The Journal of Emergency Medicine, Vol. 44, No. 1, pp. 28–35, 2013

0736-4679/$ - see front matter

ELSEVIER

http://dx.doi.org/10.1016/j.jemermed.2012.05.001

Original Contributions

USE OF THE RELATIONSHIP BETWEEN ABSOLUTE LYMPHOCYTE COUNT AND CD4 COUNT TO IMPROVE EARLIER CONSIDERATION OF PNEUMOCYSTIS PNEUMONIA IN HIV-POSITIVE EMERGENCY DEPARTMENT PATIENTS WITH PNEUMONIA

Anthony M. Napoli, MD, FACEP,* Brandon Maughan, MD,* Ryan Murray, MD,† Kevin Maloy, MD,† and David Milzman, MD, FACEP†

*Department of Emergency Medicine, Providence, Rhode Island and †Department of Emergency Medicine, Washington Hospital Center, Georgetown University School of Medicine, Washington, DC

Reprint Address: Anthony M. Napoli, MD, FACEP, 593 Eddy Street, Davol 142, Providence, RI 02903

□ **Abstract—Background: The ability to accurately assess the level of immunosuppression in HIV+ patients in the emergency department (ED) is often limited and can affect management of these patients. Objective: To evaluate the relationship between the absolute lymphocyte count (ALC) and CD4 count in HIV patients admitted through the ED with pneumonia and how utilization of this relationship may affect early consideration and evaluation of *Pneumocystis jiroveci* pneumonia (PCP). Methods: Retrospective multicenter 5-year study of HIV+ patients with an ICD-9 diagnosis of pneumonia. Included patients had an ALC measured on ED presentation and a CD4 count measured in < 24 h. A receiver operator curve (ROC), decision plot analysis, and McNemar test of proportions were used to characterize the relationship between study variables. Results: Six hundred eighty six patients were enrolled, 23.2% (95% confidence interval [CI] 20.2–26.1) were diagnosed with PCP. The geometric mean CD4 count and ALC were 81 and 1089, respectively. The correlation between ALC and CD4 was r = 0.60 (95% CI 0.55–65, $p < 0.01$). The ROC was 0.78 (0.75–0.82). An ALC < 1700 cells/mm^3 had a sensitivity of 84% (95% CI 80–87) and specificity of 55% (95% CI 48–70) for a CD4 < 200 cells/mm^3. An ALC threshold of 1700 cells/mm^3 would have identified 86% of patients with PCP but falsely identified 2.5 patients without PCP for every one accurately identified. Conclusion: The ALC threshold of 1700 cells/mm^3 retains significant discriminatory value and would moderately improve identification of patients with a CD4 < 200 cells/mm^3 but is not likely to be reliable as the sole method of early recognition and evaluation of PCP.** © 2013 Elsevier Inc.

□ **Keywords—human immunodeficiency virus; absolute lymphocyte count; CD4; pneumocystis pneumonia; PCP**

INTRODUCTION

Since 2006, the Centers for Disease Control and Prevention have recommended routine screening for HIV infection among all patients aged 13–64, unless the prevalence of undiagnosed HIV in the local population is less than 0.1% (1). Current research estimates the prevalence of known HIV infection to be as high as 3% in some urban areas, with the rate of undiagnosed HIV among emergency department (ED) patients ranging from 0.7 to 16% (2–5). Management of HIV patients in the ED is challenging because differential diagnoses and treatment options depend on the level of immune suppression. In the absence of a recently documented CD4 count, the emergency physician's ability to accurately assess the level of immunosuppression in HIV-infected patients is limited. This clinical uncertainty may result in failures

RECEIVED: 2 September 2011; FINAL SUBMISSION RECEIVED: 27 January 2012;
ACCEPTED: 4 May 2012

to provide empiric treatment with trimethoprim-sulfamethoxazole (TMP-SMX) or in delayed diagnostic evaluation for *Pneumocystis jiroveci* pneumonia (PCP). The CD4 count is an important predictor of susceptibility to opportunistic infection (OI) in HIV patients, with a CD4 count < 200 cells/mm^3, indicating an increased risk for opportunistic infections (6). However, the rapid determination of the CD4 count is not available in the earliest phases of care.

