

## Matter of the Heart: The Heart Matters: Marathons and (IM) Mortality!

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### Abstract

Any kind of physical exercise is quite beneficial for our health in general and for our hearts in particular. It is important to assess the beneficial or untoward effects of extreme form of sports including marathons on the heart. Therefore, this review is presented to assess the good and not-so-good effects of marathons related to overall human health with much attention paid to the cardiac health as well.

**Keywords:** Heart; Marathons; Mortality

“Run the first two-thirds of the race with your head and the last third with your heart”.

“If you want to run, then run a mile. If you want to experience another life, run a marathon”.

### Introduction

#### History of marathon

During the Greece and Persian conflict/War, 490 BCE, a man named Phidippides ran the 26 miles (about 40 kilometres) from a battlefield near Marathon, Greece, into Athens with the exciting news of Greek victory and declared: ‘Joy, we have won!’ and then he passed out and died [1].

A news like this today will grab the national and international headlines instantaneously!

Did he have an underlying cardiac pathology e.g. cardiomyopathy leading to dangerous and fatal arrhythmia? we might never know that.

#### Case Report

Many years back I saw a man in my office who was a marathon runner. He was 62 years old at the time with BMI of 23, BP 122/80 and heart rate of 60 bpm without any history of tobacco smoking, dyslipidemia, diabetes or hypertension. There was no strong history of premature coronary artery disease (CAD) in the family. His physical and cardiac examination were unremarkable. He has been actively running about 10 miles on a daily basis. One day, he realized he could hardly jog for 5 - 10 minutes before he would develop significant shortness of breath and chest tightness. He had limited his physical activities and was sent to my office for cardiac evaluation: a man who was running about 10 miles on a daily basis could barely run 1.5 - 2 miles!

His treadmill stress test was markedly abnormal. His coronary angiography revealed 95% proximal left anterior descending artery disease (LAD) requiring stenting.

Two weeks after this procedure, he returned to see me in my office for follow up and said to me, “Doc, while my friends all their lives have been eating bad food at McDonald’s and doing everything else, I was trying to eat healthy and have been exercising and running all along. How did this happen to me?”.

In so many ways, I did not have enough satisfactory answers to his questions. However, we can review the literature of running, marathons, healthy heart, mortality and prolonged life.

In addition, for the past few years, my oldest son has been quite actively participating in 5K, 10K, ½ Marathons and Marathons. He just took part in 5K in Boston and is qualified now to participate in Marathon in Boston next year.

Therefore, it came to my mind that it is about time that I must review the Heart-Marathon-Health connection!

### **Benefits of running/exercise**

Close to 250,000 deaths in a year in the United States can be due to lack of regular physical activity. Moreover, multiple studies over time have shown the positive effects of regular exercise for many diseases including non-insulin-dependent diabetes, osteoporosis, hypertension and cancer of colon. In people with low level of exercise, a higher rate of cardiovascular events and a higher death rate have been reported.

Various guidelines have recommended to reduce body weight by exercise and thus help reduce blood pressure. Exercise can reduce LDL cholesterol levels in the blood as well as total cholesterol and can raise HDL. In diabetic patients, exercise has been shown to improve the intracellular uptake of insulin and thereby better control of blood sugar.

Physical exercise on a regular basis has been shown to:

- Improve lipid profile with HDL cholesterol rise.
- Reduce the risk of arteriosclerosis.
- Reduce stress hormones adrenaline and cortisol.
- Improve blood pressure and blood sugar
- Lower the risk of thrombosis
- Increase better immune response to fight inflammation.

### **Athlete’s heart**

Before we delve into the details of running, marathons and their effects on the heart, we must review the condition called, Athlete’s heart.

Athlete’s heart, Athletic heart syndrome (AHS), athletic bradycardia, or exercise-induced cardiomegaly is mostly a benign condition commonly seen in athletes when the heart is enlarged, and the resting heart rate can be quite low (bradycardia).

Intense exercise can lead to repeated remodeling of the myocardium and thereby leading to a condition called Athlete’s heart. This condition is more common in those athletes who exercise more than an hour a day, and more so in endurance athletes [2,3].

The heart is hypertrophied with an increase in stroke volume, an enlarged left ventricle (and sometimes both ventricles) and bradycardia. The left ventricle wall size may increase as much as 20%. The systolic function of the left ventricle remains unaffected and LV diastolic function may or may not change.

