HHS Public Access

Author manuscript

J Crit Care. Author manuscript; available in PMC 2017 December 01.

Published in final edited form as:

J Crit Care. 2016 December ; 36: 265–271. doi:10.1016/j.jcrc.2016.08.004.

Healthcare-Associated Pneumonia in the ICU: Guideline-Concordant Antibiotics and Outcomes

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Conflict of Interest Statements:

Russell Attridge: none

Christopher Frei: Dr. Frei has received grants outside the submitted work from Bristol Myers Squibb, Pfizer, and Ortho-McNeill Janssen.

Mary Jo Pugh: none

Kenneth Lawson: none

Laurajo Ryan: none

Antonio Anzueto: none

Mark Metersky: Dr. Metersky has served as a speaker for Pfizer (relationship ended in 2011).

Marcos Restrepo: Dr. Restrepo's time is partially protected by Award Number K23HL096054 from the National Heart, Lung, and Blood Institute. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, And Blood Institute, the National Institutes of Health or the Department of Veterans Affairs.

Eric Mortensen: Dr. Mortensen reports grants from NIH received during the conduct of the study.

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Abstract

Purpose—Recent data have not demonstrated improved outcomes when guideline-concordant (GC) antibiotics are given to patients with healthcare-associated pneumonia (HCAP). This study was designed to evaluate the relationship between health outcomes and GC therapy in patients admitted to an ICU with HCAP.

Materials and Methods—We performed a population-based cohort study of patients admitted to >150 hospitals in the U.S. Veterans Health Administration system to compare baseline characteristics, bacterial pathogens, and health outcomes in ICU patients with HCAP receiving either GC-HCAP therapy, GC community-acquired pneumonia (GC-CAP) therapy, or non-GC therapy. The primary outcome was 30-day patient mortality. Risk factors for the primary outcome were assessed in a multivariable logistic regression model.

Results—A total of 3,593 patients met inclusion criteria and received GC-HCAP therapy (26%), GC-CAP therapy (23%), or non-GC therapy (51%). GC-HCAP patients had higher 30-day patient mortality compared to GC-CAP patients (34% vs. 22%, p<0.0001). After controlling for confounders, risk factors for 30-day patient mortality were vasopressor use (OR, 95% CI; 1.67, 1.30–2.13), recent hospital admission (1.53, 1.15–2.02), and receipt of GC-HCAP therapy (1.51, 1.20–1.90).

Conclusions—Our data do not demonstrate improved outcomes among ICU patients with HCAP who received GC-HCAP therapy.

Keywords

pneumonia; critical care; guideline-concordant therapy; health outcomes; antibiotic therapy

INTRODUCTION

The concept of healthcare-associated pneumonia (HCAP) has been surrounded by controversy since its introduction in 2005 [1]. The growing body of HCAP literature has demonstrated that community-dwelling patients admitted to the hospital with pneumonia and HCAP risk factors have more comorbidities, are more severely-ill, and experience higher rates of mortality than similar patients without HCAP risk factors [2–11]. These studies also indicate a higher incidence of multi-drug resistant (MDR) pathogens (e.g., *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* [MRSA]) in patients with HCAP, although some data from specific geographic regions reveal a pathogen distribution more similar to community-acquired pneumonia (CAP), with low absolute rates of MDR pathogens [4,6,7,9].

Multiple studies have correlated guideline-concordant (GC) CAP therapy with improved outcomes in patients with CAP [12]; however, this does not seem to be the case for GC-

HCAP therapy. Several studies of hospitalized patients with HCAP, admitted mostly to medical wards, demonstrated either no effect, or increased mortality, with GC-HCAP therapy [5,13–16], while one found decreased mortality [17]. A study of intensive care unit (ICU) patients (including patients with HCAP, hospital-acquired pneumonia, and ventilator-associated pneumonia) at risk for MDR infections also found increased mortality with GC therapy [18].

There are few data to describe the effect of guideline-concordant antibiotic therapy in a pure cohort of ICU patients with HCAP. In the present study, we examined a cohort of ICU patients with HCAP to compare effects of GC-HCAP therapy and GC-CAP therapy on patient mortality and hospital length-of-stay (LOS).

MATERIALS AND METHODS

This study was performed using administrative data from the U.S. Veterans Health Administration (VHA) to examine pneumonia care and mortality among ICU patients with HCAP. The VHA databases are repositories of clinical data from more than 150 VHA hospitals and 850 VHA clinics. The Institutional Review Boards of The University of Texas Health Science Center at San Antonio and the VA North Texas Health Care System have approved this study.

