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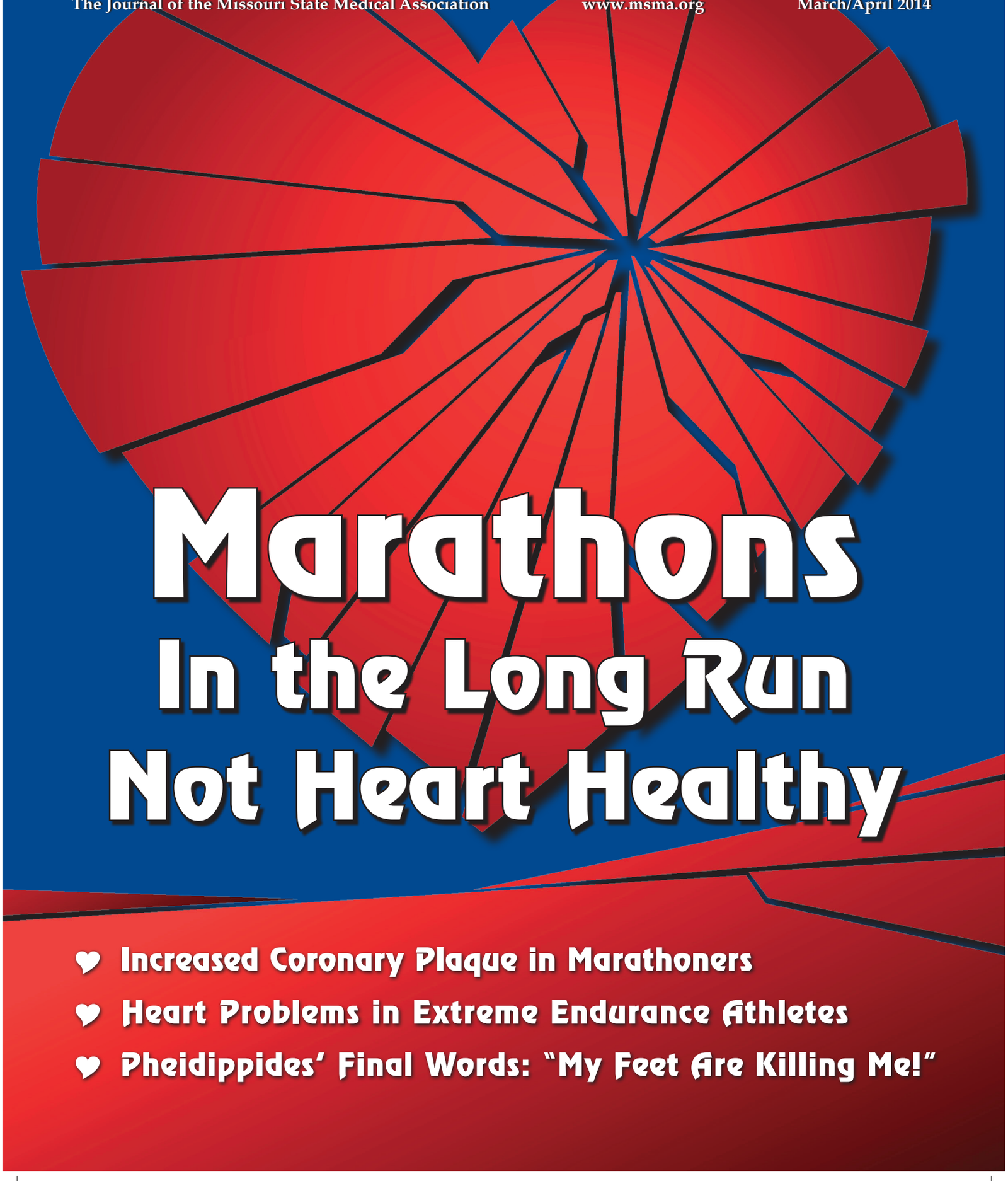

# Marathons
## In the Long Run Not Heart Healthy

- Increased Coronary Plaque in Marathoners
- Heart Problems in Extreme Endurance Athletes
- Pheidippides' Final Words: "My Feet Are Killing Me!"

# Increased Coronary Artery Plaque Volume Among Male Marathon Runners

*by Robert S. Schwartz, MD, Stacia Merkel Kraus, MPH, Jonathan G. Schwartz, MD, Kelly K. Wickstrom, BS, Gretchen Peichel, RN, Ross F. Garberich, MS, John R. Lesser, MD, Stephen N. Oesterle, MD, Thomas Knickelbine, MD, Kevin M. Harris, MD, Sue Duval, PhD, William O. Roberts, MD & James H. O'Keefe, MD*

**This study found that long-term participation in marathon training/racing is paradoxically associated with increased coronary plaque volume.**

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## Abstract

### *Background*

**Long-term marathon running improves many cardiovascular risk factors, and is presumed to protect against coronary artery plaque formation. This hypothesis, that long-term marathon running is protective against coronary atherosclerosis, was tested by quantitatively assessing coronary artery plaque using high resolution coronary computed tomographic angiography (CCTA) in veteran marathon runners compared to sedentary control subjects.**

### *Methods*

**Men in the study completed at least one marathon yearly for 25 consecutive years. All study subjects underwent CCTA, 12-lead electrocardiogram, measurement of blood pressure, heart rate, and lipid panel. A sedentary matched group was derived from a contemporaneous CCTA database of asymptomatic healthy individuals. CCTAs were analyzed using validated plaque characterization software.**

### *Results*

**Male marathon runners (n = 50) as compared with sedentary male controls (n = 23) had increased total plaque volume (200 vs. 126 mm3, $p < 0.01$), calcified plaque volume (84 vs. 44 mm3, $p < 0.0001$), and non-calcified plaque volume (116 vs. 82 mm3, $p = 0.04$). Lesion area and length, number of lesions per subject, and diameter stenosis did not reach statistical significance.**

### *Conclusion*

**Long-term male marathon runners may have paradoxically increased coronary artery plaque volume.**

*Exercise might be best understood as a drug with powerful benefits, especially for cardio-vascular health. As with any potent drug, establishing the safe and effective dose range is critically important—an inadequately low dose may not confer full benefits, whereas an excessive dose may produce adverse effects that outweigh its benefits.*

## Introduction

Regular physical activity is a key component of a healthy lifestyle. Vigorous aerobic exercise is considered protective against coronary artery plaque development based on its favorable effects on many cardiovascular (CV) risk factors including lower resting blood pressure and heart rate, improved lipid profile and glucose metabolism, reduced body mass index (BMI), and association with healthier lifestyles such as eating a nutritious diet and avoiding tobacco.[1-3] Daily physical activity and high levels of cardiorespiratory fitness are also associated with lower inflammatory markers and better life-expectancy.[4-8]

Four decades ago, Thomas Bassler, MD, an American physician, notably hypothesized that marathon running confers immunity against coronary atherosclerosis.[9] Exercise might be best understood as a drug with powerful benefits, especially for CV health. As with any potent drug, establishing the safe and effective dose range is critically important—an inadequately low dose may not confer full benefits, whereas an excessive dose may produce adverse effects that outweigh its benefits.

Two recently published long-term large observational studies independently showed that runners, as compared to non-runners, have increased life expectancy. However, these longevity benefits were most significant for those obtaining moderate doses of running; individuals chronically performing high-intensity long-distance running appeared to lose the mortality benefit.[10, 11] Indeed, an emerging body of scientific data suggests that chronic, excessive, high-intensity exercise may induce oxidative stress and myocardial fibrosis, accelerate atherosclerosis, increase vascular wall thickness, and increase cardiac chamber stiffness.[12, 13] Demand ischemia related to significant coronary narrowing may also occur in endurance running, and rarely this may even result in myocardial infarction and cardiac arrest.[14, 15] Male marathon runners have also been shown to have paradoxically increased coronary artery calcified plaque as measured by computed tomography (CT) coronary calcium scoring.[16] However, a study using high resolution coronary computed tomographic angiography (CCTA) for quantifying coronary artery plaque volume in marathoners has not been previously performed.

