Challenges of evaluating endurance athletes with symptoms of possible AMI during or after a race

Triathlon – triple challenge to athletes and doctors

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Summary

Acute myocardial infarction (AMI) in endurance athletes such as triathletes is rare but not impossible. However, the assessment of endurance athlete with possible AMI is very challenging because application of the classical diagnostic tools, i.e., history, electrocardiogram and cardiac troponin testing is different from their use in "normal" AMI patients and requires specific knowledge regarding the cardiovascular phenotype of the endurance athlete in general and during a competitive event. To illustrate this, we report on three different subjects referred with similar presentations but very different underlying problems on a single day during one single triathlon event.

Key words: acute myocardial infarction; exercise; endurance; cardiac troponin; electrocardiogram

Introduction

Triathlon, i.e., swimming, cycling and running over moderately long to ultra-long distances in a row, is one of the most demanding endurance sports disciplines as it requires a both highly trained and very versatile athlete. It does not come as a surprise that athletes completing a long distance triathlon (3.8 km swimming, 180 km cycling, 42.195 km running) are referred to as "ironmen" and "ironwomen". Although heart disease is very rare in such endurance athletes, and regular exercise reduces the lifetime risk of acute myocardial infarction (AMI), it is well known that there are athletes with previously unknown significant cardiac disease that may manifest for the first time, and potentially in a fatal manner, during a sports competition [1–3]. In particular, AMI has been reported during endurance sport events such as marathon running [4].

However, the assessment of the endurance athlete with possible AMI is very challenging because application of the classical diagnostic tools, i.e., history, electrocardiogram (ECG) and cardiac troponin (cTn) testing is different from their use in the "normal" AMI patients and requires specific knowledge regarding the cardiovascular phenotype of the endurance athlete in general, and during and early after a competitive event. Intense endurance training over years leads to adaptations of the cardiovascular system including remodelling of the left ventricle and right ventricle [5] and the atria ("athlete's heart") with associated changes of the ECG [6], which makes ECG interpretation challenging. In addition, prolonged and intense exercise has been repeatedly shown to be associated with an acute rise of circulating cTn [7]. Thus, cTn testing to exclude or diagnose AMI may be challenging or even impossible in the setting of an endurance exercise competition. To illustrate the problem of the assessment of these athletes in the emergency setting, we report on three different subjects referred with similar presentations but very different underlying problems on a single day during one triathlon event.

Case series

On a Sunday in June 2017, a middle-distance triathlon (1.9 km swimming, 70 km cycling, and 21.1 km running) took place in eastern Switzerland. Among 2036 athletes taking part in the race, 1940 were able to finish within 7.5 hours. The 2017 race was notable because of the hottest temperatures in the history of this particular triathlon event (>30°C) [8]. We herein report on three athletes who were referred to our cardiology service by the local hospital or ambulance teams because of suspected AMI.

Case 1

A 47-year-old experienced male Caucasian triathlete (>10 triathlons) with possible mild dyslipidaemia (total cholesterol 4.9 mmol/l, low-density lipoprotein cholesterol not measured) but no other cardiovascular risk factors had to give up the race during the cycling course because of acute chest pain, which had started during swimming and which was ongoing and prevented the patient from faster cycling. He was assessed by the local medical team and because of ongoing chest pain an ECG was performed, which showed widespread ST segment elevation (fig. 1). The patient was

