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# The Ventilator-Associated Pneumonia PIRO Score*

## A Tool for Predicting ICU Mortality and Health-Care Resources Use in Ventilator-Associated Pneumonia

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***Background:*** **No score is available to assess severity and stratify mortality risk in ventilator-associated pneumonia (VAP). Our objective was to develop a severity assessment tool for VAP patients.**

***Methods:*** **A prospective, observational, cohort study was performed including 441 patients with VAP in three multidisciplinary ICUs. Multivariate logistic regression was performed to identify variables independently associated with ICU mortality. Results were converted into a four-variable score based on the PIRO (predisposition, insult, response, organ dysfunction) concept for ICU mortality risk stratification in VAP patients.**

***Results:*** **Comorbidities (COPD, immunocompromise, heart failure, cirrhosis, or chronic renal failure); bacteremia; systolic BP < 90 mm Hg; and ARDS. A simple, four-variable VAP PIRO score was obtained at VAP onset. Mortality varied significantly according to VAP PIRO score ($p < 0.001$). On the basis of observed mortality for each VAP PIRO score, patients were stratified into three levels of risk: (1) mild, 0 to 1 points; (2) high, 2 points; (3) very high, 3 to 4 points. VAP PIRO score was associated with higher risk of death in Cox regression analysis in the high-risk group (hazard ratio, 2.14; 95% confidence interval [CI], 1.19 to 3.86) and the very-high-risk group (hazard ratio, 4.63; 95% confidence interval, 2.68 to 7.99). Moreover, medical resource use after VAP diagnosis was higher in high-risk and very-high-risk levels compared to patients at mild risk, evaluated using length of ICU stay (mean ± SD, 22.0 ± 10.6 d vs 18.7 ± 12.8 d, $p < 0.05$) and duration of mechanical ventilation (18.3 ± 10.1 d vs 15.1 ± 11.5 d, $p < 0.05$).**

***Conclusions:*** **VAP PIRO score is a simple, practical clinical tool for predicting ICU mortality and health-care resources use that is likely to assist clinicians in determining VAP severity.**

***(CHEST 2008; 134:1208–1216)***

**Key words:** PIRO; sepsis; ventilator-associated pneumonia

**Abbreviations:** APACHE = acute physiology and chronic health evaluation; AUROC = area under the receiver operating characteristic; CI = confidence interval; *df* = degree of freedom; OR = odds ratio; PIRO = predisposition, insult, response, organ dysfunction; ROC = receiver operating characteristic; VAP = ventilator-associated pneumonia

Severity scores and class risk stratification have been successfully incorporated in the management of patients with a variety of respiratory conditions including COPD (Global Initiative for Chronic Obstructive Lung Disease),[1] pulmonary hypertension (World Health Organization classification),[2] and community-acquired pneumonia (CURB65 [confusion, urea, respiratory rate, BP, age > 65]).[3] However, no score has been developed to assess severity and to stratify mortality risk in ventilator-associated pneumonia (VAP). The use of biological markers[4–6] for severity assessment remains premature. A score identifying different levels of risk for VAP would be useful to improve decision making in terms of comparison in clinical trials or between different series, for benchmarking, to predict outcome, to anticipate

clinical failure or requirement for prolonged ventilatory support, and to define better the criteria for improving therapy.

In 2003, an international panel of experts provided the basis for introducing the PIRO concept as a hypothesis-generating model for future research.[7] The elements of the PIRO (predisposition, insult, response, organ dysfunction) concept are as follows: predisposition (chronic illness, age, and comorbidities), insult (injury, bacteremia, and endotoxin), response (neutropenia, hypoxemia, and hypotension), and organ dysfunction. Moreno et al[8] used the PIRO concept to construct a 12-variable model for severity assessment in septic patients admitted to ICU. The objectives of the present study are to develop a severity assessment tool able to stratify critically ill patients with VAP into mortality risk groups; and to evaluate the association between a PIRO score and health-care resource use in VAP patients.

## Materials and Methods

This is a cohort study including all patients with VAP prospectively recorded for surveillance purposes at three different multidisciplinary ICUs. Institutional review board approval was obtained in accordance with local requirements, and informed consent was waived due to the observational nature of the study.