Recent advances in CCTA provide quantitative, noninvasive assessment of coronary artery plaque, and permit accurate measurement of plaque volume and location. In this study we used CCTA to examine whether long-term marathon running in men is associated with quantitative coronary artery plaque differences compared to a sedentary control group.

## Methods

The study was approved by the Institutional Review Board of Abbott Northwestern Hospital (Minneapolis, MN). It was a single-center observational study of male long-term, very long-distance runners who participated in the Twin Cities' Marathon (Minneapolis-St. Paul, MN). Eligible individuals were identified and invited to participate by reviewing marathon race records. After reviewing eligible subjects, participation thresholds were chosen as a minimum of 25 consecutive races for men.

A sedentary group of men was obtained from a coronary screening study of individuals who underwent CCTA scanning for clinical indications.[17, 18] All subjects in this group were self-reported to lead sedentary lifestyles. Attempts were made to match the marathon runners to the sedentary controls for coronary disease risk factors.

## Inclusion Criteria

All subjects signed informed consent. Exclusion criteria were those who declined to participate, were allergic to x-ray contrast, and had serum creatinine ≥ 2.0. Scans were not scheduled if a subject had run a marathon within the previous two weeks or intended to run a marathon within the following two weeks (to avoid potential nephrotoxic effects from intravenous contrast, since marathon running is associated with a transient creatinine rise).[19]

## Procedures

CCTA was performed per standard clinical practice using Siemens Dual Source or FLASH CT in a minimum x-ray dose protocol. At or near the time of the CCTA, the following procedures were performed: 12-lead electrocardiogram, height, weight, blood pressure, resting heart rate, serum lipid panel, historical life-style and risk factor questionnaire, and serum creatinine.

## Data Analysis

CCTA scans were evaluated for all measurable plaque, both calcified and non-calcified. Plaque was manually identified and characterized for volume and stenosis severity using validated, commercial software on a commercial CCTA 3-D workstation (Vitrea, Vital Images, Minnetonka, MN).

Descriptive statistics were calculated and included means and standard deviations or numerical counts and percentages. Chi-squared or Fisher's exact tests were used to assess the statistical significance of categorical variables and t-tests or Wilcoxon tests were 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 non-parametric comparisons. A p value of ≤ 0.050 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).

Table 1
Demographic Characteristics of Subjects

| Men | | | |
|---|---|---|---|
| **Characteristic** | **Sedentary (n=23)** | **Marathon (n=50)** | **p value** |
| Age, years | 55.43 ± 10.39 | 59.44 ± 6.66 | NS, 0.051 |
| Systolic BP, mmHg* | 134.00 ± 18.35 | 127.02 ± 13.74 | NS |
| Diastolic BP, mmHg | 79.30 ± 10.39 | 79.04 ± 9.40 | NS |
| Heart Rate, bpm | 70.83 ± 10.57 | 52.36 ± 9.31 | < 0.001 |
| Height, inches* | 70.39 ± 2.10 | 70.10 ± 2.44 | NS |
| Weight, kg* | 96.8 ± 17.0 | 76.9 ± 11.5 | < 0.001 |
| BMI, $kg/m^2$* | 30.29 ± 5.16 | 24.16 ± 2.88 | < 0.001 |
| Hypertension | 15/23 (65.2) | 12 / 47 (25.5) | 0.001 |
| Hyperlipidemia | 19/23 (82.6) | 22 / 47 (46.8) | 0.004 |
| Diabetes | 4 / 23 (17.39) | 0 / 50 (0) | 0.008 |
| History of Smoking, % | 9 / 23 (39.1) | 26 / 50 (52.0) | NS |
| Creatinine, mg/dl* | 1.03 ± 0.20 | 1.15 ± 1.00 | NS |
| Total Cholesterol, mg/dl* | 183.56 ± 48.59 | 186.44 ± 28.83 | NS |
| HDL, mg/dl | 46.67 ± 8.86 | 58.02 ± 11.58 | < 0.001 |
| LDL, mg/dl* | 108.13 ± 45.23 | 111.90 ± 26.09 | NS |
| Triglycerides, mg/dl* | 130.80 ± 63.00 | 83.36 ± 38.58 | NS |

*Values presented are mean ± SD or n (%), p values from Fisher's Exact Test/T-test/Wilcoxon test for non-normal data*
**Indicates failure of the normality assumptions based on Shapiro-Wilk test*
†*BMI-body mass index, ‡HDL-high-density lipoprotein, §LDL-low-density lipoprotein, ||CAD-coronary artery disease*

## Results

Fifty male marathon runners and 23 sedentary male control subjects were enrolled. All male runners reported no CV symptoms and had no CV or coronary history. The marathoners and controls were similar in age, resting blood pressure, height, smoking history, serum creatinine, total cholesterol, and low density lipoprotein (LDL) cholesterol (p = NS for all) (See Table 1). Marathoners had significantly lower resting heart rate, weight, BMI and triglyceride levels, but had higher high density lipoprotein (HDL) levels, and were less likely to have a history of diabetes and hypertension (See Table 1).

Tables 2 and 3 summarize coronary CT lesion analysis. There were 46 lesions in 12 of the 23 sedentary subjects and 95 lesions in 30 of the 50 marathon

Table 2
Lesion Prevalence across Runners and Sedentary Subjects

| Lesion Prevalence - Men | | | |
|---|---|---|---|
| **Characteristic** | **Sedentary (n=23)** | **Marathon (n=50)** | **p value** |
| Number of lesions | 47 | 95 | - |
| Lesion prevalence | 12 (52.2) | 30 (60.0) | NS |

*Values presented are mean ± SD or n (%)*
*p values from Fisher's Exact Test/T-test*

Table 3
CT derived Lesion Characteristics

| Lesion Data - Men | | | |
|---|---|---|---|
| **Characteristic** | **Sedentary (n=47 lesions)** | **Marathon (n=95 lesions)** | **p value** |
| Lesion area* | 43.4 ± 26.0 (44) | 46.9 ± 24.2 (94) | NS |
| Lesion diameter* | 42.0 ± 22.4 (43) | 41.7 ± 19.9 (94) | NS |
| Lesion length* | 15.1 ± 8.0 (43) | 20.0 ± 17.3 (94) | NS |
| Plaque volume* | 125.5 ± 80.5 (46) | 200 ± 144.2 (95) | 0.002 |
| Calcified Plaque volume* $mm^3$ | 44.0 ± 36.8 (46) | 83.8 ± 67.7 (95) | < 0.0001 |
| Non-calcified Plaque volume $mm^3$* | 81.5 ± 58.1 (46) | 116.1 ± 95.7 (95) | 0.039 |

*p values from T-test/Wilcoxon test for non-normal data*
**Indicates failure of the normality assumptions based on Shapiro-Wilk test*

participants. There was no difference in lesion prevalence between groups. Male marathon runners however had paradoxically increased total plaque volume (200 vs. 126 $mm^3$, $p = 0.002$), calcified plaque volume (84 vs. 44 $mm^3$, $p < 0.0001$), and non-calcified plaque volume (116 vs. 82 $mm^3$, $p = 0.04$) (See Figure 1). Lesion area, diameter stenosis, and length differences did not reach statistical significance between the two groups.

