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Community-, Healthcare- and Hospital-Acquired Severe Sepsis Hospitalizations in the University HealthSystem Consortium

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Abstract

Objectives—Severe sepsis poses a major burden on the U.S. healthcare system. Previous epidemiologic studies have not differentiated community-acquired severe sepsis from healthcare-associated severe sepsis or hospital-acquired severe sepsis hospitalizations. We sought to compare and contrast community-acquired severe sepsis, healthcare-associated severe sepsis, and hospital-acquired severe sepsis hospitalizations in a national hospital sample.

Setting—United States

Interventions—None

Measurements & Main Results—Prevalence of community-acquired severe sepsis, healthcare-associated severe sepsis, and hospital-acquired severe sepsis, adjusted hospital mortality, length of hospitalization, length of stay in an ICU, and hospital costs. Among 3,355,753 hospital discharges, there were 307,491 with severe sepsis, including 193,081 (62.8%) community-acquired severe sepsis, 79,581 (25.9%) healthcare-associated severe sepsis, and 34,829 (11.3%) hospital-acquired severe sepsis. Hospital-acquired severe sepsis and healthcare-associated severe sepsis exhibited higher in-hospital mortality than community-acquired severe sepsis (hospital-acquired [19.2%] vs healthcare-associated [12.8%] vs community-acquired [8.6%]). Hospital-acquired severe sepsis had greater resource utilization than both healthcare-associated severe sepsis and community-acquired severe sepsis, with higher median length of hospital stay (hospital acquired [17 d] vs healthcare associated [7 d] vs community-acquired [6 d]), median length of ICU stay (hospital-acquired [8 d] vs healthcare-associated [3 d] vs

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community-acquired [3 d]), and median hospital costs (hospital-acquired [\$38,369] vs healthcare-associated [\$8,796] vs community-acquired [\$7,024]).

Conclusions—In this series, severe sepsis hospitalizations included CA-SS (62.8%), HCA-SS (25.9%) and HA-SS (11.3%) cases. HA-SS was associated with both higher mortality and resource utilization than CA-SS and HCA-SS.

Keywords

Sepsis; Severe Sepsis; Epidemiology; Hospital-acquired; Healthcare-Associated; Community-acquired

Introduction

Severe sepsis, the syndrome of microbial infection complicated by systemic inflammation and organ dysfunction, is associated with over 750,000 hospital hospitalizations, 572,000 Emergency Department (ED) visits and 200,000 deaths annually in the United States (US). [1-5] Sepsis is the single most expensive disease process in US hospitalizations, accounting for over \$20 billion expenditures annually and 5.2% of national hospital expenditures.[6] Severe sepsis care is complex, potentially requiring aggressive fluid resuscitation, early antibiotics, infective source control, vasopressors and blood products.[7]

Numerous studies have described the epidemiology of severe sepsis in the US through the use of hospital discharge data. [1, 7-15] These studies have largely followed the strategy of Angus, et al., identifying the presence of severe sepsis using combinations of hospital discharge diagnoses for serious infections and organ dysfunction.[4] However, a this approach combines all severe sepsis into a single category without distinguishing clinically important subgroups. For example, the characteristics, etiology, hospital course, outcomes and optimal management strategies may differ between severe sepsis presenting on hospital admission (“community acquired” severe sepsis – CA-SS), those with prior healthcare exposures (“healthcare-associated severe sepsis - HCA-SS) or cases developing at a later points of hospitalization (“hospital-acquired” severe sepsis – HA-SS). Information regarding the patient source and discharge diagnoses present on hospital admission could help to distinguish these severe sepsis phenotypes.

The University HealthSystem Consortium (UHC) is a national collaborative of hospitals affiliated with many of the nation's leading academic medical centers.[16] The objective of this study was to compare and contrast hospitalizations for CA-, HCA- and HA-SS in the UHC.

Methods

Design

We analyzed hospital discharge data from The University HealthSystem Consortium (UHC) in a retrospective, observational study.[16] The Institutional Review Board of The University of Alabama at Birmingham approved this study.

