Sensitivity, Specificity, and Positivity Predictors of the Pneumococcal Urinary Antigen Test in Community-Acquired Pneumonia

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Abstract

Rationale: Detection of the C-polysaccharide of *Streptococcus pneumoniae* in urine by an immune-chromatographic test is increasingly used to evaluate patients with community-acquired pneumonia.

Objectives: We assessed the sensitivity and specificity of this test in the largest series of cases to date and used logistic regression models to determine predictors of positivity in patients hospitalized with community-acquired pneumonia.

Methods: We performed a multicenter, prospective, observational study of 4,374 patients hospitalized with community-acquired pneumonia.

Measurements and Main Results: The urinary antigen test was done in 3,874 cases. Pneumococcal infection was diagnosed in 916 cases (21%); 653 (71%) of these cases were diagnosed exclusively by the urinary antigen test. Sensitivity and specificity were 60 and 99.7%, respectively. Predictors of urinary antigen positivity were female sex; heart rate ⩾125 bpm, systolic blood pressure <90 mm Hg, and Sa_{O_2} <90%; absence of antibiotic treatment; pleuritic chest pain; chills; pleural effusion; and blood urea nitrogen ⩾30 mg/dl. With at least six of all these predictors present, the probability of positivity was 52%. With only one factor present, the probability was only 12%.

Conclusions: The urinary antigen test is a method with good sensitivity and excellent specificity in diagnosing pneumococcal pneumonia, and its use greatly increased the recognition of community-acquired pneumonia due to *S. pneumoniae*. With a specificity of 99.7%, this test could be used to direct simplified antibiotic therapy, thereby avoiding excess costs and risk for bacterial resistance that result from broad-spectrum antibiotics. We also identified predictors of positivity that could increase suspicion for pneumococcal infection or avoid the unnecessary use of this test.

Keywords: community-acquired pneumonia; pneumococcal urinary antigen; sensitivity; specificity; positive predictor factors

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Community-acquired pneumonia (CAP) is a common entity, with an incidence of 2 per 1,000 adults (1), and is the most frequent cause of both admission to hospital and death due to a community-acquired infection (2). *Streptococcus pneumoniae* is the most commonly identified bacterial pathogen. Traditional microbiological diagnosis is based on microscopic examination of a Gram-stained sputum specimen, sputum culture, and blood culture. Sputum cultures combine the difficulty of obtaining a good-quality sample (3) (<50% of cases) with uncertain specificity of a positive culture result. Blood cultures are positive (4) in no more than 20 to 25% of cases of pneumococcal pneumonia (5, 6).

Recent guidelines (7–10) have also recommended routine testing of urine for antigens of *S. pneumoniae* in patients hospitalized with CAP. The most widely used method for detecting urinary pneumococcal antigen uses a membrane immune-chromatographic test that detects the C-polysaccharide antigen common to all serotypes. Studies (11–21) have shown that this technique is positive in 60 to 85% of patients who have definitive pneumococcal pneumonia (*S. pneumoniae* isolated from a normally sterile site in a patient with a new pulmonary infiltrate and symptoms consistent with pneumonia) and 40 to 65% of patients with presumptive pneumococcal pneumonia (*S. pneumoniae* isolated only from sputum in a patient with a similar clinical presentation). With one exception (14), these have been small-scale studies, and none has addressed factors that predict positivity of this technique.

The objective of our study was to determine the frequency of positivity, the sensitivity and specificity, and the predictors of pneumococcal urinary antigen positivity in a series of more than 4,000 patients diagnosed with CAP. In addition, we aimed to create a probabilistic model for this test. Our hypothesis was that identifiable predictive factors might help clinicians to select patients with CAP for obtaining a better sensitivity of *S. pneumoniae* urinary antigen test.

Methods

We performed a prospective, multicenter, observational study in 13 Spanish hospitals from November 2005 to November 2007. Pneumonia was defined as the presence of a new infiltrate on a chest radiograph together with clinical symptoms that were suggestive of lower respiratory tract infection (e.g., fever, cough, sputum production, and pleuritic chest pain). We excluded patients who were immune suppressed (patients with AIDS or those undergoing immunosuppressant treatments, including chronic administration of >10 mg/d of prednisone or equivalent), patients diagnosed with tuberculosis, and those who had pneumonia in the previous 3 months. Patients provided written informed consent to participate in the trial. The study was approved by the Ethics Committees (ISS, Hospital La Fe, Valencia, Spain).