## Discussion

The association of decades-long marathon training/racing with coronary artery plaque was examined in this study. Few prior studies have focused on this association, and none using plaque quantitation by CCTA. We found that long-term marathon running in men may not engender protection against coronary artery plaque development, despite conferring advantages in many traditional coronary risk factors including favorable changes in lipid levels, glucose metabolism, and blood pressure. To the contrary, this study found that long-term participation in marathon training/racing is paradoxically associated with increased coronary plaque volume (despite comparable plaque prevalence).

A recent study found the incidence of sudden death in marathon running is approximately 1 in 100,000 participants,[15] with coronary artery disease (CAD) accounting for the majority of fatalities.[14] Fortunately, these deaths, though tragic and disturbing, are rare. However, the bigger concern may be the fact that excessive exercise ultimately deprives the individual from reaping the significant longevity benefits conferred by moderate exercise.

The Copenhagen City Heart Study followed 1,878 runners and 10,158 non-runners for up to 35 years.[10] The runners had an impressive 44% lower risk of mortality during follow-up, with an increase in life expectancy of about six years for both genders. Importantly though, U-shaped curves were apparent for mortality with respect to dose of running, whereby the benefits of running were most significant for those who jogged between 1 to 2.5 hours per week, at a slow to moderate pace, with a frequency of about three times per week.[10] In those runners who were performing higher volume, higher intensity running, the long-term mortality rates were not significantly different from non-runners. In other words, excessive running may have abolished the remarkable improvements in longevity conferred by lower doses of running.

Strikingly concordant data were seen in a large decades-long observational study of 54,000 Americans.[11] Highly significant mortality reductions were seen in the

runners compared to the non-runners, but U-shaped curves again showed that the lowest mortality rates were seen in those running 5 to 20 miles/week, and that the longevity benefits of running completely disappeared with distances greater than 25 to 30 miles/week. Still, the mortality rates in the high mileage runners were similar to but did not exceed those for sedentary individuals).[11]

Cardiac over-use injury is a term that we have proposed for problems that arise with chronic excessive high intensity exercise. Reports have documented myocardial fibrosis and scarring, potentially dangerous rhythms, and accelerated coronary atherosclerosis (a constellation of pathology which has been labeled Pheidippides' Cardiomyopathy by Peter McCullough, MD).[12, 13, 19] The number of individuals running in marathons and other extreme endurance events has been rising dramatically during the past 40 years (See Figure 2).[12, 13] We suspect some runners might choose shorter, less exhausting challenges if they were aware of the potential adverse cardiac effects of chronic extreme endurance efforts.

The metabolic and mechanical stresses produced by excessive running could constitute a causal role in accelerated atherosclerosis. Runners who train and race over very long-distances experience protracted elevations in heart rate, blood pressure, cardiac output, and atrial and ventricular volumes for up to several hours per day. Intense exercise generates large quantities of free-radicals that outstrip the buffering capacity of the system after approximately one hour of vigorous continuous exercise, leaving these individuals susceptible to oxidative stress, atherogenic modification of cholesterol particles, and endothelial dysfunction.[20] Ultra-endurance efforts also cause multiple other disturbances within the system including sustained elevations of catecholamines and resultant coronary vasoconstriction, protracted sinus tachycardia which reduces the diastolic filling time of the coronary arteries, changes in free fatty acid metabolism, lactic acidosis, and other metabolic derangements.[12, 13, 19]

Figure 1
Marathoners had significantly more total coronary plaque volume, non-calcified plaque volume and calcified plaque volume compared to control subjects.

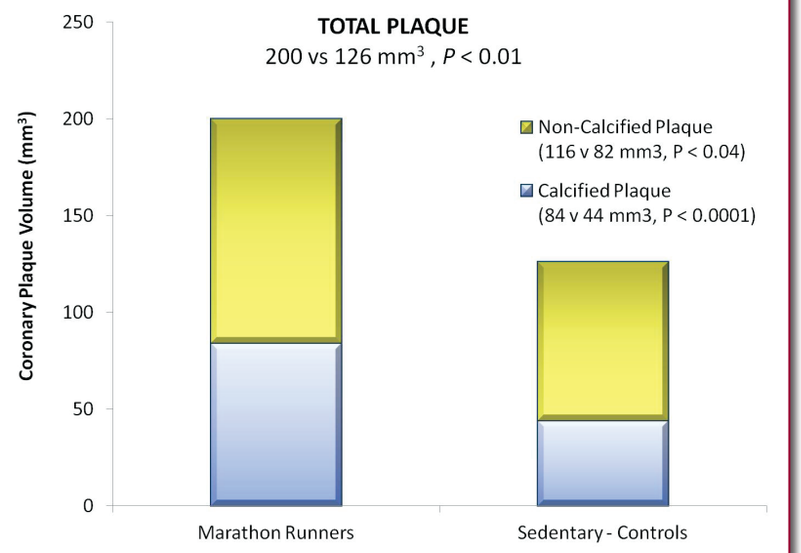
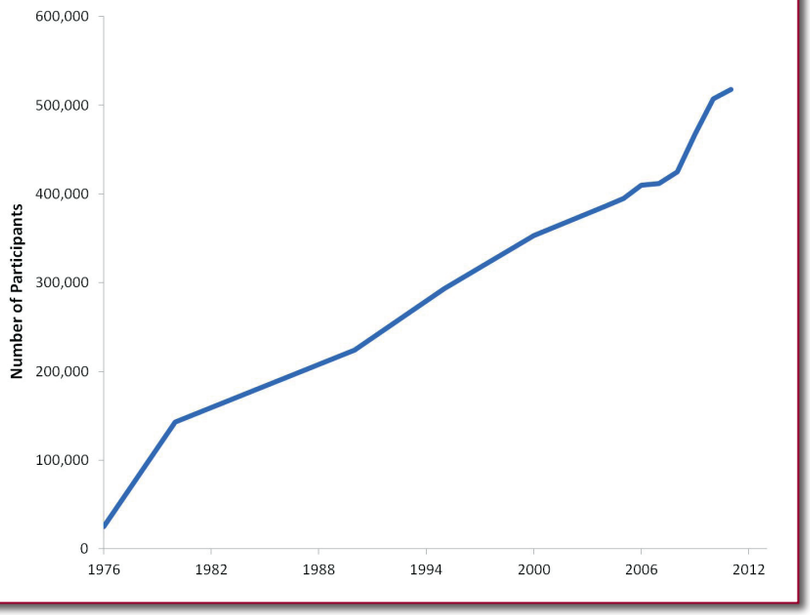



Figure 2
Marathon running trends in the United States from 1976 through 2011.



## Limitations

The control group, although matched for age, gender and several CV risk factors, was unable to be matched to the marathoners for resting heart rate, weight and HDL levels, likely the result of chronic high intensity aerobic exercise. Still, these differences would be expected to protect against atherosclerosis, thereby favoring the marathoners. However, the sedentary controls had significantly less coronary plaque despite the marathoners' more favorable CV risk factors.

This was a single-center observational study, based on recruitment from known runners who chose to participate. However, a study that randomly assigned individuals to either run marathons for 25 years or be sedentary for 25 years is practically impossible, and will never be done. Thus, a cause-and-effect relationship between marathon running and accelerated coronary plaque development cannot be established. Nonetheless, multicenter studies comparing coronary plaque volume in larger numbers of marathoners and matched sedentary control subjects would be of great interest.

## Conclusion

Long-term training for and competing in marathons may in men be paradoxically associated with accelerated coronary artery plaque formation.

## Acknowledgments

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## Disclosures

None reported.

