Preoperative functional optimization for better surgical outcome

Francesco Carli
McGill University
Montreal, Canada
franco.carli@mcgill.ca
F Carli is recipient of a grant of the Rossy Cancer Network (Canada)
Learning Objectives

• Address the pathophysiological factors which can influence outcome following surgery and cancer

• Introduce the concept of surgical *prehabilitation*

• Review the literature of surgical prehabilitation and preliminary results
What if surgery could be done without:

• Stress response
• Pain
• Organ dysfunction
• Complications
• Fatigue

...then recovery will be fast, and then length of stay and costs will decrease too
postoperative recovery, 1980

- Loss of body weight, less muscle mass
- Deconditioning
- Increased heart rate with work
- Decrease in muscle strength
Need for Surgery Identified

Preoperative Phase

Enhanced Recovery After Surgery Program

Intraoperative Phase

Fast-Track

Postoperative Phase

Continuum of care
fast-track-enhanced recovery 1990

- Preoperative Optimization
- Modulation of stress response
- Pain Control
- Nutrition
- Activity

Accelerated convalescence and reduced morbidity
High rate of postoperative morbidity after elective abdominal surgery

NSQIP database (2005-2006)

Table 1. Relative Contribution of 36 Procedures to Adverse Events and Excess Length of Stay in General Surgery, American College of Surgeons – National Surgery Quality Improvement Program, 2005–2006

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Procedures</th>
<th>% of total</th>
<th>Adverse event rate, %</th>
<th>Proportion of all adverse events, %</th>
<th>Average excess length of stay for adverse event, d</th>
<th>Proportion of all excess length of stay, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Colectomy ± colostomy</td>
<td>12,767</td>
<td>9.9</td>
<td>28.9</td>
<td>24.3</td>
<td>9.8</td>
<td>23.5</td>
</tr>
<tr>
<td>2. Small intestine resection</td>
<td>3,576</td>
<td>2.8</td>
<td>32.9</td>
<td>7.7</td>
<td>13.9</td>
<td>10.6</td>
</tr>
<tr>
<td>3. Cholecystectomy/inpatient</td>
<td>11,718</td>
<td>9.1</td>
<td>7.5</td>
<td>5.7</td>
<td>8.7</td>
<td>4.9</td>
</tr>
<tr>
<td>4. Ventral hernia repair</td>
<td>7,477</td>
<td>5.8</td>
<td>10.1</td>
<td>4.9</td>
<td>6.3</td>
<td>3.1</td>
</tr>
<tr>
<td>5. Pancreatectomy</td>
<td>1,927</td>
<td>1.5</td>
<td>34.9</td>
<td>4.4</td>
<td>6.8</td>
<td>3.0</td>
</tr>
<tr>
<td>6. Appendectomy</td>
<td>9,016</td>
<td>7.0</td>
<td>7.2</td>
<td>4.3</td>
<td>4.4</td>
<td>1.9</td>
</tr>
<tr>
<td>7. Bariatric procedures</td>
<td>6,167</td>
<td>4.8</td>
<td>8.3</td>
<td>3.4</td>
<td>3.7</td>
<td>1.2</td>
</tr>
<tr>
<td>8. Proctectomy ± colectomy ± anastomosis</td>
<td>1,402</td>
<td>1.1</td>
<td>31.5</td>
<td>2.9</td>
<td>6.2</td>
<td>1.8</td>
</tr>
<tr>
<td>9. Lysis of adhesions</td>
<td>1,323</td>
<td>1.0</td>
<td>23.1</td>
<td>2.0</td>
<td>10.5</td>
<td>2.1</td>
</tr>
<tr>
<td>10. Liver resection</td>
<td>1,045</td>
<td>0.8</td>
<td>27.0</td>
<td>1.9</td>
<td>8.8</td>
<td>1.6</td>
</tr>
<tr>
<td>11. Mastectomy/simple, radical, or subcutaneous</td>
<td>4,313</td>
<td>3.3</td>
<td>5.6</td>
<td>1.6</td>
<td>0.9</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Schilling et al. JACS 2008
Still high rate of postoperative morbidity after elective abdominal surgery........
...............5 years later

- 76,076 resections for esophageal, gastric, pancreatic, hepatobiliary, and colorectal cancers at 316 hospitals from the 2006 to 2011 ACS NSQIP

