Μπορεί η υπερβολική άσκηση να έχει δυσμενή αποτελέσματα στη φυσιολογική καρδιά?

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Σύγκρουση συμφερόντων

Honoraria, consultancy fees and grants

• - ABBVIE
• - MEDTRONIC
• - MENARINI
• - NOVARTIS
• - GALENICA
• - GUIDOTTI
The benefits of exercise

Most of these benefits are attributable to moderate exercise.

However, athletes perform way beyond the recommended levels of physical activity and constantly push back the frontiers of human endurance!
Can lifelong endurance exercise hurt the heart?

**Acute cardiovascular risks**
- ↑ risk for sudden cardiac death
- ↑ risk for acute myocardial infarction
- ↓ ventricular function of the heart

**Evidence of acute myocardial injury**
- ↑ CK and CK-MB concentrations
- ↑ cardiac troponin concentrations
- ↑ BNP and NT-proBNP concentrations

**Cardiac remodeling**
- ↑ dimensions of right and left ventricle
- ↑ dimensions of right and left atria
- ↑ wall thickness

**Potential cardiac maladaptations**
- = / ↓ Carotid intima media thickening
- ↑ ↓ Coronary artery calcification
- ↑ prevalence of myocardial fibrosis
- ↑ risk for atrial fibrillation
- ↑ risk for bradycardia
- ↑ aortic diameter
- ↑ progression of ARVC

**Longevity**
- ↑ life expectancy
- ↓ risk for cardiovascular mortality
FIGURE 1. Trends in United States race finishers 1990–2012. (Data from Running USA.)
CV and peripheral adaptation to exercise in athletes

**Structural changes**
- ↑ LVWT 10-25%
- ↑ LV and RV cavity 15%
- Bi-atrial dilatation

**Electrical changes**
- Sinus bradycardia
- Sinus arrhythmia
- First degree AV block
- Voltage LVH, and RVH
- Incomplete RBBB
- TWI in V1-V4 in black athletes

**Functional changes**
- ↑ diastolic filling
- E’ > 9 cm/s
- E/E’ < 6
- S’ > 9
- ↑ Stroke volume

**Peripheral changes**
- ↑ skeletal muscle fibres
- ↑ capillary conductance
- ↑ oxidative capacity
- ↑ mitochondrial enzymes
- ↑ O₂ Peak consumption
Differential effect of exercise type on cardiac structure & function

Characteristic Adaptations for Normal "Pre-training" Cardiac Structure and Function:
- Mild to Moderate Eccentric LVH and RV dilation
- Bialtrial enlargement
- Normal to slightly reduced resting LVEF
- Normal or enhanced Early LV Diastolic Function
- Normal or enhanced LV twisting / untwisting

Characteristic Adaptations for Endurance Training:
- RV Dilation +/- Mild RVH
- Eccentric LV Hypertrophy

Characteristic Adaptations for Strength Training:
- RV No Δ
- Concentric LV Hypertrophy
- Mild concentric LVH but No RV remodeling
- Normal to mildly enlarged left atrial size
- Normal to hyperdynamic resting LVEF
- Normal to slightly reduced early LV diastolic function
- Compensatory increase in late LV diastolic function

Right Ventricle
Left Ventricle
Physiological adaptation to exercise or underlying cardiomyopathy?
CONCLUSIONS: RV remodeling occurs in Olympic athletes, with male sex and endurance practice playing the major impact. A significant subset (up to 32%) of athletes exceeds the normal TF limits; therefore, we recommend referring to the 95th percentiles here reported as referral values; alternatively, only major diagnostic TF criteria for arrhythmogenic RV cardiomyopathy may be appropriate.
Distribution of CV causes of sudden death in 1,435 young competitive athletes

- HCM (36%)
- Indeterminate LVH-possible HCM (8%)
- Coronary artery anomalies (17%)
- Myocarditis (6%)
- ARVC (4%)
- MVP (4%)
- Tunneled LAD (3%)
- CAD (3%)
- AS (3%)
- Dilated C-M (2%)
- Aortic rupture (2%)
- Sarcoidosis (1%)
- Ion channelopathies (3%)
- Other congenital HD (2%)
- Other (3%)
- Normal heart (3%)
Speculated mechanisms for the detrimental effects of exercise
Exercise-induced cardiac troponin elevation: evidence, mechanisms, and implications.

