Comparison of CPIS (clinical pulmonary infection score) and Clinical Criteria in the Diagnosis of Ventilator-associated Pneumonia in ICU Complex Patients

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Background --- Accurate data on the epidemiology of ventilator-associated pneumonia (VAP) are limited by the lack of standardized criteria for its diagnosis. The difficulties of diagnosis are mostly a results of the following factors: possibility of multiple other causes of systemic inflammatory reactions, pre-existing antibiotic usage in ICU patients and the absence of a standard test to detect and diagnose VAP. The accuracy of clinical criteria (infiltrates on the chest radiograph and 2 of the following: leukocytosis, fever, purulent secretions) for the diagnosis of pneumonia was reasonable with sensitivity of 69% and specificity of 75%. On the other hand, the Clinical Pulmonary Infection Score (CPIS), which combined the clinical signs recorded on the day of the clinical suspicion of VAP to the tracheal aspirate gram stain and culture and PaO2/Fio2 ratio, proved to achieve 72% sensitivity and 85% specificity. This study evaluated the validity of the CPIS and Clinical criteria in the diagnosis of VAP in ICU complex patients and determined the length of ICU stay and mortality rate of patients who had VAP.

Methods --- A prospective cohort study was conducted involving patients who had been under mechanical ventilation for more than 48 hours, suspected for VAP and admitted in the ICU complex of the Philippine Heart Center from July 2006 to January 2007. The criteria for diagnosis of VAP using the clinical criteria as well as the CPIS were applied to them. Patients were followed up for occurrence of death until discharge.

Results --- Forty patients admitted at ICU complex were enrolled. The mean age of the subjects was 59.6 + 14.8 years. Length of ICU stay was 19.2 + 14.5 days with mean duration of mechanical ventilation of 13.6 + 12.3 days. Sensitivity showed 35.3% and 78.3% on the 1st and 3rd day of referral respectively. Specificity revealed 95.7% and 81.3% on the 1st and 3rd day of referral respectively. Five patients (13%) died, all of them were females. The causes of death were arrhythmia (3 patients) and septic shock (2 patients).

Conclusion --- This study would still recommend the use of the clinical criteria over CPIS in the diagnosis of VAP. However, VAP continues to be an important challenge to the critical care physician and it is difficult to diagnose accurately, and a high index of suspicion is required. ***Phil Heart Center J 2007;13(2):135-138.***

Key Words: Ventilator-associated Pneumonia ■ diagnostic criteria ■ validation study ■ Clinical Pulmonary Infection Score

Ventilator associated pneumonia (VAP) is an important form of hospital acquired pneumonia (HAP), specifically developing in a mechanically ventilated patient more than 48 hours after tracheal intubation.[1] Despite major advances in techniques for the management of VAP and the routing use of effective procedures to disinfect respiratory equipment, VAP continues to complicate the course of 8 to 28% of the patients receiving mechanical ventilation.[2] Pulmonary complications are common after surgical procedures, accounting for nearly one of every four deaths that occur in the first post-operative week. In the intensive care unit, pneumonia accounts for 28 to 47% of all nosocomial infections. The single greatest risk factor for VAP is related to the duration of mechanical ventilation. The risk peaks at day 5 on the ventilator, plateaus after day 15, and then declines significantly, with the result that VAP is uncommon in patients on long term mechanical ventilation.[8] The risk of VAP is highest early in the course of hospital stay, and is estimated to be three percent per day during the first five days of ventilation, two percent per day during days 5 to 10 of ventilation, and one percent per day after this.[3] Accurate data on the epidemiology of VAP are limited by the lack of standardized criteria for its diagnosis. The absence of a gold standard continues to fuel controversy about the adequacy and relevance studies in this field.[2] In 1991, Pugin and colleagues proposed to combine the clinical signs recorded on the day of the clinical suspicion of VAP to the tracheal aspirate gram stain and culture and PaO2/FiO2 ratio into a CPIS as a diagnostic tool of pneumonia. The score varied from 0 to 12 points with a CPIS of more than six being associated with a high likelihood of pneumonia.[4] (Table 1). The score proved to