- 3% esophagectomy, 5% gastrectomy, 16% pancreatectomy, 4% hepatectomy, 63% colectomy, and 9% proctectomy

- 21-45% of patients experienced a postoperative complication and 1.1-4.4% died. The incidence of patients with any complication 24%

Lucas DJ, Surgery, 2013
Despite intraoperative interventions & advances in anesthesia and surgical care

Complications are still between 25 and 55%
Postoperative complications are a burden and impact on long term outcomes


Reduced survival by 69% at 8 yr (from 18.4 yr to 5.6 yr)
Redesigning Surgical Decision Making for High-Risk Patients

Laurent G. Glance, M.D., Turner M. Osler, M.D., and Mark D. Neuman, M.D.

Surgical risk stratification
Surgical risk attenuation
ACS risk calculator
15 variables predicting higher risk

Model generated from N=28,863 colorectal procedures at 182 hospitals

**Not Modifiable**
- ASA III/IV
- Sepsis
- Indication for surgery
- Disseminated cancer
- Extent of surgery
- Emergent
- **Age >65**
- Creatinine
- COPD
- Wound class
- PTT >35

**Potentially Modifiable**
- Functional health status
- BMI
- Dyspnea
- Albumin ≤35

*Cohen et al., Bilimoria, Ko, Hall. JACS 2009*
Optimizing Surgical Care of Colon Cancer in the Older Adult Population

Gregory D. Kennedy, MD, PhD*, Victoria Rajamanickam, MS†, Erin S. O'Connor, MD*, Noelle K. Loconte, MD‡, Eugene F. Foley, MD*, Glen Leverson, PhD†, and Charles P. Heise, MD*

• Factors that predict complications:
  - Age >75 y
  - BMI >25
  - COPD
  - ETOH
  - Duration of surgery

the United States continues to age. Surgeons will have to operatively approach an older group of patients with multiple preoperative comorbidities. It is clear from these data that preoperative health and functional status as well as operative approach contribute to short-term outcomes.
## Preoperative Risk Assessment

<table>
<thead>
<tr>
<th>Test</th>
<th>Predicting</th>
<th>Scoring</th>
<th>Evidence level</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>P possum</td>
<td>Mortality and Morbidity</td>
<td>12 physiological and 6 operative variables</td>
<td>High</td>
<td>Strong</td>
</tr>
<tr>
<td>Lees index</td>
<td>Perioperative Cardiac complication</td>
<td>6 preoperative clinical factors</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
<tr>
<td>Shuttle Walk Test</td>
<td>Perioperative complications</td>
<td>Aerobic fitness</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Shuttle Walk Test</td>
<td>Screening tool to proceed to CPET / echocardiography etc</td>
<td>Aerobic fitness</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
<tr>
<td>Cardiopulmonary Exercise testing (CPET)</td>
<td>Perioperative complications</td>
<td>Aerobic exercise – AT and VO₂ max</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
<tr>
<td>Cardiopulmonary Exercise testing (CPET)</td>
<td>Selecting patient’s suitability for surgery</td>
<td>Aerobic exercise – AT and VO₂ max</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

With permission of Scott MJ. 2015
Risk factors for prolonged recovery of Independent Activities of Day Living (IADL) after major abdominal surgery in elderly people

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious complication</td>
<td>0.61</td>
<td>0.39-0.96</td>
<td>0.03</td>
</tr>
<tr>
<td>Physical performance status*</td>
<td>1.20</td>
<td>1.02-1.41</td>
<td>0.02</td>
</tr>
<tr>
<td>Geriatric Depression Scale</td>
<td>0.95</td>
<td>0.92-0.98</td>
<td>0.003</td>
</tr>
<tr>
<td>Folstein Mini-Mental State</td>
<td>1.04</td>
<td>0.98-1.11</td>
<td>0.22</td>
</tr>
<tr>
<td>Creatinine &gt; 133 umol/L</td>
<td>0.83</td>
<td>0.47-1.47</td>
<td>0.52</td>
</tr>
<tr>
<td>Albumin &lt; 30 g/L</td>
<td>0.63</td>
<td>0.15-2.66</td>
<td>0.53</td>
</tr>
<tr>
<td>CHF on CXR</td>
<td>0.94</td>
<td>0.46-1.92</td>
<td>0.87</td>
</tr>
<tr>
<td>Male</td>
<td>1.25</td>
<td>0.8-1.87</td>
<td>0.29</td>
</tr>
<tr>
<td>Age, y</td>
<td>1.0</td>
<td>0.97-1.02</td>
<td>0.80</td>
</tr>
</tbody>
</table>

