Sudden cardiac death in athletes: in perspective and from different perspectives

Prof. Dr. Hein Heidbuchel

Disclosures

National Coordinator of RE-LY/Rely-able (Boehringer Ingelheim), Rocket-AF (Bayer, J&J), ENGAGE-AF (Daiichi-Sankyo) and of other studies sponsored by Sanofi-Aventis, Cardiome, Bayer J&J, Daiichi-Sankyo.

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Shareholder: none
Sudden cardiac death in athletes: is it a big problem?

- Difficult to have good data
- Veneto region (Italy): 300 SD during 29 million y of FU

<table>
<thead>
<tr>
<th></th>
<th>Athletes (n = 55)</th>
<th>Non-Athletes (n = 245)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yrs)</td>
<td>23.1 ± 7</td>
<td>23.9 ± 9</td>
<td>1.0</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>50</td>
<td>170</td>
<td>0.002</td>
</tr>
<tr>
<td>Females</td>
<td>5</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Circumstances of death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise-related</td>
<td>49 (89%)</td>
<td>22 (9%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>During effort</td>
<td>40</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>After effort</td>
<td>9</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Unrelated to exercise</td>
<td>6 (11%)</td>
<td>225 (91%)</td>
<td></td>
</tr>
</tbody>
</table>

- relative risk in athletes is 2.5 (p<0.0001)
- no manifest increased risk in women

Corrado et al, JACC 2003

Sudden cardiac death in athletes: is it a big problem?

- Sports-related SCD is dependent on population:
  - 1 in 43000 in NCAA athletes (US)
  - 1 in 18000 in black NCAA athletes
  - 1 in 3000 in male competitive basketball players

- Incidence is dependent on registration
  - media and/or insurance claim data underestimate 2x to 5x

- There is no official recording of sports-related SCD
  - not in Belgium
  - not in Europe
  - not in the world

Sudden cardiac death in athletes: is it a big problem?

- Sports-related SCD is highly age-dependent:

Table. Estimated Incidence Rates of Sports-Related Sudden Death According to Sex and Age

<table>
<thead>
<tr>
<th>Age group, y</th>
<th>No. of Participants</th>
<th>Overall Incidence/ Million Sport Participants/Year (95% CI)</th>
<th>No. of Participants</th>
<th>Incidence/ Million Male Participants/Year (95% CI)</th>
<th>No. of Participants</th>
<th>Incidence/ Million Male Participants/Year (95% CI)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19</td>
<td>160</td>
<td>2.96 (2.30-3.42)</td>
<td>11</td>
<td>0.43 (0.18-0.69)</td>
<td>149</td>
<td>5.23 (4.39-6.07)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>20-24</td>
<td>357</td>
<td>5.63 (5.94-7.31)</td>
<td>13</td>
<td>0.49 (0.23-0.76)</td>
<td>344</td>
<td>12.47 (11.15-13.77)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>25-29</td>
<td>258</td>
<td>7.31 (6.80-8.43)</td>
<td>11</td>
<td>0.65 (0.27-1.03)</td>
<td>247</td>
<td>14.18 (12.42-15.94)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Overall</td>
<td>775</td>
<td>5.45 (5.07-5.83)</td>
<td>35</td>
<td>0.51 (0.34-0.68)</td>
<td>740</td>
<td>9.07 (8.34-9.81)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

* Statistical tests used were categorical comparisons and tests for trends.

1. Marijon et al, JAMA 2013

Death in athletes cardiac vs. non-cardiac

- US data:

273 deaths/ 1.97 million athlete years

1. Harmon et al, Circulation 2011
Death in athletes cardiac vs. non-cardiac

• US data:\(^1\)

<p>| | |</p>
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<tr>
<td>273 deaths/ 1.97 million athlete years</td>
<td></td>
</tr>
<tr>
<td>Traumatic</td>
<td>Medical</td>
</tr>
<tr>
<td>±70%</td>
<td>±30%</td>
</tr>
</tbody>
</table>

1. Harmon et al, Circulation 2011
Sudden death in athletes
Other causes:

• Non-cardiac
  – trauma
  – dissection/rupture of the aorta (Marfan syndrome)
  – intracranial bleeding
  – asphyxia through food aspiration
  – drugs
  – drowning
  – hypothermia
  – hyperthermia
  – …

• Unknown

Sudden death in athletes
What’s the cause?

