Ventilator Associated Pneumonia in Intensive Care Unit: Incidence, patient characteristics, outcome and validation of VAP-PIRO score in a local Chinese cohort

Arthur Ming-Chit Kwan, King-Chug Chan, Arthur Chun-Wing Lau, Wing-Wa Yan

Abstract

***Objective*: Despite a systematic scoring system has been developed to assess the severity and to stratify the mortality risk of Ventilator-Associated Pneumonia (VAP), few clinical studies had published in validating this scoring system. We intend to study the incidence of VAP in a local Chinese cohort and to validate the VAP-PIRO (Predisposition, Insult, Response, Organ Dysfunction) score.**

***Design*: A prospective, observational cohort study.**

***Setting*: A 20-bed mixed medical-surgical adult Intensive Care Unit (ICU) of a regional referral centre serving 650,000 populations.**

***Patients and participants*: 269 consecutive patients who had been intubated and mechanically ventilated for more than 24 hours during an 8-month study period.**

***Interventions*: None.**

***Measurements and results*: VAP was diagnosed by National Healthcare Safety Network (NHSN) PNU1 criteria. Clinical characteristics, medical resource use and outcome of the cohort were studied. The VAP-PIRO score of each VAP case was calculated. The medical resource use and mortality in each PIRO risk group were compared. Of 269 patients admitted to ICU during the study period there were 59 VAP cases. The VAP incidence was 47.81 per 1,000 ventilator days. VAP-PIRO score was unable to stratify medical resource use and mortality in our cohort.**

***Conclusion*: VAP-PIRO score cannot significantly differentiate mortality and usage of medical resources in our cohort. This is likely due to the severity of VAP in our cohort is modest when compared to the original cohort.**

Key words: Ventilator-Associated Pneumonia, Pneumonia, PIRO.

Introduction

Critically ill patients in Intensive Care Unit (ICU) are at risk of dying not only from their critical illness *per se* but also from secondary process with the initial intention of organ support. Ventilator-Associated Pneumonia (VAP) is one of the typical examples and is one of the most frequent nosocomial infections associated with significant mortality, morbidity and healthcare cost. (1)

The definition of VAP is a highly debatable topic in critical care and there is no "gold standard" in the diagnostic criteria so far. Parallel to the lack of gold standard in the diagnostic criteria of VAP is the absence of measures to assess the severity and to stratify mortality risk. (2) In 2003 an international panel of experts participated in a consensus

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conference sponsored by the Society of Critical Care Medicine, European Society of Intensive Care Medicine, American College of Chest Physicians (ACCP), American Thoracic Society (ATS), and Surgical Infection Society and provided the basis for introducing Predisposition, Insult, Response and Organ Dysfunction (PIRO) as a hypothesis-generating model for future research. (3)

So far few papers had utilized the PIRO concept to gradate the severity of VAP and to predict its mortality. (4-6) It has been shown that VAP-PIRO score had a better performance than Acute Physiology and Chronic Health Evaluation II (APACHE II) and ATS/IDSA criteria in mortality prediction in the original study. (6) Our study will attempt to validate the VAP-PIRO score in our cohort and to assess the performance of VAP-PIRO score in risk stratification and mortality differentiation.

Materials and methods

Patients

A prospective, observational cohort study was conducted in Pamela Youde Nethersole Eastern Hospital, Hong Kong. The mixed medical-surgical adult ICU was a 20-bed unit which provided a comprehensive intensive care service except burns, cardiothoracic surgery and transplant surgery. Patients were recruited between April and November 2010. Consecutive adult patients older than 18 years who had been intubated and mechanically ventilated prior ICU admission and those who were intubated in ICU were included. Patients who had been intubated and mechanically ventilated for less than 24 hours in ICU and those who died within 24 hours after ICU admission were excluded. A patient could only be included once per single ICU admission regardless of the number of intubations (or re-intubations) or VAP episodes during that ICU admission.