Patient Eligibility

Similar methods are described in a previous study from our research group [13]. All patients were required to have a discharge diagnosis of pneumonia: either a primary diagnosis of pneumonia/influenza (International Classification of Disease-ninth edition [ICD-9] codes 480.0–483.99 or 485–487) or a secondary discharge diagnosis of pneumonia/influenza with a primary diagnosis of respiratory failure (ICD-9 code 518.81) or sepsis (ICD-9 code 038.xx), in fiscal years 2002 to 2007, and at least one documented HCAP risk factor. HCAP risk factors were defined as hospital admission in the previous 90 days, residence in a nursing home in the previous 90 days, receipt of outpatient intravenous antibiotics in the previous 90 days, and hemodialysis. Patients were also required to be admitted to the ICU and to have received antibiotics within 48 hours of hospital admission. Excluding patients who did not receive antibiotics within 48 hours minimizes the potential inclusion of cases of nosocomial pneumonia.

Baseline Characteristics

ICD-9 codes from outpatient and inpatient care at the time of admission were used to determine baseline characteristics in accordance with the Charlson comorbidity scoring system [19]. Patient race was recorded for white and black patients, and ethnicity was reported for patients identifying themselves as Hispanic. Native Americans, Hawaiians, and patient records missing race information were reported as “other.” Tobacco use was defined as patients with a diagnosis of nicotine dependence, a recorded visit to a VHA tobacco cessation clinic, a current procedural terminology (CPT) treatment code for smoking (99406 or 99407), or an outpatient prescription for a smoking cessation product (Zyban®, varenicline, Nicotrol®, or nicotine replacement). Alcohol abuse/dependence and organ

failure were identified through ICD-9 codes, and medication use in the 90 days prior to admission was documented by medication classes, as previously described [13].

Antibiotic Therapy and Bacterial Pathogens

Current consensus guidelines were reviewed to evaluate antibiotic therapy received within the first 48 hours of hospital admission (Table 1) [1,12]. Patients receiving additional antibiotics beyond the minimum required to satisfy GC-HCAP or GC-CAP therapy remained in their respective treatment groups. The subset of patients who received both GC-HCAP and GC-CAP therapy was considered to have received GC-HCAP therapy. Patients receiving antibiotics that were not concordant with either CAP or HCAP guidelines were considered to have received non-GC therapy.

Pneumonia pathogens were identified using ICD-9 discharge diagnosis codes. Codes used during the study period do not differentiate between methicillin-sensitive *S. aureus* and MRSA; however, HCAP data in the U.S. suggest that methicillin-resistance is present in more than half of all *S. aureus* isolates [2,3,14].

Patient Mortality and Hospital Length-of-Stay

Our primary outcome was 30-day patient mortality. Admission and discharge dates were extracted for each hospital stay and length of stay (LOS) was defined as the date of hospital discharge minus the date of hospital admission plus one day. Mortality was determined using date of death provided by the VHA vital status file.

Statistical Analysis

For bivariable comparisons, a two-tailed alpha ≤0.05 was used for statistical significance. In comparisons among the three treatment groups, GC-HCAP was used as the reference group and was compared with both the GC-CAP and non-GC groups. In our multivariable logistic regression model, a two-tailed alpha ≤0.05 indicated statistical significance.

Patient demographics, baseline characteristics, comorbid conditions, bacterial pathogens, and health outcomes (hospital LOS and mortality) were compared between groups. Dichotomous variables were compared using Chi-square or Fisher’s Exact tests. The Wilcoxon Rank Sum test was used to compare continuous variables after all were tested for normality and were found to have non-normal distributions. A multivariable logistic regression model was used to examine the association between the receipt of GC antibiotics and 30-day patient mortality. Patients who received non-GC therapy were excluded from the regression analysis to isolate the effects of GC therapy (GC-HCAP vs. GC-CAP). We included variables that the investigative team believed were clinically important. Then, those variables were simultaneously entered into the regression model. The dependent variable was 30-day patient mortality and covariates included individual HCAP risk factors, comorbid conditions, mechanical ventilation, vasopressor use, and guideline-concordant antibiotic therapy.

All statistical analyses were conducted using JMP 8.0® (SAS Corp., Cary, NC, USA) and SPSS (SPSS, Inc., Chicago, IL, USA).

