Acute and Chronic Cardiovascular Risks of Endurance Exercise:

What the Operator Needs to Know!

Francis G. O’Connor, MD, MPH
Professor, Department of Military and Emergency Medicine
Medical Director, Consortium for Health and Military Performance
Associate Director, Sports Medicine Fellowship Program
Uniformed Services University of the Health Sciences

DISCLOSURE

- I have no relevant financial disclosures in reference to this lecture.
- That being said, I was a physician in the US Army, and currently work for the Department of Defense.

My opinions and assertions contained herein are private views and are not to be construed as official or as reflecting the views of the U.S. Army Medical Department, Uniformed Services University or the Department of Defense at large.

The Legend Of Pheidippides
A Second Look at the Legend of Pheidippides

- Pheidippides was a legendary Athenian runner (530 to 490 BC).
- History tells us that he ran to Athens with the news of the great victory his people had over the Persians at Marathon (about 26 miles).
- He actually ran before the Marathon run, ran from Athens to Sparta and back, to solicit the help of the Spartan Army…round trip distance of 280 miles.
- Celebrated today as the Spartathlon.

Cardiovascular Benefits of Regular Exercise

Bassler Hypothesis

- "...if a non-smoking individual was in sufficient good health to run a complete marathon in four hours or less the probability of that individual dying of heart attack within six years of completion of the marathon was negligible."

Inverse Relationship between Physical Activity and Cardiovascular Events

- Examined the physical activity and other life-style characteristics of 16,068 Harvard alumni, aged 35 to 74, for relations to rates of mortality from all causes and for influences on length of life.
- Rates were one quarter to one third lower among alumni expending 2000 or more kcal during exercise per week than among less active men.
- With or without consideration of hypertension, cigarette smoking, extremes or gains in body weight, or early parental death, alumni mortality rates were significantly lower among the physically active.
- By the age of 80, the amount of additional life attributable to adequate exercise, as compared with sedentariness, was one to more than two years.


However…

Marine Corps Marathon Runner Dies
The Associated Press
Monday, October 30, 2006; 2:27 AM
WASHINGTON -- A man collapsed more than halfway through the Marine Corps Marathon and died Sunday, and another runner had a heart attack near the starting line.

And More Perplexing….
More may not be Better!

- Hazard ratios for joggers adjusted for the confounders in were 0.68 for <1 hour per week of jogging, 0.58 for 1–2.4 hours per week for 0.79 2.5–4 hours per week, and 0.86 for >4 hours per week.
- These results showed a tendency of a U-shaped relation to mortality risk, so the optimal quantity of jogging seemed to be 1–2.4 hours per week.

Faster may not be Better!

- RESULTS:
  - Compared with sedentary non-joggers, 1 to 2.4 h of jogging per week was associated with the lowest mortality (multivariable hazard ratio [HR]: 0.29; 95% confidence interval [CI]: 0.11 to 0.80).
  - The optimal frequency of jogging was 2 to 3 times per week (HR: 0.32; 95% CI: 0.15 to 0.66) or ≤1 time per week (HR: 0.29; 95% CI: 0.12 to 0.72).
  - The optimal pace was slow (HR: 0.51; 95% CI: 0.24 to 1.10) or average (HR: 0.38; 95% CI: 0.22 to 0.66).
  - The joggers were divided into light, moderate, and strenuous joggers.
  - The lowest HR for mortality was found in light joggers (HR: 0.22; 95% CI: 0.10 to 0.47), followed by moderate joggers (HR: 0.66; 95% CI: 0.32 to 1.38) and strenuous joggers (HR: 1.97; 95% CI: 0.48 to 8.14).

The Fine Print...

- Death rates declined steadily as energy expended on activity increased from less than 500 to 3500 kcal per week, beyond which RATES INCREASED SLIGHTLY.


The Legend Of Pheidippides

Acute Sudden Cardiac Arrest, or…

Acute Event on Chronic Cardiomyopathic Condition?

Objectives

- Discuss the acute Risk-Benefit ratio with Acute Exercise
- Explore the emerging literature on potential Long Term Harm from Excessive Endurance Exercise
- Describe current “Gaps” in the Exercise and Cardiovascular Risks and Benefits literature
- Discuss considerations in making a Prudent Recommendation
- ShareThree video pearls.

Exercise and Acute Cardiovascular Risks and Benefits
Epidemiology of Sudden Death in Athletes

- Sudden cardiac death in athletes is an uncommon event.
- Risk in young athletes is approximately 1:50,000 - 100,000/yr.
- Risk ranges from 1:15,000 to 1:50,000/yr in older athletes.