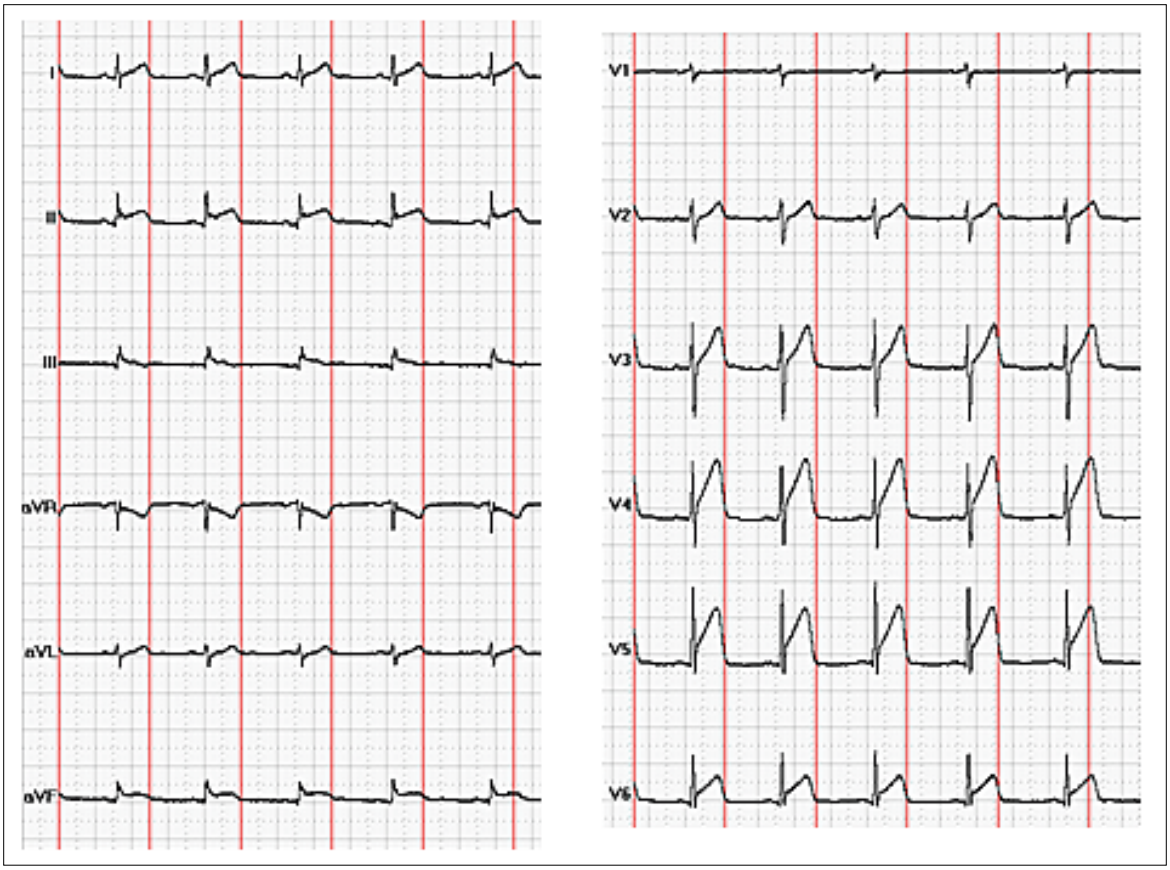

Figure 1: 12-lead ECG showing widespread ST segment elevation (II, III, aVF but also V3–6) and ST segment depression in aVR resulting from thromboembolic occlusion of the distal left anterior descending artery, which runs around the cardiac apex to the inferior wall (please also see fig. 2).