RESULTS

Baseline Characteristics

A total of 3,593 patients met inclusion criteria for our study (Figure 1). The most common HCAP risk factor was recent hospitalization in the past 90 days (72%), 27% had more than one HCAP risk factor, and invasive or non-invasive mechanical ventilation was necessary in 42% and 16%, respectively (Table 2).

Of the 3,593 ICU patients with HCAP, 944 (26%) received GC-HCAP therapy and 808 (23%) received GC-CAP therapy. Compared to patients who received GC-CAP therapy, those receiving GC-HCAP therapy were more likely to have been hospitalized in the past 90 days (75% vs. 59%, p<0.0001) and have more than one HCAP risk factor (31% vs. 22%, p<0.0001). Intensity of care was higher in GC-HCAP vs. GC-CAP, with patients receiving GC-HCAP therapy being more likely to receive vasopressors (40% vs. 15%, p<0.0001) and invasive mechanical ventilation (54% vs. 29%, p<0.0001). Patients receiving GC-HCAP therapy were also more likely than patients receiving GC-CAP therapy to experience organ failure (77% vs. 64%, p<0.0001), and when divided by type, had a statistically-significant higher rate of respiratory, cardiovascular, renal, and hematologic failure.

Patients receiving non-GC therapy had baseline characteristics, pathogens, and outcomes that were more similar to patients receiving GC-HCAP therapy vs. GC-CAP therapy. Of 1,841 patients in the non-GC therapy group, 33.4% receiving anti-MRSA therapy, 51.7% received antipseudomonal therapy, and 31.7% received both. Antibiotics with activity against atypical pathogens was prescribed in 40.4% of patients who received non-GC therapy. Macrolides were prescribed in 10.9% of patients who received non-GC therapy.

Bacterial Pathogens

Bacterial pathogens were identified in 26% of the cohort (Table 3). Among these patients, 86% had a single pathogen identified. The three most common pathogens were *S. aureus* (38%), *Pseudomonas* spp. (17%), and *S. pneumoniae* (16%). Patients receiving GC-HCAP therapy were more likely to be culture-positive than patients receiving GC-CAP therapy (36% vs. 19%, p<0.0001) or non-GC therapy (36% vs. 23%, p<0.0001). Compared to patients receiving GC-CAP therapy, those receiving GC-HCAP therapy were more likely to have pneumonia due to potentially drug-resistant pathogens including *S. aureus* (43% vs. 27%, p=0.0005) and *Pseudomonas* spp. (22% vs. 7%, p<0.0001) and less likely to have pneumonia due to *Streptococcus pneumoniae* (12% vs. 33%, p<0.0001) and *H. influenzae* (1% vs. 11%, p<0.0001).

Culture-positive patients with only one HCAP risk factor were more likely to have HCAP secondary to *S. pneumoniae* (19.1%) vs. those with two (9.6%) or three or more HCAP risk factors (10%) [p=0.002]. The opposite was true with pneumonia secondary to *Pseudomonas* spp., although this was not statistically-significant (15.3%, 21.7%, and 20% for one, two, and three or more risk factors, respectively, p=0.08). Rates of *S. aureus* pneumonias were similar regardless of the cumulative number of HCAP risk factors.

Outcomes

The overall 30-day patient mortality rate was 37.6%. Thirty-day patient mortality was significantly higher in patients receiving GC-HCAP vs. GC-CAP therapy (34% vs. 22%, p<0.0001). Patients receiving non-GC therapy experienced a higher rate of 30-day mortality (46%) than either of the other groups (p<0.0001 for both comparisons). The median hospital LOS was 11 days (IQR 6–20). Patients receiving GC-HCAP therapy had a nearly-double hospital LOS compared to patients in the GC-CAP group (median, IQR; 18, 11–34 vs. 10, 6.25–17, p<0.0001) or non-GC group (18, 11–34 vs. 9, 4–16, p<0.0001). Patients who received macrolide therapy (31% of total cohort) had lower 30-day mortality than those patients who did not receive this therapy (24.2% vs. 43.6%, p<0.0001). Additionally, macrolide therapy was a part of most GC-CAP therapy (78.1%), nearly one-third of GC-HCAP therapy (29.9%), and only 10.9% of non-GC therapy.

