Intense prolonged exercise causes acute right ventricular injury which may not be completely reversible.

A La Gerche¹,⁴, AT Burns², DJ Mooney², AJ Taylor³, AI MacIsaac², H Heidbuchel⁴, DL Prior¹,²

¹Department of Medicine, University of Melbourne
²Cardiology Department, St Vincent’s Hospital Melbourne
³Alfred Hospital and Baker IDI Melbourne
⁴University Hospital of Leuven, Belgium

André La Gerche
St Vincent’s Hospital, University of Melbourne
University Hospital, Leuven, Belgium

No Disclosures
Background

- Moderate exercise has proven efficacy in improving cardiovascular health
- The benefits of intense endurance exercise are less certain
- Elevations in cardiac biomarkers have raised the possibility of cardiac injury
- LV abnormalities are inconsistently reported and mild
Background

• Functional abnormalities of the RV may be more common than the LV
  La Gerche et al. Heart 2008

• In athletes, ventricular arrhythmias are:
  – most commonly of RV origin
  – associated with RV functional abnormalities
  – may be life threatening
  – distinct from ARVC
  Heidbuchel et al. EHJ 2003
  La Gerche et al. Heart 2010
Intense endurance exercise may induce *right ventricular* remodelling which may represent an arrhythmogenic substrate.
Aims

- To compare RV and LV morphology and function after endurance exercise
- To assess whether post-race elevations in cardiac biomarkers may be explained by changes in RV function
- To assess whether post-race changes are influenced by exercise duration
- To assess whether all post-race changes completely recover
Methods

- 40 well-trained endurance athletes over 4 events of increasing duration

<table>
<thead>
<tr>
<th>Race</th>
<th>Distance (km)</th>
<th>No. of study subjects</th>
<th>average finishing time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marathon</td>
<td>42.2</td>
<td>7</td>
<td>2 hrs 59 mins ±30 mins</td>
</tr>
<tr>
<td>Endurance Triathlon</td>
<td>1.9/ 90/ 21.1</td>
<td>11</td>
<td>5 hrs 24 mins ± 25 mins</td>
</tr>
<tr>
<td>Alpine Cycling race</td>
<td>207</td>
<td>9</td>
<td>8 hrs 5 mins ± 42 mins</td>
</tr>
<tr>
<td>Ultra-endurance Triathlon</td>
<td>3.8/ 180/ 42.2</td>
<td>13</td>
<td>10 hrs 52 mins ±1 hr 16 mins</td>
</tr>
</tbody>
</table>
Methods

**BASELINE**
- Cardiac Magnetic Resonance Imaging (including DGE)
- Echocardiography
- Troponin (cTnI) and B-type natriuretic peptide (BNP)

**POST-RACE**
- Echo
- cTnI and BNP

**DELAYED**
- Echo

14 – 21 days

6 – 11 days
Methods - echocardiography

- **3D Echo (GE Vivid 7)**
  - LV and RV full volume acquisitions
  - TomTec software
  - Validated against CMR

- **Strain and SR imaging**
  - 2D speckle tracking
  - RV and LV separately
  - 60 - 90 frames per second

- **Traditional**
  - RV Fractional Area Change
  - Tricuspid Annular Plane Systolic Excursion
Methods – Cardiac Magnetic Resonance

• 1.5-T scanner (Signa Excite, GE)

• Volumetric analysis
  ➢ Short axis stack (8mm, no gaps)
  ➢ Endo and epicardial tracing

• Delayed enhancement
  ➢ Gadolinium-DTPA (0.2 mmol/kg)
  ➢ T1 weighted images
  ➢ DGE assessed by two blinded independent observers
  ➢Confirmed by mean signal intensity > 2SD that of neighbouring myocardium (Osirix software)

Inversion time 300 – 400 ms
Methods

• Statistical analysis
  – Pre and post-race comparisons by paired T-test
  – Time point measures were compared by ANOVA
  – Changes according to race duration by FANOVA
  – Relation between $\Delta$ EF and biomarkers by linear regression
  – $p < 0.05$ significant
# Results: Post-race biomarker increase

