Rehabilitation after Critical Illness: What Should this Look Like?

Margaret Herridge MD MPH
Associate Professor of Medicine
Interdepartmental Division of Critical Care
University of Toronto
Canadian Critical Care Trials Group
I have no conflict of interest to declare
Overview

- Rehabilitation Framework
- Heterogeneity of Disability
- Changes in Morbidity over time
- Different Risk Strata
- Challenges and Opportunities
Phase-specific Approach to Rehabilitation in Critical Illness: Targeting Muscle, Nerve and Brain during and after the ICU Stay

Rehabilitation in ICU

- Resuscitation: Steroids, NMB, Ventilation
- Glycemic Control: Sedation
- Delirium Treatment
- Wakefulness: Early Mobility, Physical Therapy

Phase-specific Approach to Rehabilitation in Critical Illness: Targeting Muscle, Nerve and Brain during and after the ICU Stay

Rehabilitation after ICU - Phase-Specific Needs

<table>
<thead>
<tr>
<th>Hospital Ward</th>
<th>Preparing for Discharge</th>
<th>Early Community Adjustment</th>
<th>Late Community Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk stratify Inpt vs Outpt &amp; Intensity of Rehab</td>
<td>Education Preparation</td>
<td>Optimizing ADLs and Independence</td>
<td>Facilitate Return to work or job Re-training</td>
</tr>
</tbody>
</table>

Herridge Crit Care Med 2009

Five-Year Outcomes in ARDS

Herridge et al. NEJM 2011; 364: 1293-304

Persistent exercise limitation and reduction in Physical QOL at 5-years after ICU discharge
Quality of life in the five years after intensive care: a cohort study

Brian H Cuthbertson, Siân Roughton, David Jenkinson, Graeme MacLennan, Luke Vale

Results: 300 level 3 intensive care patients of median age 60.5 years and median length of stay 6.7 days, were recruited. Physical quality of life fell to 3 months (P = 0.003), rose back to pre-morbid levels at 12 months then fell again from 2.5 to 5 years after intensive care (P = 0.002). Mean physical scores were below the population norm at all time points but the mean mental scores after 6 months were similar to those population norms. The utility value measured using the EuroQOL-5D quality of life assessment tool (EQ-5D) at 5 years was 0.677. During the five years after intensive care unit, the cumulative quality adjusted life years were significantly lower than that expected for the general population (P < 0.001).

Garland et al. Chest 2004; 126: 1894-904
Heterotopic Ossification

Spectrum of Disability

- Weakness
- Mental Health & Cognition

Alopecia

Tracheal stenosis

Cosmesis - Scars from CVC, Art line, CT, drain sites

- Nerve and Muscle
- Brain

- Hearing Loss
- Pulmonary fibrosis
- Frozen joints
- Contractures
- Renal Impairment

- Weakness
- Mental Health & Cognition

Ischemic digits

- Bronchiectasis
- Taste changes
- Striae

Spectrum of Disability
1 & 2 Year Cognitive Outcomes

[Graph showing percent with deficits in processing speed, memory, executive function, attention, and IQ over 1, 2, and 3 years post-Hospital DC.]

Hopkins et al. AJRCCM 1999; 160:50
### Table 2. Difference in Follow-up Cognitive Scores by Hospitalization Status<sup>a</sup>

