h: 137 (9.4-5192) 3 h: 211 (11.2-659) 4 h: 182 (11.2-659) 5 h: 141 (12.1-559) 6 h: 118 (10.6-437) 24 h: 24.7 (3.1-80.6)	

TABLE 2. Main Studies on Hs-cTnT Rise After Sport *(Continued)*

Authors	Population	Type of Sport	Timing of Sample Collection	Highest Hs-cTnT Increase	Hs-cTnT-Values	
					4 h: 17.5 (8.8-291) 5 h: 16.7 (8.6-255) 6 h: 15.8 (6.6-208.3) 24 h: 4.0 (2.9-24.79)	
Roca et al,[26] 2017, Spain		57 M, 22 F, age 39 ± 6 yrs	Marathon	Baseline, at 2 and 48 h	100% above URL of 14 ng/L	Pre: 2.9 (1.77) 2 h: 46.9 (24.1-91.1) 48 h: 4.7 (2.4-8.85)
Baker et al,[2,19] 2019, United Kingdom	26 (18 M, 8 F), age 40 yrs	Marathon	Baseline, immediately after the race, at 3, 6, and 24 h	100% above URL of 14 ng/L	NR	
Aggard et al,[38] 2014, Sweden	42 M, age 50.5 ± 5	Marathon	Baseline, immediately after	97% above URL of 14 ng/L	Pre: 3.2 (3.0-5.7) Post: 39 (26-68)	
Cires-Sastre et al,[9] 2020, Spain	36 M, 24 children, age 10.7 ±1.6 yrs, 12 adults, age 37.5 ± 12.7 yrs	Football 7	Baseline, at 3 h	70.3% of children and 66.7% of adult above the URL of 13.5 ng/L	Children Pre: 4.64 (3.65-12.7) Post: 22.9 (4.67-200) Adults Pre: 6.54 (4.88-11.7) Post: 18.6 (8.31-60.2)	
Peretti et al,[31] 2020, Italy	21 M, age 9.2 ± 1.7 yrs cyclist	Cyclist	150 minutes after race	30% above URL of 14 ng/L	Post: 20.37 ± 7.45 (range 15.0-34.8) ng/L	
Richardson et al,[13] 2018, USA	52 (39 M, 13 F), age 39 ± 11 yrs	Marathon	Baseline, 5 minutes after the race	100% above URL of 14 ng/L	Pre: 5.6 ± 3.27 ng/L Post: 74.52 ± 30.39 ng/L No differences among sexes	
Mingles et al,[32] 2009, The Netherlands	85 (70 M, 15 F), age 47 (45-49)	Marathon	Baseline, 0-2 h, 24 h	86% above URL of 14 ng/L	Pre: mean 0.004 ng/L, median 0.004 ng/L 0 h: mean 0.042 ng/L, median 0.03 ng/L 24 h: mean 0.012 ng/L, median 0.010 ng/L	
Wedin et al,[64] 2014, Sweden	23 M, age 19 (16-34)	Football	Baseline, 0-2 h	86% above URL of 14 ng/L at 2 h	Pre: 6.2 (5.5-7.7) 0 h: 8.6 (7.1-10.4) 2 h: 9.0 (7.9-19.5)	

cTn, cardiac troponin; Hs-cTnT, high-sensitivity cardiac troponin T; NR, not reported; URL, upper reference limit.

(eg, number of previous marathons, years of training/distance performed before the race) have been used alone[20,22,24-26,28,20,31,58] or in combination[8,9,17,35,40,42-44,47-49,51,63] to define the training status. Regardless of the method used to define the training level, there is consensus[20,23,29,32] that lower trained athletes are those with higher postexercise cTn rise. Regarding the potential influence of age and sex, a few data are available for children and adolescents,[1,8,9,16,25,31,36,52,64] whereas the evidence in women is very limited.[8,27,42,45,50,58,64] The influence of ethnicity has not been evaluated so far, and data in non-White are extremely limited.[23,37,52]

Pathophysiological and Clinical Interpretation of Increased Cardiac Troponin Values: Limitations and Perspectives

