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Impact of Older Age and Nursing Home Residence on Clinical Outcomes of U.S. Emergency Department Visits for Severe Sepsis

Adit A. Ginde, MD, MPH, **Marc Moss, MD**, **Nathan I. Shapiro, MD, MPH**, and **Robert S. Schwartz, MD**
Department of Emergency Medicine (AAG), Division of Pulmonary Sciences and Critical Care Medicine (MM), and Division of Geriatric Medicine (RSS), University of Colorado School of Medicine, Aurora, CO; and Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, MA (NIS)

Abstract

Purpose—To compare the impact of older age and nursing home residence on the incidence and morbidity of severe sepsis.

Materials and Methods—This was a retrospective analysis of 19,460 emergency department (ED) visits from the 2005–2009 National Ambulatory Medical Care Surveys with diagnosis of infection with or without severe sepsis (acute organ dysfunction). Clinical outcomes included intensive care unit (ICU) admission, hospital length of stay (LOS), and in-hospital mortality.

Results—Older adults (age ≥65 years) were five-fold more likely to have infections classified as severe sepsis than younger adults (6.5% vs. 1.3%), and nursing home residents were seven-fold more likely to have a severe sepsis diagnosis compared to non-nursing home residents (14% vs. 1.9%). Among visits for severe sepsis, older adults, compared to younger adults, had modestly higher rates of ICU admission (27% vs. 21%), hospital LOS (median 6 vs. 5 days), and in-hospital mortality (24% vs. 16%). Nursing home residents with severe sepsis, compared to non-nursing home residents, had significantly higher rates of ICU admission (40% vs. 21%), hospital LOS (median 7 vs. 5 days) and in-hospital mortality (37% vs. 15%).

Conclusions—Older adults, and particularly nursing home residents, have a disproportionately high incidence of and morbidity from severe sepsis.

Keywords

sepsis; infection; organ failure; critical care; emergency medicine; geriatrics; nursing home; epidemiology

Address manuscript correspondence to: Adit A. Ginde, MD, MPH; Department of Emergency Medicine; University of Colorado School of Medicine; 12401 E. 17th Avenue, B-215; Aurora, CO 80045, Phone: (720) 848-6777, Fax: (720) 848-7374, adit.ginde@ucdenver.edu.

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INTRODUCTION

Severe sepsis is a syndrome of infection-related acute organ dysfunction that hospitalizes 750,000 annually, resulting in 215,000 deaths and an estimated $16.7 billion in direct medical costs in the U.S (1). While the incidence of severe sepsis increased four-fold from 1979 to 2000, the mortality decreased from 27.8% o 17.9% (2). Emphasis on early recognition and aggressive intervention for severe sepsis in emergency department (ED) and intensive care unit (ICU) patients has reduced associated morbidity (3,4). However, severe sepsis remains the 10th leading cause of death in the U.S. and the leading cause of death in non-cardiac ICUs, with 51% mortality at 1 year and 74% mortality at 5 years (5,6). Additionally, the rate of discharge to rehabilitation or long-term care facilities after hospitalizations for severe sepsis has markedly increased (2).

Older adults suffer the majority of the severe sepsis burden in the U.S., with a steep increase in incidence with advancing age (2,7–9). In addition, the mortality from severe sepsis rises with increased age and frailty (1,2,5,7). Prior national studies of outcomes using hospital discharge data have included a substantial proportion of hospital-acquired infections and severe sepsis. Recent efforts through the Surviving Sepsis campaigns aimed at early detection and treatment of severe sepsis patients presenting to the ED setting have successfully reduced morbidity (4). National data on outcomes after ED visits for severe sepsis could help to inform future research efforts and treatment decisions, including anticipated prognosis. However, prior national ED-based studies of severe sepsis have lacked important data on hospital outcomes and nursing home residence prior to presentation, an potentially important risk stratification variable in addition to age (8,9).