*score combining Timed Up and Go, Functional Reach, and Hand Grip Strength using Components Analysis

Cox Proportional Hazards Regression
Lawrence et al, JACS, 2009
Poor physical fitness/reserve is associated with:

- **all-cause mortality**  
  *Wilson et al, BJA 2010*

- **postoperative complications**  
  *TN Robinson et al, Am J Surg 2013*

- **length of hospital stay and discharge destination**  
  *JJ Dronkers et all, Anaesthesia 2013*

- **hospital and healthcare costs**  
  *TN Robinson et all, Am J Surg 2011*
Preoperative functional status and postoperative outcome

Surg Endosc 2015
Preoperative nutritional state

elective abdominal surgery, n=1085
Nutritional Risk Screening > 4

* $p = 0.008$

Optimization in the preop period. What do not we do now?

Pre-existing Medical Conditions

Functional Capacity

Psychological Status

Pharmacological/Procedural interventions

Nutritional

Physical

Mental
Current practice is to predict postoperative complications and to adjust postoperative resources (e.g. if AT < 9.8, postop ICU)

and wait until after surgery to intervene to help patients to recover

Rehabilitation
Is the postoperative period the right time to intervene?

Patients are tired, depressed, weak

What about modify the preoperative risk assessment?

Can we improve patient’s fitness before surgery, while waiting?

Prehabilitation
Need for Surgery Identified

Preoperative Phase

Intraoperative Phase

Postoperative Phase

Enhanced Recovery After Surgery Program

Fast-Track

Surgery

Continuum of care
Trajectory of Surgical Care

Enhanced Recovery After Surgery Program

Prehabilitation
Preoperative Phase
Fast-Track
Intraoperative Phase
Postoperative Phase
Continuum of care

Need for Surgery Identified
Surgery
Increase physiological reserve to overcome the stress of surgery and accelerate the recovery process.

Level of Functional ability

Prehabilitation phase | Surgical Procedure | Rehabilitation phase | Post rehabilitation phase

Prehab patient
Non-prehab patient

Carli F, Zavorsly G 2005,
The effects of preoperative exercise therapy on postoperative outcome: a systematic review

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Risk ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>Dronkers et al. 2006</td>
<td>3</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Hulzebos et al. 2006pilot</td>
<td>1</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Hulzebos et al. 2006RCT</td>
<td>9</td>
<td>139</td>
<td>22</td>
</tr>
<tr>
<td>Weiner et al. 1998</td>
<td>1</td>
<td>42</td>
<td>3</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td>205</td>
<td>201</td>
</tr>
</tbody>
</table>

Total events: 14, 34
Heterogeneity: Chi² = 0.36, df = 3 (P = 0.95); I² = 0%
Test for overall effect: Z = 3.11 (P = 0.002)

Figure 2 Effect of preoperative inspiratory muscle training on postoperative pulmonary complications after cardiac or abdominal surgery.

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean difference IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
</tr>
<tr>
<td>Beaupre et al. 2004</td>
<td>6.7</td>
<td>2.2</td>
<td>65</td>
</tr>
<tr>
<td>D'Lima et al. 1996-11</td>
<td>6.29</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>D'Lima et al. 1996-12</td>
<td>6.1</td>
<td>1.99</td>
<td>10</td>
</tr>
<tr>
<td>Wijgman et al. 1994</td>
<td>15.7</td>
<td>3.4</td>
<td>31</td>
</tr>
<tr>
<td>Williamson et al. 2007</td>
<td>6.49</td>
<td>1.99</td>
<td>60</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td></td>
<td></td>
<td>176</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 3.80, df = 4 (P = 0.43); I² = 0%
Test for overall effect: Z = 0.38 (P = 0.70)

Figure 4 Effect of preoperative exercise therapy on length of hospital stay after joint replacement surgery.
Systematic Review & Meta-Analysis of Systemic Prehabilitation

