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Palliative care consultation in patients with *Staphylococcus aureus* bacteremia

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Abstract

Background: Palliative care consultation has shown benefits across a wide spectrum of diseases, but the utility in patients with *Staphylococcus aureus* bacteremia remains unclear despite its high mortality.

Aim: To examine the frequency of palliative care consultation and factors associated with palliative care consult in *Staphylococcus aureus* bacteremia patients in the United States.

Design: A population-based retrospective analysis using the Nationwide Inpatient Sample database in 2014, compiled by the Healthcare Costs and Utilization Project of the Agency for Healthcare Research and Quality.

Setting/subjects: All inpatients with a discharge diagnosis of *Staphylococcus aureus* bacteremia (ICD-9-CM codes; 038.11 and 038.12).

Measurements: Palliative care consultation was identified using ICD-9-CM code V66.7. Patients' baseline characteristics and outcomes were compared between those with and without palliative care consult.

Results: A total of 111,320 *Staphylococcus aureus* bacteremia admissions were identified in 2014. Palliative care consult was observed in 8,140 admissions (7.3%). Palliative care consultation was associate with advanced age, white race, comorbidities, higher income, teaching/urban

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Conflict of interest

None

hospitals, Midwest region, Methicillin-resistant *Staphylococcus aureus* bacteremia and the lack of echocardiogram. Palliative care consult was also associated with shorter but more expensive hospitalizations. Crude mortality was 53% (4314/8140) among admissions with palliative care consult and 8% (8357/10,318) among those without palliative care consult ($p < 0.001$).

Conclusions: Palliative care consultation was infrequent during the management of *Staphylococcus aureus* bacteremia, and a substantial number of patients died during their hospitalizations without palliative care consult. Given the reported benefit in other medical conditions, palliative care consultation may have a role in *Staphylococcus aureus* bacteremia. Selecting patients who may benefit the most should be explored.

Keywords

staphylococcus bacteremia; palliative care consultation; mortality; staphylococcus aureus

Background

Staphylococcus aureus is the leading cause of bacteremia in both community and healthcare settings. *S. aureus* bacteremia (SAB) may arise from breaches of the skin, as with indwelling catheters, after surgery or other procedures, or in the setting of local *S. aureus* infections such as pneumonia or cellulitis. Its clinical presentations vary, ranging from asymptomatic, to fever alone, to sepsis. While they may be difficult to recognize initially, complications can be critical such as endocarditis, embolization to the central nervous system and other visceral organs, vertebral osteomyelitis and other bone and joint infections. Mortality rates associated with SAB are high at 15 to 25 percent.[1] However, the mortality is higher among patients with comorbidities, methicillin-resistant *S. aureus* (MRSA) infection, and time to positivity of blood cultures less than 12 hours.[2–4]

Palliative care improves quality of life for both patients and families by relieving pain and stress from serious illness.[5] Palliative care consult (PCC) is associated with favorable clinical outcomes including pain relief, symptom control, and decreased depression and anxiety, resulting in increased satisfaction among both patients and their families.[6] Currently no specific guidance or recommendation exist on when to consider PCC in patients with infections except for human immunodeficiency virus.[7] Furthermore, there is a paucity of studies assessing the value of PCC for serious infectious diseases. The role of PCC in patients with SAB is incompletely elucidated despite the high mortality and morbidity associate with SAB.[8, 9]

We examined the frequency of utilization of PCC and factors associated with PCC in SAB patients in the United States.

Methods

A population-based retrospective analysis was conducted using the Nationwide Inpatient Sample (NIS) database in 2014, compiled by the Healthcare Costs and Utilization Project (HCUP) of the Agency for Healthcare Research and Quality. NIS is one of the largest all-payer inpatient databases in the United States and represents approximately 7 million

hospital stays in the United States each year.[10] NIS captures a stratified sample (20%) of all discharges from community and teaching hospitals, excluding rehabilitation and long-term acute care hospitals in the United States.