<table>
<thead>
<tr>
<th></th>
<th>Following Noncritical Illness Hospitalization</th>
<th>$P$ Value</th>
<th>Following Critical Illness Hospitalization</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up CASI</td>
<td>$-2.27 \ (-2.61$ to $-1.93)$</td>
<td>&lt;.001</td>
<td>$-2.92 \ (-5.00$ to $-0.86)$</td>
<td>.006</td>
</tr>
<tr>
<td>Adjusted difference&lt;sup&gt;c&lt;/sup&gt;</td>
<td>$-1.01 \ (-1.33$ to $-0.70)$</td>
<td>&lt;.001</td>
<td>$-2.14 \ (-4.24$ to $-0.03)$</td>
<td>.047</td>
</tr>
<tr>
<td>Follow-up CASI IRT</td>
<td>$-0.28 \ (-0.32$ to $-0.24)$</td>
<td>&lt;.001</td>
<td>$-0.27 \ (-0.45$ to $-0.09)$</td>
<td>.003</td>
</tr>
<tr>
<td>Adjusted difference&lt;sup&gt;c&lt;/sup&gt;</td>
<td>$-0.12 \ (-0.16$ to $-0.08)$</td>
<td>&lt;.001</td>
<td>$-0.19 \ (-0.38$ to $-0.01)$</td>
<td>.04</td>
</tr>
</tbody>
</table>

Abbreviations: CASI, Cognitive Abilities Screening Instrument; CI, confidence interval; IRT, item response theory.

<sup>a</sup>Linear regression with generalized estimating equations to account for repeated observations, specifying an exchangeable correlation matrix and robust variance estimates.

<sup>b</sup>The reference category in each comparison was no hospitalization.

<sup>c</sup>Adjusted for age at study visit, sex, baseline cognitive score, years of education, time since baseline visit, and the baseline comorbidities coronary heart disease and cerebrovascular disease.

Mental Health Issues in Patients

- Anxiety - 23-48%
- Depression - 17-43%
- Post Traumatic Stress Disorder - 21-35%
- Family Dysfunction

Davydow et al. Psychosom Med 2008; 70:512-9
Adhikari et al. Chest 2011

Jones et al. Critical Care 2010; 14(5): R168
Myhren et al. Crit Care 2010 ;14: R14
Davydow Crit Care 2010; 14: 125
Kapfhammer et al. Am J Psychiatry 2004; 161: 45-52
### Long-term Cognitive and Psychological Outcomes in the Awakening and Breathing Controlled Trial

James C. Jackson¹,²,³,⁴, Timothy D. Girard¹,²,⁵, Sharon M. Gordon²,⁵, Jennifer L. Thompson⁶, Ayumi K. Shintani⁶, Jason W. W. Thomason⁷, Brenda T. Pun¹, Angelo E. Canonico⁸, Janet G. Dunn⁹, Gordon R. Bernard¹, Robert S. Dittus²,⁵, and E. Wesley Ely¹,²,⁶

#### TABLE 3. LONG-TERM OUTCOMES

<table>
<thead>
<tr>
<th>Outcome</th>
<th>3-mo Follow-up</th>
<th>12-mo Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention</td>
<td>Control</td>
</tr>
<tr>
<td>Cognitive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite T-score</td>
<td>40 (36–47)</td>
<td>40 (36–45)</td>
</tr>
<tr>
<td>Impaired, %</td>
<td>70</td>
<td>91</td>
</tr>
<tr>
<td>Psychological</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI-II score</td>
<td>13 (7–20)</td>
<td>11 (7–17)</td>
</tr>
<tr>
<td>Prevalence, %</td>
<td>64</td>
<td>58</td>
</tr>
<tr>
<td>Posttraumatic stress disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTSS-10 score</td>
<td>22 (12–29)</td>
<td>20 (14–26)</td>
</tr>
<tr>
<td>Prevalence, %</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Functional</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADL impairment, %</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Functional disability, %</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Quality of life</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-36 scores</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental component</td>
<td>53 (42–57)</td>
<td>53 (43–57)</td>
</tr>
<tr>
<td>Physical component</td>
<td>27 (19–32)</td>
<td>28 (23–36)</td>
</tr>
<tr>
<td>Worse than baseline, %</td>
<td>72</td>
<td>74</td>
</tr>
</tbody>
</table>

*Jackson et al. AJRCCM 2010; 182: 183-91*
Caregiver Burden- Risk Modifier

Psychiatric illness in the next of kin of patients who die in the intensive care unit

Mark D. Siegel, MD, FCCP; Earle Hayes, DO, MS; Lauren C. Vanderwerker, PhD; Diane B. Loseth, RN, MSN, APRN, BC-PCM; Holly G. Prigerson, PhD

CCM 2008; 36: 1722-1728

PTSD symptoms consistent with a moderate to major risk of PTSD were found in 33% of family members.