### *Study Patients*

Patients enrolled were consecutive patients aged ≥ 18 years with suspicion of VAP, defined by new, persistent pulmonary infiltrates, not otherwise explained, appearing on chest radiography plus the presence of local (purulent respiratory secretions) and systemic signs of inflammatory response (WBC count > 10.000/μL, rise in WBC count > 20% in the absence of leukocytosis or fever) in patients receiving mechanical ventilation for at least 48 h.[9]

Inclusion in the study required collection of both respiratory and blood samples for microbiological examinations due to clinical suspicion of VAP, and the absence of any other infection. Fiberoptic bronchoscopic examination using quantitative respiratory cultures samples with protected specimen brush or BAL or quantitative tracheal aspirates was performed within 6 h of the onset of a new pulmonary infiltrate. Nosocomial infection management includes a standardized protocol in which two sets of blood cultures were obtained by venopuncture in all patients with suspected VAP in conjunction with respiratory cultures. The study excluded patients with respiratory infection other than VAP (including acute tracheobronchitis) and patients with multiple episodes of VAP.

### *Variables*

Patient demographic characteristics, comorbidities, clinical and laboratory variables, factors associated with VAP, onset of VAP, etiology, appropriateness of empirical antibiotic therapy and ICU mortality were recorded prospectively. In addition, the severity of illness was assessed by APACHE (acute physiology and chronic health evaluation) II within 24 h of ICU admission. The variables used to develop the new score were selected from the current literature as the most significant in VAP prognosis,[10–14] or because they were considered clinically important, in accordance with PIRO concept.

### *Definitions*

Patients were aggregated according to admission diagnosis in three categories: trauma, surgical, and all other medical conditions. Trauma was defined as either presence of injury in more than one body area or system or the presence of major cranial trauma isolated. Preexisting COPD was defined as a disease state characterized by the presence of airflow limitation due to chronic bronchitis or emphysema.[15] Immunocompromise was defined as primary immunodeficiency or immunodeficiency secondary to radiation treatment, use of cytotoxic drugs or steroids (daily doses > 20 mg of prednisolone or the equivalent for > 2 weeks), or AIDS or malignancy. Chronic heart failure was considered in patients admitted with New York Heart Association class III and IV. Chronic hepatopathy was considered in patients with documented biopsy-proven cirrhosis, documented portal hypertension, episodes of past upper-GI bleeding attributed to portal hypertension, or previous episodes of hepatic encephalopathy. Chronic renal failure was considered in patients receiving long-term hemodialysis.

An etiologic diagnosis of VAP was upheld when protected specimen brush yielded ≥ $10^3$ cfu/mL, BAL ≥ $10^4$ cfu/mL, or quantitative tracheal aspirate ≥ $10^5$ cfu/mL of at least one pathogenic microorganism. Episodes with more than one pathogenic microorganism isolated in respiratory samples were considered polymicrobial episodes. Recent antibiotic therapy was considered when a patient received antimicrobial agents during the 15 days preceding the VAP episode, with the exception of antibiotics administered for perioperative prophylaxis. VAP episodes were classified as early or late onset according to the American Thoracic Society/Infectious Diseases Society of America.[9]

Bacteremic episodes were defined as at least one positive blood culture result not related to another source of infection and at least one positive respiratory sample obtained within 48 h of each other. In addition, at least one of the microorganisms isolated in respiratory samples had to be isolated in blood cultures, whereas all isolates in blood cultures were required to grow in simultaneously obtained respiratory samples to meet the complete definition of bacteremic pneumonia.[12] Severe hypoxemia was defined as a $PaO_2$/fraction of inspired oxygen < 300. Multilobar compromise was considered when more than single-lobe opacities were observed in chest radiography. Presence of systolic BP < 90 mm Hg within 24 h of VAP diagnosis, or need of

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vasopressor drugs to maintain this BP level, in response to infection was recorded[16]; ARDS was diagnosed according to American-European Consensus Conference Committee criteria.[17] Appropriate antibiotic therapy was defined as the use of at least one antibiotic to which all isolates were susceptible *in vitro* from the moment a respiratory specimen was obtained.[18,19]

### *Score Construction and Calculation*

Univariate analysis was used to identify significant risk factors associated with mortality in the study. Variables associated with mortality in the univariate analysis ($p < 0.1$) or those with a clear relationship described in literature were included in a multivariate analysis model. Independent factors associated with mortality were identified and, then, used to build a score, based on the PIRO concept.

A clinical score (VAP PIRO score) was calculated based on four variables independently associated with mortality in multivariate analysis (presence of comorbidities, bacteremia, shock and ARDS), and one point was given for each feature present (range 0 to 4 points). The VAP PIRO score is the sum of these four variables. Then, mortality in the different VAP PIRO score level was assessed. Moreover, we randomly extracted two roughly equal-sized parts from the database to estimate the variability and stability of the prediction model. The quality of prediction was assessed by the goodness-of-fit statistics and discriminative ability of the model (area under receiver operating characteristic [ROC] curve) [AUROC].