Data Source

The UHC is a collaborative group of 300 academic hospitals and associated community hospital affiliates spanning 42 states. The goal of the consortium is to foster collaboration with hopes of improving clinical outcomes and implement more cost-effective healthcare. To facilitate quality improvement efforts, the UHC maintains a Clinical Database/Resource Manager (CDB/RM) containing administrative data for all hospital discharges from contributing members in the consortium. For this analysis, the dataset encompassed information from the 213 hospitals that contribute to the CDB/RM.

The CDB/RM's core elements include patient demographics, *International Classification of Diseases, 9th Revision* (ICD-9) diagnosis codes, procedures performed and patient outcomes. The CDB/RM records up to 99 unique ICD-9 discharge codes for each hospitalization. Additional variables include hospital costs as well as a proprietary mortality risk predictor. This CDB/RM dataset has been previously used for epidemiological studies of sepsis.[3, 11, 17, 18]

Selection of Population

We included all hospital discharges from January 1 – December 31, 2012. We excluded all patients that were under the age of 18 at the time of hospitalization, incarcerated, pregnant, admitted for a psychiatric condition, under the care of a hospice organization or transferred from an outside facility.

We defined severe sepsis using the methodology of Angus, et al., identifying hospitalizations with the presence of ICD-9 discharge diagnoses for both a serious infection as well as organ dysfunction (Appendix 1, Supplemental Digital Content 1, <http://links.lww.com/CCM/B354>).[2, 4, 5]

Outcomes

The primary outcomes of this study were hospital mortality, length of hospitalization, length of intensive care unit (ICU) stay and cost of hospitalization. Trained coders at each hospital assigned discharge diagnoses for each hospitalization using medical record review. A unique feature of the UHC database is the indication of discharge diagnoses that were present on hospital admission. Present on hospitalization diagnoses encompassed conditions that were present at the time the patient was placed in inpatient status and diagnoses that were present in outpatient encounters, in the ED, during an observational stay or during outpatient surgery.[16]

We categorized severe sepsis hospitalizations by whether or not an infection was present on admission. Discharges that had no infection present on admission were categorized as HA-SS. Hospitalizations with an infection present on admission were subdivided based on the whether or not there were risk factors for HCA-SS. Patients that were admitted from an inpatient nursing facility or were receiving home health care, had been discharged from the same facility within the past 30 days or were on hemodialysis prior to admission were categorized as HCA-SS; patients without these exposures were categorized as CA-SS.

Characteristics of Patients, Hospital Course and Outcomes

Patient demographics included age, sex, and race. We determined the infection types and organ dysfunctions associated with each hospitalization.[2, 4, 5, 13] (Appendix 1, Supplemental Digital Content 1, <http://links.lww.com/CCM/B354>) Using established classification codes for identifying surgical cohorts, we categorized hospitalizations as surgical if a discharge code for a major surgical procedure was documented for that hospitalization. (Appendix 2, Supplemental Digital Content 1, <http://links.lww.com/CCM/B354>) [19] We categorized all other discharges as medical.

We determined expected mortality using the UHC mortality prediction models. UHC uses logistic regression to generate expected mortality by Medicare Severity Diagnosis-Related Groups (DRGs) having the same reason for care, collapsing those without chronic/comorbid conditions, with chronic/comorbid conditions, and with major chronic/comorbid conditions. Predictor variables included but were not limited to age, sex, race, chronic/comorbid conditions, other conditions present on admission and admission point of origin.[16]

Outcomes assessed in the analysis included hospital mortality, length of hospitalization, length of ICU stay and total cost of hospitalization. Hospitals reported total costs for each case as the sum of all line-item charges for a given hospitalization multiplied by the institution's cost-to-charge ratio.

