Characteristics of Hospitalized Patients with Acute Bacterial Skin and Skin Structure Infections (ABSSSI) Treated with Vancomycin and at Greatest Risk for Prolonged Hospital Length of Stay in an Integrated Delivery Network (IDN)

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ABSTRACT

Background: Care for ABSSSI patients places a major financial burden on the US healthcare system, largely due to hospitalization costs. Limited data are available on populations at greatest risk for prolonged hospital length of stay (LOS). This study identified adult patients who were hospitalized with ABSSSI, treated with vancomycin, and at greatest risk for prolonged LOS (at least 8 days).

Methods: A retrospective study of adult patients hospitalized with a primary diagnosis of ABSSSI was done using the Geisinger IDN medical encounter 2010-2015 database. All study patients were required to have at least 1 year enrollment in the IDN before their first ABSSSI diagnosis during the study period (index date). Inclusion criteria also required a prescription of vancomycin on day 1 or 2 of a hospitalization for ABSSSI and continued for at least 2 days. Demographics and clinical characteristics of patients in the overall cohort and in the subgroup with LOS ≥ 8 days were examined. Multivariate logistic modeling with stepwise variable selection (p=0.2 for entry and p=0.05 for stay in the final model) was used to determine predictors for the prolonged length of stay.

Results: Among 651 patients hospitalized with a primary diagnosis of ABSSSI in the final cohort, additional diagnoses at admission included cellulitis (84.8%), major abscess (42.7%), lower extremity ulcer (21.0%), post-surgical wound infection (8.1%), and post-traumatic wound infection (5.5%). Nearly 70% had a Charlson comorbidity index (CCI) score of 0 or 1, and 35.0%, 42.7% and 22.3% were classified as ERON Classes I-II, III and IV, respectively. Demographic characteristics included male (57.0%), age 65+ (39.0%), BMI 36+ (31.5%), current smokers (28.3%), and past smokers (32.6%). About half (47.2%) had commercial insurance and 38.6% had Medicare. Prior medical history included previous ABSSSI (1.7%) and diabetes with complications (4.1%) and without (8.8%). Overall, the geometric mean (median, SD) LOS was 5.9 (6.0, 1.7) days. There were 183 (28.1%) in the cohort who were hospitalized ≥ 8 days. Of those 183 patients, 114 (62.3%) had a CCI score of 0-1 and most were ERON Class III (42.6%) or Class IV (29.5%). Additionally, of patients hospitalized ≥ 8 days, 9.3% were readmitted within 30 days. In contrast, of patients with LOS <8 days, 4.3% were readmitted within 30 days. Severity of illness, as measured by the ERON classification, was associated with increased LOS in the cohort. Controlling for other covariates, hospitalized patients in the higher severity ERON Class IV had 2.3 times the odds (95% CI: 1.4-3.7) of staying in the hospital for at least 8 days compared to those in the lower severity ERON classes I-II. In the multivariate model where ERON class was not included as a covariate, both diabetes (OR=2.2, 95% CI: 1.4-3.5) and lower extremity ulcer (OR=2.1, 95% CI: 1.4-3.2) were statistically significantly associated with LOS ≥ 8 days.

Conclusions: Approximately one-fifth of ABSSSI patients were hospitalized for at least 8 days, and the majority of those patients had no or only one comorbidity. Readmission rates for patients with prolonged LOS were higher than those with a LOS < 8 days. Older age, severity ERON class IV, diabetes, lower extremity ulcer and major abscess were associated with the prolonged LOS. These findings provide important leads for further prospective research as they suggest that many patients without comorbid conditions are hospitalized for ABSSSIs for prolonged periods of time, while a robust association exists between ABSSSI severity and prolonged LOS.

INTRODUCTION

- Care for ABSSSI patients places a major financial burden on the US healthcare system, largely due to hospitalization costs
- Limited data are available on populations at greatest risk for prolonged hospital length of stay (LOS)
- This study identified adult patients who were hospitalized with ABSSSI, treated with vancomycin, and at greatest risk for prolonged LOS (at least 8 days)

RESULTS

- A total of 651 ABSSSI patients were hospitalized during the study period.
- The mean LOS for hospitalized patients was 7 days (SD = 5; Median = 6.0)
- Demographic and clinical characteristics of 651 hospitalized ABSSSI patients who received Vancomycin IV on hospitalization day 1 or 2 and continued for at least 2 days are shown in **Table 1**
  - 57.0% were male, 39.0% were age 65+, 31.5% had BMI of 36+, and 28.3% were current smokers
  - About half (47.2%) had commercial insurance and 38.6% had Medicare.
  - Diagnoses at admission included cellulitis (84.8%), major abscess (42.7%), lower extremity ulcer (21.0%), post-surgical wound infection (8.1%), and post-traumatic wound infection (5.5%)
  - 68.2% of patients had CCI ≤1 and 67.3% had CCI=0
  - 8.6% of patients were ERON class I, 26.4% were ERON class II, 42.7% were ERON class III, and 22.3% were ERON class IV
- Bivariate associations between baseline characteristics and LOS ≥ 8 days are shown in **Table 1**
  - Of 651 hospitalized patients, 183 (28.1%) had a hospital length of stay greater than or equal to 8 days

