Letters

RESEARCH LETTER

Readmission Diagnoses After Hospitalization for Severe Sepsis and Other Acute Medical Conditions

Patients are frequently rehospitalized within 90 days after having severe sepsis.1 Little is known, however, about the reasons for readmission and whether they can be reduced. We sought to determine the most common readmission diagnoses after hospitalization for severe sepsis, the extent to which readmissions may be potentially preventable by posthospitalization ambulatory care, and whether the pattern of readmission diagnoses differs compared with that of other acute medical conditions.

Methods | We studied participants in the nationally representative US Health and Retirement Study,2 a multistage probability sample of households with adults aged 50 years or older, that is linked to Medicare claims (1998-2010). We identified hospitalizations with severe sepsis using a validated approach that requires International Classification of Diseases, Ninth Revision, Clinical Modification codes for both infection and acute organ dysfunction.3,4 We matched hospitalizations for severe sepsis to hospitalizations for 15 common acute medical conditions (Table) 1:1 by age, sex, postdischarge comorbidity burden (Charlson Comorbidity Index), prehospitalization functional disability (limitations of activities and instrumental activities of daily living), and length of hospitalization using coarsened exact matching.5

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 (ACSCs), which are diagnoses for which effective outpatient care may reduce hospitalization rates.6 We used ACSCs identified by the Agency for Healthcare Research and Quality,6 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 χ² tests with significance at P < .001 (2-sided) given 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 3494 hospitalizations for severe sepsis, of which 2843 (81.4%) survived to discharge. Of these, 2617 (92.1%) were matched to hospitalizations for other acute medical conditions. The cohort’s mean age was 78.9 years (SD, 8.9 years), 57.3% were female, and they had some preexisting functional disability (median, 1 limitation; interquartile range [IQR], 0-4 limitations). At discharge, patients had moderate comorbidity burden (median Charlson Index, 6; IQR, 3-8). Median hospitalization length was 7 days (IQR, 4-11 days). Age, sex, co-

<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>

Abbreviation: COPD, chronic obstructive pulmonary disease.

* Listed from most frequent to least frequent. The most frequent readmission diagnoses accounted for 51.5% of all readmissions within 90 days after hospitalization for severe sepsis.

* Principal diagnoses were heart failure, pneumonia, cardiac arrhythmia, COPD exacerbation, acute myocardial infarction, acute cerebrovascular disease, complication of a device, implant, or graft, chest pain, fluid or electrolyte disorder, urinary tract infection, hip fracture, gastrointestinal hemorrhage, complication of surgical or medical care, syncope, and diabetes with complication.

* Calculated using McNemar χ² tests.
morbidity burden, functional status, and hospitalization length did not differ between severe sepsis and matched acute medical conditions ($P > .05$ for each).

There were 1115 severe sepsis survivors (42.6%) rehospitalized within 90 days. The 10 most common readmission diagnoses following severe sepsis included several ACSCs (eg, heart failure, pneumonia, chronic obstructive pulmonary disease exacerbation, and urinary tract infection; Table). Collectively, ACSCs accounted for 22.2% (95% CI, 20.3%-24.5%) of 90-day readmissions. Using the expanded definition, ACSCs accounted for 41.6% (95% CI, 39.1%-44.1%) of 90-day readmissions after severe sepsis.

Patterns of readmission differed between survivors of severe sepsis and matched acute medical conditions (Table and Figure). Rates of readmission for sepsis and renal failure were higher and accounted for a greater proportion of the total readmissions after severe sepsis. Readmissions for a primary diagnosis of infection (sepsis, pneumonia, urinary tract, and skin or soft tissue infection) occurred in 11.9% (95% CI, 10.6%-13.1%) of severe sepsis survivors compared with 8.0% (95% CI, 7.0%-9.1%) of matched acute medical conditions ($P < .001$). Readmissions for ACSCs were more common after severe sepsis (21.6%; 95% CI, 20.0%-23.2%) vs matched acute conditions (19.1%; 95% CI, 17.7%-20.7%) ($P = .02$) and accounted for a greater proportion of all 90-day readmissions (41.6% [95% CI, 39.2%-44.1%] vs 37.1% [95% CI, 34.8%-39.5%], respectively; $P < .009$).

