Epidemiologic Changes in Bacteremic Pneumococcal Disease in Patients With Human Immunodeficiency Virus in the Era of Highly Active Antiretroviral Therapy

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Background: The use of highly active antiretroviral therapy (HAART) may change the incidence of, and the risk and prognostic factors for, invasive pneumococcal disease in patients with human immunodeficiency virus (HIV).

Methods: We prospectively studied 142 episodes of pneumococcal bacteremia in 122 HIV-infected adults. Eighty-five episodes occurred in the pre-HAART era (1986-1996) and 57 in the HAART era (1997-2002). A case-control study was conducted to identify risk factors for pneumococcal bacteremia in the HAART era.

Results: The incidence of pneumococcal bacteremia dropped from 24.1 episodes per 1000 patient-years in the pre-HAART era to 8.2 episodes per 1000 patient-years in the HAART era (P=.01). Compared with patients in the pre-HAART era, patients in the HAART era had more associated comorbidity (42% vs 26%; P=.04), fewer recurrences of bacteremia (4% vs 15%; P=.04), and a higher 30-day mortality rate (26% vs 8%; P=.004). High antibiotic resistance rates were observed in both periods. By multivariate analysis, the major risk factors for pneumococcal bacteremia in the HAART era were associated comorbidity (adjusted odds ratio [OR], 3.36), alcohol abuse (adjusted OR, 5.28), prior hospitalization (adjusted OR, 3.38), current smoking (adjusted OR, 5.19), and CD4 cell count lower than 100 cells/µL (adjusted OR, 2.38); while use of HAART (adjusted OR, 0.37) and pneumococcal vaccine (adjusted OR, 0.39) were protective factors.

Conclusions: The widespread use of HAART and pneumococcal vaccine may decrease the incidence of invasive pneumococcal disease in HIV-infected patients. Risk factors and prognosis of pneumococcal bacteremia in the HAART era are more similar to those reported in non-HIV-infected individuals.

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TREPTOCOCCUS PNEUMONIAE IS one of the most important bacterial pathogens in patients with human immunodeficiency virus (HIV). The incidence of invasive pneumococcal disease in HIV-infected patients has been reported to be about 46 to 100 times greater than in the general population, and recurrences are common.1-3 The increased risk of pneumococcal infections in HIV-infected patients could be related to the deep impairment of the immune system, particularly the humoral immune response.4

The use of highly active antiretroviral therapy (HAART) is associated with a restoration of the cellular-mediated immune system and, consequently, with a decline in the incidence of HIV-related opportunistic infections as well as the overall mortality.5-6 Preliminary data have suggested that the incidence of invasive pneumococcal infection is decreasing in the HIV-infected population.5,7 The improvement of B-cell-mediated immune response associated with HAART and the use of pneumococcal vaccination could be responsible, at least in part, for this decline.

In the present study, we have analyzed a cohort of HIV-infected adults to look for differences in the incidence of pneumococcal bacteremia and to compare its clinical presentation and outcome during the pre-HAART and HAART
erans. In addition, we carried out a case-control study to investigate the risk factors for pneumococcal bacteremia in the HAART era.

**METHODS**

**SETTING AND STUDY POPULATION**

This study was performed at Hospital de Bellvitge, a 1000-bed tertiary teaching hospital in Barcelona, Spain, that admits only adult patients and serves a population of about 1 million people. Our institution has an active program for HIV-infected patients (inpatient and outpatient care) and is the reference center for our geographic area. All HIV-infected patients are included in a computerized database. From January 1986 to December 2002, a total of 3143 HIV-infected persons were included in this database.

During the last 2 decades, all cases of invasive pneumococcal disease have been prospectively studied at our institution. For the present study, we have included the episodes of pneumococcal bacteremia that occurred in HIV-infected adults and analyzed several variables, including demographic, clinical, laboratory, and microbiological data; vaccination status; antiretroviral therapy; and mortality.

The annual incidence of pneumococcal bacteremia was calculated using as denominator the number of HIV-infected persons alive each year registered in the database from our geographic area. We compared several clinical, epidemiologic, and microbiological variables of patients treated in our hospital in the pre-HAART (1986-1996) and HAART (1997-2002) eras. In addition, we carried out a case-control study to investigate the risk factors for pneumococcal bacteremia in the HAART era. We conducted a case-control study. A “case” was defined as the occurrence of pneumococcal bacteremia in an HIV-infected patient in the period 1997 to 2002. (If a patient had recurrent pneumococcal bacteremia, only the first episode was recorded.) The duration of follow-up for cases was considered from the first visit to the HIV day care center to the date of positive blood culture for *S. pneumoniae*.