This benign Athlete’s heart condition has to be differentiated from more malignant hypertrophic cardiomyopathy which is a well-known familial pathology and the most common cause of sudden cardiac death in young athletes [4].

Feature	Athletic heart syndrome	Cardiomyopathy
Left ventricular hypertrophy	< 13 mm	> 15 mm
Left ventricular end-diastolic diameter	< 60 mm	> 70 mm
Diastolic function	Normal (E:A ratio > 1)	Abnormal (E:A ratio < 1)
Septal hypertrophy	Symmetric	Asymmetric (in hypertrophic cardiomyopathy)
Family history	None	May be present
BP response to exercise	Normal	Normal or reduced systolic BP response
Deconditioning	Left ventricular hypertrophy regression	No left ventricular hypertrophy regression

Aerobic exercises like running, jogging, intense running on a treadmill can lead to Athlete’s heart when the dynamic exercise is performed for more than 5 hours a week. This can lead to increase in the left ventricular size, mass and wall thickness.

How do we diagnose this condition? Well, Athlete’s heart is mostly an incidental finding found on the tests performed for some other medical complaints. Most commonly a chest x-ray or EKG in the emergency department will report cardiomegaly and that leads to a visit to a cardiologist and having a 2D-echocardiography.

The most common cardiac condition leading to sudden cardiac death during the sports and marathon running is likely to be hypertrophic cardiomyopathy leading to ventricular tachycardia, ventricular fibrillation, asystole and death. The other potential causes could be asymptomatic congenital heart defects or asymptomatic arrhythmia becoming manifest with fatal arrhythmia during sporting events.

**Is marathon so good?**

Jeremy Morris was an army physician in India and Burma during the world war II years. He carried out a very interesting study, “Coronary heart disease and the physical activity of work,” which was published in *The Lancet*, 1953). That study looked at the cardiac outcomes of London transport workers-the bus drivers who sat all day while driving versus the ticket collectors who walked up 600 stairs a day on London’s double-decker buses. His conclusion was that the ticket collectors suffered 30% fewer myocardial infarctions and if they did, these were much less severe [5].

Dr Morris continued to investigate this concept by another study of 17,000 civil servants in England between the ages of 40 and 64, and his findings showed that those who frequently burned about 450 calories per hour in exercise had 33% less myocardial infarctions than those who had little or no exercise. He concluded, “vigorous exercise is a natural defense of the body, with a protective effect on the aging heart against ischemia and its consequences.”

In 1975, Dr Thomas Bassler, a pathologist/runner, believed in a theory that if you could run a marathon, you were immune to death from coronary artery disease [6]. He thought that the marathoners were like the Masai warriors of Kenya and the Tarahumara Indians of Mexico-these groups of people have been found to have little or no heart disease. “Marathon runners have much in common with these primitive populations,” Bassler wrote. Of course, this myth has long since been disproven.

Runners Association database compared 538 runners with 423 matched non-runners from the Lipid Research Clinics database after adjusting for baseline age, gender and functional ability and reported a 39% lower risk of all-cause mortality [7].

Similar mortality findings were reported by the Copenhagen City Heart Study in 1,878 joggers, compared with non-joggers [8]. There was a U-shaped relationship between jogging time and mortality. Compared with no jogging, weekly jogging < 150 minutes was associated with mortality reduction, however, > 150 minutes of weekly jogging did not show significant mortality benefits.

On the other hand, there are studies showing a linear dose-response relation between jogging/running and cardiac death risk with more benefits at higher doses of exercise [9].

In 2014, a large study was published examining the associations of running with all-cause and cardiac mortality risks in 55,137 adults, aged 18 to 100 years (mean age, 44) [10]. That study concluded that running, even 5 - 10 minutes per day and slow speeds < 6 mph, is associated with markedly reduced risks of death from all causes and cardiac disease.

Other conclusions from this study were: First, runners had consistently lower risks of all-cause and cardiac mortality compared with non-runners. Second, lower amount of running or slower speed of running was associated with significant mortality benefits. Third, regular running on a long-term basis was strongly correlated with mortality reduction [10].

