The Relationship Between Hospital Spending and Mortality in Patients With Sepsis

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Background: Sepsis is common, highly morbid, and costly, yet little is known about differences in the care or outcomes of patients with sepsis across hospitals. We sought to characterize variations in hospital spending and mortality rates and to determine whether higher levels of spending are associated with better hospital survival.

Methods: We conducted a cross-sectional study of hospitals that treated at least 100 adult patients with sepsis between 2004 and 2006. We developed multivariable models for expected patient mortality and costs and calculated standardized mortality and cost ratios for each hospital. We defined clinically significant variation as observed outcomes that differed from expected outcomes by at least 10%. We examined the association between hospital-level spending and mortality rate using a model that adjusted for hospital characteristics.

Results: Among 166,931 patients with sepsis at 309 hospitals, we observed wide variations in hospital-level mortality and cost. Of 61 hospitals (19%) at the median expected mortality rate, observed mortality ranged from 9% to 32%. More than a third (34%) of hospitals exceeded expected costs by at least 10%, with a median average excess cost of $5207. We found lower-than-expected costs and mortality rates at 22 hospitals (7%). An adjusted model did not show a significant association between hospital spending and mortality.

Conclusions: Hospital spending and adjusted mortality rates for patients with sepsis vary substantially, but higher hospital expenditures are not associated with better survival. Efforts to enhance the value of sepsis care could be modeled on hospitals that achieve lower-than-expected mortality and costs.

Arch Intern Med. 2011;171(4):292-299

ORIGINAL INVESTIGATION

THREE DECADES OF HEALTH services research has documented striking variations in the care and outcomes of patients each year in the United States and the world. Sepsis affects approximately 750,000 patients each year in the United States and is in many ways a model condition for examining the relationship between hospital spending and patient outcomes and for identifying potential opportunities to improve the value of hospital care. First, the mortality rate of patients with sepsis approaches 20% and the annual costs attributable to sepsis care have been estimated at $17 billion, similar in magnitude to the costs of ischemic heart disease. Second, because sepsis is a condition that often involves multiple organ systems, the care of patients with sepsis is complex and frequently requires the coordination of multiple disciplines throughout the hospital. Thus, one of the potential drivers of the costs of care may be the quality of care coordination and the overall efficiency of the hospital environment. And, unlike cancer or heart failure, sepsis is an acute rather than chronic disease, so it lends itself to studies of acute care hospitalizations. Given the impera-
effective to improve quality of care while reducing the growth of health care spending, we sought to characterize variations in hospital costs and hospital mortality rates of patients with sepsis and to examine whether higher spending is associated with better outcomes.

**METHODS**

**SETTING AND SUBJECTS**

We conducted a cross-sectional study using data from 309 hospitals that cared for at least 100 patients with sepsis and participated in the Perspective database (Premier Healthcare Informatics, Charlotte, North Carolina) between June 1, 2004, and June 30, 2006. Perspective has been previously described. In brief, it is a voluntary, fee-supported database created to measure quality and health care utilization. In addition to the elements found in hospital claims derived from the uniform billing 04 (UB-04) form, Perspective contains an itemized, date-stamped log of all items and services charged to the patient or insurer, including medications, laboratory tests, and diagnostic and therapeutic services. Approximately 75% of hospitals that participate in Perspective submit information on actual hospital costs, taken from internal cost accounting systems, whereas the remaining hospitals provide cost estimates based on Medicare cost to charge ratios. Participating hospitals are drawn from all regions of the United States, and, similar to the composition of acute care hospitals nationwide, they are predominantly small to mid-sized nonteaching facilities and serve a largely urban population. In 2003, 5.5 million hospital discharges, or approximately 15% of all US hospitalizations, were included in the database.

