Assessment of Coronary Atherosclerosis Using Calcium Scores in Short- and Long-Distance Runners

Omar Jafar; Jason Friedman, MD; Ian Bogdanowicz; Aamir Muneer; Paul D. Thompson, MD, FACC; Julie Ling, MD, FACC; Anthony Messina, MD, FACC; Michael Yen, MD, FACC; Dorothy Wakefield, MS; Pranav Varanasi; and Kamran Haleem, MD, FACC

Abstract

Objective: To determine whether there is a "dose-dependent" relationship between coronary atherosclerosis and the burden of exercise.

Background: Recent data have suggested there may be negative consequences related to strenuous exercise. Previous studies evaluating the presence of coronary atherosclerosis as assessed by coronary calcium scores have been confounded by the presence of other cardiovascular risk factors. We aimed to assess whether there was a relationship between the burden of coronary calcium and the amount of running in a local cohort.

Patients and Methods: Eighty-five runners were screened on the basis of an exercise questionnaire that was later used to determine the experimental groups from January 2016 through October 2016. Twenty-nine individuals were excluded from the study because of the presence of preexisting cardiovascular risk factors. Runners were divided into 3 categories: Group A comprised runners who had competed in at least 10 ultramarathons and/or Ironman competitions in 10 years. Group B included runners who had participated in more than 9 marathons over 10 years. Group C comprised runners who had competed in more than 9 shorter races over 10 years. Coronary artery calcium (CAC) scores were assessed by computed tomography. Statistical analysis was performed using chi-square analyses. Logistic regression models were used to assess the relationship between runner groups and calcium score greater than 100, calcium score percentile, and calcium score greater than 0.

Results: There were no differences between groups A and B for CAC scores greater than 0 or greater than 100, and a similar percentage of group A and B athletes had scores greater than the 50th percentile. Groups A and B were combined for further analysis. Among those runners participating in extreme distance running (groups A and B), 73% of runners had CAC scores greater than 0 whereas only 21% of group C runners had CAC scores greater than 0 (P=.0002). Moreover, 70% of group A + B athletes ranked above the 50th percentile of their age and sex as assessed by a national database (Hoff JA, Chomka EV, Krainik AJ, Daviglus M, Rich S, Kondos GT. Age and gender distributions of coronary artery calcium detected by electron beam tomography in 35,246 adults. *Am J Cardiol*. 2001;87(12):1335-1339), whereas only 19% of group C runners were ranked above the 50th percentile (P=.0001). One-third of runners in group A + B had CAC scores greater than 100 as compared with only 12% of runners in group C (P=.05). When controlling for age, sex, and number of years running, the study group was not a significant predictor of CAC greater than 100 (P=.12). In contrast, group A + B was 10 times more likely than group C to have CAC scores in the 50th percentile or greater (P=.02) and 8.8 times more likely to have a abnormal calcium score when controlling for covariates (P=.03).

Conclusion: A significantly higher rate of coronary artery calcification existed in long-term marathon, ultramarathon, and extreme runners than in submarathon runners. Marathoners and ultramarathoners also had a higher incidence of calcification, as well as higher average plaque burden, as compared to a standard database. Marathoners and ultramarathoners also had above-average coronary calcium scores as compared to a national database.

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The cardiovascular benefits of regular aerobic exercise are well documented. However, recent evidence suggests that long-term strenuous exercise may have deleterious cardiovascular effects. Data from large-scale prospective studies have indicated that the increased longevity ascribed to regular physical activity may vanish as the duration and intensity of the exercise exceeds a moderate threshold.[1-6] Multiple studies find a "U- or J-shaped" relationship between exercise volumes and mortality, with the lowest mortality rates occurring at modest activity levels and the highest rates occurring in individuals who exercise the most and at high intensity. Individuals at the highest end of the spectrum for activity actually have mortality rates similar to the sedentary population.

Coronary atherosclerosis increases the risk of cardiovascular events. Coronary calcium as measured by computed tomography (CT) scan is a marker for calcified atherosclerotic plaque and a predictor of adverse cardiac events.[7] A higher coronary artery calcium (CAC) score indicates a larger extent of coronary atherosclerosis and is associated with an increased risk of atherosclerotic cardiac events in the general population. However, both the etiology and the clinical significance of an increased CAC score have yet to be determined in athletic populations.

