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Bacterial Pathogen–Positive Patients Hospitalised With Suspected Community-Acquired Bacterial Pneumonia (CABP) Have Worse Outcomes Than Those With Negative or No Culture: A Multi-Centre Retrospective Cohort Study

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INTRODUCTION & PURPOSE

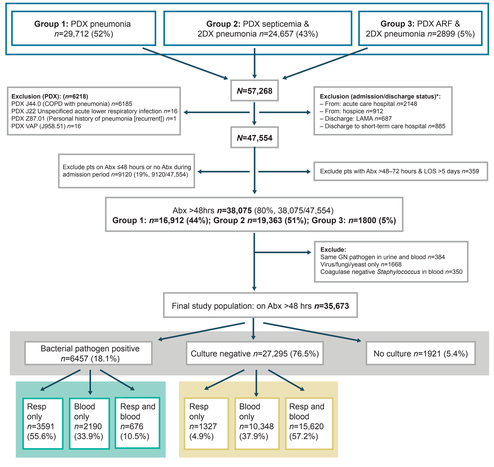
- Community-acquired pneumonia affects >1.5 million admissions each year in the United States and is associated with significant morbidity and mortality[1]
- The microbiological diagnosis of suspected community-acquired bacterial pneumonia (CABP) has proven difficult with standard culture methods and can vary by clinical setting. Failure to identify a pathogen in most cases of pneumonia, including healthcare and non–healthcare-associated pneumonia, complicates efforts at appropriate empiric treatment and antimicrobial stewardship
- We hypothesised that the outcomes among patients hospitalised with CABP would differ based on whether they had a sample taken for pathogen identification and whether such pathogen was identified
- We explored the impact of guideline-concordant empiric therapy on the outcomes in these three groups

METHODS

Study Design

- This was a retrospective cohort study of data from 104 US acute care hospitals from October 2015 through December 2017 (**Figure 1**)

Figure 1. Case Tree for Community-Acquired Bacterial Pneumonia



ARF=acute respiratory failure; Abx=antimicrobial therapy; COPD=chronic obstructive pulmonary disease; GN=Gram-negative pathogens; LAMA=left against medical advice; LOS=length of stay; PDX=primary diagnosis code, International Classification of Diseases, Tenth Revision; pts=patients; VAP=ventilator-associated pneumonia; 2DX=secondary diagnosis code, International Classification of Diseases, Tenth Revision.
*Reasons for exclusion were not mutually exclusive.

Data Source

- BD Insights Research Database (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), including microbiological results, general laboratory results, pharmacy orders, and administrative data

METHODS (continued)

Patients

- Adult patients (aged ≥18 years) hospitalised for suspected CABP
- Suspected CABP was identified by any of the following International Classification of Diseases, Tenth Revision (ICD-10) code algorithms plus evidence of antimicrobial treatment for >48 hours:
  - In addition to a positive respiratory and/or blood culture result, urine antigen tests were used to identify *Streptococcus pneumoniae* and *Legionella pneumophila*; blood serologies were used to identify *Mycoplasma pneumoniae*
  - Primary ICD-10 diagnosis code for pneumonia
  - Primary ICD-10 diagnosis code for sepsis AND a secondary diagnosis code for pneumonia
  - Primary ICD-10 diagnosis code for acute respiratory failure AND a secondary diagnosis code for pneumonia
- Healthcare-associated pneumonia (HCAP) was identified as an admission from a skilled nursing/long-term care facility, previous hospital discharge within 90 days, dialysis, or a cancer diagnosis[2]

Outcomes Evaluated

- In-hospital death
- Length of stay (LOS)
- Total hospital stay cost as calculated by each institution (eg, cost accounting system)

Statistical Analysis

- Univariate analysis on patient characteristics and outcomes based on the results of diagnostic testing
- Mixed models to estimate the impact of pathogen identification from blood and/or respiratory source on outcomes compared with those for which a pathogen was not identified, or where culture was not done, adjusting for the following
  - Demographics (eg, age and sex)
  - Comorbidities (Agency for Healthcare Research and Quality [AHRQ] Comorbidity Software [Elixhauser Comorbidity Index])[3]
  - Healthcare-associated status
  - Intensive care unit (ICU) admission status within 3 days of admission
  - Acute Laboratory Risk of Mortality Score (ALaRMS), a published clinical severity score incorporating demographics and 24 laboratory test results on admission[4]
  - Infectious Diseases Society of America (IDSA) guidelines[5] concordance/discordance with empiric treatment status defined as
    - Guideline concordance in the non-ICU during the admission period: antimicrobial order(s) for at least either a respiratory fluoroquinolone (R-FQ) or β-lactam + macrolide or R-FQ
    - Guideline concordance in the ICU during the admission period: antimicrobial order(s) for at least a β-lactam + macrolide or FQ
    - Episodes not meeting the above were considered guideline discordant

