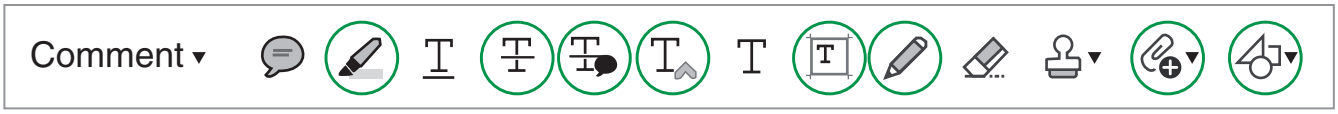
Page Proof Instructions and Queries

Journal Title: European Journal of Preventive Cardiology (CPR)

Article Number: 820203

Thank you for choosing to publish with us. This is your final opportunity to ensure your article will be accurate at publication. Please review your proof carefully and respond to the queries using the circled tools in the image below, which are available **by clicking "Comment"** from the right-side menu in Adobe Reader DC.*

Please use *only* the tools circled in the image, as edits via other tools/methods can be lost during file conversion. For comments, questions, or formatting requests, please use T. Please do *not* use comment bubbles/sticky notes.



*If you do not see these tools, please ensure you have opened this file with Adobe Reader DC, available for free at get.adobe.com/reader or by going to Help > Check for Updates within other versions of Reader. For more detailed instructions, please see us.sagepub.com/ReaderXProofs.

No.	Query
	Please confirm that all author information, including names, affiliations, sequence, and contact details, is correct.
	Please review the entire document for typographical errors, mathematical errors, and any other necessary corrections; check headings, tables, and figures.
	Please confirm that the Funding and Conflict of Interest statements are accurate.
	Please ensure that you have obtained and enclosed all necessary permissions for the reproduction of artistic works, (e.g. illustrations, photographs, charts, maps, other visual material, etc.) not owned by yourself. Please refer to your publishing agreement for further information.
	Please note that this proof represents your final opportunity to review your article prior to publication, so please do send all of your changes now.
AQ: 1	Ref 5: please provide precise date of e publication and the doi number
AQ: 2	Please provide in-text citations of refs 8 and 9

Research letter

European Journal of Preventive Cardiology

ESC European Society of Cardiology

European Journal of Preventive Cardiology
0(00) 1–3

DOI: 10.1177/2047487318820203
journals.sagepub.com/home/ejpc

SAGE

The acute impact of a high-altitude ultra-trail race on the ECG

Alessandro Zorzi[1], Flavio D'Ascenzi[2], Francesca Anselmi[2], Lucia Spera[2], Aladino Ibrahim[2], Chiara Ceccon[2], Sergio Mondillo[2], Domenico Corrado[1], Francesco Antonini-Canterin[3] and Leopoldo Pagliani[3]

Ultra-endurance competitions, defined as sports events that exceed 6 hours in duration, are becoming increasingly popular, but there is concern that these extreme physical activities may carry negative health consequences in particular in older athletes.[1] A previous study demonstrated that athletes engaging in ultra-endurance sports show a transient rise in cardiac biomarkers and right ventricular dysfunction after a competition.[2] It has been hypothesised that repetitive bouts of myocardial damage may translate into an adverse arrhythmic remodeling exposing the athlete to the risk of sudden cardiac death.[3] However, the consequences of ultra-endurance sports activity on the heart rhythm is still a debated issue. The aim of our study was to evaluate the acute effects on heart rhythm after an endurance (48 km) and ultra-endurance (120 km) high-altitude race. We used a portable single-lead electrocardiogram (ECG) recording device which allowed us to recruit a large number of participants.

The study was performed during the 2018 North Face Lavaredo Ultra Trail mountain run (Cortina D'Ampezzo, BL, Italy). Athletes running the Lavaredo Ultra Trail (120 km and elevation gain of 5800 m) and the Cortina Trail (48 km and elevation gain of 2600 m) were offered participation in the study on a voluntary basis. We recorded the ECG with the US Food and Drug Administration (FDA)-approved MyDiagnostick device (Applied Biomedical Systems BV, The Netherlands). Holding the device by the handles with both hands, it records a 1-minute, single-lead ECG tracing. Recordings were performed at baseline the day before the run and immediately after the run. Variables that were assessed at the time of enrollment were age, gender, years of sports activity and average number of hours of training per week.