Based on this study, it was concluded that the mortality can be reduced by 30% by running: Just for the sake of benefit comparison: smokers giving up smoking would reduce mortality by 11%.

### Is marathon not-so-good?

#### Cardiovascular Effects from Excessive Exercise

Vigorous exercise for more than 1-2 hours per day could potentially lead to volume overload of the right ventricle leading to overstretching and small tears in the myocardium. There could be a transient elevation in cardiac biomarkers, including troponin and B-natriuretic peptide and a fall in the RV ejection fraction [11]. Patchy myocardial fibrosis can be seen in the atria and RV, and these fibrotic scars could lead to atrial and potentially malignant ventricular arrhythmias. There are studies showing that the aging of the heart can be exacerbated by excessive physical exercise via the mechanism of increased coronary artery calcification, diastolic ventricular dysfunction and stiffening of cardiac structures [12-14].

A very interesting study from Mayo Clinic, Minnesota evaluated a group of runners who had completed at least 25 marathons over 25 years and found a 60% increase in coronary plaque burden compared with sedentary age-matched controls [15]. Similar findings were reported by another study from Germany, with increased coronary plaque in 108 chronic marathoners compared with sedentary controls [16].

Another study reported a 3-fold increased scattered fibrosis and scarring in the walls of the atria, interventricular septum and RV in marathon runners for decades by having MRI scans of their hearts [17].

This amount of significant scarring/fibrosis could be a nidus for various arrhythmia as noted with 5-fold higher chance of atrial fibrillation in marathon runners [14].

Similar findings were reported in mice after going through extensive exercise programs for 4 months with scarring, cardiac enlargement and potentially dangerous arrhythmia. Most of these changes reversed to normal after mice were withdrawn from intense physical exercise [18].

#### Odds of dying during marathon

Having sudden cardiac death during a marathon is least likely, about 0.5 to 1 in 100,000 participants [19]. One more dataset gives another perspective of someone's chance of sudden cardiac death during a marathon or half-marathon is about 1 in 259,000.

On the other hand, according to the National Safety Council, the lifetime odds of our dying from:

- Motor Vehicle Accident - 1 in 88
- Falling Down - 1 in 171
- Fire or Smoke - 1 in 1,116
- Drowning - 1 in 1,123
- While riding a bike - 1 in 4,717
- Being struck by lightning - 1 in 84,079
- Legal Execution - 1 in 96,691
- Earthquake - 1 in 148,756
- Flood - 1 in 175,803

The overall risk of dying during marathon is extremely low. However, the risk is 4 times more for marathon runners than half-marathon runners. Our odds of surviving a cardiac arrest out of a hospital is about 5 - 8% while marathon runner have about 30% survival rate during the race. We can compare these statistics with the lifetime odds of dying of heart disease as 1 in 6 and stroke being 1 in 28.

### Downside of marathons in your city

Road closures on the Marathons days may increase the risk of death from heart attacks as reported recently [20]. Medicare data were analysed on hospitalizations for acute myocardial infarction or cardiac arrest among Medicare beneficiaries ( $\geq 65$  years of age) in 11 U.S. cities that were hosting major marathons during the period 2002 - 2012 and compared 30-day mortality among the beneficiaries who were hospitalized on the date of a marathon, those who were hospitalized on the same day of the week as the day of the marathon in the 5 weeks before or the 5 weeks after the marathon, and those who were hospitalized on the same day as the marathon but in surrounding ZIP Code areas unaffected by the marathon. The findings suggested that marathon-affected hospitals with acute myocardial infarction or cardiac arrest on marathon dates had longer ambulance transport times before noon (4.4 minutes longer) and higher 30-day mortality than patients who were hospitalized on non-marathon dates. It showed that someone who is hospitalized on a race day has about a 13 - 15% higher mortality rate compared to identical days of the week and surrounding weeks. These findings are consistent with the likely idea that delays in care attributable to infrastructure disruptions are a possible explanation.

### Deaths during marathons

In London, cardiologist Daniel Tunstall Pedoe served as London Marathon medical director from the inaugural 1981 marathon, which he ran in 3:19, through the 2007 event. Pedoe has studied marathoner deaths during all 27 London Marathons. Almost 712,000 runners have completed the race, with 8 dying from heart attacks, a rate of one in every 89,000. The eight London deaths included five attributed to coronary artery disease (CAD) and three to structural heart abnormalities.