We compared patients receiving GC-HCAP and GC-CAP therapy in a multivariable logistic regression model, with 30-day patient mortality as the dependent variable (Table 4). After controlling for possible confounders, several characteristics maintained significant associations with 30-day patient mortality, including vasopressor use (odds ratio [OR], 95% confidence interval [CI]; 1.67, 1.30–2.13), recent hospital admission in the past 90 days (1.53, 1.15–2.02), and the receipt of GC-HCAP therapy (1.51, 1.20–1.90).

DISCUSSION

This study examined the effects of guideline-concordant HCAP therapy in ICU patients with HCAP. Our results demonstrated that guideline-concordant HCAP therapy, compared to guideline-concordant CAP therapy, is not associated with improved outcomes and, after controlling for possible confounders, remains a significant risk factor for 30-day patient mortality.

The reason that GC-HCAP therapy did not improve outcomes in this cohort of ICU patients with HCAP is unclear. There are data to indicate that patients with HCAP are more likely to have restrictions on care (e.g., “do not resuscitate” or “not for ICU” orders) that may negatively affect survival [7]. By limiting our cohort to ICU patients, we expected that restrictions on care would have a smaller role, and that GC-HCAP antibiotics might be more likely to be beneficial. Despite this approach, the effects of GC-HCAP therapy remained consistent with prior studies, where GC-HCAP therapy given to patients in the medical ward or mixed ward/ICU patients either increased mortality or had no effect on mortality [5,13–15]. Data using a less strict combination of guideline-similar antibiotics (e.g., one anti-MRSA antibiotic and only one antipseudomonal antibiotic) in mixed ward/ICU cohorts have also demonstrated similar results to our study [15,16].

A recent meta-analysis by Troitino et al had similar findings, with GC-HCAP therapy being associated with increased mortality and no effect on hospital length of stay or time to clinical stability [20]. We do not believe the antibiotic regimens alone are fully responsible for these findings since GC-HCAP antibiotics have a high likelihood of being active against the isolated pathogens; however, we hypothesize that increases in adverse events with GC-HCAP therapy and fewer options for oral transition therapy (and thus increased intravenous

[IV] therapy duration and increased hospital LOS) may have contributed to the association between GC-HCAP therapy and poor outcomes. Duration of IV therapy is responsible for a significant amount of variation among LOS in CAP patients [21], and shorter LOS minimizes exposure to hospital environments that may increase the risk of additional complications, including *Clostridium difficile* infection [22].

A lack of activity against atypical pneumonia pathogens with some GC-HCAP regimens and/or the absence of macrolides (and their potential immunomodulatory effects) may have had a role in poorer outcomes in patients receiving GC-HCAP therapy. While there are data to highlight potential risks of macrolide therapy [23], our finding that patients who received macrolides had lower 30-day mortality compared to those who did not is consistent with other published data [24,25]. Similarly, it is possible that a lower rate of atypical coverage (whether by macrolide or another antibiotic) in conjunction with inconsistent coverage of MRSA and *Pseudomonas* spp. may have been partially responsible for the poor outcomes of the non-GC therapy group.

After controlling for confounders, several other baseline characteristics were significantly-associated with 30-day mortality in our study. Vasopressor use increased mortality, but mechanical ventilation (invasive or non-invasive) did not. Among HCAP risk factors, recent hospital admission was the only factor associated with mortality. In most HCAP data, including the current data, it is the most common reason for classification as HCAP [26]. Several other studies, although not all [6,27], analyzing individual risk factors have indicated that recent hospitalization is an important factor in mortality [9,13,17,28] and in the recovery of resistant pathogens [10,29,30]. Recent hospitalization may be a particularly important HCAP risk factor, and it is prudent for clinicians to be aware of this history, especially in those receiving recent antibiotic therapy [7,9,10,27,28,31,32]. Further studies that review characteristics of recent hospitalizations (e.g., principal hospital diagnosis, receipt of antibiotic therapy) and/or measure changes in functional status as a measure of physiologic reserve may provide further insights into this risk factor.

Many findings, and a recent meta-analysis, support the idea that differences in baseline characteristics (comorbidities, severity of illness, and/or functional status) between patients with CAP and HCAP are a major driving factor behind HCAP mortality [7–9,11,17,27,28,33,34]. A meta-analysis from Chalmers et al, which included 24 eligible studies comparing patients with CAP and HCAP, found significantly higher mortality rates among those with HCAP. However, after including the only four studies that adjusted for age and comorbidities, there was no mortality difference between the two groups [34]. Our cohort of ICU patients with HCAP had increased mortality with GC-HCAP therapy, even after adjusting for comorbidities, which may suggest additional unmeasured confounders.