Patients were included in the analysis if they were 18 years or older, had a principal or secondary diagnosis of sepsis as defined by Martin et al, underwent blood culture, and received antibiotics within the first 2 days of hospitalization. Diagnostic information was assessed using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM). We restricted the analysis to patients in whom treatment for sepsis was initiated within the first 2 days of hospitalization because we sought to focus our investigation on the care of patients who present with sepsis rather than those who develop sepsis later during the hospitalization. We defined initial treatment as treatment administered during the first 2 days of hospitalization (rather than just the first day) because in administrative data sets the duration of the first hospital day includes partial days that can vary in length. Surviving patients who received less than 3 consecutive days of antibiotics were excluded to ensure that we did not include cases of suspected sepsis that were not confirmed. We also excluded patients who were transferred from or to another acute care facility because we could not accurately determine the onset or subsequent course of their illness. Permission to conduct the study was obtained from the institutional review board at Baystate Medical Center, Springfield, Massachusetts.

**HOSPITAL AND PATIENT INFORMATION**

For each hospital included in the study, we recorded bed size, teaching status, geographic region, and whether it served an urban or rural population. We additionally obtained information on local wage index, disproportionate share of low-income patients, and ratio of resident physicians to beds as defined by the Centers for Medicare and Medicaid Services. For each patient, we recorded age, sex, marital status, insurance status, race, and ethnicity (as recorded by admission or triage staff of participating hospitals using hospital-defined options). Using software provided by the Healthcare Costs and Utilization Project of the Agency for Healthcare Research and Quality, we recorded the presence of 30 comorbid conditions; in addition, we used diagnosis codes to assess the source (lung, abdomen, urinary tract, blood, or other) and type of infection (gram positive, gram negative, mixed aerobic, or fungal). We categorized patients as medical or surgical, and if surgical, according to the nature of the operation. To characterize presenting severity of illness, we noted initial admission to the intensive care unit (ICU), treatment with mechanical ventilation, and use of vasopressors during the first 2 hospital days.

**STATISTICAL ANALYSIS**

We calculated patient and hospital-level summary statistics using frequencies for categorical data and medians and interquartile ranges for continuous variables. We constructed a multilevel (hierarchical) mixed-effects logistic regression model to predict mortality at the patient level while accounting for the random effects of patients being treated within the same hospital. We included patient characteristics and comorbidities in the patient-level mortality prediction model as well as admission to the ICU and use of mechanical ventilation and vasopressors on day 1 or 2. We calculated a predicted mortality for each patient (eTable 1; http://www.archintermed.com) and then defined the expected mortality rate for each hospital as the mean patient-level model-predicted mortality. We calculated the standardized mortality ratio as the observed vs expected hospital mortality and derived 95% confidence intervals for each using the method described by Rapoport et al. We predicted total patient-level costs using a multilevel (hierarchical) mixed-effects linear regression model with a logarithmic link of costs owing to its highly skewed distribution (eTable 2). Predicted costs were then transformed into their original scale using a smearing technique. The model included patient characteristics, comorbidities, and the use of intensive monitoring, mechanical ventilation, and vasopressors on days 1 and 2. We defined the expected costs for each hospital as the mean of patient-level model-predicted costs and derived the mean residual costs at the hospital level as the difference between the hospital-level observed and model-predicted costs, transformed to a standardized normal distribution. We used a 1-sample t test to identify hospitals with mean residual costs significantly different from zero.

We defined “clinically significant” differences in cost and mortality as both meeting statistical significance and showing outcomes that differed from expected by at least 10%. We also examined the relationship between observed costs and severity-adjusted mortality rate using a hospital-level regression model. In this model, adjusted hospital mortality rate was the dependent variable and predictor variables included mean observed cost per case, bed size, geographic region, resident to bed ratio, disproportionate share of low-income patients, rates of transfer in and out, urban location, and local wage index.

