The Effect of Chemotherapy on Aerobic Power and Cardiac Function in Early-stage Breast Cancer Patients

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BREAST CANCER IN AUSTRALIA

NUMBER OF WOMEN DIAGNOSED IN 2017

17,586

1 IN 8 WILL DEVELOP BREAST CANCER

5-YEAR SURVIVAL RATE

90%

[1] AIHW, 2017
Cardiovascular disease in cancer patients is an important public health issue

Cardiovascular disease is the leading cause of non-cancer related death in breast cancer survivors [2-4]

Figure 1: Women with breast cancer (dash), women without breast cancer (solid line)
Chemotherapy may lead to cardiac injury

Anthracycline-chemotherapy is the primary treatment for solid tumours and is associated with cardiotoxicity\textsuperscript{[5]}

Figure 2: Cardiac reserve decreases with chemotherapy and increases risk of heart failure

\textsuperscript{[5]} Cristietello, La Gerche et al., 2012
Cardiac imaging and testing

- Resting echocardiography
  - Left ventricular ejection fraction (LVEF) [5-9]
  - Global longitudinal strain (GLS) [5-9]

- Biochemical markers
  - Troponin [6]
  - B-type Natriuretic Peptide (BNP) [6]

- Cardiopulmonary exercise testing [9-13]
Exercise training during chemotherapy

- Exercise training has been proven to be well-tolerated and safe in breast cancer during chemotherapy [13-15]

- One study has demonstrated VO$_2$peak ↑ 11% during chemotherapy but others studies have not. [13-16]

- In patients who do not exercise, VO$_2$peak ↓ ~10% after 12-weeks of chemotherapy treatment [14-17]
Research aim and hypotheses

Aim: We sought to assess the association between resting cardiac function measures and VO$_2$peak and whether exercise training could attenuate changes in VO$_2$peak during therapy.

Hypotheses:

- VO$_2$peak will decrease in early-stage breast cancer patients treated with anthracycline-based chemotherapy
- Changes in cardiac function will not be associated with changes in VO$_2$peak
- Exercise will attenuate falls in VO$_2$peak and cardiac function
28 early-stage breast cancer patients recruited into a observational non-randomised study
• Scheduled for anthracycline-based chemotherapy
• Aged 18-70 years
• Capable of exercise

Prior to scheduled chemotherapy

Resting echo
CPET
Biomarkers

12-week exercise intervention

15 breast cancer patients during chemotherapy
-Exercise training

13 breast cancer patients during chemotherapy
- Usual care

~3-weeks after the final (4th) cycle anthracycline-chemotherapy
Repeat outcome measures resting echo, CPET and biomarkers
## Exercise intervention

<table>
<thead>
<tr>
<th>Exercise training principles</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>Three sessions per week (two supervised, one unsupervised)</td>
</tr>
<tr>
<td><strong>Intensity</strong></td>
<td>Moderately-vigorous - 70-85% exercise intensity</td>
</tr>
<tr>
<td><strong>Type</strong></td>
<td>Mix method of aerobic training (stationary cycling) and resistance training</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td>150 minutes per week</td>
</tr>
<tr>
<td><strong>Progression/Regression method</strong></td>
<td>Progressed every 4 weeks using a submaximal progressive exercise test</td>
</tr>
</tbody>
</table>
Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Usual care (n=13)</th>
<th>Exercise training (n=15)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>51.8 ± 12.3</td>
<td>45.8 ± 9</td>
<td>0.15</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>151 ± 8.5</td>
<td>152 ± 9.1</td>
<td>0.77</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>75.4 ± 17.6</td>
<td>68.1 ± 20.5</td>
<td>0.32</td>
</tr>
<tr>
<td>Breast cancer diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• HER2+</td>
<td>4 (30%)</td>
<td>2 (13%)</td>
<td></td>
</tr>
<tr>
<td>• ER-, PR-, HER2-</td>
<td>3 (23%)</td>
<td>8 (62%)</td>
<td></td>
</tr>
<tr>
<td>• Other</td>
<td>6 (46%)</td>
<td>5 (33%)</td>
<td></td>
</tr>
<tr>
<td>VO$_2$peak (ml.kg$^{-1}$.min$^{-1}$)</td>
<td>21.2 ± 5.6</td>
<td>26.9 ± 4.9</td>
<td>0.007</td>
</tr>
<tr>
<td>VO$_2$peak (%predicted)</td>
<td>65.9± 22.9</td>
<td>83.5± 20.7</td>
<td>0.04</td>
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</tbody>
</table>
Exercise training during chemotherapy preserved VO$_2$peak

Changes in VO$_2$peak

![Graph showing changes in VO$_2$peak](image)