<table>
<thead>
<tr>
<th>Activity</th>
<th>First Author (Ref. #)</th>
<th>Distance</th>
<th>Number of Participants</th>
<th>Troponin Isoform Measured</th>
<th>cTn Diagnostic Threshold</th>
<th>Prevalence of Positive cTn Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walking</td>
<td>Eijsvogels et al. (48)</td>
<td>30-50 km (4 consecutive days)</td>
<td>103</td>
<td>cTnl</td>
<td>&gt;0.01 ug/ml</td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&gt;0.2 ug/ml</td>
<td></td>
</tr>
<tr>
<td>Running</td>
<td>Lippi et al. (45)</td>
<td>HM</td>
<td>17</td>
<td>cTnT</td>
<td>0.03 ng/ml</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Jassal et al. (49)</td>
<td>HM</td>
<td>61 (HM)</td>
<td>cTnT</td>
<td>“Detectable”</td>
<td>HM: 30.6% immediately after race; 45.9% at 1 h after</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>FM</td>
<td></td>
<td></td>
<td>FM: 35.7% immediately after race; 52.8% at 1 h after</td>
</tr>
<tr>
<td></td>
<td>Mingels et al. (36)</td>
<td>FM</td>
<td>85</td>
<td>hs-cTnT</td>
<td>&gt;99th percentile</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>cTnI</td>
<td>&gt;99th percentile</td>
<td>45%</td>
</tr>
<tr>
<td></td>
<td>Fortescue et al. (37)</td>
<td>FM</td>
<td>482</td>
<td>cTnT</td>
<td>&gt;0.01 ng/ml</td>
<td>68%</td>
</tr>
<tr>
<td></td>
<td>Mousavi et al. (38)</td>
<td>FM</td>
<td>14</td>
<td>cTnT</td>
<td>&gt;0.01 ng/ml</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>Middleton et al. (2)</td>
<td>FM</td>
<td>9</td>
<td>cTnT</td>
<td>&gt;0.01 ug/ml</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>Scott et al. (50)</td>
<td>160 km</td>
<td>25</td>
<td>cTnT</td>
<td>&gt;0.01 ug/ml</td>
<td>20%</td>
</tr>
<tr>
<td></td>
<td>Giannitsis et al. (51)</td>
<td>216 km</td>
<td>10</td>
<td>hs-cTnT</td>
<td>&gt;99th percentile</td>
<td>50%</td>
</tr>
<tr>
<td>Cycling</td>
<td>Serrano-Ostariz et al. (52)</td>
<td>206 km</td>
<td>91</td>
<td>cTnI</td>
<td>&gt;0.04</td>
<td>43%</td>
</tr>
<tr>
<td>Triathlon</td>
<td>La Gerche et al. (53)</td>
<td>IM</td>
<td>26</td>
<td>cTnI</td>
<td>&gt;0.16 ng/ml</td>
<td>58%</td>
</tr>
</tbody>
</table>
Proposed pathogenesis of cardiomyopathy in endurance athletes

Extreme exercise efforts (e.g. marathon)
- ↑Catecholamine
- ↑O₂ Demand
- ↑↑↑Preload and ↑afterload
- ↑Troponin, ↑CK-MB, ↑BNP

Chronic training
- LV dilatation
- LV hypertrophy
- ↑LV mass

Long-term effects
- ↑Cardiac chamber sizes
- Patchy areas of fibrosis
- ↑Atrial arrhythmias
- ↑Ventricular arrhythmias
- ↑Incidence of SCD

Immediate effects
- Right heart strain
- RA/RV dilatation
- RV hypokinesis
- Diastolic dysfunction

Subacute effects
- Cardiac fibrosis
Dose of jogging and long-term mortality: the Copenhagen City Heart Study.

