Short Strenuous Training-Induced Changes in Blood Coagulation in Sportsmen and Sportswomen

Tünde Paska[1], Elemér Sipos[2]*, Ákos Tóth[3], Sára Jeges[1], Sándor Szabados[2] and Gábor L. Kovács[4,5]

[1]Faculty of Health Sciences, University of Pécs, H-7623, Hungary

[2]Heart Center, University of Pécs, H-7623, Hungary

[3]Institution of Physical Education and Sport Sciences, University of Pécs, H-7623, Hungary

[4]Department of Laboratory of Medicine, University Pécs, H-7623, Hungary

[5]Szentágothai Research Centre, University Pécs, H-7623, Hungary

*Corresponding author: Elemer Sipos, Heart Center, University of Pecs, H-7623, Hungary, Tel: +49-7834-970-136; E-mail: sipa6080@gmail.com

Abstract

Objective: To observe how a short vigorous exercise influences certain coagulation and fibrinolytic parameters in sportsmen and sportswomen.

Design: Pre-post parallel-groups.

Setting: Heart Centre and Department of Laboratory of Medicine, University Pécs, H-7623, Hungary

Participants: A total of 31 healthy individuals (mean age [+SD] 35 + 8 years; 18 males, 13 female), participated in the study at the Heart Centre of the University of Pécs. Participants were active and well-trained active sportsmen (and women) continuously involved in competitive sport activities (basketball, handball or water polo) for at least 10 years.

Main Outcome Measures: All participants performed an exercise test on a cycle ergometer. Venous blood samples were obtained for rotational thrombelastometry (ROTEM).

Results: In the case of sportsmen significant differences were obtained related to physical exercise in certain nonactivated thrombelastometry (NATEM) measurements. After exercise, the mean clotting time (CT) was shorter (329.3 ± 85.3 vs. 276.7 ± 91.7 seconds, P=0.041) and the maximum clot firmness (MCF) was broader (53.7 ± 4. vs. 60.4 ± 13.7 mm, P=0.034) than before exercise. In sportswomen mean CT was shorter (292.9 ± 65.2 vs. 247.8 ± 105.9 seconds, P=0.04), and the MCF was broader after exercise (59.0 ± 4.1 vs. 65.2 ± 9.7 mm, P=0.04) by NATEM measurements.

Conclusions: A tendency for a post-exercise hypercoagulation state following a short-term strenuous exercise has been documented.

Introduction

The cardiovascular benefit of regular physical activity is well documented [1]. Regular exercise is generally associated with favorable alterations in risk of cardiovascular morbidity and mortality. Strenuous exercise, on the other hand, has been implicated in the pathogenesis of sudden death [2]. Physical exertion occurring 1-2 h before the onset of symptoms has been identified as triggering acute myocardial infarction (MI). Triggering acute MI by physical exertion has been reported to be more common in men and in younger patients [3]. However, it is known that fit people, too, can die during or after exertion [4]. Occurrence of sudden cardiac death was an important factor prompting us to investigate the coagulation in a selected population of sportsman. Thompson reviewed several studies on the incidence of sudden death during exercise [5]. While the incidence of sudden cardiac death during exercise is very low, the evidence seems to prove that exercise is likely to trigger or cause sudden cardiac death in athletes with underlying heart disease.

Sportsmen have not been investigated following short-term strenuous ergometry for their coagulation disturbances supposedly representing a risk factor from the point of view of sudden death. In most European countries (except for Germany and France) cardiac ultrasound examinations and ECG stress testing is not used routinely as a regular means of control, even in the case of professional sportsmen. Cardiac complications in sportsmen are susceptible to coagulation disturbances. These coagulation disorders may contribute to death caused by hidden cardiac complications [6]. Therefore, the examination of coagulation disturbances may be important from a medical point of view. Until now, different types of stress tests have been performed, e.g. the long term strenuous exercise during Marathon race. It has not been investigated whether there are measurable changes in the coagulation parameters in well-trained sportsmen during the course of a short distance exertion. According to our hypothesis, the risk of sudden death can significantly increase; e.g. symptomless coronary scleroses plus prothrombotic state means a higher risk for sudden death. Thus, a sensitized myocardium plus a trigger factor can lead to sudden death. Timothy at al. have enlisted the following factors which, under physical stress, can lead to sudden death: changes in the vegetative nervous system, increased tromboxan A2 level, coronary vasospasm, increased coagulation activity, increased serum lactate level, intraextracellular electrolyte changes, increased fatty acid concentration, increased body temperature [7]. We performed a standard stress test in all the participants and studied the coagulation factors by using thrombelastometry and some routine laboratory parameters of blood coagulation.