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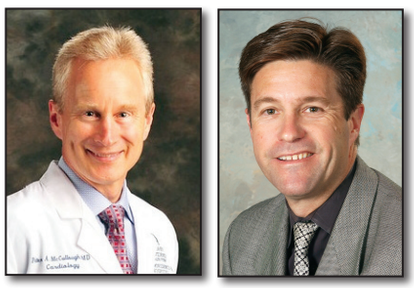
# Coronary Artery Plaque and Cardiotoxicity as a Result of Extreme Endurance Exercise

*by Peter A. McCullough, MD, MPH & Carl J. Lavie, MD*

**To summate present knowledge in early 2014, studies support a potential increased risk of coronary artery disease, myocardial fibrosis, and sudden cardiac death in those with considerable experience as marathoners (25 or more races completed).**



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## Fallible Logic: '*Some Exercise is Good, More Must Be Better*'

Aerobic exercise and fitness has been generally viewed in a positive light among the lay public and health care providers for decades.[1] The impressive and consistent reductions in cardiovascular (CV) mortality among those fit compared to sedentary individuals has lead to many conclusions which now appear to be challenged with recent studies.[2] The previous chain of logic was that if CV morbidity and mortality is reduced among those with higher physical activity (PA) and exercise training (ET) and who are more fit (See Table 1),[3] then there must be a reduction in atherosclerosis in terms of presence or absence or potentially a reduction in the general plaque burden. Furthermore, if some exercise is good, then more should be better. Thus, marathoners, among all recreational athletes, should be most free of atherosclerosis. The report by Schwartz and colleagues[4] in this issue of *Missouri Medicine* is a sobering reminder that all forms of deduction or chains of logic in clinical medicine should be challenged with scientific investigation.

Among those with considerable experience as marathoners (25 or more races completed), the cases in this study undoubtedly had many years of endurance training and cumulatively logged distances traveled that could be 100-fold greater than average sedentary individuals. Thus, the summative physiological environment of the marathoners was no doubt extremely different than the control group of sedentary individuals. As the authors pointed out, exercise is a transient oxidative stress on the systemic vasculature, creates greater shear stress in the coronary arteries, and is associated with a variety of additional adverse effects which are short-term, provided the aerobic activity is brief.[4] The important point is that marathoners have sustained increases in aerobic activity and cardiac demand for hours at a time. Therefore, the biologic plausibility for these factors to promote atherosclerosis is tenable, despite improved risk factor profiles, and this thread of concern has been evident in the literature for several decades.[5] It is important that CV risk factors were developed as associated variables for binary events of nonfatal myocardial infarction (MI) or CV death, not for the presence or absence of atherosclerosis.[6] Thus, despite the healthier CV risk profiles on the surface, the burden of atherosclerosis and potentially worrisome noncalcified plaques which could be more susceptible to rupture and result in MI is a reality that must be understood among adult marathoners and their physicians.[7]

**Table 1**
**Potential Benefits of Physical Activity and Exercise Training**

***Improvements in Exercise Capacity***
- Maximal Oxygen Consumption (Peak VO2)
- Estimated METs

***Improvements in Lipids***
- Total cholesterol
- HDL-C
- LDL-C
- Triglycerides
- Total cholesterol/HDL-C
- LDL-C/HDL-C

***Reduction in Obesity Indices***
- Weight
- Percentage Body fat
- Body Mass index

***Improvements in Blood Rheology***
- Reduction in Homocysteine Levels
- Improvement in Viscosity

***Improvement in Psychosocial Factors***
- Depression Score
- Anxiety Score
- Hostility Score

***Major Morbidity and Mortality***
- Reduction in Overall Mortality
- Reduction in Hospital Costs
- Reduction in Non-Fatal Myocardial Infarction

## Sudden Cardiac Death

Besides potential detrimental changes in the coronary arteries, there are several other forms of cardiotoxicity associated with marathon running or extreme endurance exercise (EEE).[2, 8-10] Perhaps the most serious is sudden cardiac death (SCD). Although episodes of SCD often generate considerable publicity in major running road races or other long distance endurance events, SCD remains relatively uncommon.

A recent study reviewed all marathons and half-marathons in the United States from 2000 - 2010 (10.9 million runners; 59 cardiac arrests) and reported that SCD occurred in only 0.54/100,000 participants.[11] Although other studies suggest that the true occurrence may be two- to four-fold higher than this,[12,13] due to the fact that the Kim et al.[11] data may be contaminated by large numbers of half marathoners and only accounts for SCD during the race itself and not soon afterwards, still the fatality in marathons is relatively uncommon, but still "too high." The fatality rate of triathlons is approximately two-fold higher than that of marathons, but largely because of increased CV events and SCD during the swim portion of the race.[14] The high catecholamine state of competition superimposed on forms of either preexisting training-induced structural myocardial abnormalities is the most tractable explanation for cases of SCD after common causes such as hypertrophic cardiomyopathy, coronary artery disease, anomalous coronary arteries, channelopathies, and other etiologies are excluded.

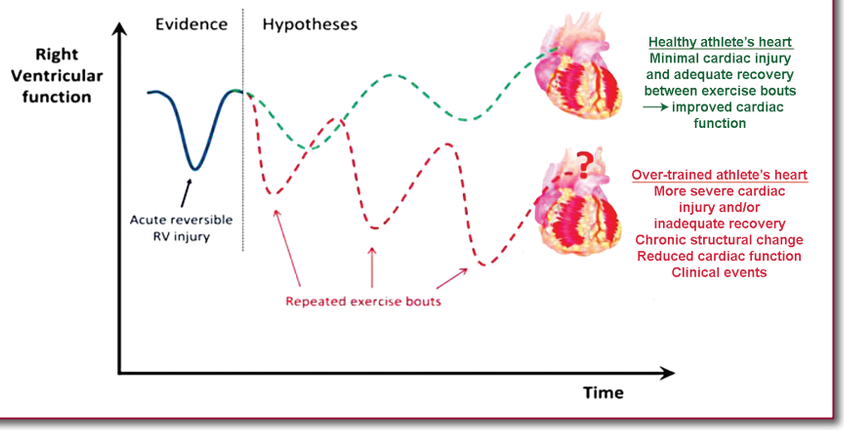
## Adverse Effects of Cardiac Structure and Function

Besides potential adverse effects on CAD discussed above, EEE has potential adverse effects on cardiac structure and function (See Figures 1 and 2).[2,8-10] In fact, animal studies have suggested considerable potential cardiotoxicity of EEE.[15,16] In one recent study, rats were trained to run strenuously for 60 consecutive minutes daily for 16 weeks.[16] Compared with control rats, the exercise rats developed left ventricular (LV) hypertrophy, right ventricular (RV) hypertrophy, diastolic dysfunction, and dilation of both atria, as well as collagen deposition in the cardiac chambers. Ventricular tachyarrhythmias were inducible in 42% of the running rats compared with only 6% of the controls ($p=0.05$). After de-training, the adverse changes and elevated electrical irritability largely reversed.[16]

Similarly, adverse structural remodeling following EEE has been noted in humans.[2,8-10] For example, following a marathon, studies have demonstrated that almost 30% of runners develop acute dilation of cardiac structures, especially the RV and right atrium, and dysfunction of both the LV (at least in the ventricular septum) and, especially, the RV.[2,8-10,17,18] Serologic markers of cardiac damage, including cardiac troponin and creatinine kinase myocardial band, two enzymes released in acute MI and used to diagnose MI, and B-type natriuretic peptide (or BNP), which is used to monitor patients for heart failure, are elevated in close to 30% and up to 50% of participants during a marathon.[2,8-10,17,19-22] Although these abnormalities typically reverse within days of an acute bout of EEE, concern has been expressed that repeated episodes may lead to myocardial cell damage at sites of myocyte slippage of one cell above another due to loss of integrity of desmosome connections, and chronic multiple injuries may lead to stimulation of resident fibroblasts to produce extracellular collagen resulting in patches of fibrosis, the substrate for anisotropy and lethal arrhythmias. The predisposing genetic substrate, dose, and duration of endurance training and competition are all unknown, but

based on the totality of evidence, we believe that high levels of EEE may predispose some individuals to long-term cardiotoxicity resulting in more extensive coronary atherosclerosis and calcification as well as myocardial fibrosis.[23]