ECG tracings were reviewed independently by two cardiologists (AZ, FD) and a third (LP) was consulted in case of disagreement. Athletes with at least one unreadable recording or those who withdrew from the run or arrived beyond the time limit were excluded. The ECGs were analysed for heart rate, QRS duration, QT-interval duration corrected according to the Bazett correction formula and the presence of at least one beat of presumed ventricular origin (different QRS morphology and full compensatory pause) during the 1-minute recording, hereafter called premature ventricular beat (PVB). As the P waves were clearly identifiable in both tracings in only 176 of 545 (32%) athletes and many showed irregular RR intervals that could be caused by either sinus arrhythmias or premature atrial beats/atrial fibrillation, analysis of supraventricular arrhythmias was not performed. Analysis of the QT-interval in both tracings was possible in 498 (91%) athletes.

Data are expressed as number (%) or mean (± standard deviation). Dichotomous variables were compared with the chi-square or the Fisher exact test as appropriate. Continuous variables were compared with the Wilcoxon signed-rank test for paired samples (comparison between pre-run and post-run data) or the rank sum test for independent samples (comparison between athletes who run the 120 and 48 km run). A two-tailed $P < 0.05$ was considered statistically significant. All analyses were performed using SPSS 18 (SPSS Inc., Chicago, IL, USA).

Athletes who agreed to participate were 315 of 1391 who completed the 48 km run and 248 of 1179 who completed the 120 km run. Eighteen athletes were excluded because either the pre or the post-run ECG was unreadable due to low QRS voltages and/or

[1]Department of Cardiac, Thoracic, Vascular and Public Health sciences, University of Padova, Italy
[2]Department of Medical Biotechnologies, University of Siena, Italy
[3]Department of Cardiology, High Specialization Rehabilitation Hospital, Italy

Corresponding author:
Flavio D'Ascenzi, Department of Medical Biotechnologies, Division of Cardiology, University of Siena, Viale M Bracci 16, 53100 Siena, Italy.
Email: flavio.dascenzi@unisi.it

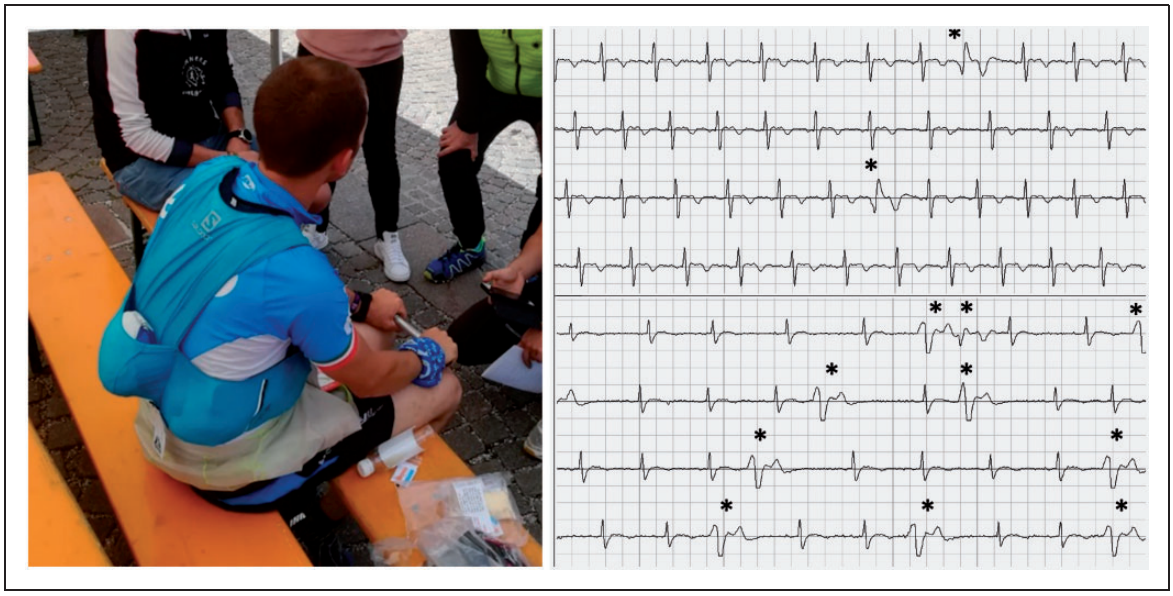


Figure 1. Example of two post-run ECG recordings with the MyDiagnostick device showing premature ventricular beats that were not present before the race.

muscular artifacts. Hence, a total of 545 athletes (83% men, mean age 40 ± 9 years), 241 running the 120 km race and 304 running the 50 km race, were included. Athletes running the 120 km race were more often men (92% vs. 77%, $P < 0.001$) and showed a similar age (41 ± 8 vs. 40 ± 9 years, $P = 0.40$) to those running the 48 km race.

