European Heart Journal (2008) **29**, 1800–1802
doi:10.1093/eurheartj/ehn273

EDITORIAL

The risk of marathon runners–live it up, run fast, die young?

Axel Schmermund*, Thomas Voigtländer, and Bernd Nowak

Cardioangiologisches Centrum Bethanien, Im Prüfling 23, D-60389 Frankfurt am Main, Germany

Online publish-ahead-of-print 13 June 2008

This editorial refers to 'Running: the risk of coronary events. Prevalence and prognostic relevance of coronary atherosclerosis in marathon runners'† by S. Möhlenkamp *et al.*, on page 1903

Marathon running enjoys an astonishing popularity. Because of the enormous number of applicants, it is quite difficult to get a starting place for one of the marathon races in Berlin, London, or New York. Almost every European city appears to have its own marathon race in the months between April and October. Regularly, out of the tens of thousands of runners, one or two succumb to an acute coronary syndrome or sudden arrhythmias.

It is quite evident that the extreme exertion of a marathon race, as mentally rewarding as it may be, offers little benefit in terms of health and longevity. Indeed, in clinically healthy runners, markers of cardiac injury are elevated after a race.[1,2] An inverse relationship between myocardial injury and the amount of training for the race has been described, with the greatest amount of injury incurred by runners with the least training mileage.[2] However, the clinical relevance of acute post-race elevations in markers of myocardial injury remains open. There is little evidence to suggest permanent cardiac damage in healthy runners, but the issue is complex. With increasingly sophisticated biomarkers and imaging methods to measure cardiac damage—what is a healthy runner?

Möhlenkamp and colleagues from the University Clinic Essen, Germany, have collected unique data in 108 male recreational marathon runners aged $\geq$50 years.[3] The runners had completed at least five marathon races during the preceding 3 years and were free of clinical coronary heart disease, diabetes mellitus, and other major cardio-renal disease. An important aspect of this study is that the authors in part are investigators of the Heinz Nixdorf Recall study, a large epidemiological study in the general, unselected population in the Ruhr area in Germany. This ongoing study examines the predictive value of state-of-the-art risk factor analysis compared with coronary calcium measurements and other methods regarding cardiovascular 'hard' end-points in >4800 subjects.[4]

The data on the marathon runners were obtained in analogy to the Heinz Nixdorf Recall study, providing for the most comprehensive characterization of marathon runners presented so far. Of particular interest, coronary artery calcium assessment was for the first time available in a sizeable group of marathon runners. Coronary calcium scanning allows for an *in vivo* quantitative measure of coronary atherosclerosis in asymptomatic subjects[4,5] and is thus well suited to detect occult disease. An increased calcium score, signifying advanced coronary atherosclerosis, is associated with an increased cardiovascular risk and has prognostic implications over and above the traditional cardiovascular risk factor analysis.[5–7]

The major findings of the Essen Marathon study can be summarized as follows. (i) Marathon runners had a much more favourable risk factor profile compared with age-matched males in the Heinz Nixdorf Recall study. (ii) Coronary calcium was found less frequently in marathon runners than in age-matched controls from the Heinz Nixdorf Recall study. (iii) Compared with males with a similarly low risk profile, coronary calcium was more frequent in the marathon runners, and their coronary calcium score was higher. The amount of training activity (weekly metabolic equivalents) was not associated with coronary calcium scores. (iv) Using cardiac magnetic resonance imaging (MRI) in 102 runners, late gadolinium enhancement with a subendocardial distribution typical for ischaemic scar formation was observed in five subjects (5%). In another seven subjects (7%), late enhancement with a different intramural distribution was seen. Overall, late gadolinium enhancement was associated with high coronary calcium scores and an increased number of completed marathon races. (v) During a mean follow-up of 21 months, four coronary events occurred, including resuscitation of two runners after physical exertion. Accordingly, these marathon runners with a mean age of 57 years had a 10-year event rate ('hard events' plus revascularization) of 21%, although their mean Framingham risk score

The opinions expressed in this article are not necessarily those of the Editors of the *European Heart Journal* or of the European Society of Cardiology.

* Corresponding author. Tel: +49 69 9450 28 0, Fax: +49 69 461613, Email: A.Schmermund@ccb.de

† doi:10.1093/eurheartj/ehn163

placed them in a low-risk category. All coronary events occurred in runners with a coronary calcium score >100.