Finally, to further examine the relationship between spending and outcome, we divided hospitals into quintiles of mean cost per case and compared adjusted mortality rate across quintiles and by size and teaching status. We used a 1-way analysis of variance weighted for number of patients per hospital to determine if there was a significant difference in mortality across cost quintiles. Within spending quintiles, we calculated the relative contribution of service categories (including room and board, diagnostic imaging, respiratory therapy, and pharmacy costs) to determine whether the percentage of spending on service categories varied by quintile. We also examined whether length of stay varied by spending quintile. All analyses were done using STATA 10.1 (StataCorp, College Station, Tex).
The 309 hospitals included in the analysis contributed a total of 166,931 patients during the study period, with values ranging from 103 to 1932 patients per hospital. Approximately 80% of hospitals operated more than 200 beds (Table 1). Two-thirds of hospitals (67%) were not engaged in house staff training. The majority of hospitals (84%) were located in urban areas, and approximately one-half (49%) were in the southern United States. The median age of patients was 70 years; approximately one-half (49%) were in the southern United States. The median unadjusted hospital mean cost per case was $18,256, and 15% were placed on mechanical ventilation. The mortality model (eTable 1) showed good discrimination as evidenced by an area under the receiver operating characteristic curve of 0.78. The median expected mortality rate was 19.4%, with an interquartile range (IQR) of $14,213-$23,851. Overall, 33,192 patients (20%) died in the hospital. The average, median (IQR) hospital-level mortality rate was 19.4%, with an IQR of 16.3% to 23.0%.

The mortality model (eTable 1) showed good discrimination as evidenced by an area under the receiver operating characteristic curve of 0.78. The median expected mortality rate for all hospitals was 19.2%. Among the 61 hospitals with expected mortality between 18.5% and 19.5%, observed mortality ranged from 9.2% to 32.3% (Figure 1A). Overall, 66 hospitals (21%) had a clinically and statistically significantly higher-than-expected mortality rate, with 20 hospitals between 10% and 25% above expected mortality rate and 46 hospitals with observed mortality exceeding predicted mortality by more than 25%. The median average expected (fixed effects only) cost per case at the hospital level was $18,659;
Table 2. Characteristics, Treatments, and Outcomes of Patients with Sepsis at 309 US Hospitals (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall Across Patients (n=168,931)</th>
<th>Across Hospitals (n=309)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary, primary or secondary</td>
<td>63,648 (38.1)</td>
<td>37.2 [33.0-42.8]</td>
</tr>
<tr>
<td>Lung, primary or secondary</td>
<td>52,753 (31.6)</td>
<td>31.4 [27.7-36.0]</td>
</tr>
<tr>
<td>Abdominal, primary or secondary</td>
<td>23,728 (14.2)</td>
<td>13.7 [10.3-16.3]</td>
</tr>
<tr>
<td>Other (eg, skin, bone/unknown)</td>
<td>43,208 (25.9)</td>
<td>25.0 [22.0-30.0]</td>
</tr>
<tr>
<td>Infection type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram positive</td>
<td>29,152 (17.5)</td>
<td>17.4 [13.9-21.3]</td>
</tr>
<tr>
<td>Gram negative</td>
<td>28,622 (16.8)</td>
<td>16.3 [13.5-19.5]</td>
</tr>
<tr>
<td>Other (fungal, viral, anaerobic, mixed)</td>
<td>2491 (1.5)</td>
<td>1.4 [0.9-2.0]</td>
</tr>
<tr>
<td>Unknown</td>
<td>107,226 (64.2)</td>
<td>64.8 [58.2-70.2]</td>
</tr>
<tr>
<td>Medical (vs surgical)</td>
<td>139,139 (83.4)</td>
<td>84.1 [80.9-87.5]</td>
</tr>
<tr>
<td>Surgical type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General or GI</td>
<td>10,433 (6.3)</td>
<td>6.1 [4.8-7.5]</td>
</tr>
<tr>
<td>Cardiac or vascular</td>
<td>2661 (1.6)</td>
<td>1.0 [0.4-2.0]</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>4439 (2.7)</td>
<td>2.6 [1.7-3.3]</td>
</tr>
<tr>
<td>Other</td>
<td>5527 (3.3)</td>
<td>3.1 [2.1-4.1]</td>
</tr>
<tr>
<td>Treatments, by day 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU care at least 1 d</td>
<td>59,871 (35.9)</td>
<td>36.4 [29.9-41.1]</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>24,936 (14.9)</td>
<td>13.7 [10.1-17.7]</td>
</tr>
<tr>
<td>Vasopressors</td>
<td>36,965 (22.1)</td>
<td>21.6 [17.2-25.4]</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOS, d</td>
<td>8 [5-14]</td>
<td>11.0 [9.6-12.5]</td>
</tr>
<tr>
<td>Patient costs, US$</td>
<td>11,413</td>
<td>18,256</td>
</tr>
<tr>
<td>(range)</td>
<td>[56316-22,488]</td>
<td>[14,213-23,851]</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>33,192 (19.9)</td>
<td>19.4 [16.3-23.0]</td>
</tr>
</tbody>
</table>

