What Happens to our Septic Patients after Hospital Discharge?

Hallie Prescott, MD, MSc
Ohio Hospital Association
July 19, 2016
Disclosures

• I have no relevant financial conflicts of interest

• Key Funding
  – NIH/NIGMS
  – American Thoracic Society Foundation

• This talk does not necessarily represent the views of the U.S. Government or Department of Veterans Affairs
Outline

• A patient case
• Life after sepsis

In August:
• What can we do to help improve long-term outcomes
Case

49 year old female, mid-level manager at a large corporation.

PMH: HTN, mild asthma

- Presented to ED with fevers, chills, sore throat, cough
- Admitted with community-acquired pneumonia
- Treated with IV antibiotics
Situation

- ARDS
- Septic Shock

- Day #36: extubated
- Day #43: to rehab
3 Weeks of Inpatient Rehab
IQ Testing, 1

Before ICU

139
IQ Testing, cont’d

- Before ICU: 139
- Post-ICU (8 months): 106
Interview with Gordon Bernard, 2004

*Is there a residue in sepsis survivors who have had multi-organ failures or dysfunctions?*
Interview with Gordon Bernard, 2004, cont’d

Is there a residue in sepsis survivors who have had multi-organ failures or dysfunctions?

“Most people return to normal or near-normal lives even if they have had severe organ failures…

Most surviving patients come back to being normal.”
Our Patient

“I just don’t feel right…

Is this because of my sepsis?”
Symptoms

- Weight loss
- Muscle weakness
- Fatigue
- Reduced QOL
- Reduced walk distance
- Inability to return to work
Neurologic Critical Care

Six-month neuropsychological outcome of medical intensive care unit patients

James C. Jackson, Fyodor Robert P. Hart, PhD; Sharon M. Gordon, Fyodor; Ayumi Shintani, PhD; Brenda Truman, MSN, Lisa May, BSN, E. Wesley Ely, MD, MPH

Objective: To examine neuropsychological function, depression, and quality of life 6 months after discharge in patients who received mechanical ventilation in the intensive care unit.

Design: Prospective cohort study.

Setting: Tertiary care, medical and coronary intensive care unit of a university-based medical center.

Study Population: A total of 224 consecutive, mechanically ventilated patients from a medical intensive care unit were prospectively followed. At 6 months, 157 were alive, of whom 41 (26%) returned for extensive follow-up testing.

Measurement and Health Results: Neuropsychological testing and assessment of depression and quality of life were performed at 6-month follow-up. Seven of 41 patients were excluded from further analysis due to surprising cognitive impairments determined via cognitive interviews using the Modified Mini-Mental State Exam and a review of medical records. On the basis of criteria selected from normative data, we found that 11 of 34 patients (32%) were neuropsychologically impaired. Impairment was generally diffuse but occurred primarily in areas of psychomotor speed, visual and working memory, verbal fluency, and visuoconstruction. The rate of neuropsychological deficits in the study population was markedly higher than population norms for mild dementia. Scores on the Geriatric Depression Scale—Short Form were significantly more abnormal in the neuropsychologically impaired group than in the nonimpaired group at hospital discharge (p = .04) and at 6-month follow-up (p = .02), and clinically significant depression was found in 27% of impaired subjects at hospital discharge and in 36% at 6-month follow-up. No differences were observed between groups in quality of life as measured with the Short Form Health Survey-12 at discharge or 6-month follow-up.

Conclusion: Prolonged neuropsychological impairment is common among survivors of the medical intensive care unit and occurs with a greater degree of severity when compared with normative data. Future investigations are warranted to elucidate the nature of the association between critical illness, neuropsychological impairment, depression, and decreased quality of life. (Crit Care Med 2003; 31:1228–1234)

The table shows cognitive impairment at baseline and 6-month follow-up and associated neuropsychological scores. The table shows that 80% of survivors in one cohort were found to have impaired memory, attention, concentration, and decreased processing speed a year after hospital discharge (36), and in another report, nearly 25% had mild cognitive impairment even 6 years after their intensive care unit (S36) stay (138). However, there are no prospective reports documenting neuropsychological impairment in the general medical ICU population. In addition, no information is currently available on the predictive significance of depression during an ICU stay in regard to long-term neuropsychological outcomes. The data from this study of general medical patients in studies that take into account preexisting cognitive impairment suggest that long-term mental status is worse in patients with a history of depression (23-24).