Statistical Analysis

We compared the patient and hospitalization characteristics of CA-SS, HCA-SS and HA-SS hospitalizations using bivariate logistic regression. To compare mortality between CA-, HCA and HA-SS, we fit a mixed-effects logistic regression model with hospital-specific random intercepts, specifying hospital mortality as the outcome and type of severe sepsis as the exposure, adjusting for UHC expected mortality. We also assessed the association between hospitalization type (medical vs. surgical) and mortality stratified by SS type.

We performed all analyses using Stata v.13.1 (Stata, Inc. College Station, Texas).

Results

Of 4,639,442 total hospital discharges during the study period, we excluded 1,283,689 hospitalizations for patients who were <18 years old, incarcerated, under the care of hospice, hospitalized for a psychiatric condition, pregnant or transferred from another facility. (Figure 1) Of the remaining 3,355,753 hospital discharges, 307,491 (9.2%) involved severe sepsis.

Among the severe sepsis discharges, 193,081 (62.8%) involved CA-SS, 79,581 (25.9%) involved HCA-SS and 34,829 (11.3%) involved HA-SS. While HA-SS patients were slightly younger than HCA-SS and CA-SS (HA: 63.3y; HCA: 64.6; CA: 65.0y), they exhibited fairly similar sex and racial distribution. (Table 1) HA-SS hospitalizations were much more likely to involve surgical conditions (HA: 36.3%; HCA: 11.0%; CA: 12.5%). Bloodstream, pulmonary and genitourinary infections were the most common types of infections in all groups. The most common organ dysfunctions in all groups were

cardiovascular, pulmonary and renal. Cardiovascular and pulmonary dysfunction was more common in the HA-SS group.

Median costs of hospitalization were higher for HA-SS than for CA-SS and HCA-SS hospitalizations (HA: \$38,369; CA: \$7,024; HCA: \$8,796). (Table 2) Among hospitals in this series, hospital costs for CA-SS, HCA-SS and HA-SS totaled \$2.86, \$1.44 and \$2.14 billion, respectively. Median length of hospitalization was longer in HA-SS compared to CA-SS and HCA-SS (HA: 17 days; CA: 6 days; HCA: 7 days). Among discharges involving ICU care, ICU stays were longer in the HA-SS group (HA: 8 days; HCA: 3 days; CA: 3 days). Hospital mortality was highest in HA-SS (HA: 19.2%; HCA: 12.8%; CA: 8.6%) with an even more pronounced difference when adjusting for expected mortality (Adjusted OR HA vs. CA 3.22, 95% CI: 3.11-3.34; Adjusted OR HCA vs. CA 1.46, 95% CI: 1.41-1.50).

HCA-SS patients were identified based on the presence of previous hemodialysis (23.5%), readmission within 30 days from the same hospital (73.5%) and admission from an inpatient nursing facility or receiving home health (14.7%). Patients on hemodialysis had a higher cost of hospitalization, length of stay, ICU length of stay and mortality when compared to nursing home patients and readmissions. (Table 3)

When stratified by medical versus surgical hospitalizations, surgical hospitalizations uniformly had higher cost of hospitalization, length of stay and ICU length of stay. (Table 4) Surgical patients had higher hospital mortality in CA and HCA-SS, while medical patients that went on to develop HA-SS had higher mortality than surgical patients (adjusted OR 1.60, 95% CI: 1.50-1.70). Medical patients that developed HA-SS were the subgroup with highest mortality (22.8%, 95% CI: 22.1-23.6%).

Discussion

Prior epidemiologic studies highlight the prominence and public health importance of severe sepsis hospitalizations in the US. In this study of over 200 hospitals affiliated with the UHC, we affirmed that the cohort of severe sepsis hospitalizations is comprised of three distinct subsets: 1) patients presenting to the hospital with “community-acquired” severe sepsis 2) patients presenting to the hospital with severe sepsis that have “healthcare-associated” risk factors and 3) those developing “hospital-acquired” sepsis during the course of hospital care. Although comprising only 11.3% of SS hospitalizations, HA-SS posed significant healthcare burdens, accounting for 20% of severe sepsis deaths and over 34.9% of all severe sepsis-related hospital costs in the consortium. While previous studies have characterized CA-SS and HA-SS, these efforts used smaller series and focused on individual infection groups (e.g. ventilator-associated pneumonia, catheter-associated urinary tract infection, etc.). [20, 21] In addition to providing national perspectives of these important SS subgroups, our study offers epidemiologic and healthcare utilization data to deepen our understanding of the national burden of SS.

