Rehabilitation in the ICU: Timing it Right

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Critical Care Canada Forum

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  – Canada Foundation for Innovation
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  – Canadian Respiratory Research Network Emerging Research Leaders Initiative
  – Ontario Thoracic Society
  – Canadian Institutes for Health Research

• Restorative Therapies for bike loans at Toronto General Hospital and London Health Sciences
What is the optimal timing of rehabilitation in the ICU?

1. Is there any urgency for rehab in the ICU?
2. What do we know about early rehabilitation interventions in the ICU?
   - What don’t we know?
3. How do we design an optimal early rehab intervention in the ICU?
4. Ongoing research
Rehab in the ICU: Timing it right

• When do we start?
• What interventions across the course of the patient’s ICU stay?
  – Frequency
  – Intensity
  – Type
  – Time
1. IS THERE ANY URGENCY FOR REHAB IN THE ICU?
Quadriceps muscle cross sectional area decreases quickly in the ICU

3x more than healthy people on bedrest!

Within 7 days of ICU admission, involuntary quadriceps force is very low

Figure 1 Quadriceps twitch tension (Twq) in ICU patients.

Vivodtzev et al., Critical Care. 2014. 18:431.
$\dot{V}O_2$ changes occur early after exposure to bedrest in healthy people (19 studies)
Prospective 1 and 5-year follow-up study of 109 ICU survivors

Setting: 4 Canadian ICUs
Population: Adult patients with ARDS

Outcomes:
Primary – 6 minute walk test
Pulmonary function tests
Health-related quality of life

6 minute walk distance
N=83 281 m 49% predicted
N=82 396 m 64% predicted
N=83 422 m 66% predicted
N=64 436 m 76% predicted

Patients developing ICUAW have longer LOS & MV, higher costs, and higher 1-year mortality.

Hermans et al., AJRCCM. 2014; 190(4):410-420.

ICUAW = ICU-acquired weakness
MRC = Medical Research Council Strength
2. WHAT DO WE KNOW ABOUT EARLY REHAB INTERVENTIONS IN THE ICU?
Is “rehabilitation” in the ICU the right term?

What is the time frame of Rehabilitation?
Typically rehabilitation occurs by a specific period of time....and can be needed from the acute or initial phase immediately following recognition of a health condition.
Continuum of physical activity

Sedentary Physiology

Bedrest

Completely Passive

Exercise Physiology

Completely Active

Increasing physical activity and patient engagement in rehab

Methodologically rigorous and clinically relevant systematic review

Included trials published up to April 2014
- Rehab vs. usual care in ICU (excl. neuro, trauma)
- 7 trials: 6 RCTs; 4 RCTs started intervention within 1st 7 days of ICU
# Neuromuscular Electrical Stimulation

<table>
<thead>
<tr>
<th>Intervention (n enrolled)</th>
<th>ICU start</th>
<th>Primary Outcome Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>55 min daily NMES(^1) vs control (N=142)</td>
<td>2 days</td>
<td>Fewer patients with ICUAW @ ICU awakening ✔ 13% (3/24) vs 39% (11/28);</td>
</tr>
</tbody>
</table>

Continuum of physical activity

Sedentary Physiology
- sleep
- sedentary behaviour

Exercise Physiology
+ light activity
+ moderate physical activity
+ intense exercise

Increasing physical activity and patient engagement in rehab

METS

Bedrest
Completely Passive

Completely Active

RCT of early PT/OT in the ICU

**Primary Outcome:**
Independent functional status @ hospital discharge (composite)
(6 ADLs + independent walking)

Medical ICU

- Daily interruption of sedation + Early OT/PT
  - 7d/wk
  - N=49
  - 59% (29/49)
  - p=0.02

- Daily interruption of sedation + Standard care
  - OT/PT
  - N=55
  - 35% (19/55)

Schweickert et al., Lancet. 2009. 373: 1874-82.
Early physical rehabilitation in intensive care patients with sepsis syndromes: a pilot randomised controlled trial

**Primary Outcome:**
Acute Care Index of Function @ ICU discharge

<table>
<thead>
<tr>
<th>Group</th>
<th>Number (Mean (SD))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined early PT intervention</td>
<td>61.1 (33.1)</td>
</tr>
<tr>
<td>Standard care</td>
<td>55.0 (24.4)</td>
</tr>
</tbody>
</table>