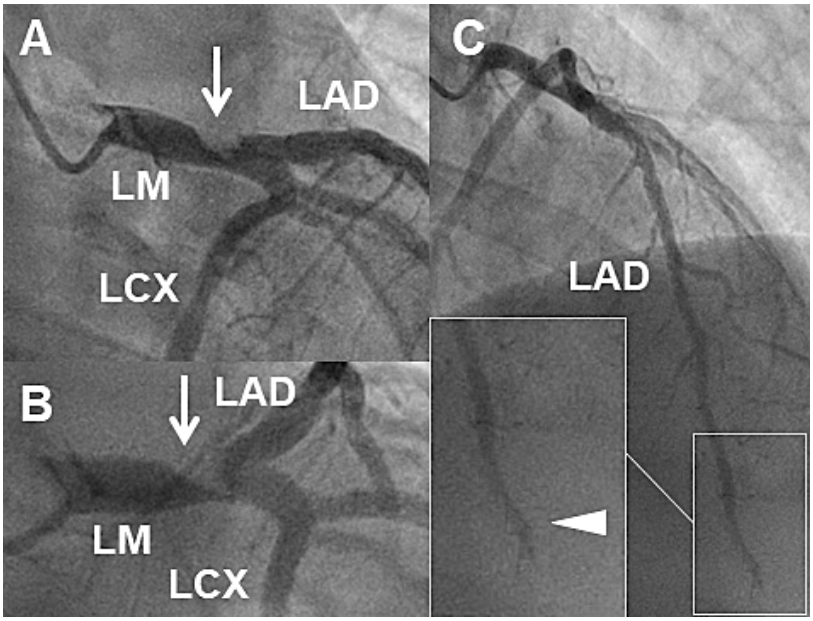

Figure 2: Coronary angiography (left coronary artery) showing plaque rupture and thrombus (panels A and B, arrow) in the distal left main (LM) and thromboembolic occlusion of the distal left anterior descending artery (LAD, panel C, triangle).
LCX: left circumflex artery.
Panel A: right anterior oblique (RAO) 30°, caudal 20° projection. Panel B: caudal 30° projection. Panel C: RAO 10°, left anterior oblique 30° projection.

transferred immediately from the field directly to our catheter laboratory by helicopter. He had been given aspirin, ticagrelor and heparin by the emergency physician. Coronary angiography revealed a left dominant coronary circulation with plaque rupture and thrombus formation in the distal left main and thrombotic occlusion of the distal left anterior descending artery (fig. 2). Cardiac troponin I at that time was 223 ng/l (cut-off <30 ng/l). An intra-aortic balloon pump was placed, and owing to the presence of a complex left main lesion in a left-domination circulation with a significant risk of further embolisation during a percutaneous intervention, as well as the very large diameter of the left main, the patient was transferred for emergency bypass surgery. The in-hospital course after surgery was uneventful, and the patient was discharged one week later.

Case 2

A 46-year-old Caucasian man without cardiovascular risk factors (low-density lipoprotein cholesterol 1.6 mmol/l) was referred because he experienced chest

discomfort starting during the cycling course. He had been exercising on a regular basis for years, but had not specifically trained for this race. He was able to complete the entire race but had to reduce speed and to walk slowly several times during the final half-marathon. On admission he had no chest pain but felt unwell. The ECG showed significant ST segment elevation in the precordial leads (fig. 3) and T wave inversions in leads II, III and aVF; cTn was above the cut-off for AMI (cardiac troponin I 245 ng/l; cut off <30 ng/l). The patient was initially treated in the local hospital and was then urgently transferred to our emergency department by helicopter. An echocardiogram revealed a structurally normal heart with overall normal left ventricular ejection fraction but possible mild anteroapical hypokinesia. Coronary angiography revealed mild atherosclerosis, but no stenosis or occlusion of a coronary artery. The patient then remembered that he had been told in the past that his ECG was abnormal. All three ECGs during the hospital course of 24 hours looked the same, i.e., there were no dynamic ECG changes. The patient's symptoms resolved within two hours after rehydration. The ECG was interpreted as a normal variant, the cTn rise was attributed to the triathlon race *per se*, and the patient's symptoms were attributed to exhaustion and dehydration in the context of suboptimal training status and extreme weather conditions.

Case 3

A 37-year-old Caucasian woman experienced sudden onset of shortness of breath and chest discomfort during swimming. She was unable to complete the swimming course because of these symptoms, and she was subsequently admitted to the local hospital with a peripheral oxygen saturation of 88%. Chest x-ray revealed mild pulmonary oedema (fig. 4), the ECG was abnormal (fig. 5), and cTn was above the local threshold for the diagnosis of AMI. The patient was given furosemide, aspirin, ticagrelor and heparin, and she was transferred to our cardiology department by helicopter. On admission, she had no symptoms, but there was a further rise in cTn (cardiac troponin I 244 ng/l; cut-off <30 ng/l). An echocardiogram revealed left ventricular hypertrophy most prominent at the apex ,but normal left ventricular ejection fraction and regional wall motion (fig. 6), and normal diastolic left ventricular function with no evidence of an increased left ventricular filling pressure (ratio of peak early [E] to atrial mitral