For each patient, we recorded age, sex, smoking habits, alcohol consumption, prior antimicrobial treatment, and comorbid conditions (chronic obstructive pulmonary disease, asthma, diabetes mellitus, chronic heart failure, chronic kidney failure, chronic liver disease, cerebrovascular disease, and cancer). Symptoms and signs were noted. Laboratory results included complete blood count, glucose, blood urea nitrogen (BUN), creatinine, electrolytes, and C-reactive protein. Chest radiograph was obtained in every case. The severity of disease was graded using the Pneumonia Severity Index (PSI) (22) and the CURB-65 score (23).

Microbiological Studies

On admission, blood was cultured aerobically and anaerobically, and serum was obtained for serologic studies (complement fixation tests) for *Legionella pneumophila*, *Chlamydophila pneumoniae*, *Mycoplasma pneumoniae*, *Chlamydophila psittaci*, *Coxiella burnetii*, syncytial respiratory virus, influenza virus A and B, and adenovirus and parainfluenza viruses. A second (convalescent) serum was taken 4 to 6 weeks later for a paired analysis.

Urine samples were collected in the emergency department or on the ward in the first 24 hours to test for antigens of *S. pneumoniae* and *L. pneumophila* serogroup 1, using the Binax NOW immunochromatography method (Alere BinaxNOW, *Streptococcus pneumoniae* Antigen Card; Alere Inc., Waltham, MA) in accordance with the manufacturer's instructions. Investigators agreed in advance that the urinary antigen test would be requested routinely in all patients.

Sputum was cultured if a suitable sample (>25 polymorphonuclear leukocytes, <10 epithelial cells per field at 100× magnification) could be provided. Respiratory secretions were obtained from intubated patients or from patients with mechanical ventilation by means of bronchial aspiration, bronchoalveolar lavage, or telescoping catheter brush. Pleural fluid was extracted and cultured when a sufficient amount was present.

We considered the diagnosis to be definitive in the following instances: (*1*) a likely bacterial pathogen was isolated in blood samples or pleural fluid, (*2*) there was a ⩾4-fold increase in antibody titers between the acute phase and convalescence serum, (*3*) the urinary antigen test was positive, and (*4*) a likely bacterial pathogen was isolated in the bronchial aspirate ($\geqslant 10^5$ colony forming units [cfu]/ml), protected brush specimen ($\geqslant 10^3$ cfu/ml), or bronchoalveolar lavage ($\geqslant 10^4$ cfu/ml). Diagnosis was considered probable if the bacterium was isolated in good-quality sputum and was supported by Gram staining or by means of fiberoptic bronchoscopy when the cfu/ml count was below the above-mentioned limits.

Statistical Analysis

Statistical calculations were performed using SPSS version 17.0. A descriptive analysis was performed. Quantitative variables were expressed as mean (SD), and qualitative variables were expressed as proportions. In the univariate analysis we included all the variables described previously; the *t* test was used to compare means, and the Mann–Whitney *U* test was used where the variables showed nonnormal distribution. The Pearson chi-squared test was used to compare qualitative variables, and the Fisher exact test was used where necessary.

A multivariate logistic regression analysis was performed on variables that were statistically significant in the univariate analysis ($P < 0.1$). The odds ratio and 95% confidence intervals were calculated for significant variables throughout the study. The level of significance was set at 0.05 (two-tailed). To calculate the yield of the test, we analyzed sensitivity and specificity, predictive values, and probability ratios.

Sensitivity was obtained (following the usual formulas) by using three reference groups: (*1*) patients with a definitive

Table 1. Demographic and clinical findings in patients with community-acquired pneumonia with and without pneumococcal urinary antigen testing