**Discussion** | Readmissions within 90 days after hospitalization for severe sepsis were common, and 42% occurred for diagnoses that could potentially be prevented or treated early to avoid hospitalization compared with 37% after matched acute medical conditions.

A limitation of the present study is that we inferred the potential preventability of rehospitalizations by measuring readmissions for ACSCs. Whether these diagnoses represent preventable admissions, especially after sepsis, is not clear. Nonetheless, the high prevalence and concentration of specific diagnoses during the early postdischarge period suggest that further study is warranted of the feasibility and potential benefit of postdischarge interventions tailored to patients’ personalized risk for a limited number of common conditions.

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Left Atrial Appendage Closure for Atrial Fibrillation

To the Editor The study by Dr Reddy and colleagues1 reported the 3.8-year follow-up of the PROTECT AF trial that randomized patients with atrial fibrillation (AF) to receive percutaneous left atrial appendage (LAA) closure with the WATCHMAN device or warfarin. We had a number of questions and concerns about the study.

First, patients randomized to receive warfarin were older and more often had cardiovascular comorbidities and permanent AF than the patients randomized to receive the LAA closure. In Table 1 in the article, P values were missing, so it is unclear if these differences were statistically significant and may in part explain the higher mortality in the warfarin group.

Second, why do the patient-years for the different end points in Table 2 differ?

Third, after LAA closure, warfarin was discontinued for 345 of 370 patients at the 12-month transesophageal echocardiographic evaluation. What was the reason for continuation of warfarin in the remaining 25 patients, and what were their outcomes?

Fourth, according to Table 3, 53 patients in the LAA closure group died. How many of these patients underwent autopsy, and what were the pathoanatomic findings of the left atrium and LAA? Were there any thrombi or leaks between the LAA wall and the device, and was the device completely endothelialized in all cases?

Fifth, the LAA is known to play a hemodynamic role in pressure and volume overload of the left ventricle and is a site for release of atrial natriuretic peptides.2 Thus, it would be of interest to know whether patients in the LAA closure group developed new or worsening heart failure more frequently than patients in the warfarin group.

Sixth, only 3 of the 12 authors reported no potential conflict of interest with the manufacturer of the closure device. Furthermore, the senior author has contracted rights to receive royalties from the license of the device. The sponsor of the study was the manufacturer of the device and was responsible for data collection, analysis, interpretation, and drafting of the manuscript. Thus, a bias in favor of the device cannot be excluded.3 Reanalysis of the data by independent scientists is needed.

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In Reply Drs Stöllberger and Schneider raise a number of questions about our article. First, with regard to baseline patient characteristics, as stated in the Results section, there were no significant differences in principal baseline characteristics between the groups.

Second, the number of patient-years in Table 2 varies between end points because cumulative patient-years for each row were determined by the time to first event. In the case of the primary end point, the first event could be any component of the composite, whereas the individual rows would only include patients experiencing the specific outcome listed, thus allowing for small variations in the denominator.

Third, the reason for warfarin continuation in 25 of 370 patients at 12 months was because of a residual shunt in 10 patients and physician discretion for 15 patients.

Fourth, there was no systematic autopsy evaluation of patients who died during the course of the trial, so there are no pathology data for these patients. However, we have previously published an analysis1 of patients receiving the WATCHMAN device in PROTECT AF comparing those with no peridevice leak (68% of the cohort) and those with at least some small degree of leak (32% of cohort). In that analysis,2 we found no significant difference in the primary efficacy outcome between groups if the leak was small.

Fifth, the protocol did not include the systematic collection of left ventricular ejection fraction or heart failure status during follow-up, so we cannot comment on the possibility of differential development or worsening of heart failure. However, both cardiovascular mortality and all-cause mortality (both of which are known to track with severe congestive heart failure) occurred more frequently in the warfarin group. As shown in Table 3 in the article, there was no difference in heart failure–related deaths between groups.

Sixth, Stöllberger and Schneider note that the manufacturer of the WATCHMAN device was responsible for the data collection and compilation. However, a data and safety monitoring board that was independent of both the company and the steering committee of the trial reviewed all of the data. Furthermore, as part of the US regulatory process, the study data were monitored in compliance with US Food and Drug Administration requirements for investigational device exemption protocols, and all data were independently reviewed and analyzed by the agency.

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