Long-Term Marathon Running Is Associated with Low Coronary Plaque Formation in Women

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ABSTRACT

ROBERTS, W. O., R. S. SCHWARTZ, S. M. KRAUS, J. G. SCHWARTZ, G. PEICHEL, R. F. GARBERICH, J. R. LESSER, S. N. OESTERLE, K. K. WICKSTROM, T. KNICKELBINE, and K. M. HARRIS. Long-Term Marathon Running Is Associated with Low Coronary Plaque Formation in Women. *Med. Sci. Sports Exerc.*, Vol. 49, No. 4, pp. 641–645, 2017. **Introduction**: Marathon running is presumed to improve cardiovascular risk, but health benefits of high volume running are unknown. High-resolution coronary computed tomography angiography and cardiac risk factor assessment were completed in women with long-term marathon running histories to compare to sedentary women with similar risk factors. **Methods**: Women who had run at least one marathon per year for 10–25 yr underwent coronary computed tomography angiography, 12-lead ECG, blood pressure and heart rate measurement, lipid panel, and a demographic/health risk factor survey. Sedentary matched controls were derived from a contemporaneous clinical study database. CT scans were analyzed for calcified and noncalcified plaque prevalence, volume, stenosis severity, and calcium score. **Results**: Women marathon runners (n = 26), age 42–82 yr, with combined 1217 marathons (average 47) exhibited significantly lower coronary plaque prevalence and less calcific plaque volume. The marathon runners also had less risk factors (smoking, hypertension, and hyperlipidemia); significantly lower resting heart rate, body weight, body mass index, and triglyceride levels; and higher high-density lipoprotein cholesterol levels compared with controls (n = 28). The five women runners with coronary plaque had run marathons for more years and were on average 12 yr older (65 vs 53) than the runners without plaque. **Conclusion**: Women marathon runners had minimal coronary artery calcium counts, lower coronary artery plaque prevalence, and less calcified plaque volume compared with sedentary women. Developing coronary artery plaque in long-term women marathon runners appears related to older age and more cardiac risk factors, although the runners with coronary artery plaque had accumulated significantly more years running marathons. **Key Words:** CARDIAC RISK, CORONARY CALCIUM COUNTS, FEMALE RUNNERS, CAD

The number of runners finishing marathons in the United States has increased from 25,000 in 1976 to 541,000 in 2013, and the percent of women finishers has increased from 10% in 1980 to 43% in 2013 (14). Typically, marathon running engenders excellent cardiovascular (CV) risk factor profiles and remarkable cardiorespiratory fitness, but little is known about the effects of long-term marathon participation on the coronary vasculature among middle-age and older women.

Möhlenkamp et al. (9) demonstrated higher than expected calcified coronary plaque characteristics in men 50 yr of age or older who had run at least five marathons in the previous 3 yr, many of whom had risk factors for CAD before starting running, including prior tobacco use. Within 2 yr, four men with coronary artery calcium counts (CACC) >100 had coronary events. We previously studied 50 male runners who had run one or more marathons each year for 25 or more consecutive years using coronary computed tomography angiography (CCTA) and found significantly greater accumulations of coronary plaque volume compared with a control group of sedentary age-matched men (15). No information has been published describing the effects of chronic marathon training and racing on coronary plaque formation among women runners. This study looked at both the coronary plaque formation in women who had run at least one marathon per year for 10–25 consecutive years

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Submitted for publication June 2016.
Accepted for publication October 2016.

0195-9131/17/4904-0641/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0000000000001154

compared with sedentary women of similar age, and the cardiac risk factors and demographics of the women marathon runners with and without coronary artery calcification.

METHODS

The study was approved by the Institutional Review Board of Abbott Northwestern Hospital (Minneapolis, MN) as a single-center observational study of women runners who had participated annually in the Twin Cities Marathon (Minneapolis-St. Paul, MN) for at least 10 consecutive years. Eligible women were identified and invited to participate by reviewing marathon race records.