Characteristic	Total (*n* = 4,374)	With Pneumococcal Urinary Antigen Testing (*n* = 3,874)	Without Pneumococcal Urinary Antigen Testing (*n* = 500)	*P* Value
Sex, n (%)				0.78
Male	2,859 (65.4)	2,535 (65.4)	324 (64.8)	
Female	1,515 (34.6)	1,399 (34.6)	176 (35.2)	
Age, yr, mean (SD)	66 (18)	66 (18)	71 (16)	<0.001
Underlying diseases, n (%)				
COPD	1,026 (23.5)	882 (23.2)	144 (29.2)	0.003
Diabetes mellitus	939 (21.5)	828 (21.4)	111 (22.2)	0.66
Heart failure	644 (14.7)	535 (13.8)	109 (21.8)	<0.001
Active cancer	249 (5.7)	209 (5.4)	40 (8.0)	0.018
Chronic renal failure	307 (7.0)	256 (6.6)	51 (10.2)	0.003
Cerebrovascular disease	498 (11.4)	411 (10.6)	87 (17.4)	<0.001
Chronic liver disease or cirrhosis	183 (4.2)	161 (4.2)	22 (4.4)	0.80
Severity-of-illness scores, n (%)				
PSI high mortality risk classes (IV and V)	2,105 (48.1)	1,811 (46.7)	294 (58.8)	<0.001
CURB-65 high mortality risk group (⩾3 points)	1,370 (31.3)	1,170 (30.2)	200 (40.0)	<0.001
Respiratory failure, n (%)	1,976 (49.6)	1,736 (49.0)	240 (53.8)	0.057
Severe sepsis, n (%)	1,700 (38.9)	1,501 (38.7)	199 (39.8)	0.65
ICU admission, n (%)	306 (7.0)	296 (7.6)	10 (2.0)	<0.001

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; CURB-65 = consciousness, urea, respiratory rate, blood pressure, 65 yr old; ICU = intensive care unit; PSI = pneumonia severity index.

diagnosis of pneumococcal pneumonia, (*2*) patients with probable pneumococcal pneumonia, and (*3*) all patients with pneumococcal pneumonia (definitive and probable). When determining specificity, we considered two control groups: (*1*) patients with a definitive or probable diagnosis of nonpneumococcal pneumonia and (*2*) patients who had pneumonia proven to be due to a causative agent other than *S. pneumoniae*. Mixed pneumonias (*S. pneumoniae* with other pathogens) were not included to calculate the specificity.

Results

We enrolled 4,374 patients in the study, of whom 2,859 (65.4%) were men. The mean age was 66 (±18) years. Mortality during hospitalization was 5% and was higher at 30 (6%) and 90 (8%) days. Urine was studied for pneumococcal antigen in 3,874 cases. The differences in demographic and clinical data for patients with CAP across the 13 sites are summarized in Table E1 in the online supplement. We compared patients in whom urine pneumococcal antigen was sought with 500 patients in whom it was not. Demographic and clinical data for patients with CAP with and without pneumococcal urinary antigen testing are shown in Table 1.

Patients whose urine antigens were not studied were significantly older; they presented more comorbidities, especially chronic obstructive respiratory disease, heart failure, active cancer, chronic renal failure, and cerebrovascular disease. A greater proportion had PSI severity scores of IV and V as well as CURB65 scores ⩾3, but ICU admissions were less frequent compared with patients in whom the urine antigen tests were performed.

Blood was cultured in 2,718 patients (62%), and the cultures were positive for *S. pneumoniae* in 305 cases (11%). Pleural fluid was cultured in 270 cases (6%) with positive results in 51 cases (19%). Using all available laboratory methods, an etiologic diagnosis was established in 1,608 cases (37%) (Table 2). The most commonly identified microorganism was *S. pneumoniae* either as the sole agent or in mixed-etiology pneumonias; this organism was implicated in 916 of all 4,374 patients studied (21%). *Legionella* urine antigen was positive in 106 of 3,852 cases (3%).

The microbiological methods by which *S. pneumoniae* was identified as a cause of CAP are shown in Table 3. Of the 916 patients with documentation of pneumococcal infection, the diagnosis was made without the urine pneumococcal antigen in only 263 (29%) cases. The urine pneumococcal antigen was studied in 3,865 cases and was positive in 871 (23%). Thus, of 916 cases of pneumococcal CAP, 653 (71%) were diagnosed exclusively by means of urinary antigens, markedly increasing the diagnostic yield in this group.