At baseline, athletes showed a mean heart rate of 64 ± 14 beats per minute (bpm) and a mean QRS duration of 92 ± 18 ms. Three (0.5%) showed at least one PVB. Analysis of QTc-interval duration showed a mean value of 412 ± 25 ms. After the race, athletes showed a higher heart rate (91 ± 13 bpm, $P < 0.001$), a similar QRS duration (94 ± 16 ms, $P = 0.32$) and a longer QTc-interval duration (447 ± 25 ms, $P < 0.001$) as compared with baseline data. The number of athletes showing at least one PVB increased significantly to 18 (3.3%, $P = 0.004$) as compared with the pre-race evaluation (Figure 1 and Supplementary Figure 1).

There was no statistically significant difference in the prevalence of PVBs after the run according to age, gender and run length. Athletes engaged in the 120 km run showed a slightly longer but statistically significant post-run QTc-interval (450 ± 24 vs. 444 ± 25 ms, $P = 0.009$) while the post-run QRS duration was similar between the two groups. There was no statistically significant correlation between post-run QRS duration and QTc-interval and age or gender. The presence of PVBs after the race was not correlated with the QTc-interval.

One of the most debated issues in sports cardiology is whether intense exercise enhances the burden of ventricular arrhythmias. Recent studies showed that both young athletes and older endurance athletes show a prevalence of ventricular arrhythmias on 24-hour ambulatory ECG monitoring similar to sedentary individuals.[4,5] This finding is in line with our observation that the prevalence of one or more PVBs during a baseline 1-minute ECG recording was low (0.5%) also in middle-aged athletes (mean age 40 years) engaging in endurance or ultra-endurance mountain runs when they are evaluated at baseline before the competition. However, we found that the prevalence of PVB increases by six times after the run, in parallel with the prolongation of QT-interval. This observation suggests that prolonged intense physical activity may cause a transient increase in the electrical instability of the ventricular myocardium, secondary to myocardial fatigue and to electrolytic imbalances that are typically found after ultra-endurance competitions in athletes.[2,6] We may speculate that increased ventricular ectopic activity and QT prolongation recorded shortly after an intense and prolonged exercise may contribute to the increased risk of arrhythmias that persists after the finish line of endurance competitions.[7]

Acknowledgements

The authors would like to thank Medtronic Italia's unconditional support for technical support and device usage specifications. The authors would like to thank the organising committee of the North Face Lavaredo Ultra Trail mountain run in the person of Mrs Cristina Murgia for organisational help.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

References

1. Chugh SS and Weiss JB. Sudden cardiac death in the older athlete. *J Am Coll Cardiol* 2015; 65: 493–502.
2. La Gerche A, Burns AT, Mooney DJ, et al. Exercise-induced right ventricular dysfunction and structural remodelling in endurance athletes. *Eur Heart J* 2012; 33: 998–1006.
3. La Gerche A, Claessen G, Dymarkowski S, et al. Exercise-induced right ventricular dysfunction is associated with ventricular arrhythmias in endurance athletes. *Eur Heart J* 2015; 36: 1998–2010.
4. Zorzi A, De Lazzari M, Mastella G, et al. Ventricular arrhythmias in young competitive athletes: prevalence, determinants, and underlying substrate. *J Am Heart Assoc* 2018; 7(pii): e009171.
5. Zorzi A, Mastella G, Cipriani A, et al. Burden of ventricular arrhythmias at 12-lead 24-hour ambulatory ECG monitoring in middle-aged endurance athletes versus sedentary controls. *Eur J Prev Cardiol*. Epub ahead of print 2018. DOI: [AQ1].
6. Scotney B and Reid S. Body weight, serum sodium levels, and renal function in an ultra-distance mountain run. *Clin J Sport Med* 2015; 25: 341–346.
7. Hart L. Marathon-related cardiac arrest. *Clin J Sport Med* 2013; 23: 409–410.
8. Kim JH, Malhotra R, Chiampas G, et al. Race Associated Cardiac Arrest Event Registry (RACER) Study Group. Cardiac arrest during long-distance running races. *N Engl J Med* 2012; 366: 130–140 [AQ2].
9. Zorzi A, Cipriani A and Corrado D. Circumstances of cardiac arrest during sports activity recorded on video. *Eur J Prev Cardiol* 2018; 25: 1452–1454.