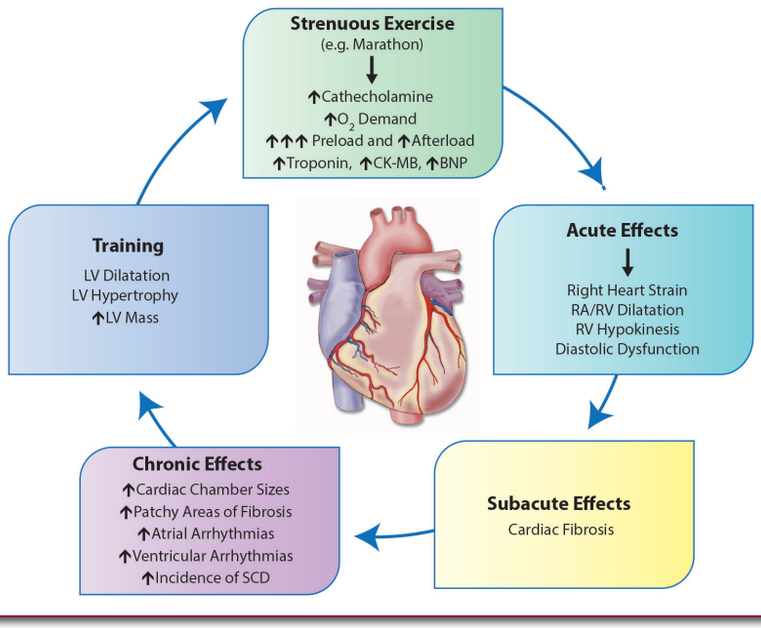
Figure 1
Potential impact of repeated bouts of ultra-endurance exercise on right ventricular structure and function. Reproduced from Patil et al. [10]




## Proarrhythmic Environment of Training and Competition

It appears that in some athletes, the adverse cardiac remodeling induced by EEE can create an arrhythmogenic substrate, some of which may increase the risk of dangerous ventricular arrhythmias and SCD.[2, 8-10,18,24] At times, malignant ventricular arrhythmias can develop in competitive athletes, similar to that present in patients with familial arrhythmogenic RV dysplasia, possibly due to sustained volume overload of the right sided cardiac chambers for several hours.[25] This in combination with high levels of catecholamines may alter the arrhythmogenic potential in some patients. In addition, it has been reported that heavy endurance exercise, including EEE, increases the rate of atrial fibrillation by as much as five-fold, presumably due to similar mechanisms of periodic and sustained volume overloading of the left atrium resulting in fibrosis and electromechanical remodeling.[2, 26-29]

**Figure 2**
**Proposed pathogenesis of endurance athlete's cardiomyopathy. RA=Right atrium, RV= Right ventricle, LV= Left ventricle, SCD= Sudden Cardiac Death. Reproduced from Patil et al. [10]**




## Current Recommendations

Clearly, the United States and most of the Westernized World are currently plagued by lack of physical activity and exercise training.[23] Certainly, lack of physical activity and exercise training are much greater problems for our society than is the potential adverse effects of excessive endurance exercise. We must recognize that most participants in excessive endurance exercise, including marathon runners, are not doing this activity for health reasons alone, but are driven by the thrill of competition, fellowship, and the attainment of personal goals. In a similar vein, people jump from planes and mountains, race cars and boats, and participate in many other sports or recreational activities, without the primary purpose being health improvement. We should stress that the benefits of PA and ET seem to occur and be maximized after the first 40-60 minutes,[2, 8-10,23] and more prolonged ET, such as EEE in marathon runners and triathletes, improves athletic performance and burns calories, but does not typically promote additional health benefits and as we have pointed out, may cause harm including greater risk of CAD as reported by Schwartz and colleagues,[4]

and cardiac fibrosis and SCD as published by others.[2, 8-10] Simply stated, the platform of "more is better" for aerobic exercise training recommendations is not supportable at this time.

Future research will need to take this work a step further to really understand the relative stability or instability of atherosclerosis among various patient populations. It is possible that the original chain of logic is still somewhat intact; that is, marathoners may have relative freedom from myocardial infarct, not because they are free of atherosclerosis, but because atherosclerosis that forms in those who exercise regularly is in some way "protected" against instability and MI. In addition to better phenotypic characterization, the future holds the promise for genetic susceptibility testing to understand individual profiles that are very favorable towards endurance training and those that potentially indicate harm to both the coronaries and the myocardium with this form of exercise and competition.[30] To summate present knowledge in early 2014, studies support a potential increased risk of coronary artery disease, myocardial fibrosis, and sudden cardiac death in marathoners.[2,5, 8-10,31-33]

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## Disclosures

None reported.

MM

# Pheidippides' Final Words: "My Feet Are Killing Me!"

*by John C. Hagan, III, MD*

**In the long run, you may end up with a broken heart.**

*Missouri Medicine* Editor John C. Hagan, III, MD, was very confident that his long-distance running would guarantee a healthy heart. He now believes 45 years of maximum endurance exercising contributed to his atrial fibrillation and high coronary artery calcium score. Above, Dr. Hagan runs the Kansas City Hospital Hill Half Marathon in 1988.
This is a modification of an editorial that appeared in *Missouri Medicine: The Journal of the Missouri State Medical Association* in July/August 2012.
*Contact: jhagan@bizkc.rr.com*

Let me "run" something by you. Whoa, I forgot, that was the old Marathoner/100-mile Bicyclist/Half-Ironman Triathlon® -Me talking. Let the new Easy-Exercising-Me "walk" you through this.

A sea of change is occurring in the understanding of heart disease and extreme endurance exercise like marathon running. A growing number of influential cardiologists, including *Missouri Medicine's* Preventive Medicine Editorial Board member James H. O'Keefe, MD, and his collaborators, report persuasive evidence that prolonged (>one hour) maximal or near maximal aerobic exercise, especially after age 50, may be lead to heart damaging atheroma in the myocardium and coronary arteries. (See pages 85-92 for Schwartz et al. article and McCullough/Lavie editorial) Part of this body of evidence is the finding that veteran (a code word for "older") marathoners and other endurance athletes have higher than normal coronary artery calcium scores (CACS) and rates of atrial fibrillation. Been there; got that!

I have been a long-distance runner since about 1967. If I didn't run at least 12 miles at a time, I felt it was a wasted effort. I was especially influenced by Kenneth Cooper, MD, and his book "*Aerobics*" and the pioneering work of Scottish physician Jeremiah N. Morris, MD, who established the inverse relationship between mild to moderate physical activity with cardiovascular disease, and American preventive cardiologist Jeremiah Stamler, MD, who first coined the term "risk factors" for the association of hypertension, obesity, lack of exercise, and lipid abnormalities with heart disease.

Running Pied Pipers appeared. Among them was pathologist Thomas Bassler, MD, who, in 1977, stated that running long distances prevented coronary artery disease and that no marathoner had died of a myocardial infarct in a 10-year study he conducted. This was first disproven by Timothy Noakes, MD, who presented four marathoners who had died of autopsy-proven coronary artery disease. Popular running author Jim Fixx, at age 52 in 1984, died of a heart attack while running; Olympic marathoner and three-time winner of the New York Marathon Alberto Salazar, 47, was technically dead for 14 minutes due to a heart attack before being revived. He was found to have extensive coronary artery disease. (Note to self: pay attention to things like that next time).