Studies on postexercise release of troponin have a practical relevance from a clinical point of view; indeed, chest pain after exercise is a common cause of access to the emergency department[2,4] and is often associated with cTn rise above URL.[2,4] According to the document Forth Universal Definition of Myocardial Infarction,[72] only one cTn value above the 99th percentile URL indicates a myocardial injury. As a consequence, this generates anxiety, cardiology assessment requirement, and often it leads to unnecessary third-level expensive and time-consuming examinations, such as cardiac magnetic resonance imaging or even coronary angiography. However, although guidelines state that cTn values above the 99th percentile URL suggest the presence of myocardial injury, they do not indicate the underlying pathophysiological mechanisms.[72] Mild troponin elevation may be due to multiple factors other than acute coronary syndromes[7] including preload-induced mechanical stretch or physiological stresses in otherwise normal hearts.[72] Accordingly, the current evidence demonstrates that troponin peak after sport competitions may be considered a physiological phenomenon at all ages.[1-5] However, in limited cases, the troponin peak after sport may indicate myocardial injury that may be reversible or irreversible.[69,72,74-79] Adult individuals with asymptomatic cardiovascular disease may more frequently show increased cTn levels after intense physical activity than healthy subjects.[69,72,76-79] These individuals may be at higher risk for early progression to symptomatic heart failure.[69,72,76-79] Thus, the troponin rise after sport is usually considered as a benign phenomenon that does not require second-level and

TABLE 3. Main Studies Reporting cTnT Rise After Sport

Authors	Population	Type of Sport	Timing of Sample Collection	Highest cTnT Increase	cTnT Values
Shave et al,[12] 2002, United Kingdom	26 M, age 41 ± 10 yrs	Ultramarathon	Pre, immediately after, day 2	Postrace 50% had values above the URL of 0.01 ng/L	Immediately after: (0-0.035); day 2: 0.001 (0-0.017)
Tulloh et al,[24] 2006, Australia	32 M, age 38 ± 5.2 yrs	Triathlon	Baseline, 20 minutes, 14-24 h	86.5% at 20 minutes, 23.7% at 12-24 h, above the URL 0.01 ng/mL, 16.2% >0.10 ng/mL	20 min: 0.095 (0.19) ng/mL; 12-24 h: 0.017 (0.04) ng/mL
Hermann et al,[29] 2003, Germany	46 (40 M, 6 F), age 40, (7) yrs	Marathon	Baseline, <15 min, at 3, 24 h	51% at 15 min, 40% at 3 h, 0% at 24 h above URL of 0.01 ng/L, 8% at 15 min, and 8% at 3 h above AMI cut-off of 0.03 ng/L	15 min: 0.006 (0.000-0.103) ng/L; 3 h: 0.07 (0.000-0.74) ng/L
Frassl et al,[27] 2008, Germany	15 F, age 37, 26-45 yrs	Marathon	Baseline, immediately after the race, 1 d, 3 d	Postrace 53% above the URL cut-off of 0.01 ng/L; at 1 and 3 day all normal	Immediately after race; median 0.032 ng/L
Fortescue et al,[23] 2006, USA	482 (45.6% F)	Marathon	Postrace	Postrace 68% above the URL of 0.01 ng/L; 11% significant increase above AMI of 0.075 ng/L	NR
Jassals et al,[40] 2009, Canada	61 half marathons (40 M): age 40 ± 12 yrs; 68 marathons (44 males): age 42 ± 14 yrs	Marathon	Baseline, immediately post, 1 h, 3 h	Postrace 31%, at 1 H 50% above the URL of 0.01 ng/L	Half marathon 1 h: 0.027 (0.011-0.156) 3 h: 0.038 (0.011-0.251) Full marathon 1 h: 0.036 (0.011-0.225) 3 h: 0.061 (0.011-0.432)
Neilan et al,[33] 2006, USA	41 M and 19 F, age 41 (range 21-65) yrs	Marathon	Immediately after	Postrace, >60% of above the URL >0.01 ng/mL, whereas 40% had a cTnT level at or above the AMI cut-off of ≥0.03 ng/mL	<35 miles/wk 0.09 (0.07-0.21) 36-45 miles/wk 0.02 (0.02-0.04) <45 miles/wk <0.01 (<0.01-0.01)
Siegel et al,[51] 1997, Boston, USA	25: 20 M, 5 F, age 41.2 ± 12 yrs	Ultramarathon	Immediately after	After the race, 20% of above the URL >0.01 ng/mL	NR
Sahlen et al,[48] 2008, Sweden	43: 37 M, 6 F, age 61 ± 3.6 yrs	Long distance	Before and immediately after	Postrace, 44% of above the URL >0.03 ng/L	Pre >0.01 0 h: 0.02 (0.010-0.05)
Ma et al,[52] 2013, China	28 M, age 7.21 ± 1.11 yrs	Table tennis	Pre, 0, 4, 24, and 48 hours after	14.29% at 0 h, 32.14% at 4 h, 17.14% at 24 h above the cut-off of 0.01 ng/mL, and 17.4% at 4 h above the AMI cut-off	Pre: 0.005 0 h: 0.023 (0.005-0.044) 4 h: 0.026 (0.005-0.43) 24 h: 0.021 (0.005-0.32) 48 h: 0.005