<table>
<thead>
<tr>
<th>DOSE OF JOGGING</th>
<th>NO. OF PARTICIPANTS</th>
<th>ALL-CAUSE MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>DEATHS</td>
</tr>
<tr>
<td>Adjusted for age and sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary nonjogger (reference)</td>
<td>413</td>
<td>128</td>
</tr>
<tr>
<td>Light jogger</td>
<td>576</td>
<td>7</td>
</tr>
<tr>
<td>Moderate jogger</td>
<td>262</td>
<td>8</td>
</tr>
<tr>
<td>Strenuous jogger</td>
<td>40</td>
<td>2</td>
</tr>
<tr>
<td>Adjusted for age, sex, smoking, alcohol intake, education, and diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary nonjogger (reference)</td>
<td>394</td>
<td>120</td>
</tr>
<tr>
<td>Light jogger</td>
<td>570</td>
<td>7</td>
</tr>
<tr>
<td>Moderate jogger</td>
<td>252</td>
<td>8</td>
</tr>
<tr>
<td>Strenuous jogger</td>
<td>36</td>
<td>2</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The findings suggest a U-shaped association between all-cause mortality and dose of jogging as calibrated by pace, quantity, and frequency of jogging. Light and moderate joggers have lower mortality than sedentary nonjoggers, whereas strenuous joggers have a mortality rate not statistically different from that of the sedentary group.
The U-shaped curve: moderate exercise is better than no exercise; extreme exercise may be harmful.
Leisure-time running reduces all-cause and cardiovascular mortality risk.

Mortality benefits were slightly less at the highest quintile of weekly running time of \( \geq 176 \text{ min/week} \).

Thus, future studies are needed on this dose-response issue about whether there is an optimum upper limit of vigorous-intensity activities, beyond which additional activity provides no further mortality benefits.

<table>
<thead>
<tr>
<th>Variable</th>
<th>0</th>
<th>&lt;51</th>
<th>51-80</th>
<th>81-119</th>
<th>120-175</th>
<th>( \geq 176 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (min/wk)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distance (miles/wk)</td>
<td>0</td>
<td>&lt;6</td>
<td>6-8</td>
<td>9-12</td>
<td>13-19</td>
<td>( \geq 20 )</td>
</tr>
<tr>
<td>Frequency (times/wk)</td>
<td>0</td>
<td>1-2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>( \geq 6 )</td>
</tr>
<tr>
<td>Total amount (MET-min/wk)</td>
<td>0</td>
<td>&lt;506</td>
<td>506-812</td>
<td>813-1199</td>
<td>1200-1839</td>
<td>( \geq 1840 )</td>
</tr>
<tr>
<td>Speed (mph)</td>
<td>0</td>
<td>&lt;6.0</td>
<td>6.0-6.6</td>
<td>6.7-7.0</td>
<td>7.1-7.5</td>
<td>( \geq 7.6 )</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** Running, even 5 to 10 min/day and at slow speeds <6 miles/h, is associated with markedly reduced risks of death from all causes and cardiovascular disease. This study may motivate healthy but sedentary individuals to begin and continue running for substantial and attainable mortality benefits.
Limited (if any) clinical trial data

- Prospective clinical trials proving that physical activity reduces CVD incidence in healthy subjects have **NOT** been performed:
  - NNT and treatment time required to document an effect is large
  - Long term compliance with assignment to active or sedentary behavior would be difficult to enforce
  - The cost of such a study would be enormous
Speculated mechanisms for the detrimental effects of exercise

- Atrial Fibrillation
  - Atrial Stretch
  - ↑ Vagal tone
- Sinus Node disease
  - AV block
- Ventricular arrhythmias
  - ? Fibrosis
- ↑ Troponin
- Adverse cardiac remodelling
- ? Atherosclerosis
- ↑ Oxidative stress
  - Shear forces
- ? Dilated cardiomyopathy
- ? Exercise induced ARVC
CONCLUSIONS: There is a graded, inverse relationship between cardiorespiratory fitness and incident AF, especially among obese patients.
Suspected mechanisms of AF in endurance athletes

- Increased atrial pressures (during exercise)
- Left atrial enlargement
- Elevated inflammatory markers
- Myocardial fibrosis
- Bradyarrhythmias
- Increased vagal tone
- Role of genetic predisposition?
**Left Atrium Size in Elite Athletes.**