Our data indicate a high prevalence of *S. aureus* and *Pseudomonas* spp. among patients with HCAP, a finding consistent with the majority of HCAP literature [2,3,13,14,17,31,33,34]. There are data postulating that inappropriate initial antibiotic therapy, partially because of an increased prevalence of *S. aureus* and *Pseudomonas* spp., might have been responsible for higher rates of mortality in HCAP patients [2]; however, there are other data that do not support this notion [7,8,11]. Even among studies in which patients had very low rates of

resistant pathogens and thus, were more likely to receive appropriate initial therapy, the population with HCAP (vs. CAP) had lower survival [4,6,7,9].

If GC-HCAP therapy does not improve outcomes among patients with HCAP, what strategy should be used to initiate empiric therapy in these patients? To date, there is no clear answer to this question. Research of risk factors for potentially drug-resistant pathogens has highlighted the suboptimal predictive ability of the HCAP criteria [31,32,34,35]. Several risk scores have been developed that perform better than the HCAP criteria in selecting resistant pathogens [8,10,35,36], and risk score strategies that separate out MRSA from other MDR organisms might prove to be useful [10,29,30]. Some have demonstrated that severity of illness might be used to help predict pneumonia pathogens [7,8,33]; however, this is not supported by all published studies [10]. In our study, patients with HCAP who received GC-HCAP therapy and GC-CAP therapy had no difference in Charlson Comorbidity Index scores, yet the pneumonia pathogens differed significantly between the two groups.

Quick de-escalation, improved diagnostics, and a restructuring of HCAP criteria may also be beneficial. At least for now, a quick de-escalation strategy, particularly in culture-negative patients, may be useful [37]. Improved and continued evaluation of diagnostics might improve our ability for either early de-escalation, or broadening of empiric therapy, when necessary. Based on the entirety of the HCAP data, calls to restructure criteria and separate recently-hospitalized patients and immunosuppressed patients from HCAP are logical [11,38].

Our study has several limitations that should be addressed. First, while the large, national sample is a strength of our study, the retrospective cohort study design is subject to limitations inherent to this type of research. Patients in the treatment groups had several significant differences in baseline characteristics (as outlined in Table 2). We performed multivariable logistic regression with a number of covariates to minimize confounding; however, this method will not account for unmeasured variables and is not as robust as a randomized, controlled trial. Prospective studies to assess outcomes for pneumonia patients with HCAP and other risk factors for multi-drug resistant pathogens may help validate our results. We also included Charlson Index scores as a measure of comorbidity burden, but we did not have sufficient data to classify patients with conventional pneumonia severity-of-illness scoring systems (e.g., Pneumonia Severity Index, CURB-65) [39,40]. Second, the use of ICD-9 codes to identify pneumonia patients and pathogens enabled us to analyze a large sample size but limited our ability to provide specific microbiologic information that would be of interest, including antibiotic susceptibilities, and may be responsible for a relatively low rate of culture positivity. We acknowledge that our method for identifying pathogens is suboptimal and may have missed some patients with known bacterial etiology because we did not have complete microbiologic information. ICD-9 codes did not allow us to differentiate between methicillin-sensitive and methicillin-resistant *Staphylococcus aureus*, and we were unable to return to individual patient records to review for any serologic tests that may have identified additional pathogens. For these reasons, we did not include the bacterial pathogens in the multivariable regression model. Third, our definition of guideline-concordant therapy was a strict, guideline-based definition. Less strict definitions, to include patients receiving only one antipseudomonal agent, patients receiving empiric

antipseudomonal therapy and not anti-MRSA therapy, or patients receiving anti-MRSA therapy and not antipseudomonal therapy, may provide different results and should continue to be investigated in future studies. Additionally, while we were able to account for some potential confounders, we did not have data available on functional status. A positive relationship between poor outcomes and poor functional status has been demonstrated in some recent HCAP studies [9,28], and this may have had an effect on our finding of increased mortality among patients receiving GC-HCAP therapy.

CONCLUSION

GC-HCAP therapy, compared to GC-CAP therapy, was not associated with improved outcomes in ICU patients with HCAP.

Acknowledgments

This project was supported by a grant from the U.S. National Institute of Nursing Research (R01NR010828). The content is solely the responsibility of the authors and does not necessarily represent the official views of the U.S. National Institute of Nursing Research or the National Institutes of Health.