There was a study reported in *New England Journal of Medicine* in 2012, The Race Associated Cardiac Arrest Event Registry (RACER) assessing the incidence and outcomes of cardiac arrest associated with marathon and half-marathon races in the United States from January 1, 2000, to May 31, 2010. The clinical characteristics of cardiac arrests were assessed by interviewing survivors and the next of kin of non-survivors, reviewing medical records, and analyzing post-mortem data [19].

Of 10.9 million runners, 59 had cardiac arrest (incidence rate 0.54 per 100,000 participants). Cardiovascular disease accounted for the majority of cardiac arrests. The incidence rate was significantly higher during marathons (1.01 per 100,000) than during half-marathons (0.27) and 5 times more common among men than women. 80% of non-survivors of cardiac arrest collapsed in the final 25% of the distance of marathons and half-marathons or shortly after the finish line.

This study also showed that younger runners (< 40) experiencing cardiac arrest were 7 times less likely to survive than runners over 40. The underlying cardiac disease shown was clearly different: In those under 40 the most common cause was hypertrophic cardiomyopathy whereas older runners had coronary artery disease. One of the reasons for low survival in younger runners is that the ventricular tachycardia preceding the cardiac arrest responds to portable cardiac defibrillator only in the 1<sup>st</sup> 1-2 minutes of the event and once it turns into ventricular fibrillation, it very poorly responds to a defibrillator.

A similar 10-year review study of sudden death during sporting activities [21]. was recently reported from Australia.

All autopsies conducted at a forensic medicine facility in Australia between the years 2006 - 2015 (inclusive) were reviewed. Sporting related deaths amongst those 7 - 65 years of age were identified. Data collected included subject height, weight, gender, circumstances of death, and pathologic findings at autopsy and their conclusion was: sudden cardiac death during sport is rare. Deaths are largely due to coronary artery disease in adults and cardiomyopathy or arrhythmia in children. The majority of sports deaths were witnessed and so presents an opportunity to enhance outcomes via CPR (cardiopulmonary resuscitation) training and increased availability of AEDs (defibrillators) at venues [21].

The British Medical Journal published a study of deaths during marathons [22]. It surveyed 750 separate marathon days that were taken from 26 marathons over 30 years. The total number of runners in these races was 3,292,268, and the newspaper articles noting 26 heart-attack deaths. Hence, the ratio is one death in 126,000 runners. The author's most striking finding was that nearly half of all deaths occurred in the last mile of the race, or after the finish. Overall, the authors concluded: "Clinicians interested in preventing sudden cardiac death might be surprised by the low risk associated with marathon running. It is about the same as the baseline hourly risk of death for a middle-aged man".

### **Proarrhythmic Effects of Excessive Endurance Exercise**

Adverse cardiac remodeling induced by excessive exercise can create an arrhythmogenic substrate and rhythm abnormalities may be the most common CV problems encountered by these athletes. Long-term sustained aerobic exercise e.g. marathon or ultra-marathon running, or professional cycling has been associated with as much as a 5-fold increase in the prevalence of atrial fibrillation [23].

The association of long-term excessive exercise and atrial fibrillation are not well known however it may include increased vagal and sympathetic tone, bradycardia, inflammatory changes, atrial wall fibrosis and increased atrial size [24].