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achieve 72% sensitivity and 85% specificity.[9] These results do not indicate a superiority of CPIS to Johansson's criteria, and given that the CPIS is more time consuming to calculate, there is no evidence to recommend this score in routine clinical practice. The accuracy of clinical criteria (infiltrates on the chest radiograph and 2 of the following: leukocytosis, fever, purulent secretions) for the diagnosis of pneumonia was reasonable with sensitivity of 69% and specificity of 75%.5 (Table 2). Thus, available evidence indicates that clinical diagnosis of VAP is associated with around 30-35% false-negative and 20-25% false-positive results. The high rate of false-positive results is probably due to alternative diagnoses that may cause pulmonary infiltrates mimicking VAP such as alveolar hemorrhage, atelectasis, pulmonary infarction and the fibroproliferative phase of acute respiratory distress syndrome (ARDS). False-negative results may result from initial phases of pneumonia not detected on chest radiograph.[9] Noninvasive (TBA) and invasive (PSB, BAL, protected BAL) sampling techniques were not superior to these clinical criteria.[5] Recently, several studies have suggested that the use of quantitative cultures of endotracheal aspirate may have similar diagnostic value compared with invasive techniques, such as protected specimen brush (PSB) and bronchoalveolar lavage (BAL). The advantage of quantitative endotracheal aspirates is its reliance on the simplicity and cost effectiveness of the method, as well as the lack of side effects. In fact, it has been suggested that using lavage in mechanically ventilated patients with pneumonia can lead to systemic and sepsis-like effects. Furthermore, deterioration of blood gas exchange has been described.[10] The difficulties of diagnosis are mostly a results of the following factors: possibility of multiple other causes of systemic inflammatory reactions, pre-existing antibiotic usage in ICU patients and the absence of a standard test to detect and diagnose VAP.[6] This study aimed to validate CPIS and clinical criteria in the diagnosis of VAP in ICU complex (RR, SICU, MICU, CCU) patients. Specifically, it aimed to evaluate the sensitivity and specificity of clinical criteria and CPIS on patients suspected of VAP as well as to determine the length of ICU stay and mortality rate of patients who had VAP.

Table 1. CPIS (clinical pulmonary infection score)

Criteria		Points
Temperature (°C)		
	>or equal to 36.5 and < or equal to 38.4	0
	>or equal to 38.5 and < or equal to 38.9	1
	>or equal to 39 and < or equal to 36	2
Blood leukocytes, mm³		
	>or equal to 4,000 and < or equal to 11,000	0
	< 4,000 or > 11,000	1
	< 4,000 or > 11,000 + band forms> equal to 50%	2
Tracheal secretions		
	Absence of tracheal secretions	0
	Presence of non purulent tracheal secretions	1
	Presence of purulent tracheal secretions	2
Oxygenation:PaO2/FIO2, mmHg		
	>240 or ARDS (ARDS defined as PaO2/FIO2 ≤ 200), pulmonary arterial wedge pressure ≤ or equal to 18 mmHg and acute bilateral infiltrates)	0
	≤ 240 and no ARDS	2
Pulmonary radiography		
	No infiltrate	0
	Diffuse (or patchy) infiltrate	1
	Localized infiltrate	2
Progression of pulmonary infiltrate		
	No radiographic progression	0
	Radiographic progression (after CHF and ARDS excluded)	2
Culture of tracheal aspirate		
	Negative	0
	Positive	2

NOTE: score of > 6 is considered suggestive of pneumonia. 7

Table 2. Clinical Criteria

1.) New infiltrate on chest radiograph (or radiographically confirmed worsening of pre-existing infiltrate) and
2.) At least 2 of the following:
- Leukocytosis (>12,000/mm3)
- Leucopenia (< 4,000/mm3)
- Fever (>38 0 C)
- Hypothermia (< 35 oC)
- Purulent tracheal secretions

