Letters

RESEARCH LETTER

Hospital Deaths in Patients With Sepsis From 2 Independent Cohorts

Sepsis, the inflammatory response to infection, affects millions of patients worldwide.[1] However, its effect on overall hospital mortality has not been measured. We quantified the contribution of sepsis to mortality in 2 complementary inpatient cohorts from Kaiser Permanente Northern California (KPNC) and the Healthcare Cost and Utilization Project Nationwide Inpatient Sample (NIS).

Methods | The KPNC cohort included 482 828 adults (aged ≥18 years) with overnight, nonobstetrical hospitalizations at 21 KPNC hospitals between 2010 and 2012.[2] Compared with all Northern California patients, KPNC patients have broadly similar health characteristics but higher income and educational attainment.[3] The NIS, a nationally representative sample of 1051 hospitals, included 6.5 million unweighted adult hospitalizations in 2010.[4]

We used 2 approaches to identify patients with sepsis from *International Statistical Classification of Diseases, Ninth Revision, Clinical Modification* codes. The explicit approach identified those with codes 038 (septicemia), 995.91 (sepsis), 995.92 (severe sepsis), or 785.52 (septic shock). Because of the known underrecognition of sepsis, we also used an implicit approach adding patients with evidence of both infection and acute organ failure using the Angus implementation[5] of sepsis consensus criteria. Within KPNC data, we delineated diagnoses when coded as present on admission, an important consideration for improving identification and treatment efforts. Furthermore, we linked 97.9% (n = 19 621) of all explicit sepsis cases present on admission in 2012 to KPNC quality improvement data, permitting stratification of patients by common sepsis severity criteria including early goal-directed therapy (EGDT) eligibility and serum lactate levels.[6]

In each cohort, we calculated the percentage of all inpatients admitted with sepsis, the sepsis hospital mortality rate, and the percentage and 95% confidence interval of hospital deaths occurring in patients with sepsis using Stata version 11.2 (StataCorp). The KPNC institutional review board approved the use of KPNC data with a waiver of informed consent and exempted NIS data from review.

Results | In the KPNC cohort, there were between 55 008 explicit (11.4% of total; 95% CI, 11.3%-11.5%) and 80 678 implicit (16.7%; 95% CI, 16.6%-16.8%) sepsis hospitalizations (**Table 1**); most occurrences of sepsis were present on admission. From the NIS cohort, 280 663 (4.3%; 95% CI, 4.3%-4.3%) hospitalizations met explicit sepsis criteria while 717 718 (10.9%; 95% CI, 10.9%-11.0%) met implicit criteria.

Of 14 206 KPNC inpatient deaths, 36.9% (95% CI, 36.1%-37.7%; explicit) to 55.9% (95% CI, 55.1%-56.7%; implicit) occurred among patients with sepsis, which was nearly all present on admission. Of 143 312 NIS deaths, 34.7% (95% CI, 34.4%-34.9%; explicit) to 52.0% (95% CI, 51.7%-52.2%; implicit) occurred among patients with sepsis. In the 2012 linked KPNC subset (**Table 2**), patients with sepsis meeting criteria for EGDT (n = 2536) comprised 32.6% (95% CI, 30.4%-34.7%) of sepsis deaths. In contrast, patients with sepsis, normal blood pressure, and measured lactate levels of less than 4 mmol/L (n = 15 095) comprised 55.9% (95% CI, 53.6%-58.1%) of sepsis deaths.

Discussion | In 2 complementary hospital cohorts, we found that sepsis contributed to 1 in every 2 to 3 deaths, and most of these patients had sepsis at admission. Given the prominent role it plays in hospital mortality, improved treatment of sepsis (potentially a final hospital pathway for multiple other underlying conditions) could offer meaningful improvements in population mortality.