For each case, we chose 3 controls from the HIV-infected patient database. A “control” was an HIV-infected patient without pneumococcal bacteremia who presented to the HIV clinic within 6 months before or after the first visit of the corresponding case. The duration of follow-up of the control had to be at least that of the corresponding case. For each control, we recorded demographic, clinical, and laboratory data; vaccination status; and antiretroviral therapy.

**DEFINITIONS**

Diagnosis of bacteremic pneumococcal infection was based on clinical findings and the simultaneous isolation of *S. pneumoniae* in 1 or more blood cultures. Pneumococcal pneumonia was considered in patients with signs or symptoms of an acute lower respiratory tract infection together with a new pulmonary infiltrate on chest radiography. Other origins of bacteria (eg, peritonitis, soft tissue infection, meningitis, and endocarditis) were defined according to current accepted criteria. The infection was considered community acquired if it was evident on admission or within the first 48 hours thereafter; hospital acquired if signs or symptoms occurred at least 72 hours after admission and it was not in the incubation period.

Prior pneumonia was recorded when the patient had a diagnosis of bacterial pneumonia in the previous year. Prior hospitalization was defined as any hospital admission during the previous 6 months. Prior antibiotic therapy was defined as the intake of any antibiotic for treatment or prophylaxis for more than 48 hours during the previous 3 months. Use of antiretroviral therapy was defined as receipt during the previous and current 30 days of bacteremic episode.

The diagnosis of septic shock was based on a systolic blood pressure below 90 mm Hg and peripheral hypoperfusion together with clinical and/or bacteriologic evidence of uncontrolled infection. Polysaccharide pneumococcal vaccination was ascertained in patients with written documentation of pneumococcal vaccination 2 weeks or more before the episode of pneumococcal bacteremia. Recurrent bacteremia was defined as the subsequent isolation of *S. pneumoniae* from blood 1 week or more after a previous episode. Mortality was considered when the patient died within 30 days of positive blood cultures. The classification of the HIV infection followed the 1992 recommendations of the Centers for Disease Control and Prevention.

**MICROBIOLOGICAL METHODS**

Strains of *S. pneumoniae* were identified by the typical colonial morphologic characteristics, gram stain, bile solubility, and optochin susceptibility. The antibiotic susceptibility was determined by microdilution according to the current recommendations from the National Committee for Clinical Laboratory Standards. Two strains of *S. pneumoniae* were used as controls: ATCC 49619 (serotype 19) and ATCC 6303 (serotype 3). The minimum inhibitory concentration was defined as the lowest concentration of antibiotic that prevented visible growth after 18 to 20 hours of incubation at 35°C. To define resistance to different antibiotics we used the 2004 National Committee for Clinical Laboratory Standards criteria. Pneumococcal strains were serotyped at the Spanish Pneumococcal Reference Laboratory (Madrid, Spain) by the quellung reaction with the use of 46 antiserum preparations provided by the Statens Serum Institut (Copenhagen, Denmark).

**STATISTICAL ANALYSIS**

Statistical analyses were carried out with SPSS 11.0 for Windows 2000 (SPSS Inc, Chicago, Ill). Continuous variables were compared by *t* test; categorical variables, by *χ²* or Fisher exact test when appropriate.

To determine risk factors for pneumococcal bacteremia in the case-control study, we performed univariate analysis (unadjusted odds ratio [OR]) using logistic regression models; for the multivariate analysis (adjusted OR), we used a multiple logistic regression model that included age and those variables statistically significant in the univariate analysis. In addition, we used multiple logistic regression models to investigate risk factors for resistance to penicillin and for prognosis (30-day mortality). *P* values < .05 (2-sided) were considered statistically significant.