Methods

This was a prospective study of patients who were admitted in ICU complex (RR, SICU, MICU, CCU) of Philippine Heart Center between July 2006 to January 2007. All patients had been under mechanical ventilator for more than 48 hrs and were suspected of having contracted VAP and were subsequently referred to pulmonary service. Patients with immunosuppression (organ transplantation, HIV infection and AIDS, severe neutropenia < 1.0 x 10 9/l, steroid therapy equivalent to prednisone in a dose of >20 mg/day) were excluded. Data gathering includes age, sex, type of surgical procedure, duration of mechanical ventilation, length of stay and co-morbidities were recorded. Each patient was then scored by clinical criteria and CPIS on the day of the referral as baseline and was repeated 72 hours after for reassessment. Clinical and laboratory evaluation. All clinical (body temperature and endotracheal secretion) and laboratory (CBC, Chest radiograph, arterial blood gas and microbiological assay of endotracheal secretion) were recorded. Chest radiograph were also reviewed by one of the investigators and an independent radiologist. The endotracheal aspirate (ETA) was collected using French size 60 cm suction catheter with mucus trap and introduced through the endotracheal tube for approximately 24 cm. Gentle aspiration was then performed without instilling saline and the catheter was withdrawn from

the endotracheal tube. Sample was immediately taken to the laboratory for processing. The result of the gram stain was obtained within 24 hours and quantitative culture was obtained within the following 48 to 72 hours.

Microbiological processing

Sample was then inoculated into different culture media (blood agar plate and MacConkey by Biomerauex). The plates were incubated within 18-24 hours at 370°C. After initial characteristics of the isolates by colony morphology and gram stain, species identification and susceptibility testing were done using the disc diffusion method.

Results

Forty patients admitted at ICU complex (RR, SICU, MICU, and CCU) of the Philippine Heart Center were enrolled in this study from July 2006 to January 2007. Table 1 shows that the mean age was 59.6 years. The average number of days of referral and ICU stay were 7.0 days and 19.2 days, respectively. More than half of the patients were male (58%). Five patients (13%) died, all of them were females. The causes of death were arrhythmia (3 patients) and septic shock (2 patients).

Table 3. Clinical Characteristics of Patients Included in the Study

Characteristics	N(%) or mean (SD)
Age, years	59.6 ± 14.8
Day(s) of referral	7.0 ± 8.7
Length of ICU stay (days)	19.2 ± 14.5
Duration of Mechanical Ventilation, days	13.6 ± 12.3
Gender	
Male	23 (57.5)
Female	17 (42.5)
Mortality	
Expired	5 (13.2)
Recovered	33 (86.8)

*Data are presented as mean ± SD or No. (%) unless otherwise indicated

For the first-day diagnosis, the sensitivity of clinical pulmonary infection score method was 35.3%. That means that 35.3% of those with ventilator associated pneumonia, as diagnosed by clinical criteria, were detected using clinical pulmonary infection score. On the 3rd day diagnosis, the sensitivity went up to 78.3%. Its specificity on the 1st and 3rd day diagnosis was 95.7% and 81.3%, respectively. Thus, on the 1st and 3rd day diagnosis, 95.7% and 81.3%, respectively, of those without VAP were identified as such using CPIS. Positive predictive values were the same for the 1st and 3rd day diagnosis. Among those identified by CPIS as positive, the likelihood that they really have the disease was 85.7%. On the other hand, the negative predictive values were 66.7% and 72.2% for the 1st and 3rd day, respectively. Those with negative CPIS result, the likelihood that they do not have VAP were 66.7% and 72.2% during the 1st and 3rd day, respectively. ROC curve had area under the curve of 0.655 and 0.798 on the 1st and 3rd day diagnosis, respectively. This showed that the VAP determination of CPIS is better in the 3rd day diagnosis than the 1st day. One patient was transferred to another hospital, thus, a decrease to 39 patients on the 3rd day diagnosis from 40 patients on the 1st day diagnosis. (Table 4 and 5)

Table 4. Sensitivity and Specificity of CPIS in Detecting VAP on Day One

CPIS	Clinical Criteria		Total
	Positive	Negative	
Positive	6	1	7
Negative	11	22	33
Total	17	23	40

Sensitivity 35.3, Specificity 95.7

Positive Predictive Value. 85.7, Negative Predictive Value 66.7 AUC 0.655

Table 5. Sensitivity and Specificity of CPIS in Detecting VAP on Day Three

CPIS	Clinical Criteria		Total
	Positive	Negative	
Positive	19	3	21
Negative	5	13	18
Total	23	16	39