We used the International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) codes to characterize the records, identifying patients with a discharge diagnosis of *Staphylococcus aureus* bacteremia (ICD-9-CM codes; 038.12 of methicillin-resistant *S. aureus* (MRSA) bacteremia and 038.11 of methicillin-susceptible *S. aureus* (MSSA) bacteremia). These codes have been used in previous studies.[111213] Palliative care consultation was identified using ICD-9-CM code V66.7. The sensitivity and specificity of V66.7 code were validated in a previous study and were 81% and 97%, respectively.[14] Patient-level characteristics (age, sex, race, baseline comorbidities, Elixhauser score, household income, and insurance status), hospital-level characteristics (hospital bed size, location, and region), proportion of MRSA (number of MRSA / all SABs), and the use of an echocardiogram were obtained. Hospital bed size definitions can be found in the website of Agency for Healthcare Research and Quality.[10] The Census Bureau region definition was used for the hospital region.[15] Echocardiogram was identified using the corresponding ICD-9-CM procedure code (88.72). The cost of hospitalization was calculated from hospital charges according to the guidance provided by the HCUP. To calculate the estimated costs of hospitalization, the NIS data were merged with cost-to-charge ratios.

Summary statistics for all measures were calculated for the full sample and stratified by PCC status. Continuous measures were represented as means (SDs) or medians (IQRs), depending on the distribution, and categorical variables were represented as percentages. Tests for differences of the variables between PCC and non-PCC groups were conducted using two-sample t-, Wilcoxon rank-sum, and Pearson's chi-square tests.

All subsequent analyses utilized the generalized linear modeling (GLM) framework, allowing us to specify the distribution of each outcome. The primary outcome was whether a patient with SAB received PCC (binary distribution, logit link). Univariate models predicting PCC were fit using all other measures. Variables with a univariate p-value < 0.15 were included in a multivariate model to assess the significance and any adjustments of the odds ratio estimates.

Secondary outcomes included length of stay (LOS, Poisson distribution, log link), hospitalization cost (gamma distribution, log link), and death (binary distribution, logit link). Comparisons of patient characteristics and clinical outcomes between PCC and non-PCC were assessed both unadjusted and adjusting for age, sex, race and Elixhauser score, providing mean ratio estimates for cost and length of stay and odds ratio estimates for death. All comparisons were assessed at the $\alpha = 0.05$ level. Data extraction and analysis were carried out using SAS 9.4 (SAS Institute Inc, Cary, North Carolina). Because NIS contains publicly available data, approval from an Institutional Review Board was not necessary.

Results

A total of 111,320 SAB admissions were identified in 2014. PCC was observed in 8,140 admissions (7.3%, table 1). Compared to admissions without PCC, the PCC group was older (mean age, 70 vs. 59, $p < 0.001$), more likely to be white (75% vs. 68%, $p < 0.001$), had higher prevalence of chronic heart failure, chronic pulmonary disease, coagulopathy, liver disease, metastatic cancer, solid tumor (p values < 0.05 respectively), MRSA rather than MSSA bacteremia (53% vs. 48%, $p < 0.001$) and a higher Elixhauser score (mean 20 vs. 13, $p < 0.001$). Admissions with PCC were also significantly associated with Medicare insurance (71% vs. 56%, $p < 0.001$), Midwest region (26% vs. 21%, $p < 0.001$), large hospitals (59% vs. 54%, $p < 0.001$) and urban teaching hospitals (73% vs. 65%, $p < 0.001$). Conversely, the PCC group was less likely to have echocardiography (13% vs. 19%, $p < 0.001$). Crude mortality was 53% (4314/8140) among admissions with PCC and 8% (8357/10,3180) among those without PCC ($p < 0.001$).