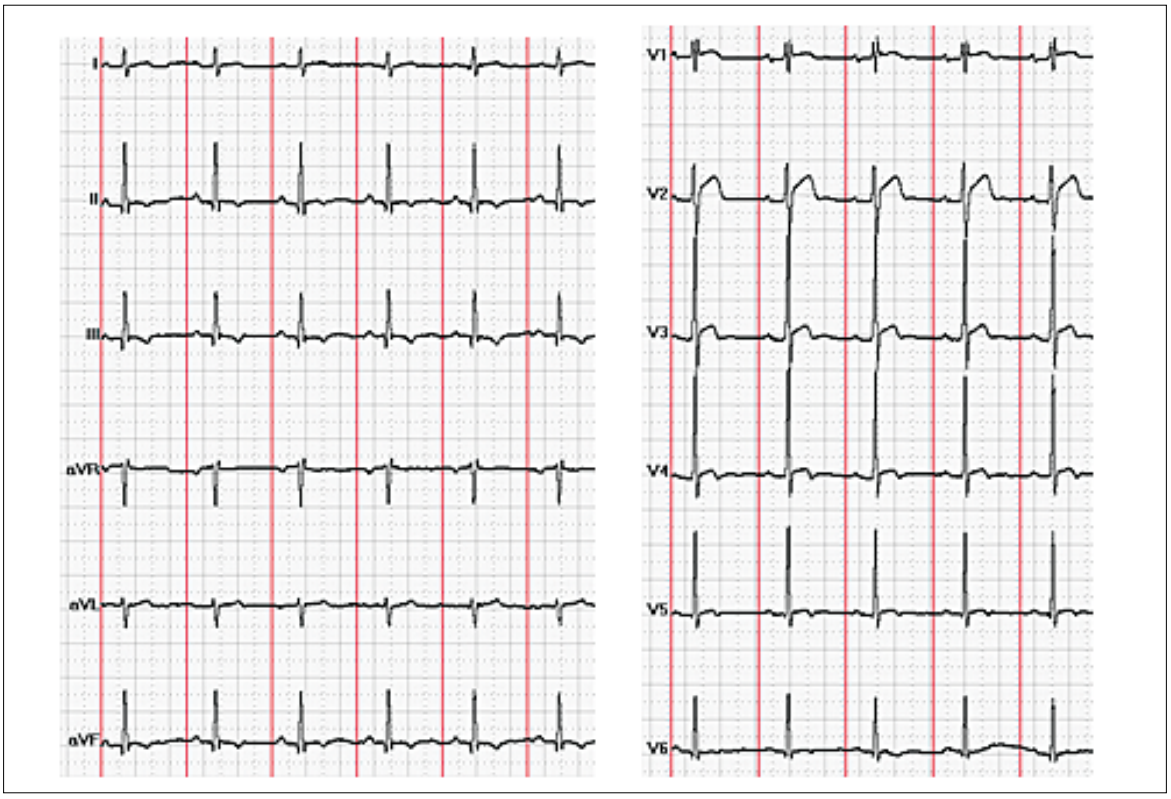

Figure 3: 12-lead ECG showing incomplete right bundle-branch block, ST segment elevation in leads V1–5, and negative T waves in II, III and aVF. There is an elevated J point by 0.1 mV in leads V2–4 (borderline V5), and associated terminal T wave inversions in V3–5.