Abbreviations: GI, gastrointestinal; ICU, intensive care unit; LOS, length of stay.

Data are given as number (percentage) of patients or median [IQR] value.

Data are given as median percentage [IQR] unless otherwise specified in “Variable” column.

of the 42 hospitals whose expected costs were within $500 of this amount, actual mean costs per case ranged from $12,271 to $37,095 (Figure 1B). More than a third (34%) of hospitals exceeded expected costs by at least 10%, with a median average excess cost per case of $5,207. When examining costs and mortality concurrently, 22 hospitals (7%) had both significantly lower-than-expected costs and lower-than-expected mortality rates, and 30 hospitals (10%) had both higher-than-expected costs and mortality rates (Figure 2). In an adjusted model that included cost and hospital-level characteristics (bed size, region of the country, share of low-income patients, wage index, ratio of residents to beds, and transfer rates), there was no significant association between hospital spending and mortality (eTable 3).

We divided hospitals into quintiles based on mean cost per patient, with the lowest spending hospitals in quintile 1 and the highest spending hospitals in quintile 5. Using an analysis of variance weighted for the number of patients per hospital, we determined that the differences by quintile were significant (P < .001), though when the highest-spending quintile was removed, the differences between groups was nonsignificant (P = .57). This pattern persisted when stratified by size and teaching status (Figure 3). We further divided spending quintiles into the various categories of services provided to patients (eg, room and board, respiratory care, laboratory, pharmacy, diagnostic imaging, etc.) and found that the proportional contributions of each service line were similar across quintiles (Figure 4). Room and board (which includes nursing care) represented the largest proportion, approximately 50% including both ICU and non-ICU room and board, of hospital costs. Other sizable contributors, such as laboratory costs, diagnostic imaging, and pharmacy, were also proportional across quintiles. We found similar, proportional results when examining fixed vs variable spending. Because mean length of stay increased as spending quintile increased (quintile 1, 8.6 days; quintile 2, 9.9 days; quintile 3, 11.1 days; quintile 4, 11.8 days; and quintile 5, 14.0 days), we compared cost per day between spending quintiles to determine whether the increased spending was due solely to the longer lengths of stay or was the result of higher use as well. We found that in addition to longer lengths of stay, hospitals in the higher spending quintiles also spent more per day (P < .001) (Figure 5).
In a large nationwide sample of hospitals, we observed substantial variation in risk-adjusted cost and mortality rates among hospitals that cared for patients with sepsis, yet found little correlation between overall levels of spending and hospital survival, implying that, on average, additional expenditures at high-cost hospitals do not translate into better short-term clinical outcomes. As a consequence of these investigations, we also identified a subset of institutions that had both significantly lower-than-expected mortality rates and lower-than-expected costs. These findings highlight potential opportunities to improve the value of sepsis care. For example, the 63,833 study patients treated at the 105 hospitals with higher-than-expected mean costs represent a potential $332 million in excess hospital spending (using the median of $5207 above expected costs).

