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Predictors of Pneumonia Severity in HIV-Infected Adults Admitted to an Urban Public Hospital

Kara W. Chew, M.D.,[1] Irene H. Yen, Ph.D., M.P.H.,[2] Jonathan Z. Li, M.D.,[3] and Lisa G. Winston, M.D.[4]

Abstract

Data on outcomes of community-acquired pneumonia (CAP) in the HIV-infected population are mixed and the perception of worse outcomes in HIV may lead to excess hospitalization. We retrospectively evaluated the utility of the Pneumonia Severity Index, or PORT score, as a prediction rule for mortality in 102 HIV-infected adults hospitalized at an urban public hospital with CAP. Primary outcome was survival at 30 days. Secondary outcomes included survival on discharge, intensive care unit (ICU) admission, length of stay, and readmission within 30 days. The cohort was predominantly male (70%) with a mean age of 45.4 years (standard deviation [SD] ± 7.4). Mean CD4 cell count was 318 cells per microliter; 40 (39%) had CD4 less than 200 cells per microliter. Forty-three percent were on antiretroviral therapy at the time of admission and 31% on prophylactic antibiotics. Twelve patients had bacteremia on admission, predominantly with *Streptococcus pneumoniae.* Of the 46 patients with admission sputum cultures, 20 yielded an organism, most commonly *Haemophilus influenzae* and *S. pneumoniae.* Overall survival in the cohort was high, 96%. Most patients (81%) had a low PORT risk score (class I–III). PORT score predicted 30-day survival ($p = 0.01$) and ICU admission ($p = 0.03$), but antiretroviral use did not. In contrast to a prior study, we did not find that CD4 cell count predicted CAP outcome. Lack of stable housing was not associated with worse outcomes. The PORT score may be a valid tool to predict mortality and need for hospital admission in HIV-infected patients with CAP.

Introduction

HIV-infected individuals are at increased risk for bacterial community-acquired pneumonia (CAP) as compared to HIV-negative individuals,[1] with inpatient mortality estimated at 5–12%.[2–6] Despite the use of effective antiretroviral therapy (ART), CAP remains one of the most common reasons for hospital admission and a leading cause of death in HIV-infected individuals.[3,7–15] Published studies evaluating the impact of HIV infection on CAP outcomes have shown mixed results. Four studies found that HIV-infected patients with CAP have higher mortality than their HIV-negative counterparts,[7,16–18] whereas other studies have found no difference.[6,19,20] In clinical practice, the lack of reliable information regarding outcomes in the HIV-infected population may lead to excess hospitalization of HIV patients for CAP, as they are perceived to have worse outcomes.[20]

The Pneumonia Severity Index, or PORT score, is a frequently utilized clinical prediction rule for CAP that was developed excluding patients with HIV.[21] Consensus guidelines from the Infectious Diseases Society of America and American Thoracic Society for management of CAP recommend using the PORT score, along with other scoring methods for severity of illness, to identify appropriate candidates for outpatient treatment.[22] Two studies in the early ART era attempted to create a pneumonia severity scoring system for HIV-infected patients with CAP,[4,23] but neither has become widely utilized.

Our aim was to identify prognostic factors for outcomes in HIV-infected patients with CAP and to evaluate the utility of the PORT score as a prediction rule for mortality in HIV-infected patients admitted to an urban public hospital with CAP. If the PORT score is an effective predictor, it could be used with HIV-infected patients.

[1]Division of Infectious Diseases, Department of Medicine, David Geffen School of Medicine at the University of California, Los Angeles, Los Angeles, California.
[2]Division of General Internal Medicine, [4]Division of Infectious Diseases, Department of Medicine, University of California, San Francisco, San Francisco, California.
[3]Division of Infectious Diseases, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts.