A previous study finding increased plaque volume in male marathon runners was confounded by the fact that more than half the male marathoners of the study were current or former smokers.[8] In our study, CAC scores were compared across long-term endurance runners and regular short distance runners. Coronary artery calcium scores in the greater than 50th percentile were defined using a national database.[9] We also assessed whether the incidence of CAC in runners is "dose dependent" by comparing CAC scores in master (>40 years old) marathon and ultramarathon participants with those in regular exercisers running lower durations at milder intensities.

PATIENTS AND METHODS

Runners were recruited from the local road runner clubs and by advertising in a local newspaper and at local competitive races. We recruited 85 respondents who completed an exercise questionnaire (Supplemental Appendix, available online at http://www.mcpiqojournal.org) that was later used to determine the experimental groups. Twenty-nine individuals were excluded using the following exclusion criteria: those younger than 45 years; those with a history of active or remote tobacco use, known coronary artery disease (CAD), a family history of premature CAD, diabetes mellitus, hypertension, or hyperlipidemia; and women who were pregnant. Thus, our sample included 56 runners who had run competitively for 10 or more years. Runners were divided into 3 categories: Group A comprised runners who had competed in at least 10 ultramarathons (races covering >50 km) and/or Ironman competitions (consisting of a 3.2 km swim, 161 km bicycle ride, and 42 km run) in 10 years. Group B included runners who had participated in more than 9 marathons over 10 years. Group C comprised runners who had competed in more than 9 shorter races, defined as races covering less than 13.1 miles over 10 years. Coronary artery calcium was measured using a 160-slice CT scanner (Toshiba Medical Systems). Coronary artery calcium was assessed by a noncontrast study, with scanning parameters of 120 kV and 10 mAs. The radiation dose was 0.7 to 1.5 mSv/subject. Calcium within coronary vessels was estimated to have a cutoff density of greater than 130 Hounsfield units. The CAC score was based on the Agatston scoring system. A CAC score of greater than 100 was used to define a group at a higher risk of future cardiovascular events by using previous definitions.[9] Women of childbearing potential were given a urine pregnancy test before the CT scan to exclude pregnancy. Institutional Review Board approval was obtained before the study initiation.

Runner characteristics were compared using analysis of variance for continuous variables and chi-square analyses for categorical variables. Because of the skewness of the calcium scores, we created categories of calcium scores 100 or less and calcium scores greater than 100 and used chi-square analyses for comparisons. For analyses, we combined

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From the The Heart Center, Vassar Brothers Medical Center, Poughkeepsie, NY (O.J., J.F., I.B., A.M., J.L., A.M., M.Y., P.V., K.H.); Hartford Healthcare Heart and Vascular Institute, Hartford Hospital, Hartford, CT (P.D.T.); and University of Connecticut Center for Public Health and Health Policy, Farmington, CT (D.W.)

ultramarathon (group A) and marathon (group B) runners and compared them with nonmarathon (group C) runners. Logistic regression models examined the relationship between runner groups (marathon vs nonmarathon) and calcium score greater than 100 (model 1), calcium score percentile (model 2), and calcium score greater than 0 (model 3). Covariates included in the model were age, sex, and number of years running. Statistical analyses were performed using SAS 9.4 (SAS Institute), and a P value of less than .05 was considered significant.

RESULTS

Table 1 lists the runner characteristics by running group. Marathon runners (group B) were younger ($P<.03$) and had been running for fewer years than the other groups ($P=.007$). There were no differences between groups A and B for CAC scores greater than 0 (76.2% vs 66.7%; $P=.59$) or greater than 100 (38.1 vs 22.2; $P=.67$), and a similar percentage of group A and B athletes had scores greater than 50% (71.4% vs 66.7%; $P=.79$). Men were almost 5 times more likely than women to have CAC scores greater than 0 (odds ratio, 4.6; 95% CI, 1.4-15.6; $P=.01$), but women in groups A and B also had higher CAC scores compared with athletes running shorter distances. Four of 6 women (66.7%) in groups A and B had CAC scores in the greater than 50th percentile vs 0 of 13 women in group C ($P=.004$).

These 2 groups were combined for all further analyses (Table 2). Among those runners participating in extreme distance running (groups A and B), 73.3% of runners had CAC scores greater than 0 whereas only 23.1% of group C runners had CAC scores greater than 0 ($P=.0002$). A CAC score greater than 0 indicated the presence of calcium within the coronary vessels. Furthermore, 70% of group A + B athletes ranked above the 50th percentile of their age and sex as assessed by a national database,[9] whereas only 19.2% of group C runners were ranked above the 50th percentile ($P=.0001$). One-third of runners in group A + B had CAC scores greater than 100 as compared with only 11.5% of runners in group C ($P=.05$).