RESULTS

- Results of the multivariate analyses are shown in **Tables 2 and 3**
  - The result of the multivariate model where ERON class was included as a covariate indicated that being 65+ compared to 18-64, ERON class IV, having diabetes, lower extremity ulcer, and major abscess all statistically significantly increased the odds of having prolonged LOS
  - In the multivariate model without ERON class included as a covariate, both diabetes and lower extremity ulcer were statistically significantly associated with prolonged length of stay

Table 1. Demographic and clinical characteristics of 651 hospitalized ABSSSI patients who received Vancomycin IV on hospitalization day 1 or 2 and continued for at least 2 days

Characteristics	All		LOS < 8 days		LOS ≥ 8 days		p value for difference
	n	%	n	%	n	%	
Overall	651	100.0	468	100.0	183	100.0	
Gender							0.2374
Male	371	57.0	260	55.6	111	60.7	
Female	280	43.0	208	44.6	72	39.3	
Age group							0.2921
18-64	397	61.0	298	63.7	99	54.1	
≥ 65	254	39.0	170	36.3	84	45.9	
Race							0.2921
White	639	98.2	461	98.5	178	97.3	
Black	12	1.8	7	1.5	5	2.7	
Smoking Status							0.0238
Never smoking	244	37.5	173	37.0	71	38.8	
Current smoking + past smoking	396	60.8	291	62.2	105	57.4	
Others/Unknown	11	1.7	4	0.9	7	3.8	
BMI group							0.5874
BMI ≤ 30	317	48.7	231	49.4	86	47.0	
BMI > 31	334	51.3	237	50.6	97	53.0	
Payer							0.8238
Commercial	307	47.2	223	47.6	84	45.9	
Medicare	251	38.6	177	37.8	74	40.4	
Others/Unknown	93	14.3	68	14.5	25	13.7	
12-month baseline comorbidity							
ABSSSI (not including current ABSSSI)	11	1.7	10	2.1	1	0.5	0.1570
Asthma	9	1.4	6	1.3	3	1.6	0.7256
Burns	2	0.3	2	0.4	0	0	NA
Cerebrovascular disease	16	2.5	10	2.1	6	3.3	0.3976
Congestive heart failure	30	4.6	19	4.1	11	6.0	0.2858
Chronic pulmonary diseases	37	5.7	26	5.6	11	6.0	0.8215
COPD/Bronchitis	26	4.0	18	3.8	8	4.4	0.7583
Other chronic pulmonary disease	12	1.8	8	1.7	4	2.2	0.6846
Acute respiratory failure	13	2.0	7	1.5	6	3.3	0.1438
Clostridium difficile	3	0.5	2	0.4	1	0.5	0.8402
Coronary heart disease	87	13.4	60	12.8	27	14.8	0.5145
Myocardial infarction	3	0.5	2	0.4	1	0.5	0.8402
Unstable cardiac disease	67	10.3	48	10.3	19	10.4	0.9620
Other coronary heart disease	42	6.5	27	5.8	15	8.2	0.2571
Dementia	6	0.9	4	0.9	2	1.1	0.7750
Hemiplegia/Paraplegia	2	0.3	2	0.4	0	0	NA
Immunocompromising conditions	52	8.0	42	9.0	10	5.5	0.1376
HIV/AIDS	1	0.2	1	0.2	0	0	NA
Cancer	47	7.2	37	7.9	10	5.5	0.2793
Other immunocompromising conditions	12	1.8	10	2.1	2	1.1	0.3734
Neutropenia, leukocytopenia	9	1.4	6	1.3	3	1.6	0.7256
Liver disease	16	2.5	10	2.1	6	3.3	0.3976
Non-severe liver disease	11	1.7	6	1.3	5	2.7	0.1969
End-stage liver disease (e.g., ascites, hepatic encephalopathy)	5	0.8	4	0.9	1	0.5	0.6855
Malnutrition	4	0.6	2	0.4	2	1.1	0.3286
Rheumatoid Arthritis	3	0.5	3	0.6	0	0	NA
Peripheral vascular disease	21	3.2	10	2.1	11	6.0	0.0119
Acute renal failure	27	4.1	13	2.8	14	7.7	0.0051