Abbreviations

GC	guideline-concordant
HCAP	healthcare-associated pneumonia
MDR	multi-drug resistant
LOS	length-of-stay
VHA	Veterans Health Administration

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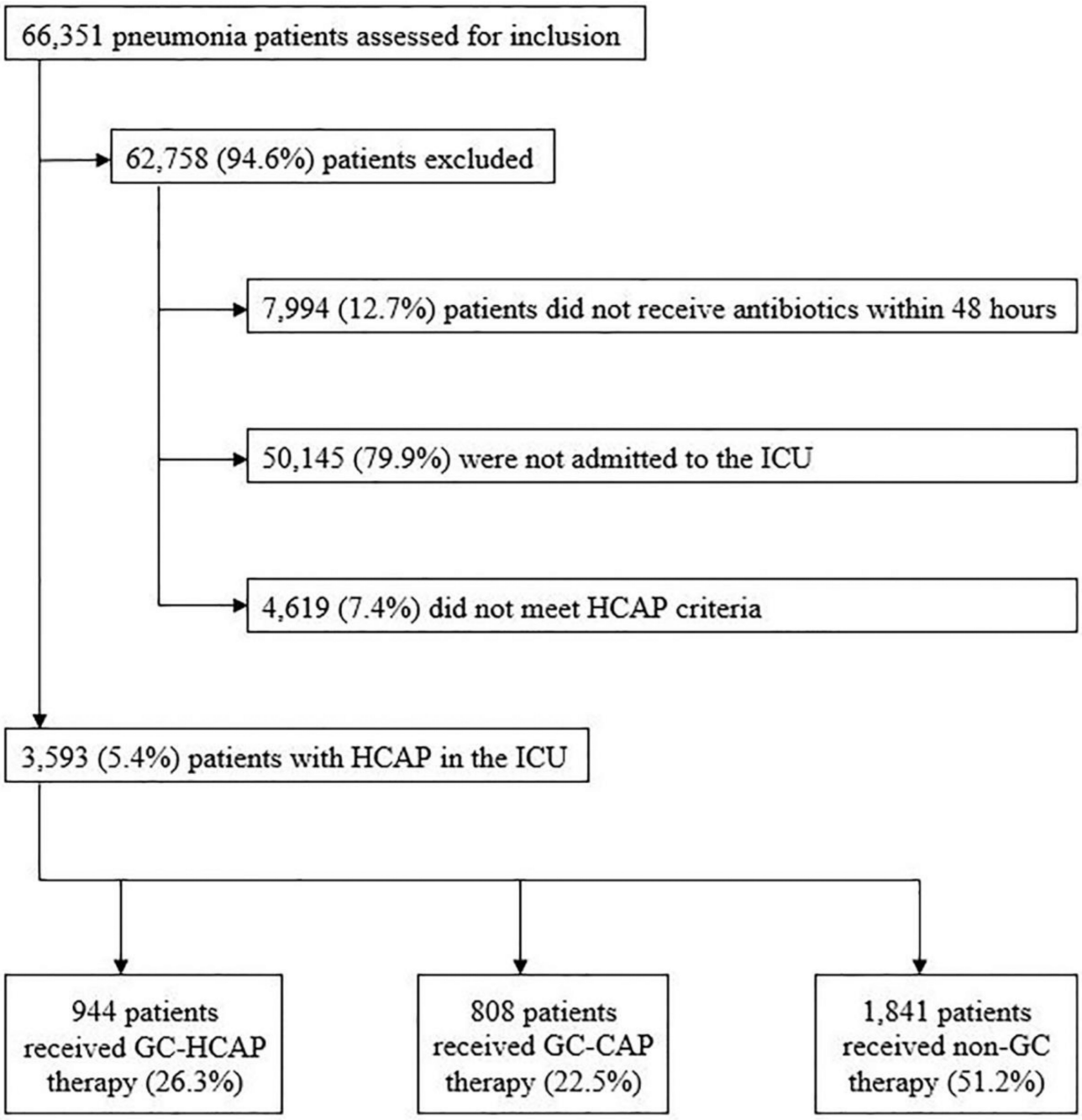

Figure 1.
Patient inclusion and exclusion flow diagram

Table 1

Definitions of CAP and HCAP Guideline-Concordant Therapy (ICU Patients)