AMI, acute myocardial infarction; cTn, cardiac troponin; cTnT, cardiac troponin T; NR, not reported; URL, upper reference limit.

third-level examinations, but uncertainties remain in selected cases.[2,4] Diagnostic algorithms[2,4] have been proposed to differentiate between physiological postexercise cTn rise and pathologic conditions.[2] Baker et al[2] suggest that cTn rise <×3 URL are probably because of exercise unless subjects have a high cardiovascular risk, whereas cTn rise above >×5 URL may alert for an acute coronary syndrome. Physiological factors influencing postexercise troponin release (eg, the type of sport, its intensity and duration, age, sex, and level of training) should also be evaluated when assessing the troponin peak after exercise.

Pitfalls in the Evaluation of Troponin Values in Master and Junior Athletes

Some studies have recently reported that cTn levels, measured with high-sensitivity assays, progressively increase after the 55 years in both sexes[67-69] and that cardiovascular risk (including mortality risk and major adverse cardiovascular events) also increases with a similar and parallel trend of cardio-specific biomarkers in the general population.[79] The 2020 ESC guidelines on physical exercise in patients with cardiovascular diseases state that regular physical activity is associated with lower cardiovascular risk in the general population and in patients with cardiac diseases.[80] According to these guidelines, despite the substantial health benefits provided by regular physical activity, intense exercise may paradoxically act as a trigger for major cardiovascular adverse events (also including life-threatening ventricular arrhythmias) in individuals with underlying cardiovascular disease.[80] Taking as a whole, the data reported in this review support the recommendations made by the guidelines that the physical exercises for persons aged older than 65 years should be designed after an accurate evaluation of the cardiovascular risk score according to their biological age and exercise experience.[80] Two recent expert documents recommend the use of cTn measurement with