45 NCAA athletes, sudden death between 2004-2008
36 available autopsies

31% no diagnosis!

Harmon et al., Circ AE 2014
Athletic death vs. other mortality in young people

Annual absolute number of death (US) 15 to 24 year old

1. Maron et al, JACC 2014 (note: many different data sources)

Sudden cardiac death in athletes: Can we disregard it?

- Survival is similar to matched Swiss male population\(^2\)
  (n=62 former athletes participating Tour de Suisse 1955-1975)

- Standardized mortality ratio < male general population\(^1\)
  (n=786 French participants Tour de France 1947-2012)

Sudden cardiac death in athletes: Can we disregard it?

- Genetic selection (“the healthy worker effect”), and
- positive health effects related to sports (direct or indirect)…
- … do not negate recognition of possible negative effects.

La Gerche & Heidbuchel, Circulation 2014 (in press)

Sudden death and sports
Underlying heart disease

- ≤35 years: (VS data)

Maron et al., JAMA 1996

- >35 years: 75% = ischemic heart disease
1. Sport as trigger for arrhythmias

- Physical activity affects in general:
  - autonomic tone
  - ion disturbances
  - temperature
  - ischemia
  - direct stretch activated electrophysiological perturbations
    - cf. functional triad of gap junctions with sodium channels\(^1\)
  - ...

1. Delmar & McKenna, Circ Res 2010

Who can safely participate?
2. Sport as substrate promoter

- Sport leads to global cardiac adaptations at all levels.
- If underlying ARVC:

=> sports will lead to progression of the substrate.

symptoms at younger age
more likely to meet Task Force Criteria
more VT/VF (and regression if reduction in exercise after VT/VF)²

Pulmonary artery pressure during exercise

- 40 athletes & 15 non-athletes\(^1\)\(^-\)\(^3\)

![Graph showing pulmonary artery pressure vs. cardiac output with athletes and non-athletes plotted separately. The graph includes a note: (Near) linear increase in pulmonary artery pressures with exercise intensity. Independent of athletic status (\(p = 0.71\)).]


RV vs. LV end-systolic wall stress
Laplace equation: ESWS = P.r/2h

- TEE max exercise on semi-supine bicycle + radial artery catheter; CMR

![Graph showing comparison of left vs. right ventricle end-systolic wall stress. The graph includes a note: *\(p < 0.0001\) and \(p = 0.083\).]

1. LaGerche, Prior & Heidbuchel, Med Sci Sports Exerc 2010
3. Sport as substrate inducer

Even in the absence of desmosomal mutations: “Exercise-induced ARVC”1-3

1. Heidbuchel et al, Eur Heart J 2003;
Athlete heart evaluation: Positive or negative remodeling?

- Can be very complex, including
  - morphologic evaluation
  - genetic evaluation
  - electrical evaluation
    - resting 12-lead ECG
    - exercise testing
    - Holter
    - late potentials
    - electrophysiological study

Electrophysiological Study
Freedom from sustained VT or sudden death

**Relative Risk 3.4**
Heidbuchel et al, Eur Heart J 2003
What happens to the heart during exercise?

Exercise CMR + invasive pressure measurements


Cardiac volumes @ 181 bpm

Post-race study: design

**BASELINE**

3 weeks

**POST-RACE**

5 hours

150 km cycling race

n = 14 athletes

age: 36 ± 6 years

training history

- 11 ± 7 years
- 13 ± 5 h/week

exercise CMR + biochemistry at baseline and post-race

**Post-race study:**

Unchanged LV EF but reduced RV EF

Exercise MRI:
RV contractility measure

EA: elite athletes; NA: non-athletes; VA: ventricular arrhythmias

A. La Gerche, G. Claessen & H. Heidbuchel (submitted)

How to help them if anything goes wrong?
If we cannot prevent SCD…

- Prospective registry sports-related SD 10-75y (France)\(^1\)
- 10-fold regional disparity of survival (3.4 to 42.6%, \(p<0.001\))

- related to bystander CPR and shockable rhythm
  - prompt CPR and AED use can lead to survival of up to 64% \(^2\)


Can she participate?

Lady X
Can athletes with an ICD continue?