Materials and Methodology

Investigations were approved by the Regional Ethical Committee of the University of Pécs (No. 3757.316-4443/KK4/2010). A total of 31 healthy individuals (mean age [+SD] 35 + 8 years, 18 males, 13 females), participated in the study at the Heart Centre of University of Pécs. All participants were non-smokers, free of known cardiopulmonary or metabolic diseases and did not take any medication at the time of the study. All patients were investigated for cardiovascular risk, using the Framingham score. All patients had a cardiovascular risk of <1% for the next 10 years. Informed consent was obtained from all patients prior to testing. Participants were active and well-trained sportsmen (and women) continuously involved in competitive sport activities (basketball, handball or water polo) for at least 10 years. All patients were negative with routine 2-D echocardiography measurements with pulsed wave Doppler, continuous wave Doppler and color flow mapping for valve problems and measurement of left ventricular volume using modified Simpson's method or peak ejection velocity for systolic function and mitral valve motion for diastolic function. None of the athletes suffered from prolonged or shortened partial thromboplastin time (PTT) before testing. They did not take medication known to interfere with PTT testing.

All participants performed an incremental exercise test on a cycle ergometer (GE Medical System) based on Bruce protocol until volitional exhaustion. The loading was measured in MET (MET is a term used to describe oxygen utilization by the body, and stands for metabolic equivalents. One MET equals 3.5 ml oxygen uptake/kg body weight/min). The work-rate was increased every 3 min until an age-dependent maximal heart rate or until volitional exhaustion. Throughout the test a pedaling frequency of 55-65 rev/min was maintained and heart rate was measured continuously with ECG. Venous blood samples were obtained from a prominent antecubital vein with minimal stasis immediately before starting and immediately after finishing ergometry for ROTEM analyses.

The blood samples were collected in vacuum tubes containing EDTA and 3.8% trisodium citrate (Vacutainer, Becton Dickinson, Heidelberg, Germany). The blood samples were immediately transferred to the laboratory and analyzed within a time period of less than 1 hour. Haemostatic alterations induced by physical exercise were measured by rotational thrombelastometry (ROTEM, Pentapharm GmbH, Munich, Germany). Citrated whole venous blood was drawn immediately before and after finishing spiroergometry for rotational thrombelastometry analyses. To yield the highest sensitivity, blood coagulation was initiated by recalcification. The 3 principal dedicated ROTEM test applications NATEM (recalcification), INTEM (intrinsic pathway) and EXTEM (extrinsic pathway) were performed. The following key parameters were recorded: clotting time (CT: this parameter describes the time period from the initiation of coagulation to initial recognizable clot formation), clot formation time (CFT: this parameter measures the subsequent period from the beginning of clot formation until the amplitude of the thrombelastogram has reached a width of 20 mm and represents the dynamics of clot formation), alpha angle (the angle is given between the center line in the thrombelastogram and the tangential line to the developing curve of the thrombelastogram and represents the kinetics of fibrin buildup and cross-linking), maximum clot firmness (MCF: this parameter is identical to the maximal width of the clot, reflecting the achieved clot strength that is dependent on the number and function of platelets and interaction of platelets and fibrin), maximum lyses (ML: this parameter is a reduction of clot firmness after MCF in relation of MCF), amplitude reduction 5,-10,-15,-20 min after MCF (A5, A10, A15, A20). In the case of normal distribution, the paired t- test was
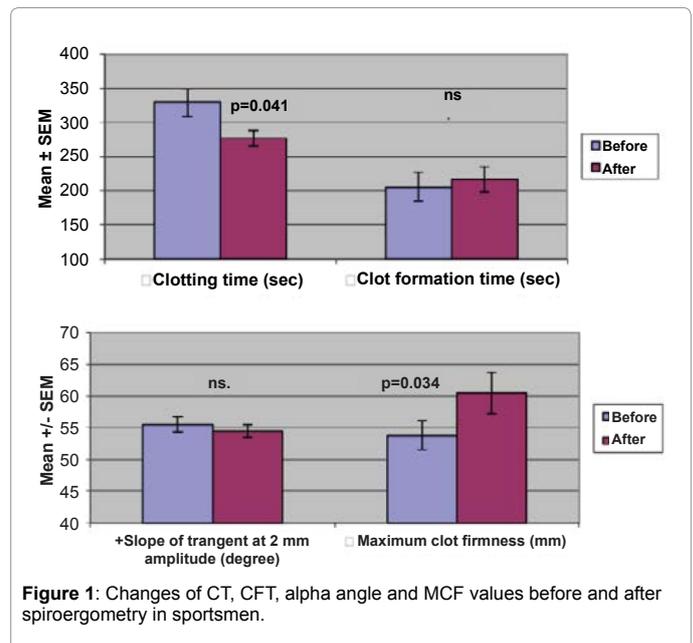