Sudden cardiac arrest is the leading cause of nontraumatic exertional death in Young Athletes!

Epidemiology of Sudden Death in Young Athletes

- Estimated death rates in male athletes are 5X higher than in female athletes.
- Estimated death rates in college athletes are 2X higher than in high school athletes.
- Non-cardiac deaths account for 22% of deaths.
- Football and basketball account for the majority of sudden deaths.
- AAs appear to be at greater risk.


**Sudden Death in the Military**

- PAR 6.3 million men and women ages 18 to 35 (recruits).
- 126 nontraumatic sudden deaths; 86% related to exercise.
- 51% had a cardiac abnormality; 35% unexplained.
- Coronary anomaly was leading cause of cardiac death 61%; HCM was present in 13%.

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**Not so Fast!!**

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Cause-Specific Findings in 902 Cases of Adjudicated Unexplained Sudden Cardiac Death Stratified by Age &lt;35 Years and ≥35 Years in a Cohort Undergoing Active Surveillance</th>
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</thead>
<tbody>
<tr>
<td><strong>Findings</strong></td>
<td><strong>&lt;35 Years of Age (n = 339)</strong></td>
</tr>
<tr>
<td>Sudden unexplained death</td>
<td>27 (8.0%)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>24 (7.1%)</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>6 (1.8%)</td>
</tr>
<tr>
<td>Myocarditis-related cardiomyopathy</td>
<td>5 (1.5%)</td>
</tr>
<tr>
<td>Arteriovenous malformation</td>
<td>5 (1.5%)</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Arrhythmogenic RV cardiomyopathy</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (2.4%)</td>
</tr>
</tbody>
</table>

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**Tragedy at Great Lakes**

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Epidemiology of Sudden Death in Older Athletes

Risk for Sudden Cardiac Death Associated with Marathon Running

- 215,413 completed the Marine Corps and the Twin Cities Marathon.
- Four exercise-related sudden deaths occurred; three during the race, one right after completion.
- Risk for sudden death with marathon running: 1:50,000; this was 1/100 the risk of overall living for 1 year.
Evidence for Decreasing Occurrence of Sudden Cardiac Death Associated with the Marathon

Estimated death rate of 1:220,000


Sudden Death in Joggers

- In the six years from 1975 through 1980, a total of 12 men died during jogging in the state of Rhode Island. The cause of death in 11 was coronary heart disease (CHD).
- The incidence of death during jogging for men of this age group was one death per year for every 7,620 joggers, or approximately one death per 396,000 man-hours of jogging.
- This rate is seven times the estimated death rate from CHD during more sedentary activities in Rhode Island and suggests that exercise contributes to sudden death in susceptible persons.
- The occurrence of only one death per 7,620 joggers per year demonstrates that the risk of exercise is small and suggests that the routine exercise testing of healthy subjects before exercise training is not justified.


ACUTE Cardiovascular Risks of Exercise

- Habitual physical activity reduces coronary heart disease events, but vigorous activity can also acutely and transiently increase the risk of sudden cardiac death and acute myocardial infarction in susceptible persons.
- Exercise-associated acute cardiac events generally occur in INDIVIDUALS WITH STRUCTURAL CARDIAC DISEASE.
- The incidence of both acute myocardial infarction and sudden death is greatest in the habitually least physically active individuals.

Exercise: The Double Edged Sword in Adults

- Prospective, nested case-crossover design within the Physicians' Health Study

**GENERAL CONSENSUS:**
Exercise acutely INCREASES but ultimately DECREASES, the risk of Sudden Cardiac Death.

- Habitual vigorous exercise attenuated the relative risk of sudden death that was associated with an episode of vigorous exertion (P value for trend=0.006).


Don’t Forget the Supplements!

- Of the 48 sudden deaths temporally associated with supplement use, the mean age was 34.2 ± 10.0 years and predominantly male (n = 44, 91.7%).
- The underlying cause of death was fatal atherosclerotic coronary disease in 18 (37.5%), sudden unexplained death in 16 (33.3%), and hypertrophic cardiomyopathy in six (12.5%).
- Compared with controls, there were no statistically significant differences in adjudicated cause of death.
- Ergogenic supplements increase risk of SCD 5 fold in soldiers >35 years


Exercise and Potential Chronic Long-Term Cardiac Risks
Is there a Cardiac Overtraining Syndrome?

- Just as runners can develop stress fractures, it may also be that endurance athletes may develop sports-related cardiac injuries.
- Despite exercise being our oldest and most efficacious therapy, there is an incomplete understanding of the entire dose–response relationship.
- Faced with the modern inactivity pandemic there has been an appropriate focus on the harm associated with too little exercise.
- Extreme training can result in profound cardiac remodeling, termed the “athlete’s heart,” and the prognostic significance of the resulting structural, functional, and electric changes remains uncertain.