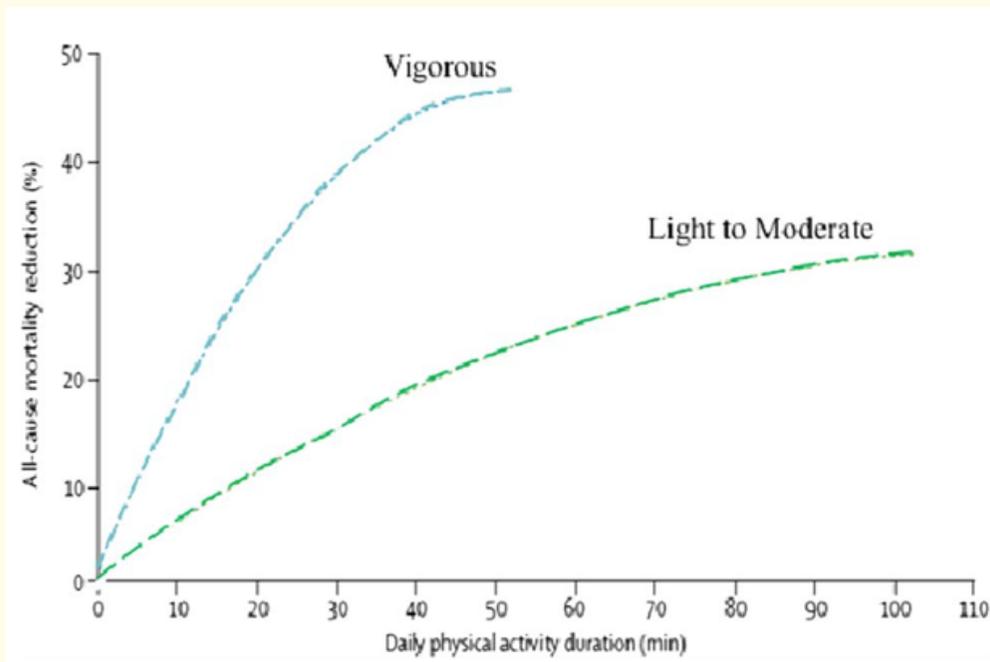
The patchy myocardial fibrosis that may develop as a reparative response to damaged myocardium can favor re-entry, a substrate well known causing for arrhythmia [25].

Long-term endurance exercise also stimulate multiple other disruptions, including episodic release of excessive catecholamines with resultant coronary vasoconstriction, chronic tachyarrhythmia, changes in free fatty acid metabolism, lactic acidosis and metabolic derangements [26].

### **The best course of action: exercise in moderation?**

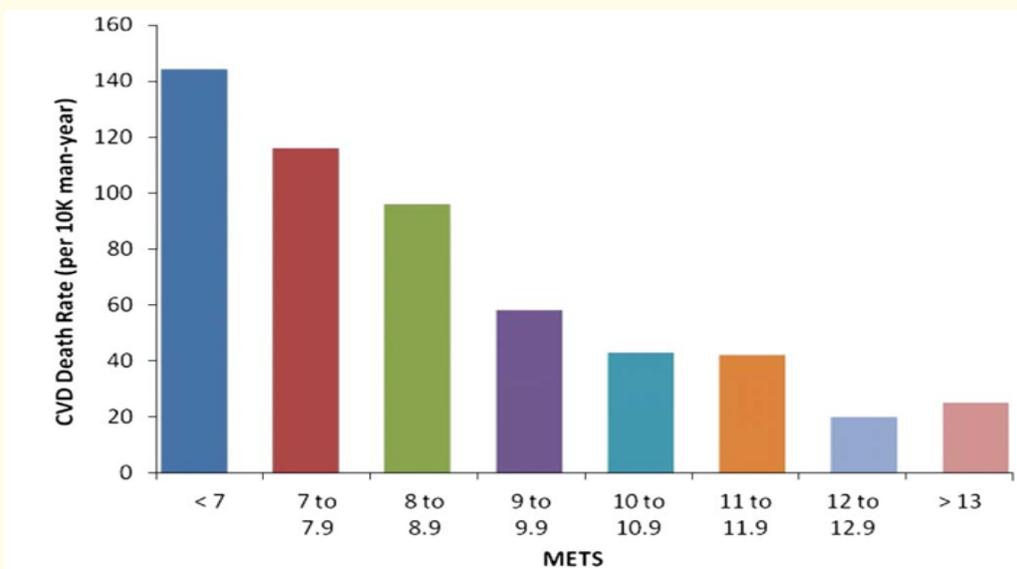
Human evolution studies tell us that our ancient ancestors probably walked 4 - 10 miles on a daily basis.

In a study of 416 000 adults followed for a mean of 8 years, 40 - 50 min per day of vigorous exercise reduced risk of death by about 40% (Figure 1). At about 45 minutes, a point of diminishing returns is reached whereby longer exercise efforts do not appear to translate into lower death risk as seen in figure 1 [27]. It is well known that about 30 - 45 minutes of daily vigorous exercise significantly reduces risks for many diseases including early death, Alzheimer's disease, diabetes, osteoporosis, CAD and depression.