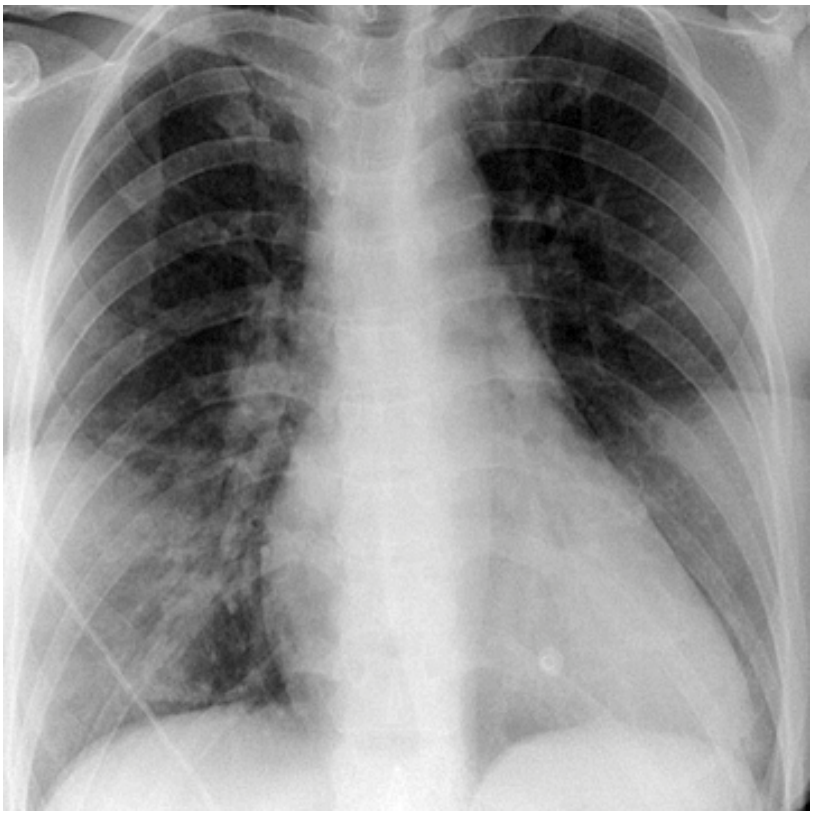

Figure 4: Chest x-ray (anteroposteror) showing pulmonary oedema.

inflow velocities 1.6, peak early mitral annular velocity [e'] averaged from the septal and lateral annulus 8 cm/s, E/e' 10). Computed tomography coronary angiography excluded coronary artery disease, but still showed mild pulmonary oedema. Eighteen hours later, there was a fall in cardiac troponin I to 114 ng/l. On further questioning it turned out that a cardiomyopathy had been known for years, but that the patient had missed regular follow-up appointments and had stopped beta-blocker therapy. An apical form of hypertrophic cardiomyopathy was diagnosed. However, for the acute symptoms during the race, we considered swimming-induced pulmonary oedema the most likely diagnosis. A follow-up visit was organised, and future participation in competitive sports events was discouraged.

Discussion

Our series of three triathletes taking part in exactly the same competition on exactly the same day all presenting with a similar combination of symptoms and findings – chest discomfort and acute exercise intolerance, abnormal ECG, and abnormal cTn – but very dif-