Methods

Patient selection and definitions

We conducted a retrospective observational study of HIV-infected adult (≥18 years) patients consecutively admitted to the Internal Medicine or Family Practice inpatient services at San Francisco General Hospital with CAP from November 2005 to July 2006. We performed a search of the San Francisco General Hospital electronic medical record system for discharges carrying the ICD-9 codes for bacterial pneumonia (481-486) and HIV-related disease (042-044). This search excluded patients who were transferred from another inpatient setting or Laguna Honda Hospital, an affiliated skilled nursing facility. Cases were excluded if the chart was unavailable, patients were found not to be HIV-infected, were also treated for pneumocystis pneumonia or tuberculosis, did not have evidence of an infiltrate on chest imaging within 48 h of admission, were recently hospitalized (<10 days, as excluded in the Pneumonia PORT Cohort Study[21]), or if the admitting team did not feel the patient had CAP.

The following data were abstracted from the medical record using a standardized collection form: age; CD4 cell count; viral load; prior opportunistic diseases (including bacterial pneumonia); use of ART or prophylactic antibiotics at time of admission; use of alcohol, tobacco, or illicit drugs; pneumococcal vaccination history; housing status; comorbid psychiatric disease; baseline cognitive impairment; blood and sputum culture results; PORT score components (nursing home status, coexisting neoplastic disease, liver disease, congestive heart failure, cerebrovascular accident, renal disease, altered mental status, emergency department [ED] triage vital signs, admission laboratory results); length of stay; intensive care unit (ICU) admission; discharge condition and discharge housing status; survival on discharge; survival at 30 days; and readmission within 30 days.

PORT score and risk class were determined as described by Fine et al.[21] Prophylactic antibiotics recorded included trimethoprim-sulfamethoxazole (TMP-SMX), dapsone, azithromycin, and "other." Patients were considered to be "on ART" or "on prophylactic antibiotics" if they reported consistent use at the time of admission. Active substance use included any use in the month prior to admission. CD4 count and viral load data included were those values closest to admission and within 1 year prior to admission or 6 months following admission. For statistical analysis, CD4 values were further categorized as follows: CD4 < 200, CD4 = 200–349, CD4 = 350–500, CD4 > 500. CD4 count was also analyzed as a dichotomous variable, CD4 < 200 and ≥200. Viral load was analyzed as a continuous variable. Housing status was analyzed as a dichotomous variable, with unstable housing defined as being homeless or marginally housed (such as single-room occupancy residency). Survival at 30 days was determined by electronic and paper chart review and was the main outcome variable. Secondary outcome variables were length of stay, ICU admission, survival on discharge, and readmission within 30 days.

Data analysis

All statistical analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC). Continuous variables were compared using paired Student's *t* tests. Categorical variables were compared using χ^2 or Fisher's exact tests. The association between PORT score, PORT class, CD4 count, HIV viral load and previously described outcome variables were investigated in bivariate linear and logistic regression models. A two-sided p value < 0.05 was considered significant.

The study was reviewed and approved by the University of California, San Francisco Institutional Review Board.

Results

Patient characteristics

The study period included 102 admissions for CAP from November 2005 to July 2006. Table 1 summarizes patient characteristics. The majority of cases (70%) occurred in men. Mean age was 45 years. There was no significant difference in mean age between survivors and nonsurvivors ($p = 0.51$). Mean CD4 cell count (available for 101 of 102 patients) was 318 cells per microliter. Mean HIV viral load (available for 101 of 102 patients) was 61,651 copies per milliliter. Twenty-eight (28%) had an undetectable viral load. Eighty-two (80%) had prior history of opportunistic infection, including 51% with prior history of bacterial pneumonia. Forty-three percent reported actively taking antiretrovirals and 31% reported routine use of prophylactic antibiotics at the time of admission, including 22% on TMP-SMX and 7% on azithromycin. Ninety (88%) reported a history of smoking and 73 (72%) were known

Table 1. Characteristics of 102 HIV-Infected Adults Admitted with Bacterial Community-Acquired Pneumonia from November 2005 to July 2006