As is elegantly discussed by the authors, the question arises of whether marathon running in and by itself plays a causal role regarding coronary atherosclerotic plaque formation (i.e. coronary calcification) and myocardial infarction as determined by cardiac MRI. As a note of caution, the majority of runners with myocardial late gadolinium enhancement had myocardial fibrosis distinct from the typical ischaemic subendocardial distribution. Classically, this non-subendocardial distribution is explained by mechanisms other than ischaemia, e.g. myocarditis, with late enhancement appearing in bands rather than being patchy.[8] However, experimental animal studies have demonstrated patchy necrosis and late enhancement with a seemingly random myocardial distribution after coronary microembolization.[9,10] Can subclinical plaque rupture and inflammation cause such MRI findings in humans? If so, does marathon running play a role in this regard? Detailed results from the ongoing study on myocardial scar formation and its prognostic significance in the runners are eagerly awaited.

Marathon running is part of a healthy lifestyle. There is overwhelming evidence for the cardiovascular protective effects of physical activity.[11] In the current report, weekly energy expenditure (probably corresponding to training mileage) was not associated with the amount of coronary artery calcium. However, the number of completed marathon races was. Is training for a marathon healthy—as previous data suggest and common belief holds—while the race itself is risky?

The Framingham risk of marathon runners in the current report was only about half the risk observed in age-matched controls. At first glance, the amount of coronary calcium and myocardial scar ormation appears all the more disturbing. However, we believe participant recruitment for the marathon study may account for some of these findings. Subjects participating in the Heinz Nixdorf Recall study served as a control group. They were approached by the investigators on the basis of a random sample from German mandatory citizen registries. Thus, they represent a truly unselected population.[4] The marathon runners were mainly recruited by advertising. Who among recreational marathon runners would undergo a lengthy cardiovascular examination which did *not* include formal performance diagnostics, but rather blood tests and cardiac imaging? There may have been a selection bias favouring runners with health worries to volunteer for this study. More than 50% were former smokers. One can deduce that they had not been sportsmen all their lives but rather took up running relatively late. Certainly, some were pondering about running as a means to reverse the effects of a decade-long unhealthy lifestyle.

The current report demonstrates a high prevalence of advanced coronary atherosclerosis and myocardial scar formation in seemingly healthy marathon runners aged >50 years. Cardiologists will have to consider these findings when seeing a marathon running patient aged >50 years who asks about his individual risk and prognosis. Active runners usually have a favourable actual risk factor profile (which does not necessarily mean it has always been that way) and are able to perform exercise stress testing very well. An uneventful stress test does not preclude severe coronary artery disease in these subjects.[12] In the current study, all four coronary events occurred in runners with a coronary calcium score >100, signifying advanced coronary atherosclerosis. This underscores the potential value of coronary calcium scanning in this setting. Awaiting further data, a calcium score >100 should alert the attending physician towards an increased risk in his marathon running male patient.

Training and competition need to be tailored to each individual's cardiorespiratory fitness and risk status. Cardiologists with the respective expertise should be intimately involved in this process. They need to consider not only the actual risk factor profile, but also the possibility of cumulative risk exposure due to previous smoking, overweight, or genetic predisposition. Frequently, formal performance diagnostics with determination of the anaerobic threshold will help to avoid excessive exhaustion. Running at the right pace is beneficial,[11] and cardiologists have an important role in defining the dose and intensity of running. At times, they will have to advise patients to refrain from competitive running. After having lived it up for a long time, it may be prudent for a patient not to run so fast (and long).

The Essen marathon study has the unique merit of demonstrating a high prevalence of advanced coronary atherosclerosis and myocardial scar formation in seemingly healthy marathon runners aged >50 years. Regular running in mid-life was unable to prevent this damage. Whether marathon racing itself had a causal role in this respect remains open. However, it is quite plausible that some subjects with prior risk factor exposure, endothelial dysfunction and increased coronary atherosclerosis are vulnerable to developing further damage in the setting of extreme physical exertion. Although much remains to be learned, it is clear that cardiologists have an important role in determining their patients' risk and giving advice to those who are aspiring marathon runners.

Conflict of interest: none declared.