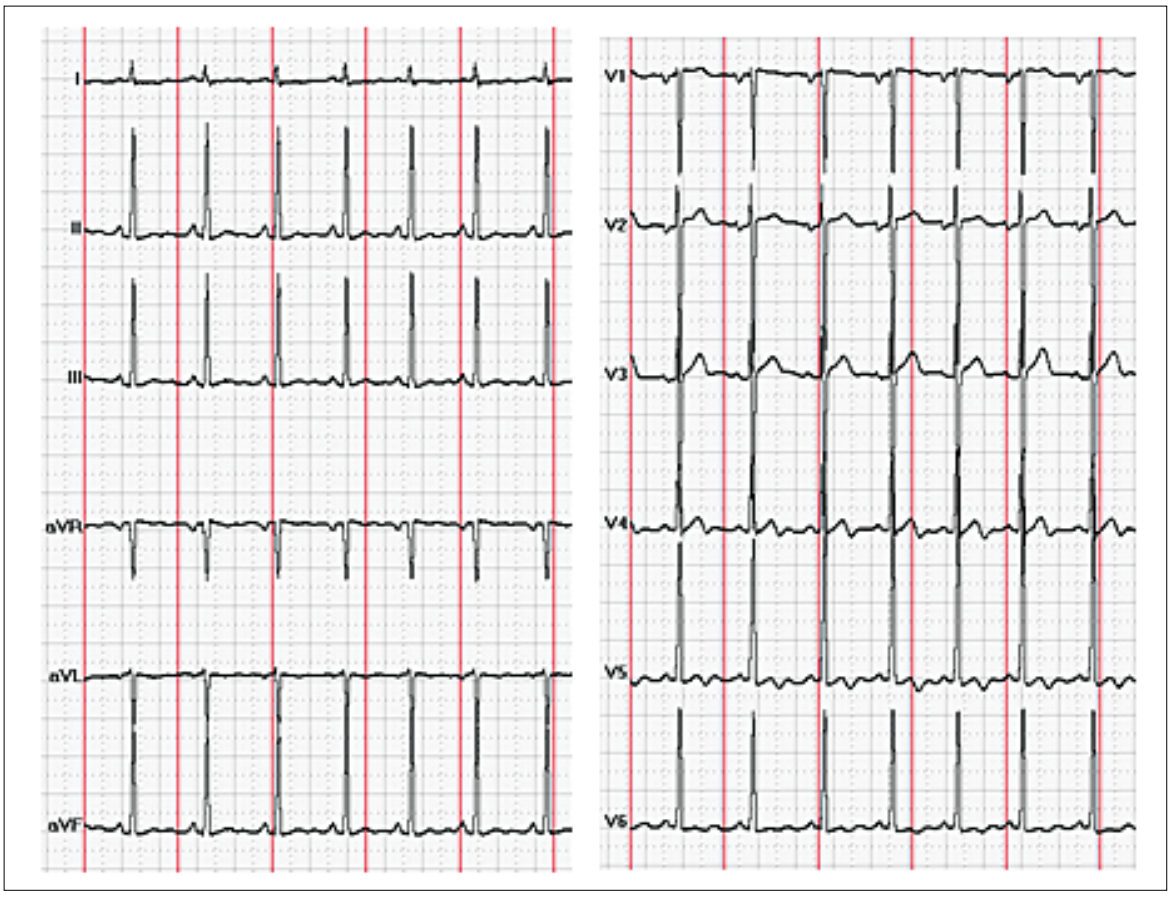

Figure 5: 12-lead ECG with positive Sokolov index and T wave abnormalities in leads V4–6.

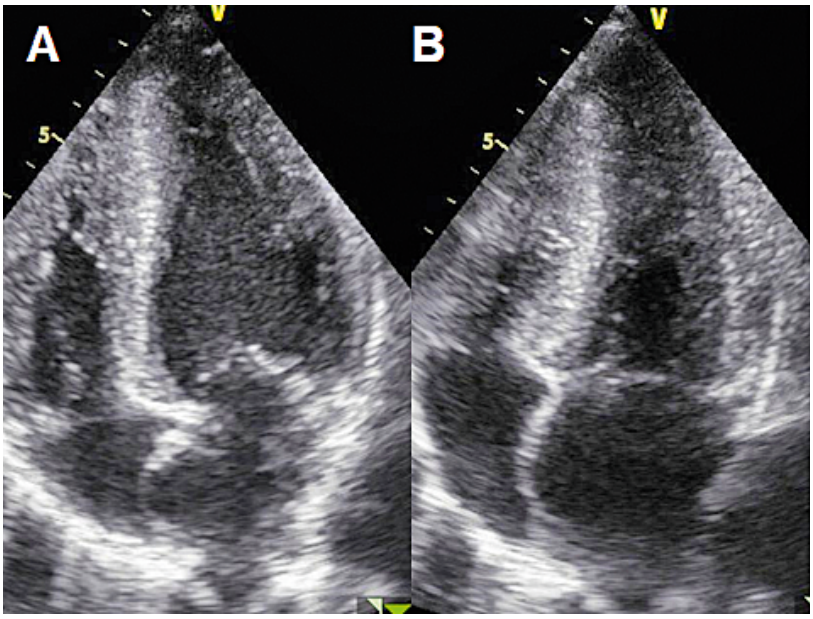

Figure 6: Transthoracic echocardiography, apical four-chamber view, showing left ventricular hypertrophy predominantly at the apex. A: end-diastolic still frame, B: end-systolic still frame

ferent underlying cardiac status highlights the difficulties in the acute assessment of these athletes during and after a race if the conventional noninvasive diagnostic tools usually applied for the evaluation of possible AMI are used. The diagnosis of AMI is primarily based on symptoms, ECG and cTn [9, 10]. However, although physicians are generally familiar with the interpretation of history, ECG and cTn findings in "normal" patients admitted to the emergency department, special knowledge and considerations are required when using these tools in endurance athletes after a race. Here, we briefly discuss these aspects.