**Inclusion criteria:**

- Total body MSK ± aerobic exercise & postop outcomes

**Results:**

- 1996-2011
- K=21 (17 RCTs); median sample n=54
  - 13 orthopaedic, 1 abdominal, 3 cardiac
- Moderate-poor methodological quality
- Majority found improved postop:
  - Pain, LOS, physical function
- Equivocal benefits to:
  - Aerobic fitness, complications & QOL
- Adverse event in 2/669 prehab patients

(Santa Mina et al, 2014, Physiotherapy)
Surgical Prehabilitation

- Medical optimization
- Physical activity
- Glycemic control
- Alcohol & smoking cessation
- Nutrition
- Occupational care
- Relaxation strategies
- Pain & symptom control
Prehabilitation to enhance postoperative recovery for an octogenarian following robotic-assisted hysterectomy with endometrial cancer  Carli F, Brown R, Kennephol S. CJA 2012; 59: 779-84

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>88 y</td>
</tr>
<tr>
<td><strong>Past Medical History</strong></td>
<td>CAD, Stent x2, CABG x3, AS, HTN, periods of CHF, postoperative delirium x2, UTI, Mild MCI</td>
</tr>
<tr>
<td><strong>Weight loss</strong></td>
<td>30 lbs in 1 year</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td>MA Theology at the age of 60 years!</td>
</tr>
<tr>
<td></td>
<td>Sedentary, Depressed, Frustrated and Malnourished</td>
</tr>
<tr>
<td>Time of assessment</td>
<td>SF36</td>
</tr>
<tr>
<td>-------------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td></td>
<td>Physical Component</td>
</tr>
<tr>
<td>Initial Assessment</td>
<td>33.7 (-0.7)</td>
</tr>
<tr>
<td>4 Weeks before Surgery</td>
<td>39.6 (-0.1)</td>
</tr>
<tr>
<td>8 Weeks after Surgery</td>
<td>65.3 (1.2)</td>
</tr>
</tbody>
</table>

* Repeatable Battery or the Assessment Neuropsychological Status
Preop: Nutrition prehab improved 20.8 ± 42.6 m, while placebo improved by 1.2 (65.5).

Postop: Four weeks after surgery, recovery rates were similar between groups.

Multimodal Prehabilitation: The McGill Experience

**Exercise Program**
- Aerobic (walking, cycling)
- Strength (elastic band)
- Flexibility

**Nutritional Intervention**
- Caloric balance (match intake and expenditure)
- Protein supplementation (1.5g/kg/day)
- Multivitamins, Calcium (in elderly)
- Immunonutrition (arginine and omega-3 containing formulas) in cancer patients

**Medical Optimization**
- Anemia correction
- Glycemic control (use of hypoglycemic agents if HbA1C >5.7)
- Blood pressure control
- Alcohol reduction
- Smoking cessation
- Preoperative carbohydrate

**Psychological Intervention**
- Relaxation strategies
- Visualisation exercises
- Concentration exercises (Sudoku, crossword puzzles)
- Breathing exercises

**Functional Reserve**
Multimodal Prehabilitation to Increase Functional Reserve

- Up to 1/3 of patients are at nutrition risk

Whey Protein Supplementation

Aerobic and resistance exercise

- 20% of patients may have mood changes like anxiety / depression while waiting for surgery

Anxiety Reduction Strategies
Increase in muscle protein synthesis following exercise with whey proteins (Anabolic Window)

Outcome measure of recovery: functional walking capacity

Six-Minute Walk Test
- Objective, Reproducible
- Essential to everyday activities
- Integrates balance, force, speed, endurance
- Cheap, no equipment needed
- Validated measure of surgical recovery (Moriello, 2008, Pecorelli 2015)

Minimal important difference = 20 meters
the smallest change in an outcome measure perceived as beneficial by patients undergoing colorectal surgery

Predicted 6MWT = 868 – (age x 2.9) – (female x 74.7)
Patients with multimodal prehabilitation are stronger before and after surgery for colorectal cancer.
Previous Trial Comparisons: Preoperative Period

Difference in 6MWT assessments between baseline and immediately pre-surgery

- Prehabilitation (Pilot)
- Prehabilitation
- Rehabilitation/No Prehab
- Nutrition Counselling + Placebo
- Nutrition Counselling + Whey

\[ \Delta 6\text{MWT} (\text{m}) \]

