Is Marathon Running Hazardous to Your Cardiovascular Health? The Jury Is Still Out

Kibar Yared, MD, FRCPC
Malissa J. Wood, MD

In this issue of Radiology, Breuckmann et al report on the prevalence and pattern of late gadolinium enhancement (LGE) in 102 male marathon runners aged 50 or more years (1). Predominantly subendocardial regions of LGE typical of myocardial infarction (dubbed the coronary artery disease [CAD] pattern) were distinguished from regions with a predominantly midmyocardial patchy pattern of LGE (dubbed the non–CAD pattern) with cardiac magnetic resonance (MR) imaging. The prevalence of LGE was higher in marathon runners than in control subjects; however, this difference was not significant ($P = .077$).

Adenosine perfusion defects were found in the same territory as LGE in runners who had a CAD pattern of LGE. In contrast, no perfusion defects were found in runners with a non–CAD pattern of LGE. Runners without LGE and control subjects did not undergo adenosine perfusion imaging.

The first individual known to have completed the marathon distance died at the conclusion of his 26-mile journey, which—if history is correct—was run soon after he completed a 280-mile round-trip journey from Athens to Sparta (2). Since that time, a great deal of mystique and curiosity has been associated with long-distance running. There has been active debate about whether the overall health benefits of regular physical exercise outweigh the potentially harmful cardiovascular effects. While the benefits of repetitive high-intensity exercise are well known, the harmful consequences of this activity are less certain.

A number of theories have arisen in an attempt to explain the cardiac MR findings described in this study population. These include an exertion-induced, direct myocardial toxic effect leading to myocardial and cellular injury with resultant fibrosis and scarring. Another possibility is that the LGE detected in this study results from myocardial ischemia from large- or small-vessel CAD. It is also possible that regular endurance exercise unmasks cellular and molecular defects that result in myocardial necrosis and scarring even though the cause-and-effect relationship between these two entities has yet to be elucidated. Alternatively, exercise may increase the susceptibility of the myocardium to injury from microbiologic organisms.

Concerns about possible myocardial necrosis and fibrosis resulting from endurance exercise have been raised for years. While the sedentary community has been eager to highlight the detrimental long-term effects of regular endurance exercise, to our knowledge, there has been no conclusive evidence to directly support this claim. There is, however, an abundant body of literature to support the positive physiologic and biochemical response of healthy myocardium after exposure to prolonged exercise.

Numerous authors have reported biochemical evidence of a possible myocardial insult, including an elevation in the serum troponin level, following the completion of an endurance event (3,4). To our knowledge, the cause of this increase has not been determined, and the link between the postrace elevation in the serum troponin level (5) or creatinine kinase–MB fraction (6) and demonstrable myocardial ischemia has yet to be made. In healthy runners, the release of serum troponin occurs fairly early in the course of endurance exercise, and prolonged exercise is not necessarily required to stimulate the mechanisms responsible for its release (7). Mechanisms postulated to be responsible for the exercise-induced release of serum troponin include myocardial ischemia, increased permeability of myocardial membranes leading to leakage of se-
rum troponin, increased right or left ventricular strain due to hemodynamic changes, and release of serum troponin by peripheral stem cells (8). Our group and other researchers have demonstrated variable acute biochemical responses to marathon running that are seemingly dependent on the runner’s length of training, prior marathon history, and marathon finish times, with traditional cardiac risk factors having no relationship with the increase in serum troponin levels (9). Data about the subject’s fitness level (including his training mileage), marathon finish times, and time since his most recent marathon would help better define this population and perhaps help explain the changes seen with cardiac MR imaging.

Myocardial function appears to be only temporarily affected by prolonged exercise. These physiologic changes may be a direct result of prolonged tachycardia and its associated sequelae: changes in myocardial contractility and compliance due to cellular and molecular energy deficits, relative myocardial ischemia, and myocardial fatigue. Follow-up studies in endurance athletes have demonstrated only minor persistent abnormalities (10). Data on left ventricular structural and functional changes in this study population would shed more light on the mechanisms of myocardial adaptation to endurance exercise and would help correlate the changes seen at cardiac MR imaging.

MR imaging is rapidly becoming the reference standard in the evaluation of myocardial scarring, be it secondary to ischemic heart disease or some other disorder, such as inflammatory or infectious diseases of the myocardium, cardiomyopathy, cardiac neoplasms, or congenital or genetic cardiac abnormalities.