We therefore undertook the current investigation to study the prevalence and type of neuropsychological impairment among medical ICU patients who had developed respiratory failure requiring mechanical ventilation.
Disability

- In national sample with baseline measurement, new and persistent disability is common after sepsis
Post-Intensive Care Syndrome

Mental Health
- Depression
- Anxiety
- PTSD

Cognitive Impairments
- Executive Function
- Mental Processing Speed
- Visuo-spatial
- Memory
- Attention

Physical Impairments
- Muscle Weakness
- Pulmonary Function

Measurements and Main Themes: Three major themes emerged from the consensus reporting: (1) raising awareness and education, (2) understanding and addressing barriers to practice, and (3) identifying research gaps and resources. Predischarge care was agreed upon as the recommended term to describe new or worsening problems in physical, cognitive, or mental health arising after a critical illness and permitting delayed acute care hospitalization. The term could be applied to either a survivor or family member.

Conclusion: Improving care for intensive care survivors and the development of appropriate practice guidelines and resources in both the inpatient and outpatient settings warrant further development to address the major themes arising from the consensus conference to improve outcomes for survivors and families.

Critical Care Med 2013. 40(4S):S2

Copyright © 2010 by the Society of Critical Care Medicine and Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

Our Patient,

“Am I going to die from this?”
More Research Needed

Evidence for a causal link between sepsis and long-term mortality: a systematic review of epidemiologic studies

Manu Shankar-Hari\textsuperscript{1,2*}, Michael Ambler\textsuperscript{1*}, Viyaasan Mahalingasivam\textsuperscript{1}, Andrew Jones\textsuperscript{1,2}, Kathryn Rowan\textsuperscript{3} and Gordon D. Rubenfeld\textsuperscript{4}

**Conclusions:** Epidemiologic criteria for a causal relationship between sepsis and post-acute mortality were not consistently observed. Additional epidemiologic studies with recent patient level data that address the pre-illness trajectory, confounding, and varying control groups are needed to estimate sepsis-attributable additional risk and modifiable risk factors to design interventional trials.
Mortality Link

Late mortality after sepsis: propensity matched cohort study

Hallie C Prescott,¹,²,³,⁴ John J Osterholzer,¹,⁴ Kenneth M Langa,¹,²,³,⁵ Derek C Angus,⁶ Theodore J Iwashyna¹,²,³,⁴,⁵,⁷

Hypothesis:
Sepsis itself is associated with excess late mortality.
Late mortality after sepsis: propensity matched cohort study

Hallie C Prescott,1, 2, 3, 4 John J Osterholzer,1, 4 Kenneth M Langa,1, 2, 3, 5 Derek C Angus,6 Theodore J Iwashyna1, 2, 3, 4, 5, 7

1. Adults not actively hospitalized
2. Non-Sepsis Infection
3. Sterile Inflammation

37,000 Older Americans Studied

Late mortality after sepsis: propensity matched cohort study

Hallie C Prescott,1, 2, 3, 4 John J Osterholzer,1, 4 Kenneth M Langa,1, 2, 3, 5 Derek C Angus,6 Theodore J Iwashyna1, 2, 3, 4, 5, 7

- NIA-funded cohort
- 1992 - ongoing
- 37,000 older Americans
- Detailed survey data
- Linked Medicare records

Study Cohort

Late mortality after sepsis: propensity matched cohort study

Hallie C Prescott,1,2,3,4 John J Osterholzer,1,4 Kenneth M Langa,1,2,3,5 Derek C Angus,6 Theodore J Iwashyna1, 2, 3, 4, 5, 7

Demographics
- Age
- Gender
- Race
- Ethnicity
- Married/partnered

Healthcare Utilization
- Hospitalization
- Sepsis Hospitalization
- Residence in Nursing Facility

Economic Status
- Total Wealth
- Government Assistance

Health Status
- Functional Limitations
- Self-Rating of Health
- Body Mass Index

Comorbidity Burden
- Charlson Index
- CHF
- Cancer
- Connective Tissue Disease
- Dementia
- Liver Disease
- Renal Disease

Hospitalization Variable

Late mortality after sepsis: propensity matched cohort study
Hallie C Prescott,1, 2, 3, 4 John J Osterholzer,1, 4 Kenneth M Langa,1, 2, 3, 5 Derek C Angus,6 Theodore J Iwashyna1, 2, 3, 4, 5, 7

- Sepsis versus Non-hospitalized

Adjusted Odds Ratio for Late* Mortality:

Absolute Increase in Late Mortality:

*Late mortality = mortality in the 31 days – 2 years post-sepsis
Late Mortality Increase

Sepsis versus Non-hospitalized

Adjusted Odds Ratio for Late* Mortality:

3.5  \( (p < 0.001) \)

Absolute Increase in Late Mortality:

22%

*Late mortality = mortality in the 31 days – 2 years post-sepsis
Sepsis vs Non-Sepsis Infection

Adjusted Odds Ratio for Late* Mortality:

1.6 \quad (p = 0.01)

Absolute Increase in Late Mortality:

10%

*Late mortality = mortality in the 31 days – 2 years post-sepsis

Sepsis versus Sterile Inflammation

Adjusted Odds Ratio for Late* Mortality:

2.3 \ (p < 0.001)

Absolute Increase in Late Mortality:

16%

*Late mortality = mortality in the 31 days – 2 years post-sepsis
Overall Factors Studied
Mortality Conclusions

Conclusions:

- More than 1 in 5 sepsis survivors with a late death not explained by pre-sepsis health status

- Amenable to intervention?
Our Patient,

“If I do survive, what will the next year look like?”
Our Patient, 4

“If I do survive, what will the next year look like?”

- Cognitive Impairment
- Physical Disability
- Mental Health Impairment
Cognitive Impairment

Before sepsis

After sepsis

Cognitive impairment
- Mild
- Moderate to severe

Patients With Cognitive Impairment, %

Second Survey Before Sepsis  Last Survey Before Sepsis  First Survey After Sepsis  Second Survey After Sepsis
Not Just Older Patients

![Box plot showing RBANS Global Cognition Score for different age groups and time points (3 Mo, 12 Mo). The age groups are ≤49 Yr, 50–64 Yr, and ≥65 Yr, with corresponding sample sizes (N=97, 147, 130, 89, 138, 98). The box plots indicate the distribution of scores across Normal, MCI, and TBI categories.]
## Not Just Sickest Patients

### TABLE 2. RISK OF DEMENTIA DID NOT VARY BASED ON SEVERITY OF INFECTION*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of Cases</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>320</td>
<td>2.24</td>
<td>1.62–3.11</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pneumonia with organ dysfunction†</td>
<td>82</td>
<td>2.06</td>
<td>0.92–4.61</td>
<td>0.07</td>
</tr>
<tr>
<td>Pneumonia without organ dysfunction</td>
<td>240</td>
<td>2.19</td>
<td>1.52–3.16</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>198‡</td>
<td>2.28</td>
<td>1.38–3.77</td>
<td>0.001</td>
</tr>
<tr>
<td>Other infections</td>
<td>1,049§</td>
<td>1.98</td>
<td>1.61–2.43</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Physical Disability

Limitations at baseline
- Severe
- Mild to moderate
- None

Before sepsis

After sepsis

Mean Number of ADL and IADL Limitations

Third Survey Before Sepsis  Second Survey Before Sepsis  Last Survey Before Sepsis  First Survey After Sepsis  Second Survey After Sepsis  Third Survey After Sepsis

New physical disability was common in general ward patients with sepsis, even in those with good baseline function.
for every 100 patients with severe sepsis:
for every 100 patients with severe sepsis:

18 patients die in the hospital
Back of Envelope, ³

for every 100 patients with severe sepsis:

18 die in days 1-90 after discharge
Back of Envelope, 4

for every 100 patients with severe sepsis:

8 patients die in days 91-365 after discharge
Back of Envelope, 5

for every 100 patients with severe sepsis:

11 have moderate-severe cognitive impairment
for every 100 patients with severe sepsis:

37 have ≥1 ADL limitation
Mental Health
Mental Health, 2

Review Article

Anxiety symptoms in survivors of critical illness: a systematic review and meta-analysis

Sina Nikayin, M.D. a,b, Anahita Rabiee, M.D. a,b, Mohamed D. Hashem, M.D. a,b, Minxuan Huang, Sc.M. a,b, O. Joseph Bienvenu, M.D., Ph.D. a,c, Alison E. Turnbull, D.V.M., M.P.H., Ph.D. a,b,d, Dale M. Needham, F.C.P.A., M.D., Ph.D. a,b,e,*

In Meta-Analysis of 22 Studies, Prevalence of Anxiety:
• 32% at 2-3 months
• 40% at 6 months
• 34% at 12-14 months
• did not differ by ICU admission diagnosis in 4 of 4 studies.
Mental Health, 3

Depressive Symptoms After Critical Illness:  
A Systematic Review and Meta-Analysis

Anahita Rabiee, MD1,2; Sina Nikayin, MD1,2; Mohamed D. Hashem, MD1,2; Minxuan Huang, ScM1,2; Victor D. Dinglas, MPH1,2; O. Joseph Bienvenu, MD, PhD1,3; Alison E. Turnbull, DVM, MPH, PhD1,2,4; Dale M. Needham, FCPA, MD, PhD1,2,5

In Meta-Analysis of 22 Studies, Prevalence of Depression:

• 29% at 2-3 months
• 34% at 6 months
• 29% at 12-14 months
• Did not differ by ICU admission diagnosis in 5 of 6 studies.
Posttraumatic Stress Disorder in Critical Illness Survivors: A Metaanalysis*