The control group was generated from a pool of 159 women who were subjects in the Personalized Risk Evaluation and Diagnosis in the Coronary Tree trial (CardioDX, Palo Alto, CA) using a propensity match based on self-reported sedentary lifestyle and age. The Personalized Risk Evaluation and Diagnosis in the Coronary Tree is a clinical trial evaluating CAD screening in women and men who were referred for CCTA but had no known history of myocardial infarction, CAD, or coronary revascularization procedure (either performed or recommended).

All subjects signed an informed consent for participation in the study and the CCTA. Potential participants were excluded if they had an allergy to x-ray contrast, had a serum creatinine ≥2.0, or were pregnant. All the women underwent a pregnancy test before CCTA, unless they were surgically sterilized or postmenopausal. Scans were scheduled at least 2 wk from a marathon race to protect renal tissue from potential intravenous contrast nephrotoxic effects.

CCTA was performed using Siemens Dual Source or FLASH CT with a minimum x-ray dose protocol per standard clinical best practice. At or near the time of the CCTA, a 12-lead ECG, serum lipid panel and serum creatinine, height, weight, resting blood pressure (BP), and resting heart rate measures were obtained, and a historical lifestyle and risk factor questionnaire, including history of hyperlipidemia, hypertension, diabetes, smoking, and family history of CAD, was completed by each participant.

CCTA scans were evaluated for all measurable plaque. Plaque was manually identified and characterized for volume and stenosis severity using validated, commercial software on a 3-D workstation (Vitrea, Vital Images, Minnetonka, MN). CACC were risk stratified with as follows: 0, no plaque; 1–10, minimal; 11–100, mild; 101–400, moderate; or >400 extensive plaque. Coronary artery obstruction was rated as minimal, mild, moderate, or severe.

Descriptive statistics were calculated and included means and standard deviations or numerical counts with either percentages or ranges. Chi-squared test or Fisher exact test was used to assess the statistical significance of categorical variables, and *t*-test or Wilcoxon test was used for continuous variables where appropriate. The Shapiro–Wilk test was used to test for normality of continuous data. If normality assumptions failed, conclusions were based on nonparametric comparisons. A P value of ≤0.05 was considered statistically significant, and all reported P values were two sided. Statistical calculations were done with SAS software version 9.2 (SAS Institute Inc., Cary, NC) or Excel Data Analysis Toolpack (Microsoft Corp., Redmond, WA).

RESULTS

Twenty-six women marathon runners were compared with 28 sedentary controls; neither the marathon nor sedentary control groups had any known history of CV disease. The statistical differences between the runners and the controls are outlined in Table 1.

Calcified coronary artery plaque was found in five of the 26 women marathon runners and 14 of the 28 sedentary controls demonstrating a statistically significant lower lesion prevalence (19.2% vs 50%, $P = 0.014$) and less total calcified plaque volume (43 vs 77 mm^3, $P = 0.014$) in the women marathon runners. No differences were found in total plaque volume, noncalcified plaque, lesion area, diameter stenosis, or length between women runners and sedentary controls. Table 2 summarizes CCTA lesion data analysis.

The running history, cardiac risk factors, and marathon times for the 26 women runners, ages 42 to 82 yr old, who had completed a combined total of 1217 marathons are outlined in Table 3. All but three of the women used alcohol in moderation: one <1 time per month, seven 2–4 times per month, five 2–3 times per week, and nine >4 $d \cdot wk^{-1}$; 18 had one drink at each use; and five had up to two drinks per time.

The women with and without coronary artery plaque are compared in Table 4. There were five women marathoners with asymptomatic CAD (CACC of three in one runner and one in four runners) profiled in Table 5 who had been running marathons for 23–33 yr. All but one had normal BP, one had hypertension for 20 yr, three had hyperlipidemia (one for 30 yr), two were taking aspirin daily, one was taking a statin, two had a family history of stroke, and 4 ran

TABLE 1. Demographic characteristics and cardiac risk factors of women subjects.