In 2005, the National Hospital Ambulatory Medical Care Survey (NHAMCS) began to collect hospital outcome data and prior nursing home residence, providing the opportunity to reanalyze current national epidemiologic data on ED visits for severe sepsis. The primary objective of this study was to compare the impact of age older age (defined as age ≥ 65 years) or present nursing home residence on the incidence and morbidity of severe sepsis.

MATERIALS AND METHODS

Study Design and Participants

This study was a secondary analysis of adult (age ≥ 18 years) ED visits in the five most recent years (2005–2009) of the NHAMCS database, a nationally representative survey of ED visits, conducted annually by the National Center for Health Statistics. We received a waiver from our institutional review board as an exempt study.

Details of survey methodology are described elsewhere (10). Briefly, the NHAMCS is a four-stage probability sample of visits to EDs associated with U.S. non-institutional, general and short stay hospitals. During 2005–2009, a sample of 2,390 hospitals was selected for participation in NHAMCS. Of the 1,968 hospitals deemed eligible based on type of hospital, 1,768 (90%) participated and a total of 174,020 ED visits were abstracted. Trained National Center for Health Statistics staff collected data during a randomly assigned 4-week data period for each of the sampled hospitals. When the data collection forms were completed, they were sent to the Constella Group (Durham, NC), where they were coded using the International Classification of Disease, Ninth Revision, Clinical Modification (11). NHAMCS data provide ED diagnoses (at the time of discharge from the ED or hospital admission) and do not represent hospital discharge diagnoses for admitted patients. For visits resulting in hospital admission, hospital course was also tracked.

Identification of Severe Sepsis

We used standard consensus criteria to define *severe sepsis* as concurrent bacterial or fungal infection plus acute organ dysfunction (4,12). To identify cases of severe sepsis, we used ICD-9-CM for infection and acute organ dysfunction in any of the three recorded ED diagnosis fields. This case definition did not include visits by patients whose infection or acute organ dysfunction was recognized or developed after the ED visit (e.g., during the hospitalization). ICD-9-CM codes were based on previously validated methodology to define presence of a bacterial or fungal infection, or acute organ dysfunction (Appendix Tables 1 and 2) (1,5). These codes have been used in more recent epidemiological analyses of severe sepsis in administrative datasets (9,13). We also considered endotracheal intubation performed during the ED visit or hypotension (ED triage systolic blood pressure <90 mm/Hg) to be markers of acute organ dysfunction, as previously reported (2). Finally, we added the single ICD-9-CM code 995.92 (severe sepsis/sepsis with acute organ dysfunction/sepsis with multiple organ dysfunction) to the severe sepsis criteria.

Clinical Characteristics

The primary characteristics of interest were age and residence at a nursing home immediately prior to the ED visit. While we recognize that different age thresholds to define “older adults” may be used, we dichotomized age at 65 years to compare with prior inpatient data for our primary analysis (7). Other demographic characteristics were analyzed including sex, race/ethnicity, U.S. Census Region, and urban location. ED clinical characteristics included ambulance arrival, initial ED triage vital signs, triage acuity (immediate/emergent, urgent, semi-urgent/non-urgent), and site of infection (based on the ICD-9-CM codes). The clinical outcomes of interest focused on markers of morbidity, including ED disposition (admission to an ICU setting, admission to a non-ICU setting, or discharge from the ED), hospital length of stay, and in-hospital mortality (including death in the ED).

Statistical analysis

We performed statistical analyses using Stata 12.1 (StatCorp, College Station, TX). Using survey commands, we applied the recommended sample weights to account for unequal probabilities of selection and to annualize estimates for all U.S. ED visits. We presented data as proportions with 95% confidence intervals (CI) or medians with interquartile ranges (IQR). We did not report 95% CIs for estimates with >30% relative standard errors due to unreliability, according to National Center for Health Statistics guidelines (10). Given the potential overlap between age and nursing home residence, we used multivariable logistic regression to evaluate for independent associations of age ≥65 years and nursing home residence with death and ICU admission, adjusted for sex and race/ethnicity.