In the multivariate model, factors associated with PCC were advanced age, white race, comorbidities, higher income, teaching/urban hospitals, Midwest regions, MRSA bacteremia and the lack of echocardiogram (table 2). Adjusted estimates of the effect of PCC on our secondary outcomes show a shorter length of stay (mean ratio = 0.95, CI = 0.93 – 0.96) but a higher cost (MR = 1.10, CI = 1.05 – 1.15, table 3).

Discussion

Our study revealed that PCC was observed in 7% of patients with SAB in the United States. PCC was associated with advanced age, white race, comorbidities, higher income, teaching/urban hospitals, Midwest region, MRSA bacteremia and the lack of echocardiogram. PCC was also associated with shorter LOS but higher hospitalization costs. A considerable number of patients died during their hospitalizations without PCC.

PCC, especially when initiated early in the disease course, improves patient and family experience and quality of care.[16, 17] While guidelines exist on the utility of PCC in patients with cancer [18], its role in patients with sepsis or bloodstream infection is not well described. *S. aureus* is among the most common causes of bloodstream infection and sepsis, with the rate of SAB having remained largely stable over time, while the proportion of SABs due to MRSA decreased during 2012–2017.[19]

Our study revealed that PCC was placed in 7% of all patients with SAB, 53% of whom died during their hospitalizations. A similar study demonstrated that PCC was placed in 11 and 15% of patients with ST-segment elevation myocardial infarction and abdominal aortic rupture, respectively.[920] The lower rate of PCC in SAB may be explained by infection being viewed as more treatable (with antibiotics) than other conditions considered to be irreversible. However, PCC was used in only one third of SAB patients who died during their hospitalization (34% of 12971; 4314 patients).

The lower PCC utilization in younger patients, non-White race, lower income patient and smaller/non-teaching hospitals has been reported in previous studies with other medical issues.[921] Though our study does not identify subsets of patients that would benefit most

from PCC, there is likely room to improve patient-selection for appropriate PCC in patients with SAB. In addition, a recent study revealed that SAB leads to a significant impact on the quality of life among survivors.[22] Therefore, PCC may need to be considered more proactively for patients with SAB not only during admission but also in the outpatient setting. Given higher mortality reported in prior studies, the target population would be SAB patients with age > 60, MRSA infection, septic shock, endocarditis, underlying cirrhosis or time to positivity of blood cultures less than 12 hours.[2342324]

Patients who received PCC were less likely to undergo an echocardiogram. This may be because more severely ill patients who require PCC may be judged unable to tolerate an invasive procedure like a transesophageal echocardiogram (TEE). However, this remains speculative as the ICD 9 code used in our study can capture both transthoracic echocardiogram and TEE. Interestingly, MRSA was more frequent in the PCC group. Previous studies revealed that MRSA bacteremia had higher mortality, higher cost, and longer LOS than MSSA bacteremia.[25] On the other hand, PCC has been associated with decreased costs and shorter LOS in two other similar studies.[2627] However, our findings were different from non-SAB studies; while LOS was shorter, higher costs were seen in the PCC group. Possible explanations are that physicians and/or family may think the patient's status will improve with antibiotics, or conversely, the SAB course was fulminant. PCC might not have been performed soon enough to cause a significant difference.

There are several limitations to this analysis. First, the study is subject to biases associated with observational studies. Second, the purpose of the PCC could not be evaluated. PCC could be obtained for goals of care discussion or pain management, and such data may have made the analysis even more informative. Third, the timing of PCC could not be identified. Therefore, the LOS and cost analysis are affected by whether the PCC was obtained early or later in the disease course. Fourth, the availability of PCC in each institution could not be evaluated. Fifth, we did not investigate the data surrounding clinical features of SAB such as bone/joint involvement, endocarditis, presence of hardware or central line, source control, and treatment taken. These features are likely to help select patients who may benefit from PCC most. Sixth, diabetes was associated with lower likelihood of PCC. One prior report demonstrated worse outcomes in diabetic patients with SAB. Our result might be biased by unmeasured confounding factors.[28]

In conclusion, the palliative care service was infrequently consulted during management of SAB, and many patients died during hospitalization without PCC. Given the benefit of PCC in other medical problems, PCC may have a greater role in selected SAB patients.

