Decreased prevalence of cardiac arrhythmias during and after vigorous and prolonged exercise in healthy male marathon runners

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Background Vigorous exercise such as marathon running results in an increased risk of sudden cardiac death. Malignant arrhythmias seem to be the primary cause. However, continuous electrocardiographic monitoring for detection of arrhythmias during a marathon race has not been performed yet.

Methods Twenty male marathon runners (age 45 ± 8 years) free of cardiovascular disease underwent 24-hour Holter monitoring 5 weeks before a marathon race (baseline). Subsequently, wireless Holter monitoring started immediately before the race, recorded up to 70 hours postrace. Electrocardiograms were analyzed for the presence of arrhythmias. Additionally, cardiac troponin, interleukin-6 (IL-6), and electrolytes were assessed prerace and postrace.

Results At baseline Holter recordings, runners showed a median of 9 (interquartile range 3-25) atrial premature complexes (APCs) and 4 (2-16) ventricular premature complexes (VPCs) per 100,000 beats. Compared to baseline, the number of APCs decreased significantly during and 1 hour after the marathon race (0 [0-3] and 0 [0-0], all $P < .001$) as well as the number of VPCs during the race (0 [0-0], $P = .008$). No malignant arrhythmias occurred. Mean postrace levels for troponin and IL-6 were significantly augmented after the race (prerace to postrace: troponin 4 times, IL-6 17 times, all $P < .001$); however, no significant influence of these biomarkers or electrolytes on the prevalence of arrhythmias was observed (all $P > .05$).

Conclusions In this cohort of male runners free of cardiovascular disease, the prevalence of arrhythmias during and after a marathon race was decreased. Arrhythmogenic risk was independent of changes in biomarkers assessing cardiac injury, inflammation, and changes in electrolytes. (Am Heart J 2015;170:149-55.)

Regular moderate physical activity benefits cardiovascular risk factors, prevents cardiovascular disease (CVD), and reduces cardiovascular mortality.[1,2] In contrast, the risk of exercise-related sudden cardiac death (SCD) is increased during vigorous exercise such as marathon running.[2-4] Malignant arrhythmias due to CVD account for the majority of marathon race–related cardiac arrests with an increased risk of SCD[2,5,6] Especially middle-aged men with exercise-induced frequent ventricular premature complexes (VPCs) seem to be at increased risk of death from CVD.[7] Until now, several risk factors have been identified that might promote arrhythmias during exercise; but their importance regarding marathon running has not been clarified.

Structural heart diseases (eg, cardiomyopathy or coronary artery disease) predispose to life-threatening arrhythmias during exercise.[8] It is well established that men with structural heart disease and VPCs have a higher mortality of CVD than those without VPCs.[9-11] Prolonged and vigorous exercise increases the levels of cardiac biomarkers such as troponin, which might reflect cardiac strain or temporary myocardial impairment triggering malignant arrhythmias.[12] Furthermore, exercise induced changes in activity of central nerve system (sympathetic stimulation); and an altered cardiac repolarization may increase the susceptibility to arrhythmias.[8,13] Electrolyte disturbances (particularly hyponatremia) are also known to be a cause of race-related cardiac arrest.[5]

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The purpose of this study was to detect exercise-induced arrhythmias by Holter electrocardiogram (ECG) during a marathon race in a cohort of male runners without structural heart disease.

Materials and methods

Subjects

This substudy, "Enzy-Magic-Holter," was a part of the Enzy-Magic trial, a prospective randomized, double-blind, placebo-controlled, and monocenter trial.[14] This study was conducted in accordance with Good Clinical Practice guidelines, the guiding principles of the Declaration of Helsinki 2008. The study protocol has been approved by the ethics committee of the University Hospital Klinikum rechts der Isar, Munich, Germany (approval reference number 5820/13) and the Federal Institute for Drugs and Medical Devices, Germany (approval reference number 4039219). The trial is registered at ClinicalTrials.gov (NCT01916408). Funding for the study was partly provided by MUCOS Pharma GmbH, Germany. They did not influence the study design or data analyses at any time. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

Male patients who were between 20 and 65 years, had previously successfully completed at least 1 half marathon, intended to participate at the 2013 Munich Marathon, and submitted a written informed consent were included in the study. Patients with the following characteristics were excluded from the study: known allergy against the active ingredient of the study medication or pineapple, papaya, or kiwi; known lactose intolerance, cardiac disease or severe coagulopathy, musculoskeletal or psychiatric disease, neoplasia, acute or chronic infection, renal, liver, or inflammatory disease; and if participants take medications or supplements that influence immune function as well as pharmaceutical treatment for diabetes mellitus or arterial hypertension.