**TABLE 3 Results of Base Case and Subgroup Analyses of LA Diameter in Elite Athletes Compared With Controls**

<table>
<thead>
<tr>
<th>Study-Level Factor</th>
<th>n</th>
<th>Meta-Regression Analysis: Adjusted Difference of LA Diameter, mm (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base case analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participant type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Athlete</td>
<td>7,018</td>
<td>4.1 (2.8-5.4)*</td>
</tr>
<tr>
<td>Control</td>
<td>1,044</td>
<td>Reference</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5,089</td>
<td>2.3 (0.8-3.7)*</td>
</tr>
<tr>
<td>Mixed</td>
<td>1,440</td>
<td>3.2 (1.1-5.3)*</td>
</tr>
<tr>
<td>Female</td>
<td>1,533</td>
<td>Reference</td>
</tr>
<tr>
<td><strong>Subgroup analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Training type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endurance athletes</td>
<td>2,626</td>
<td>4.6 (3.2-6.0)*</td>
</tr>
<tr>
<td>Strength athletes</td>
<td>411</td>
<td>2.9 (0.5-5.4)*</td>
</tr>
<tr>
<td>Combined trained athletes</td>
<td>875</td>
<td>3.5 (1.9-5.1)*</td>
</tr>
<tr>
<td>Mixed trained athletes</td>
<td>3,106</td>
<td>4.2 (0.9-7.6)*</td>
</tr>
<tr>
<td>Control subjects</td>
<td>1,044</td>
<td>Reference</td>
</tr>
</tbody>
</table>

**CONCLUSIONS:** To our knowledge, this is the largest compilation of studies documenting that elite athletes have larger LA dimensions compared with controls when evaluated by either LA diameter or LA volume corrected for body surface area. The largest average LA diameters were reported in endurance athletes. Physicians evaluating athletes should be aware that the LA is increased in both strength- and endurance-trained elite athletes.
Is the risk of atrial fibrillation higher in athletes than in the general population? A systematic review and meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Controls</th>
<th>Athletes</th>
<th>OR (95% CI)</th>
<th>%Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karjalainen et al.⁸</td>
<td></td>
<td></td>
<td>5.83 (1.29–26.38)</td>
<td>8.49</td>
</tr>
<tr>
<td>Heidbuchel et al.⁹</td>
<td></td>
<td></td>
<td>4.67 (1.77–12.30)</td>
<td>18.94</td>
</tr>
<tr>
<td>Elosua et al.¹⁰</td>
<td></td>
<td></td>
<td>2.86 (1.28–6.40)</td>
<td>28.38</td>
</tr>
<tr>
<td>Molina et al.¹¹</td>
<td></td>
<td></td>
<td>7.45 (1.59–34.87)</td>
<td>6.36</td>
</tr>
<tr>
<td>Mont et al.¹²</td>
<td></td>
<td></td>
<td>6.54 (3.58–11.97)</td>
<td>35.89</td>
</tr>
<tr>
<td>Baldesberger et al.¹³</td>
<td></td>
<td></td>
<td>14.38 (0.79–261.05)</td>
<td>1.94</td>
</tr>
<tr>
<td>Overall (95% CI)</td>
<td></td>
<td></td>
<td>5.29 (3.57–7.85)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Test of OR = 1: P = 0.0001
Heterogeneity: P = 0.633; I² = 0%

CONCLUSION: The risk of AF is significantly higher in athletes compared with not athletes. However, this finding should be confirmed further in large-scale prospective longitudinal studies.
CONCLUSIONS: Among male participants of a 90 km cross-country skiing event, a faster finishing time and a high number of completed races were associated with higher risk of arrhythmias. This was mainly driven by a higher incidence of AF and bradyarrhythmias. No association with SVT or VT/VF/CA was found.
We found that intense physical activity, like leisure-time exercise of more than 5 h/week at the age of 30 years, increased the risk of developing atrial fibrillation later in life. By contrast, moderate-intensity physical activities, like walking or bicycling of more than 1 h/day later in life at older age decreased the risk.
Wide variation in risk estimates among studies evaluating the association between sports participation and AF incidence

- Poor quality studies e.g. case-control or cohort studies report the highest risk
- No consensus on what defines an athlete or sports participant; most studies relied on self-report of training or sports history
- No standardized method of AF ascertainment:
  - 12.5% AF prevalence amongst sports participations when relied on self-report
  - 2.7% AF prevalence amongst skiers when using electronic health records
Putative risk factors and therapeutic interventions for exercise-related AF

