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Chronic Critical Illness: No Good Deed Goes Unpunished

Kathleen J. Haley, MD
Associate Physician
Department of Medicine, Division of Pulmonary and Critical Care Medicine
Brigham and Women's Hospital
Assistant Professor of Medicine
Harvard Medical School

CONTINUING MEDICAL EDUCATION
DEPARTMENT OF MEDICINE

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Conflict of Interest/Financial Disclosure

I am a co-investigator on the NIH-funded PrecISE Trial Network and the IDEA Trial. Within the last three years, the following companies have provided study drugs for the PrecISE Trial Network: GlaxoSmithKline, Laurel, Sun Pharma, Vifor, Vitaeris/CSL Behring, Vitaflo, Sanofi-Aventis/Regeneron, and Organon.

I am also a co-investigator on an industry-sponsored trial, KALOS, which uses study drugs supplied by Sanofi.

Kathleen Haley, MD

Pennsylvania State University Medical College
Medicine Residency and Pulmonary Medicine Fellowship @ NEDH
Critical Care and Research Fellowship @ BWH
Assistant Professor of Medicine @ HMS

- Clinical focus: Critical Care Medicine
- Research focus: Chronic Critical Illness and Asthma
- Member of the BWH Ethics Committee
- Director, Spaulding Cambridge Hospital Ventilator Service

Outline

What is chronic critical illness?
Prolonged vent support
Tracheostomies
ICU-acquired weakness
Neurocognitive dysfunction

Background

Designation first used in 1985

- Chronically critically ill survive initial crisis but require continued advanced support

Incidence: approximately 5 – 10% of patients needing mechanical ventilation

- Resource intense: 20 – 40% ICU bed days
  - 18% of all BWH ICU patient-days
- Long length of stay (LOS)
  - BWH (21.1 days) and LTAC (28.8 days)
- High 30 day readmission rate – nationally 40% in first year
  - 40% from SHC FY2012
- High annual payer costs
  - $20 billion/year in the US
  - 13% of healthcare expenditures

Substantial Morbidity & Mortality

Patients

- Approximately 50% 1-year mortality
  - Very stable over past 20yrs
  - Variability within patient subgroups
- About 10% at home and independent at 1-yr
- Decreased 6-minute walk c/w normal even at 5yr
- Recovery better for patients <45 yr old

Families

- >80% of families caring for patients at home quit or changed work to provide care for patient
  - Financial hardship common
- High rates of depression
  - Higher rates in families of institutionalized patients

Clinical Features

Prolonged respiratory insufficiency
Weakness
- Loss of lean muscle mass

Poor nutrition
- Occurs despite apparently adequate calorie and protein delivery
- Impaired anabolism
- Anasarca is very common

Neurocognitive dysfunction
Chronic pain
Skin breakdown
Immune dysfunction

What Is Chronic Critical Illness?

Is it just the consequence of critical illness?

Is it an ongoing process?

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Is it just the consequence of critical illness?

Is it an ongoing process?

Why Differentiate?

Ongoing process has potential for reversing

- Some evidence to support a persistent immune dysregulation
- Persistent inflammation, immunosuppression, and catabolism syndrome[1]

Possible lessons from COVID-19

- The SHC post-COVID patients had had better return of function than other cohorts
  - –Significantly higher rates of decannulation and home DC
  - –Is this the disease or patient age/functional status?

Reference:
1. R.B. Hawkins et al. Frontiers in Immunol 2018; vol. 9: article 1511

Prolonged Ventilator Dependence

Common in chronically critically ill patients

- Frequently used as the defining trait for chronic critical illness

About 50% still need ventilator after 1 year[1]

- Average 1 month for liberation from ventilator
- >2 months unsuccessful liberation attempts is poor prognostic sign
- Successful weaning portends good prognosis[2]
  - 67% alive at 1y vs 16% not liberated (53% overall)
  - 85% would have ventilation again (at 6m and 1y)

References:

1. L Rose and IM Fraser. Can Respir J 2012; vol. 19: pp 216 - 220
2. A. Jubran et al. Am J Resp Crit Care Med 2019; vol. 199: pp 1508 - 1516

Approach to Vent Liberation

Trach mask trials surprisingly effective

- A Jubran and colleagues, JAMA 2013
  - 160/500 (32%) did not require “weaning”
  - TM performed as well as PSV, but had faster liberation times (approximately 2 wks)