Figure 1: Changes of CT, CFT, alpha angle and MCF values before and after spiroergometry in sportsmen.
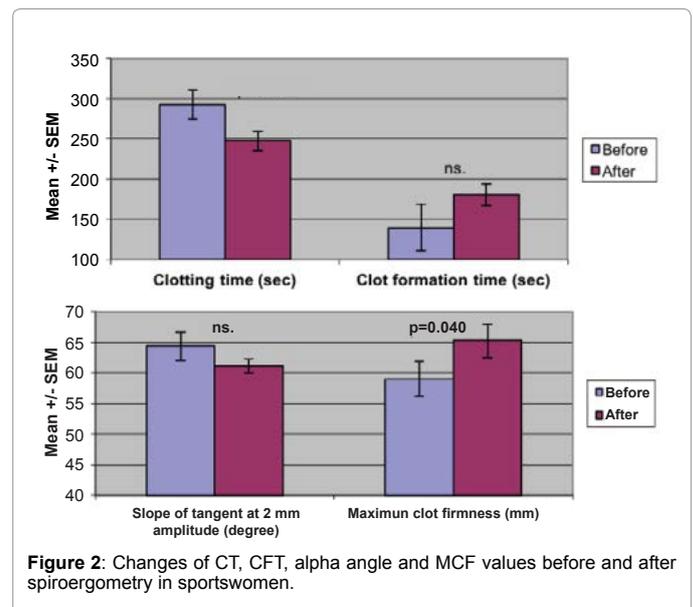

Figure 2: Changes of CT, CFT, alpha angle and MCF values before and after spiroergometry in sportswomen.

used, if the distrbution was not normal, the Wilcoxon's Signed Rank Test was used. Differences were considered statistically significant at P<0.05.

Results

In the case of sportsmen statistically significant differences were obtained related to physical exercise in certain NATEM measurements (but not with INTEM or EXTEM parameters). Accordingly, after exercise the mean CT was shorter (329.3 ± 85.3 vs. 276.7 ± 91.7 seconds, P=0.041) and the MCF was broader (53.7 ± 4. vs. 60.4 ± 13.7 mm, P=0.034) than before exercise. INTEM or EXTEM results and the other NATEM parameters (e.g. CFT, alpha angle) were statistically not different before versus after the loading test (Figure 1).

In the case of sportswomen mean CT was shorter (292.9 ± 65.2 vs. 247.8 ± 105.9 seconds, P=0.043). The MCF was broader after exercise

(59.0 ± 4.1 vs. 65.2 ± 9.7 mm, P=0.040) by NATEM measurements. Other ROTEM parameters were not different if compared before and after exercise (Figure 2).