Patients with initially less severe sepsis made up the majority of sepsis deaths. Performance improvement efforts in the treatment of sepsis have primarily focused on standardizing care for the most severely ill patients, whereas interventions for treating other patients with sepsis are less well defined. Given their preva-

Table 1. Inpatients With Sepsis Diagnoses in the Kaiser Permanente Northern California Cohort and the Healthcare Cost and Utilization Project Nationwide Inpatient Sample[a]

	Inpatients With Sepsis Diagnoses[b]					
	Kaiser Permanente Northern California (2010-2012) (n = 21 Hospitals) (14 206 Deaths/482 828 Admissions)				Nationwide Inpatient Sample (2010) (n = 1051 Hospitals) (143 312 Deaths/6 555 621 Admissions)	
	Explicit	Explicit POA[c]	Implicit	Implicit POA[c]	Explicit	Implicit
Hospitalizations	55 008 (11.4) [11.3-11.5]	50 520 (10.5) [10.4-10.5]	80 678 (16.7) [16.6-16.8]	73 933 (15.3) [15.2-15.4]	280 663 (4.3) [4.3-4.3]	717 718 (10.9) [10.9-11.0]
Hospital mortality	6272 (11.4) [11.1-11.7]	5238 (10.4) [10.1-10.6]	7941 (9.8) [9.6-10.0]	7391 (10.0) [9.8-10.2]	49 664 (17.7) [17.6-17.8]	74 451 (10.4) [10.3-10.4]
% (95% CI) of all hospital deaths among patients with sepsis	44.2 (43.3-45.0)	36.9 (36.1-37.7)	55.9 (55.1-56.7)	52.0 (51.2-52.8)	34.7 (34.4-34.9)	52.0 (51.7-52.2)

Abbreviation: POA, present on admission.

[a] Case definitions are based on explicit sepsis diagnosis codes or the addition of cases identified using the Angus implementation[5] of the International Consensus Conference Definition of Severe Sepsis (implicit).

[b] Values expressed as No. (%) [95% CI] unless otherwise indicated.

[c] Indicates diagnoses were POA.

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Table 2. Hospital Mortality Among Patients With Sepsis Present on Admission[a]

		Sepsis Severity Group[b]				
		Lactate[c]			Early Goal-Directed Therapy	
	Overall (n = 19 621)	Normal (n = 9067)	Intermediate (n = 6028)	None (n = 1990)	Yes (n = 1200)	No (n = 1336)[d]
Age, mean (SD), y	69 (17)	69 (17)	70 (16)	69 (17)	67 (16)	73 (16)
Laboratory and Acute Physiology Score, mean (SD)[e]	104 (40)	94 (33)	110 (39)	79 (43)	145 (39)	149 (39)
Direct admission to ICU, No. (%) [95% CI][f]	3790 (19.3) [18.7-19.9]	879 (9.7) [9.1-10.3]	976 (16.2) [15.3-17.1]	267 (13.4) [11.9-14.9]	1087 (90.6) [88.9-92.2]	581 (43.5) [40.8-46.1]
Hospital deaths, No. (%) [95% CI]	1817 (9.3) [8.9-9.7]	477 (5.3) [4.8-5.7]	538 (8.9) [8.2-9.6]	211 (10.6) [9.2-12.0]	212 (17.7) [15.5-19.8]	379 (28.4) [25.9-30.8]
% (95% CI) of all sepsis deaths[g]		26.3 (24.2-28.3)	29.6 (27.5-31.7)	11.6 (10.1-13.1)	11.7 (10.2-13.1)	20.9 (19.0-22.7)

Abbreviation: ICU, intensive care unit.

[a] Based on explicit diagnosis criteria and stratified by clinical characteristics using linked 2012 Kaiser Permanente Northern California quality improvement data. A total of 420 (2.1%) patients meeting explicit sepsis diagnosis criteria could not be matched with quality improvement data.

[b] Patients were grouped sequentially into sepsis severity groups starting with those meeting standard criteria for early goal-directed therapy.

[c] Remaining patients were stratified by lactate values: less than 2 mmol/L (normal), between 2 mmol/L or greater and less than 4 mmol/L (intermediate), or not obtained (none).

[d] These patients were eligible for early goal-directed therapy but they did not receive it.

[e] Score range is from zero to a theoretical maximum of 414.[2]

[f] Determined based on whether patients were transferred to a critical care hospital ward directly from the emergency department.

[g] Row total may exceed 100% due to rounding.

lence, improving standardized care for patients with less severe sepsis could drive future reductions in hospital mortality.

Even though our findings were broadly consistent, the study's primary limitation results from potential inaccuracies and inconsistencies in case identification across cohorts. Prior strategies, based on administrative data, have demonstrated variability with respect to prevalence estimates and case accuracy, a factor that may have contributed to differences between cohorts in explicit sepsis mortality.[5] Thus, we present granular data from the KPNC sepsis quality improvement program whose components include standardized case identification, manual chart validation, severity of illness risk adjustment, and treatment data; replication in other samples with similar granularity could be valuable.

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