### *Statistical Analysis*

Data were analyzed using statistical software (Version 11.0 for Windows; SPSS; Chicago, IL). Continuous variables were described as mean values and SDs, and were compared with *t* test or Mann-Whitney *U* test as appropriate according to distribution; Categorical variables were compared with Pearson $\chi^2$ and, if appropriate, Fisher exact test.

The association between the PIRO score for VAP and mortality was first assessed by stratifying patients according to different levels of VAP PIRO score and later into distinct risk groups. Risk classes according to the VAP PIRO score were calculated in all patients. The patients were stratified according to VAP PIRO score and survival curves were compared using Cox proportional hazards regression. The operative indexes (sensitivity, specificity, and positive and negative predictive values) of VAP PIRO score were determined for different cut-off points, and the positive likelihood ratio was calculated.

The discriminative power of PIRO score for VAP was assessed through measuring and comparing the AUROC, considered a composite index of discrimination.[20] The Hosmer-Lemeshow goodness-of-fit statistic was used to evaluate calibration of the developed prognostic model. The area under the curve, SE, and 95% confidence intervals (CIs) are given, and values were compared using the Student *t* test. The results are expressed as odds ratios (ORs) and p values with 95% CIs. The significance level was defined as $p < 0.05$.

## Results

We included 441 patients with VAP diagnosis. Mean APACHE II score was 18.3 ± 6.7, and mean age was 53.8 ± 18.4 years. There were 344 male patients (77.1%). Mean length of stay in the ICU was 30.1 ± 24.9 days, and duration of mechanical ventilation was 27.3 ± 22.3 days ± SD. Distribution of admission diagnosis category included the following: 194 medical (44.0%), 100 surgical (22.7%), and 147 trauma patients (33.3%). Definite etiology was documented in 328 patients (74.4%). There were 58 polymicrobial episodes (13.2%). Overall ICU mortality rate was 37.0%. Mortality in medical patients was 38.1%, in surgical patients was 58.0%, and in trauma patients was 21.1% ($\chi^2 = 35.009$; degrees of freedom [*df*] = 2; $p < 0.001$). The baseline characteristics of survivors and nonsurvivors are described in Table 1. Etiology of VAP episodes is described in Table 2.

Presence of comorbidities, admission diagnostic category, age, bacteremia, recent antibiotic therapy, severe hypoxemia, systolic BP < 90 mm Hg, and ARDS were identified in univariate analysis as significantly associated with mortality in VAP patients (Table 1). A multivariate model analysis (logistic regression) including these risk factors (presence of comorbidities, admission diagnostic category, age, bacteremia, recent antibiotic therapy, severe hypoxemia, systolic BP < 90 mm Hg, and ARDS) associated with mortality in the univariate analysis identified four variables independently associated with mortality in VAP patients ($\chi^2 = 146.3453$; *df* = 4; $p < 0.001$) [Table 3]. VAP PIRO score was then calculated based on the presence of these four variables (Table 4).

According to the VAP PIRO score, patients were distributed as follows: 102 patients (23.1%) had 0 points, 135 patients (30.6%) had 1 point, 121 patients (27.4%) had 2 points, 68 patients (15.4%) had 3 points, and 15 patients (3.4%) had 4 points. The mean VAP PIRO score for all patients was 1.4 ± 1.1, higher in nonsurvivors than survivors (2.2 ± 1.0 vs 1.0 ± 0.9; median, 2.0 vs 1.0; Mann Whitney *U* test z statistic = − 11.177; $p < 0.001$). ICU mortality rate increased significantly (Pearson $\chi^2 = 134,482$; *df* = 4; $p < 0.001$; linear-by-linear association = 126.213, $p < 0.001$) according to the VAP PIRO score (Fig 1). Table 5 shows predictive values for different cut-off points of the VAP PIRO score. A VAP PIRO score cut-off ≥ 2 points was associated with the best performance to predict ICU mortality with a sensitivity of 79.8% and specificity of 73.4%.