*Note: N=19 for Combined early PT intervention group, N=23 for Standard care group.*

**Single centre**
N=50

Feasibility and safety of early combined cognitive and physical therapy for critically ill medical and surgical patients: the Activity and Cognitive Therapy in ICU (ACT-ICU) trial

Primary Outcome:
Tower Test
3 months post-ICU

- Cognitive Therapy + Early PT
  - N=43
  - 10.0 [8.0-11.0]

- Early PT
  - N=22
  - 11.0 [11.0-12.0]  p=0.20
  - N=14

- Usual Care
  - N=22
  - 10.0 [8.8-12.0]
  - N=12

Normal = 7 to 13
Higher scores = better

# Exercise rehabilitation for patients with critical illness: a randomized controlled trial with 12 months of follow-up

Linda Denehy\(^1\)*, Elizabeth H Skinner\(^2\), Lara Edbrooke\(^1\), Kimberley Haines\(^2\), Stephen Warrillow\(^3\), Graeme Hawthorne\(^4\), Karla Gough\(^5\), Steven Vander Hoorn\(^6\), Meg E Morris\(^7\) and Sue Berney\(^2\)

## Primary Outcome:
6 minute walk test @ 12 months (model estimates)

<table>
<thead>
<tr>
<th>Group</th>
<th>Distance (SD)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive exercise in ICU, on ward, and post-ICU</td>
<td>409.6 (22.9) m</td>
<td>41</td>
</tr>
<tr>
<td>Standard care</td>
<td>404.9 (23.0) m</td>
<td>38</td>
</tr>
</tbody>
</table>

\(^*\) Indicates statistical significance: p=0.884


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**Medical/Surgical ICU**

**Intensive exercise in ICU, on ward, and post-ICU**

N=74

**Standard care**

N=76

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**Single centre**

N=150
# Summary of early intervention RCTs

<table>
<thead>
<tr>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>✔ Daily NMES(^1)</td>
</tr>
<tr>
<td>Daily NMES(^2)</td>
</tr>
<tr>
<td>✔ Daily OT and PT(^3)</td>
</tr>
<tr>
<td>Multimodal PT(^4)</td>
</tr>
<tr>
<td>BID Cognitive and daily PT(^5)</td>
</tr>
<tr>
<td>Intense exercise(^6)</td>
</tr>
</tbody>
</table>

Implementing the Evidence - FITT:
Identifying the “dose” of therapy

Frequencty: how often
Intensity: how difficult
Time: how long
Type: what types of activity
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Intervention Freq/ Intensity/ Time/ Type</th>
<th>Usual Care FITT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily NMES(^1)</td>
<td>Daily in ICU / visible muscle contraction / <strong>55 min</strong> / NMES</td>
<td>Not reported (NR)</td>
</tr>
<tr>
<td>Daily NMES(^2)</td>
<td>Daily in ICU / visible muscle contraction / <strong>60 min</strong> / NMES</td>
<td>Daily in ICU / N/A / 60 min / Sham</td>
</tr>
</tbody>
</table>

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## What interventions started within 7 days are ready for implementation NOW?

<table>
<thead>
<tr>
<th>Intervention</th>
<th>ICU start</th>
<th>Primary Outcome Results</th>
</tr>
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<tbody>
<tr>
<td>✔ NMES 55 min daily</td>
<td>2 days</td>
<td>Fewer patients with ICUAW @ ICU awakening</td>
</tr>
<tr>
<td>NMES 60 min daily</td>
<td>4 days</td>
<td>No difference in lower extremity muscle strength @ hospital d/c</td>
</tr>
</tbody>
</table>

Early mobilization and recovery in mechanically ventilated patients in the ICU: a bi-national, multi-centre, prospective cohort study

Setting: 12 Australian / New Zealand ICUs
Population: Adult MV patients

Clinical Course

- ICU Admission
- MV >24 h
- < 3 Days ICU stay

Outcomes:
- Primary – receipt of early active mobilization
- Secondary – muscle strength, health-related quality of life, employment status

Median time from ICU admission to mobilization:
5 [3 to 8] days

Day 14 MV or d/c MV or (whichever 1st)

6 months
- QOL
- Employment

Patients mobilized w/ MV
N=70/192

Episodes of mobilization
during MV
N=209/1,288

37 out of 100 received any mobilization

16 out of 100 mobilization activities occurred
Highest mobilization activities during MV (n=209)