Ann M. Parker, MD\(^1,2\); Thiti Sricharoenchai, MD\(^3\); Sandeep Raparla, MD\(^4\); Kyle W. Schneck, BA\(^5\); O. Joseph Bienvenu, MD, PhD\(^3,6\); Dale M. Needham, FCA, MD, PhD\(^1,2,7\)

In Meta-Analysis of 22 Studies, Prevalence of PTSD:

- 44% at 1-6 months
- 34% at 7-12 months.
- did not differ by ICU admission diagnosis in 7 of 7 studies.
Is Critical Illness a Marker or Mediator of Mental Health Impairments?

Depressive symptoms

New Psychoactive prescriptions

Wunsch, et al. JAMA. 2014
Survivors

Increased 1-Year Healthcare Use in Survivors of Severe Sepsis

Hallie C. Prescott¹, Kenneth M. Langa¹,²,³, Vincent Liu⁴, Gabriel J. Escobar⁴, and Theodore J. Iwashyna¹,²,³

¹Department of Medicine, University of Michigan, Ann Arbor, Michigan; ²VA Center for Clinical Management Research, HSR&D Center for Excellence, Ann Arbor, Michigan; ³Institute for Social Research, Ann Arbor, Michigan; and ⁴Kaiser Permanente Division of Research, Oakland, California
Post-Acute Care Increase

**Conclusion:** Sepsis is followed by significant increases in healthcare use.

- Median: 10% of days alive in healthcare facility.
- Most is increase is post-acute care use.
# Most Common Index Diagnosis & Most Costly Cause of Readmission

## Table 1. High-volume conditions ranked by rate of readmission for all causes within 30 days, 2013

<table>
<thead>
<tr>
<th>Rank</th>
<th>Principal diagnosis for index hospital stay</th>
<th>Number of index admissions</th>
<th>Number of all-cause readmissions</th>
<th>Aggregate cost of readmissions, $ millions</th>
<th>Rate of all-cause readmission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total index admissions for any cause</td>
<td>28,124,869</td>
<td>3,900,556</td>
<td>52,398</td>
<td>13.9</td>
</tr>
<tr>
<td>1</td>
<td>Congestive heart failure, non-hypertensive</td>
<td>782,079</td>
<td>183,534</td>
<td>2,728</td>
<td>23.5</td>
</tr>
<tr>
<td>2</td>
<td>Schizophrenia and other psychotic disorders</td>
<td>366,256</td>
<td>83,245</td>
<td>772</td>
<td>22.7</td>
</tr>
<tr>
<td>3</td>
<td>Respiratory failure, insufficiency, arrest (adult)</td>
<td>290,892</td>
<td>62,684</td>
<td>961</td>
<td>21.5</td>
</tr>
<tr>
<td>4</td>
<td>Diabetes mellitus with complications</td>
<td>486,886</td>
<td>99,108</td>
<td>1,204</td>
<td>20.4</td>
</tr>
<tr>
<td>5</td>
<td>Acute renal failure</td>
<td>431,452</td>
<td>87,537</td>
<td>1,190</td>
<td>20.3</td>
</tr>
<tr>
<td>6</td>
<td>Chronic obstructive pulmonary disease and bronchiectasis</td>
<td>570,077</td>
<td>114,067</td>
<td>1,384</td>
<td>20.0</td>
</tr>
<tr>
<td>7</td>
<td>Complication of device, implant or graft</td>
<td>581,289</td>
<td>111,838</td>
<td>1,973</td>
<td>19.2</td>
</tr>
<tr>
<td>8</td>
<td>Alcohol-related disorders</td>
<td>261,072</td>
<td>50,081</td>
<td>366</td>
<td>19.2</td>
</tr>
<tr>
<td>9</td>
<td>Septicemia</td>
<td>1,011,496</td>
<td>191,156</td>
<td>3,154</td>
<td>18.9</td>
</tr>
<tr>
<td>10</td>
<td>Fluid and electrolyte disorders</td>
<td>358,640</td>
<td>65,704</td>
<td>839</td>
<td>18.3</td>
</tr>
</tbody>
</table>
Our Patient,

“What might I be hospitalized for? Will my sepsis come back?”
Risk of Recurrence: After Surviving Sepsis
A Matched Cohort Study

Hsiu-Nien Shen, MD, PhD; Chin-Li Lu, MS; Hsi-Hsing Yang, MD

Cumulative incidence of sepsis and death in sepsis survivors (left) and matched controls (right)

Event-free
Severe sepsis
Death

35%
5%

How Common is Recurrent Sepsis? New or Relapsed Infection?