The combination of serious infection and organ dysfunction discharge diagnosis codes has been applied in a range of studies characterizing severe sepsis epidemiology.[2, 4, 12] None of these studies have distinguished CA- from HA- and HCA-SS. Our contrasting study was

able to distinguish the three entities using healthcare-associated risk factors and “present on admission” flags recorded for each coded discharge diagnosis allowing for risk adjustment and comparative analyses of conditions that occur subsequent to entering the hospital. This distinction has important clinical implications because CA-SS, HCA-SS and HA-SS likely have differing clinical presentations as well as ideal methods for detection and strategies for management.[4] For example, CA-SS typically results from community acquired infections and pathogens, while we demonstrated that most HA-SS has a higher rate of having been exposed to surgical procedures. While our study illustrates one potential strategy for distinguishing SS phenotypes using administrative data, other approaches are possible.

The clinical presentation of sepsis is often cryptic, requiring the assimilation of clinical context with physical and laboratory findings. Sepsis care guidelines are geared toward early recognition of CA-SS presenting to the ED. However, different strategies may be needed for detecting HA-SS developing in the course of hospitalization. For example, in contrast to the ED, inpatient ward settings often lack the resources necessary to frequently monitor vital signs or laboratory test results. Comprehensive sepsis treatment bundles are designed for rapid deployment in the ED, but timely implementation of these aggressive therapies in the inpatient setting often requires transfer to an intensive care unit. While not indicating the best care strategies, our observations affirm that the HA-SS group comprises a large number of patients with a disproportionately large healthcare burden, supporting development of customized approaches for this subset.

Hospitals seeking to improve sepsis outcomes have developed different strategies for improving sepsis recognition and care in both the ED and inpatient settings. For example, the UHC endorses sepsis screening in EDs through the use of electronic medical record-based tools as well as inpatient screening through daily nursing protocols evaluating for new signs of infection.[16] The use of lactic acid assays in the ED and procalcitonin and c-reactive protein assays in the intensive care unit have been studied as screening modalities to aid in sepsis recognition.[22-24] Management strategies in the ED have focused on time-based bundles created to help direct resuscitation, while inpatient sepsis management strategies have focused on appropriate antibiotic stewardships, lung-protective ventilation strategies and the use of hospital rapid response teams.[9, 16, 25]

HA-SS consists of a much higher proportion of surgical patients than CA-SS. This may be due to the exposure of the patient to surgery, anesthesia, the operating room or procedures performed in surgical patients (intubation, arterial lines, etc.) that may be more common in the operating room than on medical floors. Given the increased rate of HA-SS in surgical patients, further consideration should be given to both early recognition of SS in hospitalized surgical patients as well as the prevention of HA-SS through sterile technique in the operating room, peri-operative antibiotics and researching novel SS prevention techniques.

In this study, while mortality was higher for surgical than medical CA-SS and HCA-SS; mortality was higher for medical than surgical HA-SS. There are several potential explanations for these findings. Medical and surgical HA-SS may have different pathophysiologic processes; for example, medical HA-SS may be more likely due to

nosocomial microbes while surgical HA-SS may be exhibiting a SIRS-like response to anesthesia or surgery. Another possibility is the presence of disparate sepsis recognition and care between medical and surgical inpatient units. For example, surgical units may be accustomed to more vigilant screening for infectious etiologies as well as providing aggressive intravenous fluid therapy in post-operative patients. Additional study must identify the reasons for these outcome differences, although this study does highlight the significant mortality associated with medical patients that develop SS during their hospitalization.