In the setting of a triathlon competition, symptoms may be difficult to interpret since some sort of chest discomfort, shortness of breath and exhaustion is not uncommon in such a race where athletes go to, or sometime beyond, their limits, particularly if there are extreme additional external factors (e.g., extreme temperature and/or humidity). General exhaustion, dehydration, gastrointestinal problems, hypothermia, heat stroke and muscular problems are common phenomena, which are far more common than AMI in the triathlon setting but which may be hard to differentiate clinically in the acute setting. All three patients had symptoms leading to medical contact. First of all, the fact that an athlete asks for professional medical advice and support is an alarming sign itself, since these athletes typically know their body well, have longstanding experience in interpreting symptoms and a strong will to suppress those during the race, and will well recognise if anything is happening that they are not familiar with. Thus, the problem has to be taken seriously, although the differential diagnosis is broad, and only a small minority of such patients will end up having AMI [1]. Notably, the probability of any coronary artery disease in endurance athletes is not extremely low [11, 12]. Among 152 master marathon runners >50 years, nearly 50% of men have been shown to have coronary plaques, and this prevalence was higher than in age-matched sedentary men. Interestingly, plaque composition was different in athletes and sedentary men, with more calcified plaques in athletes and more mixed plaques in sedentary men [12], which may explain the relatively low incidence of plaque rupture and AMI in these athletes. In recent years, the participation in demanding endurance exercise competitions such as marathon running has become very popular among middle-aged subjects [3], and these subjects may have cardiovascular risk factors and silent coronary artery disease. The vast majority of sports-related sudden cardiac deaths occurs in athletes older than 35–40 years [13] and, in contrast to young patients, sports-related cardiac events in this age group are mostly related to coronary artery disease rather than cardiomyopathies [14]. Our first patient had plaque rupture and extensive thrombus formation in the left main in a left-dominant coronary system, and thus timely and correct diagnosis was crucial.

The ECG is the primary tool for risk stratification in patients with possible AMI [10]. Patients with ST segment elevation must immediately undergo cardiac catheterisation to establish reperfusion, whereas in those without ST segment elevation, a secondary risk stratification is based on serial cTn measurements and other clinical factors [10]. Physicians involved in the management of patients with possible AMI are usually well trained in the interpretation of the ECG. However, although the typical AMI patient is a non-athlete older than 40–50 years, younger patients and particularly athletes often show abnormal ECGs even when there is no underlying coronary artery disease [6, 15]. The differentiation of the athlete's ECG from a pathological ECG is difficult, and has been subject of numerous papers and a recent expert consensus statement [6]. Whereas most often ECGs in athletes are performed in the context of screening for a clinically silent cardiomyopathy, i.e. ,in an outpatient setting where there is time to think about the need of further examinations, in particular an echocardiogram [6], the setting of possible AMI is less common but requires a quick decision. Some degree of ST segment elevation and J point elevation, particularly in the precordial leads in men <40 years, is normal [15], and most often previous ECGs will

not be available in the emergency setting. In the first patient, the ECG showed widespread ST segment elevation. The infarct-related artery was not absolutely clear (ST segment elevation in V3–6 but also II, III, and aVF, ST segment depression in aVR), but the highly abnormal ECG in combination with suggestive symptoms made the decision for an emergency angiogram easy. Retrospectively, the ECG was explained by the fact that the patient had thromboembolic obstruction (resulting from embolisation from the left main) of the distal left anterior descending artery, which runs around the cardiac apex to the inferior wall. In our second patient, the ECG was clearly abnormal, and angiography was required to clarify the situation. The ST segment elevation in the precordial leads was most likely a form of early repolarisation (defined as elevation of the J point by ≥0.1 mV in the precordial or inferior leads [6]) although it was not an absolutely typical pattern. The terminal T wave inversion preceded by J point elevation and convex ST segment elevation is often seen in athletes [6]. In contrast, T wave inversions in leads II, III, and aVF are usually regarded as abnormal and requiring further examination with echocardiography and cardiac magnetic resonance imaging, depending on the findings of the echocardiogram [6]. T wave inversions in the lateral leads (not present in our patient) are particularly relevant and may reflect an underlying cardiomyopathy and an adverse outcome [16]. Athletes with these ECG changes should be evaluated with cardiac magnetic resonance imaging and require regular follow-up [6]. In our second patient, an abnormal ECG was obviously known before, and the echocardiogram was not suggestive of a cardiomyopathy. The third patient also had an abnormal ECG, but from her history an underlying cardiomyopathy was suspected early in the diagnostic work-up. With this in mind and her very low cardiovascular risk, we performed computed tomography coronary angiography to prove that the cTn rise was not a reflection of AMI. In particular, we wanted to exclude spontaneous coronary artery dissection, a non-atherosclerotic cause of AMI that has been reported in young women after exercise [17].