- Be aware of high heart rates during exercise: use dependence associated with class IC AAD
- Be aware of resting bradycardia: reverse use dependence associated with class III AAD
<table>
<thead>
<tr>
<th><strong>Atrial Fibrillation (AF)</strong></th>
<th><strong>Atrial Flutter (AFL)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Athletes with AF should undergo a workup that includes thyroid function tests, queries for drug use, ECG, and echocardiogram (Class I; Level of Evidence B). Athletes with low-risk AF that is well tolerated and self-terminating may participate in all competitive sports without therapy (Class I; Level of Evidence C). In athletes with AF, when antithrombotic therapy, other than aspirin, is indicated, it is reasonable to consider the bleeding risk in the context of the specific sport before clearance (Class IIa; Level of Evidence C). Catheter ablation for AF could obviate the need for rate control or antiarrhythmic drugs and should be considered (Class IIa; Level of Evidence B).</td>
<td>Athletes with AFL should undergo an evaluation that includes thyroid function tests, queries for drug use, ECG, and echocardiogram (Class I; Level of Evidence B). Catheter ablation for typical AFL has a high likelihood of success and should be considered (Class I; Level of Evidence B). When anticoagulation, other than with aspirin, is indicated in an athlete, it is reasonable to consider the bleeding risk in the context of the specific sport before clearance (Class IIa; Level of Evidence C).</td>
</tr>
</tbody>
</table>

Abbreviations: ECG, electrocardiograph.
### The main targets and goals

<table>
<thead>
<tr>
<th>Target</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Smoking</strong></td>
<td>No exposure to tobacco in any form.</td>
</tr>
<tr>
<td><strong>Diet</strong></td>
<td>Low in saturated fat with a focus on wholegrain products, vegetables, fruit and fish.</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td>At least 150 minutes a week of moderate aerobic PA (30 minutes for 5 days/week) or 75 minutes a week of vigorous aerobic PA (15 minutes for 5 days/week) or a combination thereof.</td>
</tr>
<tr>
<td><strong>Body weight</strong></td>
<td>BMI 20–25 kg/m². Waist circumference &lt;94 cm (men) or &lt;80 cm (women).</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
<td>&lt;140/90 mmHg&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

### Lipids<sup>b</sup>

- **LDL** is the primary target
- **Very high-risk:** <1.8 mmol/L (<70 mg/dL), or a reduction of at least 50% if the baseline is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL)<sup>d</sup>
- **High-risk:** <2.6 mmol/L (<100 mg/dL), or a reduction of at least 50% if the baseline is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL)
- **Low to moderate risk:** <3.0 mmol/L (<115 mg/dL).

| HDL-C           | No target but >1.0 mmol/L (>40 mg/dL) in men and >1.2 mmol/L (>45 mg/dL) in women indicate lower risk. |
| Triglycerides   | No target but <1.7 mmol/L (<150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors. |

### Diabetes

- HbA1c <7% (<53 mmol/mol)

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### Table 8: Cardiovascular and other conditions independently associated with atrial fibrillation

<table>
<thead>
<tr>
<th>Characteristic/comorbidity</th>
<th>Association with AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Habitual vigorous exercise&lt;sup&gt;214&lt;/sup&gt;</td>
<td>RR:</td>
</tr>
<tr>
<td>Non-exercisers</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>&lt;1 day/week</td>
<td>0.90 (95% CI 0.68–1.20)</td>
</tr>
<tr>
<td>1–2 days/week</td>
<td>1.09 (95% CI 0.95–1.26)</td>
</tr>
<tr>
<td>3–4 days/week</td>
<td>1.04 (95% CI 0.91–1.19)</td>
</tr>
<tr>
<td>5–7 days/week</td>
<td>1.20 (95% CI 1.02–1.41)</td>
</tr>
</tbody>
</table>

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2016 ESC CVD Prevention guideline

2016 ESC AF guideline
Take home message

• Exercise and physical activity appear to have remarkably beneficial effects for the majority of the population.

• The problem for most developed societies is **too little** and **NOT too much exercise**.

• Nevertheless, the possibility that prodigious amounts of exercise could adversely affect cardiac function and disease risk in some individuals or populations should be considered and examined