Exercise – Oncology Research: Current Status & Future Directions

Lee W. Jones, PhD
Background

• Therapeutic properties of exercise been recognized since ancient Greeks and Chinese

• 1995 American College of Sports Medicine (ASCM) – first exercise guidelines for US adults

• 2002 American Cancer Society recommended exercise to prevent risk of certain forms of cancer

• Exercise after cancer diagnosis comparatively less attention
Significant improvements in survival after cancer

5-year survival

- Nation’s cancer death rate has dropped 18 percent since early 1990s
- ~13 million cancer survivors are alive today – up from 3 million in 1970s
- Patients living longer and, as a result, greater risk of late effects of cancer therapy
Original Published Articles on ‘Exercise and Cancer 1986-2011’ (PubMed)

- McVicar publishes 1st Ex & Ca Study
- ACS guidelines CA J Clinicians
- Segal publishes in JCO
- Holmes publishes in JAMA
- Courneya et al. first RCT on survival
- Meyerhardt interaction btw exercise & tumor molecular features
Exercise-oncology framework

Pre-Diagnosis

PEACE Framework – Courneya & Friedenreich, Ann Behav Med, 1997
Past: What do we know?

PEACE – 3 major timepoints

1. Pre-treatment
2. During treatment
   1. Toxicity
   2. Efficacy
3. Post treatment
   1. Chronic & late-effects
   2. Recurrence & cancer-specific mortality
   3. Non-cancer mortality
   4. All-cause mortality

Jones & Alfano, *Acta Oncologica*, in submission
1. Pre-treatment

- Improve fitness prior to surgical resection
- ~5 studies
- Ltd data suggests that exercise training is feasible & safe in this setting

2. During-treatment  - (a) off-set toxicity

- Speck et al. 40% of studies conducted in this setting
- Patients with early-stage disease (breast cancer)
- Feasible, safe, & efficacious on select outcomes (considerable heterogeneity)

Jones & Alfano, Acta Oncologia, in submission
2. During-treatment - (b) efficacy

- One clinical trial (Courneya et al. J Clin Oncol, 2007) – resistance training ↑ treatment completion rates
- Insufficient data

3. Post treatment – (a) chronic & late-effects

- Speck et al. ~50% of studies conducted in this setting
- Patients with early-stage disease (breast cancer)
- Feasible, safe, & efficacious on select outcomes (considerable heterogeneity)

Jones & Alfano, Acta Oncologia, in submission
4. Post treatment – (b) recurrence (biomarkers) & cancer-specific mortality

- No RCTs
- n=9 epidemiological studies – significant inverse relationship between higher exercise & lower risk of recurrence & mortality in breast, colorectal, & prostate
- n=14 animal studies – mixed results
- n=24 studies examining changes in plasma biomarkers
  - Metabolic factors
  - Immune factors
  - No clear conclusions

Jones & Alfano, Acta Oncologia, in submission
4. Post treatment – (b) non-cancer mortality

- No studies to date – epidemiological studies only examined cancer-specific & all-cause mortality

4. Post treatment – (c) all-cause mortality

- No RCTs
- N=16 epidemiological studies – prognostic value of exercise or fitness
- Higher levels of exercise & fitness associated with significant reductions in risk of death – breast, colorectal, lung, brain, prostate, ovarian

Jones & Alfano, *Acta Oncologica*, in submission
Current: What are we doing (Clinical Trials.gov)?

- PEACE timepoint
  1. Pre-treatment (n=5; 6%)
  2. During therapy (a) toxicity (n=40; 50%); (b) efficacy (n=0)
  3. Post therapy (a) late-effects (n=29; 36%); (b) recurrence (n=5; 6%); non-cancer mortality (n=0); (c) all-cause mortality (n=1; 2%)

- Sample size
  - Mean: n= 171 (10 – 1070)

Clinical Trials.Gov (Aug 1st, 2012)
Current: What are we doing?

- Study characteristics
  - Study design – n=51 (64%) 2-arm RCTs
  - Cancer type – breast cancer n=32 (40%)
  - Exercise intervention – aerobic training only (n=20; 25%) or combined aerobic & resistance training (n=20; 25%)
  - Traditional exercise prescriptions
  - n=51 different primary endpoints;
    - >75% QOL, fatigue, or physical functioning
### Future: Future direction / gaps in knowledge

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Major Gap in Knowledge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Pre-Treatment</strong></td>
<td>• Adequately powered trials to determine the effects of pre-surgical exercise training on surgical complications and recovery in patients undergoing extensive surgical resections for operable disease</td>
</tr>
<tr>
<td><strong>2. During Treatment</strong></td>
<td></td>
</tr>
<tr>
<td>(a) toxicity</td>
<td>• Effects and mechanisms of exercise training on common but currently understudied physiological toxicities (e.g., cardiotoxicity, peripheral neuropathy, thrombosis, bone loss)</td>
</tr>
<tr>
<td>(b) efficacy</td>
<td>• Differential effects and mechanisms of exercise training on the efficacy of conventional and forthcoming anticancer therapies adopting a translational bench-to-bedside approach</td>
</tr>
</tbody>
</table>
## Future: Future direction / gaps in knowledge

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Major Gap in Knowledge</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Post-Treatment</td>
<td></td>
</tr>
<tr>
<td>(a) Chronic &amp; late-effects</td>
<td>• Effects and mechanisms of exercise training to prevent and/or treat common and emerging chronic and late-effects of treatment</td>
</tr>
<tr>
<td>(b) recurrence</td>
<td>• Elucidation of the optimal dose of exercise to inhibit tumor progression / metastasis in mouse models of solid tumors to guide the dose of exercise to be tested in phase II randomized trials</td>
</tr>
<tr>
<td>(c) non-cancer mortality &amp; (d) all-cause mortality</td>
<td>• Utilize mouse models to determine the effects and mechanisms of exercise on non-cancer related morbidity and mortality in cancer mouse models</td>
</tr>
</tbody>
</table>
Conclusion

• Tremendous gains in scope, clinical and patient interest, and impact exercise in the oncology setting

• Time to launch exercise – oncology research into the next generation of research

• Today’s presentations:

1. Anna Enblom: *Level of physical, leisure, and daily living activities in cancer patients undergoing radiotherapy: Which patients will need additional support?*

2. Andreas Holst Andersen: *A modified exercise protocol may promote continuance of exercise after intervention in lung cancer patients*

3. Randi Reidunsdatter: *Fatigue after breast cancer may be related to conditions other than the cancer. The impact of comorbidity is essential*