Characteristic (total n = *102)*	n *(%)*
Men	71 (70)
Women	31
Age (years), mean ± standard deviation	45.4 ± 7.4
CD4 (cells/μL), mean	318 [range 3–1262, 1 missing]
<200	40 (39)
200–349	25 (25)
350–500	19 (19)
>500	17 (17)
HIV viral load (HIV-1 RNA copies/mL), mean	61651 [range <75 to >500,000, 1 missing]
Undetectable viral load	28 (28)
Housing status	
Homeless	30 (29)
Marginally housed	24 (24)
Housed	33 (32)
Nursing home	3 (3)
Other	12 (12)
On antiretroviral therapy	44 (43)
On prophylactic antibiotics	32 (31)
Prior opportunistic infection	82 (80)
Prior bacterial pneumonia	52 (51)
Ever substance use	
Tobacco	90 (88)
Alcohol	63 (62)
Illicit drug use	90 (88)
Comorbid psychiatric disease	38 (37)
Baseline cognitive impairment	6 (5)
Documented pneumococcal vaccination	34 (33)

to be current smokers. Thirty-three percent had documentation of having received pneumococcal vaccination prior to hospitalization. Fifty-three percent of patients did not have stable housing at the time of admission. The majority (81%) had low PORT scores with risk class of I–III.

Microbiologic data

One hundred of 102 patients had blood cultures drawn on admission. Of these, 12 had bacteremia, with the majority (8/12) having *Streptococcus pneumoniae*. Forty-six patients had sputum cultures done on admission, with 20 yielding an organism. Five had more than one organism isolated on culture. *Haemophilus influenzae* was the most commonly isolated organism (isolated in 8 specimens), followed by *S. pneumoniae* (6), *Staphylococcus aureus* (4), and *Pseudomonas aeruginosa* (4).

Primary outcome: 30-day survival

Overall 30-day survival was high (96%, 98/102) and was the same as survival on discharge. All four deaths were pneumonia-related. Table 2 shows the number of deaths in each PORT risk class. Bivariate analysis showed PORT risk class was predictive of 30-day survival. Mean PORT score for survivors was 69.2 versus 105.5 for nonsurvivors ($p=0.01$), and mean PORT risk class for survivors was 2.43 versus 3.75 for nonsurvivors ($p=0.02$). CD4 count (<200 or ≥ 200) and ART status were not associated with survival at 30 days ($p=1.0$ and $p=0.31$). There was no difference in mean CD4 count between 30-day survivors and nonsurvivors ($p=0.50$). All deaths occurred in the stably housed group ($p=0.02$). There was no difference in mean PORT risk class between stably and unstably housed groups ($p=0.80$), or difference in housing distribution within high- and low-PORT risk classes ($p=0.62$).

Secondary outcome measures

Six of 102 patients required ICU admission. Two patients requiring ICU admission had low PORT scores, with risk class of II. High PORT score was predictive of ICU admission ($p=0.03$). CD4 count and ART status were not predictive of ICU admission ($p=1.0$ and $p=0.40$). On linear regression analysis, severity of pneumonia was predictive of length of stay (B = 1.7, $p=0.01$). Sixteen patients required readmission within 30 days, although not all for pneumonia-related disease. CD4 count, ART status, PORT class and housing status were not predictive of readmission ($p=1.0$, $p=0.58$, $p=0.17$ and $p=0.11$, respectively).

Table 2. Distribution of PORT Class, Deaths, and Secondary Outcomes

PORT risk class	*No. of patients (total n = 102)*	*No. of deaths at 30 days (% of class)*	*Length of stay, mean no. of days*	*No. requiring ICU admission*
I	19	0 (0)	3.8	0
II	39	1 (3)	4.8	2
III	25	0 (0)	5.6	0
IV	15	2 (13)	8.7	3
V	4	1 (25)	12.0	1

PORT, Pneumonia Severity Score; ICU, intensive care unit.

Discussion

The PORT score predicted mortality in our cohort of HIV-infected patients. Overall inpatient mortality was low, only 4% as compared to 8% in the PORT validation cohort,[21] and the majority (81%) of patients had low PORT scores (risk class I–III). This suggests that some patients could be managed on an outpatient basis, despite the perception that their HIV status may predict worse outcomes. Of interest, two of the six ICU admissions were in patients with low PORT scores (risk class II), which underscores the importance of combining both clinical judgment and objective measures to determine need for hospital admission. In both cases, the patients' initial triage vital signs and studies supported a low PORT score, but they had clinical decline while in the emergency department necessitating early ICU admission. Notably, one had demonstrated him/herself to be unreliable for follow-up, having presented twice in the preceding days to an emergency department, leaving without recommended treatment. Also of note, one had multilobar infiltrates on initial chest imaging, a finding suggesting more severe disease, which is not distinguished by the PORT score, and the other had rapid progression to multilobar disease, with initial chest imaging showing single lobe involvement.