To our knowledge, detailed cardiac MR evaluation of endurance athletes had not been performed prior to the study of Breuckmann et al. (1). We believe they are the first to report on the prevalence of LGE in athletes of such age and caliber. Of the 102 runners, 12 (12%) had LGE; however, only four (4%) of the 102 age-matched control subjects had LGE. Breuckmann et al reported two patterns of LGE: a CAD pattern (specific to a coronary territory) and a non–CAD pattern. LGE in a specific coronary territory reflects an acute ischemic injury and occurs only in areas of irreversibly injured myocardium. As predicted by the wavefront theory of ischemia and/or infarction, myocardial necrosis (and eventual scar formation) begins at the subendocardium and, to a variable extent, spreads toward the epicardium. Thus, LGE that involves the subendocardium generally reflects ischemic damage and may be referred to as the CAD pattern. LGE of any other pattern, including midmyocardial and/or subepicardial LGE, may be seen in patients with other nonischemic syndromes (mentioned previously) and, in turn, may be referred to as the non–CAD pattern. Breuckmann et al then attempted to correlate the presence of LGE with perfusion defects on adenosine perfusion cardiac MR images. Only subjects with LGE underwent perfusion imaging. Breuckmann et al concluded that the presence of perfusion defects and the corresponding LGE in a given coronary territory placed the runners at higher-than-anticipated risk for a coronary event. While this may be true, the ischemic burden on subjects who do not have LGE remains unknown. These subjects would have served as an important control subpopulation, and additional perfusion imaging of these individuals would have enabled Breuckmann et al to more accurately estimate the risk incurred by runners with LGE. Furthermore, correlation of areas of LGE with abnormalities in wall motion may have helped to clarify the ischemic origin of such changes.

Breuckmann et al (1) presented several theories to explain the patterns of LGE. Although most of their theories are feasible, we cannot ignore or minimize other nonischemic causes of LGE, such as myocarditis, hypertensive or hypertrophic cardiomyopathy, and athlete’s heart. Left ventricular structural and functional data also may have helped eliminate some of these other diagnoses.

It is curious that LGE was located in the territory of the left anterior descending artery in runners with a CAD pattern of LGE, whereas LGE was located in the right coronary artery territory in the other two groups. CAD does seem to occur more often in the left anterior descending artery; however, it usually occurs in patients younger than 40 years (11). The cross-sectional area of the left coronary artery increases with athletic training (12). Furthermore, physical exercise is an important stimulus for plaque disruption (13). It is conceivable that the larger coronary artery (the left anterior descending artery) will receive the larger volume of blood during high-intensity exercise. When combined with vigorous cardiac contraction, this may predispose the subject to increased shear stress and plaque rupture or erosion and subsequent microembolization of overlying thrombus, thereby creating a CAD pattern of LGE. It is unclear why LGE clustered in the right coronary artery territory (nine of 17 segments), even in the control group and runners with the non–CAD pattern of LGE in the Breuckmann et al study. As the pattern of LGE is presumably not subendocardial, the location of LGE should not have any bearing.

The higher prevalence of LGE in marathon runners is slightly concerning; therefore, we must examine this cohort more closely. Of the 12 subjects with LGE, five had a pattern typical of myocardial ischemia. Marathon runners volunteered for this study, and this may have led to a recruiting bias in that runners who were concerned about underlying cardiovascular disease were more likely to enroll in the study. The subjects involved were apparently healthy men, 51.8% of whom were former smokers and 4.6% of whom were current smokers (14). The percentage of participants who were current or former smokers was much greater than that in the present study. Fewer than 5% of participants in the marathon research study conducted by Neilan et al (4) reported a smoking history. Neither cardiac catheterization nor computed tomographic (CT) angiography was performed in these subjects; thus, any conclusions about underlying significant CAD as a possible cause of LGE would
be somewhat speculative. On the other hand, given the runners’ smoking history and age, it is conceivable that LGE is solely a result of CAD and the associated endothelial dysfunction. In fact, runners with LGE had higher coronary artery calcium scores than did runners without LGE (14). We cannot be certain that marathon running contributes directly to LGE; rather, it may uncover underlying CAD. More importantly, this study has shown that conversion to a healthier lifestyle that includes running may not resolve the coronary and myocardial damage created by many years of cigarette smoking. While many of the previously described changes in cardiac function that occur in response to prolonged exercise are seen in healthy young subjects, it is possible that the presence of underlying microvascular disease could result in more permanent changes.

Moreover, we cannot ignore the fact that the presence of LGE portends a worse prognosis (15). Breuckmann et al (1) followed up the runners for a mean of 21 months ± 3 (standard deviation) after initial presentation and found a diminished event-free survival rate in runners with LGE. It is important to remember that only four events occurred during the follow-up period (three in runners with LGE, one in a runner without LGE). Unfortunately, we did not receive event-free survival data on the control group; thus, we cannot be sure that the event-free survival rate in runners differs significantly from that in sedentary individuals. Furthermore, the follow-up period was short, and it is difficult to predict what will happen to these survival curves 5 and 10 years in the future.

Nonetheless, this is an important study. Certainly, one cannot ignore the smoking history of these participants. At this time, there is not enough evidence to implicate marathon running in the development of a dangerous substrate for coronary events. On the other hand, it is becoming clear that an improvement in lifestyle, even with complete cessation of risky activities, may not completely eliminate the potentially dangerous sequelae of such activities. Perhaps individuals with a history of smoking, hypertension, and/or hyperlipidemia or a family history of CAD who wish to undergo exhaustive physical exercise should undergo a thorough medical evaluation that could include noninvasive CT coronary angiography or cardiac MR imaging to exclude significant CAD and the presence of preexisting myocardial fibrosis and/or scarring.

References