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Key statement

What is already known about the topic?

- Mortality rates associated with *Staphylococcus aureus* bacteremia (SAB) remain high at 15 to 25 percent.
- While palliative care consultation (PCC) has shown benefits across a wide spectrum of diseases, there has been very limited work examining the utility of PCC for patients with SAB despite its high mortality.

What this paper adds

- Palliative care consultation was infrequent during the management of SAB (7%).
- PCC was associated with advanced age, white race, comorbidities, higher income, teaching/urban hospitals, Midwest regions, methicillin-resistant *S. aureus* bacteremia and the lack of echocardiogram.
- Two thirds of SAB patients who died during their hospitalization did not use PCC.

Implications for practice, theory or policy

- Given the reported benefit of PCC in other medical problems, PCC may have a greater role in patients with SAB.
- Further research is needed to identify which subsets of SAB patients would benefit most from PCC.

Table 1:

Characteristics of hospitalized patients with *Staphylococcus aureus* bacteremia, National Inpatient Sample, 2014

	Total	Without palliative consult	Palliative consult	p-value
N	111320	103180	8140	
Age, mean (SD)	60.1 (18.4)	59.3 (18.4)	70.0 (15.3)	< 0.0001
<65	56.0	57.9	32.7	< 0.0001
65–79	28.4	27.8	35.9	
>80	15.6	14.3	31.5	
Female	41.2	41.1	42.8	0.1742
Race/ethnicity				
White	68.9	68.4	74.9	< 0.0001
Black	16.5	16.7	13.5	
Hispanic	9.3	9.5	6.8	
Asian	2.2	2.3	1.8	
Native American	0.8	0.9	0.7	
Other	2.3	2.3	2.4	
AIDS	0.3	0.3	0.3	0.6070
Alcohol use disorder	5.4	5.4	5.4	0.9703
Rheumatoid arthritis/collagen vascular disease	4.3	4.3	3.7	0.2180
CHF	22.3	21.5	31.9	< 0.0001
chronic pulmonary disease	22.8	22.6	25.5	0.0070
coagulopathy	17.7	16.9	28.3	< 0.0001
depression	12.1	12.3	9.9	0.0045
DM	22.8	23.1	19.6	0.0012
DM with chronic complication	17.2	17.6	11.9	< 0.0001
Intravenous drug use	9.9	10.3	4.7	< 0.0001
Liver disease	8.0	7.9	9.5	0.0169
lymphoma	1.9	1.8	2.5	0.0788
metastatic cancer	3.4	2.9	9.1	< 0.0001
Obesity (BMI >30)	17.5	17.9	12.2	< 0.0001
renal failure	33.3	33.2	34.8	0.1705
solid tumor without metastasis	3.2	3.0	5.6	< 0.0001
Elixhauser score, mean (SD)	13.5 (26.8)	13.0 (26.5)	20.4 (26.3)	< 0.0001
Household income by Zip code				
1st quartile (1–39,999)	32.2	32.5	27.9	< 0.0001
2nd quartile (40,000 – 50,999)	28.6	28.6	27.8	
3rd quartile (51,000 – 65,999)	22.2	22.2	23.2	
4th quartile (66,000+)	17.0	16.7	21.2	