Discussion

The cardiovascular benefits of regular physical activity are well founded. Regular exercise is generally associated with favorable alterations in risk of cardiovascular morbidity and mortality. Strenuous exercise, on the other hand, has been implicated in the pathogenesis of sudden death. Physical exertion occurring 1-2 h before the onset of symptoms has been identified as trigger of acute myocardial infarction. Such triggering has been reported to be more common in men and in younger patients [8]. It is known that fit people, too can die during or after exertion [4], and this was an important factor why we investigated the population of sportsmen. Thompson reviewed several studies on the incidence of sudden death during exercise [5]. He reported that the absolute incidence of exercise-related sudden cardiac death to be 0.75 and 0.13 per 100,000 young male and female athletes, respectively. 6 per 100,000 middle-aged men die during exertion per year. Thus, while the incidence of sudden cardiac death during exercise is very low, the evidence suggests that exercise may trigger or cause sudden cardiac death in athletes with underlying heart disease [3].

The data of Siscovick et al. show that persons who have undetected heart disease and who are therefore at risk of sudden death reduce their overall risk if they exercise regularly [9]. During exercise, however, their risk is increased acutely. The majority of death cases in athletes are due to underlying cardiovascular disease, which is often not diagnosed. Sudden cardiac death in older athletes (>35 years) is predominately caused by atherosclerotic coronary artery disease. In contrast, sudden cardiac death in young athletes (<35 years of age) is associated with a number of inherited cardiac diseases, particularly the cardiomyopathies and ion channelopathies [10]. In the USA, the most common cardiovascular causes were hypertrophic cardiomyopathy (36%) and congenital coronary artery anomalies (17%) [8]. The incidence rates of sport-related sudden cardiac death in noncompetitive and competitive athletes are not different. Importantly, however, sudden cardiac death in the general population is much more prevalent than in sportsmen in all age groups [11].

There are three essential mechanisms by which vigorous physical activity may develop myocardial ischemia in athletes with coronary artery disease [7]. First, the initial surge of blood pressure with initiation of exercise might precipitate the fissuring of a vulnerable atherosclerotic plaque with the subsequent thrombus formation transforming a previously non-occlusive lesion into a total occlusion. Second, it is possible that a non-occlusive atherosclerotic plaque may bring about transient ischemia by inducing an imbalance between myocardial oxygen demand and supply. Third, myocardial ischemia during exercise might result from coronary-artery spasms. It is believed that a combination of the triggering event and a susceptible myocardium combine to initiate potentially lethal arrhythmias especially ventricular fibrillation. Coagulation disorders can contribute to sudden death in case of susceptible myocardium, since coagulation disorders during physical exertion may lead to triggering events [6]. The aim of our study was to observe how a short vigorous exercise influences certain coagulation and fibrinolytic parameters in a physically fit, well-trained organism. The tendency for a post-exercise hypercoagulation state has been documented (higher circulating platelet counts, shorter activated partial thromboplastin time, higher activity of factor VIII, increased thrombin generation, elevated von Willebrand factor, global increase in fibrinolytic activity (increase in tissue plasminogen activator, decrease in plasminogen activator inhibitor) [12,13]. We investigated the potentially enhanced blood coagulation with ROTEM, since Sucker et al. found that ROTEM is sensitive tool to exercise-induced hemostatic alterations [14]. Our present result confirms these conclusions by showing decreased CT, increased MCF in ROTEM following a short strenuous exercise in well-trained subjects of both genders. Under homeostatic conditions, the body is maintained in a finely tuned balance of coagulation and fibrinolysis. Fibrinolytic responses to acute exercise are clinically important. The magnitude of the fibrinolytic response to exercise is dependent upon both exercise intensity and duration.

Womack et al. found that intensity is more important than duration for eliciting acute fibrinolytic responses [15]. The acute fibrinolytic response to exercise occurs primarily due to an increased release of tPA [13]. Vasopressin is a potential mediator of fibrinolytic exercise responses [16]. There are no data in the literature whether strenuous exercise of short duration may or may not alter fibrinolysis in the well-trained organism. In the ROTEM analysis, maximum lyses (ML), is an indicator of fibrinolysis. In the current experiment, however, ML was not affected by strenous exercise, suggesting that the fibrinolytic activity was not affected in a significant manner.