Diagnostic Yield of the Urinary Antigen for *S. pneumoniae*

Table 4 shows a summary of the sensitivity, specificity, and predictive values of a positive pneumococcal urinary antigen test. Overall sensitivity, including

Table 2. Etiologic agents in 4,374 patients hospitalized for community-acquired pneumonia

Microorganism	n (%)
Streptococcus pneumonia	916 (20.9)
Mixed	134 (3.1)
With *S. pneumoniae*	90 (2.1)
Without *S. pneumoniae*	44 (1.0)
Legionella pneumophila	109 (2.5)
Pseudomonas aeruginosa	51 (1.2)
Coxiella burnetii	51 (1.2)
Mycoplasma pneumoniae	50 (1.1)
Chlamydophila pneumoniae	48 (1.1)
Haemophilus influenzae	46 (1)
Enteric gram-negative bacilli	45 (1)
Staphylococcus aureus	44 (1)
Viruses	43 (1)
Methicillin-resistant *S. aureus*	10 (0.2)
Others	61 (1.4)
Not diagnosed	2,766 (63.2)

Table 3. Diagnosis of pneumococcal pneumonia

Microbiological Test	n (%)
Blood culture	167 (18)
Pleural fluid	16 (1.7)
Patients whose only positive test for *Streptococcus pneumoniae* was urine pneumococcal antigen	653 (71)
Sputum	66 (7.2)
Protected specimen brush	6 (0.7)
Tracheal aspirate	5 (0.5)
Bronchoalveolar lavage	3 (0.3)

The urine pneumococcal antigen was studied in 3,865 cases and was positive in 871 (23%).

pneumococcal pneumonia with definitive and probable diagnoses, was 60%; the sensitivity was 68% in patients with a definitive diagnosis and 44% in those with a probable diagnosis. Specificity was 99.7%, based on one positive test in 375 patients with proven diagnoses of nonpneumococcal pneumonia; the urine pneumococcal antigen was positive in one patient whose blood culture was positive for *Pseudomonas aeruginosa*. The area under the receiver operating characteristic curve was 0.64 (95% confidence interval, 0.58–0.70) for predicting a positive urine pneumococcal antigen test (Figure 1).

In patients with PSI risk class V, the overall sensitivity of the urine pneumococcal antigen test for all patients with pneumococcal pneumonia (definitive and probable diagnoses) was 65%, and the specificity was 98%, based on one positive test in 42 patients with proven diagnoses of nonpneumococcal pneumonia (Table E2). In patients with CURB-65 risk group 3, the overall sensitivity, including pneumococcal pneumonia with definitive and probable diagnoses, was 71%, and the specificity was 99% based on one positive test in 84 patients with proven diagnoses of nonpneumococcal pneumonia (Table E3).

Predictors of Positivity of the Pneumococcal Urinary Antigen

Several variables were significantly associated with the positivity of the urine pneumococcal antigen test in the univariate logistic regression analyses (Table 5). After performing an adjusted logistic regression analysis, the following remained significant: female sex; heart rate ⩾125 bpm, systolic blood pressure <90 mm Hg, and Sa_{O_2} <90%; absence of antibiotic treatment before admission; pleuritic chest pain; chills; pleural effusion; and BUN ⩾30 mg/dl. Figure 2 demonstrates that the risk of having a positive urinary antigen testing for *S. pneumoniae* could be predicted by assessing the number of clinical predictors present.

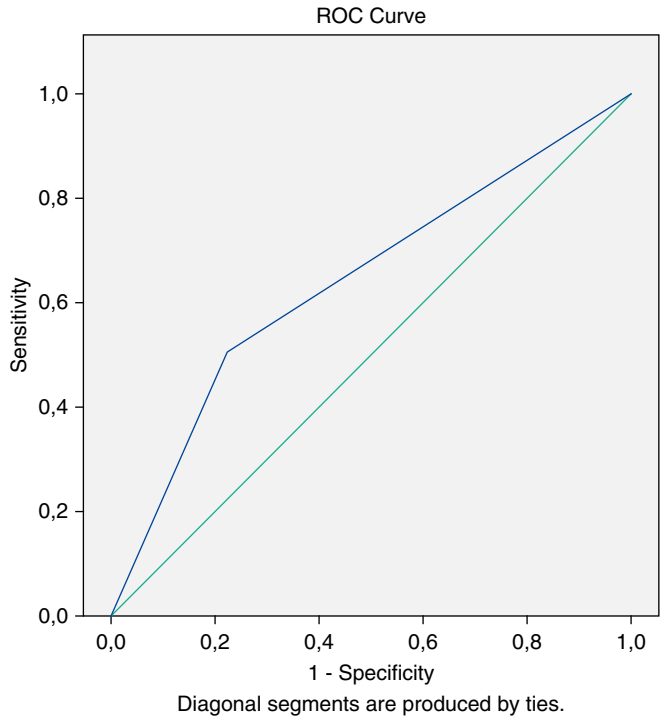

Figure 1. Receiver operating characteristic (ROC) analysis of significant variables derived from the logistic regression model in their capacity to predict positivity of the urine pneumococcal antigen test.