	Total	Without palliative consult	Palliative consult	p-value
Expected payer				
Medicare	57.3	56.2	70.7	< 0.0001
Medicaid	17.8	18.3	11.6	
Private insurance	18.2	18.7	12.6	
Self pay	4.1	4.2	2.3	
No charge	0.4	0.4	0.1	
Other	2.3	2.2	2.7	
Hospital bed size				
Small	16.7	16.8	14.4	0.0001
Medium	29.0	29.2	26.3	
Large	54.4	54.0	59.3	
Hospital location				
Rural	8.0	8.3	4.6	< 0.0001
Urban non-teaching	26.2	26.5	22.1	
Urban teaching	65.8	65.2	73.3	
Hospital region				
Northeast	18.0	18.1	16.8	0.0001
Midwest	21.6	21.2	25.9	
South	38.5	38.7	35.5	
West	22.0	22.0	21.8	
Total cost, median (IQR)	$20,423 ($11,951 – $38,305)	$20,198 ($11,923 – $37,891)	$23,524 ($12,466 – $44,645)	< 0.0001
Length of stay, median (IQR)	9 (6 – 16)	9 (6 – 16)	9 (5 – 16)	< 0.0001
Mortality	11.4	8.1	53.0	< 0.0001
MRSA	48.7	48.3	53.4	< 0.0001
Echocardiogram	18.8	19.2	13.4	< 0.0001

Abbreviations

SD: standard deviation, AIDS: acquired immunodeficiency syndrome, CHF: chronic heart failure, DM: diabetes mellitus, IQR: interquartile range, MRSA: methicillin resistant staphylococcus aureus.

Table 2:

Variables associated with palliative care consultation in hospitalized *Staphylococcus aureus* bacteremia patients, National Inpatient Sample, 2014.

	Univariate		Multivariate	
	Odds ratio (95% Cl)	**p value**	**Odds ratio (95% Cl)**	**p value**
Age, mean (SD)				
<65	reference		reference	
65–79	2.21 (1.94 – 2.51)	<.0001	2.2 (1.86 – 2.59)	<.0001
>80	3.73 (3.26 – 4.27)	<.0001	3.47 (2.89 – 4.15)	<.0001
Female	1.10 (0.99 – 1.22)	0.0855	1.11 (0.99 – 1.25)	0.0611
Race/ethnicity				
White	reference			
Black	0.75 (0.64 – 0.88)	0.0003	0.83 (0.7 – 0.98)	0.0303
Hispanic	0.66 (0.53 – 0.82)	0.0001	0.79 (0.63 – 0.98)	0.0355
Asian	0.73 (0.48 – 1.11)	0.1464	0.61 (0.39 – 0.94)	0.0244
Native American	0.65 (0.32 – 1.32)	0.2303	0.75 (0.36 – 1.57)	0.4493
Other	0.89 (0.62 – 1.29)	0.5477	0.92 (0.63 – 1.34)	0.6614
AIDS	0.68 (0.21 – 2.17)	0.5139		
Alcohol	1.00 (0.79 – 1.26)	0.9754		
Rheumatoid arthritis/collagen vascular disease	0.83 (0.62 – 1.10)	0.1882		
CHF	1.67 (1.48 – 1.87)	<.0001	0.95 (0.82 – 1.09)	0.46
chronic pulmonary disease	1.16 (1.03 – 1.31)	0.016	0.92 (0.81 – 1.05)	0.2189
coagulopathy	1.93 (1.71 – 2.17)	<.0001	1.13 (0.97 – 1.32)	0.1236
depression	0.82 (0.69 – 0.97)	0.0217	1.07 (0.89 – 1.28)	0.4954
DM	0.77 (0.67 – 0.88)	0.0001	0.69 (0.6 – 0.8)	<.0001
DM with chronic complication	0.62 (0.52 – 0.73)	<.0001	0.73 (0.61 – 0.88)	0.0006
drug	0.45 (0.35 – 0.57)	<.0001	0.85 (0.65 – 1.12)	0.2526
Liver disease	1.27 (1.06 – 1.52)	0.0103	1.38 (1.13 – 1.68)	0.0016
lymphoma	1.26 (0.88 – 1.80)	0.204		
metastatic cancer	3.04 (2.48 – 3.72)	<.0001	1.84 (1.46 – 2.32)	<.0001
obesity	0.60 (0.51 – 0.71)	<.0001	0.92 (0.77 – 1.1)	0.3713
renal failure	1.05 (0.94 – 1.17)	0.3922		
solid tumor without metastasis	1.92 (1.51 – 2.43)	<.0001	1.4 (1.09 – 1.81)	0.0086
Elixhauser score	1.05 (1.05 – 1.05)	<.0001	1.04 (1.03 – 1.04)	<.0001
Median household income by Zip code				
1st quartile	reference			
2nd quartile	1.14 (0.99 – 1.31)	0.0754	1.06 (0.92 – 1.24)	0.4182
3rd quartile	1.25 (1.07 – 1.45)	0.0038	1.06 (0.9 – 1.25)	0.4593
4th quartile	1.50 (1.29 – 1.75)	<.0001	1.2 (1.01 – 1.42)	0.0371
Expected payer				