Demographic data, admission source, specialty, admission types, co-morbidities, duration of mechanical ventilation, the date when bronchoscopy and tracheostomy were performed, length of ICU and hospital stay were recorded prospectively. The severity of illness of patients was assessed by APACHE II and IV within 24 hours of ICU admission.

Definitions

Non-metastatic cancer was defined as cancer which could include regional lymph nodes. Chronic renal failure was defined as chronic renal supportive therapy (i.e., chronic hemodialysis, hemofiltration, or peritoneal dialysis) for irreversible renal disease or history of chronic renal insufficiency associated with clinical adverse effects (creatinine >300 μmol/L). COPD was defined as chronic obstructive pulmonary disease, chronic bronchitis, or emphysema requiring prescribed treatment.

Chronic respiratory failure was defined as permanent shortness of breath on light activity attributable to pulmonary (chronic restrictive or obstructive) disease and those who had been documented chronic hypoxemia, hypercarbia, secondary polycythemia, severe pulmonary hypertension (mean pulmonary artery pressure >40 mmHg), or requirement for chronic respiratory support (e.g., home oxygen therapy).

Chronic heart failure was defined as patients who had been documented as New York Heart Association class III and IV. Chronic hepatopathy was diagnosed either by biopsy taken before or during ICU admission or by clinical features such as portal hypertension, presence of esophageal/gastric varices, the demonstration of retrograde splenic-venous flow by ultrasound, history of variceal bleeding, episodes of acute hepatic failure/encephalopathy/coma. Alcoholism was defined as alcohol intake of greater than 80 g of alcohol per day for at least 6 months before ICU admission and that was responsible for clinical adverse effects such as encephalopathy, neurologic disorder, nutritional disorder, and cirrhosis.

Diabetes mellitus was defined as diabetes which required daily insulin therapy.

Immunosuppression was defined as primary immunodeficiency or immunodeficiency secondary to radiation treatment, use of cytotoxic drugs or steroids (daily doses greater than 20 mg prednisolone or equivalent for more than 2 weeks), AIDS or malignancy. (6)

The definition of NHSN-PNU1 in the Ventilator-Associated Pneumonia guideline published by NHSN (7) was adopted. Late-onset VAP was defined as VAP with its onset of 4

days (96 hours) after intubation. VAP diagnosed before day 4 was defined as early-onset VAP. (8) An etiological diagnosis of VAP was confirmed when endotracheal aspirate or bronchoalveolar lavage grew at least one pathogenic organism by qualitative culture method. Episodes of VAP with more than one pathogenic organism isolated from the specimen were considered as polymicrobial VAP. Recent antibiotic therapy was defined as patient received antimicrobial agents within 14 days preceding VAP episode with the exception of pre-operative antibiotic prophylaxis. Bacteraemia was defined as at least one positive blood culture result not related to another source of infection and at least one positive respiratory sample (ETA or BAL) obtained within 48 hours of each other.

The VAP-PIRO score was calculated based on 4 variables independently associated with mortality documented in the original study. For each variable present in a patient, 1 point would be given and the VAP-PIRO score was the sum of these 4 variables. The definition of parameters, scoring method and risk stratification can be referred to VAP-PIRO schema diagram as shown. (6)

Establish the diagnosis

The attending physician attended the patient regularly and standard level of care was practiced. Blood parameters (including white cell count and PaO2) were checked at least daily at a fixed time of the day. Radiological images including chest radiographs or computer tomography of the thorax were reviewed everyday with the presence of all ICU staff including respiratory physician. Routine qualitative culture of endotracheal aspirate was performed twice weekly. Endotracheal aspirates were also sampled additionally upon the discretion of attending physician whenever indicated. Routine bronchoscopy or bronchoalveolar lavage (BAL) was not performed and was left upon discretion of attending physician.

Various prevention of VAP measures were routinely practiced in the ICU before and during the study period: Avoidance of continuous muscle relaxants or over-sedation, avoidance of routine suction or saline instillation, practice of sedation interruption, promotion of weaning, maintenance of adequate tracheal cuff pressure, proper patient positioning of semi-recumbent position and regular antiseptic oral care.