TABLE 4. Main Studies Reporting cTnI Rise After Sport

Authors	Population	Type of Sport	Timing of Sample Collection	Tn-I Increase	Values
Hs-cTnI					
Christou et al,[10] 2019, Greece	25 (19 M, 8 F): age 45 ± 7 yrs	Ultraendurance running	Baseline and 10 min after race	Postrace: 62% above URL of 47 ng/L	Mean post: 115 ± 81 ng/L
Skadberg et al,[42] 2017, Norway	74 M, 43 F: age 42.8 ± 9.6 yrs	Cyclist	Pre, 0, 3, and 24 h	At 0 h 70% had cTnI above the URL >30.0 ng/L). At 3, 82% and at 24 h 21%	0 h: 50.5 (28.5-71.9) ng/L 3 h: 69.3 (42.3-97.7) ng/L 24 h: 14.2 (8.5-27.9) ng/L
cTnI					
Frassl et al,[27] 2008, Germany	15 F: age 37, 26-45 yrs	Marathon	Baseline, immediately after the race, 1 d, 3 d	33% above the URL cut-off of 0.03 ng/L. At 1 d, only 4 borderlines. At 3 d, all normal	Immediately after race: median 0.098 ng/L
Neumayr et al,[28] 2001, Austria	38 M: age 35 yrs	230 km mountain cycle	Baseline, immediately after the race, at 1 d	34% after the race and 24% at 24 h above URL of 0.05 ng/L	NR
Hermann et al,[29] 2003, Germany	46 (40 M, 6 F): age 40 (7 yrs	Marathon	Baseline, <15 min, at 3, 24 h	60 at 15 min, 73.3% at 3 h, 2% (1 case) at 24 h above URL of 0.04 ng/L; 37.7% at 15 min, 60% at 3 h above; AMI cut-off of 0.06 ng/L	15 min: 0.05 (0.010-0.360) ng/L 3 h: 0.07 (0.02-0.930) ng/L
Hubble et al,[43] 2007, Australia	92 (65 M): age 43.4 ± 8 yrs	Marathon	Baseline, immediately after the race	Postrace: 32% above the URL of 0.1 ng/L	Pre: 0.01 (0.01) Post: 0.14 (0.23)
Vidotto et al,[58] 2005, Austria	12 M: age 42.8 ± 7.3; 13 F: age 39.0 ± 6.5	Half-marathon	Baseline, 0, and 2 h	13% after the race and 32% at 2 h above URL of 0.11 ng/mL	Pre M: **0.038 ± 0.026** F: **0.025 ± 0.018** 0 h M: **0.051 ± 0.032** F: **0.055 ± 0.018** 2 h M: **0.086 ± 0.042** F: **0.098 ± 0.057**
La Gerche et al,[30] 2008, Australia	27 (20 M, 7 F): age 32, 22-54 yrs	Ultraendurance triathlon	Baseline, immediately after the race, 1 wk	Postrace: 33% above URL of 0.03 ng/L; 58% above URL for AMI of 0.16 ng/L; at 1 wk 0%	NR
Ashley et al,[55] 2006, Toronto, Canada	85; 62 M, 23 F: age 34 ± 5 yrs	Ultraendurance	Baseline, immediately after the race	Postrace: 41% above URL of 0.01 ng/L	
Ma et al,[52] 2013, China	28 M: age 7.21 ± 1.11 yrs	Table tennis	Pre, 0, 4, 24, and 48 h after	14.29% at 0 h, 25% at 4 h, and 7.14% at 24 h above the cut-off of 0.01 ng/mL	Pre: **0.02 (0.001-0.057)** 0 h: **0.057 (0.053-0.09)** 4 h: **0.054 (0.045-1.89)** 24 h: **0.055 (0.05-0.12)** 48 h: **0.021 (0.011-0.053)**

cTn, cardiac troponin; cTnI, cardiac troponin I; NR, not reported; URL, upper reference limit.

high-sensitivity methods for a more accurate stratification of cardiovascular risk and especially for an early detection of individuals in the general population with asymptomatic cardiac disease at higher risk to progression to symptomatic heart failure,[79,81] although further evidence is needed to support this approach.

Finally, it is very difficult to discuss the pathophysiological interpretation of increased levels of cTn after intense physical activity in pediatric age in accordance with the definition of myocardial injury, as requested by international guidelines.[72] Indeed, there are no reliable data on the accurate estimate of 99th percentile URL from neonatal age to 18 years. The limited data available on hs-cTnI and hs-TnT circulating levels in pediatric age suggest that biomarker values are greatly increased in the neonates with a successive trend to progressively reduction up to adolescence.[67,82-85] However, hs-cTnI and hs-cTnT values in apparently healthy boys and girls on average tend to remain significantly higher than those measured in adults.[67,82-85]

CONCLUSIONS

The results of this systematic review confirm that postexercise cTn rise can be observed in both young (<35 years) and master (>35 years) athletes, especially when the biomarker levels are measured with high-sensitivity methods. The peak of troponin values after exercise is usually physiological, although more rarely it may unmask a subclinical cardiac disease, especially in older individuals. Further and larger studies are required to establish individualized cut-off/algorithms of risk for troponin rise after exercise. These studies should be conducted on a large population of individuals with different ages, sex, and ethnicity (with a special attention to master, junior, female, and non-White athletes) and should evaluate a series of variables that may have a significant impact on postexercise cTn rise, including training levels, type of sport, and methods used for cTn assay.