**RESULTS**

From January 1986 to December 2002 we prospectively studied 1043 episodes of pneumococcal bacteremia in adult patients, 142 (13.6%) of them in persons with HIV infection. The annual incidence of pneumococcal bacteremia in HIV-infected patients has decreased in recent years (Figure), with a 2.9-fold decrease comparing the pre-HAART era (24.1 episodes per 1000 patient-years) with the HAART era (8.2 episodes per 1000 patient-years) (*P* = .01).

Of the 142 episodes that occurred in 122 HIV-infected patients, 118 (83%) were bacteremic pneumo-
coccal pneumonias, and 24 (17%) were pneumococcal bacteremias from other origins: spontaneous peritonitis in patients with cirrhosis (n=12); sepsis without an apparent focus (n=4); meningitis (n=3); soft tissue infection (n=2); and endocarditis (n=2). Nine episodes (6%) were polymicrobial infections, including the isolation in blood cultures of *S pneumoniae* and 1 or more of the following: *Staphylococcus aureus* (n=2); *Salmonella enteritidis* (n=2); *Haemophilus influenzae* (n=1); *Escherichia coli* (n=3); *Pseudomonas aeruginosa* (n=1); and coagulase-negative staphylococci (n=1). The infection was community acquired in 135 episodes (95%) and hospital acquired in 7 (5%).

We compared the demographic and clinical characteristics of episodes that occurred in the pre-HAART and HAART eras (Table 1). Patients in the pre-HAART era were significantly younger than those in the HAART era. The major risk factor for HIV infection was intravenous drug use in both pre-HAART and HAART eras, but in the latter period there was a trend toward increased heterosexual transmission: 7 (8%) of 85 pre-HAART vs 11 (19%) of 57 HAART (*P*=.05). Patients in the HAART era had a history of AIDS and associated comorbidities such as liver cirrhosis more frequently than those in the pre-HAART era. Recurrent pneumococcal bacteremia decreased in the HAART era, and the 23-valent pneumococcal polysaccharide vaccine was administered more frequently in the HAART era. No differences in variables indicating a greater severity of pneumococcal infection at presentation (eg, shock) were observed between the 2 periods.

Overall, the 30-day mortality in HIV-infected patients with pneumococcal bacteremia was 15% (22/142), but it was greater in the HAART era (26%; 15/57) than in the pre-HAART era (8%; 7/85) (Table 1). In a multiple logistic regression model, including only the patients in the HAART era, associated comorbidity (adjusted OR, 13.6; 95% confidence interval [CI], 2.3–79.76; *P*=.004), and particularly the presence of liver cirrhosis (adjusted OR, 13.3; 95% CI, 2.5-1.45; *P*=.002), was independently associated with increased mortality after adjustment for age, HIV status, and CD4 cell count.

In the HAART era, patients with bacteremic pneumococcal infections caused by penicillin-nonsusceptible (intermediate and highly resistant) strains had higher mortality than those with penicillin-susceptible strains (42% vs 15%; OR, 3.99; 95% CI, 1.14-13.96; *P*=.03). However, after adjustment for other prognostic variables (age, HIV status, CD4 cell count, and associated comorbidities), this did not reach statistical significance (adjusted OR, 3.38; 95% CI, 0.68-16.78; *P*=.13).

In addition, we compared the mortality rate of bacteremic pneumococcal infection in HIV-infected and non–HIV-infected persons. In the pre-HAART era (1986-1996), the 30-day mortality rate was significantly lower in HIV-infected than in non–HIV-infected persons (8% [7/85] vs 24% [128/523]; *P*=.001). However, in the HAART era (1997-2002), the 30-day mortality rate was similar in HIV-infected and in non–HIV-infected persons (26% [15/57] vs 25% [91/366]; *P*=.81), and this could be related, at least in part, to an increased number of comorbidities in HIV-infected patients in the HAART era (Table 1).

### ANTIBIOTIC RESISTANCE AND CAPSULAR SEROTYPES

The overall prevalence of nonsusceptible strains (intermediate and highly resistant) to penicillin was 40%; ceftriaxone and/or cefotaxime, 2%; erythromycin, 20%; trimethoprim-sulfamethoxazole, 51%; and tetracycline, 34%. No statistically significant differences were observed in antibiotic resistance rates between periods, and no pneumococcal strains with decreased susceptibility to fluoroquinolones were found.
Of the 142 episodes of pneumococcal bacteremia in HIV-infected patients, 117 isolates (82%) were available for serotyping. Overall, the most frequent serotypes or serogroups of *S. pneumoniae* isolated in our HIV-infected patients were 19 (14%) and 9 (12%). Serotypes or serogroups included in the 23-valent polysaccharide vaccine accounted for 86% of strains, and those included in the 7-valent conjugate vaccine accounted for 60% of isolates; this percentage did not vary significantly during the study period.