The Hong Kong East Cluster Ethics Committee approved this study and informed consent was waived since no patient intervention was involved. No patient identifiers were used during data collection and maintenance.

Statistical analysis

Continuous variables were described as mean values and standard deviations, and were compared with Student's t-test or Mann-Whitney U test as deemed appropriate. Categorical variables were compared with Pearson *Chi*-square test. The association between the VAP-PIRO score and mortality was first assessed by stratifying patients according to different VAP-PIRO scores as described in the original article. (6)

The area under the receiver-operating characteristic curve (AUROC) was then obtained as to assess the discriminating capability of the VAP-PIRO score. Comparison of the AUROC would then be made with the AUROC using APACHE II score and APACHE IV score respectively. Data analysis was performed by Statistical Package for Social Sciences (SPSS version 15.0 for Windows, Chicago, IL).

Results

Over the 8-month study period from April 2010 to November 2010 there were 799 admissions to the ICU. 263 patients who had been intubated and mechanically ventilated for more than 24 hours were included into the study. The mean APACHE II score was 26±9 and APACHE IV score was 94±38 respectively. The mean age was 66±16 years. There were 148 males (56.3%). The mean (± 2 SD) duration of mechanical ventilation was 4.69±5.42 days, ICU length of stay was 7.62±7.66 days, and hospital length of stay was 26.02±24.58 days. The overall ICU mortality in was 16.7% (44/263) and the hospital mortality was 25.1% (66/263).

There were 59 VAP cases (22.43%) and the VAP rate by NHSN-PNU1 criteria was 47.81 per 1,000 ventilator days. Among the 59 VAP cases there were 31 late-onset VAP (52.5%) and the median time for development of VAP was day 5. The baseline characteristics, admission source, admission specialties and co-morbidities of patient with VAP versus those without were listed in **Table 1**. No significant difference was noticed in the baseline co-morbidities except

more patients in the VAP group had received antibiotics prior its onset (**Table 1**).

Patients with VAP were more likely to had bronchoscopy performed (12.3% vs 30.5%, p<0.001), to be re-intubated (5.9% vs 23.7%, p<0.001) and tracheostomised (7.8% vs 40.7%, p<0.001) (**Table 1**). A significantly longer duration of mechanical ventilation (9.93±8.37 days vs 3.18±2.76 days, p<0.001), ICU length of stay (15.36±11.26 days vs 5.39±4.13 days, p<0.001), and hospital length of stay (42.65±31.67 days vs 21.58±20.22 days, p<0.001) were observed in VAP cases (**Table 2**). A higher ICU mortality (15.7% vs 20.3%, p=0.519) and a significantly higher hospital mortality (21.08% vs 38.98%, p=0.009) were noticed in VAP cases (**Table 1**).

The VAP-PIRO score of our cohort was calculated based on the presence of 4 variables published in the original paper. (6) In our cohort 24 patients (40.7%) had 0 points, 23 patients (39%) had 1 point, 11 patients (18.6%) had 2 points and 1 patient (1.7%) had 3 points. The mean VAP-PIRO score for all patients was 0.81±0.298 (**Figure 1**). A non-significant trend towards a higher VAP-PIRO score was observed among non-survivors (1.167±0.937 vs 0.723±0.743, Mann-Whitney U test, z statistics -1.348; p=0.178). A non-significant increase in ICU and hospital mortality was noted in patients with a higher VAP-PIRO score (Pearson Chi square =5.181; df=3; p=0.159, linear by linear association=2.948; p=0.086) (**Figure 2**).

ICU resource use in terms of days of mechanical ventilation, ICU days free from mechanical ventilation and ICU length of stay in patients with different VAP-PIRO score were tabulated in **Table 3**, which showed no significant difference in patients with a higher VAP-PIRO score. Finally, the discrimination of VAP-PIRO score was assessed by using ROC curves. The AUROC of VAP-PIRO score was 0.595, while the AUROC for APACHE II was 0.72 and AUROC for APACHE IV was 0.692 in our cohort (**Figure 3**).