Discussion

There are three main findings of this study. First, in a large number of carefully studied patients who were hospitalized with CAP, *S. pneumoniae* was the most commonly identified causative organism, but it was found in only 21% of cases, consistent with the decreasing frequency with which pneumococcus has been implicated in CAP during the past two decades (24–26). Second, in 71% of cases of pneumococcal pneumonia, the diagnosis was made exclusively by means of urinary antigen test; in other words, using classical microbiological techniques of Gram stain and culture, pneumococcus would have been identified in only 29% of cases. Because of the large size of this case series, we were able to calculate both the sensitivity and specificity of urine antigen test; these values were 60 and 99.7%, respectively.

Third, we detected predictors that could be useful for clinicians to increase the suspicion for pneumococcal infection. Certain factors associated with severity (systolic blood pressure ⩽90 mm Hg, Sa_{O_2} ⩽90%, and BUN ⩾30 mg/dl) are more common in cases of bacteremic pneumococcal CAP (27), which may explain the higher sensitivity in cases with definitive etiology. Severity, as shown by the PSI or CURB65 scales, was not predictive, although several of the variables found form part of these scales.

Previous studies of the pneumococcal urinary antigen test have been much smaller than this one; the largest study to date by Roson and colleagues (14) included only 959 patients. None has reported the receiver operator characteristics, which in our case showed an area under the curve of 0.64. This is also the first study to report factors that predict a positive urinary antigen *S. pneumoniae* test. Previous studies have determined that factors such as days of clinical course until diagnosis (19), prior administration of

Table 4. Diagnostic accuracy of detection of pneumococcal antigen in urine

Reference Groups	n	Positive AgP (AgP performed)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	+PV (%) (95% CI)	−PV (%) (95% CI)	+LR (95% CI)	−LR (95% CI)
Diagnosis of pneumococcus								
Definitive diagnosis	182	112 (165)	67.9 (60.5–75.3)		99.1 (97.0–100)		254.6 (35.9–1,807.4)	
Probable diagnosis	80	33 (75)	44.0 (32.1–55.9)		100 (98.5–100)		—	
Overall	262	145 (240)	60.4 (54.0–66.8)		99.3 (97.6–100)		1,749.1 (245.8–12,445.8)	
Diagnosis of nonpneumococcus								
Definitive diagnosis	404	1 (375)		99.7 (99.0–100)		87.6 (84.3–90.8)		0.32 (0.26–0.40)
Probable diagnosis	198	0 (177)		100 (99.7–100)		80.8 (75.4–86.3)		0.56 (0.46–0.68)
Overall (includes diagnoses of unknown cause)	3,135	1 (2,895)		100 (99.9–100)		96.9 (96.3 to −97.6)		0.40 (0.34–0.46)

Definition of abbreviations: AgP = pneumococcal antigen; CI = confidence interval; LR = likelihood ratio; PV = predictive value.

antibiotics (11, 21), decreased renal function (especially if prerenal) (28), and severity according to the PSI score (14) are associated with detection of pneumococcal antigen in urine. Some clinical data suggest that CAP due to *S. pneumoniae* is also associated with a positive result, such as chills or pleuritic pain (9). However, none of these studies included an adjusted multivariate analysis, as done in the present study.

This analysis enabled us to determine the probability of diagnosing pneumococcal pneumonia by the pneumococcal urine antigen test according to the number of factors present. The probability is very low when only one factor is present (12%) but is substantially greater when six or more factors are present (52%). These results give a clear understanding of the pretest probability of a positive test and might help to set up recommendations for future guidelines in diagnosing and treating CAP. Although this study did not show in how many positive cases it was possible to simplify treatment, other studies have shown a change in treatment about one third of cases (17, 29).