Characteristic	Controls ($n = 28$)	WM ($n = 26$)	P
Age (yr)[a]	61 ± 10	56 ± 10	NS
Lesion prevalence	14 (50)	5 (19)	0.014
Systolic BP (mm Hg)[a]	130 ± 21	120 ± 13	NS
Diastolic BP (mm Hg)	75 ± 11	78 ± 10	NS
Heart rate (bpm)	72.2 ± 12.1	57.1 ± 7.6	<0.001
Height (inches)	64.5 ± 2.6	65.3 ± 2.7	NS
Weight (kg)	86.4 ± 23.8	60.5 ± 9.5	<0.001
BMI ($kg \cdot m^{-2}$)[a]	32 ± 8	22 ± 3	<0.001
Total cholesterol ($mg \cdot dL^{-1}$)	198.9 ± 32.3	189.4 ± 31.9	NS
HDL ($mg \cdot dL^{-1}$)	54 ± 16	73 ± 15	<0.001
LDL ($mg \cdot dL^{-1}$)[a]	119 ± 36	103 ± 23	NS
Triglycerides ($mg \cdot dL^{-1}$)[a]	127.7 ± 60.3	70.5 ± 20.9	<0.001
Hypertension	16/25 (64)	3/26 (12)	<0.001
Hyperlipidemia	15/25 (60)	6/26 (23)	0.011
Diabetes	1/25 (4)	0/26 (0)	NS
Smoking Hx	15/27 (56)	5/25 (20)	0.011
Family Hx CAD	24/28 (86)	13/26 (50)	0.005

Values are presented as mean ± SD or n (%). P values from the Fisher exact test/*t*-test/Wilcoxon test for nonnormal data.
WM, women marathoners; BMI, body mass index; Hx, history.
[a]Failure of the normality assumptions based on Shapiro–Wilk test.

TABLE 2. Lesion data in control and marathon women.

Characteristic	Control (n = 28)	Marathon (n = 26)	P
No. lesions	28	7	–
Lesion prevalence	14 (50.0)	5 (19.2)	0.014
Lesions per person[a]	2.0 ± 1.3	1.4 ± 0.89	NS
Lesion area	50.8 ± 28.2 (28)	37.1 ± 31.3 (7)	NS
Lesion diameter	53.3 ± 21.9 (28)	35.4 ± 18.5 (7)	NS
Lesion length[b]	18.9 ± 11.0 (28)	13.6 ± 8.4 (7)	NS
Plaque volume (mm^3)[b]	169.8 ± 111.8 (28)	96.5 ± 87.8 (7)	NS
Calcified plaque volume (mm^3)[b]	76.6 ± 67.9 (28)	42.5 ± 51.4 (7)	0.043
Noncalcified plaque volume (mm^3)[b]	92.9 ± 51.6 (28)	54.0 ± 45.2 (7)	NS

Five marathon women had lesions; one with three and four with one each. Values are presented as mean ± SD or n (%). P values from Fisher exact test/t-test/Wilcoxon test for nonnormal data.
[a]Average number of lesions in participants where at least one lesion was present.
[b]Failure of the normality assumptions based on Shapiro–Wilk test.

year around. These five women, although on average older, were not statistically different from the marathon women without coronary plaque except for the number of years running marathons ($P < 0.001$). The sum of CV risk factors was greater in this coronary calcium positive group and approaching the significant level ($P = 0.085$).

The 21 women without coronary plaque had run marathons for 10 to 30 yr and had completed 10–99 marathons each (Table 4). Among these 21 women, 3 had systolic BP > 140 mm Hg, 4 had diastolic BP > 85 mm Hg, 20 ran year round, 7 had a family history of stroke, 4 were on daily aspirin, 1 was on antihypertensive medication, 3 had HDL cholesterol <65 $mmol \cdot L^{-1}$, and 10 had LDL cholesterol >100 $mmol \cdot L^{-1}$ (all were <130 $mmol \cdot L^{-1}$).

