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Review

Troponin and exercise

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ABSTRACT

Cardiac troponins are the preferred biomarkers in diagnostic of myocardial infarction, but these markers also can rise in response to exercise. Multiple studies have assessed troponins post-exercise, but the results have varied and there have been disagreements about the mechanism of troponin release. The aim of this paper was to review the literature, and to consider factors and mechanisms regarding exercise-induced increase of troponin. 145 studies were found after a search in pubmed and inclusion of additional articles found in the reference list of the first articles.

Results showed that troponin rises in 0–100% of subjects after prolonged heavy exercise like marathon, but also after short-term and intermittent exercise like 30 min of running and basketball. The variation can be due to factors like intensity, age, training experience, variation in sample size, blood sample timing and troponin assay. The pattern of troponin level post-exercise corresponds to release from the cytosolic compartment of cardiomyocytes. Increased membrane permeability might be caused by production of reactive oxygen species or alterations in calcium, pH, glucose/fat metabolism or in communication between integrins. Other suggested mechanisms are increased cardiovascular stress, inflammation, vasculitis, release of troponin degradation products in "blebs", dehydration, impaired renal clearance and expression of cardiac troponin in skeletal muscle.

It can be concluded that both heavy and light exercise may cause elevated troponin, which have to be considered when patient are suspected to have a myocardial infarction. Several factors probably influence post-exercise levels of troponin, but the mechanism of release is most likely physiologic.

1. Introduction

The last years, the cardio specific troponins have been the preferred biomarkers in diagnostic of myocardial infarctions [1]. Cardiac troponin T (cTnT) and troponin I (cTnI) are only found in cardiomyocytes [2], which is why elevated circulating levels might imply necrosis of the myocardium. The last years, it has also been discovered that elevated cTn is frequent under many other circumstances as well. Exercise is one of these circumstances, even in a healthy population [1]. This phenomenon has been referred to as a "doubled edged sword" [3], considering that regular exercise is also known to have multiple beneficial effects. The first study where troponin was measured in subjects after exercise, was published in 1987 [4], and this was the beginning of a long debate. Two main questions have been discussed in literature; 1) does exercise lead to elevation of cardiac troponin? And 2) is exercise-induced elevation of cTn physiological or pathological? Studies published before year 2000 were not consistent regarding either of these questions. Most authors had measured troponin in participants of endurance exercise events like ultramarathons, cycling races, triathlons and marathons. The limitations of these studies were many. Sample sizes were often small, first generation assay of cTnT had cross-reactivity with skeletal troponin [2] and the subjects were highly selected considering that only trained individuals are capable of strenuous exercise for several hours. Results ranged from 0 to 100% of subjects having elevated cTn [5,6]. As the assays of troponin improved, with development of high sensitive methods capable of detecting a few nanograms of troponin, sample sizes increased and several types of populations were examined, it has become clear that exercise may cause elevation of cardiac troponins. A recent published article reported increase of troponin in 96% of subjects post-exercise when a high sensitive method was used [7]. In the largest study, 482 participants of the Boston marathon 2002 had their blood analyzed for troponins after completing the race, and 68% had an increased level [8]. Multiple other studies have reported post-exercise elevation of troponin, including assessments of short-term exercise. Treadmill sessions of only 30 min [9], and exercise like basketball [10] and soccer [11] have all affected levels of cTn. Even playing table tennis is sufficient to cause elevation of troponin in children [12]. However, most studies have not found positive samples in all subjects and this makes the mechanism hard to explain. What are the factors contributing to elevation of cTn in response to exercise? And what is the mechanism? Is it myocardial cell death or damage? The aim of this paper was to review these topics by searching the literature.

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2. Methods

We used the mesh terms "exercise AND troponin" in pubmed/medline and found 636 articles (Fig. 1). By reading the headlines 385 could be excluded because they did not concern exercise-induced elevation of troponin in healthy subjects. Of the 151 remaining articles, another 35 were excluded because they were reviews, comments, case rapports or full text was not available in English, in addition to a few examples where only the baseline level of cTn had been measured in athletes. I was left with 116 articles. All studies were published between 1987 and 2015 and had measured troponin in subjects after exercise. The references of the articles were searched to find more relevant studies, and another 29 were found.

2.1. Results of different exercise protocols (Table 1)

2.1.1. Marathons

Cardiac troponin has been measured in runners of multiple marathons and often in large events like Boston, Berlin and London marathons.

In addition to Boston marathon and 2002, where 68% of 482 runners demonstrated increased cTn postrace [8], studies were done in 1993 [13], 1995 [14], 1997–2001 [15,16] and 2004–2007 [17–20]. The -95 study did not find post-exercise elevation of cTnT using a second generation assay, but 20% had elevations of cTnT or cTnI measured by first generation methods. Results from the other competitions proved elevated levels of troponin.

Runners of the Berlin marathon have been assessed at 4 occasions [5,21–25]. The result of the study from 1990 should be interpreted with caution, due to low cardiac specificity of the assay. The articles from later contests have reported troponin elevation in range from 38% of all subjects [23], to 94% of subjects above the upper reference limit [25].