Two factors suggest that this test could have a greater impact on limiting antibiotic treatment. The first is the time when the test is performed. Because the specificity approaches 100%, a positive result could be used to limit treatment to antibiotics directed against pneumococcus. A positive result at the moment of diagnosis of CAP would also reduce the need for further tests to establish an etiologic agent. The second factor is that some physicians may prefer to continue broad-spectrum antibiotics despite a positive urinary pneumococcal antigen (30). With our finding of a 99.7% specificity, this problem could be overcome by better education. The fact that the urine pneumococcal antigen test is only 60% sensitive simply means that the remaining 40% of patients will receive the same empiric, broad-spectrum coverage that all patients now receive without the urine antigen test.

A potential problem for antibiotic deescalation in CAP in the presence of a positive pneumococcal urinary antigen is the probability that several etiologic agents are involved. It is very unusual to have more than one bacterial species as the cause of pneumonia. When another pathogen is identified, it is nearly always viral, so there would be no impact from

Table 5. Significant univariate and multivariate logistic regression analyses of the predictive factors of positive pneumococcal urinary antigen testing

Factor	Univariate			Multivariate*		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Female sex	1.21	1.03–1.41	0.018	1.37	1.12–1.68	0.003
Pleuritic chest pain	1.61	1.38–1.87	<0.001	1.54	1.26–1.88	<0.001
Purulent expectoration	1.28	1.08–1.51	0.038	—	—	—
Chills	1.28	1.09–1.49	0.002	1.38	1.14–1.68	0.001
Days of clinical course (<3)	1.16	0.98–1.37	0.074	—	—	—
Chronic liver disease	1.51	1.07–2.13	0.020	—	—	—
No prior antibiotic treatment	1.39	1.15–1.68	0.001	1.46	1.13–1.89	0.004
HR ⩾125 bpm	1.64	1.31–2.06	<0.001	1.43	1.08–1.91	0.014
SBP <90 mm Hg	2.69	1.97–3.69	<0.001	2.16	1.43–3.28	<0.001
DBP ⩽60 mm Hg	1.6	1.34–1.92	<0.001	—	—	—
RR ⩾30 rpm	1.36	1.13–1.65	0.001	—	—	—
Interpretation of auscultation	1.34	1.07–1.69	0.012	—	—	—
Sa_{O2} ⩽90%	1.46	1.24–1.73	<0.001	1.29	1.05–1.59	0.017
Pa_{O2} ⩽60 mm Hg	1.32	1.12–1.57	0.001	—	—	—
Leukocyte count ⩾10,000 /mm^3	1.37	1.15–1.62	<0.001	—	—	—
BUN ⩾30 mg/dl	1.92	1.62–2.28	<0.001	1.76	1.39–2.23	<0.001
Na <130 mmol/l	1.43	1.08–1.89	0.013	—	—	—
Multilobe involvement	1.18	0.99–1.40	0.060	—	—	—
Pleural effusion	1.45	1.19–1.76	<0.001	1.49	1.16–1.94	0.002
PSI risk classes IV to V	1.58	1.36–1.84	<0.001	—	—	—
CURB-65 risk groups 2 and 3	1.46	1.21–1.75	<0.001	—	—	—

Definitions of abbreviations: BUN = blood urea nitrogen; CI = confidence interval; CURB-65 = consciousness, urea, respiratory rate, blood pressure, 65 yr old; DBP = diastolic blood pressure; HR = heart rate; OR = odds ratio; PSI = pneumonia severity index; RR = respiratory rate; SBP = systolic blood pressure.
*Hosmer-Lemeshow goodness-of-fit test; $P > 0.05$.

limiting antibiotic therapy (31). Although older studies have implicated *Mycoplasma* or *Chlamydia* as common causes of CAP, often together with bacteria, the methods used have been serologic, and these are of questionable validity (32). Recent studies using PCR technology suggest that these organisms will only rarely cause pneumonia in an older adult that is severe enough to require hospitalization (33), and a study comparing a cephalosporin alone or together with a macrolide showed no difference in outcome, further indicating the unimportant role played by *Mycoplasma* or *Chlamydia* (34).

