Paracelcus Reloaded: Searching for the Perfect Dose of Exercise?

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Conflicts/Disclosures: None
Objectives

• To provide a brief overview of the recognised benefits of physical activity on cardiovascular health.

• To discuss the currently recommended dose of physical activity for all individuals.

• To question whether too much exercise may have a deleterious impact on an otherwise normal heart.
Physical activity and CVD: Early Work

The first study to show an association between physical activity and risk of heart disease.

Morris et al. (1953) Lancet
Risk Hazard of CHD in Relation to Physical Activity

N = 44,452 professional males
Follow up of 475,755 person years

Tenesescue M et al JAMA 2002
Death Rates as a Function of Cardiovascular Fitness

13% reduction per MET

6.4 km/h

9 km/h

Church TS. Arch Int Med 2005
Kokkinos P et al Circulation 2008
15 year observational study.

55,137 individuals.

Mean age 44 years old.

Runners had a 30% all cause reduction in mortality and a 45% reduction in CVD events.
1098 joggers and 3,950 healthy non joggers.

Jogging 1-2.4 hours, over 2-3 times per week and a slow to moderate pace (6-10 MET equivalents) was associated with the best results for reduction in all cause mortality.

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Hazard Ratio
Current Physical Activity Guidelines

• **Adults:**

  30 mins of moderate intensity physical activity at least 5 days per week

  or 25 min vigorous activity 3 days per week

• **Children:** at least 60 minutes per day of moderate intensity physical activity.

(Chief Medical Officers Report 2004)
Endurance Athletes
Dose-Benefit Relationship

Cardiovascular Benefit

Benefits of exercise

Risks and harms

Exercise intensity
The Young Athlete’s Heart

10% increase in LV and RV cavity.

10-20% increase in left ventricular wall thickness
Left Ventricular Cavity Dimensions in Highly Trained Athletes

48%

14%

Cardiac Risk in the Young
Centre for Sports Cardiology
44 Italian Olympian males with LVH (> 13 mm) and enlarged LV cavity (> 60 mm).

De-trained for a mean of 53 months.

LV wall thickness and LV mass normalised.

Remodeling of Left Ventricular Hypertrophy in Elite Athletes After Long-Term Deconditioning
Antonio Pelliccia, Barry J. Maron, Rosanna De Luca, Fernando M. Di Paolo, Antonio Spataro and Franco Culasso
Circulation 2002;105:944-949; originally published online Feb 4, 2002;
DOI: 10.1161/he0802.104534
The Ugly Side of Exercise: Sudden Cardiac Death

90% during or just after exercise

90% in males

80% don’t have prodromal symptoms

40% in age < 18 years old
Triggers for Sudden Cardiac Death

- Dehydration
- Adrenergic surges
- Electrolyte imbalance
- Acid/base disturbance

[Diagram showing the relationship between these triggers]

[ECG trace image]
Can Exercise Induce Cardiomyopathy in a Normal Heart?

Endurance athletes exercise 10-15 x the daily recommended exercise.

2 million marathon participants each year.

Can you get too much of a good thing?
Evidence of Transient Cardiac Injury Post Marathon Running

• Raised cardiac troponin levels post race (EXERCISE INDUCED CARDIAC DAMAGE)

• Impaired left ventricular function (EXERCISE INDUCED CARDIAC FATIGUE)
Could Too Much Exercise Be Cardiotoxic?
Troponin Release
High BNP concentrations

SEROLOGICAL MARKERS

PATHOLOGY

Adverse cardiac remodelling
Cardiac Dysfunction
+ Arrhythmias

HISTOLOGICAL CHANGES

Myocardial inflammation
Myocardial fibrosis

CARDIAC RISK in the Young Centre for Sports Cardiology
Animal model of Endurance Training

Exercised for 60mins daily for 16 weeks

Compared with sedentary rats

Enlarged Atria and RVH/LVH
Fibrosis

Diastolic dysfunction

VT in 42%
102 healthy males aged 50-72 years old.

Completed at least 5 marathons in the past 3 years.

12 had late gadolinium enhancement which was 3-fold commoner than in age-matched controls.

5 had LGE with a coronary artery disease pattern.