Conclusion

In conclusion, several data indicate changes of blood coagulation and/or fibrinolysis related to exercise. Coagulations disturbances in sportsmen (and women) can contribute to death caused by hidden cardiac complications. On a routine base, sportsmen (and women) are not investigated for risk of sudden death. Cardiovascular screenings and preparticipation examinations (regular screening with cardiac ultrasound investigation and ergometry) as well as regular laboratory investigation of coagulation parameters may be recommended to prevent sudden death. Even in the case of outstanding sportsmen (and women) cardiac ultrasound examination or ECG stress testing is not used routinely in most of the European countries, except for Germany and France; though this practice may undergo positive changes in the near future. The degree and the direction of the coagulation/fibrinolysis imbalance may largely depend on the level of training (fitness), duration and intensity of exercise. As such, the current observations on the potentially activated coagulation in the well-trained subjects following a short-term strenous exercise are new in the literature. The importance of early identification of clinically silent cardiovascularer diseases at a presymptomatic stage relies on the concrete possibility of SCD prevention by lifestyle modification, including restriction of competitive sports activity, but also treatment with implantable defibrillator and drugs. In the current manuscript significance of simultaneous cardiological and laboratory investigation in preventing sudden death are emphasized.

Conflict of Interest

None declared.

References

1. El-Sayed MS, Ali N, El-Sayed Ali Z (2005) Haemorheology in exercise and training. Sports Med 35: 649-670.

2. Smith JE (2003) Effects of strenuous exercise on haemostasis. Br J Sports Med 37: 433-435.

3. de Noronha SV, Sharma S, Papadakis M, Desai S, Whyte G, et al. (2009) Aetiology of sudden cardiac death in athletes in the United Kingdom: a pathological study. Heart 95: 1409-1414.

4. Corrado D, Migliore F, Basso C, Thiene G (2006) Exercise and the risk of sudden cardiac death. Herz 31: 553-558.

5. Thompson PD (1996) The cardiovascular complications of vigorous physical activity. Arch Intern Med 156: 2297-2302.

6. Koenig W, Ernst E (2000) Exercise and thrombosis. Coron Artery Dis 11: 123-127.

7. Timothy ND (1998) Sudden death and exercise. Sportscience 2: 4.

8. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO (2009) Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980-2006. Circulation 119: 1085-1092.

9. Siscovick DS, Weiss NS, Fletcher RH, Lasky T (1984) The incidence of primary cardiac arrest during vigorous exercise. N Engl J Med 311: 874-877.

10. Sheppard MN (2012) Aetiology of sudden cardiac death in sport: a histopathologist's perspective. Br J Sports Med 46: i15-21.

11. Risgaard B, Winkel BG, Jabbari R, Glinge C, Ingemann-Hansen O, et al. (2014) Sports-related sudden cardiac death in a competitive and a noncompetitive athlete population aged 12 to 49 years: data from an unselected nationwide study in Denmark. Heart Rhythm 11: 1673-1681.

12. El-Sayed MS, El-Sayed Ali Z, Ahmadizad S (2004) Exercise and training effects on blood haemostasis in health and disease: an update. Sports Med 34: 181-200.

13. Womack CJ, Nagelkirk PR, Coughlin AM (2003) Exercise-induced changes in coagulation and fibrinolysis in healthy populations and patients with cardiovascular disease. Sports Med 33: 795-807.

14. Sucker C, Zotz RB, Senft B, Scharf RE, Kroger K, et al. (2010) Exercise-induced hemostatic alterations are detectable by Rotation Thrombelastography (ROTEM): A Marathon Study. Clin Appl Thromb Hemost 16: 543-548.

15. Womack CJ, Rasmussen JM, Vickers DG, Paton CM, Osmond PJ, et al. (2006) Changes in fibrinolysis following exercise above and below lactate threshold. Thromb Res 118: 263-268.

16. El-Sayed MS (1990) Exercise intensity-related responses of fibrinolytic activity and vasopressin in man. Med Sci Sports Exerc 22: 494-500.