Our findings support the association between PORT risk class and mortality in HIV-infected populations. In notable contrast to the Spanish study by Curran et al.,[5] CD4 count was not a significant predictor of mortality in our study. This is a significant distinction, as CD4 values are not always readily available at the time of evaluation and patients may be considered for admission due to concern for potential low CD4 count as a risk factor for poor outcome. A Canadian study evaluated the validity of the PORT score in immunocompromised hosts as compared to non-immunocompromised hosts,[24] considering HIV infection "low-risk" immunosuppression (the cohort also included solid-organ transplant recipients and individuals on immunosuppressive drugs). The authors found that this low-risk cohort had PORT score-controlled mortality similar to non-immunocompromised patients.

A number of studies evaluating CAP outcomes in HIV-infected patients have included non-bacterial cases of pneumonia, such as *Pneumocystis jirovecii* and other fungal pneumonias.[18] This may substantially affect the mortality rates described in their cohorts and overestimate morbidity and mortality outcomes in HIV-infected patients with presumed bacterial CAP. Our study focused on outcomes in hospitalized patients with bacterial CAP and found a population with both low PORT scores and mortality rates. This is consistent with the findings of the Community-Acquired Pneumonia Organization (CAPO) cohort,[6] which showed that HIV-infected patients were hospitalized with a lower pneumonia severity risk class than patients without HIV infection.

Strengths of our study include its focus on patients with only presumed bacterial CAP, rather than all causes of CAP, which may allow for more accurate assessment of outcomes. We additionally examined housing status as a possible predictor of poor outcome, as it may be considered an indication for hospital admission, and did not find that unstable housing predicted death at 30 days. Housing status also did not appear to affect the rates of admission, as patients were admitted with low PORT scores irrespective of their housing situation.

Limitations include the retrospective nature of the study, small size of our cohort, and few deaths limiting multivariate analysis. Case selection was done by ICD-9 coding, and one could postulate the low overall mortality was due to missing CAP cases by this method of case identification, but we would expect this would similarly affect and exclude both more severe and milder cases of disease. Our study also only included hospitalized patients and so cannot estimate outpatient mortality, which would be important to describe.

We recognize that there are factors not included in the PORT score which may be relevant to the need for hospital admission in our patient population, including marginal housing status, active drug use, cognitive impairment, and comorbid psychiatric disease. These factors may limit adherence to outpatient treatment and make certain individuals, even with low PORT score, inappropriate for outpatient management. Additionally, the risk of opportunistic pulmonary infections, which may present similarly to bacterial CAP in HIV-infected patients,[25] may complicate the initial diagnosis of CAP. From our clinical experience, however, a significant proportion of HIV-infected patients present with an acute febrile respiratory illness of sufficiently short duration and with characteristic lobar infiltrates on chest imaging to support a presumptive diagnosis of and directed therapy for bacterial CAP. However, it is reasonable to consider empiric therapy for multiple infectious etiologies or closer observation for individuals at higher risk of opportunistic infections (e.g., those with low CD4 counts) and radiologic and clinical findings atypical for CAP.

In our study of HIV-infected patients hospitalized with presumed bacterial CAP, overall mortality was low and PORT score was predictive of mortality, adding to the growing data that suggest HIV-infected patients have no worse outcomes than HIV-negative patients with CAP. The lack of an association between CD4 count and CAP mortality in our study suggests that the PORT score may be applicable for HIV-infected patients at varying levels of immunosuppression. Our findings support use of the PORT score, in conjunction with individualized clinical assessment, for determination of which HIV patients with bacterial CAP may be appropriately treated in an outpatient setting.

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Author Disclosure Statement

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Address correspondence to:
Kara W. Chew, M.D.
Division of Infectious Diseases
Department of Medicine
David Geffen School of Medicine at UCLA
10833 Le Conte Avenue, 37-121 CHS
Los Angeles, CA 90095

E-mail: kchew@mednet.ucla.edu