Limitations

While widely used in studies of sepsis epidemiology, the Angus, et al. criteria have known limitations, including potential classification bias from coding practices and errors, and the unclear clinical link between documented infections and organ dysfunctions. The patients in the study sampled from academic medical centers and their affiliates may not be representative of community hospitals in the US. While we differentiated CA- from HA- and HCA-SS using discharge diagnoses and present-on-admission flags, errors or discrepancies in coding may have altered the relative numbers of each severe sepsis type, particularly if infections were present but not recognized on admission. The UHC database is only able to identify patients that are readmitted to the same facility, therefore some patients that were initially admitted at a different facility may be inappropriately categorized as CA-SS when they truly represent HCA-SS.

While HA-SS exhibited higher mortality than CA-SS and HCA-SS, and while there were differences in surgical and medical SS mortality, the etiology for these differences remains unknown. Further, it is unclear what proportion of surgical discharges represent primary surgical conditions (e.g. acute cholecystitis) compared to those who develop infection as a result of a surgery (e.g. elective orthopedic surgery leading to sepsis).

Conclusion

In this series of discharges from hospitals of the UHC, severe sepsis hospitalizations included CA-SS (62.8%), HCA-SS (25.9%) and HA-SS (11.3%) cases. HA-SS was associated with higher mortality and resource utilization compared to CA- and HCA-SS. HCA-SS discharges were much more similar to CA-SS than to HA-SS. These findings have important implications for the organization and delivery of severe sepsis care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Overview of study population.

Table 1
Characteristics of Severe Sepsis Hospitalizations

Characteristic	Community-Acquired Severe Sepsis N = 193,081	Healthcare-Associated Severe Sepsis N = 79,581	Hospital-Acquired Severe Sepsis N = 34,829
Mean Age (SD)	65.0 (17.1)	64.6 (16.7)	63.3 (16.4)
Sex			
Male	49.9%	51.1%	55.8%
Female	50.1%	48.9%	44.2%
Race			
White	66.2%	63.0%	68.6%
Black	22.1%	25.7%	19.5%
Other or Unknown	11.7%	11.3%	11.9%
Type of Hospitalization			
Medical	87.5%	89.0%	63.6%
Surgical	12.5%	11.0%	36.3%
Organ Dysfunction (95% CI)			
Cardiovascular	26.8% (26.56-26.95)	32.2% (31.85-32.50)	45.1% (44.54-45.59)
Hematologic	19.1% (18.93-19.29)	20.4% (20.09-20.65)	25.1% (24.64-25.55)
Hepatic	2.3% (2.19-2.32)	2.4% (2.26-2.47)	5.1% (4.83-5.29)
Neurological	12.9% (12.70-13.00)	15.5% (15.27-15.77)	22.4% (21.98-22.85)
Renal	57.8% (57.60-58.04)	54.2% (53.81-54.50)	54.0% (53.52-54.56)
Pulmonary	31.5% (31.27-31.69)	32.5% (32.19-32.85)	41.8% (41.31-42.34)
Median number of Organ Systems Involved (IQR; min, max)	1 (1-2; 1-6)	1 (1-2; 1-6)	2 (1-3; 1-6)
Infection Type (95% CI)			
Blood Stream & Parasitic	49.7% (49.48-49.93)	58.5% (58.11-58.80)	58.7% (58.16-59.20)
Central Nervous System	1.1% (1.10-1.19)	1.1% (1.03-1.18)	0.8% (0.68-0.86)
Cardiac	0.8% (0.72-0.80)	1.3% (1.20-1.35)	0.4% (0.29-0.42)
Pulmonary	38.3% (38.09-38.52)	33.8% (33.52-34.18)	36.1% (35.61-36.62)
Gastrointestinal	13.5% (13.34-13.64)	15.4% (15.13-15.64)	8.0% (7.73-8.30)
Genitourinary	40.3% (40.07-40.51)	38.3% (37.94-38.61)	37.9% (37.37-38.39)
Skin & Soft Tissue	10.7% (10.60-10.87)	9.7% (9.48-9.89)	5.7% (5.45-5.93)
Musculoskeletal	3.6% (3.55-3.72)	4.68% (4.53-4.82)	0.6% (0.51-0.67)
Infection, Not Otherwise Specified	7.6% (7.49-7.73)	14.9% (14.64-15.13)	16.7% (16.32-17.10)
Median Number of Infections (IQR; min, max)	1 (1-2; 1-8)	2 (1-2; 1-7)	1 (1-2; 1-6)

Table 2

Severe sepsis hospitalization care and outcomes.