	Univariate		Multivariate	
	Odds ratio (95% Cl)	**p value**	**Odds ratio (95% Cl)**	**p value**
Medicare	reference			
Medicaid	0.51 (0.43 – 0.61)	<.0001	1.12 (0.91 – 1.39)	0.2842
Private insurance	0.56 (0.48 – 0.66)	<.0001	0.93 (0.77 – 1.13)	0.4696
Self pay	0.44 (0.31 – 0.63)	<.0001	1.13 (0.77 – 1.64)	0.5367
No charge	0.26 (0.06 – 1.05)	0.059	0.7 (0.17 – 2.94)	0.6308
Other	0.99 (0.71 – 1.38)	0.9536	1.78 (1.25 – 2.54)	0.0014
Hospital bed size				
Small	reference			
Medium	1.06 (0.89 – 1.26)	0.5313	1.11 (0.93 – 1.33)	0.2594
Large	1.30 (1.11 – 1.52)	0.0013	1.42 (1.21 – 1.68)	<.0001
Hospital location				
Rural	reference			
Urban non-teaching	1.51 (1.15 – 1.98)	0.0028	0.65 (0.49 – 0.86)	0.0027
Urban teaching	2.06 (1.60 – 2.66)	<.0001	1.56 (1.37 – 1.78)	<.0001
Hospital region				
Northeast	reference			
Midwest	1.37 (1.16 – 1.62)	0.0003	1.53 (1.28 – 1.83)	<.0001
South	0.97 (0.83 – 1.13)	0.6872	1.11 (0.94 – 1.31)	0.2067
West	1.12 (0.94 – 1.33)	0.2019	1.29 (1.08 – 1.56)	0.0057
MRSA	1.22 (1.10 – 1.36)	0.0003	1.19 (1.07 – 1.33)	0.0021
Echocardiogram	0.66 (0.57 – 0.77)	<.0001	0.63 (0.54 – 0.74)	<.0001

Abbreviations

SD: standard deviation, AIDS: acquired immunodeficiency syndrome, CHF: chronic heart failure, DM: diabetes mellitus, IQR: interquartile range, MRSA: methicillin resistant staphylococcus aureus.

Table 3:

Total charge and length of stay in patients with palliative care consult after adjustment with age, sex, race, and mortal score

	PCC vs. No PCC			
Outcome	**Unadjusted**	**p-value**	**Adjusted**	**p-value**
Total cost, MR (CI)	1.15 (1.10 – 1.20)	<.0001	1.10 (1.05 – 1.15)	<.0001
Length of stay, MR (CI)	0.97 (0.96 – 0.99)	<.0001	0.95 (0.93 – 0.96)	<.0001
Death, OR (CI)	12.80 (11.47 – 14.28)	<.0001	9.60 (8.53 – 10.81)	<.0001

Abbreviations

PCC: palliative care consult, Cl: confidential interval, OR: odds ratio, MR: mean ratio