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post-race</th>
<th>Follow-up</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>52 ± 7</td>
<td>72 ± 9</td>
<td>54 ± 6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic BP (mm/Hg)</td>
<td>147 ± 14</td>
<td>117 ± 13</td>
<td>134 ± 20</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic BP (mm/Hg)</td>
<td>77 ± 7</td>
<td>70 ± 11</td>
<td>74 ± 10</td>
<td>0.001</td>
</tr>
<tr>
<td>PASP (mmHg)</td>
<td>21.5 ± 3.8</td>
<td>18.0 ± 3.3</td>
<td>20.0 ± 3.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Biochemical Measures

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post-race</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detectable cTnI (≥0.015µg/L) / total</td>
<td>9/40</td>
<td>40/40</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>cTnI (µg/L) median, range</td>
<td>&lt;0.015, 0.21</td>
<td>0.08, 0.97</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BNP (ng/L)</td>
<td>13.1 ± 14.0</td>
<td>25.4 ± 21.4</td>
<td>0.003</td>
</tr>
</tbody>
</table>
Cardiac Biomarkers correlate with RVEF

No correlation with LV measures
Results: RV but not LV dysfunction

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post-race</th>
<th>Follow-up</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Right Ventricular Measures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVEF (%)</td>
<td>51.0 ± 3.6</td>
<td>46.4 ± 6.5</td>
<td>50.0 ± 3.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RVFAC (%)</td>
<td>51.5 ± 6.0</td>
<td>44.3 ± 11.2</td>
<td>49.8 ± 6.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TAPSE</td>
<td>24.9 ± 3.9</td>
<td>24.0 ± 4.5</td>
<td>26.5 ± 4.1</td>
<td>0.035</td>
</tr>
<tr>
<td>RV strain (%)</td>
<td>27.2 ± 3.4</td>
<td>23.7 ± 3.7</td>
<td>25.6 ± 3.0</td>
<td>0.001</td>
</tr>
<tr>
<td>RV SRs (s⁻¹)</td>
<td>1.42 ± 0.24</td>
<td>1.26 ± 0.23</td>
<td>1.29 ± 0.19</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Left Ventricular Measures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>56.4 ± 5.2</td>
<td>57.5 ± 5.6</td>
<td>58.8 ± 5.1</td>
<td>0.147</td>
</tr>
<tr>
<td>LV strain (%)</td>
<td>18.4 ± 3.7</td>
<td>16.9 ± 2.8</td>
<td>17.7 ± 2.3</td>
<td>0.071</td>
</tr>
<tr>
<td>LV SRs (s⁻¹)</td>
<td>0.98 ± 0.26</td>
<td>0.95 ± 0.15</td>
<td>0.89 ± 0.13</td>
<td>0.13</td>
</tr>
</tbody>
</table>

**ALL RV measures decreased whilst NO LV measures changed**
RV *dilates* whilst the LV *shrinks*

**End-diastolic Volume**
- **Baseline**: 170 ±30 ml, 150 ±23 ml
- **Post-race**: 179 ±25 ml, 143 ±21 ml

**End-systolic Volume**
- **Baseline**: 83 ±17 ml, 66 ±14 ml
- **Post-race**: 96 ±19 ml, 61 ±12 ml
Results: RV Ejection Fraction

Duration dependent reduction in RV measures
Results – delayed gadolinium enhancement

Focal DGE observed in 5/39 athletes (12.8%)

