hypoglycemia (14). Whether severe hypoglycemia was associated with adverse outcome could not be directly addressed by Dr. Arabi et al, as many factors are involved and as most periods of hypoglycemia were probably of short duration due to strict vigilance. It is remarkable that, in spite of very strict and frequent (hourly and even every 20 mins when glucose was <54 mgd/L) monitoring of blood glucose, still a 50-fold increase in hypoglycemia was found in the intensive insulin group. Apparently, the protocol used by Dr. Arabi et al was not adequate in preventing hypoglycemia, only nonresponsiveness to earlier low blood glucose readings may explain why several patients achieved glucose levels of <18 mg/dL, as proper treatment with 50% glucose, being part of the protocol, would have instantaneously raised blood glucose concentrations. Unfortunately, intervention-related risk factors for hypoglycemia were not analyzed. Thus, Dr. Arabi et al present more data adding to the exciting and important field of intensive insulin therapy, with up to one of three patients suffering from hypoglycemia, emphasizing the need for improved algorithms that should be both effective and safe. The rate of insulin infusion and the response to hypoglycemia (prompt correction, but avoid overcorrection) are critical aspects to consider. Future studies should specifically target the question as to why, in spite of strict protocol vigilance, hypoglycemias occur and even persist.

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Ventilator-associated pneumonia prevalence: To benchmark or not to benchmark*

Comparing performance across intensive care units (ICUs) analyzing preventable nosocomial infections, such as ventilator-associated pneumonia (VAP), for benchmarking is a current trend. Approaches aiming at the "zero" VAP prevalence have suggested that VAP could be used as a quality indicator and benchmarking in the ICU. However, VAP is not always preventable and some risk factors for VAP are not modifiable. Accurate benchmarking for VAP prevalence seems to be currently unfeasible as there is considerable uncertainty in rendering a VAP diagnosis (1, 2).

Classically, VAP diagnosis is based on the presence of pulmonary inflammatory reaction in patients ventilated and systemic signs of sepsis. Clinical criteria, defined by the Centers for Disease Control and Prevention (3), had a high sensitivity but very low specificity in mechanically ventilated patients. The clinical signs of pneumonia (fever, pulmonary opacities, and purulent respiratory secretion) presence in ICU patients are due to VAP in only 30% to 40% (2, 4).

Using quantitative culture of respiratory samples is advocated as a measure to improve the accuracy of VAP diagnosis. However, no study to date has demonstrated any effect on reducing antibiotic use, rates of superinfection, or improvement in outcomes associated with such strategy (1). In addition, the presence of positive cultures of respiratory secretions is only moderately specific for VAP (4, 5). Some of these patients may have purulent tracheobronchitis or ventilator-associated tracheobronchitis that is defined as the presence of clinical signs or symptoms of infection and purulent respiratory secretion, but no evidence of new opacities on chest radiograph (6) (Fig. 1). It was suggested that adding microbiological results to this definition

***See also p. 2545.**

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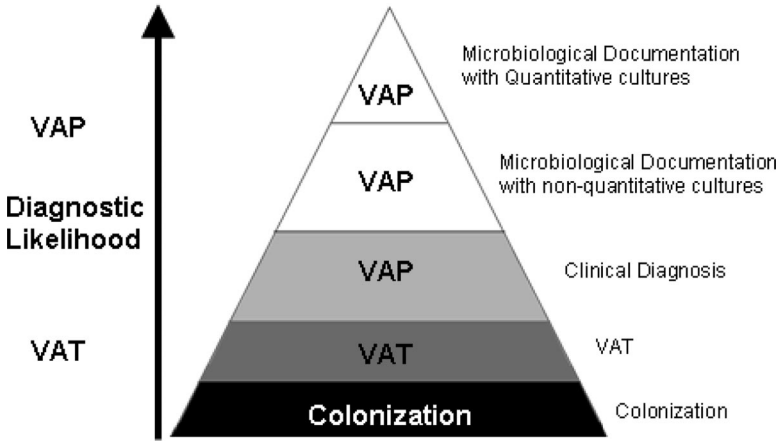