Studies conducted by the Dartmouth Atlas and others have generally found little or no relationship between spending and outcomes at the regional level and have suggested that high-intensity regions have poorer outcomes. However, hospital-level variations in the costs and outcomes of patients with sepsis or other acute conditions have received little attention. A previous study of 1028 septic patients at 8 academic medical centers reported that mortality ranged from 20% to 50% and found that after adjustment for age, sex, comorbidity, organ dysfunction, and discharge diagnosis related group, the odds of death at the highest mortality hospital were 4 times that of the hospital with the lowest mortality. Knaus et al examined variations in mortality across 42 ICUs in the United States and found that top-performing ICUs had 10 fewer unexplained deaths per 100 patients than the poorest performing hospitals; however, the study included all ICU patients, regardless of diagnosis, and did not assess the relationship between cost and outcome.

Previous studies have estimated the costs of sepsis care regionally and nationally but have not examined variation in costs of care for sepsis among hospitals.

A recent study by Jha et al found no association between average cost per Medicare case and 30-day risk-adjusted hospital mortality rate for Medicare beneficiaries treated for myocardial infarction, congestive heart failure, and pneumonia. Our finding that hospital spending is unrelated to risk-adjusted mortality rate for sepsis extends that finding to another high-impact condition. Our method of risk adjustment, which incorporated data elements not available within standard administrative data sources, increases our confidence that the observation is real and not the result of residual confounding.

Our detailed data set also allowed us to conduct exploratory analyses into potential sources of variation in spending. We observed that spending by category of service increased proportionally across spending quintiles: higher spending hospitals did not spend proportionately more on any specific service, such as pharmacy or diagnostic imaging. Furthermore, while longer length of stay explained some of the difference across quintiles, the highest spending hospitals also had the highest costs per day. While we cannot determine from these data whether this finding is the result of higher acquisition or production costs on all (or the majority of) services at high-cost hospitals or the result of greater intensity of care, an analysis of fixed and variable costs suggested that higher fixed costs did not explain spending patterns.

The identification of a subset of hospitals that consistently achieve better-than-expected mortality rates at lower-than-expected costs is perhaps the most important finding of our study. While such results highlight potential opportunities to improve the value of care, they do not offer a specific prescription for change. Future work should more closely examine system factors that contribute to high-value care. Previous studies of regional variation suggest that high-quality, low-cost health systems integrate inpatient and outpatient care effectively (eg, The Mayo Clinic). In a similar way, hospitals that are better able to standardize and coordinate the care of patients with sepsis may perform fewer procedures and diagnostic tests, mandate use of the most cost-effective therapies, and minimize the time patients spend in the ICU, resulting in lower costs without adversely affecting patient outcomes. Indeed, several recent studies examining the use of individual strategies that coordinate care for sepsis, such as sepsis bundles, protocols for mechanical ventilation and ICU procedures, and interventions to integrate ICU team members, have shown reductions in both mortality and costs. Qualitative methods, such as those described by Bradley et al, may be a useful approach for identifying quality improvement and care coordination strategies used by low-mortality, low-cost hospitals in sepsis care.

Strengths of this study are its large sample of hospitals and patients, far exceeding what has been previously reported. In addition, we developed robust models to assess mortality and cost that incorporate clinically detailed information about patients at the time of hospital admission. We included patients treated both in and
outside of the ICU setting, thereby overcoming the issue of differing selection criteria for ICU admission across hospitals. We also examined the relationship between cost and outcome in several different ways. We calculated expected vs observed values for mortality and cost, then examined a fully adjusted model, and finally examined the relationship between spending and adjusted mortality stratified by teaching status.