Discussion

To our knowledge, the present study is the first one to report a detailed overview in VAP and its impact to ICU in Hong Kong using an up to date diagnostic criteria. The data suggest that VAP is a common nosocomial infection in ICU as 22% of patient who had been ventilated for more than 24 hours is involved. Our data also represents a more realistic scenario in ICU: the APACHE II score of our cases is relatively high (26±9), and an adequate representation from various specialties. Moreover, the duration of mechanical ventilation and ICU length of stay are comparable to the large US database. (9)

The incidence of VAP in our study is slightly higher when compared to the reported figure of 18% in the ANZPIC group (10) and 14.2% in the EU-VAP/CAP group. (11) There is a wide variation in the incidence of VAP in terms of ventilator days. It has been reported in the EU-VAP group the incidence of VAP was 18.3 episodes per 1,000 ventilator days and was even lower in the NASCENT group. (12) The difference mainly lies on the diagnostic criteria of VAP, which varies in different studies in particular those required a positive quantitative culture result. (13) Concord to such finding is the fact that the reported range in the incidence of VAP lies from 4.9 to 42.8 per 1000 ventilator days. (14,15)

Consistent to studies worldwide the development of VAP significantly prolong the duration of mechanical ventilation and ICU length of stay. In our cohort patients with VAP required 6 more days of mechanical ventilation and stayed in ICU for 10 more days. Such result was similar to the findings in Europe (10 more days of mechanical ventilation and 12 more days of ICU stay) (11) and the United States (9 more days of mechanical ventilation and 6 more days in ICU stay). (9) Bronchoscopy was performed in 30.5% of our patients with VAP, a result comparable to the EU-VAP/CAP group (23.3%) (11) and ANZPIC group (29.7%). (10) The hospital mortality of 38.9% in our cohort was again comparable to other parts of the world, which ranged from 30.4% in the Rello group (9) and 35.5% in the EU-VAP/CAP group. (11)

It has been proposed a scoring system which merges the severity of sepsis and the presence of organ dysfunction would be a potentially useful tool in risk stratification and even mortality prediction. In 2001, the International Sepsis Definition Conference proposed the PIRO concept of sepsis staging and subsequently a more practical version of the PIRO staging model for risk stratification in severe sepsis was developed with the presence of scores and validation from two large databases around the world. It has been shown that a higher PIRO score was associated with a higher

mortality in patient with severe sepsis. (4,5)

However it was not until 2008 the first paper concerning the usage of PIRO score in VAP was published. (6) A prospective, observational cohort study was performed which included 441 patients with VAP in three multidisciplinary ICUs. In this study, mortality varied significantly according to the VAP-PIRO score. Moreover, the score can also be used to stratify the medical resource use in terms of ICU length of stay, duration of mechanical ventilation, and discriminate mortality. The authors concluded the VAP-PIRO score was a simple and practical clinical tool for prediction of ICU mortality and stratification of healthcare resource use.

The study has been commented with the presence of limitations: no measure of severity of shock was included and the three centers where the study was conducted were all in Spain. Until now, the VAP-PIRO score has never been validated in other historical databases or prospective cohorts.

We intend to validate the VAP-PIRO score in our cohort but we are unable to repeat the results as in the original study. First, the disease severity of our cohort is modest when compared to the original study. Only 20.3% (12/59) patients in contrast to 46.4% in the original study had a VAP-PIRO score of greater than 2, a point regarded as "high risk" in mortality stratification. Such difference is also reflected in a lower mean VAP-PIRO score of 0.81±0.298 in our cohort (1.4±1.1 in the original study).