Sensitivity 78.3, Specificity 81.3

Positive Predictive Value. 85.7, Negative Predictive Value 72.2 AUC 0.798

Discussion

VAP (ventilator associated pneumonia) is a common and serious infection in the Intensive Care Unit patients, and is often difficult to diagnose. The difficulties of diagnosis are mostly a result of the following factors: the possibility of multiple other causes of systemic inflammatory reactions in these patients, pre-existing antibiotic usage in ICU patients and the absence of a standard test to detect and diagnose VAP.[13] There is no doubt that the best diagnostic strategy in patients with suspected ventilator associated pneumonia (VAP) remains contentious. The central problem is the difficulty in striking a balance between avoiding a delay in starting antibiotics when they are required and reducing inappropriate use of broad-spectrum antibiotics.[11] In this study, we have evaluated the clinical diagnosis of ventilator associated pneumonia, assessed on either the routine clinical criteria on the first day and on the 3rd of referral and the CPIS (clinical pulmonary infection score) and the contribution of the respiratory specimens gram stains result to the diagnosis of VAP, taking endotracheal aspirate culture as the reference test.[4] The mortality rate of ventilator-associated pneumonia (VAP) was 13% in this study, which is

secondary to cardiac arrhythmia and septic shock. However, the mortality rate has been reported to be 30%.[12] In the study by Nieto et al, the mortality of ventilator associate pneumonia (VAP) ranges from 20-70%. The sensitivity and specificity of clinical criteria in diagnosing ventilator-associated pneumonia were noted to be 35.3%, 78.3% and 95.7%, 81.3% on the first and third day of referral respectively. This showed a comparable result in terms in the diagnosis of VAP especially on the third day of diagnosis. In the study of Fabregas et al, this result was reasonable with sensitivity of 69% and specificity of 75%.[5] In another study by Fagon et al, found that clinical predictors about the presence or absence of definite and probable VAP were accurate in 62% and 84% of VAP patients respectively.[8] Disappointingly the use of scoring systems, such as the clinical pulmonary infection score, seems to add little to diagnostic acccuracy.[14] The positive predictive values were 85.7% and 85.7% on the first and third day of referral respectively. However, In the study by Fagon et al, this was contradictory because the clinical diagnosis of VAP is associated with around 20-25% false positive results.[8] Many investigators have claimed that the incidence of VAP may be overestimated when clinical criteria alone are used. In a recent postmortem study the combination of infiltrates on the chest radiographs and at least 2 of 3 clinical criteria (fever, leukocytosis, and purulent secretions) had a sensitivity of 69% and a specificity of 75% for diagnosing VAP. Moreover, there have been studies that demonstrated a similar diagnostic yield with invasive and noninvasive techniques and similar patient outcomes in terms of mortality, ICU stay, and duration of mechanical ventilation. However, the VAP rates in the various studies cannot be compared because of differences in survey methods, lack of uniform diagnosis criteria, different length of ICU stay, and the lack of an adequate system to compare illness severity and invasive diagnostic or therapeutic procedures.[15] Prognostic factors for a poor outcome from nosocomial pneumonia include inappropriate antibiotic treatment.[10] This study would recommend that clinical criteria could be used as a tool in the diagnosis of ventilator associated pneumonia and reassess on the third day if antibiotic could be withhold. CPIS has a lot of variable, which include endotracheal aspirate and arterial blood gas that could further add expenses on the part of the patient. However, endotracheal aspirate is an important part in the diagnosis of ventilator-associated pneumonia which is very important in the diagnosis as well as therapeutic option in the management of ventilator-associated pneumonia. And because clinical suspicion alone is overly sensitive and lack of specificity, further diagnostic tests are required for optimal management. Ideally, microbiological data should be obtained before the start of antibiotic therapy.[14] The main drawbacks of the CPIS are that all of its elements are weighted equally (for example, the presence of an infiltrate is given the same weight as a WBC count of 11,000/mm3, even though it is substantially more suggestive of pneumonia) and that assessment of chest x-rays and sputum production is necessarily subjective, meaning that an equivocal CPIS could lead to an inappropriate treatment decision. VAP continues to be an important challenge to the critical care physician and is the most common nosocomial acquired infection among patients with acute respiratory failure. It is difficult to diagnose accurately, and a high index of suspicion is required.[14]

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