We compared the antibiotic susceptibility in blood pneumococcal isolates of patients with and without HIV infection (Table 2 and Table 3). Patients with HIV, compared with non–HIV-infected patients, had a higher proportion of nonsusceptible strains to penicillin (40% vs 29%; *P* = .08), trimethoprim-sulfamethoxazole (51% vs 42%; *P* = .04), and tetracycline (34% vs 26%; *P* = .05). The overall prevalence of nonsusceptible pneumococcal blood isolates to 1 or more antibiotics was higher in HIV-infected patients than in non–HIV-infected patients (62% vs 51%; *P* = .01). The most frequent resistant patterns are shown in Table 3. The serogroups or serotypes 6, 9, 14, 15, 19, and 23, which more commonly show penicillin and multiple antibiotic resistance, tended to be more frequently observed in HIV-infected patients than in non–HIV-infected patients (49% vs 41%; *P* = .08).
RISK FACTORS FOR PNEUMOCOCCAL BACTEREMIA IN THE HAART ERA

As summarized in Table 4, there were no statistically significant differences between cases (HIV-infected patients with pneumococcal bacteremia) and controls (HIV-infected patients without pneumococcal bacteremia) with respect to age, sex, history of AIDS-defining illness, or cotrimoxazole use. Cases were more likely than controls to have intravenous drug use as mode of HIV transmission (76% vs 56%; \(P = .01\)), current smoking (93% vs 77%; \(P = .02\)), alcohol abuse (43% vs 11%; \(P < .001\)), prior pneumonia (26% vs 7%; \(P < .001\)), prior hospitalization (49% vs 19%; \(P < .001\)), associated comorbidity (43% vs 15%; \(P < .001\)), and CD4 cell count lower than 100 cells/\(\mu\)L (42% vs 20%; \(P = .002\)). However, cases were less likely than controls to receive HAART (35% vs 63%; \(P = .001\)) and 23-valent pneumococcal vaccine (22% vs 46%; \(P = .003\)).

In a multivariate analysis (Table 5), after adjustment for age and the statistically significant variables in the univariate analysis, we found that the independent factors associated with an increased risk of pneumococcal bacteremia in HIV-infected persons in the HAART era were alcohol abuse (adjusted OR, 5.28), prior hospitalization (adjusted OR, 3.38), and associated comorbidity (adjusted OR, 3.36). Although they did not reach statistical significance, current smoking (adjusted OR, 5.19; \(P = .06\)) and CD4 cell count lower than 100 cells/\(\mu\)L (adjusted OR, 2.38; \(P = .06\)) showed a trend toward an increased risk (Table 5). When we considered all the comorbidities, liver cirrhosis showed the strongest association with pneumococcal bacteremia (adjusted OR, 3.22; 95% CI, 1.07-9.71; \(P = .04\)). On the other hand, patients in the HAART era who received a potent combination of antiretroviral therapy (adjusted OR, 0.37) as well as those who received the 23-valent pneumococcal vaccine (adjusted OR, 0.39) had a lower risk of pneumococcal bacteremia (Table 5).

**COMMENT**

It is well known that the wide use of HAART has changed the natural history of HIV infection, with a noteworthy decline in the incidence of, and mortality from, opportunistic infections.\(^5,6\) Several studies carried out before the introduction of HAART found high rates of pneumococcal disease in HIV-infected patients\(^1,4\) and also found that the risk for pneumococcal disease may decrease in association with an improvement of immunoresponse in those who receive antiretroviral therapy.\(^1,4\) One recent study found a significant decrease in the incidence of invasive pneumococcal disease in patients with AIDS and suggested that this could be owing to the wide use of HAART.\(^2\) Our study shows a decrease in the incidence of pneumococcal bacteremia in HIV-infected patients in the HAART era (Figure), and in the case-control study, the use of HAART was an independent protective factor (Table 5).