Figure 1. Spectrum of respiratory infections in intubated patients. *VAP*, ventilator-associated pneumonia; *VAT*, ventilator-associated tracheobronchitis.

could improve its clinical relevance (6). Others have suggested using an objective clinical score to refine diagnosis (7). Whether microbiological data should derive from an invasive approach with quantitative cultures or from qualitative cultures is not defined. Actually, no difference in outcomes was documented when using either approach (8). A challenging approach would be to stratify the severity of patients with VAP using the VAP PIRO score (9).

Difficulty in rendering an accurate diagnosis of VAP makes it an unreliable basis for quality control or interhospital benchmarking of quality of care (1, 2). For example, the prevalence of VAP may be up to two times higher in patients diagnosed by qualitative or semiquantitative secretion cultures compared with quantitative cultures of lower respiratory tract secretions (4, 10). Overemphasizing quantitative culture results to improve homogeneity may be misleading, as factors like previous antibiotic exposure affect the result of microbiological techniques. The absence of an objective and specific diagnostic criteria or biomarker for VAP compromises reproducibility and difficult comparison of VAP rates among different ICUs.

In this issue of *Critical Care Medicine*, Dr. Zahar and colleagues (11) report a clinical study aiming to develop a patient-based score for predicting VAP. They develop and validate a score for computing a theoretical VAP rate based on the characteristics of the patient population to be compared with the observed VAP rate in each institution. Variables associated with VAP risk in the analysis of 1856 patients in the OUTCOMEREA high-quality database were mechanical ventilation duration, admission Sequential Organ Failure Assessment (SOFA) score, absence of parenteral nutrition, and broad-spectrum antimicrobial therapy during the first 2 days on mechanical ventilation. Authors derive an accurate model with good discrimination and good calibration in both training and validation set. This interesting study deals with the limitation of using VAP for benchmarking, adjusting observed VAP rate according to theoretical VAP rate. The standardized VAP ratio allows more reliable comparisons of VAP prevalence across ICUs, using similar definitions, and may be useful as a benchmarking tool.

Limitations to use VAP for benchmarking include differences in case-mix, different diagnosis practices, and finally, different VAP definition (12). First, we should agree on what we mean when use the term "VAP." The developed benchmarking score limits analysis only to microbiologically documented episodes based on the criteria for quantitative cultures. It represents only the top of the iceberg (Fig. 1). In Europe, data from the EU-VAP Study (13) demonstrated that only approximately one of five patients with suspected VAP have respiratory samples for microbiological documentation obtained by bronchoscopy methods and 42.7% of patients with clinical diagnosis of VAP had a qualitative tracheal aspirate performed for microbiological documentation. Negative or nonsignificant bacterial burden in quantitative cultures of tracheal aspirate or bronchoalveolar lavage only decreases the probability of VAP, but do not exclude it (4).

Nonetheless, as discussed by the authors, the prevalence of trauma, a recognized higher risk population for VAP, was very low. It limits applicability of the VAP score to units with higher prevalence of trauma. Patient differences in age, disease severity, traumatic and surgical status, or comorbidities may affect benchmarking results. In addition, specialized units, such as trauma, neurosurgery or postsurgical ICUs, handle specific patients with different risk factors for VAP (1). Using a score unadjusted for any of these aspects would generate unreliable rates for hospitals admitting and caring for high-risk patients.

Risk factors for developing VAP and episodes etiology vary importantly according to the time to onset of pneumonia and to the presence of risk factors for specific pathogens, such as *Pseudomonas aeruginosa*, MRSA, and *Acinetobacter baumannii* (3). Although an overall model presented a good discrimination for both early- and late-onset episodes, variables associated with VAP might have a different effect in early- or late-onset episodes.

