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Ventilator-associated pneumonia: caveats for benchmarking

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Abstract *Objective:* To determine the influence of using different denominators on risk estimates of ventilator-associated pneumonia (VAP). *Design and setting:* Prospective cohort study in the medical ICU of a large teaching hospital. *Patients:* All consecutive patients admitted for more than 48 h between October 1995 and November 1997. *Measurements and results:* We recorded all ICU-acquired infections using modified CDC criteria. VAP rates were reported per 1,000 patient-days, patient-days at risk, ventilator-days, and ventilator-days at risk. Of the 1,068 patients admitted, VAP developed in 106 (23.5%) of those mechanically ventilated. The incidence of the first episode of VAP was 22.8 per 1,000 patient-days (95% CI 18.7–27.6), 29.6 per 1,000 patient-days at risk (24.2–35.8), 35.7 per 1,000 ventilator-days (29.2–43.2), and 44.0 per 1,000 ventilator-days at risk (36.0–53.2). When considering all episodes of VAP (n=127), infection rates were 27.3 episodes per 1,000 ICU patient-days (95% CI 22.6–32.1) and 42.8 episodes per 1,000 ventilator-days (35.3–50.2). *Conclusions:* The method of reporting VAP rates has a significant impact on risk estimates. Accordingly, clinicians and hospital management in charge of patient-care policies should be aware of how to read and compare nosocomial infection rates.

Keywords Nosocomial infection · Nosocomial pneumonia · Critical care · Ventilator-associated pneumonia · Benchmarking

Introduction

Nosocomial pneumonia is the leading infection in critical care and significantly impacts on patient mortality and morbidity [1, 2]. The proportion of patients who acquire the infection ranges from 10% to 65% [3, 4]. Ventilator-associated pneumonia (VAP) occurs in approx. 8–28% of mechanically ventilated patients, with a reported incidence of 1–3% per day of mechanical ventilation [4, 5, 6]. A comparison of rates is difficult due not only to differences in diagnostic procedures, definitions used, and population case-mix but also to the frequent lack of appropriate denominators [5, 6, 7]. To facilitate and foster benchmarking between units and hospitals, the National Nosocomial Infection Surveillance (NNIS) system of the Centers for Disease Control and Prevention (CDC) recommends expressing VAP as the number of infectious episodes per 1,000 ventilator-days. In its latest data report covering the period from January 1995 to June 2001 VAP ranged from 4.9 (25th–75th percentiles 1.4–7.7), 7.3 (3.8–9.0), and 8.4 (4.1–11.4) to 13.2 (7.7–14.9) episodes per 1,000 ventilator-days in pediat-

Table 1 Incidence of ventilator-associated pneumonia according to different denominators; medical ICU 1995–1997, University of Geneva Hospitals

[a] Only the first episode of VAP is considered (n=106)

	Total of days	Median (range)	Infection rates per 1,000 (95% CI)[a]
ICU days	4,651	7 (2–134)	22.8 (18.7–27.6)
ICU days at risk	3,579	6 (2–67)	29.6 (24.2–35.8)
Ventilator-days	2,969	3 (1–123)	35.7 (29.2–43.2)
Ventilator-days at risk	2,408	3 (1–53)	44.0 (36.0–53.2)

ric, medical, coronary, and surgical ICUs, respectively [8].

The present study describes the epidemiology of VAP in a medical ICU, underscores the effect of the use of different denominators on risk estimates, and highlights some poorly recognized caveats of risk and rate comparison [9].

Materials and methods

The University of Geneva Hospitals are a 2300-bed tertiary care center admitting approx. 40,000 patients annually. An average of 1400 patients are admitted each year to the 18-bed medical ICU, for a mean length of stay of 4 days. During the study period 1,049 patients were surveyed for 1,068 distinct ICU stays. Median age was 63 years (range 16–92); 622 patients (58%) were male. Median ICU stay was 5 days (range 2–134). Main admission diagnoses concerned infectious (39%), cardiovascular (24%), and pulmonary (18%) conditions. Overall 452 patients (42%) benefited from mechanical ventilation for a median duration of 3 days (range 1–123); 27% were mechanically ventilated for 1 day.

Prospective, on-site surveillance was conducted by an infection control nurse who was also fully trained in intensive care medicine. She visited the ICU daily (5/7) and extracted data from medical records, kardex, interviews with nurses and physicians, microbiology, and radiographic reports. All surveillance records were validated by two infection control physicians and one intensive care specialist [10]. All patients admitted for more than 48 h between October 1995 and November 1997 were prospectively followed during their entire ICU stay and 5 days after discharge.