Measure	Community-Acquired Severe Sepsis N = 193,081	Healthcare-Associated Severe Sepsis N = 79,581	Hospital-Acquired Severe Sepsis N = 34,829
Median Cost of Hospitalization (IQR)	\$7,024 (3,786– 4,609)	\$8,796 (4,650–17,978)	\$38,369 (20,005–73,171)
Median Length of Stay in days (IQR)	6 (3–10)	7 (4-12)	17 (10-29)
Median ICU days (IQR) [†]	3 (2-7)	3 (2-7)	8 (4-17)
Hospital Mortality (95% CI)	8.6% (8.5-8.7)	12.8% (12.5-13.0)	19.2% (18.7-19.6)
OR (95% CI)	Ref	1.56 (1.52-1.60)	2.52 (2.44-2.60)
Adjusted OR (95% CI) *	Ref	1.46 (1.41-1.50)	3.22 (3.11-3.34)

[†] = Patients who spent no time in an ICU were excluded

* = Adjusted for UHC expected mortality, clustering by hospital

Table 3

Healthcare-associated severe sepsis hospitalization care and outcomes.

Healthcare-Associated Severe Sepsis			
Measure	Dialysis N = 26,736	Readmissions N = 83,545	Skilled Nursing Facility/Home Health N = 16,704
Median Cost of Hospitalization (IQR)	\$16,282 (7,567–37,785)	\$9,940 (4,986–21,488)	\$ 8,514 4,668–17,255)
Median Length of Stay in days (IQR)	9 (5–19)	7 (4–13)	7 (4–12)
Median ICU days (IQR)	5 (2–12) [†]	4 (2–8) [†]	4(2–9) [†]
Hospital Mortality (95% CI)	16.8% (16.3–17.2)	13.0% (12.7–13.2)	14.4% (13.9–14.6)

[†] = Patients who spent no time in an ICU were excluded from analysis

Table 4**Medical vs. surgical severe sepsis outcomes**

Measure	Medical vs. Surgical Admissions					
	Community-Acquired Severe Sepsis		Healthcare-Associated Severe Sepsis		Hospital-Acquired Severe Sepsis	
Median Cost of Hospitalization (IQR)	Medical N = 164,393 \$6,096 (3,470-11,614)	Surgical N = 23,470 \$22,211 (11,689-46,011)	Medical N = 68,440 \$7,751 (4,277-14,956)	Surgical N = 8,470 \$28,071 (14,650-58,861)	Medical N = 19,783 \$23,247 (12,351-42,325)	Surgical N = 11,303 \$49,072 (26,770-90,375)
Median Length of Stay in days (IQR)	5 (3-9)	12 (7-21)	6 (3-10)	14 (8-25)	14 (8-23)	19 (11-31)
Median ICU days (IQR) [†]	3 (2-6)	5 (2-12)	3 (2-6)	6 (3-13)	6 (3-13)	10 (4-20)
Hospital Mortality (95% CI)	7.9% (7.8-8.0)	10.3% (9.9-10.7)	12.2% (12.0-12.5)	14.1% (13.4-14.9)	22.8% (22.1-23.6)	15.1 (14.6-15.6)
Adjusted OR (95% CI) *	Ref	1.40 (1.33-1.48)	Ref	1.37 (1.28-1.48)	1.60 (1.50-1.70)	Ref

[†] = Patients who spent no time in an ICU were excluded from analysis

* = Adjusted for expected mortality, hospital clustering