RESULTS

From 2005 to 2009, severe sepsis accounted for an estimated 350,000 (0.4%) and infection without severe sepsis for an additional 14 million (15%) of all adult ED visits in the U.S. annually. Accordingly, 2.4% (95%CI, 2.2–2.7) of all ED visits for infection had severe sepsis. The proportion of all infection-related visits classified as severe sepsis, increased with older age: 0.7% (95%CI, 0.5–0.9) for 18–44 years; 2.9% (95%CI, 2.3–3.6) for 45–64 years; 5.9% (95%CI, 4.6–7.3) for 65–79 years; and 7.3% (95%CI, 6.0–8.8) for ≥80 years. Fourteen percent (95%CI, 11–17) of infection-related visits by nursing home residents were classified as severe sepsis, compared to 1.9% (95%CI, 1.6–2.2) of visits by non–nursing home residents.

Table 1 displays the characteristics of severe sepsis visits, compared to visits for infection without severe sepsis. Severe sepsis was associated with higher patient age, nursing home residence, ambulance arrival, and ED triage acuity. The median systolic blood pressure was lower and heart rate was higher among severe sepsis visits. As expected, respiratory and genitourinary were the most common sites of infection in both groups. Skin and soft tissue infections were less commonly associated with severe sepsis (representing 0.7% of all skin and soft tissue infection visits), while ICD-9-CM codes indicating multiple sites of infection were more commonly associated with severe sepsis (representing 7.6% of all multiple sites of infection visits). Compared to visits for infection without severe sepsis, severe sepsis visits had a three times greater hospital admission rate, an 8-fold higher ICU admission rate, two times longer median hospital length of stay, and 7-fold greater in-hospital mortality rate. Patient and clinical characteristics of ED visits for infection without severe sepsis were similar to those without infection diagnoses (Table 1).

Comparison of age and nursing home residence among severe sepsis visits with in-hospital death (vs. discharged alive) and ICU admission (vs non-ICU admission) are provided in Table 2. Older age and nursing home residence were both associated with a greater likelihood of death and with ICU admission. In-hospital mortality of severe sepsis visits was 37% (95%CI, 26–49) for those admitted to the ICU and 8.4% (95%CI, 4.5–15) for those admitted to a non-ICU setting. Additional characteristics of severe sepsis visits stratified by death or ICU admission are presented in Appendix Table 3 and by age and nursing home residence in Appendix Table 4.

When the analysis was limited to age ≥65 years, the association between nursing home residence and worse outcomes remained strong. Nursing home residents comprised 38% (95%CI, 30–46) of these older adults and had a higher rate of ICU admission (34% vs. 24% for older non-nursing home residents); higher in-hospital mortality (32% vs. 9.9% for older non-nursing home residents). Multivariable models adjusting for other demographic characteristics also suggest that nursing home residence was strongly associated with higher mortality and ICU admission, while the independent association with older age with these outcomes was limited (Table 3). These results did not change with age analyzed as a continuous variable (data not shown).

DISCUSSION

Infection is a common ED presentation accounting for 15% of all adult ED visits nationally. While only a small fraction (2.4%) of infection-related visits to the ED had severe sepsis, significant resource utilization (e.g., ICU admission) and high mortality (21%) resulted from these visits. Severe sepsis occurs throughout the adult age spectrum, but older adults (age ≥65 years), and particularly nursing home residents, had a disproportionately higher incidence of severe sepsis and subsequent mortality. Indeed, adults ≥65 years old accounted for 57% of all ED visits for severe sepsis with an associated in-hospital mortality of 24%. Nursing home residents accounted for 25% of all ED visits for severe sepsis with an associated in-hospital mortality of 37%. Nursing home residence appeared to be the primary determinant of higher mortality among older adults.

