Exercise in Metabolic Myopathies

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1942 Packard
Measuring capacity at the metabolic level
Defects in Glycolysis
McArdle’s disease
Symptoms

- Muscle cramps
- Fatigue
- Myoglobinuria
Lactate in McArdle’s Disease

Riley et al. 1993
Subj: SB–McArdle's disease  EXERCISE PERFORMANCE REPORT
Protocol: 5W min⁻¹ bicycle ramp
(10 sec average after second by second interpolation)
Gender: M  Age: 36  Weight: 74kg  Height: 1.73m  Indication: McArdle's research
73m Indication: McArdle’s research
Riley et al. 1993
2A

VE (liter/min) vs. $VO_2$ (liter/min)

2B

VE (liter/min) vs. lactate (mM)
\[ O_2\text{-pulse (}\dot{\text{VO}}_2/\text{HR}) \]

\[ \dot{\text{VO}}_2 = \dot{Q} \times C(a-v)\text{O}_2 \]

\[ \dot{Q} = \text{HR} \times \text{SV} \]

\[ \dot{\text{VO}}_2/\text{HR} = \text{SV} \times C(a-v)\text{O}_2 \]
Normal $O_2$-pulse
Arteriovenous O$_2$ difference (ml dl$^{-1}$)

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Maximum exercise</th>
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<tbody>
<tr>
<td>Normals (n=8)</td>
<td>5.3 ± 1.2</td>
<td>16.6 ± 1.4</td>
</tr>
<tr>
<td>McArdle’s</td>
<td>4.9</td>
<td>6.5</td>
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Haller et al. 1983
\( \dot{Q} - \dot{VO}_2 \) relationship in McArdle’s

Lewis et al. 1984
O’Dochartaigh et al. 2004
Plasma Ammonia (μM)

NH₃

Riley et al. 1993
Source of ammonia during exercise

- **Myokinase Reaction**

\[
2 \text{ADP} \rightarrow \text{ATP} + \text{AMP}
\]

- **Myoadenylate Deaminase Reaction**

\[
\text{AMP} \rightarrow \text{Inosine} + \text{NH}_3
\]

? gluconeogenesis with amino acid deamination
McArdle’s Disease

- Low VO$_2$
- Low RER and absent LAT
- Brisk HR response with low O$_2$ pulse
- High Q – VO$_2$ and high VO$_2$– WR relationships
- Low lactate
- High ammonia
Mitochondrial myopathy
Ragged Red myopathy
Ragged red fibres

succinate dehydrogenase staining

cytochrome c oxidase staining
Symptoms

- Muscle cramps
- Fatigue
- Dyspnoea
Premature lactate accumulation in heart disease
Bogaard et al. 1988
Wallace et al. 1988
Taivassalo et al. 2003

A

Peak Work (Watts/Kg)

B

Peak VO$_2$ (ml·kg$^{-1}$·min$^{-1}$)

C

Peak Q (ml·kg$^{-1}$·min$^{-1}$)

D

Peak a-VO$_2$ difference (ml/dl)

MM | Controls

*
\[ \dot{V}O_2 = CO \times \text{arteriovenous } O_2 \text{ difference} \]

Sullivan et al. 1989

Cardiac output (l min\(^{-1}\))

\[ P\dot{V}O_2 \text{ (ml min}\quad^1) \]

Sullivan et al. 1989
Taivassalo et al. 2003

**Panel A**

- Graph showing the relationship between Peak Q and Peak VO₂ with a correlation coefficient of $r^2 = 0.08$.

**Panel B**

- Graph showing the relationship between Peak a-vO₂ difference and Peak VO₂ with a correlation coefficient of $r^2 = 0.69$, and $P < 0.01$. 

**Legend**

- $r^2$: Coefficient of determination
- $P$: Probability
Taivassalo et al 2003

$r^2 = 0.70$
$P < 0.01$
Near infra-red spectroscopy
\[ \Delta(\text{deoxyHb}) \text{ rest-peak} \]

Grassi et al. 2006
Mitochondrial Myopathy

\( \dot{\text{VO}}_2 \) – work rate slope 12.9 ml min\(^{-1}\) W\(^{-1}\)
Ammonia

- 5 patients with MM and 5 patients with McArdle’s disease
- McArdle’s disease patients had very elevated ammonia, but MM patients had similar values to controls, but at lower $\dot{\text{VO}}_2$ (leftward shift)

Chaussain et al. 1992
Metabolic myopathies

- Muscle cramp/pain
- Low maximum VO$_2$
- Abnormalities of lactic acidosis threshold
- High VO$_2$ - work rate slope
- Low oxygen-pulse
- Elevated NH$_3$
- Elevated lactate
- Elevated creatine kinase