References

1. Cirer-Sastre R, Legaz-Arrese A, Corbi F, et al. Cardiac biomarker release after exercise in healthy children and adolescents: a systematic review and meta-analysis. *Pediatr Exerc Sci.* 2019;31:28–36.
2. Baker P, Leckie T, Harrington D, et al. Exercise-I nduced cardiac troponin elevation: an update on the evidence, mechanism and implications. *Int J Cardiol Heart Vasc.* 2019;22:181–186.
3. Vilela EM, Bastos JC, Rodrigues RP, et al. High-sensitivity troponin after running—a systematic review. *Neth J Med.* 2014;72:5–9.
4. Shave R, George KP, Atkinson G, et al. Exercise-induced cardiac troponin T release: a meta-analysis. *Med Sci Sports Exerc.* 2007;39:2099–2106.
5. Donaldson JA, Wiles JD, Coleman DA, et al. Left ventricular function and cardiac biomarker release—the influence of exercise intensity, duration and mode: a systematic review and meta-analysis. *Sports Med.* 2019;49: 1275–1289.
6. Masri W, Le Guillou E, Hamdi E, et al. Troponin elevation in other conditions than acute coronary syndromes. *Ann Biol Clin (Paris).* 2017; 75:411–441.
7. Gresslien T, Agewall S. Troponin and exercise. *Int J Cardiol.* 2016;221: 609–621.
8. Legaz-Arrese A, Carranza-García LE, Navarro-Orocio R, et al. Cardiac biomarker release after endurance exercise in male and female adults and adolescents. *J Pediatr.* 2017;191:96–102.
9. Cirer-Sastre R, Legaz-Arrese A, Corbi F, et al. Cardiac troponin T release after football 7 in healthy children and adults. *Int J Environ Res Public Health.* 2020;17:956.
10. Christou GA, Pagourelias ED, Anifanti MA, et al. Exploring the determinants of the cardiac changes after ultra-long duration exercise: the echocardiographic Spartathlon study. *Eur J Prev Cardiol.* 2020;27: 1467–1477.
11. Skalenius M, Mattsson CM, Dahlberg P, et al. Performance and cardiac evaluation before and after a 3-week training camp for 400-meter sprinters - an observational, non-randomized study. *PLoS One.* 2019;14: e0217856.
12. Shave RE, Dawson E, Whyte G, et al. Evidence of exercise-induced cardiac dysfunction and elevated cTnT in separate cohorts competing in an ultra-endurance mountain marathon race. *Int J Sports Med.* 2002;23:489–494.
13. Richardson AJ, Leckie T, Watkins ER, et al. Post marathon cardiac troponin T is associated with relative exercise intensity. *J Sci Med Sport.* 2018;21:880–884.
14. Nie J, Zhang H, Kong Z, et al. The impact of exercise modality and menstrual cycle phase on circulating cardiac troponin T. *J Sci Med Sport.* 2020;23:309–314.
15. Legaz-Arrese A, López-Laval I, George K, et al. Individual variability of high-sensitivity cardiac troponin levels after aerobic exercise is not mediated by exercise mode. *Biomarkers.* 2015;20:219–224.
16. López-Laval I, Legaz-Arrese A, George K, et al. Cardiac troponin I release after a basketball match in elite, amateur and junior players. *Clin Chem Lab Med.* 2016;54:333–338.
17. Legaz-Arrese A, López-Laval I, George K, et al. Impact of an endurance training program on exercise-induced cardiac biomarker release. *Am J Physiol Heart Circ Physiol.* 2015;308:H913–H920.
18. Saravia SG, Knebel F, Schroeckh S, et al. Cardiac troponin T release and inflammation demonstrated in marathon runners. *Clin Lab.* 2010;56: 51–58.
19. Baker P, Davies SL, Larkin J, et al. Changes to the cardiac biomarkers of non-elite athletes completing the 2009 London Marathon. *Emerg Med J.* 2013;31:374–379.
20. Scherr J, Braun S, Schuster T, et al. 72-h kinetics of high-sensitive troponin T and inflammatory markers after marathon. *Med Sci Sports Exerc.* 2011; 43:1819–1827.
21. Legaz-Arrese A, George K, Carranza-García LE, et al. The impact of exercise intensity on the release of cardiac biomarkers in marathon runners. *Eur J Appl Physiol.* 2011;111:2961–2967.
22. Serrano-Ostáriz E, Terreros-Blanco JL, Legaz-Arrese A, et al. The impact of exercise duration and intensity on the release of cardiac biomarkers. *Scand J Med Sci Sports.* 2011;21:244–249.
23. Fortescue EB, Shin AY, Greenes DS, et al. Cardiac troponin increases among runners in the Boston Marathon. *Ann Emerg Med.* 2007;49:137–43.
24. Tulloh L, Robinson D, Patel A, et al. Raised troponin T and echocardiographic abnormalities after prolonged strenuous exercise—the Australian Ironman Triathlon. *Br J Sports Med.* 2006;40:605–609.