Hypothesis:

Recurrent sepsis is common and most commonly due to new infections.
How Common is Recurrent Sepsis?

1,588 UMHS Hospitalizations
Principal Dx: Sepsis & Discharged Alive
(May 15 2013 - May 14 2015)
How Common is Recurrent Sepsis?

1,588 UMHS Hospitalizations
Principal Dx: Sepsis & Discharged Alive
(May 15 2013 - May 14 2015)

472 (29.7%)
Readmissions within 90 days
How Common is Recurrent Sepsis?

1,588 UMHS Hospitalizations
Principal Dx: Sepsis & Discharged Alive
(May 15 2013 - May 14 2015)

472 (29.7%) Readmissions within 90 days

137 (29.1%) readmissions for sepsis
335 (70.9%) readmissions for other diagnoses
### New or Relapsed Infection?

<table>
<thead>
<tr>
<th>Organism Concordance</th>
<th>Site Concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Different Site</td>
<td>Same Site</td>
</tr>
<tr>
<td>Different Organism</td>
<td></td>
</tr>
<tr>
<td>Same Organism</td>
<td></td>
</tr>
<tr>
<td>Culture Negative</td>
<td></td>
</tr>
</tbody>
</table>
New or Relapsed Infection?

<table>
<thead>
<tr>
<th>Organism Concordance</th>
<th>Site Concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Different Site</td>
</tr>
<tr>
<td>Different Organism</td>
<td>14 (10%)</td>
</tr>
<tr>
<td>Same Organism</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Culture Negative</td>
<td>17 (12%)</td>
</tr>
</tbody>
</table>

- 64 (47%) are new infections (new site and/or new organism).
### New or Relapsed Infection?

<table>
<thead>
<tr>
<th>Organism Concordance</th>
<th>Site Concordance</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Different Site</td>
<td>Same Site</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Different Organism</td>
<td>14 (10%)</td>
<td>30 (22%)</td>
<td>3 (2%)</td>
<td></td>
</tr>
<tr>
<td>Same Organism</td>
<td>0 (0%)</td>
<td>26 (19%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture Negative</td>
<td>17 (12%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- 64 (47%) are new infections (new site and/or new organism).
- 26 (19%) are relapsed infections (same site and same organism).
### New or Relapsed Infection?

<table>
<thead>
<tr>
<th>Organism Concordance</th>
<th>Site Concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Different Site</td>
</tr>
<tr>
<td>Different Organism</td>
<td>14 (10%)</td>
</tr>
<tr>
<td>Same Organism</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Culture Negative</td>
<td>17 (12%)</td>
</tr>
</tbody>
</table>

- 64 (47%) are new infections (new site and/or new organism).
- 26 (19%) are relapsed infections (same site and same organism).
- 47 (34%) are unclear (culture negative or unknown site).
Our Patient,  

“What other types of medical set-backs am I at risk for?”
Q1: What are the most common readmission diagnoses after sepsis?

Q2: To what extent are readmissions after sepsis potentially preventable?

Hypothesis: A limited number of diagnoses will explain the bulk of post-sepsis readmissions.
Potentially Preventable Readmissions

• “can potentially be avoided if ambulatory care is provided in a timely and effective manner”¹

• “[diagnoses] for which timely and effective outpatient care can help reduce the risks of hospitalization by either preventing the onset of an illness or condition, controlling an acute episodic illness or condition, or managing a chronic disease or condition”²

Potentially Preventable Readmissions, cont’d

1. Pneumonia
2. Dehydration
3. UTI
4. CHF
5. Asthma
6. COPD exacerbation
7. Uncontrolled diabetes
8. Diabetes w/ complication
9. LE amputation in diabetics
10. Perforated appendix
11. Angina without procedure
12. HTN
13. Sepsis
14. Skin/soft tissue infection
15. Acute renal failure
16. Aspiration pneumonitis
# Post-Sepsis Readmission Diagnoses

## Table. Most Frequent Readmission Diagnoses After Hospitalization for Severe Sepsis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Severe Sepsis (n = 2617)</th>
<th>No. of Survivors</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td></td>
<td>167</td>
<td>6.4 (5.4-7.3)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td></td>
<td>144</td>
<td>5.5 (4.6-6.4)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
<td>92</td>
<td>3.5 (2.8-4.2)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td></td>
<td>87</td>
<td>3.3 (2.6-4.0)</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td></td>
<td>74</td>
<td>2.8 (2.2-3.5)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td></td>
<td>65</td>
<td>2.5 (1.9-3.1)</td>
</tr>
<tr>
<td>Complication of device, implant,</td>
<td></td>
<td>52</td>
<td>2.0 (1.5-2.5)</td>
</tr>
<tr>
<td>or graft</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td></td>
<td>49</td>
<td>1.9 (1.4-2.4)</td>
</tr>
<tr>
<td>Aspiration pneumonitis</td>
<td></td>
<td>47</td>
<td>1.8 (1.3-2.3)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td></td>
<td>44</td>
<td>1.7 (1.2-2.2)</td>
</tr>
</tbody>
</table>
Preventable Readmissions Among Survivors

Figure. Total and Potentially Preventable 90-Day Readmissions Among Survivors of Severe Sepsis and Matched Hospitalizations for Acute Medical Conditions.
Readmission Conclusions

Readmissions are common. Many potentially preventable.