Furthermore, the components of VAP-PIRO score are also influential in mortality stratification. When the constituents of VAP-PIRO score were broken down in our cohort, we only have 6 out of 59 patients attained a PIRO-ARDS score and 2 out of 59 attained a PIRO-bacteraemia score. Most of the patients who attained a PIRO score of 1 are either by PIRO-hypotension (or the use of vasopressor, 24/59) or PIRO-co-morbidities (16/59). However, the severity of shock differs and so do the co-morbidities. Patient with brief period of hypotension with the use of low dose vasopressor and a patient with refractory shock can both score a "1" in PIRO-hypotension. A patient with mild COPD will have a same score as a patient severe COPD with long term oxygen support. Thus, it is possible that some patients who have a PIRO score of 1 by PIRO-hypotension or PIRO-co-morbidities can be "less-ill". Moreover, the weighing of the VAP-PIRO score also bear difference. A patient with PIRO-co-morbidities of 1 can have a less challenging clinical course than a patient with a PIRO-ARDS score of 1, which has a more objective inclusion criteria and, as expected, a higher mortality.

Finally, our cohort is small when compared to the original study. A larger historical database or cohort of bigger size in the future study can provide us with a clearer validation of VAP-PIRO score.

Limitations

The diagnosis of VAP in our study is clinical despite there are presence of up-to-date diagnostic criteria supported by positive qualitative culture results. Inclusion of patients without genuine VAP cannot be completely ruled out even if they are supported by a positive culture result, which can possibly be a coloniser. Moreover, although quantitative culture can enhance the acuity of diagnosis and further exclude the possibility of bacterial colonization in patients without genuine VAP, our laboratory was still unable to provide a quantitative culture service.

Some of the known risk factors of VAP including witnessed aspiration, underlying respiratory diseases, the use of paralytics and immunocompromised status are under-represented and this results in an insignificant difference despite the presence of a trend towards a higher incidence (**Table 1**). Our sample size is only 10% the size of the EU-VAP/CAP study group with 27 participating centers and 12% of the ANZPIC II study with 14 participating centers. Such problem also accounted for the reason why we are unable to repeat the results of VAP-PIRO score by the Rello group. (6)

Conclusion

The present study is the first prospective study which provides an overview in the incidence and outcome of patients with VAP in Hong Kong using an up-to-date diagnostic criteria. The additional burden posed on ICU (in term of number of days of mechanical ventilation and ICU length of stay) and the hospital mortality are on par with recent large scale studies worldwide. We were unable to reproduce a similar result as in the Rello Group (6) concerning the VAP-PIRO

score in stratification of medical resource use and prediction of mortality as our sample size is limited and the disease severity in our cohort is relatively modest when compared to the original study. Further multicenter studies with adequate representation of wide spectrum of VAP cases are required for an accurate validation of this promising tool.

Table 1. Baseline characteristics, co-morbidities, admission source and outcome of VAP vs Non-VAP cases