DISCUSSION

Women who completed marathons annually for 10–25 yr had lower CACC, had lower calcified plaque volumes, were leaner, and smoked tobacco less compared with sedentary counterparts in the same age-group. Running marathons annually for up to 33 yr does not appear to accelerate atherosclerotic plaque formation in women runners.

Only 5 of these 26 women marathon runners had any coronary artery calcium plaque, and the CACC were in the minimal range. By contrast, the companion study of 50 men who had run at least one marathon a year for 25 yr showed greater plaque volume with no difference in CACC compared with the control group (16). However, the men marathon runners were on average 4 yr older, less lean, had higher systolic and diastolic BP, carried more diagnoses of hypertension and hyperlipidemia, and 50% were previous smokers (16).

TABLE 3. Running demographics of the women marathoners.

Characteristic	Median	Mean	Range
Age started running (yr)	30	27	10–53
Age first marathon (yr)	34	34	19–55
Current age (yr)	53	56	42–82
Best marathon time (h:min)	3:39	2:42	2:30–5:37
Most recent marathon time (h:min)	4:34	3:28	2:49–7:07
Total marathons completed	35	47	10–157
Total marathons started	35	48	10–160
Marathons run per year	2	2.5	1–8
Peak training ($miles \cdot wk^{-1}$)	55	58	30–210

TABLE 4. Comparison of women marathoners with and without coronary artery plaque.

Characteristic	WM with CAC (n = 5)	WM without CAC (n = 21)	P
Age (yr)	65 [52–82]	53 [42–63]	0.10
Lesion prevalence	5	0	0.025
Systolic BP (mm Hg)	123 [106–132]	119 [88–146]	–
Diastolic BP (mm Hg)	80 [71–86]	77 [58–103]	–
BMI ($kg \cdot m^{-2}$)	25 ± 5	21 ± 4	NS
HDL ($mg \cdot dL^{-1}$)	83 ± 18	70 ± 17	NS
LDL ($mg \cdot dL^{-1}$)	122 ± 23	98 ± 19	0.10
Hypertension	1/5 (20)	2/21 (10)	NS
Hyperlipidemia	3/5 (60)	3/21 (14)	NS
Diabetes	0/5 (0)	0/21 (0)	–
Smoking Hx	1/5 (20)	4/21 (19)	NS
Family Hx CAD	2/5 (40)	11/21 (52)	NS
Mean sum five risk factors	2.6 [1–4]	1.2 [0–3]	0.085
Postmenopausal	4 (80)	11 (52)	–
Total marathons run	272 [28–99]	945 [10–157]	NS
Age started running	36 ± 13	25 ± 9	NS
Age at first marathon	38 ± 13	33 ± 7	NS
Years running marathon	27 ± 3	20 ± 7	<0.001
Marathons run	54 ± 14	45 ± 36	NS
Marathons run per year	3 ± 1.4	2 ± 1.8	NS
Peak training ($miles \cdot wk^{-1}$)	56 ± 24	59 ± 36	NS

Values are presented as mean ± SD, n (%), or [range].
P values from Student t-test.
WM, women marathoners; CAC, coronary artery calcium; BMI, body mass index; Hx, history.

The differences between men and women participating in prolonged marathon training and racing is not easily explained but is likely multifactorial involving genetic predisposition to CAD, sex differences, personal risk factors, and lifestyle choices affecting coronary plaque formation. Both the number and the percent of women participating in marathon running have been rising since the 1980s (15). The percent of women participating in the Twin Cities Marathon, where the study cohorts were recruited, has increased from 10% in 1982 to 40% in 2009 (14). Thus, fewer women with 25 yr of consecutive annual marathon finishes were available for this study, but the study cohort did have a large volume of marathon finishes.