Table 3 presents the results of the logistic regression models. When controlling for age, sex, and number of years running, the study group was not a significant predictor of CAC scores greater than 100 ($P=.12$). In contrast, group A + B was 10 times more likely than group C to have CAC scores in the 50th percentile or greater and 8.8 times more likely to have a positive CAC when controlling for covariates.

TABLE 1. Runner Characteristics[a]

Characteristic	Group A (ultramarathon runners)	Group B (marathon runners)	Group C (nonmarathon runners)	P value
Sample size	21	9	26	
Age (y)	60.9±7.6	53.0±7.7	59.3±7.3	.03
Sex				.06
Female	4 (19.1)	2 (22.2)	13 (50.0)	
Male	17 (80.9)	7 (77.8)	13 (50.0)	
Number of years running	35.4±11.7	19.1±7.7	27.3±15.0	.007
Miles per week[b]	42.9±12.3	40.0±10.9	33.5±15.6	.08
Days per week	5±0	5±0.6	4.3±1.2	.06
Hours per week				.56
<5	1 (4.8)	0	4 (16.0)	
5-≤10	14 (66.7)	5 (62.5)	13 (52.0)	
>10	6 (28.6)	3 (37.5)	8 (32.0)	
Calcium score in the ≥50th percentile	15 (71.4)	6 (66.7)	5 (19.2)	.0007
Calcium score >0	16 (76.2)	6 (66.7)	6 (23.1)	.0008

[a]Data are presented as mean ± SD or as No. (percentage).
[b]SI conversion factor: To convert values in miles per week to kilometers per week, multiply by 1.6.

DISCUSSION

We designed this study to exclude any runners with risk factors for CAD, including a history of previous or active tobacco use, diabetes, hypertension, hyperlipidemia, or a family history of premature CAD (first-degree relative with a coronary event at age <60 years). In addition, we wanted to compare short distance runners with marathoners and ultramarathoners in terms of presence of coronary calcium. We observed that a significantly higher rate of coronary artery calcification existed in long-term marathon, ultramarathon, and extreme runners than in submarathon runners. Marathoners and ultramarathoners also had a higher incidence of calcification, as well as higher average plaque burden, as compared to a standard database.[9] Marathoners and ultramarathoners also had above-average coronary calcium scores as compared to a national database.

There have been 2 recent studies evaluating the prevalence of CAD in endurance athletes. Merghani et al[10] evaluated 152 master athletes who were older than 40 years and had competed in more than 10 marathons, half marathons, or 10K races. There was no difference between athletes and controls in the percentage of athletes with calcium scores greater than 0 (52% vs 59%). However, athletes had a higher prevalence of CAC scores greater than 300 (11.3% vs 0%; P=.009). In addition, the median CAC score in male athletes with CAC scores greater than 1 was higher than that in the sedentary population (86 vs 3; P=.02). There was also a stronger trend toward CAC scores greater than 100 in athletes in comparison to the sedentary population (18.9% vs 7.4%; P=.06). In addition, there was a higher percentage of purely calcified plaque in runners vs the sedentary population (72.7% vs 30.8%; P=.0002). This study differed from our study in 1 key aspect. The runners in this study were a heterogeneous group that included short and long distance runners. We compared long distance runners with short distance runners to determine whether there is a U-shaped effect of endurance running with respect to calcium scores.

Aengevaeren et al[11] analyzed the relationship between coronary atherosclerosis and lifelong exercise volume in the Measuring Athlete's Risk of Cardiovascular Events study. This study evaluated only men who were free of known CAD but may have had coronary risk factors. In addition, athletes with CAC scores in this study were older and had higher systolic and diastolic blood pressures, total cholesterol, more frequent use of statins, and higher prevalence of former smokers than did athletes with CAC scores of 0. Athletes were divided into 3 groups on the basis of lifelong history pattern (<1000, 1000-2000, >2000 metabolic equivalent tasks/min per week). The most active group (>2000 metabolic equivalent task/min per week) had a higher CAC score in a multivariate analysis with an odds ratio of 3.2 (P=.002) vs the lower volume group.