On the basis of the observed ICU mortality according to VAP PIRO score (Fig 1), the patients were stratified into three levels of risk: (1) mild, 0 to 1 point; (2) high, 2 points; and (3) very high, 3 to 4 points. Differences in distribution and mortality associated with each level of risk are shown in Table 6. The effect of VAP PIRO risk levels was tested with the Cox proportional hazards regression analysis controlled for age and severity of illness (APACHE II

**Table 1—*Univariate Analysis for ICU Mortality in 441 VAP Patients**

| Variables | Survivors (n = 278) | Nonsurvivors (n = 163) | p Value† | Statistic Test |
|---|---|---|---|---|
| Age, yr | 49.2 ± 18.9 | 61.2 ± 14.8 | <0.05 | −6.951‡ |
| APACHE II score at admission | 17.9 ± 6.4 | 18.8 ± 7.0 | 0.17 | −1.376‡ |
| Admission category | | | | 35.009§ |
| Trauma | 116 (41.7) | 31 (19.0) | <0.05 | 23.844‖ |
| Surgical | 42 (15.1) | 58 (35.6) | <0.05 | 23.414‖ |
| Medical | 120 (43.2) | 74 (45.4) | 0.73 | 0.127‖ |
| Comorbidities | 94 (33.8) | 106 (65.0) | <0.05 | 40.404‖ |
| COPD | 47 (16.9) | 45 (27.6) | <0.05 | 6.493‖ |
| Immunocompromise | 36 (12.9) | 32 (19.6) | 0.08 | 3.024‖ |
| Chronic heart failure | 26 (9.3) | 44 (27.0) | <0.05 | 22.645‖ |
| Chronic hepatopathy | 8 (2.9) | 12 (7.4) | 0.05 | 3.793‖ |
| Chronic renal failure | 5 (1.8) | 9 (5.5) | 0.06 | 3.501‖ |
| Recent antibiotic therapy | 119 (42.8) | 102 (62.6) | <0.05 | 16.066‖ |
| Diagnostic method performed | | | | |
| Bronchoscopy | 12 (4.3) | 6 (3.7) | 0.94 | 0.006‖ |
| Quantitative tracheal aspirate | 266 (95.7) | 157 (96.3) | 0.94 | 0.006‖ |
| Definite etiology | 212 (76.3) | 116 (71.2) | 0.28 | 1.144‖ |
| Polymicrobial VAP | 38 (13.7) | 20 (12.3) | 0.78 | 0.176‖ |
| Late-onset VAP | 170 (61.2) | 109 (66.9) | 0.26 | 1.447‖ |
| Bacteremia | 27 (9.7) | 37 (22.7) | <0.05 | 13.969‖ |
| Severe hypoxemia | 251 (90.3) | 156 (95.7) | 0.04 | 4.239‖ |
| Multilobar compromise | 131 (47.1) | 83 (50.9) | 0.50 | 0.451‖ |
| Systolic BP < 90 mm Hg | 91 (32.7) | 127 (77.9) | <0.05 | 83.909‖ |
| ARDS | 66 (23.7) | 93 (57.1) | <0.05 | 49.463‖ |
| Inappropriate empirical antibiotic therapy | 26 (9.3) | 26 (16.0) | 0.05 | 3.690‖ |

*Data are presented as mean (SD).
†Pairwise comparisons between survivors and nonsurvivors.
‡Continuous variables, *t* test.
§$\chi^2$, *df* = 2.
‖Categorical variables, $\chi^2$.

score). High-risk level (hazard ratio, 2.14; 95% CI, 1.19 to 3.86) and very-high-risk level (hazard ratio, 4.63; 95% CI, 2.68 to 7.99) were significantly associated with higher risk of death when compared to mild risk category (Fig 2). When comparing episodes in subgroups such as trauma ($\chi^2 = 57.066$; *df* = 4; $p < 0.001$) and nontrauma patients ($\chi^2 = 69.717$; *df* = 4; $p < 0.001$), according to diagnosis on admission as trauma ($\chi^2 = 57.066$; *df* = 4; $p < 0.001$), surgical ($\chi^2 = 25.196$; *df* = 4; $p < 0.001$) or medical ($\chi^2 = 46.181$, *df* = 4; $p < 0.001$) patients, early ($\chi^2 = 42.767$; *df* = 4; $p < 0.001$) and late-onset VAP ($\chi^2 = 93.293$; *df* = 4; $p < 0.001$), episodes with ($\chi^2 = 104.175$; *df* = 4; $p < 0.001$) or without definite etiology ($\chi^2 = 30.662$; *df* = 4; $p < 0.001$), and episodes with appropriate ($\chi^2 = 95.160$; *df* = 4; $p < 0.001$) and inappropriate empiric antibiotic treatment ($\chi^2 = 11.690$;