Characteristics	Non-VAP case (204)	VAP case (59)	P value
Age (mean)	67	64.6	0.318
APACHE II (230 cases)	25±9 (187)	28±9 (53)	0.032
APACHE IV (230 cases)	92±38 (187)	103±35 (53)	0.065
Sex –male	111/204 (54.4%)	37/59 (62.7%)	0.326
Specialty:			
Medical	88/204 (43.1%)	27/59 (45.8%)	0.899
Surgical	54/204 (26.5%)	17/59 (28.8%)	
Neurosurgery	43/204 (21.1%)	10/59 (16.9%)	
Others	19/204 (9.3%)	5/59 (8.5%)	
Source:			
Ward	78/204 (38.2%)	32/59 (54.2%)	0.132
OT	82/204 (40.2%)	17/59 (28.8%)	
AED	36/204 (17.6%)	8/59 (13.6%)	
Others	8/204 (3.9)	2/59 (3.4%)	
Type of admission:			
Elective	9/204 (4.4%)	3/59 (5.1%)	0.96
Emergency	189/204 (92.6%)	54/59 (91.5%)	
Trauma	6 (2.9%)	2/59 (3.4%)	
Co-morbidities:			
COPD	18/204 (8.8%)	3/59 (5.1)	0.509
Immunocompromised	11/204 (5.4%)	5/59 (8.5%)	0.573
Chronic heart failure	9/204 (4.4%)	4/59 (6.8%)	0.691
Chronic renal failure	18/204 (8.8%)	5/59 (8.5%)	1
Chronic respiratory failure	12/204 (5.9%)	2/59 (3.4%)	0.673
Alcoholism	6/204 (2.9%)	1/59 (1.7%)	0.948
DM	36/204 (17.6%)	12/59 (20.3%)	0.779
Witnessed aspiration	31/204 (15.2%)	12/59 (20.3%)	0.459
Received antibiotics	165/204 (80.9%)	58/59 (98.3%)	0.002
Received paralytics	15/204 (7.4%)	7/59 (11.9%)	0.404
Cancer	26/204 (12.7%)	4/59 (6.8%)	0.3
Chronic hepatopathy	7/204 (3.4%)	3/59 (5.1%)	0.843
Procedures:			
Bronchoscopy	25/204 (12.3%)	18/59 (30.5%)	<0.001
Reintubation	12/204 (5.9%)	14/59 (23.7%)	<0.001
Tracheostomy	16/204 (7.8%)	24/59 (40.7%)	<0.001
Outcome			
ICU mortality	32/204 (15.7%)	12/59 (20.3%)	0.519
Hospital mortality	43/204 (21.1%)	23/59 (38.9%)	0.009

Legend: OT=operating theatre; AED=Accident and Emergency Department; COPD=chronic obstructive pulmonary disease

Table 2. Medical resource use in VAP cases vs Non-VAP cases, overall and by various specialties (mean±2SD)

	Mean (days)	Non-VAP case (days)	VAP case (days)	P value
Duration of mechanical ventilation (overall)	4.69	3.18±2.76	9.93±8.37	<0.001
Ventilator free day in ICU LOS (overall)	2.94	2.21±2.46	5.46±5.28	<0.001
ICU LOS (overall)	7.62	5.39±41.3	15.36±11.28	<0.001
Hospital LOS (overall)	18.75	16.14±18.85	28.56±30.90	0.008

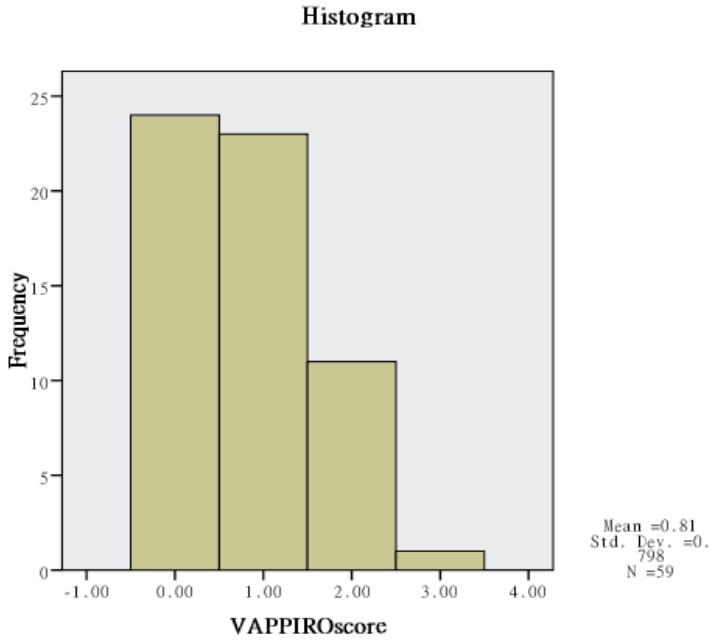
Legend: LOS=length of stay

Table 3. Medical resource use as stratified by different VAP-PIRO score

VAP-PIRO score	0	1	2	3	P value
Case number	24	23	11	1	
MV days	8.42±5.82	11.09±11.28	10.73±6.23	11	0.729
MV free days during ICU LOS	6.92±5.2	3.61±5.11	6.45±5.17	2	0.138
ICU LOS	15.17±8.53	14.78±15.14	17.18±7.86	13	0.944
Hospital LOS	33.67±32.46	27.75±34.46	22.3±19.10	13	0.616