To our knowledge, this is the first national study of ED-diagnosed severe sepsis to report hospital outcomes. Prior ED-based studies of sepsis included data from NHAMCS from 1992–2001 and 2001–2004 (8,9); however, NHAMCS data on hospital outcomes did not become available until 2005 (the first year included in the present study). A prior analysis of 2001–2008 NHAMCS data on urinary tract infections in older ED patients focused on presence of urinary symptoms, did not present data for severe sepsis, and did not include hospital outcomes data, such as mortality and hospital length of stay (14). Prior national

studies that included hospital outcomes used the National Hospital Discharge Survey or National Inpatient Sample (2,7); however these studies represent all cases seen in the hospital, including those not directly admitted through the ED (e.g., direct transfers, elective operations, hospital-acquired infections).

In comparison to Wang et al (9), we report a somewhat lower annual incidence of ED visits for severe sepsis (350,000 vs 571,000). However, the prior study included fever, in addition to ICD-9-CM codes, as criteria for the infection component of severe sepsis, and fever alone accounted for approximately half of infections among those classified as having severe sepsis. We chose not to include fever in our criteria, as it is non-specific, may include viral infections and other conditions not associated with sepsis syndromes, and is inconsistent with previously reported ICD-9-CM only methodology on identification of severe sepsis in administrative data (1,5,13). Based on our results, one may abstract that nearly half of the reported 750,000 annual U.S. cases of severe sepsis originated in the ED. These epidemiological data on severe sepsis from the ED perspective highlight the importance of developing ED-based strategies and interventions to improve outcomes for severe sepsis.

While increased susceptibility to infection among older and frailer adults is not a new concept, these data provide additional insight into their predisposition to and morbidity associated with severe sepsis. Compared to adults aged 45–64 years presenting with infection, 65–79 year olds had twice the rate of severe sepsis and ≥80 year olds had 2.5 times the rate of severe sepsis. Nursing home residents, compared to non-nursing home residents, with infection had an even more striking difference with seven-fold higher rate of severe sepsis. The increased susceptibility to severe sepsis in these groups is likely multi-factorial, including physiological differences such as impaired antimicrobial responses and prolonged inflammation.

Immunosenescence, or the age-related decline in immune function, affects both innate and adaptive immunity, reduces host protection against infection and responses to vaccines, and thus, increase risk for incident infection (15,16). Inflammation is a hallmark of sepsis syndromes, and while the ability of older adults to process antigens is impaired, the aging immune system often mounts an over-exuberant and maladaptive pro-inflammatory cytokine response that more frequently leads to severe sepsis and septic shock (17,18). Nursing home residents are often exposed to more aggressive and antimicrobial-resistant infections, similar to nosocomial infections (19). Beyond this location-related risk, nursing home residence can also be considered a marker of frailty and multi-morbidity (20, 21), both of which contribute to enhanced impairment of immune responses (22). In addition, nursing home residents likely have a high number of co-morbid acute illnesses that may impact outcomes (23). While we are unable to assess these specific mechanisms of higher morbidity in our study, this is an important area of future investigation.

Hospital outcomes were modestly worse among all older adults, but markedly worse among nursing home residents, which appeared to be the primary determinant of worse outcomes in older adults. Of note, the outcomes measured in this study (e.g., mortality) only represent a fraction of the actual disease burden. Indeed, an episode of severe sepsis often impairs the functional status of older adults, sometimes permanently (24,25), leading to the need for placement in skilled nursing facilities for rehabilitation or long-term care (2). These outcomes are important to include in future prospective investigation.

Collectively, our results add to the literature on the epidemiology on severe sepsis to focus clinical care and to direct allocation of resources and research priorities. While older adults and nursing home residents are often excluded from ED-based and ICU clinical trials, either explicitly or indirectly by other factors that are prevalent in this population (26), these

patients represent a majority of U.S. adults with severe sepsis. Thus, while evidence is predominantly derived from younger and non-nursing home populations, its application is broad and includes older adults and nursing home residents despite limited data. Further study that focuses on this high-risk population will help to understand the interface between immunosenescence and acute infection to develop strategies to reduce the high incidence and morbidity of severe sepsis in frail, older adults.