Guideline-Concordant CAP Therapy	Guideline-Concordant HCAP Therapy
Beta-lactam[1†] *plus* azithromycin Beta-lactam[1†] *plus* respiratory fluoroquinolone[2]	Antipseudomonal beta-lactam[3†] *plus* antipseudomonal fluoroquinolone[4] *plus* vancomycin *or* linezolid Antipseudomonal beta-lactam[3†] *plus* aminoglycoside[5] *plus* vancomycin *or* linezolid

CAP: community-acquired pneumonia; HCAP: healthcare-associated pneumonia; ICU: intensive care unit

[†] Aztreonam may be substituted for beta-lactam in penicillin-allergic patients

[1] Beta-lactam includes cefotaxime, ceftriaxone, or ampicillin-sulbactam

[2] Respiratory fluoroquinolone includes moxifloxacin, levofloxacin, or gatifloxacin

[3] Antipseudomonal beta-lactam includes cefepime, ceftazidime, imipenem-cilastatin, meropenem, piperacillin-tazobactam, or ticarcillin-clavulanate

[4] Antipseudomonal fluoroquinolone includes ciprofloxacin or levofloxacin

[5] Aminoglycoside includes gentamicin, tobramycin, or amikacin

Table 2

Baseline Characteristics

Patient Characteristics	**Overall (n=3,593)**	**GC-HCAP (n=944)**	**GC-CAP (n=808)**	**Non-GC (n=1,841)**	**GC-HCAP *versus* GC-CAP (p-value)**	**GC-HCAP *versus* Non-GC (p-value)**
Age in years; median, IQR	77.1, 71.8–81.8	76.8, 71.8–81.4	77.1, 71.8–81.7	77.3, 71.8–82.0	0.40	0.58
Male, %	98.4	99.3	98.6	97.9	0.20	**0.009**
Race, %					**0.05**	0.27
White	80.7	78.7	84.0	80.3		
Black	14.4	15.1	12.3	14.9		
Other	4.9	6.1	3.7	4.7		
Hispanic ethnicity, %	5.4	8.8	3.6	4.4	**<0.0001**	**<0.0001**
HCAP Risk Factors, %						
Recent hospitalization, 90d	71.6	74.9	59.4	75.2	**<0.0001**	0.87
Nursing home resident, 90d	2.1	2.8	2.6	1.6	0.84	**0.03**
Hemodialysis	45.5	46.1	50.7	42.9	0.05	0.10
Outpatient IV antibiotic therapy, 90d	10.9	10.9	11.3	10.8	0.82	0.90
≥2 HCAP Risk Factors, %	27.2	30.7	21.6	27.9	**<0.0001**	0.12
Charlson Index score; median, IQR	3, 2–5	3, 2–5	4, 2–6	3, 2–5	0.10	0.83
Comorbid conditions, %						
Myocardial infarction	12.8	12.3	14.1	12.4	0.26	0.91
Heart failure	40.1	36.7	46.3	39.1	**<0.0001**	0.21
Cerebrovascular disease	21.7	25.1	21.3	20.1	0.06	**0.002**
COPD	56.2	52.6	61.5	55.7	**0.0002**	0.13

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Patient Characteristics	Overall (n=3,593)	GC-HCAP (n=944)	GC-CAP (n=808)	Non-GC (n=1,841)	GC-HCAP *versus* GC-CAP (p-value)	GC-HCAP *versus* Non-GC (p-value)
Liver disease	1.3	1.5	1.0	1.3	0.36	0.70
CKD	33.5	32.6	39.7	31.2	**0.002**	0.45
Diabetes	40.9	41.5	45.4	38.6	0.10	0.14
Neoplastic disease	27.7	30.1	22.6	28.7	**0.0004**	0.44
HIV/AIDS	0.2	0.1	0.1	0.3	0.91	0.37
Substance abuse or dependence						
Tobacco use	35.8	35.8	35.8	35.9	0.99	0.98
Alcohol abuse or dependence	5.1	4.7	5.4	5.2	0.45	0.57
Outpatient medication use, 90d, %						
Cardiovascular medications	72.8	71.0	81.9	69.6	**<0.0001**	0.47
Antidiabetic medications	27.5	27.3	33.0	25.2	**0.009**	0.23
Inhaled corticosteroids	21.8	20.8	23.9	21.5	0.12	0.65
Systemic corticosteroids	28.0	29.1	28.1	27.3	0.63	0.31
Pulmonary medications	39.4	36.7	44.1	38.8	**0.002**	0.26
Vasopressors, %	28.8	39.5	14.9	29.4	**<0.0001**	**<0.0001**
Invasive mechanical ventilation, %	41.6	53.7	28.5	41.2	**<0.0001**	**<0.0001**
Non-invasive mechanical ventilation, %	16.3	18.2	17.1	15.0	0.53	0.03
Organ failure, %						
Any organ failure	68.9	76.6	64.4	67.0	**<0.0001**	**<0.0001**
Respiratory	46.0	55.5	36.5	45.2	**<0.0001**	**<0.0001**
Cardiovascular	18.3	18.5	12.1	20.9	**0.0002**	0.14