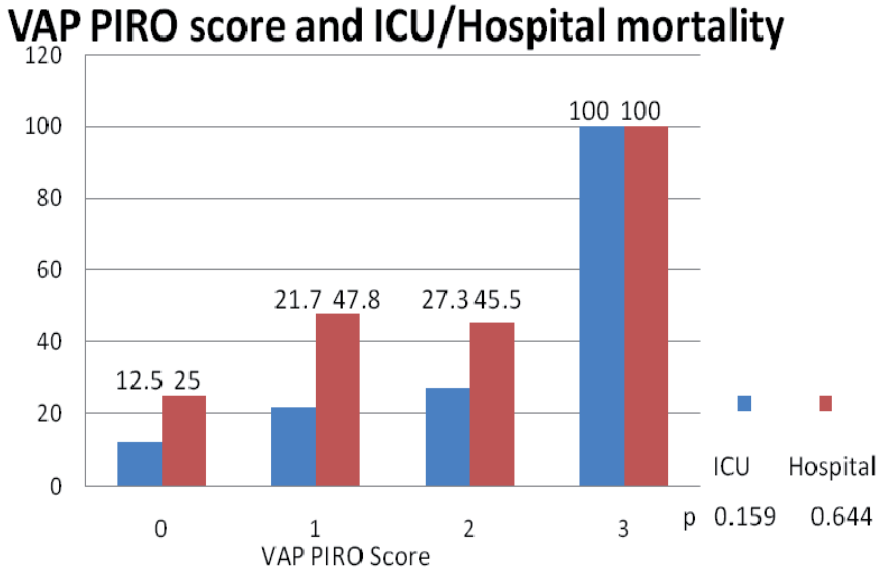
Legend: LOS=length of stay; MV=mechanical ventilation

Figure 1. Frequency distribution of VAP-PIRO scores among the 59 VAP cases



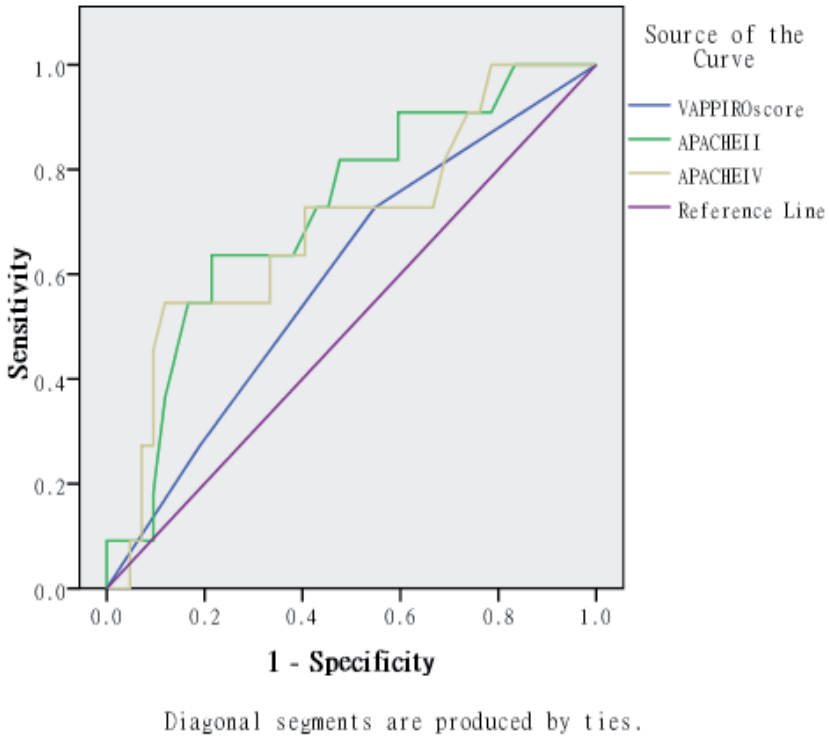
Legend: Mean VAP-PIRO score for all was 0.81±0.798; mean VAP PIRO score for survivors was 0.723±0.743; mean VAP-PIRO score for non-survivors was 1.167±0.937; z statistics - 1.348 p=0.178