The present study supports these previous observations that increased exercise increases coronary artery calcification and makes 2 important contributions to this literature. First, the only previous study to include women found no difference in the burden or morphology of atherosclerotic plaque between athletic women and controls. In contrast, we observed that a higher percentage of female athletes participating in longer endurance events had CAC scores in the greater than 50th percentile for their age than less active women. This observation suggests that female athletes are also vulnerable to the possible deleterious effects of extreme endurance exercise. Second, ours is also only the second study to stratify runners by the amount of exercise. We found that runners participating in shorter endurance events had lower CAC scores, suggesting that CAC is related not to exercise alone but to the volume of exercise. The possibility of a "threshold effect," although widely postulated, warrants further examination.

TABLE 2. Comparison of Coronary Artery Calcium (CAC) Scores in Endurance Runners and Shorter Distance Runners

Parameter	Group A + B	Group C	*P* value
Runners with CAC scores >0	73.3%	23.1%	.0002
Runners with CAC scores in the >50th percentile	70%	19.2%	.0001
Runners with CAC scores >100	33%	11%	.05
Woman with CAC scores in the >50th percentile	71.4%	7.7%	.0014

TABLE 3. Results of the Multivariate Logistic Regression Models

Variable	Odds ratio (95% CI)	*P* value
Model 1: CAC scores >100		
Group A + B vs group C	4.04 (0.70-23.39)	.12
Female vs male	0.07 (0.005-0.86)	.04
Age	1.17 (1.03-1.34)	.02
Number of years running	0.95 (0.89-1.02)	.15
Model 2: CAC scores in the ≥50th percentile		
Group A + B vs group C	10.00 (2.30-43.54)	.002
Female vs male	0.17 (0.03-0.89)	.04
Age	1.12 (1.00-1.25)	.05
Number of years running	0.95 (0.90-1.01)	.12
Model 3: CAC scores >0		
Group A + B vs group C	8.80 (2.14-36.29)	.003
Female vs male	0.26 (0.06-1.17)	.08
Age	1.11 (1.00-1.24)	.05
Number of years running	0.98 (0.92-1.03)	.37

The etiology of the increased coronary artery calcification in endurance athletes is unclear. Repeated high-intensity aerobic exercise subjects the coronary arteries to turbulent blood flow, which could produce inflammation and atherosclerosis, which then calcifies. Free radical formation causing oxidative stress may also participate in this process.[1] Exercise also acutely increases parathyroid hormone levels, which could increase the calcification of any atherosclerotic lesions.[12]

Long-term cardiovascular outcomes data that would provide perspective to the above observations are lacking. None of these studies can document that higher CAC scores observed in athletes have deleterious consequences. Endurance athletes have long been known to have enhanced survival, but such observations cannot differentiate the effects of exercise from genetic endowment. Coronary artery calcium scores do predict future cardiac events in the general population, but this may not apply to extreme endurance athletes. Increased cardiorespiratory fitness[13] and greater amounts of physical activity[14] are associated with the largest reduction in cardiac events in individuals with the highest CAC scores. Also, cardiac events decrease with increasing CAC density, making it possible that the higher CAC values in athletes are stabilizing coronary plaques, similar to the effect of statins on soft vulnerable plaque.

There are limitations to the present study. Participants were grouped based on self-reported participation. We used a convenience sample. We separated runners by their competitive events, which should reflect their volume of training, but did not measure their habitual exercise levels. We excluded subjects with known atherosclerotic risk factors, but did not measure atherosclerotic risk factors, such as serum lipids and blood pressure, and relied on self-reporting. Our study was small and included only 56 subjects in the final analysis, but this number is not remarkably different from other studies examining this topic.

CONCLUSION

Ultradistance and marathon runners had higher CAC scores than did runners participating in shorter events. The source of this difference and its clinical significance is not clear, requiring further study to better define this observation.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at: http://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **CAC** = coronary artery calcium; **CAD** = coronary artery disease; **CT** = computed tomography

Potential Competing Interests: Dr Thompson serves as a consultant to Amgen, Regeneron, Sanofi, and Esperion; he has received grants from Sanofi, Regeneron, Esperion, Amarin, and Amgen and payment for lectures from Amarin, Regeneron, Sanofi, Amgen, Kowa, and Boehringer Ingelheim; and he owns stocks of AbbVie, Abbott Laboratories, CVS, General Electric, Johnson & Johnson, Medtronic, Sarenta, Boston Scientific, and MyoKardia (all outside the submitted work). Ms Wakefield has received consultancy fees or honorarium from VBMC for statistical analysis. The other authors report no competing interests.

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Correspondence: Address to Kamran Haleem, MD, The Heart Center, Vassar Brothers Medical Center, 1 Columbia St, Poughkeepsie, NY 12601 (khaleem@health-quest.org).

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