Optimizing exercise prehabilitation in cancer care

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Energy Balance Research Seminar
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Objectives

• Describe the rationale for exercise prehabilitation in cancer care
• Provide an overview of findings from previous cancer prehabilitation studies
• Provide an overview of pancreatic cancer prehabilitation at MD Anderson
• Describe current and next steps in exercise prehabilitation for cancer
Cancer + treatment

- Reduced strength
- Muscle loss
- Reduced fitness
- Depression and anxiety
- Neuropathy
- Reduced physical functioning
- Fatigue
- Appetite loss
Exercise prehabilitation in cancer care

- Improved strength
- Muscle maintenance (or gain)
- Improved fitness
- Improved emotional affect, reduced anxiety and depressive symptoms
- Improved physical functioning
- Fatigue
- Reduced neuropathy
- Increased appetite

Improved appetite
American College of Sports Medicine
Exercise Guidelines for Cancer Survivors (2019 updates)

- Updated evidence for dose-response relationships between exercise and outcomes in cancer survivorship.

  \[ \geq 30 \text{ minutes moderate-intensity aerobic exercise} \geq 3x/\text{week} \]

  **AND**

  \[ \geq 2 \text{ weekly sessions of resistance training targeting major muscle groups} \]

  \[ (\geq 2 \text{ sets of 8-15 repetitions at } \geq 60\% \text{ of 1-repetition maximum}) \]

- **Adapt** according to age, treatment, limitations, performance status

Campbell et al., 2019
Cancer prehabilitation

• Goals
  • Optimize health before cancer treatments
  • Prevent impairments and reduce the need for reconditioning

• Targets
  • Surgical and perioperative outcomes
  • Physical functioning
  • Fitness
  • Body composition
  • Psychological well-being
  • Health-related quality of life

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<thead>
<tr>
<th>Goals and benefits of cancer prehabilitation</th>
<th>Assess and document</th>
<th>Identify and reduce</th>
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Exercise prehabilitation in cancer care

Prehab:
Pre-op treatment; no prehab

Preoperative Period

Postoperative Period

No prehab

Surgery

Functional Recovery

Esophogastric cancer

Prehab (5 weeks) and perioperative 6-minute walk distance for surgery patients

Prehab $n=26$
Control $n=25$

*significantly better improvement in aerobic functioning in the prehab group ($p<.001$)
Lung cancer

Meta-analysis and pooled estimated effect size for **postoperative length of stay** in prehab intervention group and control group

Significantly reduced postoperative length of stay (~5 days difference) in prehab patients vs. control patients following surgical resection of lung cancer.
Attitudes and Perceptions to Prehabilitation in Lung Cancer

Anna Shukla, BAppSc¹,², Catherine L. Granger, B Physio(Hons), PhD¹,³, Gavin M. Wright, MBBS, FRACS, PhD²,⁴, Lara Edbrooke, BAppSc, PhD¹,⁵, and Linda Denehy, BAppSc, PhD¹,⁵

Abstract

Background: Prehabilitation to maximize exercise capacity before lung cancer surgery has the potential to improve operative tolerability and patient outcomes. However, translation of this evidence into clinical practice is limited. Aims: To determine the acceptability and perceived benefit of prehabilitation in lung cancer among thoracic surgeons. Procedure: 198 cardiothoracic surgeons within Australia and New Zealand were surveyed to evaluate their attitudes and perceived benefits of prehabilitation in lung cancer. Results: Response rate was 14%. A moderate proportion of respondents reported that there is a need to refer lung resection patients to preoperative physiotherapy/prehabilitation, particularly high-risk patients or those with borderline fitness for surgery. 91% of surgeons were willing to delay surgery (as indicated by cancer stage/type) to optimize patients via prehabilitation. The main barriers to prehabilitation reported were patient comorbidities and access to allied health professionals, with 33% stating that they were unsure who to refer to for prehabilitation in thoracic surgery. This is despite 60% of the cohort reporting that pulmonary rehabilitation is available as a preoperative resource. 92% of respondents believe that further research into prehabilitation in lung cancer is warranted. Conclusion: The benefits of prehabilitation for the oncology population have been well documented in the literature over recent years and this is reflected in the perceptions surgeons had on the benefits of prehabilitation for their patients. This survey demonstrates an interest among cardiothoracic surgeons in favor of prehabilitation, and therefore further research and demonstration of its benefit is needed in lung cancer to facilitate implementation into practice.
Colorectal cancer

Pooled analysis of interventions for surgery patients

Unadjusted mean changes in absolute lean mass

Prehab $n=76$
Rehab $n=63$

*statistically significant change relative to baseline ($p<.05$)

…but there are some mixed findings

Gastroenterology > Colon Cancer

Can 'Prehabilitation' Help Frail Colorectal Cancer Patients Undergoing Surgery?
— First randomized trial of multi-part behavioral program

by Diana Swift, Contributing Writer    January 23, 2020

Multimodal "prehabilitation" did not improve 30-day postoperative outcomes versus postoperative rehabilitation in frail elderly patients undergoing colorectal cancer resection, a randomized trial found.