Main reasons for not receiving active mobilization
- Endotracheal tube
- Sedation

<table>
<thead>
<tr>
<th>Activity</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bed Exs</td>
<td>94</td>
</tr>
<tr>
<td>Passive t/f to sit</td>
<td>52</td>
</tr>
<tr>
<td>Dangle</td>
<td>22</td>
</tr>
<tr>
<td>Stand</td>
<td>11</td>
</tr>
<tr>
<td>Bed to chair</td>
<td>4</td>
</tr>
<tr>
<td>Walking</td>
<td>26</td>
</tr>
</tbody>
</table>

It’s about receiving therapy while on mechanical ventilation

**Intervention**

PROM -> AAROM -> AROM -> Bed Mobility -> Transfers (sitting) -> Sitting balance -> ADLs -> Transfers (standing) -> Ambulation

<table>
<thead>
<tr>
<th></th>
<th>Intervention (N=49)</th>
<th>Control (N=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time to start therapy (d)</td>
<td>1.5 [1.0 to 2.1]*</td>
<td>7.4 [6.0 to 10.9]</td>
</tr>
</tbody>
</table>

0.32 h/d = 19.2 minutes

Schweickert et al., Lancet. 2009. 373: 1874-82.
Strengths and Limitations of Existing Trials

**Strengths**
- Randomized intervention
- Varied ICU settings
- Interventions started within 1st 7 days

**Limitations**
- Optimal “dose” unknown
- Usual care poorly described
- Varied outcome measures and timing of measures
- Fully passive therapies do not allow patient engagement
3. HOW DO WE DESIGN AN OPTIMAL EARLY REHAB INTERVENTION IN THE ICU?
Considerations for designing an early ICU rehab intervention

• **Population**: Who is most likely to benefit?

• **Intervention**:
  – Starts within first 7 days of ICU stay
  – Adaptable to patients’ varying levels of consciousness/severity of illness
  – Feasible to deliver
  – Reproducible - Frequency, intensity, time, type
  – Acceptable to patients, families, and ICU clinicians
  – Use of existing vs. extra human resources

• **Comparison**: Well-documented

• **Outcomes**: Patient-centered, validated
4. ONGOING RESEARCH
# CYCLE: Critical Care Cycling to Improve Lower Extremity Strength

<table>
<thead>
<tr>
<th>CYCLE</th>
<th>Preparation phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICAN Rehab</td>
<td>Survey development: pt, family, clinician satisfaction with rehabilitation</td>
</tr>
<tr>
<td>CYCLE-R</td>
<td>Systematic Review</td>
</tr>
<tr>
<td>Uni-CYCLE</td>
<td>Retrospective chart audit ✓ JCC 2015</td>
</tr>
</tbody>
</table>

## TryCYCLE: Phase II open label study
- 1 center, 33 pt prospective cohort
  - Design the intervention; select outcomes; assess fidelity, safety, satisfaction, and acceptability ✓ submitted

## CYCLE pilot RCT: Phase II randomized pilot
- 7 center, 60 pt pilot RCT
  - Feasibility

## CYCLE RCT: Phase III randomized trial
- Multicenter RCT
- CYCLE$ Economic evaluation
- BICYCLE Behavioural Intervention for Knowledge Translation
Rationale for CYCLE

• **RCT:** PT and OT started within 1.5 days of intubation improves independence at hospital discharge
  
  – Main difference: **19.2 minutes**/ day during MV
  

• **RCT:** In-bed cycling started ICU **day 14** improved 6-minute walk test distance at hospital discharge
  

• **Question:** Can we initiate in-bed cycling with patients *earlier* in their ICU stay, and will it improve patient outcomes?
RESEARCH QUESTION:

Is it feasible to enroll newly mechanically ventilated adults in a multi-centre pilot RCT of early in-bed cycling plus routine physiotherapy versus routine physiotherapy alone to inform a larger RCT?
- Randomized intervention 5d/ wk until ICU d/c or 28 days
- If patients in cycling arm -> d/c cycling if patient can march on the spot x 2 days
CYCLE Pilot RCT Team Members

Physiotherapists / RCs

St. Joseph’s Healthcare
• Daana Ajami, Magda McCaughan, Christina Murphy, Kristy Obrovac, Laura Camposilvan; RCs Alex Molloy, France Clarke, Marnie Jakab