RESULTS

- Among 35,673 adults with suspected CABP, 33,752 (94.6%) had a respiratory culture, urine antigen test, or blood culture obtained, of which 6457 (18.1%) had a bacterial pathogen identified
- Compared to those with a negative or no culture, bacterial pathogen–positive patients
  - Were younger (mean [SD] age, 66 [16.2] vs 69 [16.4] vs 71 [16.1] years, respectively; *P*<0.0001)
  - Had more comorbidities (mean [SD] Elixhauser Comorbidity index, 4.8 [2.3] vs 4.3 [2.3] vs 4.1 [2.4], respectively; *P*<0.0001)
  - Were more likely to be admitted to the ICU (46.4% vs 26.1% vs 12.7%, respectively; *P*<0.0001)
  - Were in the highest quartile of ALaRMS score (37.2% vs 21.7% vs 13.7%, respectively; *P*<0.0001)
  - Were more likely to receive empiric therapies that were discordant to IDSA guidelines (55.0% vs 40.1% vs 42.3%, respectively; *P*<0.0001)
  - Had similar HCAP prevalence (~46%; **Table 1**)
- The unadjusted mortality rate was highest among bacterial pathogen–positive patients and lowest when no culture was obtained (10.4% vs 5.6% vs 3.7%, respectively; *P*<0.0001)
  - The risk-adjusted mortality odds ratio for bacterial pathogen–positive patients was 1.22 (95% CI: 1.07–1.39; *P*=0.0026) compared with the culture-negative group (**Table 2**)

RESULTS (continued)

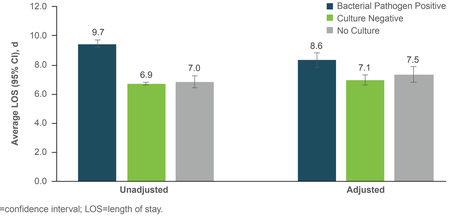
Table 1. Patient Characteristics by Bacterial Pathogen–Positive, Culture-Negative, or No Culture Status

Variable	Overall *n*=35,673		Bacterial Pathogen Positive *n*=6457 (18.1%)		Culture Negative *n*=27,295 (76.5%)		No Culture *n*=1921 (5.4%)		*P* Value
	n	%	*n*	%	*n*	%	*n*	%	
Age, y									
≤60	10,228	28.7	2090	32.4	7645	28.0	493	25.7	<0.0001
61–70	7864	22.0	1597	24.7	5879	21.5	388	20.2	
71–80	8412	23.6	1471	22.8	6514	23.9	427	22.2	
>80	9169	25.7	1299	20.1	7257	26.6	613	31.9	
Sex									
Male	17,306	48.5	3447	53.4	13,038	47.8	821	42.7	<0.0001
Female	18,367	51.5	3010	46.6	14,257	52.2	1100	57.3	
HCA admission									
Yes	16,518	46.3	3020	46.8	12,623	46.3	875	45.6	<0.5937
No	19,155	53.7	3437	53.2	14,672	53.8	1046	54.5	
ICU admission									
Yes	10,376	29.1	2997	46.4	7136	26.1	243	12.7	<0.0001
No	25,297	70.9	3460	53.6	20,159	73.9	1678	87.4	
ALaRMS (clinical severity score)[4]									
1st quartile	9152	25.7	1163	18.0	7326	26.8	663	34.5	<0.0001
2nd quartile	9015	25.3	1288	20.0	7147	26.2	580	30.2	
3rd quartile	8918	25.0	1603	24.8	6900	25.3	415	21.6	
4th quartile	8588	24.1	2403	37.2	5922	21.7	263	13.7	
AHRQ Comorbidity Index[3]									
Mean (SD)	4.4 (2.4)		4.8 (2.3)		4.3 (2.3)		4.1 (2.4)		<0.0001
Median (IQR)	4 (3–6)		5 (3–6)		4 (3–6)		4 (2–6)		
IDSA 2003 Empiric Therapy Guideline[5]									
Discordant	15,318	42.9	3548	55.0	10,957	40.1	813	42.3	<0.0001
Concordant	20,355	57.1	2909	45.1	16,338	59.9	1108	57.7	

AHRQ=Agency for Healthcare Research and Quality; ALaRMS=Acute Laboratory Risk of Mortality Score; HCA=healthcare-associated; ICU=intensive care unit; IDSA=Infectious Diseases Society of America; IQR=interquartile range; SD=standard deviation.