-20  -10   0   10   20   30   40   50
Randomized clinical trial of prehabilitation before planned liver resection

<table>
<thead>
<tr>
<th></th>
<th>Prehabilitation</th>
<th>Standard care</th>
<th>Study arm comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline*</td>
<td>Post*</td>
<td>Change†</td>
</tr>
<tr>
<td>$V_{O_2}$ at AT (ml per kg per min)</td>
<td>10.0(0.9)</td>
<td>11.9(2.2)</td>
<td>1.9 (0.1, 3.6)</td>
</tr>
<tr>
<td>$V_{O_2}$ at peak (ml per kg per min)</td>
<td>16.1(2.2)</td>
<td>18.9(4.7)</td>
<td>2.8 (-0.4, 5.9)</td>
</tr>
<tr>
<td>Oxygen pulse at AT (ml/beat)</td>
<td>8.1(1.9)</td>
<td>9.3(2.2)</td>
<td>1.2 (0.1, 2.3)</td>
</tr>
<tr>
<td>Oxygen pulse at peak (ml/beat)</td>
<td>9.9(1.9)</td>
<td>11.3(2.2)</td>
<td>1.3 (-0.1, 2.9)</td>
</tr>
<tr>
<td>Peak work rate (W)</td>
<td>117(20)</td>
<td>130(34)</td>
<td>13 (0, 27)</td>
</tr>
<tr>
<td>Heart rate reserve (beats/min)</td>
<td>54(18)</td>
<td>58(23)</td>
<td>4 (-4, 13)</td>
</tr>
<tr>
<td>SF-36® scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall physical health</td>
<td>53(27)</td>
<td>66(27)</td>
<td>13 (2, 24)</td>
</tr>
<tr>
<td>Overall mental health</td>
<td>63(25)</td>
<td>75(24)</td>
<td>12 (1, 23)</td>
</tr>
<tr>
<td>Overall QoL</td>
<td>59(25)</td>
<td>73(23)</td>
<td>14 (1, 27)</td>
</tr>
</tbody>
</table>

Values are *mean(s.d.) and †mean (95 per cent c.i.). $V_{O_2}$, oxygen uptake; AT, anaerobic threshold; QoL, quality of life. ‡Paired t test; §independent t test.
Do patients with poor functional capacity benefit the most from prehabilitation?
< 400 m walk distance: indicator of poor functional capacity

1) 400-meter walk test → related to frailty and major mobility disability in older adults

2) < 409 m = VO2peak < 15 ml/Kg/min

3) < 406 m → cardio-resp complications after CR surg

Pahor M et al, JAMA 2014
Sinclair RCF et al, BJA 2012
## Baseline Patients Characteristics

<table>
<thead>
<tr>
<th></th>
<th>&gt; 400 m (n=70)</th>
<th>&lt; 400 m (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6MWD, m</td>
<td>485 (61)*</td>
<td>308 (76)</td>
</tr>
<tr>
<td>Age, years</td>
<td>65 (10)*</td>
<td>75 (13)</td>
</tr>
<tr>
<td>Male gender</td>
<td>46 (66%)</td>
<td>17 (47%)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.6 (4.6)</td>
<td>27.2 (4.3)</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>54.5 (10.8)</td>
<td>52.5 (10.7)</td>
</tr>
<tr>
<td>ASA class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-II</td>
<td>56 (80%)</td>
<td>23 (64%)</td>
</tr>
<tr>
<td>III-IV</td>
<td>14 (20%)*</td>
<td>13 (36%)</td>
</tr>
<tr>
<td>Colon surgery</td>
<td>30 (43%)</td>
<td>22 (61%)</td>
</tr>
<tr>
<td>Laparoscopic surgery</td>
<td>65 (93%)</td>
<td>33 (92%)</td>
</tr>
</tbody>
</table>

Data presented as mean (SD) or n(%).
ASA: American Society of Anesthesiologists Classification, BMI: Body Mass Index

*P < 0.05
In the **preoperative period**, less fit patients had a greater improvement in walking capacity.

![Graph showing the improvement in walking capacity before surgery](image-url)

- **Baseline**: 0 m for both groups.
- **Before surgery**: 0 m for the group < 400 m, 46 ± 50.4 m for the group > 400 m.