Azoulay et al. AJRCCM 2005; 17: 987-994
Jones et al. Int Care Med 2004; 30: 456-460

Caregiver depression risk was 34%, 31% and 23% at 2, 6, 12 months
Lifestyle disruption and employment reduction were common.
Compromised HRQOL similar to caregivers of stroke/dementia
Depressive symptomatology associated with depression in ARDS survivors

Van Pelt et al. AJRCCM 2007; 175: 167-173
Cameron et al. Crit Care Med 2006;34:26-33
Caregiver Burden- Risk Modifier

- Distress from fluctuation in mental status and cognition
- Lack of support after hospital discharge
- Difficult to explain situation to children and balancing child care and work
- Distance in relationship with ARDS patient
- Lingering feelings of regret- “...your life is changed forever...”

## Change in Morbidity over Time

### Table 2. (Continued.)

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>At 1 Year (N=83)</th>
<th>At 2 Years (N=69)</th>
<th>At 3 Years (N=71)</th>
<th>At 4 Years (N=63)</th>
<th>At 5 Years (N=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median SF-36 score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical functioning</td>
<td>60</td>
<td>70</td>
<td>70</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Role, physical</td>
<td>25</td>
<td>50</td>
<td>100</td>
<td>75</td>
<td>88</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>62</td>
<td>62</td>
<td>72</td>
<td>74</td>
<td>74</td>
</tr>
<tr>
<td>General health</td>
<td>52</td>
<td>62</td>
<td>55</td>
<td>59</td>
<td>62</td>
</tr>
<tr>
<td>Vitality</td>
<td>55</td>
<td>55</td>
<td>50</td>
<td>50</td>
<td>55</td>
</tr>
<tr>
<td>Social functioning</td>
<td>63</td>
<td>75</td>
<td>75</td>
<td>69</td>
<td>75</td>
</tr>
<tr>
<td>Role, emotional</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Mental health</td>
<td>72</td>
<td>76</td>
<td>72</td>
<td>76</td>
<td>76</td>
</tr>
<tr>
<td><strong>Mean costs after initial hospitalization — Canadian $</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication costs</td>
<td>1,441</td>
<td>1,652</td>
<td>2,288</td>
<td>2,713</td>
<td>2,152</td>
</tr>
<tr>
<td>Rehospitalization costs</td>
<td>11,875</td>
<td>3,727</td>
<td>2,217</td>
<td>1,945</td>
<td>2,700</td>
</tr>
<tr>
<td>Outpatient costs</td>
<td>8,993</td>
<td>4,506</td>
<td>1,558</td>
<td>1,091</td>
<td>714</td>
</tr>
<tr>
<td>Total</td>
<td>22,309</td>
<td>9,885</td>
<td>6,063</td>
<td>5,749</td>
<td>5,566</td>
</tr>
</tbody>
</table>

Herridge et al. NEJM 2011; 364: 1293-304
Five-Year Outcomes in Severe ARDS - relatively young, previously working, few comorbidities - almost 1/3 survivors on HFV

Most patients have modest exercise limitation, return to original work over 2-3 years, have accommodated to disability

Needham and ICAP study (future ARDS cohorts - Fan, Lamontagne)
Older patients / spectrum of age, larger study sample, Identification of more risk factors for poor functional outcome

Fill in the gaps in spectrum of outcome in ARDS
Figure 3. Functional Trajectories by Baseline Functioning

Limitations at baseline:
- Severe
- Mild to moderate
- None

Before sepsis:
- Third Survey Before Sepsis
- Second Survey Before Sepsis
- Last Survey Before Sepsis

After sepsis:
- First Survey After Sepsis
- Second Survey After Sepsis
- Third Survey After Sepsis