A small number of conditions account for the bulk of the problem:

<table>
<thead>
<tr>
<th>Table, Most Frequent Readmission Diagnoses After Hospitalization for Severe Sepsis</th>
<th>Table, Most Frequent Readmission Diagnoses After Hospitalization for Other Acute Medical Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severe Sepsis (n = 2017)</strong></td>
<td><strong>Readmission</strong></td>
</tr>
<tr>
<td><strong>No. of Diagnoses</strong></td>
<td><strong>% (95% CI)</strong></td>
</tr>
<tr>
<td>Septic shock</td>
<td>167</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>544</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>32</td>
</tr>
<tr>
<td>Infection</td>
<td>87</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>38</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>251</td>
</tr>
<tr>
<td>Complication of device, implant, or graft</td>
<td>187</td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td>59</td>
</tr>
<tr>
<td>Aspiration pneumonitis</td>
<td>47</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>47</td>
</tr>
</tbody>
</table>

*Abbreviation: COPD, chronic obstructive pulmonary disease.*

1 Listed are most frequent to least frequent. The most frequent readmission diagnoses accounted for 53.3% of all readmissions within 90 days after hospitalization for severe sepsis.

Conclusions

Readmissions are common. Many potentially preventable.

A small number of conditions account for the bulk of the problem:

- Infection (particularly recurrent sepsis)
- CHF exacerbation
- COPD exacerbation
- Acute renal failure
- Aspiration pneumonia

We measured the rate and 95% confidence interval of 90-day readmissions. Using the Healthcare Cost and Utilization Project's Clinical Classification Software, we determined the most common readmission diagnoses. To gauge what proportion of rehospitalizations may be potentially preventable, we measured ambulatory care sensitive conditions (AGSs), which are diagnoses for which effective outpatient care may reduce hospitalization rate. We used AGSs identified by the Agency for Healthcare Research and Quality and an expanded definition also including sepsis, skin or soft tissue infection, acute renal failure, and aspiration pneumonitis, all of which could plausibly be prevented or treated early to avoid rehospitalization.

We compared readmission rates using McNemar's tests with significance at \( P < 0.001 \). Odds ratios for multiple comparisons. The University of Michigan Institutional Review Board approved this study. Patients provided oral informed consent at enrollment and for Medicare linkage.

Results: We identified 4494 hospitalizations for severe sepsis, of which 2645 (59%) survived to discharge. Of those, 2577 (92.1%) were matched to hospitalizations for other acute medical conditions. The cohort's mean age was 70.5 years (SD, 15.9 years). 2226 were female, and they had some presenting functional disability (median Charlson index, 4; IQR, 3–4). Median hospitalization length was 7 days (IQR, 4–11 days). Age, sex, co-

Table. Most Frequent Readmission Diagnoses After Hospitalization for Severe Sepsis

<table>
<thead>
<tr>
<th>Diagnosis*</th>
<th>Severe Sepsis (n = 2437)</th>
<th>Matched Hospitalizations for Other Acute Medical Conditions (n = 2437)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tachy...</td>
<td>167</td>
<td>4.4 (4.2–4.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Sepsis</td>
<td>144</td>
<td>5.5 (4.5–6.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>92</td>
<td>3.3 (2.8–3.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>87</td>
<td>3.1 (2.6–3.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>74</td>
<td>2.8 (2.2–3.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>65</td>
<td>2.5 (1.9–3.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Complication of device, implant, or graft</td>
<td>52</td>
<td>2.2 (1.6–2.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td>49</td>
<td>1.8 (1.4–2.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Aspiration pneumonitis</td>
<td>47</td>
<td>1.8 (1.3–2.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>44</td>
<td>1.7 (1.2–2.2)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Abbreviations: COPD, chronic obstructive pulmonary disease
* Listed in order of most frequent to least frequent. The most frequent readmission diagnoses accounted for 75% of all readmissions within 90 days after hospitalization for severe sepsis.
* Principal diagnosis was heart failure, pneumonia, cardiac arrhythmias, COPD exacerbation, acute renal failure, or acute coronary disease.