25. Tian Y, Nie J, Huang C, et al. The kinetics of highly sensitive cardiac troponin T release after prolonged treadmill exercise in adolescent and adult athletes. *J Appl Physiol.* 2012;113:418–425.
26. Roca E, Nescolarde L, Lupón J, et al. The dynamics of cardiovascular biomarkers in non-elite Marathon runners. *J Cardiovasc Transl Res.* 2017;2:206–208.
27. Frassl W, Kowoll R, Katz N, et al. Cardiac markers (BNP, NT-pro-BNP, Troponin I, Troponin T) in female amateur runners before and up until three days after a marathon. *Clin Lab.* 2008;3:81–87.
28. Neumayr G, Gaenze H, Pfister R, et al. Plasma levels of cardiac troponin I after prolonged strenuous endurance exercise. *Am J Cardiol.* 2001;87: 369–371.
29. Herrmann H, Scharhag J, Urhausen A, et al. Postrace kinetics of cardiac troponin T and I and N-terminal pro-brain natriuretic peptide in marathon runners. *Clin Chem.* 2003;49:831–834.
30. La Gerche A, Connelly KA, Mooney DJ, et al. Biochemical and functional abnormalities of left and right ventricular function after ultraendurance exercise biochemical and functional abnormalities of left and right ventricular function after ultra-endurance exercise. *Heart.* 2008;94: 860–866.
31. Peretti A, Mauri L, Masarin A, et al. Cardiac biomarkers release in preadolescent athletes after an high intensity exercise. *High Blood Press Cardiovasc Prev.* 2018;25:89–96.
32. Mingels A, Jacobs L, Michielsen E, et al. Reference population and marathon runner era assessed by highly sensitive cardiac troponin T and commercial cardiac troponin T and I assays. *Clin Chem.* 2009;55: 101–108.
33. Neilan TG, Januzzi JL, Lee-Lewandrowski E, et al. Myocardial injury and ventricular dysfunction related to training levels among non-elite participants in the Boston marathon. *Circulation.* 2006;114:2325–2333.
34. George K, Shave R, Oxborough D, et al. Left ventricular wall segment motion after ultra-endurance exercise in humans assessed by myocardial speckle tracking. *Eur J Echocardiogr.* 2009;10:238–243.
35. Legaz-Arrese A, López-Laval I, George K, et al. Individual variability in cardiac biomarker release after 30 min of high-intensity rowing in elite and amateur athletes. *Appl Physiol Nutr Metab.* 2015;40:951–958.
36. Cirer-Sastre R, Legaz-Arrese A, Corbi F, et al. Effect of training load on post-exercise cardiac troponin T elevations in young soccer players. *Int J Environ Res Public Health.* 2019:2;16.
37. Fu F, Nie J, Tong TK. Serum cadiac troponin T in adolescent runners: effect of exercise intensity and duration. *Int J Sports Med.* 2009;30: 168–172.
38. Aagaard P, Sahlén A, Bergfeldt L, et al. Heart rate and its variability in response to running associations with troponin. *Med Sci Sports Exerc.* 2014;46:1624–1630.
39. Eijsvogels T, George K, Shave R, et al. Effect of prolonged walking on cardiac troponin levels. *Am J Cardiol.* 2010;105:267–272.
40. Jassal DS, Moffat D, Krahn J, et al. Cardiac injury markers in non-elitemarathon runners. *Int J Sports Med.* 2009;30:75–79.
41. Shave R, Baggish A, George K, et al. Exercise induced cardiac troponin elevation: evidence, mechanisms, and implications. *J Am Coll Cardiol.* 2010;56:169–176.
42. Skadberg Ø, Kleiven Ø, Bjørkavoll-Bergseth M, et al. Highly increased Troponin I levels following high-intensity endurance cycling may detect subclinical coronary artery disease in presumably healthy leisure sport cyclists: the North Sea Race Endurance Exercise Study (NEEDED) 2013. *Eur J Prev Cardiol.* 2017;24:885–894.
43. Hubble KM, Fatovich DM, Grasko JM, et al. Cardiac troponin increases among marathon runners in the Perth Marathon: the Troponin in Marathons (TRIM) study. *Med J Aust.* 2009;190:91–93.
44. Martínez-Navarro I, Sánchez-Gómez JM, Collado-Boira EJ, et al. Cardiac damage biomarkers and heart rate variability following a 118-km mountain race: relationship with performance and recovery. *J Sports Sci Med.* 2019;18:615–622.
45. Danielsson T, Carlsson J, Schreyer H, et al. Blood biomarkers in male and female participants after an Ironman-distance triathlon. *PLoS One.* 2017; 12:e0179324.
46. Cleave P, Boswell TD, Speedy DB, et al. Plasma cardiac troponin concentrations after extreme exercise. *Clin Chem.* 2001;47:608–610.