Marathon running has been associated with rare occurrences of sudden cardiac arrest (6,8,13,14), and significant coronary artery plaque is often found during autopsy of these fatalities (1,8,13,14,17,18). Sudden death and CV events during marathon races often receive substantial lay press coverage, although these adverse outcomes are uncommon, occurring in approximately 1 per 100,000 participants (6,8,13,14). Strikingly, the risk of death during marathon participation is five to six times higher for men compared with women (6,14).

In sedentary men and women, increased coronary artery plaque volume (for both calcified and noncalcified plaque formation) has been associated with family history, tobacco use, hypertension, hyperlipidemia, diabetes, and obesity (12). These associations likely hold true in runners also. The women marathoners in this study were lean, did not currently smoke, exercised regularly, and were in good health. The five women runners with coronary artery plaque were older and on the whole had more CV disease risk factors than their counterparts without plaque. The women's cohort

TABLE 5. Characteristics of the five women marathon runners with coronary artery plaque.

Lesion Location	BMI ($m^2 \cdot kg^{-1}$)	Age Started Running (yr)	Age at First Marathon (yr)	Total Marathons Completed (*n*)	Marathons per Year (*n*)	Peak Training ($miles \cdot wk^{-1}$)	HDL Cholesterol ($mg \cdot dL^{-1}$)
2 LAD, 1 RCA	33.8	53	55	35	2	NA	84
1 LAD	26.3	33	33	99	5	45	99
1 RCA	21.5	15	19	70	3	70	79
1 LAD	20.8	32	34	40	2	60	52
1 LAD	20.8	47	49	28	1	50	102

LAD, left anterior descending; RCA, right coronary artery.

had a large lifetime endurance exercise exposure with each having completed a median of 35 and a mean of nearly 50 marathons. Thus, as a group they, could be classified as extreme endurance exercisers.

Without question, 20 to 30 min of moderate or vigorous physical activity multiple times per week will enhance CV health and longevity. However, increasing the dose of exercise beyond this level, especially to extreme endurance exercise levels, may not translate to improved health dividends (7,11). Indeed, there is concern that very high volume exercise may have detrimental health effects; however, the long-term outcomes of extreme endurance exercise are not fully understood for women or men (7,11). The women runners in this study did not seem to be adversely affected by their high volume endurance exposure. By contrast, sedentary behavior is clearly associated with greater CV risk compared with any level of exercise (2). Although an emerging body of data indicates that a single episode of very strenuous, prolonged exercise may cause acute transient myocardial dysfunction and trigger elevations of cardiac troponin and B-type natriuretic peptide levels above the usual norms, no long-term adverse effects to longevity or health have been documented (10,19).

There are limitations to this study. The number of study subjects is small and only five women had coronary plaque, so the conclusions are uncertain. The controls are a convenience sample from a group of age-matched sedentary women being evaluated for CAD who had relatively high body mass index (obese) compared with the marathoners (lean). If available, an age- and body mass index–matched control group of women who were moderately active may be a better group to assess risk of frequent and long-term marathon running. The findings of reduced coronary plaque volume among the female marathoners compared with men marathoners in previous studies may be confounded by differences in age, exposure time to running, lifestyle choices before running marathons, and varying cardiac risk factors. In addition, previous studies indicate that within the general population, women tend to have lower amounts of coronary calcification compared with men at the same age (3–5).

CONCLUSIONS

Women with 10–25 consecutive years of annual marathon running and on average 47 completed marathons had lower coronary artery plaque prevalence and less calcified plaque volume compared with sedentary women. Therefore, long-term marathon training and competition in women does not appear to adversely affect the CV risk profile. The development of coronary plaque in women marathon runners appears to be related to older age and more cardiac risk factors, although the small group of five runners with minimal coronary artery plaque had accumulated more years of running marathons and had more cardiac risk factors.

This work was supported in part by the Ken Rome Foundation, Minneapolis, MN http://kenrome5k.wordpress.com/2008/08/01/ken-rome-foundation-information. The authors have no conflicts of interest to disclose. The results of the present study do not constitute endorsement by the American College of Sports Medicine. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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