**Table 2—*Organisms Isolated in 441 VAP Episodes**

| Pathogens | Overall Prevalence (n = 441) | Mean VAP PIRO Score | Survivors (n = 278) | Nonsurvivors (n = 163) | p Value† | $\chi^2$ |
|---|---|---|---|---|---|---|
| Enterobacteriaceae | 81 (18.4) | 1.5 ± 1.1 | 50 (18.0) | 31 (19.0) | 0.75 | 0.098 |
| MSSA | 79 (17.9) | 1.1 ± 1.0 | 60 (21.6) | 19 (11.7) | 0.01 | 6.227 |
| MRSA | 60 (13.6) | 1.9 ± 1.1 | 34 (12.2) | 26 (16.0) | 0.32 | 0.914 |
| *P aeruginosa* | 49 (11.1) | 1.6 ± 0.9 | 25 (9.0) | 24 (14.7) | 0.09 | 2.862 |
| *Acinetobacter baumannii* | 48 (10.9) | 1.8 ± 1.3 | 27 (9.7) | 21 (12.9) | 0.38 | 0.763 |
| *Haemophilus influenzae* | 34 (7.7) | 1.3 ± 1.1 | 28 (10.1) | 6 (3.7) | 0.03 | 5.034 |
| *S pneumoniae* | 23 (5.2) | 0.9 ± 1.1 | 17 (6.1) | 6 (3.7) | 0.38 | 0.788 |
| Other Gram-negative bacteria | 4 (0.9) | 1.5 ± 0.6 | 3 (1.1) | 1(0.6) | 0.98 | 0.001 |
| Other cocci | 9 (2.0) | 1.0 ± 1.0 | 7 (2.5) | 2 (1.2) | 0.56 | 0.333 |
| Unknown etiology | 113 (25.6) | 1.5 ± 1.1 | 66 (23.7) | 47 (28.8) | 0.28 | 1.144 |

*Data are presented as mean (SD). MSSA = methicillin-sensitive *S aureus*; MRSA = methicillin-resistant *S aureus*.
†Survivors vs nonsurvivors, $\chi^2$, *df* = 1.

**Table 3—*Independent Variables Associated With ICU Mortality in 441 VAP Patients in Multivariate Analysis***

| PIRO Elements | Adjusted OR | 95% CI | p Value† |
|---|---|---|---|
| P: comorbidities* | 3.81 | 2.35–6.15 | <0.05 |
| I: bacteremia | 1.94 | 1.03–3.66 | <0.05 |
| R: systolic BP < 90 mm Hg‡ | 4.40 | 2.71–7.15 | <0.05 |
| O: ARDS | 3.65 | 2.23–5.98 | <0.05 |

*Comorbidities were defined as presence of COPD, immunocompromise, chronic heart failure, chronic hepatopathy, or chronic renal failure.
†Logistic regression with stepwise elimination; Hosmer-Lemeshow goodness of fit, p = 0.254.
‡Or need of vasopressor to maintain BP.

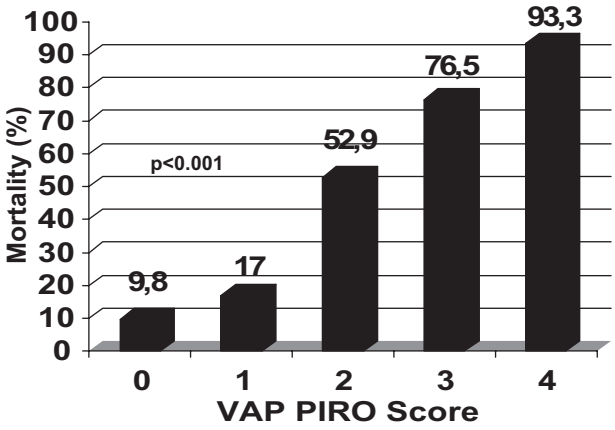


FIGURE 1. VAP PIRO score and ICU mortality in 441 VAP patients.

*df* = 4; p = 0.019), the VAP PIRO score remained significantly associated with ICU mortality in all situations. Moreover, mortality levels in different pathogens was correlated to mean simplified VAP PIRO levels ($r = 0.76$; $p < 0.05$).