Mean Number of ADL and IADL Limitations:

Time to sepsis admission, median (IQR), y:
- Third Survey Before Sepsis: -5.2 (-5.6 to -4.7)
- Second Survey Before Sepsis: -3.1 (-3.7 to -2.7)
- Last Survey Before Sepsis: -1.1 (-1.7 to -0.7)
- First Survey After Sepsis: 0.9 (0.4 to 1.4)
- Second Survey After Sepsis: 2.8 (2.3 to 3.4)
- Third Survey After Sepsis: 5.2 (4.5 to 5.5)

No. of patients, by baseline physical functioning:
- Severe limits:
  - Third Survey Before Sepsis: 87
  - Second Survey Before Sepsis: 127
  - Last Survey Before Sepsis: 159
  - First Survey After Sepsis: 159
  - Second Survey After Sepsis: 42
  - Third Survey After Sepsis: 14
- Mild to moderate limits:
  - Third Survey Before Sepsis: 105
  - Second Survey Before Sepsis: 151
  - Last Survey Before Sepsis: 195
  - First Survey After Sepsis: 195
  - Second Survey After Sepsis: 93
  - Third Survey After Sepsis: 28
- No limits:
  - Third Survey Before Sepsis: 142
  - Second Survey Before Sepsis: 206
  - Last Survey Before Sepsis: 269
  - First Survey After Sepsis: 269
  - Second Survey After Sepsis: 153
  - Third Survey After Sepsis: 56

Iwashyna et al. JAMA 2010; 304:1787-1794
Figure 2. Patient trajectories at 1 year, by health outcome.

3 Months
- 9 (7%)
- 34 (27%)
- 47 (37%)

12 Months
- 6 (4.5%)*
- 2 (1.5%)
- 1 (1%)
- 5 (4%)*
- 18 (14%)
- 4 (3%)
- 7 (6%)
- 12 (9.5%)*
- 23 (18%)
- 12 (9.5%)

Good Outcome: Alive with no functional dependencies
Fair Outcome: Alive with some functional dependencies
Poor Outcome: Alive with complete functional dependency
Dead

### TABLE 2. ADJUSTED 1-YEAR DISABILITY SCORES FOR A PROTOTYPICAL ELDERLY MV SURVIVOR COMPARED WITH A SURVIVOR HOSPITALIZED WITHOUT MV AND A SURVIVOR NOT HOSPITALIZED, MEDICARE CURRENT BENEFICIARY SURVEY 1996–2003

<table>
<thead>
<tr>
<th>Disability Score</th>
<th>Not Hospitalized Adjusted Mean (95% CI)</th>
<th>Hospitalized, no MV Adjusted Mean (95% CI)</th>
<th>Hospitalized, With MV Adjusted Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADL disability</td>
<td>8.0 (7.9–8.1)</td>
<td>11.5 (11.1–11.9)</td>
<td>14.9 (12.2–17.7)</td>
</tr>
<tr>
<td>Mobility difficulty</td>
<td>13.4 (13.3–13.6)</td>
<td>22.3 (21.8–22.9)</td>
<td>25.4 (22.4–28.4)</td>
</tr>
</tbody>
</table>

*Definition of abbreviations:* ADL = activities of daily living; CI = confidence interval; MV = mechanical ventilation.

Adjusted for prior functional status and cognitive score, demographics, Charlson comorbidity count, stroke in the year, number of hospitalizations, and days since last hospitalization. Scores are the average level of disability, ranging from 0 = not disabled to 100 = completely disabled. Scores under each scenario are calculated for the same prototypical person with average age and cognitive score, baseline ADL disability or mobility difficulty score = 10, no cerebrovascular accident, and Charlson count = 1.
Young ARDS
Modest Disability

Older Sepsis
Moderate Disability

Chronically Critically Ill Elderly
Marked Disability

Spectrum of Disability In Different Risk Strata
Rehabilitation Models

- Case-Manager Based Intervention
- Nurse-led Follow-up Clinic
- Home-based self-help instruction
- Home-based rehab program/instruction