Evidence of permanent structural remodelling
## Delayed Gadolinium Enhancement

<table>
<thead>
<tr>
<th></th>
<th>DGE +ve (n = 5)</th>
<th>DGE -ve (n = 34)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>43 ± 13</td>
<td>35 ± 8</td>
<td>0.057</td>
</tr>
<tr>
<td>Years of endurance sport</td>
<td>20 ± 16</td>
<td>8 ± 6</td>
<td>0.043</td>
</tr>
<tr>
<td><strong>Cardiac volumes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV End-diastolic Volume (ml)</td>
<td>300 ± 25</td>
<td>259 ± 39</td>
<td>0.029</td>
</tr>
<tr>
<td>RV End-systolic Volume (ml)</td>
<td>158 ± 15</td>
<td>127 ± 21</td>
<td>0.003</td>
</tr>
<tr>
<td>RV Ejection Fraction (%)</td>
<td>47.1 ± 5.9</td>
<td>51.1 ± 3.7</td>
<td>0.042</td>
</tr>
<tr>
<td>LV End-diastolic Volume (ml)</td>
<td>258 ± 25</td>
<td>226 ± 35</td>
<td>0.058</td>
</tr>
<tr>
<td>LV End-systolic Volume (ml)</td>
<td>112 ± 19</td>
<td>91 ± 21</td>
<td>0.042</td>
</tr>
<tr>
<td>LV Ejection Fraction (%)</td>
<td>56.5 ± 6.8</td>
<td>59.8 ± 5.6</td>
<td>0.242</td>
</tr>
</tbody>
</table>

DGE associated with greater (RV) remodelling
Conclusions

• Intense endurance exercise results in acute right ventricular injury but not LV injury

• RV injury:
  – correlates with cardiac biomarker elevations
  – relates to duration of exercise

• Delayed Gadolinium Enhancement:
  – may be seen in some healthy athletes
  – is associated with greater exercise exposure and more profound cardiac remodelling

• Repeated bouts of acute RV injury may lead to permanent structural remodelling in some athletes
Thanks to:

St Vincent’s Hospital, University of Melbourne, Australia
Assoc. Prof David Prior
Assoc. Prof Andrew MacIsaac
Dr Andrew Burns
Don Mooney

University Hospital, Leuven, Belgium
Professor Hein Heidbüchel
Professor Jan Bogaert

Alfred Hospital and Baker IDI Melbourne
Dr Andrew Taylor

Funding:
National Health and Medical Research Council, Australia
Heart Foundation of Australia
Pfizer CVL project grant

The Athletes
Validation of 3DE against CMR

**Left Ventricle**

(a) LV EDV (ml) - 3D Echo vs. CMR
(b) LV ESV (ml) - 3D Echo vs. CMR
(c) LV EDV (ml) - 3D Echo vs. CMR
(d) LV ESV (ml) - 3D Echo vs. CMR

**Right Ventricle**

(a) RV EDV (ml) - 3D Echo vs. CMR
(b) RV ESV (ml) - 3D Echo vs. CMR
(c) RV EDV (ml) - 3D Echo vs. CMR
(d) RV ESV (ml) - 3D Echo vs. CMR

Mean difference ± Standard deviation
- LV EDV: 79 ± 22 ml
- LV ESV: 27 ± 13 ml
- RV EDV: 94 ± 27 ml
- RV ESV: 44 ± 17 ml
Ejection fraction: 3DE against CMR

Left Ventricle

Right Ventricle

Mean difference ± Standard deviation
LV EF (%) - 3D Echo

Mean difference ± Standard deviation
RV EF (%) - 3D Echo

R Sq Linear = 0.194
p = 0.001

R Sq Linear = 0.238
p < 0.0001
### Results – RV dysfunction

#### ASE guidelines for RV assessment *(Rudski et al. *JASE* 2010)*

<table>
<thead>
<tr>
<th>Metric</th>
<th>Count</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVFAC $&lt; 0.35$</td>
<td>10/ 40</td>
<td></td>
<td>(25%)</td>
</tr>
<tr>
<td>TAPSE $&lt; 16$ mm</td>
<td>5/ 40</td>
<td></td>
<td>(12.5%)</td>
</tr>
<tr>
<td>3D RVEF $&lt; 45%$</td>
<td>17/ 40</td>
<td></td>
<td>(42.5%)</td>
</tr>
<tr>
<td>RV strain $\leq 20%$</td>
<td>8/ 40</td>
<td></td>
<td>(20%)</td>
</tr>
<tr>
<td>RV strain rate $\leq 0.85$ s$^{-1}$</td>
<td>3/ 40</td>
<td></td>
<td>(7.5%)</td>
</tr>
</tbody>
</table>
**Ventricular interaction**

**Baseline** vs. **Post-race**

**RV:LV end-systolic diameter ratio**

- Baseline: $0.54 \pm 0.14$
- Post-race: $0.69 \pm 0.19$

$p < 0.0001$