Early identification of an etiologic agent with directed treatment should substantially reduce costs for diagnostic tests and for antibiotics and limit the development of antimicrobial resistance (35). Sorde and colleagues showed that simplified therapy based on the urinary antigen test enabled directed therapy in 41 of 474 (8.6%) of patients with CAP without adverse effects and suggested that this approach could have been used in 71 patients (15%). However, in a relatively small-scaled randomized controlled trial at a single institution, Falguera and colleagues (18) found that simplifying antimicrobial treatment on the basis of positivity urinary antigen had no clinical or economic benefit. Based on very small numbers, these authors concluded that such simplification appeared to increase the likelihood of relapse (3 of 25 with simplified treatment relapsed vs. 3 of 152; $P = 0.04$).

In our study involving >4,000 cases with CAP and by performing the antigen determination within the first 24 hours of diagnosis, we diagnosed 653 patients with *S. pneumoniae* using this technique alone, which accounted for 71% of all recognized cases of pneumococcal pneumonia. Early selection of therapy directed against *S. pneumoniae* might have been expected to limit antibiotic

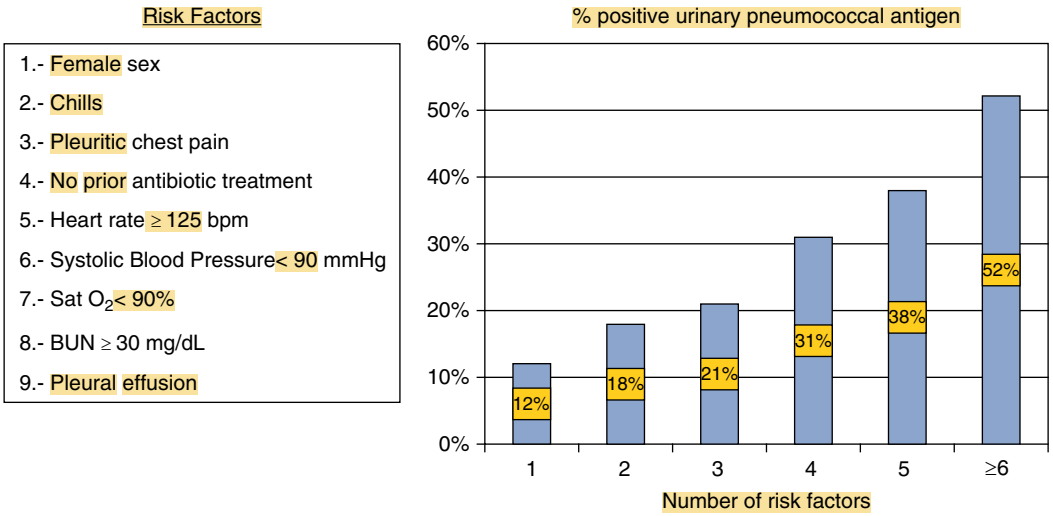

Figure 2. Risk of positive pneumococcal urinary antigen testing in patients with community-acquired pneumonia according to the number of predictors present. BUN = blood urea nitrogen.

usage, thereby reducing the risk of antibiotic resistance and costs.

The sensitivity of the pneumococcal urinary antigen test observed in this study (60%) was within the range of sensitivity observed in an earlier series of cases, in which it varied between 57 and 86% (11, 21). As has been reported previously, the sensitivity was greater (68%) in cases with a definitive diagnosis than in those with a probable diagnosis (44%), presumably reflecting a greater bacterial load in patients who are bacteremic. Concentrating the urine, which we did not do, may slightly increase the sensitivity of the assay (11). Specificity has generally been reported to be very high (11, 21) and exceeded >99% in our series, with only one case in 375 patients with proven diagnoses of nonpneumococcal pneumonia regarded as a false positive. A false-positive test might occur if a patient has had pneumococcal pneumonia in the previous 3 months (35, 36), which is not frequent in clinical practice.

Limitations of our study include the variability in usual practice from one hospital to another, but it would not be possible to obtain such a large number of patients without the collaboration of many medical centers. A urinary antigen test was not done in all patients, and those in whom it was not done tended to have more severe disease, which means that we may be slightly underestimating the overall proportion of pneumococcal cases.

In conclusion, in by far the largest prospective study to date, we identified *S. pneumoniae* as an etiologic agent in 21% of all cases of CAP. Seventy-one percent of all pneumococcal cases were diagnosed only by the urinary antigen test, which we demonstrated to be 99.7% specific. We also provided a model to predict a positive urinary antigen test. These results could be used to facilitate an early diagnosis of pneumococcal infection in patients with CAP, thereby avoiding unnecessary tests and excessive antimicrobial therapy. ■

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