*p = 0.01*
At 4 weeks after surgery, less fit patients had a greater improvement in walking capacity.
At **8 weeks** after surgery, low fit patients had a greater improvement in walking capacity.

- **< 400 m**: +53 ± 50.4
- **> 400 m**: +12.6 ± 59.8

*p=0.01*
Prehab enhances **postoperative** functional capacity in patients with low reserve

- **3.5 Lanes of Traffic**
  - 395m; 1.1m/s

- **2 Lanes of Traffic**
  - 332m; 0.8m/s

- Prehabilitation 58 m
- Rehabilitation 22 m

- A 6MWD of > 400 meters is needed to cross 4 lanes of traffic. (1.2 m/s) Criterion for independency and mobility
What is the impact of prehabilitation on clinical outcome?
### Table: Preoperative Supervised Exercise Improves Outcomes After Elective Abdominal Aortic Aneurysm Repair

#### A Randomized Controlled Trial

<table>
<thead>
<tr>
<th>Complications</th>
<th>Total</th>
<th>Exercise Group</th>
<th>Control Group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 (15.3%)</td>
<td></td>
<td>5 (8.1%)</td>
<td>14 (22.6%)</td>
<td>0.025†</td>
</tr>
<tr>
<td>5: myocardial infarction (2 fatal)</td>
<td></td>
<td>EVAR: 1 (4.3%)</td>
<td>EVAR: 3 (13.0%)</td>
<td>0.608</td>
</tr>
<tr>
<td>5: prolonged inotropic support</td>
<td></td>
<td>OAR: 4 (10.3%)</td>
<td>OAR: 11 (28.2%)</td>
<td>0.044</td>
</tr>
<tr>
<td>5: new-onset arrhythmia (without evidence of myocardial damage or ischemia)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3: new-onset arrhythmia with elevated troponin T levels</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: Unstable angina with Troponin level of 0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pulmonary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 (16.1%)</td>
<td></td>
<td>7 (11.3%)</td>
<td>13 (21.0%)</td>
<td>0.143†</td>
</tr>
<tr>
<td>14: postoperative pneumonia</td>
<td></td>
<td>EVAR: 0 (0.0%)</td>
<td>EVAR: 4 (17.4%)</td>
<td>0.109</td>
</tr>
<tr>
<td>3: severe postoperative pneumonia resulting in reintubation or respiratory support</td>
<td></td>
<td>OAR: 7 (17.9%)</td>
<td>OAR: 9 (23.1%)</td>
<td>0.575</td>
</tr>
<tr>
<td>1: postoperative pneumonia and an exacerbation of COPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: unplanned reintubation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: reintubation and aspiration pneumonia (fatal)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 (13.7%)</td>
<td></td>
<td>4 (6.5%)</td>
<td>13 (21.0%)</td>
<td>0.019†</td>
</tr>
<tr>
<td>15: more than 20% decrease in creatinine clearance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2: renal insufficiency postoperatively requiring hemodialysis/hemofiltration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Endpoints</strong></td>
<td></td>
<td>14 (22.6%)</td>
<td>26 (41.9%)</td>
<td>0.021</td>
</tr>
<tr>
<td>(composite outcome measure)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*^n (%)^.
†Chi-square test.
EVAR indicates endovascular aneurysm repair; OAR, open aneurysm repair.
The ability of prehabilitation to influence postoperative outcome. Systematic review and meta analysis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Experimental Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbalho-Moulim 2011</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>17</td>
<td></td>
<td>Not estimable</td>
</tr>
<tr>
<td>Dronkers 2008</td>
<td>3</td>
<td>10</td>
<td>8</td>
<td>10</td>
<td>20.7%</td>
<td>0.11 [0.01, 0.84]</td>
</tr>
<tr>
<td>Gillis 2014</td>
<td>12</td>
<td>38</td>
<td>17</td>
<td>39</td>
<td>42.5%</td>
<td>0.60 [0.24, 1.52]</td>
</tr>
<tr>
<td>Kulkarni 2010</td>
<td>0</td>
<td>18</td>
<td>2</td>
<td>19</td>
<td>8.8%</td>
<td>0.19 [0.01, 4.22]</td>
</tr>
<tr>
<td>Soares 2013</td>
<td>5</td>
<td>16</td>
<td>11</td>
<td>16</td>
<td>28.0%</td>
<td>0.21 [0.05, 0.92]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>97</td>
<td>101</td>
<td>101</td>
<td></td>
<td>100.0%</td>
<td>0.35 [0.17, 0.71]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>20</td>
<td>38</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity</strong></td>
<td>Chi² = 3.16, df = 3 (P = 0.37); I² = 5%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test for overall effect</strong></td>
<td>Z = 2.94 (P = 0.003)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Prehabilitation vs usual care: morbidity