Several studies have demonstrated that the absolute lymphocyte count (ALC) is a good predictor of the CD4 count but until recently these studies were primarily based on outpatient populations, mixed inpatient and outpatient populations, or on populations in resource-poor regions of the world (7–14). We recently found that ALC may be a good predictor of CD4 count in an unselected cohort of HIV patients admitted through the ED (15). However, all of these prior studies have examined general patient cohorts without targeting specific acute illnesses. As a result, prior research is limited by a spectrum bias that makes the accuracy and impact of this relationship more difficult to predict.

We sought to examine if the absolute lymphocyte count would correlate well with the CD4 count in HIV-positive ED patients with pneumonia. Additionally, we evaluated the ability of the ALC to serve as a proxy for the CD4 in identifying the need for early empiric therapy or evaluation for PCP.

MATERIALS AND METHODS

Design and Setting

This was a retrospective cohort study of consecutive HIV patients admitted through three urban emergency departments over a 5-year period. Patients were included if they were admitted to the hospital through the ED and had a known diagnosis of HIV, had an ALC measured in the ED, a CD4 count measured within 24 h of admission, and were discharged with an ICD-9 discharge diagnosis of pneumonia (ICD-9 136.3, 481–486). Patients were considered to have PCP if they were clinically diagnosed as such, regardless of diagnostic methodology, during their admission. In the case of repeat patient admissions, only the first ED admission was included.

Study Protocol

This was a retrospective chart review of demographic, laboratory, and clinical data using an electronic medical record (Amalga, Redmond, WA). The primary hypothesis, inclusion and exclusion criteria, and desired data variables were all defined prior to data abstraction. A trained chart abstractor with extensive experience using the electronic medical record, who was blinded to the hypothesis of the study, extracted the data based on the predefined inclusion and exclusion criteria above. Inter-rater reliability was not assessed since all data extracted were objective and did not require interpretation or classification. One author, who was not blinded to the hypothesis, confirmed the correct filter had been applied prior to data collection. In each study hospital, the ALC was measured using the Becton Dickinson FACSCalibur (Becton Dickson Immunocytometry Systems, San Jose, CA). CD4 lymphocyte counts were analyzed utilizing a Sysmex XT-1800 (Sysmex, Inc., Mundelein, IL). Antibiotic selection in the ED was collected and early empiric therapy was defined by administration of TMP-SMX in the ED. Data were extracted into a standard Excel database (Microsoft Corp., Redmond, WA). The Washington Hospital Center Institutional Review Board approved this study with waiver of written informed consent.

Statistical Analysis

To reduce the effects of evident skewness in the data distribution, data were log-transformed for analysis. Since some CD4 counts were zero, log transformation of the CD4 was done after adding one to each CD4 count in order to avoid undefined numbers. Back-translated geometric means and 95% confidence intervals (CI) were reported for the CD4 and ALC with the strength of association assessed using a Spearman correlation coefficient. A p value < 0.05 was considered statistically significant.

Bayesian theory suggests that a positive likelihood ratio (PLR) >10 and negative likelihood ratio (NLR) < 0.1 for a CD4 count < 200 cells/mm^3 would significantly impact clinical decision making. An ALC of 1700 cells/mm^3 was previously shown to have a negative likelihood ratio of < 0.1 (15). Thus, we sought to examine if this point or any other ALC level existed that identified a PLR >10 or NLR < 0.1 in this patient cohort. Area under the receiver operator curve (AUROC) using the Wilcoxon method and a decision plot analysis to calculate the sensitivity, specificity, and the positive and negative likelihood ratios were used to identify these prespecified optimal clinical thresholds. The proportion of patients that may receive earlier intervention or empiric TMP-SMX utilizing this pre-specified ALC of 1700 cells/mm^3 was compared with actual care using a McNemar test for comparing proportions in paired, nonparametric populations.

RESULTS

A total of 2469 patients with known HIV infection were treated over the 5-year period. Of these patients, 686 unique patients had a hospital discharge diagnosis of