London marathon has been studied several times in the 21st century [26–36]. 38–82% of subjects had elevated levels of TnT when different authors used a third generation method (Roche Diagnostics) in competitions from 2002 to 2006 [27–29,34–36]. In -07 and -08 Dawson and Wilson both used an ultra assay for TnI, and all but one runner demonstrated increased levels post-exercise [30,31]. The article from London marathon 2009 [32] only reported values above URL in a subgroup, where 20% (10/50) reached cut-off for cTnT and 9% (5/53) for TnI. Two different research groups published articles after the competition in -02, and while one reported elevation of cTnT in 26/33 participants [27] the other did not reveal increase of cTnI in 34 subjects [26]. This is one of a few studies [14,26,37] where elevated cTn has not been found post-race in marathon runners. On the opposite side, there are marathons where all participants had increased levels of cTn; London marathon 2008 and a simulated marathon on a treadmill where blood samples were taken during exercise [38]. The majority of the studies of troponin and marathon running have revealed increased levels in between 0 and 100% of subjects [4,7,39–56], and such results are also found in the 30 km Swedish race Lidingoloppet [57–63].

2.1.2. Cycling events

The same researchers who assessed runners in Berlin marathon 1990 also included 8 amateur cyclists from the Tyrolean Ötztaler Radmarathon, but did not find elevation of cTn [5]. A few years later elevated cTn was documented in 5/25 professional cyclists by the first generation assay [64]. When professional and amateur cyclists are compared, some results indicate a smaller troponin response in professionals. Neither 11 professional cyclists in a 5 day race [65] nor 9 participants of Giro d'Italia 2011 [66] had elevations of TnT, but multiple assessments of amateurs have shown positive results [52,53,67–70]. One exception is the group of cardiologists who cycled 1580 km in 8 days, but they did not take pre-exercise blood samples to document small increases of cTn [71]. However, there are several examples of troponin elevation in professional or "highly trained" cyclists [72–75], as when all volunteers had elevation of cTn at some point during Tour de France 2007 [76].

2.1.3. Ultramarathons

Ultramarathons are races covering a distance more than 42,2 km and troponin has been assessed in multiple ultramarathons since the 90's [6,52,53,77–93]. 0–100% of runners have demonstrated elevated values after a competition, but the response has often been small compared to marathon. A research group assessed both competitors of a marathon and an ultramarathon (and cycling) and found a greater proportion with elevated levels of both TnT (52% vs 21%) and TnI (73% vs 57%) among the marathon runners. Further, elevation of cTn was not detected in any subjects by conventional methods in three

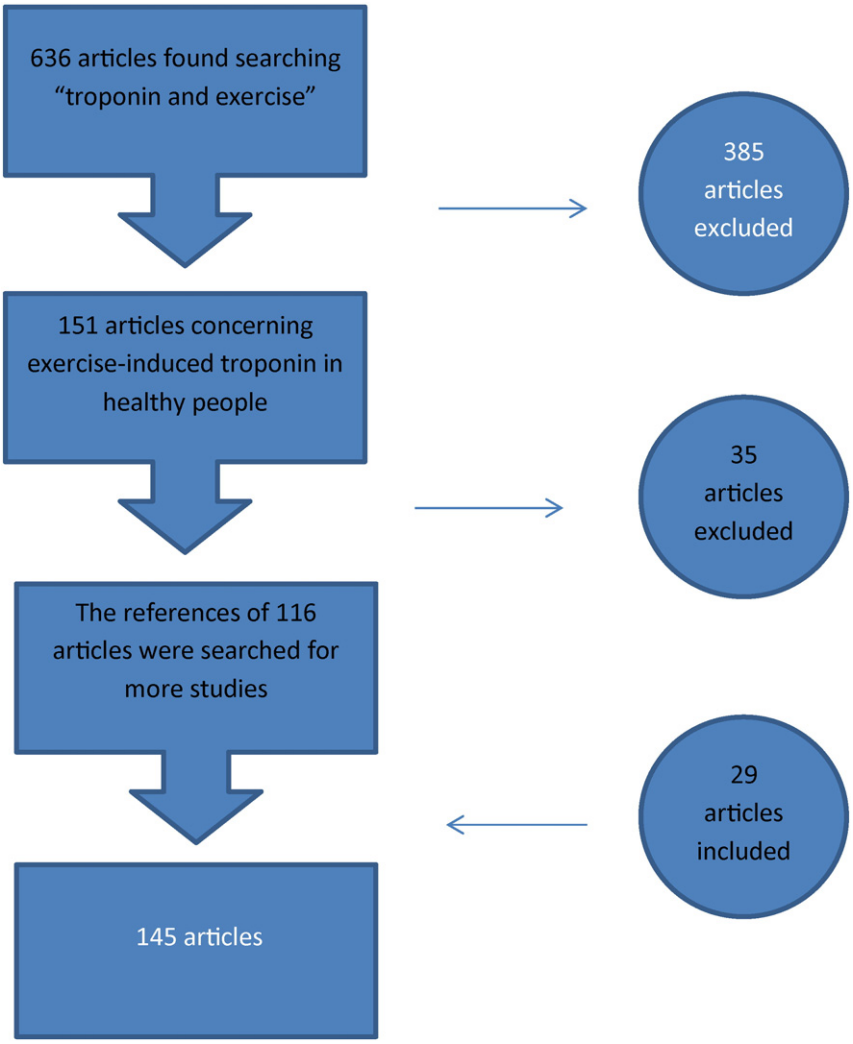

Fig. 1. The figure illustrates how the articles were chosen.