**Figure 1:** Duration of daily exercise and reduction in long term all-cause mortality (from heart.bmj.com/Dr O’Keefe’s article Jan 2013).

Studies of cardiovascular (CV) fitness as measured by peak performance on a treadmill, show a curvilinear relationship whereby improvements from unfit to moderately fit provide significant reductions in morbidity and mortality (Figure 2). However, fitness levels above 12 metabolic equivalents do not seem to translate into additional gains in cardiac health and longevity [28].



**Figure 2:** Death rates as a function of cardiovascular fitness as measured by metabolic equivalents (METs) achieved on maximal exercise treadmill testing (from heart.bmj.com/Dr O’Keefe’s article Jan 2013).

There is one prospective observational study published that followed 52,600 people for up to three decades [29]. The 14,000 runners in that study had a 19% lower risk of death compared with the 42,000 non-runners. Out of these, those who ran over 20 - 25 miles per week seemed to lose their survival advantage over the non-runners. Those who ran between 5 and 20 miles total per week enjoyed a 25% decrease in risk of death during follow-up.

Similar observation was noted for the speed of running: the fast runners, those running typically over 8 miles an hour, appeared to get no mortality benefit compared with the non-runners, whereas those who fared best usually ran about 6 - 7 miles per hour. In addition, the individuals who ran 6 or 7 days per week appeared to lose the mortality benefits, whereas the survival advantages were noted the best for those who ran 2 - 5 days per week.

A study noted before in this article, the Copenhagen City Heart Study after following 20 000 Danes since 1976 found that the joggers lived about 6 years longer than the non-runners, with a 44% lower risk of death during the study. Moreover, those who did best were the people who jogged at a slow/average pace, for 1-2.5 h per week total, accumulated during 2 - 3 sessions.

Therefore, it seems very likely that the exercise in moderation might be the best prescription for longevity just like alcohol in moderation.

Let us learn from the history.

### **And Now Comes the Good News from a Harvard Study**

Running and Marathon habits are like positive 'addiction'. Those who love running and marathons, love them to death, literally speaking! Those are definitely willing to add life to their years even at the expense of some years of their life!

However, those simply interested in improving the quality of life and prolonging their life, there comes a very timely great news.

There are 5 habits that, when done together, could add more than a decade to your life expectancy, according to a study by the Harvard T.H. Chan School of Public Health. The good news: At least 10 years can be added to our life by following habits [30]:

- Eat a healthy diet
- Exercise 30 minutes or more a day
- Maintain a healthy weight (a BMI between 18.5 and 24.9)
- Don't drink too much alcohol (No more than one 5 oz. glass of wine per day for women, and two glasses for men)
- Don't smoke (ever)

Men and women who followed the healthiest of lifestyles were 82% less likely to die from cardiovascular disease and 65% less likely to die from cancer compared with people who lived unhealthy lifestyles over the course of 30 years. The researchers analyzed 34 years of data from more than 78,000 women and 27 years of data from more than 44,000 men. The researchers estimated the women who adopted these five habits would see 14 more years of life, and men would add 12 years [30].

### **Conclusion**

"One run can change your day. Few runs can change your heart. Many runs can change your life".

"Even if you're on the right track, you'll get run over if you just sit there".

A physician named Sushruta from Varanasi, India considered exercise as a vital sign and it is known that he was the first recorded physician to prescribe exercise for his patients and to indicate that “it should be taken every day” but taken “only to half extent of his capacity” as otherwise “it may prove fatal” [31]. In addition, before prescribing exercise, it was essential for the physician to consider the age, strength, physique, exercise terrain, and diet of the patient. Sushruta advocated exercise because it made the body stout, strong, firm, compact and enhanced the growth of limbs and muscles, improved digestion and complexion, prevented inactivity and reduced senility. Sushruta was of the opinion that participation in excessive exercise, interpreted to mean strenuous or heavy physical activity, would cause multiple diseases and potentially lead to death. This is going as long back as 600 BCE [31]! This was at the time when presumably there were no data set, no clinical follow up and no randomized double-blind studies conducted!

Philippines might have been successful in delivering his esteemed message of winning the Greek war over Persian army then, however today when it comes to obesity, fitness and overall health, we have a long way to go (or jog or run or marathon)!!

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