Conclusions

Readmissions are common. Many potentially preventable.

A small number of conditions account for the bulk of the problem:

- Infection (particularly recurrent sepsis)
- CHF exacerbation
- COPD exacerbation
- Acute renal failure
- Aspiration pneumonia

PREVENTION

Letters

RESEARCH LETTER

Readmissions are common. Many potentially preventable. A small number of conditions account for the bulk of the problem: Infection (particularly recurrent sepsis), CHF exacerbation, COPD exacerbation, acute renal failure, and aspiration pneumonia, all of which could plausibly be prevented or treated early to avoid readmission.

We compared readmission rates using McNemar's test with significance at p < 0.05. Given the randomization, the expected proportions of readmissions were estimated using the McNemar's test.

Prevention

We measured the rate and 95% confidence interval of 90-day readmissions using the Healthcare Cost and Utilization Project's National Inpatient Sample. We identified readmissions with severe sepsis and severe infection using a validated approach that requires International Classification of Diseases, Ninth Revision, Clinical Modification code for both infection and acute organ dysfunction. We matched readmissions with severe sepsis to hospitalizations for 12 common acute medical conditions (Table 1). By age, sex, and discharge diagnosis burden (Charlson Comorbidity Index), prehospitalization functional disability, limitations of activities and instrumental activities of daily living, and length of hospitalization using a coarsened exact matching.

Table. Most Frequent Readmission Diagnoses After Hospitalization for Severe Sepsis

<table>
<thead>
<tr>
<th>Diagnosis*</th>
<th>No. of Patients</th>
<th>% (95% CI)</th>
<th>No. of Patients</th>
<th>% (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>1437</td>
<td>4.4 (3.4-5.3)</td>
<td>75</td>
<td>2.6 (2.2-3.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>144</td>
<td>5.5 (4.6-6.4)</td>
<td>204</td>
<td>7.8 (6.9-8.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>122</td>
<td>5.3 (4.8-5.8)</td>
<td>85</td>
<td>3.2 (2.6-3.8)</td>
<td>0.12</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>87</td>
<td>3.3 (2.6-4.0)</td>
<td>39</td>
<td>1.2 (0.7-1.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>74</td>
<td>2.1 (1.2-3.1)</td>
<td>110</td>
<td>4.4 (3.6-5.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>65</td>
<td>2.3 (1.9-2.9)</td>
<td>51</td>
<td>1.5 (1.0-2.0)</td>
<td>0.007</td>
</tr>
<tr>
<td>Complication of device, implant, or graft</td>
<td>52</td>
<td>5.9 (5.2-6.5)</td>
<td>30</td>
<td>1.2 (0.7-1.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>CVA ischemic</td>
<td>49</td>
<td>1.4 (1.2-2.0)</td>
<td>47</td>
<td>1.6 (1.2-2.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>CVA hemorrhagic</td>
<td>47</td>
<td>1.8 (1.3-2.2)</td>
<td>47</td>
<td>1.7 (1.3-2.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>46</td>
<td>1.7 (1.2-2.2)</td>
<td>47</td>
<td>1.8 (1.3-2.2)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* From most frequent to least frequent.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Diagnosis</th>
<th>Chronic obstructive pulmonary disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td></td>
<td>Infection (particularly recurrent sepsis)</td>
</tr>
<tr>
<td>CHF exacerbation</td>
<td></td>
<td>CHF exacerbation</td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td></td>
<td>COPD exacerbation</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td></td>
<td>Acute renal failure</td>
</tr>
<tr>
<td>Aspiration pneumonia</td>
<td></td>
<td>Aspiration pneumonia</td>
</tr>
</tbody>
</table>

*Principal diagnosis includes (1) severe sepsis, pneumonia, and (2) sepsis and other infections, complications of surgery and medical care, and sepsis with complications. Calculated using McNemar's test.
Different Readmission Diagnoses?

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Severe Sepsis (n = 2617)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Survivors</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>167</td>
<td>6.4 (5.4-7.3)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>144</td>
<td>5.5 (4.6-6.4)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>92</td>
<td>3.5 (2.8-4.2)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>87</td>
<td>3.3 (2.6-4.0)</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>74</td>
<td>2.8 (2.2-3.5)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>65</td>
<td>2.5 (1.9-3.1)</td>
</tr>
<tr>
<td>Complication of device, implant, or graft</td>
<td>52</td>
<td>2.0 (1.5-2.5)</td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td>49</td>
<td>1.9 (1.4-2.4)</td>
</tr>
<tr>
<td>Aspiration pneumonitis</td>
<td>47</td>
<td>1.8 (1.3-2.3)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>44</td>
<td>1.7 (1.2-2.2)</td>
</tr>
</tbody>
</table>
## Different Readmission Diagnoses?