Finally, discrimination of VAP PIRO score was assessed using ROC curves. The AUROC (Fig 3) showed consistent mortality discrimination by the VAP PIRO score (AUROC = 0.81; 95% CI, 0.77 to 0.85), which outperformed the APACHE II score (AUROC = 0.53; 95% CI, 0.47 to 0.58) for severity assessment, with significant difference between areas (z statistic = − 7.745; $p < 0.001$). There was no difference in the VAP PIRO score ability to discriminate when comparing different subgroups such as trauma vs nontrauma patients (p = 0.08), in trauma vs surgical (p = 0.16), trauma vs medical (p = 0.14), and medical vs surgical patients (p = 0.93), early vs late-onset VAP episodes (p = 0.71), episodes with or without definite etiology (p = 0.54), and patients with appropriate vs inappropriate empiric antibiotic treatment (p = 0.59) [given in electronic supplemental material, Appendix A]. A cross-validation model with Hosmer-Lemeshow goodness-of-fit analysis shows the model is well calibrated in the overall cohort (p = 0.205).

**Table 4—*Variables Included in PIRO Score for VAP***

| PIRO Elements | Variables | Points |
|---|---|---|
| Predisposition | Comorbidities* | 1 |
| Insult | Bacteremia | 1 |
| Response | Systolic BP < 90 mm Hg† | 1 |
| Organ dysfunction | ARDS | 1 |
| | Score range | 0–4 |

*Comorbidities were defined as presence of COPD, immunocompromise, chronic heart failure, chronic hepatopathy, or chronic renal failure. One point is given if any of the comorbidities listed are present.
†Or need of vasopressor agents to maintain this BP.

In survivors, medical resources use after VAP diagnosis was significantly higher in high and very-high-risk patients when compared to mild-risk patients, evaluated using ICU length of stay (22.5 ± 10.3 days vs 18.7 ± 12.9 days; median, 21.0 vs 16.0 days; Mann-Whitney *U* test Z statistic = − 3.413; $p < 0.001$) and duration of mechanical ventilation (18.9 ± 9.9 days vs 15.1 ± 11.5 days; median, 17.0 vs 12.0 days; Mann-Whitney *U* test Z statistic = − 3.454; $p < 0.001$) after VAP diagnosis.

## DISCUSSION

This is the first study designed to stratify severity of VAP episodes, using a score based on the PIRO concept. Our findings suggest that this simple four-variable score (Fig 4) is able to assess severity and to improve prediction of ICU mortality in VAP patients. Additionally, it helps to predict health-care utilization (ICU length of stay and duration of mechanical ventilation) after the VAP episode.

The PIRO concept is a classification scheme for sepsis that includes predisposing conditions, the nature and extent of insult, the nature and magnitude of the host response, and the degree of con-

**Table 5—*Test Characteristics of VAP PIRO Score for ICU Mortality in 441 Patients****

| VAP PIRO Score (n = 441) | Sensitivity, % | Specificity, % | PPV, % | NPV, % | LR (+) |
|---|---|---|---|---|---|
| ≥ 1 | 93.9 | 33.1 | 45.1 | 90.2 | 1.40 |
| ≥ 2 | 79.8 | 73.4 | 63.7 | 86.1 | 3.00 |
| ≥ 3 | 40.5 | 93.9 | 79.5 | 72.9 | 6.62 |
| 4 | 8.6 | 99.6 | 93.3 | 65.0 | 23.88 |

*PPV = positive predictive value; NPV = negative predictive value; LR(+) = positive likelihood ratio.

**Table 6—*Univariate Analysis for ICU Mortality of Different VAP PIRO Score Level of Risk in 441 Patients***

| Risk According to VAP PIRO Score | Univariate Analysis | | |
|---|---|---|---|
| | No. (%) | Death, No. (%) | OR (95% CI)* |
| Mild risk (0–1 point) | 237 (53.7) | 33 (13.9) | 1 |
| High risk (2 points) | 121 (27.5) | 64 (52.9) | 6.94 (4.03–11.99) |
| Very high risk (3–4 points) | 83 (18.8) | 66 (79.5) | 24.00 (12.01–48.54) |

*OR obtained in comparison with mild risk.

comitant organ dysfunction.[7,21–24] VAP PIRO score was built on this concept and includes variables significantly associated with mortality in multivariate analysis in a VAP database. The selection of these parameters was based on prior evidence supporting their association with poor prognosis and their good fit with the PIRO definitions.

VAP evaluation tools available in ICU are more focused on diagnosis than prognosis. The process of evaluating suspected VAP is oriented toward confirming its presence, examining the differential diagnosis, and identifying the causative organism and the presence of complications (*eg*, ARDS).[25,26] In contrast with other processes, the assessment of severity remains undeveloped.