Although there are some reports of 23-valent pneumococcal vaccine failure in HIV-infected patients, particularly in those with severe immunosuppression,\(^15-17\) several other reports have shown that this vaccine could be effective in the HIV population (ranging from 40% to 78% of effectiveness) with the best response in patients with a CD4 cell count higher than 200 cells/\(\mu\)L.\(^13,14,18\) In our study, the administration of 23-valent pneumococcal vaccine was an independent protective factor for pneumococcal bacteremia (Table 5). As recommended by the current Centers for Disease Control and Prevention guidelines,\(^19\) the 23-valent pneumococcal vaccine should be administered before the HIV-infected patient becomes severely immunosuppressed.

As disclosed in other reports,\(^4,13,14,18\) our study also demonstrated that current smoking, alcohol abuse, prior hospitalization, and CD4 cell count lower than 100 cells/\(\mu\)L were risk factors for pneumococcal bacteremia (Tables 4 and 5). The presence of associated comorbidity (mainly liver cirrhosis) was an independent risk factor for pneumococcal bacteremia. The longer survival of HIV-infected patients in the HAART era leads to the emergence of hepatitis C virus infection and chronic liver disease as an important cause of morbidity and mortality in this population.\(^20,21\) However, the use of HAART is associated with the appearance of metabolic abnormalities and lipodystrophy syndrome that can cause cardiovascular disease and diabetes mellitus.\(^22,23\) The increased prevalence of such comorbidities may increase the number of risk factors (together with HIV-related immunodeficiency) for pneumococcal disease in the HIV population.

In our study, as in others,\(^2,4,24,25\) the mortality rate observed in HIV-infected persons with pneumococcal bacteremia in the pre-HAART era was lower than that reported in the non-HIV population. This lower mortality in HIV-infected patients might be related to several factors, including younger age, lower prevalence of associ-
ated comorbidity, and a decreased inflammatory re-
sponse to pneumococci as a result of severe impairment
of the immune system.3,8 However, in our study the mor-
tality rate in HIV-infected persons with pneumococcal
bacteremia increased significantly in the HAART era
(Table 1), and this might be owing, at least partially, to
a greater prevalence of associated comorbidity (eg, liver
cirrhosis) observed in this period.

We found high rates of antibiotic resistance in
pneumococcal blood isolates from HIV-infected
patients, and no differences between periods were
observed. In contrast, we found that infections with
strains resistant to penicillin, tetracycline, and
trimethoprim-sulfamethoxazole, as well as those with
multiple antibiotic resistance, were more frequent in
HIV-infected than in non–HIV-infected persons. Other
authors found similar results,26-30 and this could be
explained, at least partially, by the frequent use of
antibiotics for treatment or prophylaxis in the HIV
population (eg, cotrimoxazole for preventing Pneumo-
cystis pneumonia).29,30 In our study, prior antibiotic
therapy was the strongest independent risk factor for
infection due to penicillin-resistant strains, and as was
noted in other reports,8 resistance to penicillin was not
associated with increased mortality after adjustment
for other prognostic factors. We also found that the
serogroups or serotypes that more frequently show
resistance to penicillin and other antibiotics (eg, 6, 9,
14, 15, 19, and 23) tended to be more frequent in
HIV-infected patients than in non–HIV-infected
patients, as reported previously.27,31,32

In summary, the present study shows a decrease in
the incidence of pneumococcal bacteremia in the HIV-
infected population that was associated with an increasing
use of HAART and 23-valent pneumococcal vac-
cine. In the HAART era, invasive pneumococcal disease