The “U” Shaped Hypothesis


What is Extreme Endurance Exercise?

- “Therefore, although cardiac alterations can be discerned in those performing ≥3 hours of sports per week, this discussion is most relevant to endurance athletes who typically perform 15 to 40 hours of training per week.”


A hypothesis explaining how multiple bouts of exercise ("overtraining") may lead to adverse cardiac remodeling.

The U Shaped Hypothesis


Evidence of Acute Myocardial Cardiac Injury with Exercise

- "Available data suggests that the increases in cTn levels ARE NOT associated with permanent cardiac damage or dysfunction."

However…Myocardial Fibrosis

- Studies have taught us that elite athletes enjoy excellent health, and athletic animal models consistently show up-regulation of molecular pathways, which are free of fibrosis and entirely different from those induced through pathological cardiac loading.
- On the other hand, extreme exercise has been associated with biochemical and functional evidence of acute damage, and some recent imaging techniques raise the possibility of small areas of myocardial scar.


Atrial Fibrillation (AF) Risk

- A total of 655 athletes and 895 controls were compared.
- Mean age was 51 ± 9 years; 93% were men. There were 147 (23%) vs. 116 (12.5%) cases of AF among athletes compared with controls.
- The overall risk of AF was significantly higher in athletes than in controls with odds ratio (95% confidence interval) = 5.29 (3.57–7.85), P = 0.0001.


Right Ventricular Dysfunction

- Forty athletes were studied at baseline, immediately following an endurance race (3–11 h duration) and 1-week post-race.
- Relative to baseline, RV volumes increased and all functional measures decreased post-race, whereas LV volumes reduced and function was preserved.
- Intense endurance exercise causes acute dysfunction of the RV, but not the LV.

Coronary Calcium Deposition

- In 108 apparently healthy male marathon runners aged >=50 years, with >=5 marathon competitions during the previous three years, the running history, Framingham risk score (FRS), CAC, and presence of myocardial late gadolinium enhancement (LGE) were measured.
- Control groups were matched by age (8:1) and FRS (2:1). The FRS in marathon runners was lower than in age-matched controls (7 vs. 11%, P < 0.0001).
- However, the CAC distribution was similar in marathon runners and age-matched controls (median CAC: 36 vs. 38, P = 0.36) and higher in marathon runners than in FRS-matched controls (median CAC: 36 vs. 12, P = 0.02).
- During follow-up after 21.3 +/- 2.8 months, four runners with CAC >=100 experienced coronary events. Event-free survival was inversely related to CAC burden (P = 0.018).
- Conventional cardiovascular risk stratification underestimates the CAC burden in presumably healthy marathon runners.


Back to Pheidippides


Current “Gaps” in the understanding of exercise and Cardiovascular Risks and Benefits
Exercise Science Challenges

- No strategies have been adequately studied to evaluate their ability to reduce exercise-related acute cardiovascular events.
- Maintaining physical fitness through regular physical activity may help to reduce events because a disproportionate number of events occur in least physically active subjects performing unaccustomed physical activity.
- Other strategies, such as screening patients before participation in exercise, excluding high-risk patients from certain activities, promptly evaluating possible prodromal symptoms, training fitness personnel for emergencies, and encouraging patients to avoid high-risk activities, appear prudent but have not been systematically evaluated.

The Major Question

“To date, there are no randomized clinical trials directly testing whether physical activity prevents cardiovascular disease.”

Proceeding with Making a Prudent Recommendation
How Much is Too Much?

- "Although it is tempting to select some arbitrary exercise dose in terms of intensity, duration, or distance, we believe that this trivializes an extremely complex interaction between the environmental, personal, and genetic factors involved in stress and repair."


Making a Recommendation


Final Thoughts
"All things are poisons, for there is nothing without poisonous qualities. It is only the dose which makes a thing poison."

Philippus Aureolus Theophrastus Bombastus von Hohenheim Aka Paracelsus

Response to La Gerche and Heidbuchel

- "Ultimately, the epidemiologic evidence is compelling: ex-Olympians, Tour de France riders, Swedish skiers, Californian runners—all live longer and better.
- The physiological evidence is striking: masters athletes have youthfully compliant hearts and blood vessels, and extraordinary coronary vasodilatory capacity; and the contrary evidence is weak, indirect, and anecdotal."


"I, for one, am heading out for a run!"

Final Thought

"Don’t be concerned if running or exercise will add years to your life; be concerned with adding life to your years."

Dr. George Sheehan