There are several potential limitations to this study. The ICD-9-CM coding algorithm relies on abstraction by National Center for Health Statistics staff and is limited by the recognition of relevant conditions by the treating ED clinician, the number of diagnoses that NHAMCS included (three), the quality of data abstraction, and the inherent accuracy of these codes to identify cases of severe sepsis. For example, 26% of severe sepsis visits were not hospitalized, which was a lower rate than anticipated and may indicate some misclassification. Additionally, we assume that infection and organ dysfunction were acute processes and related to each other, and this assumption may sometimes be incorrect. However, we used the ICD-9 coding algorithm from prior studies of severe sepsis for our analysis, which enhances consistency with prior literature (1,5,9,13). In addition, only three diagnoses are included in the NHAMCS database, which limited our ability to explore secondary diagnoses as a potential explanation for the primary results.

Other variables in this analysis, such as nursing home residence and ICU admission, were specifically categorized on the data abstraction form and thus, less subject to inaccuracy by the trained research staff. Due to limitations in NHAMCS data, we were unable to report specific results of laboratory testing or clinical monitoring nor outcomes after hospital discharge including change in functional status, placement in skilled nursing facilities, rehospitalization, and mortality after discharge. These data are important to encompass the burden of severe sepsis and are better suited to prospective study that is an active area of investigation by our and other groups.

CONCLUSIONS

Severe sepsis is a common ED presentation and despite efforts during the last decade to institute early recognition and treatment in the ED, the mortality rate is still 21%. Older adults and nursing home residents have a disproportionately high incidence and account for a large proportion of ED visits for severe sepsis. Nursing home residents have a particularly high morbidity and mortality from severe sepsis. These data provide justification to develop and investigate targeted strategies to prevent and treat severe sepsis in older adults and nursing home residents.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of U.S. emergency department visits for infection with and without severe sepsis, 2005–2009

Characteristics	Severe Sepsis % (95%CI)	Infection without Severe Sepsis % (95%CI)	No Infection % (95%CI)
Demographics			
Age, years; median (IQR)	69 (54–82)	40 (26–60)	43 (29–58)
18–44	15% (12–19)	56% (55–58)	53% (52–54)
45–64	28% (22–34)	23% (22–24)	28% (28–28)
65–79	28% (23–34)	11% (11–12)	11% (11–12)
≥80	29% (24–34)	9.2% (8.6–9.8)	7.5% (7.2–7.9)
Nursing home resident	25% (20–31)	3.9% (3.4–4.4)	2.3% (2.1–2.5)
Female sex	51% (46–56)	62% (61–63)	56% (55–56)
Race/ethnicity			
Non-Hispanic White	68% (63–73)	62% (59–65)	64% (61–66)
Non-Hispanic Black	19% (15–24)	22% (20–25)	22% (19–25)
Hispanic	8.6% (5.9–12)	12% (10–14)	11% (10–13)
Other	3.9% (nc)	3.3% (2.5–4.3)	3.4% (2.7–4.2)
Region			
Northeast	16% (12–21)	18% (16–20)	19% (17–22)
Midwest	26% (20–34)	21% (18–26)	23% (19–27)
South	38% (30–45)	42% (37–46)	39% (35–43)
West	20% (14–26)	19% (15–24)	19% (15–23)
Urban location	85% (75–92)	83% (73–90)	84% (75–90)
Clinical			
Ambulance arrival	57% (50–63)	14% (13–15)	19% (18–20)
Vital signs, median (IQR)			
Temperature, Fahrenheit	98.2 (97.4–99.3)	98.2 (97.6–98.9)	98.0 (97.4–98.5)
Systolic blood pressure	91 (80–129)	131 (118–146)	134 (120–149)
Heart rate	96 (80–113)	89 (78–102)	84 (74–96)
Respiratory rate	18 (18–24)	18 (18–20)	18 (16–20)
Oxygen saturation	96 (92–98)	98 (96–99)	98 (97–99)
Triage acuity			
Emergent	43% (37–49)	12% (11–14)	17% (16–18)
Urgent	36% (30–42)	40% (38–42)	39% (37–41)
Semi-urgent/non-urgent	12% (8.7–17)	35% (33–37)	31% (30–33)
Missing	8.8% (5.8–13)	12% (10–14)	13% (11–15)
Site of infection			
Respiratory	39% (34–44)	34% (33–35)	--
Genitourinary	20% (16–25)	24% (24–25)	--
Skin and soft tissue	5.5% (3.1–9.4)	21% (20–23)	--
Infectious and parasitic disease	9.5% (6.7–13)	3.8% (3.4–4.3)	--
Other	11% (8.2–16)	12% (11–13)	--
Multiple sites	14% (11–19)	1.1% (0.9–1.4)	--