47. Scharhag J, Herrmann M, Urhausen A, et al. Independent elevations of N-terminal pro-brain natriuretic peptide and cardiac troponins in endurance athletes after prolonged strenuous exercise. *Am Heart J*. 2005;150:1128.
48. Sahlén A, Shahgaldi K, Aminoff A, et al. Effects of prolonged exercise on left ventricular mechanical synchrony in long-distance runners: importance of previous exposure to endurance races. *J Am Soc Echocardiogr*. 2010;23:977–984.
49. Sahlén A, Winter R, Lind B, et al. Magnitude, reproducibility, and association with baseline cardiac function of cardiac biomarker release in long-distance runners aged > or =55 years. *Am J Cardiol*. 2008;102: 218–222.
50. Siegel AJ, Januzzi J, Sluss P, et al. Cardiac biomarkers, electrolytes, and other analytes in collapsed marathon runners: implications for the evaluation of runners following competition. *Am J Clin Pathol*. 2008; 129:948–951.
51. Siegel AJ, Sholar M, Yang J, et al. Elevated serum cardiacmarkers in asymptomaticmarathon runners after competition: is themyocardium stunned? *Cardiology*. 1997;88:487–491.
52. Ma G, Liu Y, Liu K. Influence of repeated bouts of table tennis training on cardiac biomarkers in children. *Pediatr Cardiol*. 2014;35:711–718.
53. Scott JM, Esch BT, Shave R, et al. Cardiovascular consequences of completing a 160-km ultramarathon. *Med Sci Sports Exerc*. 2009;41: 26–34.
54. Leers MP, Schepers R, Baumgarten R. Effects of a long distance run on cardiac markers in healthy athletes. *Clin Chem Lab Med*. 2006;44: 999–1003.
55. Ashley EA, Kardos A, Jack ES, et al. Angiotensin-converting enzyme genotype predicts cardiac and autonomic responses to prolonged exercise. *J Am Coll Cardiol*. 2006;48:523–531.
56. Denvir MA, Galloway PJ, Meighan AS, et al. Changes in skeletal and cardiac muscle enzymes during the scottish coast to coast triathlon. *Scott Med J*. 1999;44:49–51.
57. Dalla Vecchia L, Traversi E, Porta A, et al. Onsite assessment of cardiacfunction and neural regulation in amateur half marathon runners. *Open Heart*. 2014;1:e000005.
58. Vidotto C, Tschan H, Atamaniuk J, et al. Responses of N-terminal pro-brain natriuretic peptide (NT-proBNP) and cardiac troponin I (cTnI) to competitive endurance exercise in recreational athletes. *Int J Sports Med*. 2005;26:645–650.
59. Romagnoli M, Alis R, Aloe R, et al. Influence of training and a maximal exercise test in analytical variability of muscular, hepatic, and cardiovascular biochemical variables. *Scand J Clin Lab Invest*. 2014;74: 192–198.
60. Klinkenberg LJ, Res PT, van Loon LJ, et al. Strong link between basal and exercise-induced cardiac troponin T levels: do both reflect risk? *Int J Cardiol*. 2012;158:129–131.
61. Koller A, Summer P, Moser H. Regular exercise and subclinical myocardial injury during prolonged aerobic exercise. *JAMA*. 1999;282: 1816.
62. Koller A, Sumann G, Griesmacher A, et al. Cardiac troponins after a downhill marathon. *Int J Cardiol*. 2008;129:449–452.
63. Carranza-Garcia LE, George K, Serrano-Ostariz E, et al. Cardiac biomarker response to intermittent exercise bouts. *Int J Sports Med*. 2011;32:327–331.
64. Wedin JO, Henriksson AE. Postgame elevation of cardiac markers among elite floorball players. *Scand J Med Sci Sports*. 2015;25:495–500.
65. Bonetti A, Tirelli F, Albertini R, et al. Serum cardiac troponin T after repeated endurance exercise events. *Int J Sports Med*. 1996;17:259–262.
66. Sribhen K, Piyophirapong S, Wannasilp N. Cardiac troponin T concentrations in healthy adolescents. *Clin Chim Acta*. 2010;411: 1542–1543.