With the availability of sensitive and highly sensitive cTn assays the diagnosis of AMI has been refined in the last decade. Numerous published studies have shown how AMI can be ruled out and ruled in by use of baseline levels and changes of high-sensitive cTn (e.g. [18]). It must be noted, however, that cTn higher than the cut-off for exclusion of AMI often, but not always, indicates AMI. Rather cTn is an unspecific marker of myocardial injury that can be released into the blood stream through a variety of mechanisms other than AMI, including acute heart failure, myocarditis, paroxysmal tachycardia, stress cardiomyopathy and sepsis [10]. Several studies have shown that long-distance endurance exercise such as the triathlon or marathon leads to an increase in cTn above cut-offs for the exclusion of AMI in the majority of participants [19, 20] (summarised in [7]). The extent of cTn elevation in this context is modest, and cTn typically returns to baseline within 72 hours [20], which is in contrast to most patients with AMI. The exact mechanisms underlying this cTn release are unknown and may include true cardiomyocyte necrosis or increased membrane permeability with cTn leakage [7], as discussed for patients with sepsis-associated cTn release [21]. There is no evidence that this cTn release is associated with adverse long-term consequences [7]. Thus, measurement of cTn immediately after a triathlon most often will not be helpful for the exclusion or inclusion of a diagnosis of AMI, and it must be realised that cTn may be above the cut-off for the exclusion of AMI up to two days after the triathlon. Still, significantly elevated cTn after/during triathlon in an athlete with symptoms of a possible acute or chronic cardiac disease must not be attributed to the effect of triathlon alone without further thinking and consideration of additional diagnostic steps. In the first patient, cTn did not influence decision making, as in every "normal" patient presenting with suggestive ST segment elevation myocardial infarction. In the second patient, symptoms and ECG led to the decision to perform echocardiography and coronary angiography, and only after that, could cTn be attributed to intense long-distance exercise with high probability. In the third patient, the presence of pulmonary oedema was the intriguing finding. Cardiac decompensation due to cardiomyopathy and associated cTn release would have been another option. This seems unlikely, however, in a patient who had been asymptomatic and had had very good exercise capacity for years. More likely, elevated cTn was a reflection of structural heart disease exposed to additional stress. Given that the patient gave up the race already after swimming (less than one hour), cTn increase was unlikely to have been caused by exercise alone. The patient's symptoms were most likely related to swimming-induced pulmonary oedema, a known pathology in swimmers and triathletes [22]. The pathophysiology of swimming-induced pulmonary oedema is still incompletely understood. Both hydrostatic (increased pulmonary pressure) and non-hydrostatic (increased permeability) factors seem to play a role. Interestingly, left ventricular hypertrophy has been suggested as a predisposing factor [22]. In the present third patient there was no evidence of increased left ventricular filling pressure at the time of the echocardiogram. How-

ever, the patient may not have been euvolaemic after the race and without a meal (probably rather hypovolaemic) at that time, and we had not assessed her during exercise. Notably, in subjects with hypertrophic cardiomyopathy, participation in competitive sports events is generally not recommended, based on expert consensus [23].

In conclusion, our series of three triathletes participating in the same race on the same day and presenting to the same hospital and team highlights the challenges and special considerations when evaluating endurance athletes with symptoms of possible AMI during or after a triathlon race.

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