<table>
<thead>
<tr>
<th>Table 4. Univariate Analysis of Factors Associated With Bacteremic Pneumococcal Infection in the Era of HAART*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Factor</strong></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Female</td>
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<tr>
<td>Male</td>
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<tr>
<td>Mode of HIV transmission</td>
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<tr>
<td>IDU</td>
</tr>
<tr>
<td>Other</td>
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<tr>
<td>Current smoking</td>
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<tr>
<td>No</td>
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<tr>
<td>Yes</td>
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<tr>
<td>Alcohol abuse</td>
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<tr>
<td>No</td>
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<td>Yes</td>
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<tr>
<td>Prior pneumonia</td>
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<td>No</td>
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<td>Prior hospitalization</td>
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<tr>
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<td>Yes</td>
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<tr>
<td>Associated comorbidity†</td>
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<tr>
<td>Yes</td>
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<tr>
<td>History of AIDS</td>
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<tr>
<td>No</td>
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<tr>
<td>Yes</td>
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<tr>
<td>CD4 cell count &lt;100 cells/µL</td>
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<tr>
<td>No</td>
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<tr>
<td>Yes</td>
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<tr>
<td>Prophylaxis with cotrimoxazole</td>
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<td>No</td>
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<td>Yes</td>
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<tr>
<td>Use of HAART</td>
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<td>No</td>
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<td>Yes</td>
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<tr>
<td>23-Valent pneumococcal vaccine</td>
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<tr>
<td>No</td>
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<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disorder; HAART, highly active antiretroviral therapy; HIV, human
immunodeficiency virus; IDU, intravenous drug use; NA, not applicable; OR, odds ratio.

*Unless otherwise indicated, data are reported as number (percentage) of subjects.
†In cases, liver cirrhosis (n = 15), COPD (n = 6), neoplasm (n = 3), and splenectomy (n = 2); in controls, liver cirrhosis (n = 13), COPD (n = 2), neoplasm
(n = 1), splenectomy (n = 1), diabetes mellitus (n = 4), cardiovascular disease (n = 4), and end-stage renal disease (n = 1).
occurred mainly in patients with advanced HIV disease and severe comorbidities, which may explain the greater mortality in this period than during the pre-HAART era. In the HAART era, the increasing prevalence of comorbidities that are well-known risk factors for pneumococcal infection (eg, chronic liver disease, diabetes, and cardiovascular diseases) may foretell a continuing global burden of pneumococcal disease in the HIV-infected population.

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Table 5. Multivariate Analysis* of Risk Factors for Bacteremic Pneumococcal Infection in Patients With HIV

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>(P) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>0.95 (0.89-1.01)</td>
<td>.11</td>
</tr>
<tr>
<td>Mode of HIV transmission (IDU vs others)</td>
<td>1.26 (0.47-3.38)</td>
<td>.64</td>
</tr>
<tr>
<td>Current smoking</td>
<td>5.19 (0.96-28.02)</td>
<td>.06</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>5.28 (2.07-13.42)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Prior pneumonia</td>
<td>2.06 (0.63-6.81)</td>
<td>.23</td>
</tr>
<tr>
<td>Prior hospitalization</td>
<td>3.38 (1.23-9.29)</td>
<td>.02</td>
</tr>
<tr>
<td>Associated comorbidity</td>
<td>3.36 (1.32-8.52)</td>
<td>.01</td>
</tr>
<tr>
<td>CD4 cell count &lt;100 cells/µL</td>
<td>2.38 (0.98-5.79)</td>
<td>.06</td>
</tr>
<tr>
<td>Use of HAART</td>
<td>0.37 (0.15-0.88)</td>
<td>.02</td>
</tr>
<tr>
<td>23-Valent pneumococcal vaccine</td>
<td>0.39 (0.15-0.97)</td>
<td>.04</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; IDU, intravenous drug use.

*Including age and the variables statistically significant in the univariate analysis.

REFERENCES


Correction

Errors in Byline, Author Affiliations, and Figure. In the Original Investigation by Kertai et al titled “Optimizing the Prediction of Perioperative Mortality in Vascular Surgery by Using a Customized Probability Model,” published in the April 25 issue of the ARCHIVES (2005;165:898-904), errors occurred in the byline, the Author Affiliations paragraph, and the Figure. On page 898, the byline should have read as follows: “Miklos D. Kertai, MD, PhD; Eric Boersma, PhD; Jan Klein, MD, PhD; Marc van Sambeek, MD, PhD; Olaf Schouten, MD; Hero van Urk, MD, PhD; Don Poldermans, MD, PhD.” On that same page, the Author Affiliations paragraph should have read as follows: “Departments of Cardiology (Drs Kertai and Boersma), Anesthesiology (Drs Klein and Poldermans), and Vascular Surgery (Drs van Sambeek, Schouten, and van Urk), Erasmus Medical Center, Rotterdam, the Netherlands.” In the top portion of the Figure on page 902, the scores listed for “Long-term Medication” (under “Medical History”) should have been given as follows: β-blocker use, −15, and statin use, −10. The journal regrets these errors.