Surgery, 2016
Impact of Pre-operative Change in Physical Function on Surgical Recovery after Colorectal Surgery, n=156


![Graph showing the impact of pre-operative change in physical function on surgical recovery. The graph includes data points at baseline, pre-surgical phase, and 9 weeks post-surgery. The graph indicates higher rates of serious complications (18% vs 2%) in the deteriorated group compared to the no change group.]

Higher rate of serious complications
18% vs 2%
**IMPROVING PREOPERATIVE FUNCTIONAL CAPACITY DECREASES COMPLICATION AND ED VISITS**

<table>
<thead>
<tr>
<th></th>
<th>6MWD change ≥ 20 m</th>
<th></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO n = 99</td>
<td>YES n = 80</td>
<td></td>
</tr>
<tr>
<td><strong>30-day COMPLICATION (CCI), median [IQR]</strong></td>
<td>8.7 [0-22.6]</td>
<td>0 [0-8.7]</td>
<td>0.022</td>
</tr>
<tr>
<td>Participants with at least 1 complication within 30 days, n (%)</td>
<td>50 (50)</td>
<td>30 (38)</td>
<td>0.097</td>
</tr>
<tr>
<td><strong>Length of primary hospital stay (days), median [IQR]</strong></td>
<td>4 [3-6]</td>
<td>3 [3-5]</td>
<td>0.236</td>
</tr>
<tr>
<td><strong>30-day ED visit, n (%)</strong></td>
<td>25 (25)</td>
<td>10 (13)</td>
<td>0.038</td>
</tr>
<tr>
<td><strong>30-day hospital readmissions, n (%)</strong></td>
<td>14 (14)</td>
<td>5 (6)</td>
<td>0.142</td>
</tr>
</tbody>
</table>

Minnella E, unpublished
Prehabilitation in colorectal cancer and postoperative clinical outcome

International multicenter study, 2016 (Registered Clinical Trials, NTR 5947)

The Netherlands
Canada
Danemark
France
Take Home Message

• Prehabilitation requires a multidisciplinary approach
• Customize the program to each patient/surgery
• Proof of concept: increases functional capacity
• Can improve postoperative outcome (more data needed)
• Can impact on continuum of cancer care (more data needed)
• Challenges: Compliance? Recording adherence
  Costs? Caregiver, Societal, Resources?
Conference

Prehabilitation for the Surgical Patient
June 15-17 2017
Montreal, Quebec, Canada

Contact for more information:
victoria.greco@mail.mcgill.ca
Physical activity increases in the prehab group during the 4 weeks before surgery (CHAMPS,)

Chen B et al, 2016
BIA within group comparisons
Prehabilitation vs. No intervention
within an ERAS setting

Gillis C, unpublished
**Study Design**

- **n=179 pts**
  - 1 cohort + 2 RCTs

- **Baseline assessment**
- **Preoperative assessment**
- **SURGERY**
- **4 weeks post assessment**
- **8 weeks post assessment**

**Preoperative Walking Distance Improvement**
- ≥ 20 m
- < 20 m

*References*
- Gillis C et al, *Anesthesiology* 2014
- Carli F et al (unpublished)
## Type of postoperative complications

<table>
<thead>
<tr>
<th>Medical Complication, n (%)</th>
<th>6MWD change ≥ 20 m</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO n = 99</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>24 (24%)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>6 (6%)</td>
</tr>
<tr>
<td>Infectious</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>Other medical</td>
<td>5 (5%)</td>
</tr>
<tr>
<td></td>
<td>16 (16%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surgical complication, n(%)</th>
<th>6MWD change ≥ 20 m</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO n = 99</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>24 (24%)</td>
</tr>
<tr>
<td>Perforation</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Ileus</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>20 (20%)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>other</td>
<td>3 (3%)</td>
</tr>
<tr>
<td></td>
<td>1 (1%)</td>
</tr>
</tbody>
</table>
Improving preoperative functional capacity decreases severity of complication.