Safety of Sports for Athletes With Implantable Cardioverter-Defibrillators
Results of a Prospective, Multinational Registry

Rachel Lampert, MD; Brian Olshansky, MD; Hein Heidbuchel, MD; Christine Lawless, MD; Elizabeth Saare, MD; Michael Ackerman, MD; Hugh Calkins, MD; N.A. Mark Esmes, MD; Mark S. Link, MD; Barry J. Maron, MD; Frank Marcus, MD; Melvin Scheinman, MD; Bruce L. Wilkoff, MD; Douglas P. Zipes, MD; Charles J. Berul, MD; Alan Cheng, MD; Ian Law, MD; Michele Loomis, APRN; Cheryl Barth, BS; Cynthia Brandt, MD; Jannes Dolara, PhD; Fangyong Li, MS; David Cannom, MD

- US initiated (Dec 2006)
- European extension (Jul 2008)
  - European Coordinator:
    - Hein Heidbuchel, MD PhD, University of Leuven
  - Endorsed by:
    - EACPR Section on Sports Cardiology
    - EHRA Scientific Initiative Committee

Lampert, Olshansky, Heidbuchel et al, Circulation 2013

Registry on ICD in Sports Population

- 372 athletes
  - organized sports in 328; high-risk sports in 44
    - mainly running, basketball, soccer
    - mean of 5.1 h/w
  - 137 competing at interscholastic, national, international level
    - 13 h/w
- Median follow-up 31 months
- Median age 33y; 33% female; mean EF 60%
- Mainly LQTS, HCM, ARVC
- 42% secondary prevention
- 62% beta-blockers

Lampert, Olshansky, Heidbuchel et al, Circulation 2013
Registry on ICD in Sports
Results /1 Primary Endpoints

- Death or resuscitation: n = 0
- Arrhythmia- or shock-related injury: n = 0
  - 95% confidence interval: 0 – 1.5%

Lampert, Olshansky, Heidbuchel et al, Circulation 2013

Registry on ICD in Sports
Results /2 Secondary Endpoints

- Moderate injury: n = 0
- System malfunction:
  - No generator malfunctions
  - Freedom from definite lead malfunction (noise; abrasion):
    97% @5y; 90% @10y

Lampert, Olshansky, Heidbuchel et al, Circulation 2013
Registry on ICD in Sports
Results /3 ... but...

• 21% athletes received shocks
  – majority (16% athletes) during physical activity or sports (p<0.0001)
  – 13% athletes appropriate shocks
    • in 8% during physical activity or sports (p=0.006)
    • ARVC and idiopathic VF more than HCM or LQTS (p<0.05)
  – 11% athletes inappropriate shocks
    • in ±8% during physical activity or sports

• 8 episodes in 7 athletes with multiple shocks (“VT storm”)
  – of which 7 during physical activity / sports

• 30% of those who received shocks during sports: stopped sports...

Lampert, Olshansky, Heidbuchel et al, Circulation 2013

So, and she?
LQT3 carrier
“Recreational” running

Considerations:

1. Risk for damage to lead/device? ±?
2. Risk when loss of consciousness? ±
3. Effectiveness if arrhythmia during sports OK
4. Induction of arrhythmias? OK
5. Likelihood for inappropriate shocks? ±
6. Induction or progression of substrate? OK

Conclusion: likely ‘yes’

Heidbuchel & Carré, Eur Heart J 2014
So, and she?

ARVC
Competitive soccer (regional)

Considerations:
1. Risk for damage to lead/device? ±
2. Risk when loss of consciousness? ±
3. Effectiveness if arrhythmia during sports OK
4. Induction of arrhythmias? not OK
5. Likelihood for inappropriate shocks? not OK
6. Induction or progression of substrate? not OK

Conclusion: better ‘not’

Heidbuchel & Carré, Eur Heart J 2014

Ethical & philosophical considerations

• “Informed decision by athletes”
  – what is the personal freedom for choice by athlete / advising physician?
  – has society the moral right (or duty) to protect individuals?
  – we may restrict their freedom by unbalanced “yes, you can go”

• Science as a tool to defy nature?
  – Just relying on our technology to protect…?
  – Athletes, or gladiators …?

Heidbuchel & Carré, Eur Heart J 2014
Thank you!