Interaction $p = 0.07$
Pre to post $p = 0.002$
Exercise training during chemotherapy preserved power output

![Bar chart showing peak power output (Watts) before and after treatment with usual care and exercise training.](chart)

- Interaction $p = 0.07$
- Pre to post $p = 0.03$
Cardiac function is reduced during chemotherapy

Interaction $p = 0.97$
Pre to post $p = 0.02$

Interaction $p = 0.33$
Pre to post $p = 0.15$
Biomarkers of cardiac damage increased during chemotherapy

Interaction $p = 0.04$
Pre to post $p < 0.001$

Interaction $p = 0.72$
Pre to post $p = 0.99$
Linear correlation of LVEF vs VO$_2^{\text{peak}}$

$\Delta$ VO$_2^{\text{peak}}$ vs $\Delta$LVEF

$r^2 = 0.001$, $p = 0.86$
Study limitations

▪ The present study was a non-randomised observational with the primary objective of feasibility

▪ Selection bias
  o Participants allocated to each group by choice

▪ Other limitations
  o Small proportion of usual care arm completed regular exercise training
  o The single centre study
  o Small sample size (n=28)
  o Short exercise intervention (12-weeks)
Conclusion

- Chemotherapy decreased exercise capacity in early-stage breast cancer patients.
- Exercise training attenuated the decline in VO$_2$peak during chemotherapy.
- A decrease in cardiac function did not predict the decline in VO$_2$peak.
- Further studies are planned to test whether changes in VO$_2$peak predicts clinical outcomes.
Acknowledgements

Special thank you to our phenomenal participants

Honours Supervisors: A/Prof Andre La Gerche, Prof Steve Selig & Dr Steve Fraser

Sports cardiology team: Dr Erin Howden, Kristel Janssens, Rhys Beaudry & Lucie d’Udekem d’Acoz

Acknowledgements to the Baker Institute, Deakin University, Peter MaCallum Cancer Centre, St Vincent’s Hospital and Cabrini Health (Brighton) and the Australian Government Research Training Program Scholarship

Special mention to Institute of Health & Ageing, ACU and my PhD supervision team of A/Prof Prue Cormie and A/Prof Michael Baker.
‘We think with exercise, it’s going to use up all your energy, but it creates energy’ – RS - participant
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<td>BMI (kg/m$^2$)</td>
<td>23.1±5.2</td>
<td>20.7± 6.2</td>
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Breast cancer diagnosis
- • HER2+                 | 4 (30%)           | 2 (13%)                  |         |
- • ER-, PR-, HER2-       | 3 (23%)           | 8 (62%)                  |         |
- • Other                | 6 (46%)           | 5 (33%)                  |         |

Treatment
- • AC                   | 10 (76%)          | 10 (66%)                 |         |
- • AC (dose dense)      | 2 (15%)           | 3 (20%)                  |         |
- • FED-D                | 1 (7%)            | 2 (13%)                  |         |

VO$_2$ (L/min$^{-1}$)    | 1.6 ± 0.4         | 1.8 ± 0.32               | 0.11    |

VO$_2$peak (ml.kg$^{-1}$.min$^{-1}$) | 21.2 ± 5.6 | 26.9 ± 4.9 | 0.007 |

VO$_2$peak (%predicted)  | 65.9± 22.9       | 83.5± 20.7               | 0.04    |
## Fick equation

| Fick equation: \( \text{VO}_2 = \text{SV} \times \text{HR} \times [\text{O}_2]_{a-v} \) |
|---|---|
| SV and HR | \( \downarrow \text{SV} \leftrightarrow \downarrow \text{HR} \) |
| \( O_2 \) arterial (Hb) | \( \downarrow \text{Hb} \Rightarrow \downarrow [\text{O}_2]_a \) |
| Skeletal muscle utilisation of \( O_2 \) | \( \downarrow \text{SV} \leftrightarrow \downarrow \text{HR} \times \uparrow [\text{O}_2]_{a-v} \), indicated by \( \downarrow [\text{O}_2]_a \) and \( \downarrow \downarrow [\text{O}_2]_v \) across skeletal muscle |

Abbreviations: \( \text{VO}_2 \) (oxygen consumption), \( \text{SV} \) (stroke volume), \( \text{HR} \) (heart rate), \( [\text{O}_2]_{a-v} \) (arteriovenous oxygen difference across the pulmonary circulation) and Hb (haemoglobin).
Exercise intervention model

Periodisation model - Modified step periodisation model

(2:1)

Testing weeks

Percentage of relative power (Watts)

Time (weeks)

Week 1  Week 2  Week 3  Week 4  Week 5  Week 6  Week 7  Week 8  Week 9  Week 10  Week 11  Week 12