Nevertheless, the number of distance runners has swelled and races are longer and longer: 10 Kilometer, half-marathons, marathons (26.2 miles), 100 milers (including the "Leadville Colorado 100" that is run at altitudes between 9,200 feet and 12,600 feet), and the world's current longest certified foot race, the Self-Transcendence 3,100 Miler. It requires that runners complete the distance within 51 days or an average of 60.68 miles/day.

Figure 1 - Dr. Hagan in the 1993 Midwest Triathlon Championship, 1.2-mile swim, 56-mile bike, 13-mile run. He finished in 7 hours 10 minutes placing third in his age group and 34th overall.

My first published paper (1974) in *Resident and Staff Physician* "Survival of the Fittest" was about using exercise to reduce the risk of heart disease. Subsequently, I bought into the 'running more miles means better cardio-vascular health' movement. Thinking I was giving my heart just what it needed to prevent disease, I ran more than 25 Hospital Hill Half Marathons, four marathons and two Half Ironman Triathlons (See Figure 1). For many years I weekly averaged about 30-40 miles of running.

Ken Cooper, MD, to his great credit, in 1985, was among the first to express concerns about running very long distances at an all-out effort. Cooper said that anyone running over 15 miles per week was pursuing something "other than fitness." He also expressed concerns that long distances at maximum effort might suppress the immune system and predispose to neoplastic disease. Several very prominent long-distance runners, such as New York City Marathon director Fred Lebow and Olympic Marathon Champion Greta Waitz died relatively young of cancer. Cooper also felt that most, if not all, of the benefits of aerobic exercise can be obtained from much shorter exercise periods and at less than "all out" intensity. Bingo! Please re-read that last sentence, it will be the new paradigm.

At age 61, my heart served notice of overuse and abuse when I developed atrial fibrillation as described in a previous *Missouri Medicine* editorial (Fascinating Rhythm: Atrial Fibrillation—The Beat Goes On. 2006;103: 200-201)

So-called "lone" atrial fibrillation is more common in endurance athletes such as marathoners, long-distance cyclists, and cross country skiers.

I have for decades subscribed to *Runner's World,* the publication for runners. In the last 10 years it seems there have been more stories of marathoners and longer distance racers having heart attacks and/or death while running. There have been articles and letters in *Runner's World* recommending that runners determine their Coronary Artery Calcium Score (CACS). Coronary artery calcium is a presumed proxy for atheroma and the higher the number (the Agatston Scale is used: a perfect score is zero; 100 or less is mild calcification) the greater the heart artery plaque burden is felt to be. In large random populations this translates into higher rates of cardiac events (cardiac death, clinical arrhythmias, angina or myocardial infarcts). A father/son team of running cardiologists from Minnesota found marathoners had higher CACS than age matched non-runners. Europeans researchers confirmed this finding. CACS can be determined by a quick, easy and inexpensive test called a Heart CT. It is an ongoing controversy among cardiologists and public health officials when this test should be obtained. It seems running up the score is unsportsmanlike conduct.

I had asked my former cardiologists about having a heart CT, and mentioned that a disturbingly number of marathoners were reporting personal high CACS. More than a few with high CACS had work ups revealing coronary artery disease so severe that angioplasties, stents, and even coronary artery by-pass grafts were needed. I was told the heart CT would not tell those cardiologists anything they didn't already know or change how I was treated. Being basically a compliant patient I demurred.

By pure serendipity my ophthalmology practice changed health insurance plans and I had to find another cardiology group. When I again broached the heart CT question, my new cardiologist told me I could have the test

done as a walk-in any day that was convenient for $50. I soon took the test with almost a smug expectation of zero coronary calcium. The results left me 'broken-hearted.' A nurse clinician gave me the disturbing news immediately after the test that my Agatston Score was 1606. OMG, the proverbial heart of stone. I have more calcium in my heart arteries than most people have in their long bones. The cardiologist was sufficiently alarmed that he called me at home and asked me to come to his office immediately.

Another intensive round of heart tests were normal. However, this time rigorous interventions were done: I went to lipid clinic and changed a good diet into a fabulous diet. I went from a somewhat over-weight 192 pounds (BMI = 25.3) to a svelte 177 (BMI 23.3). My cholesterol was good but triglycerides borderline high. I went on statins. My lipid profile is so good I now take low dose statins every other day. My blood pressure medications were tweaked to superb levels and, with the weight loss, gradually cut back also. For the record, I am a lifetime non-smoker.

My new heart-friendly exercise program (five to six days/week walking, swimming, bicycling, weight-lifting) is never done at maximum effort and, except for moderate speed walking (with two minute stand-still recovery breaks), is less than an hour's duration. I've updated my estate planning; I take time to smell the roses every day; I'm hoping, as Agastston himself suggests, that my coronary artery plaques have been stabilized with intact lumen and any soft, lipid-filled thrombosis-causing plaque eliminated. *Missouri Medicine's* published study by Schwartz and others seems to indicate for some veteran marathoners that is not the case.

So, what's the message here? Physicians, including me, have the medicine (exercise) correct, but we definitely have got the dosage - faster and further - wrong. This happens all the time. Let me give you an example from the marathon world. In the mid-1960s most marathon race day deaths were from heat stroke brought on by inadequate hydration. The sustained message to runners was to drink as much water as possible during the run. In recent marathons most deaths have been from drinking too much water leading to fatal dilutional hyponatremia. Exercise is the same: too little can kill you, too much can kill you. Regular, moderate exercise is as close to a magic elixir as we are likely to discover.

I understand statistics; I understand the tyranny of small numbers and under-powered studies; here N = 1 and one is the loneliest number. Thus qualified, I believe 45 years of long-distance running at near maximum effort failed to prevent coronary artery disease and likely is the cause of my history of atrial fibrillation and high CACS. Almost all of my many relatives live to their mid- to late-80s. My maternal grandmother made it to 94. Workers all, none exercised.

With the qualifications that I am an ophthalmologist by way of general practice and my heart story anecdotal evidence; I present my conclusions on 'preventive cardiology' delivered from an editorial bully pulpit.

For most people, 30 minutes of walking, even if broken into multiple shorter intervals, five to six days per week will accrue almost all the benefits of exercise with the lowest possible risk of adverse events. It's a regimen that might reasonably be sold to an increasingly slothful and obese public. Please view "23 and One Half Hours" on You Tube and recommend it to your patients. Go here for the link: www.youtube.com/watch?v=aUaInS6HIGo

Maximum effort, endurance exercises/sports greater than one hour duration should be discouraged, especially in those over 40. Patients should be informed of the potential that such activities can cause increased rates of cardio-vascular disease even death in some participants.

The heart CT should be used more often as a tool for finding unsuspected coronary artery disease. Most endurance athletes over 40 should have a heart CT and be considered participating in a higher cardiovascular event risk activity.

After 40 most people should be on a statin (every cardiologist I know is so why shouldn't our patients?) and a baby aspirin. Hypertension, even pre-hypertensive states, should be treated.

Despite the personal discomfort it often engenders, physicians must regularly address our patients' problems of obesity, poor diet, smoking, lack of physical activity, and excessive alcohol use.

In 490 BC, the world's first marathon runner Pheidippides ran from Marathon to Sparta, and then to Athens to announce the Greeks had defeated the Persian army. This was about 150 miles in three days. Herodotus states Pheidippides first words on arrival were, "Joy to you, we've won." His next words were likely "My feet are killing me!" And they did; right then and there!

Why has it taken physicians over 2,500 years to understand that maximum physical exercise for very long periods of times are as unhealthy for their patients as was for Pheidippides? I don't know; it's all Greek to me.

## References and Sources

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RUNNER'S WORLD

# Heart Risk? Marathoners Have Increased Artery Plaque

**New study looks at coronary artery deposits in men who have run at least one marathon a year for 25 years**

By Amby Burfoot *(Google+)*
Published March 23, 2014

Who do you think would have more artery clogging in the heart: (A) a group of sedentary, overweight men; or (B) a group of men who are slightly older, much leaner, and have run at least one marathon annually for 25 years?