Our study also has a number of limitations. First, we used claims data from a group of hospitals that voluntarily submit data to Premier Healthcare Informatics for the purposes of quality improvement. Claims data are subject to biases that might occur as a result of variation in documenting and coding across hospitals, and findings in hospitals that participate in Perspective may not be generalizable to hospitals nationwide. Second, we used ICD-9-CM codes, blood cultures, and treatment with antibiotics to identify patients with sepsis. While this is likely to have increased the likelihood that the patients included in our study actually had sepsis, we recognize that some patients with sepsis may not routinely undergo blood
cultur ence. Third, our mortality and costs models used treat ments provided to pa tients early during the admis sion, rather than direct physiologic measurements, as indi cators of patient severity. Nevertheless, these vari ables, including the use of vasopressors and mechanical ventilation, were strongly associated with mortality, and other mortality prediction models rely on a similar frame work. It is possible that hospitals with higher spend ing achieve better outcomes that were not measured in this study, such as improved quality of life, functional status, or higher patient satisfaction. However, previous work on regional-level costs and outcomes has not found a relationship between higher costs and patient prefer ences or patient satisfaction.9 We examined in-hospital rather than 90-day mortality, and hospitals with differ ing rates of discharge to hospice or nursing care could have affected our results in unpredictable ways. How ever, the percentage of patients discharged to hospice was exceedingly small, and previous work has considered in- hospital mortality to be an effective aggregate measure of structure and process for high-mortality condi tions.10-12 We excluded transferred patients, and al though we adjusted for rates of transfer in our model, our findings may not be generalizable to patients who underwent transfer during their hospitalization. Al though we had information on actual costs for 75% of hospitals, we used cost to charge ratios for 25% of the hospitals. Finally, we were not able to account for vari ability of care within hospitals. Hospitals that use a greater number of invasive interventions for all patients may harm lower-acuity patients while simultaneously benefiting higher-acuity patients, blurring the beneficial impact of higher spending for higher-acuity patients. However, this scenario is unlikely in a real-world setting because the most common invasive interventions for severe sepsis (ie, mechanical ventilation, vasopressors) are generally not administered to patients who are not in shock and respiratory failure because the risk associated with these inter ventions is very high.

The costs and outcomes of patients with sepsis vary substantially across hospitals in the United States. How ever, higher hospital spending is not associated with bet ter survival rates. Future efforts to enhance the value of sepsis care should be guided by knowledge of the organ izational characteristics and practices of high-per form ing hospitals.

Accepted for Publication: July 20, 2010.

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Author Contributions: Drs Lagu and Lindauer had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Lagu, Rothberg, Nathanson, Steingrub, and Lindauer. Acquisition of data: Lagu and Lindauer. Analysis and interpretation of data: Lagu, Rothberg, Nathanson, Pekow, Steingrub, and Lindauer. Drafting of the manuscript: Lagu. Critical revision of the manuscript for important intellectual content: Lagu, Rothberg, Nathanson, Pekow, Steingrub, and Lindauer. Statistical analysis: Lagu, Nathanson, Pekow, and Lindauer. Obtained funding: Steingrub and Lindauer. Administrative, technical, and material support: Rothberg and Lindauer.

Financial Disclosure: Dr Steingrub has received research grant support and participates in the lecture bureau of Eli Lilly & Company. Dr Nathanson, through his company OptiStatim LLC, was paid by the investigators with funding from the Department of Medicine at Bay state Medical Center to assist in conducting the statistical analyses in this study.

Funding/Support: The study was conducted with funding from the Division of Critical Care and the Center for Quality of Care Research at Baystate Medical Center. Premier Healthcare Informatics, Charlotte, North Carolina, provided the data used to conduct this study. Dr Rothberg is the recipient of a clinical scientist development award from the Doris Duke Charitable Foundation.

Role of the Sponsor: The funding agency had no role in the study’s design, conduct, analysis, or interpretation of data or in the preparation, review, or approval of the manuscript.

Online-Only Material: eTables 1, 2, and 3 are available at http://www.archinternmed.com.

Additional Contributions: Chris Craver, MA, Senior Research Associate of Premier Healthcare Informatics, assisted in obtaining the data used in this study. Mr Craver did not receive compensation for his effort. Nicholas Hannon and Long-Chau Van helped in formatting the tables and reference sections, and Jill Ayruni helped with manuscript proofreading.

REFERENCES