Figure 2. VAP-PIRO score and ICU/hospital mortality (percentage)



Legend: Pearson Chi square=5.181 df=3 p=0.159 linear by linear association 2.948 p=0.086

Figure 3. ROC curve comparing VAP-PIRO score and APACHE II and IV score for discrimination between survivors and non-survivors in ICU



References

1. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial infections in medical intensive care units in the United States. National Nosocomial Infections Surveillance System. Crit Care Med 1999;27:887-92.
2. Napolitano LM. Use of severity scoring and stratification factors in clinical trials of hospital-acquired and ventilator-associated pneumonia. Clin Inf Dis 2010;51:S67-80.
3. Angus DC, Burgner D, Wunderink R, Mira JP, Gerlach H, Wiedermann CJ, et al. The PIRO concept: P is for predisposition. Crit Care 2003;7:248-51.
4. Moreno RP, Metnitz B, Adler L, Hoechtl A, Bauer P, Metnitz PG, et al. Sepsis mortality prediction based on predisposition, infection and response. Intensive Care Med 2008;34:496-504.
5. Finkielman JD, Dara SI, Mohammed Z, Sujay B, Afessa B. Sepsis mortality prediction based on predisposition, infection, response and organ dysfunction (PIRO). Crit Care Med 2004;32:A134.
6. Lisboa T, Diaz E, Sa-Borges M, Socias A, Sole-Violan J, Rodriguez A, et al. The ventilator-associated pneumonia PIRO score: a tool for predicting ICU mortality and health-care resources use in ventilator-associated pneumonia. Chest 2008;134:1208-16.
7. Centers for Disease Control and Prevention. Ventilator-associated Pneumonia (VAP) [Online]. 2012 Jan [cited 2012 Mar]; Available from: URL:http://www.cdc.gov/HAI/vap/vap.html
8. Kollef MH, Silver P, Murphy DM, Trovillion E. The effect of late-onset ventilator-associated pneumonia in determining patient mortality. Chest 1995;108:1655-62.
9. Rello J, Ollendorf DA, Oster G, Vera-Llonch M, Bellm L, Redman R, et al. Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. Chest 2002;122:2115-21.
10. Boots RJ, Lipman J, Bellomo R, Stephens D, Heller RF. Disease risk and mortality prediction in intensive care patients with pneumonia. Australian and New Zealand Practice in Intensive Care (ANZPIC II). Anaesth Intensive Care 2005;33:101-11.
11. Koulenti D, Lisboa T, Brun-Buisson C, Krueger W, Macor A, Sole-Violan J, et al. Spectrum of practice in the diagnosis of nosocomial pneumonia in patients requiring mechanical ventilation in European intensive care units. Crit Care Med 2009;37:2360-8.
12. Kollef MH, Afessa B, Anzueto A, Veremakis C, Kerr KM, Margolis BD, et al. Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: the NASCENT randomized trial. JAMA 2008;300:805-13.
13. Rea-Neto A, Youssef NC, Tuche F, Brunkhorst F, Ranieri VM, Reinhart K, et al. Diagnosis of ventilator-associated pneumonia: a systematic review of the literature. Crit Care 2008;12:R56.
14. National Nosocomial Infections Surveillance (NNIS) system report. Data summary from January 1992-June 2001. Am J Infect Control 2001;29:404-21.
15. Eggimman P, Hugonnet S, Sax H, Touveneau S, Chevrolet JC, Pittet D. Ventilator-associated pneumonia: caveats for benchmarking. Intensive Care Med 2003;29:2086-9.