If you picked (A), you would be wrong, at least according to a new report in the March/April 2014 issue of *Missouri Medicine*. Its supporters believe the new study adds weight to the "excessive endurance exercise hypothesis," which posits that too much exercise, like marathon training and racing, has negative effects on the heart.

The article, "Increased Coronary Artery Plaque Volume Among Male Marathon Runners," was authored by a large group of contributors including the father/son cardiologists Robert and Jonathan Schwartz; cardiologist James O'Keefe, perhaps the leading voice in the excessive exercise movement; and Runner's World "sports doc" William Roberts, who has been reporting on marathon-race fatalities for several decades.

The "artery plaque" paper investigated 50 men (average age 59) who had run at least one marathon a year for 25 years vs. a sedentary control group (average age 55). The marathoners had significantly lower weight, BMI, hypertension, lipids, diabetes, and resting heart rates. In fact, none of the 50 marathoners had diabetes vs. 17 percent of the sedentary men. The marathoners also had significantly higher HDL cholesterol levels. All good so far.

But, "Male marathon runners however had paradoxically increased total plaque volume, calcified plaque volume, and non-calcified plaque volume." The non-calcified plaque is a particularly troublesome finding, since this is the kind of softer cholesterol deposit that can become dislodged from the artery wall, and cause a heart attack or stroke.

The investigators used coronary calcium scans to measure the degree of atherosclerotic plaque in subjects. Studies have shown that high calcium scores, sometimes called Agatson scores, are linked to higher future mortality rates, even among those with no symptoms of heart disease.

The new "artery plaque" study did not look for mortality rates or longevity, but only at a measure of heart health, i.e., the calcium score. "This clearly was not an outcomes study," principal author Robert Schwartz told *Runner's World Newswire*. "In the general population, coronary calcium is unequivocally the best predictor of cardiac events, but is the same true for marathoners? No one knows. There's simply no data now. We need followup studies over time to get the answer."

Coauthor William Roberts, who's also medical director of the Twin Cities Marathon, notes: "When the sedentary group starts shoveling snow or racing after a bus, they're going to be at much higher risk than the runners. We don't see marathon runners dropping dead on a regular basis at Twin Cities. I'd rather be a marathoner than one of the sedentary guys."

The marathoners in the Schwartz et al study included a surprising number of former or current smokers, 52 percent vs. 39 percent among the controls. Since smoking is known to influence heart and other health outcomes, this could confound the results of the study.

Additionally, as with all observational studies, there is always the chicken and egg question. Runners might call it the “Jim Fixx dilemma.” Did Fixx die of a heart attack while running because he liked to log 10 miles a day and run marathons? Was he “excessive?” Or did he die because he was an overweight smoker for many years before he changed his habits?

Observational studies can’t answer these questions; they can’t unravel cause and effect. In their conclusion, the Schwartz et al authors note that the perfect experiment on marathoners and heart health “is practically impossible, and will never be done.”

It's also possible that the marathoners would have "wider pipes" than the sedentary controls. This has been a frequent finding since a 1961 autopsy report of seven-time Boston Marathon champ Clarence DeMar found his coronary arteries to be "two or three times the normal size." DeMar died of cancer at age 70 in 1958.

"Until we have more and better information, the bulk of data still suggests that you're better off running than not running," says Boston Marathon cardiologist Aaron Baggish, co-author of the RACER (Race Associated Cardiac Arrest Event Registry) that concluded, "Marathons and half-marathons are associated with a low overall risk of cardiac arrest and sudden death." Baggish adds: "I'd never suggest that anyone needs to log 26.2 miles regularly to maximize their health, but we have no reason to believe there is any danger in doing so."

Lacking better information, we know that running and occasional marathoning is healthy for the vast majority of participants who don’t have the time, desire, or talent to chase Olympic fame. We also realize that runners can die while jogging to the mailbox and back, or while running marathons. The most important guideline is: Listen to your body, and take action when you note symptoms such as unusual shortness of breath, or chest and arm tightness.

We likewise know that lifestyle is a substantial contributor to health — diet, smoking, stress, and more. They can make a big difference. Nonetheless, 30 to 50 percent of your risk for many diseases resides in your genes.

With the huge growth in running’s popularity, and the aging of the “first boom” runners, it seem likely that we will hear more stories about runners dying on the run. We just won’t know whether running shortened their lives, or added more joy and more years.

Below are some other important study results for runners looking for reassurance.

High coronary calcium scores associated with less heart disease in the highly fit.

Veteran ultramarathoners (13 years x 2,500 miles/year) exhibit greater coronary artery expansion than controls.

Tour de France cyclists live 17 percent longer than normal population.

Vasaloppet (54-miles) cross-country skiers in Sweden have roughly 50 percent lower mortality risk across all age groups.

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SPORTS

# Why Runners Can't Eat Whatever They Want

## Studies Show There Are Heart Risks to Devil-May-Care Diets—No Matter How Much You Run



By KEVIN HELLIKER CONNECT
March 25, 2014 7:23 p.m. ET

Dave McGillivray at Fenway Park in 1978 completing a cross-country charity run. *Associated Press*

As a 10-mile-a-day runner, Dave McGillivray thought he could eat whatever he wanted without worrying about his heart. "I figured if the furnace was hot enough, it would burn everything," said McGillivray, who is 59.

But a diagnosis six months ago of coronary artery disease shocked McGillivray, a finisher of 130 marathons and several Ironman-distance triathlons. Suddenly he regretted including a chocolate-chip-cookie recipe in his memoir about endurance athletics.

"My first reaction was, I was embarrassed," he said.

As race director of the Boston Marathon, McGillivray is a high-profile exhibit in a growing medical case against the devil-may-care diets of many marathoners. Their high-mileage habit tends to lower their weight, blood pressure, heart rate and cholesterol levels, leading them (and sometimes their doctors) to assume their cardiac health is robust regardless of diet.

"'I will run it off'—that attitude clearly prevails among the marathoners themselves, almost sometimes to an arrogance," said Paul Thompson, a veteran marathoner who is chief of cardiology at Hartford Hospital.

A growing body of research shows the error of that thinking. A study published in the current edition of Missouri Medicine found that 50 men who had run at least one marathon a year for 25 years had higher levels of coronary-artery plaque than a control group of sedentary men. A British Medical Journal study published this year compared the carotid

arteries of 42 Boston Marathon qualifiers with their much-less active spouses. "We hypothesized that the runners would have a more favourable atherosclerotic risk profile," says the article. As it turned out, that hypothesis was wrong.

A small body of research suggests that heart problems may arise not in spite of extreme-endurance exercise but because of it. That has led some cardiologists to theorize that, beyond a certain point, exercise stops preventing and starts causing heart disease.

"Studies support a potential increased risk of coronary artery disease, myocardial fibrosis and sudden cardiac death in marathoners," Peter McCullough, a Baylor University cardiologist, wrote as lead author of an editorial in the current Missouri Medicine.

But many cardiologists are skeptical. "The science establishing a causal link between vigorous exercise and coronary disease is shaky at best," said Aaron Baggish, a Massachusetts General Hospital cardiologist who does triathlons and marathons. Even so, he said, "I've never once told a patient they need to run marathons or race triathlons to maximize health, as this is not accurate."

McGillivray (at right) greeting a runner during a Boston 10k race in June. *Boston Globe/Getty Images*

Reports of heart disease in runners are prompting some marathoners to obtain scans of their coronary arteries. Ambrose Burfoot, winner of the 1968 Boston Marathon and editor-at-large of Runner's World magazine, is 67 years old, 6 feet tall and only 147 pounds. A lifelong vegetarian, he subsists mostly on fruits, vegetables and nuts, though he also eats "cookies and all dairy products—cheeses, ice creams etc.," he wrote in an email.