References

1. Scharhag J, Herrmann M, Urhausen A, Haschke M, Herrmann W, Kindermann W. Independent elevations of N-terminal pro-brain natriuretic peptide and cardiac troponins in endurance athletes after prolonged strenuous exercise. *Am Heart J* 2005;**150**:1128–1134.
2. Neilan TG, Januzzi JL, Lee-Lewandrowski E, Ton-Nu TT, Yoerger DM, Jassal DS, Lewandrowski KB, Siegel AJ, Marshall JE, Douglas PS, Lawlor D, Picard MH, Wood MJ. Myocardial injury and ventricular dysfunction related to training levels among nonelite participants in the Boston marathon. *Circulation* 2006; **114**:2325–2333.
3. Möhlenkamp S, Lehmann N, Breuckmann F, Bröcker-Preuss M, Nassenstein K, Halle M, Budde T, Mann K, Barkhausen J, Heusch G, Jöckel KH, Erbel R; on behalf of the Marathon Study Investigators and the Heinz Nixdorf Recall Study Investigators. Running: the risk of coronary events. Prevalence and prognostic relevance of coronary atherosclerosis in marathon runners. *Eur Heart J* 2008; **29**:1903–1910. First published on April 21, 2008. doi:10.1093/eurheartj/ehn163.
4. Erbel R, Möhlenkamp S, Lehmann N, Schmermund A, Moebus S, Stang A, Grönemeyer D, Seibel R, Mann K, Volbracht L, Dragano N, Siegrist J, Jöckel KH, on behalf of the Heinz Nixdorf Recall Study Investigative Group. Sex related cardiovascular risk stratification based on quantification of atherosclerosis and inflammation. *Atherosclerosis* 2008:**197**:662–672.
5. Erbel R, Möhlenkamp S, Kerkhoff G, Budde T, Schmermund A. Non-invasive screening for coronary artery disease: calcium scoring. *Heart* 2007;**93**: 1620–1629.
6. Greenland P, Bonow RO, Brundage BH, Budoff MJ, Eisenberg MJ, Grundy SM, Lauer MS, Post WS, Raggi P, Redberg RF, Rodgers GP, Shaw LJ, Taylor AJ, Weintraub WS, Harrington RA, Abrams J, Anderson JL, Bates ER, Grines CL, Hlatky MA, Lichtenberg RC, Lindner JR, Pohost GM, Schofield RS, Shubrooks SJ Jr, Stein JH, Tracy CM, Vogel RA, Wesley DJ; American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography); Society of Atherosclerosis Imaging and

Prevention; Society of Cardiovascular Computed Tomography. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography). *Circulation* 2007;**115**:402–426.
7. Detrano R, Guerci AD, Carr JJ, Bild DE, Burke G, Folsom AR, Liu K, Shea S, Szklo M, Bluemke DA, O'Leary DH, Tracy R, Watson K, Wong ND, Kronmal RA. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med* 2008;**358**:1336–1345.
8. Vöhringer M, Mahrholdt H, Yilmaz A, Sechtem U. Significance of late gadolinium enhancement in cardiovascular magnetic resonance imaging (CMR). *Herz* 2007; **32**:129–137.
9. Möhlenkamp S, Beighley PE, Pfeifer EA, Behrenbeck TR, Sheedy PF 2nd, Ritman EL. Intramyocardial blood volume, perfusion and transit time in response to embolization of different sized microvessels. *Cardiovasc Res* 2003;**57**:843–852.
10. Breuckmann F, Nassenstein K, Konietzka I, Bucher C, Sandner T, Kaiser G, Naber C, Konorza T, Haude M, Aker S, Skyschally A, Gres P, Erbel R, Heusch G, Barkhausen J. Visualization of experimental coronary microembolization using contrast enhanced cardiac MRI. *J Cardiovasc Magn Res* 2007; **9**:339.
11. Thompson PD, Buchner D, Pina IL, Balady GJ, Williams MA, Marcus BH, Berra K, Blair SN, Costa F, Franklin B, Fletcher GF, Gordon NF, Pate RR, Rodriguez BL, Yancey AK, Wenger NK; American Heart Association Council on Clinical Cardiology Subcommittee on Exercise, Rehabilitation, and Prevention; American Heart Association Council on Nutrition, Physical Activity, and Metabolism Subcommittee on Physical Activity. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation* 2003;**107**:3109–3116.
12. Tunstall-Pedoe DS. Marathon cardiac deaths: the London experience. *Sports Med* 2007;**37**:448–450.

The above article uses a new reference style being piloted by the EHJ that shall soon be used for all articles.