Procedures

Participants were screened to assess inclusion and exclusion criteria within 4 to 5 weeks before the marathon (visit 1, V1). Baseline data were collected, including ECG, physical examination, anthropometry, training history questionnaires, echocardiography, ultrasound of the carotid arteries, and exercise testing with spiroergometry. In 20 of 166 randomly selected participants, Holter monitoring was also performed. At V1, a 24-hour Holter ECG was recorded. In addition, Holter ECG monitoring started immediately before the marathon race (V2) and recorded until 72 hours (V4) after the race.

Blood samples were collected at V1 before the race and immediately (V2), 24 hours (V3), and 72 hours (V4) after the race. Fasting blood samples were drawn from an antecubital vein at all visits, except for the blood collection directly after the race which was in a nonfasted state. To prevent hyponatremia, participants were instructed to ingest 1 to 2 sodium-rich carbohydrate gels (0.5 g sodium/100 g) per hour during the race.

ECG analyses

Resting electrocardiography was performed using standard 12-lead placement and equipment after 5 minutes of rest in a supine position and was digitally recorded for a duration of 10 seconds (Custo Cardio 200). Further standard 3-lead ECG was recorded for 24 hours at V1 (Custo Cardio 500). Starting immediately before the marathon race and recording during the race until 72 hours after the race, we used a single-lead wireless Holter monitoring that was detected by a breast strap (Custo Cardio Guard). All ECGs were recorded and analyzed with custo diagnostics 4.3 provided by Custo Med GmbH, Ottobrunn, Germany. All ECGs were recorded with a speed of 50 mm/s and a voltage scale equivalent of 10 mm/mV. All ECG patterns were evaluated according to standard clinical criteria.[15] All ECG reports were evaluated for quality and irregularities by 2 of the 3 physicians, including at least 1 cardiologist. All ECG investigators were blinded and tested for interobserver consistency.

Normal ECG changes due to physical exertion were distinguished from suspicious abnormalities according to current guidelines.[16] The absolute values of the following resting-ECG parameters were investigated and described according to the following[17]: HR, P wave, PQ interval, QRS duration, QT, and QTc interval calculated by Bazett method.[16] Holter ECGs were analyzed for the absolute numbers of atrial and ventricular premature complexes, *sinus bradycardia* (defined as ≤30 beat/min), sinus pauses (≥3 seconds), and atrial or ventricular flutter or fibrillation.

Interleukin-6, high-sensitivity cardiac troponin T, and serum electrolytes

Inflammatory and cardiac parameters as well as serum electrolytes were determined as described previously.[12,17] The interassay coefficient of variation under actual routine conditions was as follows: interleukin-6 (IL-6): 8.5% at a concentration of 4.6 ng/L, high-sensitivity cardiac troponin T (hs-cTnT): 3.5% at 22 ng/L, potassium: 0.63% at 4.2 mmol/L, sodium: 0.41% at 146 mmol/L, magnesium: 0.58% at 0.88 mmol/L, and calcium: 0.68% at 2.56 mmol/L. Expected values for salivary cortisol (Salivette, Sarstedt) range from 0.04 to 1.41 ng/mL.

Statistical analysis

Data analysis was performed using PASW Statistics 21 (SPSS, Inc, Chicago, IL).

Quantitative statistics are described as means with their SD and ranges (for normally distributed data) or medians with interquartile ranges (IQR; for nonnormally distributed data; IQR = 25th-75th percentile). For dehydration-dependent