7 had non specific patchy fibrosis.
Atrial Fibrillation in Athletes

Long-lasting sport practice and lone atrial fibrillation

L. Mont¹, A. Sambola¹, J. Brugada¹, M. Vacca³, J. Marrugat², R. Elosua², C. Paré¹, M. Azqueta¹ and G. Sanz¹

¹Institute of Cardiovascular Diseases, Hospital Clinic, Institut d'Investigaciones Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Villarroel 170, Barcelona 08036, Spain; ²Lipids and Cardiovascular Epidemiology Research Unit, Institut Municipal d'Investigació Médica (IMIM), Barcelona, Spain

Atrial fibrillation in athletes

Atria fibrillation in endurance-trained athletes

A V Sorokin, C G S Araujo, S Zweibel, et al.

Br J Sports Med published online July 13, 2009
doi: 10.1136/bjsm.2009.057885
Atrial Fibrillation in Sportsmen

**Incidence**

5-10% of middle aged endurance athletes

Risk of lone AF over 5-fold greater than in matched sedentary individuals.

Usually sportsmen who have been exercising since youth.

Almost all male.
Risk factors for Atrial Fibrillation in Athletes

- Male sex
- Age 40-60
- Endurance sport
- Tall stature
- Exercise time 1500 hours over a lifetime
AF in Athletes

Trigger
?Increased pulmonary vein ectopy

Endurance sport practice

Modulators
Increased vagal tone:
Bradycardia
Shortening and dispersion of the atrial refractory period
Gastro-oesophageal reflux

Substrate
Pressure and volume overload:
Atrial stretch
Myocyte Hypertrophy
Atrial dilatation
Inflammatory response
Atrial fibrosis
Sinus node disease and arrhythmias in the long-term follow-up of former professional cyclists

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### Sinus node disease and arrhythmias in the long-term follow-up of former professional cyclists

Sylvette Baldesberger¹, Urs Bauersfeld², Reto Candinas¹, Burkhardt Seifert³, Michel Zuber⁴, Manfred Ritter⁵, Rolf Jenni⁶, Erwin Oechslin⁶, Pia Luthi¹, Christop Scharf¹, Bernhard Marti⁷, and Christine H. Attenhofer Jost¹*  

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*European Heart Journal*  
doi:10.1093/eurheartj/ehm555  

**Cardiac Risk in the Young Centre for Sports Cardiology**
Risk of arrhythmias in 52 755 long-distance cross-country skiers: a cohort study

Kasper Andersen¹*, Bahman Farahmand²,³, Anders Ahlbom², Claes Held¹, Sverker Ljunghall¹, Karl Michaëlsson⁴, and Johan Sundström¹

Studied participants in the Vasalopett (90k) cross country ski race between 1989-1998. 90% Male.

Followed by until December 2005.

959 had significant arrhythmias (AF, A flutter and bradyarrhythmias) which correlated with the number of races completed and faster finishing times; HR 1.30 each.
High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias: Role of an electrophysiologic study in risk stratification

Hein Heidbüchel\textsuperscript{a*}, Jan Hoogsteen\textsuperscript{b,d}, Robert Fagard\textsuperscript{a}, L. Vanhees\textsuperscript{a}, Hugo Ector\textsuperscript{a}, Rik Willems\textsuperscript{a}, Johan Van Lierde\textsuperscript{c,d}

46 endurance athletes

Symptoms \(n=36\)
- Syncope 65%
- Aborted SCD 2%
- Palpitation 15%

Complex ventricular arrhythmias
- Very abnormal ECG in 58%
- VT or RV origin in 49%
- Criteria for ARVC in 59%

9 died suddenly and 9 got ICD

Cardiac Risk in the Young Centre for Sports Cardiology
22 symptomatic athletes; cyclists (77%)

Arrhythmias of right ventricular origin

Right ventriculography revealed enlarged right ventricles with reduced ejection fraction

Possible explanations:

1. Increased RV work load may unmask heterozygotes for ARVC

2. Exercise causes adverse remodelling of the RV and increases risk of arrhythmias
Lower than expected desmosomal gene mutation prevalence in endurance athletes with complex ventricular arrhythmias of right ventricular origin

A La Gerche, C Robberecht, C Kuiperi, et al.

*Heart* 2010 96: 1268-1274 originally published online June 4, 2010
doi: 10.1136/hrt.2009.189621

- **n = 47**
  - 51% ‘Definite ARVC’ by TFC
  - 36% ‘Suspected ARVC’ by TFC

An ARVC-like phenotype may be acquired through intense exercise
Exercise-induced right ventricular dysfunction and structural remodelling in endurance athletes

André La Gerche¹,², Andrew T. Burns³, Don J. Mooney⁴, Warrick J. Inder¹, Andrew J. Taylor⁴, Jan Bogaert⁵, Andrew I. MacIsaac³, Hein Heidbüchel², and David L. Prior¹,³

40 healthy endurance athletes
Assessed immediately before, after and 7 days after an ultra-endurance race.