RESULTS

Characteristics	All		LOS < 8 days		LOS ≥ 8 days		p value for difference
	n	%	n	%	n	%	
Dialysis	4	0.6	2	0.4	2	1.1	0.3286
Severe renal disease	7	1.1	3	0.6	4	2.2	0.0858
Diabetes	84	12.9	46	9.8	38	20.8	0.0002
Diabetes without complications	57	8.8	32	6.8	25	13.7	0.0056
Diabetes with complications	27	4.1	14	3.0	13	7.1	0.0180
Infections of the musculoskeletal system	1	0.2	1	0	0	NA	0
Bursitis	4	0.6	3	0.6	1	0.5	
Seizure	8	1.2	6	1.3	2	1.1	0.8439
Other infections (Bacteremia, UTI, IAI)							
Bacteremia	3	0.5	2	0.4	1	0.5	0.8402
UTI	20	3.1	12	2.6	8	4.4	0.2296
Intra-abdominal Infections	3	0.5	2	0.4	1	0.5	0.8402
Total	26	4.0	16	3.4	10	5.5	0.2308
Charlson Comorbidity Index (CCI)							0.0430
0-1	444	68.2	330	70.5	114	62.3	
2+	207	31.8	138	29.5	69	37.7	
Pre-Index Hospitalizations							
12-month pre-index hospitalizations	195	30.0	137	29.3	58	31.7	0.5445
6-month pre-index hospitalizations	156	24.0	108	23.1	48	26.2	0.3969
3-month pre-index hospitalizations	127	19.5	88	18.8	39	21.3	0.4679
1-month pre-index hospitalizations	86	13.2	59	12.6	27	14.8	0.4670
Pre-Index ER Visits							
12-month pre-index ER visits	159	24.4	120	25.6	39	21.3	0.2477
6-month pre-index ER visits	119	18.3	91	19.4	28	15.3	0.2188
3-month pre-index ER visits	87	13.4	65	13.9	22	12.0	0.5291
1-month pre-index ER visits	45	6.9	31	6.6	14	7.7	0.6426
12-month pre-index hospital based outpatient visits	179	27.5	130	27.8	49	26.8	0.7969
12-month baseline (not including index date) systemic steroid use	174	26.7	122	26.1	52	28.4	0.5430
Index culture drawn in ER	425	65.3	291	62.2	134	73.2	0.0078
Pre-Admission Characteristics							
Prior location, including LTAC, nursing homes	9	1.4	8	1.7	1	0.5	0.2533
Surgery without implant in prior month	28	4.3	21	4.5	7	3.8	0.7082
Surgery involving implant in prior 6 months	1	0.2	0	0	1	0.5	NA
Diagnosis at Admission							
Major abscess	278	42.7	192	41.0	86	47.0	0.1663
Lower extremity ulcer	137	21.0	79	16.9	58	31.7	<.0001
Post-surgical wound infection	53	8.1	38	8.1	15	8.2	0.9742
Post-traumatic wound infection	36	5.5	25	5.3	11	6.0	0.7371
Cellulitis	552	84.8	405	86.5	147	80.3	0.0473
ABSSSI severity classes (ERON)[a]							0.0110
ERON CLASS I	56	8.6	47	10.0	9	4.9	
ERON CLASS II	172	26.4	130	27.8	42	23.0	
ERON CLASS III	278	42.7	200	42.7	78	42.6	
ERON CLASS IV	145	22.3	91	19.4	54	29.5	
Admission Source							0.4233
Admit from ED	523	80.3	370	79.1	153	83.6	
Routine Admission	17	2.6	13	2.8	4	2.2	
Others	111	17.1	85	18.2	26	14.2	
Oral antibiotics within 30 days prior to index admissions							
Bactrim/Cephalexin/Cipro/Levo/Clinda	64	9.8	46	9.8	18	9.8	0.9978
Quinolones	20	3.1	11	2.4	9	4.9	0.0879
Cephalosporines	32	4.9	26	5.6	6	3.3	0.2271
Bactrim	22	3.4	18	3.8	4	2.2	0.2919
Clindamycin	3	0.5	3	0.6	0	0	NA
Ciprofloxacin	13	2.0	7	1.5	6	3.3	0.1438
Levofloxacin	8	1.2	4	0.9	4	2.2	0.1658
Cephalexin	30	4.6	24	5.1	6	3.3	0.3116
Vancomycin switch to Daptomycin or Linezolid during inpatient stay	1	0.2	1	0.2	0	0	NA

[a] ERON CLASSES originally defined in Eron LJ, et al. Managing skin and soft tissue infections: expert panel recommendations on key decision points. *J Antimicrob Chemother*. 2003;52(suppl 1):i3-i17. doi: 10.1093/jac/dkg466.