Sometimes, a more gradual approach is needed

Patients sometimes need overnight support long-term

- Home nocturnal vent support
- Home NIV
  - Use precise language when describing indication since insurances have strict requirements

The “Almost There” Patient

Problem:

- Patients tolerate daytime weaning attempts but develop hypercarbia on prolonged trach mask

NIV can be a useful approach[1]

- Substitute NIV for mechanical ventilation via tracheostomy tube
  - Facilitates decannulation
    - Improved post-discharge function
  - Increases possible options for discharge
    - Home discharge easier with NIV compared to home vent
    - Some facilities accept NIV but not tracheostomy patients

Ensuring success

- Low-level nocturnal support needed
- Tolerance of NIV mask and settings

Reference:
1. P. Ceriana et al Pulmonology 2019; vol. 25: pp. 328 - 333

Tracheostomies

Very old procedure
Minimal difference in “early” vs “late”
- Possible faster wean
- Slightly shorter ICU, but not hospital LOS

No difference percutaneous vs surgical[1]
Advantages over ETT
- Comfort
- ADL – talking, eating
- Partial vent use
- Vocal cord dysfunction

Same as ETT
- Tracheal injury
- Infection risk

Reference:
1. D. Hashimoto et al. NEJM 2020; vol. 383: e112 (1-5)

A Caveat

Laryngectomy patients

- Presence of tracheal stoma – but very different from tracheostomy patients
- Cannot be ventilated or intubated through upper AW
- Should always have notice at bedside regarding emergent AW procedures

Decannulation

Generally done after several days RTC trach cap[1]

- Multidisciplinary team is recommended
- Markers of probable success
  - Strong spontaneous cough
  - Minimal suction requirements

Recent multicenter study from Spain suggested alternative[2]

- 330 patients (799 patients, 661 eligible for decannulation)
- Daily airway occlusion tolerance
- Compared 24h trach cap with suction frequency <q4hr
  - Suction frequency group faster decannulation (6 vs 13)
  - Similar failure rates (2.4% suction, 5.6% control)

References:
1. R.K. Singh, S. Saran, and A.K. Baronia J Int Care 2017; vol. 5:38
2. G. Hernandez Martinez et al. NEJM; vol. 383: pp 1009 - 1017

After Decannulation

Size will be significantly smaller in 24h

- Generally skin fully healed within 1 week
  - Trachea takes much longer to fully heal
- Delays seen with steroids, poor wound healing
  - Can take several days to a couple of weeks
  - Best approach is occlusive dressing
  - Suture can promote stenosis

ICU-Acquired Weakness

Old problem

- Osler describes weakness after severe sepsis in his 1892 textbook of medicine.
- Association between peripheral neuorpathy and prolonged coma reported in 1956 (Olsen, JAMA; 1956).
- Landmark article linking status asthmaticus, steroid therapy, and weakness (MacFarlane and Rosenthal, Lancet; 1977).

Scope of the Problem

Approximately 75,000 patients annually develop ICU-AW (Fan et al., AJRCCM, 2014)

Patients with ICU-AW have 30% higher acute hospital costs (Hermans et al. AJRCCM 2014) than ICU patients without weakness

- This doesn't count costs of rehabilitation, readmission, post-rehabilitation support

Patients with ICU-AW have higher mortality compared to non-weak ICU patients

- Higher post-ICU mortality in first year: 28 vs 11%
- Possible higher in-hospital mortality (inconsistent study results)

Risk Factors

Age
Sepsis
Duration of organ failure
Mechanical Ventilation
Premorbid functional status
Female gender (inconsistent)
Medication (inconsistent)

- Aminoglycosides
- Neuromuscular blockers
- Glucocorticoids

Weakness in ICU patients - Etiologies

Primary neuromuscular disease
- Increases likelihood of critical illness
- Critical illness can unmask neuromuscular disease

New, but separate, event complicating critical illness
- New CVA, embolism due to endocarditis, spinal cord ischemia

Complication of therapy
- Meds

Metabolic derrangements
- Hypokalemia

Due to critical illness
- ICU-Acquired Weakness (ICU-AW)