In conclusion, Dr. Zahar et al (11) provide an interesting approach for using standardized VAP ratio for benchmarking. Adjustment, using the ratio of observed and predicted VAP rate according to risk factors identified, is logical and the score is clear and easy to apply. The presence of not modifiable risk factors in the described model strengthen the concept that VAP is not always preventable and that "zero" VAP prevalence objective is fallacious.

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More data on epidemiology and outcome of acute kidney injury with AKIN criteria: Benefits of standardized definitions, AKIN and RIFLE classifications*

Acute renal failure or recently termed "acute kidney injury" (AKI) is an important cause of morbidity and mortality in hospitals and especially in intensive care units (ICUs) (1–6). The epidemiology and outcome of AKI varies among ICU populations and is changing with increasing critical care services worldwide. These differences can partly be attributed to the variety of existing and changing definitions of AKI (1–8). There is a growing literature on the epidemiology and outcome of AKI precipitated by great efforts to define AKI, to develop a standardized approach, and to improve research in this area (6, 7).

These efforts are helping. After the report of Acute Dialysis Quality Initiative elaborating on the RIFLE criteria (9), numerous studies contributed to the knowledge on the AKI and related mortality (6, 7, 10–13). Emergence of new data suggesting that even smaller changes in serum creatinine might be associated with adverse outcomes led to newer definitions by the AKIN (Acute Kidney Injury Network) group (14–16). AKIN criteria emphasized recognition of earlier and milder forms of AKI, and staging of AKI, and stimulated further research on the epidemiology and outcome of AKI (16).

In this issue of *Critical Care Medicine*, Dr. Thakar and colleagues (17) report their analysis of electronic data on AKI in ICU patients from 191 Veterans Administration Hospitals in the United States between 2001 and 2006. They excluded patients with <3 creatinine measurements in the ICU; patients readmitted to the ICU or transferred to other hospitals; transplant recipients; and those with chronic renal failure defined as prior dialysis, end-stage renal disease, or those with a calculated of glomerular filtration rate <15 mL/min/1.73 m^2. The remaining 325,395 patients included for analysis made this one of the largest data sets reported in AKI so far.

AKI was mostly defined by AKIN criteria according to Mehta and colleagues (16) (serum creatinine increment of >0.3 mg/dL from baseline). AKI was later categorized into three stages based on the peak serum creatinine during ICU stay, using the AKIN criteria with slight modification. Stage I: an increase in creatinine of 0.3 mg/dL to <2-fold increase; Stage II: an increase in creatinine >2 times baseline but <3 times; and Stage III: ≥3-fold increase in creatinine or a new requirement of dialysis (patients with serum creatinine >4 mg/dL but without >3-fold increase or no new dialysis requirement were not included in Stage III; and this probably led to the slight discrepancy of Stage III cases reported in their Table 3 and Fig. 1) (16, 17).

They used a logistic regression model to predict mortality risk from independent predictors (age; 31 comorbid disease groups; 84 admission diagnoses to the ICU; source of admission; and the worst value of the 11 laboratory tests within 24 hrs of ICU admission). They calculated a standardized (hospital) mortality rate for groups, using a logistic regression model (17).

Twenty-two percent of patients (n = 71,486) developed AKI; 75% of them met the AKI criteria within 48 hrs as defined by AKIN. AKI severity was usually mild (80% had Stage I, and the rest were divided into Stages II and III; this trend existed across almost all groups classified by admission diagnosis or severity of illness). A total of 3140 patients in the Stage III AKI group required dialysis. Before dialysis initiation, 27.4% had >3-fold increment in serum creatinine, and 60.7% had creatinine elevation corresponding to Stage I or II AKI before dialysis. The majority of patients requiring dialysis had preexisting renal dysfunction (17).

***See also p. 2552.**

Key Words: acute kidney injury; AKIN; RIFLE; acute renal failure

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