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Severe Sepsis (n = 2617)</th>
<th>Matched Hospitalizations for Other Acute Medical Conditions (n = 2617)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Survivors</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>167</td>
<td>6.4 (5.4-7.3)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>144</td>
<td>5.5 (4.6-6.4)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>92</td>
<td>3.5 (2.8-4.2)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>87</td>
<td>3.3 (2.6-4.0)</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>74</td>
<td>2.8 (2.2-3.5)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>65</td>
<td>2.5 (1.9-3.1)</td>
</tr>
<tr>
<td>Complication of device, implant, or graft</td>
<td>52</td>
<td>2.0 (1.5-2.5)</td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td>49</td>
<td>1.9 (1.4-2.4)</td>
</tr>
<tr>
<td>Aspiration pneumonitis</td>
<td>47</td>
<td>1.8 (1.3-2.3)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>44</td>
<td>1.7 (1.2-2.2)</td>
</tr>
</tbody>
</table>

### Different Readmission Diagnoses? Yes

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Severe Sepsis (n = 2617)</th>
<th>Matched Hospitalizations for Other Acute Medical Conditions (n = 2617)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Survivors</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>167</td>
<td>6.4 (5.4-7.3)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>144</td>
<td>5.5 (4.6-6.4)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>92</td>
<td>3.5 (2.8-4.2)</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>87</td>
<td>3.3 (2.6-4.0)</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>74</td>
<td>2.8 (2.2-3.5)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>65</td>
<td>2.5 (1.9-3.1)</td>
</tr>
<tr>
<td>Complication of device, implant, or graft</td>
<td>52</td>
<td>2.0 (1.5-2.5)</td>
</tr>
<tr>
<td>COPD exacerbation</td>
<td>49</td>
<td>1.9 (1.4-2.4)</td>
</tr>
<tr>
<td>Aspiration pneumonitis</td>
<td>47</td>
<td>1.8 (1.3-2.3)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>44</td>
<td>1.7 (1.2-2.2)</td>
</tr>
</tbody>
</table>
Cardiovascular Risks

Long-Term Mortality and Major Adverse Cardiovascular Events in Sepsis Survivors
A Nationwide Population-based Study

Shuo-Ming Ou\textsuperscript{1,2,3*}, Hsi Chu\textsuperscript{2,4*}, Pei-Wen Chao\textsuperscript{5,6}, Yi-Jung Lee\textsuperscript{2,7}, Shu-Chen Kuo\textsuperscript{2,8,9}, Tzeng-Ji Chen\textsuperscript{10}, Ching-Min Tseng\textsuperscript{2,11}, Chia-Jen Shih\textsuperscript{2,12,13‡}, and Yung-Tai Chen\textsuperscript{2,14‡}

- 1.4-fold increase over population controls
- 1.3-fold increase over hospitalized controls

Risk of Cardiovascular Events in Survivors of Severe Sepsis

Sachin Yende\textsuperscript{1,2}, Walter Linde-Zwirble\textsuperscript{3}, Florian Mayr\textsuperscript{4}, Lisa A. Weissfeld\textsuperscript{5}, Steven Reis\textsuperscript{6}, and Derek C. Angus\textsuperscript{1,2}

- 1.9-fold increase over population controls
- 1.1-fold increase over hospitalization controls
- Equivalent to ICU controls
Our Patient, 7
Our Patient,

- Multiple readmissions for infection
- Returned to work, but never 100%
- Retired early
- Participates in peer-to-peer support group
- Mentor to new sepsis survivors
IQ Testing,

- Before ICU: 139
- Post-ICU (8 months): 106
- Post-ICU (3.5 years): 120
Conclusions

Life after sepsis is scary.

- New morbidity
- Increased risk for death
- Discharge to post-acute care
- Frequent re-hospitalization
Conclusions, cont’d

• Sepsis survivors face heightened risk for death. 1 in 5 sepsis survivors with a late death due to lasting effects of sepsis.
• Over half of patients acquire new physical disability
• Cognitive decline common; ~15% with mod-severe impairment
• Anxiety, depression, PTSD each affect ~1/3 of survivors
• Healthcare use and readmission are common. Often due to the same “usual suspects”—that we know how to treat: infection, CHF, AKI, COPD, aspiration.
• Risk for Infection, AKI, aspiration, and ?CV events are increased in sepsis survivors.
In August....

We will discuss strategies to:
• reduce re-admissions
• improve long-term outcomes in sepsis survivors
Questions

@hallieprescott  hprescot@med.umich.edu