RESULTS

Table 2. Factors associated with the prolonged length of hospital stay ≥ 8 days in the final model for the cohort of 651 hospitalized ABSSSI patients who received Vancomycin IV on hospitalization day 1 or 2 and continued for ≥ 2 days*

Characteristics	Odds Ratio	95% Wald Confidence Limits		p value
Age 65 + vs 18-64	1.56	1.08	2.25	0.0186
Diabetes	2.42	1.48	3.95	0.0004
Lower extremity ulcer	2.20	1.45	3.33	0.0002
Cellulitis	0.47	0.28	0.78	0.0035
Major abscess	1.62	1.10	2.39	0.0137
ABSSSI severity classes (ERON)				
ERON CLASS I-II (reference)	1.00			
ERON CLASS III	1.41	0.92	2.16	0.1191
ERON CLASS IV	2.28	1.41	3.70	0.0008

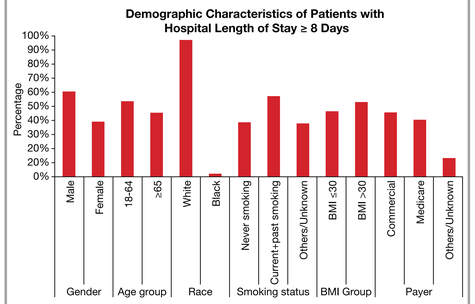
*Selected variables in Table 1 were considered for inclusion into the full multivariate model if they were present in ≥ 5% of the sample and subject matter knowledge. Covariates remained in the final multivariate model by stepwise variable selection method, p for entry = 0.2, and p to remain in the model = 0.05.

Table 3. Factors associated with prolonged length of hospital stay (≥ 8 days) in the final model for the cohort of 651 hospitalized ABSSSI patients who received Vancomycin IV on hospitalization day 1 or 2 and continued for ≥ 2 days* (Model without ERON Classes)

Characteristics	Odds Ratio	95% Wald Confidence Limits		p value
Diabetes	2.20	1.36	3.54	0.0013
Lower extremity ulcer	2.14	1.44	3.19	0.0002

*Selected variables in Table 1 were considered for inclusion into the full multivariate model if they were present in ≥ 5% of the sample and subject matter knowledge. Covariates remained in the final multivariate model by stepwise variable selection method, p for entry = 0.2, and p to remain in the model = 0.05.

Figure 1. Distributions of demographic characteristics for 183 hospitalized ABSSSI patients who received Vancomycin IV on hospitalization day 1 or 2 and continued for ≥ 2 days with hospital LOS ≥ 8 days (total n=651) (%)



RESULTS

Figure 2. Distributions of clinical characteristics for 183 hospitalized ABSSSI patients who received Vancomycin IV on hospitalization day 1 or 2 and continued for ≥ 2 days with hospital LOS ≥ 8 days (total n=651) (%)

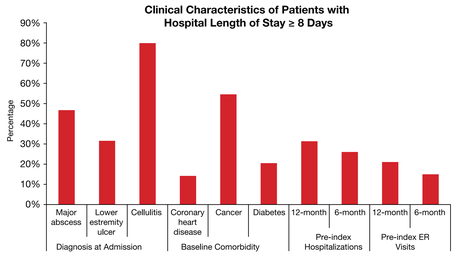
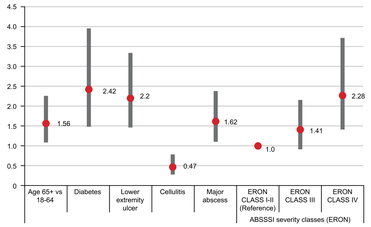


Figure 3. Factors associated with hospital stay ≥ 8 days of hospitalized ABSSSI patients (n=651) who received Vancomycin IV on hospitalization day 1 or 2 and continued for ≥ 2 days



CONCLUSIONS

- Approximately one-fifth of ABSSSI patients were hospitalized for at least 8 days
- The majority of patients with LOS ≥ 8 days had only one or no comorbidity
- Readmission rates for patients with prolonged LOS were higher than those with a LOS < 8 days
- Older age, severity ABSSSI ERON class IV, diabetes, lower extremity ulcer (not including diabetic food infections), and major abscess were significantly associated with the prolonged LOS
- These findings provide important leads for further prospective research as it suggests that many patients without comorbid conditions are hospitalized for ABSSSIs for prolonged periods of time, while a robust association exists between ABSSSI severity and prolonged LOS

ACKNOWLEDGMENTS

This study was sponsored by Paratek Pharmaceuticals, Inc. Medical editorial assistance, funded by Paratek Pharmaceuticals, Inc, was provided by Healthcare Consultancy Group.

The authors wish to thank the subjects and investigators involved in this study.

Presented at: American Society for Microbiology Microbe 2017; June 1-5, 2017; New Orleans, LA.