"Last March I learned that I have a very high coronary calcium," he said, adding that "I have a condition perhaps similar to Dave McGillivray's."

The medical profession's recommendation for such runners depends on which cardiologist they visit. James O'Keefe, a Kansas City cardiologist and ex-triathlete who believes sustained endurance exercise can damage the heart, said he would recommend no more than 20 miles a week at a modest pace.

Thompson and Baggish, however, believe that in many cases endurance athletes diagnosed with heart disease can safely continue doing marathons and triathlons, if their conditions are treated. Thompson argues that risk must be weighed against quality of life, an idea the Burfoot embraces.

"I subscribe to the old saw: 'Exercise—it might not add years to your life, but it adds life to your years,'" said Burfoot.

But cardiologists are united in their campaign against the old notion that high-calorie workouts confer a free pass to eat anything.

Those who run several hours a day often dream about cookies and ice cream. When McGillivray ran from coast to coast in 1978, he tended to finish each day at a Dairy Queen.


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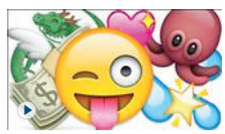

"It wasn't just replacing calories but a mental thing—that vanilla shake was my reward," he said.

Replacing thousands of calories with purely nutritious foods can be challenging. Since receiving his diagnosis last October—and radically changing his diet—the 5-foot-4 McGillivray has dropped to 128 pounds from 155, an improvement he celebrates.

Far from cutting back his workout regimen, McGillivray has amped it up, boosting his weekly mileage to 70 from about 60. As race director of the Boston Marathon, which is April 21, he plans to continue his tradition of running that course after the last runner has crossed the finish line. And to celebrate turning 60 in August, he plans to complete an Ironman-distance triathlon.

Although McGillivray says that his cardiologist, Baggish, gave him "the green light" for such challenges, Baggish said in an email that, "I do not give patients (Dave included) green or red lights. We engage in an open discussion about known and uncertain risks and benefits and come up with a collective and very individualized plan about what is reasonable.

"In Dave's case," he added, "we did just this and he is leaning toward doing the (Ironman) with full knowledge of the fact this his risk is elevated compared to the general field."

Some critics say that continuing to engage in endurance athletics despite cardiac disease is evidence of addiction. "I'm not afraid to call myself an exercise addict," said Burfoot of Runner's World. "I have always been afraid of dying on a run. But the way I look at it now, it's not that running will have killed me. Running has enhanced my life immeasurably, but it could also 'trigger' a life-ending event that probably would have happened even sooner except for my running."

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# Walk away from excess running, researchers say

By EDWARD M. EVELD
The Kansas City Star

If running 15 miles a week is heart healthy, running 45 miles a week gives you a cardiovascular system three times as clean and strong, right?

A new study sounds a serious alarm about such thinking, adding to a growing body of research on the topic of excessive endurance exercise.

You've heard of the runner's high. Researchers now want you to hear about runner's plaque — coronary artery plaque.

In short: Running super-long distances for many years might backfire on you.

"Years of extreme exercise efforts appear to erase some benefits you get from moderate exercise, so that your risk of heart disease, of dying of coronary disease, is the same as a sedentary person," said James O'Keefe, preventive cardiologist at St. Luke's Hospital.

O'Keefe said the study found that men who were marathon runners for 25 years had 62 percent more plaque buildup in their coronary arteries than men who were sedentary but were similar to the runners in other respects, including age.

And the increased quantity of plaque in the marathoners' arteries included both hard, or calcified, plaque and the more dangerous soft, fatty plaque. The latter is the kind that can be predisposed to rupture and cause a heart attack.

O'Keefe is co-author of the paper in the latest issue of Missouri Medicine, the journal of the Missouri State Medical Association. The study was conducted by Robert Schwartz and colleagues at the Minneapolis Heart Institute Foundation.

An unwavering advocate of exercise and its health benefits, O'Keefe said the new study adds weight to the idea that the potent benefits of exercise are "dose dependent."

That is, the right amount matters. Being sedentary is unhealthy. Regular, moderate exercise bestows long-term benefits.

While logging huge numbers of miles and running marathons can keep you thinner, lower your risk for type 2 diabetes and offer other benefits, it appears the subsequent wear and tear on the heart is a potential drawback, O'Keefe said.

The study's marathoners, who had run at least one 26.2-mile race a year for 25 years, had a lower weight, resting heart rate and body mass index than the non-runners. The average age of both groups was in the 50s.

That works out well for the 3-milers — keep doing that, O'Keefe said — but it's cautionary news for marathoners and ultra-marathoners, at least those who have been at it for years.

Like John C. Hagan III, a Kansas City area ophthalmologist and editor of Missouri Medicine.

"I started running in 1967, and those were the days when the police would stop you and ask you what you were running from," said Hagan, who wrote a personal article to accompany the plaque study.

A lifelong dedicated runner, Hagan participated in more than 25 half marathons, four marathons and two half Ironman Triathlons. He typically ran 30 to 40 miles a week.

So he was surprised when at age 61 he was diagnosed with atrial fibrillation, a heart rhythm problem. After learning more about runners with heart problems, he finally decided to get a heart scan for his coronary artery calcium score, an indicator of heart artery plaque.

He still felt confident that his running had provided protection. A calcium score of 100 or less is considered mild calcification, and 400 is considered extensive. His score was 1,606.

“As a physician and a runner, I felt betrayed,” he said. “I thought I was out there exhausting myself, building an absolutely indestructible heart.”

Hagan is 70 now and no longer runs, but he walks 30 minutes nearly every day and regularly swims and lifts weights.

“Do a marathon if it’s on your bucket list, when you’re young,” he said, “then cut way back.”

Two years ago, in a report published in the journal Mayo Clinic Proceedings, O’Keefe and fellow authors cited evidence that extreme endurance training may cause structural damage to the heart, making it stiff and enlarged. That paper showed that moderate running distances two to five times a week at moderate speeds offered the best health benefits and that even 15 minutes a day of physical activity was helpful.

Eladio Valdez, coach of the Runner’s Edge training group in the Kansas City area, said he is aware of recent research about the potential ill effects of years of long-distance running, and last year he held a clinic for his clients on the topic.

“I told my runners, ‘We can’t ignore this research,’ ” he said.

While such studies don’t offer definitive answers yet, Valdez said, the research is “sobering,” and he encourages his long-distance runners to see their cardiologist and to consider a scan.

Running fewer miles also reduces overuse injuries, and he has seen clients gravitate to more moderate regimens.

“Moderation may be the answer in running, as with everything else in life,” he said.

A runner for more than 30 years, Valdez has cut back his miles from about 40 a week to 20 to 25. He plans on running one more marathon this fall — the 25th anniversary of his first marathon — and then no more.

“I feel I have one more in me,” he said.

O’Keefe worries that some people will use the findings to argue against exercise. But they would be ignoring the overwhelming evidence that being sedentary is clearly dangerous for the heart, he said.

Most people will never have the super-exercisers’ issues. For every person who is overexercising, there are 19 people not getting enough exercise, O’Keefe said.

Running about 15 to 20 miles a week provides optimal health benefits, O’Keefe said. Or walking can provide benefits, from 2 miles a day to as much as 40 miles a week. Virtually all types of exercise and activities can also be protective, but moderation is best for long-term benefits, he said.

“So this really knocks the props out from under anyone with the excuse ‘I just don’t have enough time’ or ‘I’ve never been an athlete,’ ” O’Keefe said. “You can train up to be the most ultra-fit endurance athlete ever, but that’s not what’s required for longevity. Moderate exercise is.”

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