Troponin levels correlated with magnitude of RV dysfunction
**Right Ventricular Exercise Physiology**

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**EXERCISE**

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Exercise-induced arrhythmogenic right ventricular cardiomyopathy: fact or fallacy?

Sanjay Sharma* and Abbas Zaidi

Diagram:
- **Evidence**
  - Acute reversible RV injury

- **Hypotheses**
  - Healthy athlete’s heart: Minimal cardiac injury and adequate recovery between exercise bouts → improved cardiac function
  - Over-trained athlete’s heart: More severe cardiac injury and/or inadequate recovery → chronic structural change, reduced cardiac function, clinical events

**Time**
Running: the risk of coronary events†

Prevalence and prognostic relevance of coronary atherosclerosis in marathon runners

108 Males aged 50-72 years old

High calcium scores and late gadolinium enhancement in presumably healthy middle aged marathon runners compared with Framingham risk matched controls

Marathon running associated with a 2-fold increase in LGE.

56% runners were current or former smokers
Chronic endurance exercise

- Cardiac arrhythmias
  - Myocyte necrosis
  - (cTn rise)
  - ? Myocardial scars
  - RV Pressure
  - Arrhythmogenic right ventricular cardiomyopathy
  - Dilated Cardiomyopathy
  - RV Pressure
  - Arrhythmogenic right ventricular cardiomyopathy
  - Dilated Cardiomyopathy

- Atrial fibrillation
  - Adverse atrial remodelling

- High degree AV block
114 athletes (78% Male)
Mean age 22 ± 4
Continuous intensive physical training for at least 2 consecutive Olympics (2-5)
Mean training period 8.6 ± 3 years (4-17)

Rowers and canoeists (n=55), cyclists (n=19), cross-country skiing (n =15) long distance running/marathon (n=9), swimming (n=6) triathlon (n=2)
Figure 1  Serial Echocardiographic Views of the LV in an Elite Italian Marathon Runner
Aging is associated with decreased left ventricular compliance and distensibility.

4-5 sessions of intensive exercise for 30 minutes per week over 25 years prevented such age related changes.

Lower doses of exercise did not retard this normal aging process.

Masters athletes exhibited the most compliant ventricles.

and may reduce the risk of hypertension and heart failure with preserved ejection fraction.
### Dose of Jogging and Long-Term Mortality

**The Copenhagen City Heart Study**

Peter Schnohr, MD, DMSc,* James H. O’Keefe, MD,† Jacob L. Marott, MSc,* Peter Lange, MD, DMSc,*‡
Gorm B. Jensen, MD, DMSc*§

#### DOSE OF JOGGING

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Elite Endurance Athletes Live Longer than Non Athletes

Strenuous endurance exercise improves life expectancy: it’s in our genes

Jonatan R Ruiz,1 Maria Morán,2,3 Joaquín Arenas,2–4 Alejandro Lucia5

Mortality of French participants in the Tour de France (1947–2012)

Eloi Marijon1,2,3,4, Muriel Tafflet1,2,5, Juliana Antero-Jacquemin1,5, Nour El Helou1,5,6, Geoffroy Berthelot1,5, David S. Celermajer7, Wulfran Bougouin1,2,4, Nicolas Combes4, Olivier Hermine1,9,12,13, Jean-Philippe Empana1,2, Grégoire Rey10, Jean-François Toussaint1,5,14, and Xavier Jouven1,2,5,4

Review
Mortality and longevity of elite athlete

Masaru Teramotoa,*, Timothy J. Bungumb

BJSM 2011
Sudden Cardiac death in sport

Acute Myocardial infarction

Alcohol

Diabetes

Obesity

Prostate cancer

Smoking related deaths

Mortality rate per 100,000 population
Died age 51
May he rest in peace

Marathon Runners
Numerator versus Denominator

Athletes with disease phenotypes (based on case reports and small cohort studies)

Athletes with raised markers of cardiac damage

Apparently Healthy Ultra-endurance runners (millions)
Prospective Studies
Conclusions

Moderate exercise has cardiovascular benefits.

Long term endurance exercise promotes atrial fibrillation in some athletes.

Larger prospective studies are necessary to confirm or refute whether life long endurance exercise exerts a plethora of deleterious effects on an otherwise normal heart.