The two-site study by Francesco Carli, MD, MPhil, of McGill University Health Centre in Montreal, and colleagues found no inter-group difference in the primary outcome measure, the 30-day Comprehensive Complications Index, for an adjusted mean difference of -3.2 (95% CI -11.8 to 5.3, P=0.45). Nor was there a difference in secondary postoperative measures, including 30-day overall and severe complications, primary and total length of hospital stay, 30-day emergency department visits and readmissions, recovery of walking capacity, or patient-reported outcomes.
• Two centers with well-established enhanced recovery pathways and ~80% of patients underwent minimally invasive surgery

• “Effects of prehabilitation may be limited when other aspects of perioperative care are already optimized.”

• Prehabilitation program was 4-5 weeks

• Significant increases in lean body mass, muscular strength, and functional capacity require at least 12 weeks in elderly patients, even with intense exercise and protein supplementation (Karelis et al., 2015)

• Short programs may provide insufficient anabolic stimulus and fail to “move the needle” on surgery-related outcomes
Exercise prehabilitation during preoperative treatment for pancreatic cancer

• Approximately 20% of patients undergo surgical resection
  • 5-year survival rate: 18-24%

• Generally diagnosed among older adults
  • Median age at diagnosis: 71

Preoperative treatment context:

Chemotherapy (8-12 weeks) → Chemoradiation (2-6 weeks) → Off treatment “rest” (2-6 weeks) → Surgery → Recovery

(Either treatment or combination of both)
Fitness during preoperative pancreatic cancer treatment

• Muscle loss frequently accompanies preoperative treatment
• Preoperative frailty linked to adverse outcomes following surgery
• Important to optimize preoperative health!

Cooper et al., 2015; Cloyd et al., 2018
Lee et al., 2018; Broughman et al., 2015
Pancreatic cancer prehabilitation pilot study (2015-2018)
Study design: Participants and study structure

- Single-arm feasibility study
- 50 patients
  - Biopsy-proven pancreatic cancer
  - At least 6 weeks of preoperative treatment before planned surgical resection
  - Screened for safety of independent exercise (PAR-Q questionnaire and physician consultations, as necessary)

Enrollment → Preoperative therapy and exercise program → Measures → Restaging/Follow-up → Surgery
Study design: Home-based exercise program

• Exercise prescription
  • ≥60 min/week moderate-intensity aerobic exercise
  • ≥60 min/week strengthening exercise

• Participants received
  • Graded resistance tube sets
  • Photo/video instructions
  • Comprehensive instruction at baseline
  • Follow-up calls every two weeks

• Physical activity assessed using daily logs and accelerometers
Measures

- Potential exercise influences (surveys)
  - Social support from family and friends
  - Perceived walkability of home neighborhoods

- Potential exercise outcomes (surveys and “field tests”)
  - Physical functioning and fitness
  - Health-related quality of life
  - Skeletal muscle tissue
## Participant characteristics (N=50)

<table>
<thead>
<tr>
<th>Value</th>
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<tbody>
<tr>
<td><strong>Mean age at enrollment</strong>, years ± SD</td>
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<tr>
<td>66 ± 8</td>
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<td><strong>Sex, n (%)</strong></td>
</tr>
<tr>
<td>Female 24 (48)</td>
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<tr>
<td>Male 26 (52)</td>
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<tr>
<td><strong>Mean BMI at baseline</strong>, kg/m² ± SD</td>
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<tr>
<td>27.6 ± 5.3</td>
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<td>Normal weight (18.5 ≤ BMI &lt; 25), n (%)</td>
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<tr>
<td>18 (36)</td>
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<tr>
<td>Overweight (25 ≤ BMI &lt; 30), n (%)</td>
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<td>18 (36)</td>
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<tr>
<td>Obese (BMI ≥ 30), n (%)</td>
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<td>14 (28)</td>
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<td><strong>Mean exercise program duration</strong>, weeks ± SD</td>
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<td>16 (9)</td>
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</tbody>
</table>
Geographic spread of participants
Self-reported exercise and accelerometer physical activity

Average weekly minutes (Mean ± SE)

Aerobic exercise (daily logs)

Strengthening exercise (daily logs)

Moderate-to-vigorous physical activity (accelerometer)

Light physical activity (accelerometer)

ACSM weekly recommendation (aerobic)

Our weekly recommendation
Home environment influences on physical activity

More social support for exercise from family and friends

More walkable neighborhoods

More accelerometer physical activity

Both p<.05

Adjusted for age, sex, and duration of treatment and exercise program.
Outcome measures

**6-minute walk test**
- Baseline: 440 meters ± 10
- Follow-up: 500 meters ± 15
- Improvement: 60 meters
- Significance: *p* < .01