Prognosis and severity assessment are usually performed at ICU admission and do not consider complications during ICU stay. A reassessment of patient severity at the moment of VAP diagnosis allows better and more precise stratification of risk and prediction of mortality. Severity of illness, measured by mortality probability model II, when pneumonia is diagnosed was identified as an important predictor of survival,[27] suggesting that severity assessment at the time of pneumonia diagnosis could be used for therapeutic and prognostic stratification. Early assessment of severity in patients with VAP may have a role in clinical studies to stratify risk and identify potential subgroups of more severely ill patients who would benefit more from specific therapies. However, an issue that remains unexplored in VAP patients is the definition of episode severity.

Important prognostic factors have been identified for VAP episodes, such as appropriateness of antibiotic treatment,[28,29] underlying disease,[13,30–31] bacteremia presence,[12] and time to onset of pneumonia.[32,33] Trauma patients differ from medical and surgical patients, not only in terms of etiology, but they also have better prognosis than nontrauma patients.[30] The mortality difference found in our study is in concordance with these findings. Bacteremic episodes are independently associated with higher mortality.[12] Furthermore, late-onset VAP has been described as an independent factor associated with ICU mortality.[34] An assessment tool including these factors would be useful to define the episode severity.

The VAP PIRO score identified four independent variables associated with mortality, allowing assessment of VAP episode severity. A potential strength of the VAP PIRO score is its validity in different subsets of patients. The performance of diagnostic assessment tools such as Clinical Pulmonary Infection Score[25] varies according to specific subgroups of patients (*eg*, trauma).[35] Likewise, early and late-

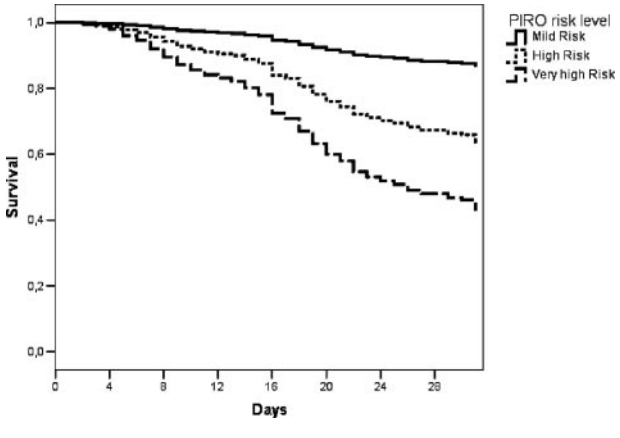


FIGURE 2. Cox regression analysis of VAP PIRO risk levels and ICU mortality in 441 patients.

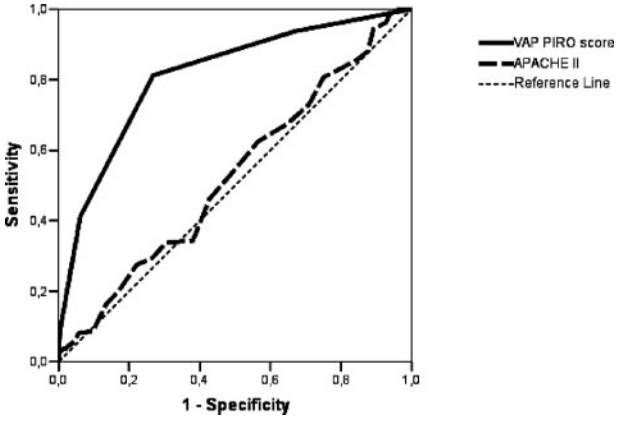


FIGURE 3. ROC curve comparing VAP PIRO score and APACHE II score for discrimination between survivors and nonsurvivors in the ICU in 441 VAP patients.

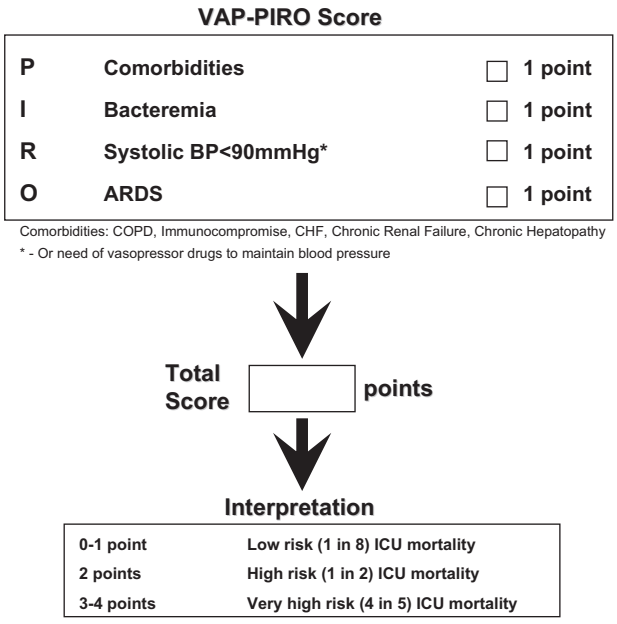


FIGURE 4. Flow chart for the use of VAP PIRO score.