Characteristics	Severe Sepsis % (95%CI)	Infection without Severe Sepsis % (95%CI)	No Infection % (95%CI)
Outcomes			
ED LOS, hours; median (IQR)	4.4 (2.9–6.0)	1.6 (2.9–4.6)	2.7 (1.6–4.5)
ED Disposition			
Admitted, intensive care	25% (20–30)	3.0% (2.7–3.4)	2.6% (2.4–2.9)
Admitted, non-intensive care	49% (42–56)	18% (17–19)	13% (12–14)
Not admitted	26% (20–34)	79% (78–80)	84% (83–85)
Hospital LOS, days; median (IQR)	6 (4–8)	3 (5–7)	4 (3–6)
In-hospital mortality	21% (15–28)	3.0% (2.4–3.8)	4.1% (3.8–4.5)

CI, confidence interval; IQR, interquartile range; ED, emergency department; LOS, length of stay; nc, not calculable due to >30% relative standard error

Table 2

Age and nursing home residence among U.S. emergency department visits for severe sepsis resulting in hospital death vs. discharged alive and intensive care unit vs. non-intensive care unit admission

Characteristics	In-hospital death % (95%CI)	Discharged alive % (95%CI)	ICU admission % (95%CI)	Non-ICU admission % (95%CI)
Age, years; median (IQR)	76 (64–82)	66 (47–80)	71 (61–83)	70 (54–82)
18–44	5% (nc)	18% (15–23)	4.3% (nc)	14% (9.1–20)
45–64	24% (nc)	28% (22–34)	32% (22–46)	25% (19–33)
65–79	31% (17–50)	28% (23–34)	32% (23–42)	32% (24–40)
≥80	39% (25–55)	26% (20–32)	28% (22–35)	29% (23–36)
Nursing home resident	48% (31–64)	20% (15–26)	39% (27–52)	21% (16–29)

ICU, intensive care unit; CI, confidence interval; IQR, interquartile range; ED, emergent department; LOS, length of stay; nc, not calculable due to >30% relative standard error

Table 3

Multivariable associations between age and nursing home residence with in-hospital death and intensive care unit admission, adjusted for sex and race/ethnicity

Characteristics	In-hospital death OR (95%CI)	ICU admission OR (95%CI)
Age ≥65 years (vs. <65 years)	1.3 (0.45–3.7)	1.0 (0.52–1.9)
Nursing home resident (vs. non-nursing home resident)	3.1 (1.2–7.8)	2.6 (1.2–5.6)
Female sex (vs. male)	1.2 (0.57–2.4)	0.88 (0.50–1.6)
Race/ethnicity		
Non-Hispanic White	Referent	Referent
Non-Hispanic Black	1.7 (0.57–4.8)	1.3 (0.62–2.6)
Hispanic	0.48 (0.12–1.9)	0.63 (0.23–1.7)
Other	0.99 (0.18–5.6)	2.4 (0.87–6.5)

ICU, intensive care unit; OR, odds ratio; CI, confidence interval