67. Giannoni A, Giovannini S, Clerico A. Measurement of circulating concentrations of cardiac troponin I and T in healthy subjects: a tool for monitoring myocardial tissue renewal? *Clin Chem Lab Med*. 2009;47: 1167–1177.
68. Clerico A, Ripoli A, Zaninotto M, et al. Head-to-head comparison of plasma cTnI concentration values measured with three high-sensitivity methods in a large Italian population of healthy volunteers and patients admitted to emergency department with acute coronary syndrome: a multi-center study. *Clin Chim Acta*. 2019;496:25–34.
69. Clerico A, Zaninotto M, Padoan A, et al. Evaluation of analytical performance of immunoassay methods for cTnI and cTnT: from theory to practice. *Adv Clin Chem*. 2019;93:239–262.
70. Eijsvogels TM, Fernandez AB, Thompson PD. Are there deleterious cardiac effects of acute and chronic endurance exercise? *Physiol Rev*. 2016;96:99–125.
71. Aakre KM, Omland T. Physical activity, exercise, and cardiac troponins: clinical implications. *Prog Cardiovasc Dis*. 2019:62:108–115.
72. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction. *J Am Coll Cardiol*. 2018;72:2231–2264.
73. Roffi M, Patrono C, Collet JP, et al. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2016; 37:267–315.
74. Mazzeschi C, Piana N, Capezzali D, et al. The impact of strenuous group physical activity on mood states, personal views, body composition, and markers of myocardial damage in overweight/obese adults: the "step-by-step Italy's coast to coast" trek. *Biomed Res Int*. 2014;2014:854129.
75. Planer D, Leibowitz D, Hadid A, et al. The effect of prolonged physical activity performed during extreme caloric deprivation on cardiac function. *PLoS One*. 2012;7:e31266.
76. Clerico A, Giannoni A, Prontera C, et al. High-sensitivity troponin: a new tool for pathophysiological investigation and clinical practice. *Adv Clin Chem*. 2009;49:1–30.
77. Hickman PE, Potter JM, Aroney C, et al. Cardiac troponin may be released by ischemia alone, without necrosis. *Clin Chim Acta*. 2010;411: 318–323.
78. Marjot J, Kaier TE, Martin ED, et al. Quantifying the release of biomarkers of myocardial necrosis from cardiac myocytes and intact myocardium. *Clin Chem*. 2017;63:990–996.
79. Mair J, Lindahl B, Hammarsten O, et al. How is cardiac troponin released from injured myocardium? *Eur Heart J Acute Cardiovasc Care*. 2018;7: 553–560.
80. Clerico A, Zaninotto M, Passino C, et al. Evidence on clinical relevance of cardiovascular risk evaluation in the general population using cardio-specific biomarkers. *Chem Lab Med*. 2020;59:79–90.
81. Pelliccia A, Sharma S, Gati S, et al; ESC Scientific Document Group. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Eur Heart J*. 2021;42:17–96.
82. Caselli C, Cangemi G, Masotti S, et al. Plasma cardiac troponin I concentrations in healthy neonates, children and adolescents measured with a highly sensitive immunoassay method: highly sensitive troponin I in pediatric age. *Clin Chim Acta*. 2016;458:68–71.
83. Caselli C, Ragusa R, Prontera C, et al. Distribution of circulating cardiac biomarkers in healthy children: from birth through adulthood. *Biomark Med*. 2016;10:357–365.
84. Jehlicka P, Huml M, Rajdl D, et al. How to interpret elevated plasmatic level of high-sensitive troponin T in newborns and infants? *Physiol Res*. 2018;67:191–195.
85. Mondal T, Ryan PM, Gupta K, et al. Cord-blood high-sensitivity troponin-I reference interval and association with early neonatal outcomes. *Am J Perinatol*. 2021. doi: 10.1055/s-0041-1722944.