Patient Characteristics	Overall (n=3,593)	GC-HCAP (n=944)	GC-CAP (n=808)	Non-GC (n=1,841)	GC-HCAP *versus* GC-CAP (p-value)	GC-HCAP *versus* Non-GC (p-value)
Neurological	4.5	5.6	5.0	3.6	0.54	**0.02**
Renal	36.9	40.8	34.2	36.2	**0.004**	**0.02**
Hematologic	6.8	9.4	5.2	6.2	**0.0008**	**0.002**
Hepatic	0.8	1.1	0.6	0.7	0.32	0.33

GC-HCAP: guideline-concordant healthcare-associated pneumonia
GC-CAP: guideline-concordant community-acquired pneumonia
GC: guideline-concordant
IQR: interquartile range
HCAP: healthcare-associated pneumonia
IV: intravenous
COPD: chronic obstructive pulmonary disease
CKD: chronic kidney disease
HIV/AIDS: human immunodeficiency virus/acquired immunodeficiency syndrome

Table 3

Bacterial Pathogen Distribution for GC-HCAP, GC-CAP, and Non-GC Patients

Patient Characteristics	Overall	GC-HCAP	GC-CAP	Non-GC	GC-HCAP *versus* GC-CAP (p-value)	GC-HCAP *versus* Non-GC (p-value)
All patients, n	3,593	944	808	1,841		
Organism identified	25.6	36.4	18.9	22.9	**<0.0001**	**<0.0001**
Single organism identified	21.9	30.1	16.8	19.9	**<0.0001**	**<0.0001**
Multiple organisms identified	3.7	6.4	2.1	3.0	**<0.0001**	**<0.0001**
Culture-positive patients, n	919	344	153	422		
Gram-positive pathogens						
S. pneumoniae	16.4	12.2	33.3	13.7	**<0.0001**	0.53
Streptococcus other	3.6	2.3	6.5	3.6	**0.02**	0.32
Staphylococcus aureus	37.5	43.3	26.8	36.7	**0.0005**	0.06
Gram-negative pathogens						
K. pneumoniae	8.7	10.2	3.3	9.5	**0.009**	0.75
Pseudomonas	17.1	21.8	7.2	16.8	**<0.0001**	0.08
H. influenzae	4.1	1.2	10.5	4.3	**<0.0001**	**0.01**
E. coli	3.6	5.2	1.3	3.1	**0.04**	0.13
Other gram-negatives	4.6	2.9	5.9	5.5	0.11	0.08
Atypical pathogens						
Legionella	1.4	1.2	2.6	1.2	0.24	0.98
Mycoplasma	0	0	0	0	--	--
Chlamydia	0	0	0	0	--	--
Anaerobes	0.4	0.6	0.7	0.2	0.92	0.45

GC-HCAP: guideline-concordant healthcare-associated pneumonia

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GC-CAP: guideline-concordant community-acquired pneumonia
GC: guideline-concordant

Table 4

Risk Factors for 30-Day Mortality in GC-HCAP and GC-CAP Patients (n= 1,752)

Risk Factors	Odds Ratio	95% Confidence Interval	p-value
HCAP risk factors			
Recent hospital admission, 90d	**1.53**	**1.15 – 2.02**	**0.003**
Nursing home admission, 90d	0.53	0.22 – 1.10	0.11
Hemodialysis	1.09	0.84 – 1.42	0.51
Outpatient IV antibiotics, 90d	1.17	0.83 – 1.62	0.37
Charlson Index score ≤4	0.91	0.72 – 1.14	0.41
Invasive mechanical ventilation	1.1	0.87 – 1.39	0.42
Non-invasive mechanical ventilation	1.2	0.91 – 1.58	0.18
Vasopressor use	**1.67**	**1.30 – 2.13**	**<0.0001**
GC-HCAP *versus* GC-CAP antibiotics	**1.51**	**1.20 – 1.90**	**0.0004**