Hamilton Health Sciences – Juravinski
• Leigh Ann Niven, Tania Brittain, Shivaun Davidson, Andrea Galli; Helen Bishop, Shannon Earl, Chelsea Hale, Gillian Manson; RC Tina Millen

Hamilton Health Sciences – General
• Ashley Eves, Annie Newman, Judi Rajczak, Julie Reid, Elise Loreto; Jennifer Duley, Sue Mahler, Matt McCaffrey, Jessica Pilon-Bigne; RC Ellen McDonald

Toronto General (co-PIs)
• Vince Lo, Sunita Mathur, PT, PhD, Gary Beauchamp, Anne-Marie Bourgeois, Sherry Harburn, Megan Hudson, Teresa Torres; RC Andrea Matte

London Health Sciences
• Kristen Abercombie, Jennifer Curry, Erin Blackwell-Knowles, Tania Larsen; RC Eileen Campbell

St. Michael’s Hospital
• Deanna Faltracco, Christine Leger, Sarah Brown, Diana Horobetz, Verity Tulloch, Anna Michalski, Natalia Zapata; RC Orla Smith

Investigators
• Dr. Michelle Kho, McMaster/ SJH (PI)
• Dr. Ian Ball, Western
• Dr. Karen Burns, St. Mike’s
• Dr. Deborah Cook, McMaster/ SJH
• Dr. Alison-Fox Robichaud, McMaster, Hamilton General
• Dr. Margaret Herridge, Toronto General
• Dr. Tim Karachi, McMaster, Juravinski
• Dr. Bram Rochwerg, McMaster, Juravinski
• Dr. Karen Koo, Western / Swedish Healthcare
• Dr. Marina Mourtzakis, U Waterloo
• Dr. Joe Pellizzari, McMaster/ SJH
• Mr. Tom Piraino, McMaster/ SJH
• Dr. Jill Rudkowski, McMaster/ SJH
• Dr. Andrew Seely, U of Ottawa / Ottawa General
• Dr. Jean-Eric Tarride, McMaster

Methods Centre (Hamilton, ON)
• Ms. France Clarke, McMaster/ SJH
• Mr. Alex Molloy, SJH
CYCLE Pilot RCT Feasibility Outcomes

1. **Accrual**: Following orientation, the overall average accrual rate will be 3 pts q 2 mo/site.

2. **Protocol violations**: The cycling protocol can be implemented with <20% protocol violations.

3. **Outcome Measures**: >80% of outcomes will be measured as scheduled.

4. **Blinded Outcome Assessment**: >80% of outcomes at hospital discharge will be assessed by personnel blinded to group allocation.
# CYCLE Pilot RCT Progress to-date

<table>
<thead>
<tr>
<th>Site</th>
<th>Bike Training</th>
<th>Ethics</th>
<th>Contracts</th>
<th>Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>St. Joe’s Hamilton</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>11 as of Oct 27</td>
</tr>
<tr>
<td>Juravinski Hamilton</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>3 as of Oct 27</td>
</tr>
<tr>
<td>Hamilton General</td>
<td>✔️</td>
<td>✔️</td>
<td>✔️</td>
<td>1 as of Oct 27</td>
</tr>
<tr>
<td>Toronto General</td>
<td>✔️</td>
<td>✔️</td>
<td>In progress</td>
<td>Pending ethics &amp; contracts</td>
</tr>
<tr>
<td>London Health Sciences</td>
<td>✔️</td>
<td>In revision</td>
<td>In process</td>
<td>Pending ethics &amp; contracts</td>
</tr>
<tr>
<td>St. Michael’s Hospital (Toronto)</td>
<td>✔️</td>
<td>Submitted</td>
<td>Submitted</td>
<td>Nov/Dec 2015</td>
</tr>
<tr>
<td>Ottawa General</td>
<td>In discussion</td>
<td>Submitted</td>
<td>Submitted</td>
<td>Jan 2016</td>
</tr>
</tbody>
</table>
What is the optimal timing of rehabilitation in the ICU?

1. Is there any urgency for rehab in the ICU?
2. Rehabilitation interventions in the ICU
   – What do we know? What don’t we know?
3. What are characteristics of an optimal rehab intervention in the ICU?
4. Ongoing research

Thank you!

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