onset VAP have different risk factors and described attributable mortality.[34] In our study, VAP PIRO score discriminate properly and no significant difference was found comparing trauma and nontrauma patients, early and late-onset VAP, and episodes with or without definite etiology. In addition, the scores differed significantly between survivors and nonsurvivors, independently of known etiology or antibiotic appropriateness. We found that mean VAP PIRO score was higher in pathogens with a higher associated mortality such as methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* and lower in pathogens with lower associated mortality such as methicillin-sensitive *S aureus* and *Streptococcus pneumoniae*. Further, we found a positive correlation between mortality and levels of VAP PIRO score according to VAP episode etiology. These findings reinforce the applicability of the score and strengthen its relevance. VAP PIRO score is the first approach to stratify patients according to severity of VAP episode. It would be useful either for benchmarking or to balance severity in randomized clinical trials.

Another potential strength of VAP PIRO score is its simplicity: it is based on four easily available variables, all with known impact on VAP mortality. It allows easy risk stratification of patients into different levels of severity with progressive rates of mortality. In order to enhance simplicity, we decided to give 1 point for each variable, in spite of difference in coefficients in multivariate analysis. Predictive ability of the score did not change when we give points to each variable according to multivariate analysis coefficients. Interestingly, Moreno et al[8] reported a 12-variable model based on the PIRO concept for prognosis in septic patients admitted to ICU, with different values based in multivariate analysis. Although it works well for sepsis severity assessment, specific risk factors associated with certain specific disease entities are not included in the model. The VAP PIRO score is a simple approach, with only four variables and specifically designed for VAP patients in comparison with the 12-variable PIRO score for sepsis[8] or Clinical Pulmonary Infection Score[25] described elsewhere. Also, on the basis of VAP PIRO score patients could be classified in three levels of mortality risk.

Attributable mortality in patients with VAP is a controversial issue because patients with VAP are severely ill patients with a high associated mortality. While some studies[32,36–37] described an attributable mortality of VAP as high as 75%, others[38–40] failed to demonstrate any excess at all. Valles et al[34] described a significant effect of time of onset of pneumonia on attributable mortality, showing that late-onset pneumonia is associated with excess mortality but early-onset VAP is not. The fact that VAP PIRO score worked well in both populations to assess severity strengthens its applicability.

The study has several limitations. First, we have performed analysis considering only ICU mortality because we lack data on hospital mortality for all patients. Secondly, although all selected variables were significantly associated with mortality, coefficient values in the multivariate analysis were different. We defined the same weight (presence/absence) for each variable in order to increase simplicity and, under these conditions, VAP PIRO score performed well for severity assessment and ICU mortality risk prediction. Interestingly, when calculating the score considering the coefficient value, the model did not change (data no shown). When including acute renal failure to the model, the results did not change. Indeed, a similar approach has been previously used to stratify patients with sepsis (*eg*, sequential organ-failure assessment score)[41] and community-acquired pneumonia (*eg*, CURB-65).[3] An additional limitation is the use of APACHE II score for severity assessment of ICU patients. Unfortunately we do not have data of newer APACHE versions for comparison. Another limitation was the low rate of patients with an invasive approach to etiologic diagnosis in the cohort. However, all patients had quantitative cultures performed. Nevertheless, a randomized controlled trial[42] did not show any significant difference in outcomes when comparing an invasive and noninvasive diagnostic approach in VAP patients. Whether VAP PIRO score appropriately assesses

severity in patients managed with an invasive diagnostic approach is an issue that should be explored in order to validate the score in this subgroup of patients. Further studies should validate VAP PIRO score in populations with specific pathogens and for hospital mortality rates. Also, we did not assess the presence of lactic acidosis in this sample. Whether this finding would add more information than the presence of hypotension and vasopressor need should be further assessed.

In conclusion, VAP-PIRO is a new, simple, four-variable tool for severity assessment that stratifies mortality risk in VAP patients. Moreover, VAP PIRO score is associated with increased medical resource use in ICU in patients after VAP develops. VAP-PIRO is likely to be a practical tool for clinicians in the prediction of disease severity in patients with VAP.

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