- The unadjusted mean hospital LOS for bacterial pathogen–positive patients vs those with a negative or no culture was 9.7 vs 6.9 vs 7.0 days, respectively; *P*<0.0001
  - The risk-adjusted incremental LOS was 1.4 days longer for the bacterial pathogen–positive group compared with the bacterial-negative group (*P*<0.0001; **Figure 2**)

Figure 2. Unadjusted and Adjusted LOS by Bacterial Pathogen–Positive Status



CI=confidence interval; LOS=length of stay.

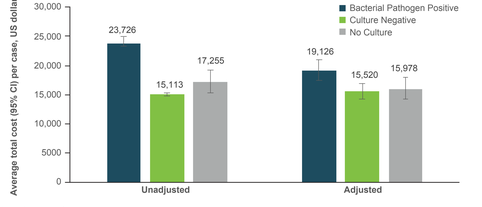
Table 2. Multivariable Mixed Model for Mortality

Variable	OR	95% CI LL	95% CI UL	*P* Value
Bacterial status				
Bacterial pathogen positive	1.22	1.07	1.39	0.0026
No culture	0.94	0.74	1.20	0.6234
Negative culture	Reference			
ICU status				
ICU	3.55	3.19	3.96	<0.0001
Non-ICU	Reference			
HCA status				
HCA	1.40	1.25	1.57	<0.0001
Non-HCA	Reference			
ALaRMS (clinical severity score)[4]				
1st quartile	Reference			
2nd quartile	2.14	1.63	2.79	<0.0001
3rd quartile	3.64	2.69	4.92	<0.0001
4th quartile	7.68	5.80	10.17	<0.0001
Age, y				
≤61	Reference			
61–70	1.14	0.98	1.33	0.1017
71–80	1.35	1.18	1.55	<0.0001
>80	1.47	1.24	1.75	<0.0001
Sex				
Male	1.16	1.04	1.30	0.008
Female	Reference			
AHRQ Comorbidity Index[3]	1.09	1.07	1.12	<0.0001
IDSA 2003 Empiric Therapy Guideline[5]				
Discordant	1.12	1.02	1.23	0.0174
Concordant	Reference			

AHRQ=Agency for Healthcare Research and Quality; ALaRMS=Acute Laboratory Risk of Mortality Score; CI=confidence interval; HCA=healthcare-associated; ICU=intensive care unit; IDSA=Infectious Diseases Society of America; LL=lower limit; OR=odds ratio; UL=upper limit.

- The unadjusted total hospital costs were highest among the bacterial pathogen–positive group vs those with a negative or no culture ($23,726 vs $15,113 vs $17,255, respectively; *P*<0.0001)
  - The risk-adjusted incremental cost was $3606 higher per case for the bacterial pathogen–positive group compared with the bacterial-negative group (*P*<0.0001; **Figure 3**)

Figure 3. Unadjusted and Adjusted Total Cost by Bacterial Pathogen–Positive Status



CI=confidence interval.

Strengths and Limitations

- The strength of this study is that it was a regionally distributed large multicentre evaluation in the US and thus generalisable to a broader population
- To avoid limitations associated with solely relying on claims data, this analysis incorporated other clinical data elements (eg, culture/serology results, measures of clinical severity of illness) and pharmacy orders to define the cases
- Because respiratory culture quality can hinder the definitive verification of the causative pathogen for suspected CABP, we referenced "suspected" CABP in this study
- This was a retrospective cohort analysis that did not include chart review and chest radiograph evaluation for suspected CABP

CONCLUSIONS

- Suspected CABP remains a significant burden, resulting in substantial mortality, morbidity, and cost
- Patients with an identified bacterial pathogen had a higher mortality, longer LOS, and higher total cost than those with negative or no culture
- The vast majority (95%) of patients hospitalised with suspected CABP had respiratory and/or blood cultures obtained, of which one-fifth identified a bacterial pathogen
- The impact of discordant therapy by bacterial pathogen–positive status should be further evaluated

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