<table>
<thead>
<tr>
<th>Severe Complication</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCI ≥ upper quartile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6MWD change ≥ 20 m</td>
<td>0.28</td>
<td>0.11-0.74</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Multivariate logistic regression analysis testing adjusted for age, gender, BMI, ASA, Charlson Comorbidities Index, cancer stage, surgical approach and surgical site.
Greater proportion of prehabilitation patients improved

\[ P < 0.001 \]
Undernutrition Before Surgery: Our Experience.

The incidence of undernutrition in all patients attending preoperative clinic at Montreal General Hospital for elective colorectal surgery

Global Assessment (n=70) score A refers to adequately nourished; B moderate or suspected undernutrition; C severely undernourished
Future directions for exercise-oncology research on cancer progression.

**Epidemiological studies**
- A greater number of large-scale studies assessing both self-reported and/or objective measures of exercise exposure with long-term follow-up and adequate event rates.
- Delineate the association no how changes in exercise behavior, functional capacity/cardiorespiratory fitness measures are associated with clinical outcome across all solid tumors.
- More studies determining the differential association between exercise and prognosis as a function of tumor phenotype/gene expression.
- More studies determining the differential association between exercise and prognosis as a function of host-related circulating factors postulated to mediate the exercise–prognosis relationship.

**Clinical biomarker intervention studies**
- Delineate the differential effects of differences in exercise prescription dose (e.g., frequency, intensity, duration, modality) on changes in salient biomarkers in randomized trials.
- Determine effects of exercise across different tumor types across the cancer continuum (i.e., from diagnosis to palliation) to expand current efforts as well as extend to other solid tumors where exercise has not been rigorously evaluated.
- Elucidate the most salient biomarkers of interest that mediate the exercise–cancer prognosis relationship to develop a standardized ‘exercise–oncology’ biomarker panel that is reproducible and can be evaluated/compared across studies.
- Determine the effects of exercise on circulating biomarkers in conjunction with procurement of tumor tissue and/or imaging biomarkers whenever possible.

**Preclinical studies**
- Orthotopic implantation of syngeneic tumor cell lines or induction of orthotopic tumors via transgenic or chemical methods in immune competent animals to enable investigation of effects on primary tumor growth and metastasis.
- Elucidate the optimal exercise frequency, intensity, duration, and progression, as appropriate. Confirmation of ‘training’ effect via muscle fiber or mitochondrial function analysis.
- Determine effects on systemic mechanisms (metabolic and sex hormones, inflammation, immunity, and products of oxidation) in conjunction with examination of intratumoral/tumor microenvironmental molecular mechanisms (e.g., cell signaling pathways, angiogenesis, metabolism, migration).

**Potential translational (cross-cutting/transdisciplinary) studies**
- 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.
- Elucidation of the effects of exercise on both circulating and intratumoral mechanisms associated with tumor growth in mouse models to guide systemic (plasma) biomarker testing in completed and ongoing clinical exercise trials in cancer patients. For further mechanistic investigations, plasma/serum from patients exposed to exercise vs. control conditions can be applied to human cancer cells in vitro to investigate effects on markers of the neoplastic phenotype.
- In epidemiological studies, identify genes or histological sub-types that may mediate the association between exercise and prognosis. Next, in preclinical studies, confirm mechanism of action by examining the effects of exercise in clinically relevant mouse models where the identified gene/pathway/histological sub-type is over-expressed or ablated. For clinical translational, plasma/serum from patients (with the identified histological sub-type or over expression of a specific pathway) exposed to exercise vs. control conditions can be applied to human cancer cells in vitro for further mechanistic studies.
Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study   BMJ, 2013

Although limited in quantity, existing randomised trial evidence on exercise interventions suggests that exercise and many drug interventions are often potentially similar in terms of their mortality benefits in the secondary prevention of coronary heart disease, rehabilitation after stroke, treatment of heart failure, and prevention of diabetes
“Marginal gains theory”

“the principle of multiple, seemingly miniscule, improvements throughout any given process, collectively achieving a far superior output”

• Identifying every single small step

• Bundle of evidence-based elements

Dave Brailsford, director of British Cycling Team, 2012