Cuthbertson et al. BMJ 2009; 339: b3723
Jones et al. Crit Care Med 2003; 31: 2456-2461
Elliott et al. Critical Care 2011, 15:R142
Rehabilitation after critical illness: A randomized, controlled trial

Christina Jones, PhD; Paul Skirrow, MPhil; Richard D. Griffiths, MD, FRCP; Gerald H. Humphris, PhD, M Clin Psych; Sarah Ingleby, BSc; Jane Eddleston, FRCA; Carl Waldmann, FRCA; Melanie Gager, RGN

Figure 2. Short-Form Health Survey (SF-36) physical function Z transformation scores (mean and SD) over time by study group. †Mean for normal population (n = 2474); ‡mean for population with severe illness (n = 256).

- A multi-centre randomised controlled trial design
- Adult intensive care patients (length of stay of at least 48 hours and mechanically ventilated for 24 hours or more)
- Graded, individualised endurance and strength training intervention was prescribed over eight weeks, with three physical trainer home visits, four follow-up phone calls, and supported by a printed exercise manual.
- The main outcome measures were blinded assessments of physical function; SF-36 physical function (PF) scale and six-minute walk test (6MWT), and health-related quality of life (SF-36) conducted at 1, 8 and 26 weeks after hospital discharge.

Elliott et al. Critical Care 2011 15:R142
### Table 4
**Mean norm-based$^a$SF-36 scores by assessment time point and group**

<table>
<thead>
<tr>
<th>SF-36 Domains</th>
<th>Week 1</th>
<th>Week 8</th>
<th>Week 26</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Physical function</td>
<td>29.1</td>
<td>27.3</td>
<td>41.0</td>
</tr>
<tr>
<td>Role function-physical</td>
<td>25.5</td>
<td>25.1</td>
<td>38.0</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>43.0</td>
<td>38.7</td>
<td>49.0</td>
</tr>
<tr>
<td>General health</td>
<td>43.5</td>
<td>41.7</td>
<td>46.0</td>
</tr>
<tr>
<td>Vitality</td>
<td>38.1</td>
<td>36.0</td>
<td>46.9</td>
</tr>
<tr>
<td>Social function</td>
<td>30.1</td>
<td>27.9</td>
<td>44.9</td>
</tr>
<tr>
<td>Role function-emotional</td>
<td>32.0</td>
<td>28.0</td>
<td>42.4</td>
</tr>
<tr>
<td>Mental health</td>
<td>43.4</td>
<td>40.1</td>
<td>48.2</td>
</tr>
<tr>
<td>PCS</td>
<td>33.0</td>
<td>31.6</td>
<td>42.7</td>
</tr>
<tr>
<td>MCS</td>
<td>40.0</td>
<td>36.6</td>
<td>47.5</td>
</tr>
</tbody>
</table>

Multi-Centre Prospective Cohort Study Evaluating 2-Year Outcomes in Survivors of Prolonged Mechanical Ventilation and their Family Caregivers

Pilot study 2007-8; Multi-centre cohort 2009- present; 500 survivors/350 caregivers
Prospective qualitative needs assessment to determine ICU survivors’ and family caregivers education and support needs corresponding to the phases of the Timing it Right Framework.
Figure 3: Total Functional Independence Measure scores at 7-days, 3, 6, and 12-months post ICU discharge
Challenges and Opportunities

- Marked heterogeneity of outcome across survivors of critical illness
- Need better characterization of caregiver outcomes and how these influence patient outcome
- Need for more international patient and caregiver longitudinal data to better inform risk stratification and potential rehabilitation needs
- Need to test rehabilitation models to determine how/if we can modify long-term functional and neuropsychological morbidity after critical illness
- Use multiple outcome measures over time to capture change
- Urgent need for translational projects to inform pathophysiology of muscle, nerve and brain injury