**5x sit-to-stand**
- Baseline: 135 seconds ± 5
- Follow-up: 120 seconds ± 10
- Improvement: 15 seconds
- Significance: *p* < .05

**Health-related quality of life (FACT-Hep)**
- Baseline: 130 score ± 5
- Follow-up: 145 score ± 7
- Improvement: 15 score
- Significance: *p* > .05

**Grip strength**
- Baseline: 30 kg ± 5
- Follow-up: 32 kg ± 6
- Improvement: 2 kg
- Significance: *p* > .05

**Self-reported physical functioning**
- Baseline: 51 score ± 5
- Follow-up: 49 score ± 6
- Improvement: 2 score
- Significance: *p* > .05
Associations among physical activity and outcomes

More self-reported aerobic exercise → Better improvement in 6-minute walk distance

More accelerometer physical activity → Better improvement in self-reported physical functioning

All $p<.05$

Adjusted for age, sex, duration of treatment and exercise program, and baseline value of the outcome.
Exercise prescription may mitigate muscle loss during preoperative pancreatic cancer treatment

Perioperative skeletal muscle mass

<table>
<thead>
<tr>
<th>Standardized skeletal muscle cross-sectional area (cm²/m²) (mean±SD)</th>
<th>Baseline</th>
<th>Preop</th>
<th>Postop</th>
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<tbody>
<tr>
<td>Control</td>
<td>n=66</td>
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<tr>
<td>Prehab</td>
<td>n=33</td>
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$p<.05$ for rates of muscle change from baseline to pre-op and baseline to post-op (models adjusted for age, sex, baseline skeletal muscle CSA)
Conclusions from pancreatic cancer prehab study

• **Exercise is feasible during preoperative pancreatic cancer treatment**
  • Capitalizing on high motivation in the preoperative “window”
  • Differences in adherence – due to differences in motivation?

• **Social support and neighborhood walkability may be important exercise influences with home-based exercise prescription**
  • Potential to mitigate barriers and maximize support

• **Exercise during preoperative pancreatic cancer treatment may confer important benefits**
  • Improving fitness and physical functioning
  • Improving health-related quality of life
  • Mitigating muscle loss
Current research

• “PancFit” randomized trial (currently accruing patients)
• Home-based aerobic and strengthening exercise prescription vs. standard care (general encouragement to exercise)
• Encouragement to maintain a high protein diet and early dietitian consultation (as needed) for both groups
• Daily physical activity measured using Fitbit Charge 2 activity monitors
• Measuring exercise motivation
• Testing effects of multi-modal exercise on fitness, body composition, quality of life, and vascular remodeling in tumors
Potential reasons for subpar adherence resistance training

- New exercise modality
  - Lack of self-efficacy
  - Lack of familiarity
- Home-based resistance training program
  - Equipment issues
  - Limited supervision/social support
  - Lack of muscular overload
  - Lack of exercise volume progression
- Structure of recommendations
  - One size does not fit all
  - Not scheduled (or periodized) to account for treatment or side effects
Resistance training 101

Overload
Place a greater demand on a muscle than it is accustomed to meeting. This leads to muscular hypertrophy and increased strength.

Progression
Increase the demand placed on a muscle over time

Periodization
Vary training volume and intensity systematically to manage fatigue and prevent training “staleness” or “plateaus”
Comparing Resistance Training Intervention Formats

In-person and supervised

- Gold standard in exercise oncology
- Greater control of training variables
- Safety
- Exercise self-efficacy
- Social support of interventionists and other facility users
- Adherence

Home-based and unsupervised

- Lower cost
- Financial
- Time
- Comfortable
- Social support of family or caregivers
- Feasibility
- Enrollment/participation
“PancStrength” feasibility study

Primary objective:

Evaluate the safety of a progressive, home-based, tele-exercise resistance training (RT) intervention in patients undergoing chemotherapy for pancreatic cancer.

Secondary objectives:

Evaluate program feasibility and acceptability.

Examine changes in exploratory outcome measures (fitness, clinical, and PROs) and their associations with RT volume.

Evaluate cancer care providers’ perspectives regarding intervention feasibility and acceptability.
“PancStrength” feasibility study

- 25 patients undergoing first-line chemotherapy for pancreatic cancer
- ~30-minute tele-RT sessions over one-to-one Zoom video conference with ACSM-certified exercise trainers

- **Progressive and individualized RT program**
  - Starting resistance based on baseline strength
  - Exercise volumes to increase based on perceived exertion
  - Training periodized based on chemotherapy treatments and potential side effects (4 sessions/2 weeks)
Optimizing exercise prehabilitation: future directions

- Applying tele-resistance training to our prehabilitation model
- Study and compare feasibility of in-person training
- Incorporate nutritional intervention and assessment
- Examine effects of prehabilitation on other important outcomes
  - Surgery-related outcomes
  - Return to baseline fitness and physical functioning
  - Mitigation of muscle loss
  - Personalized and tailored intervention for higher-risk groups
Collaborators

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Thank you! Questions?