ICU-Acquired Weakness

Can occur very early in course
- Generally seen after 1 wk in ICU

Common
- Clinically significant findings in up to 2/3 patients requiring mechanical ventilator for over 1 week
- Depending on study >80% of patients on mechanical ventilation have evidence

Persists
- 6 minute walk test only 70% age-predicted maximum in ARDS survivors 5yrs after acute illness (Herridge et al., NEJM 2003)

Subtypes
- Myopathy
- Neuropathy
- Combined myopathy/neuropathy

Diagnosis - Approach

Differential can be summarized by MUSCLES (Maramattom BV and Wijdicks EF, Critical Care Medicine 2006, vol. 34, pp 2835 – 2841)

- M: Meds – steroids, amiodarone, NMB, aminoglycosides, furosemide
- U: Undiagnosed primary neuromuscular disease
- S: Spinal cord problem such as ischemia
- C: Critical illness associated weakness
- L: Loss of muscle such as rhabodmyolysis
- E: Electrolytes: low K, low phos, high Mg
- S: Systemic illness: Hypothyroidism, adrenal insufficiency, porphyria

Diagnosis - Clinical

Relatively intact cognition required for assessment
Symmetric weakness, most pronounced in proximal muscle groups

- Facial and ocular muscles usually preserved
  –Facial can be affected with myopathy
- Respiratory muscles, including diaphragm, frequently affected
- Sensation frequently not affected, but can be if critical illness neuropathy
- Can be severe – some patients are quadriplegic

Determination of Weakness

Medical Research Council
University of Rochester Acute Care Evaluation
Functional Status Score for Intensive Care (FSS-ICU)
Chelsea Critical Care Physical Assessment tool
Physical Function Test ICU test – score (PFIT-s)

Diagnosis – Laboratory/Studies

Critical Illness Myopathy

- Primary myopathy
- Muscle biopsy shows loss of large fibers
- Muscle necrosis can be seen
- Can have small increases in CK
- Nerve conduction studies: decreased amplitude and increased duration of the compound muscle action potential
- EMG c/w decreased excitability

Diagnostic and Laboratory Studies (2)

Critical Illness Neuropathy

- Axonal degeneration without demyleination
  - –Differentiates from Guillain-Barre syndrome
- Nerve conduction studies show
  - –Normal conduction velocities
  - –Decreased sensory nerve action potential
- EMG c/w reinnervation
- Normal CK
- Edema can interfere with EMG and NCS

From: **Acute Skeletal Muscle Wasting in Critical Illness**

JAMA. 2013;310(15):1591-1600. doi:10.1001/jama.2013.278481

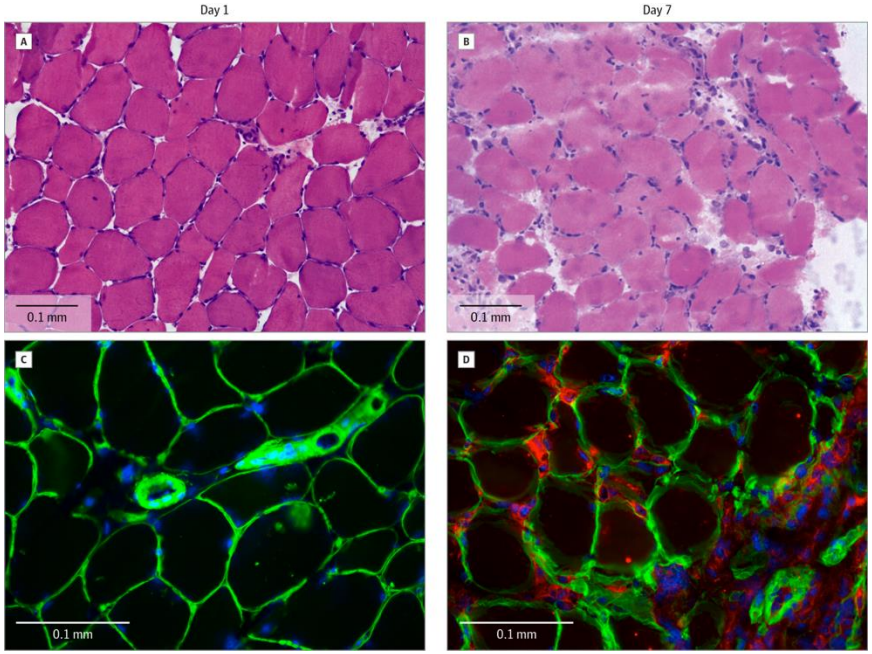

Figure Legend:

Muscle Biopsy Specimens From a Representative Patient on Day 1 and Day 7Healthy muscle is seen on day 1 (A, C) with necrosis and a cellular infiltrate on day 7 (B, D). This infiltrate was CD68 positive on immunostaining, indicating macrophage origin (red). A, B are hematoxylin and eosin stain, and C, D was immunostaining, with CD68 for red, laminin (myofiber outline) for green, and 4',6-diamidion-2-pheylidole (a nuclear marker) for blue.

Why differentiate?

Critical illness myopathy

- Occurs earlier in course

- Has a better prognosis

Mechanisms of Injury

Immobility
- Diaphragmatic wasting after 18h immobility
- Stimulates proteases to breakdown muscle
  –Ubiquitin-proteasome system

Hyperglycemia

Abnormality of fast sodium channels
- Decreases muscle excitability

Microvascular abnormality causing nerve ischemia

Catabolism

Mitochondrial dysfunction

Oxidative stress

Therapy

Preventative Strategies

- Avoid hyperglycemia
  - –Insulin may be protective, but small therapeutic index
- Early physical therapy
  - –May be an effective strategy

ICU-AW Therapy

- No specific therapy
- Continue physical therapy
- Most gains seen in first 3 months after ICU discharge

Practical Tip

Many ICU-AW patients requiring prolonged vent support may benefit from doing PT on vent

- Portable vents can be good strategy for this

Neurocognitive Dysfunction

2/3 Chronically critically ill patients at 6 months after DC from post-ICU unit had + CAM (Hope et al., Annals ATS vol 10, 2013)

- Risk factors included age, APACHE during hospitalization, poor pre-admit functional status, duration of delirium during hospitalization
- Medication use not associated

2yr after ARDS hospitalization, 32% patients had symptoms of depression (Adhikari et al., Chest vol 140, 2011)

- Decreased to 19% by 5y after hospitalization

Delirium Facts

Very common in critically ill patients
- Up to 55% of post-op patients
- Up to 80% of medical ICU patients
- Most studies 45 – 87%
- Depends on what measure is used

Associated with increased mortality
- 1-yr mortality approx 40%
- Hypoactive delirium 6-month mortality 32%

Can have either agitation or hypoactivity
- Either may benefit from therapy

Bedside scoring systems
- RASS -5 (unresponsive) to +4 (combative)
- CAM (Confusion Assessment Method)
- MMSE

Pathobiology

Endothelial dysfunction
Abnormalities in neurotramsmitter function
- ACh
- GABA
- DA

Inflammatory cytokines
- CRP
- Procalcitonin
- TNF
- IL-6, IL-2, IL-1

Genetic predisposition
- ApoE4 polymorphism – inconsistent association

Medications that can be associated with delirium

- Benzodiazepines
- Opiods
- Anticholinergics
- SSRI
- Steroids
- Metachlopropamide
- NSAIDS
- Calcineurin inhibitors
- Chemotherapy

Treatment

Prevention
- Non-pharmacologic methods effective
- No pharmacologic prophylaxis has been effective

Treatment
- Nonpharmacologic
  - –Very effective approaches
- Pharmacologic
  - –Haldol
  - –Atypical antipsychotics
    - Exact mechanism of action isn’t clear
    - Patients may have different responses to meds within class
  - –Dexmedetomidine
    - Alpha-2 receptor agonist

Question

Which of the following treatment approaches most effectively addresses critical illness-associated weakness?

1. Early weaning from mechanical ventilation
2. Daily PT/OT with initiation as soon as feasible after ICU admission
3. Early enteral nutrition with goal protein 3 gm/kg and calories 50 kcal/kg ideal body weight
4. Supplementing TF with trace minerals

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4. Supplementing TF with trace minerals

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3. MS Herridge et al. NEJM 2011 vol 364 pp1293 - 1304
4. J. Batt et al. Am J Resp Crit Care Med 2013 vol 187 pp 238 – 246
5. JE Nelson et al. AJRCCM 2010 vol 183 pp446 – 454