Definitions

All nosocomial infections were defined according to modified criteria of the CDC [10, 11]. In particular, VAP was defined according to the criteria of the American College of Chest Physicians-American Thoracic Society consensus conferences [12]. The diagnosis of VAP in a patient mechanically ventilated for 48 h or more with a clinical suspicion of pneumonia required two of the following criteria: fever (increase of >1°C or body temperature >38.3°C), leukocytosis (25% increase and a value >10,000 mm^3) or leukopenia (25% decrease and a value <5,000 mm^3); and purulent tracheal secretions (>25 neutrophils per high-power field); and one of the following: (a) new or persistent infiltrates on chest radiographs; (b) same micro-organism isolated from pleural fluid and tracheal secretions or radiographic cavitation or histopathological demonstration of pneumonia; (c) positive cultures obtained from bronchoalveolar lavage (>10^4 colony forming units/ml).

Statistical analysis

The incidence of VAP was expressed as the number of episodes per 1,000 patient-days and per 1,000 patient-days at risk, or episodes per 1,000 ventilator-days and per 1,000 ventilator-days at risk, with 95% confidence intervals (95% CI) based on the Poisson distribution. Days at risk or ventilator-days at risk were defined as the number of days or ventilator-days before the onset of first infection. All analyses were performed using the Stata software package 6.0 (Stata, College Station, Tex., USA).

Results

ICU and hospital mortality were 16.8% and 24%, respectively. A total of 554 nosocomial infections developed in 281 patients (26.3%). Rates of infection and infected patients were 70.7 and 35.8 per 1,000 patient-days, respectively. Leading sites of infection were lower respiratory tract (28.7%), bloodstream (20.4%), exit-site catheter (13.5%), and the urinary tract (11.2%). We recorded 159 episodes of pneumonia occurring in 138 patients that were ICU acquired. Of these, 127 were VAP, including 106 first episodes of VAP. When considering all episodes of VAP, infection rates were 27.3 episodes per 1,000 ICU patient-days (95% CI 22.6–32.1) and 42.8 episodes per 1,000 ventilator-days (95% CI 35.3–50.2). Rates of first episode of VAP expressed according to the different denominators are shown in Table 1. Thirty-three episodes developed within 4 days of intubation and were considered as early onset VAP.

Discussion

Successful infection control strategies are based on surveillance and feedback of infection rates [7, 13, 14]. Based on the results of the SENIC study in the 1970s, healthcare-associated infection rates decreased by an average of 32% in hospitals where infection control programs were implemented, and increased by 18% in other institutions over a 5-year period [13]. Accordingly, such programs were rapidly imposed in the United States as an important criterion for hospital accreditation [15]. Data generated by surveillance may be used for resources allocation, quality of care assessment, and benchmarking [7, 8, 16].

Determinants of VAP rates include the surveillance strategy employed, case mix, case definition, diagnostic procedures, and the way in which rates are expressed. All of these may alter infection rates and jeopardize benchmarking. The choice of the most appropriate de-

nominator is often not straightforward, and it is self-evident that rates will vary accordingly. However, this has never been explored in the field of nosocomial infection, particularly for VAP. We focus in this study on the influence of the denominator.

Diagnosis of VAP remains a controversial issue [6, 17]. We used surveillance-based criteria [11, 12, 18] which do not rely exclusively on the microbiological results obtained by invasive sampling techniques [6, 19]. Such an approach might be associated with misclassification bias but is more suitable for clinical practice or surveillance purposes and is currently used in most centers actively promoting infection control [16, 19]. Importantly, although the use of a different diagnostic strategy could have resulted in different infection rates, it would not, however, have changed the current findings regarding the impact of the use of different denominators on risk estimates.

We focused in this study on the first episode of VAP for two main reasons. First, there is still considerable debate on the definition of VAP, and the difficulty of diagnosing a second episode is enhanced, thus increasing misclassification of the second episode. Second, if considering all episodes, the concepts of "days at risk" and "ventilator-days at risk" are impossible to assess. Indeed, one should know when the first episode resolves, and when the patient is again at risk for a second episode. Most studies report VAP rates per patient-days [7], which does not take into account the main risk factor for infection, i.e., exposure to mechanical ventilation, thus leading to an important underestimation of the incidence of infection. Patient case-mix and ICU transfer policy may further bias the estimate and jeopardize benchmarking [3]. If infection rates are expressed per patient-days, a prolonged ICU stay underestimates the VAP rate, whereas an ICU with a high proportion of patients with a short length of stay is penalized by reporting a higher rate. Because the daily conditional risk of acquiring VAP peaks at around day 5 [4], a similar bias occurs when rates are expressed per ventilator-days: the longer the duration of mechanical ventilation, the lower is the rate. Considering only ventilator-days at risk, and therefore excluding ventilator-days after the onset of VAP, yields a more appropriate risk estimate and makes benchmarking feasible after case-mix adjustment [9, 20]. Because the daily conditional risk of acquiring VAP is not constant over time [4], ventilator-days may not be the best denominator to express VAP rates. Instead, stratified or standardized rates might be technically more suitable, but benchmarking is based so far on rates computed on ventilator-days. Moreover, elements such as appropriate surveillance strategies, case definition, and denominators have a greater impact on infection rates than adjustment for varying daily conditional risk.

We show that the incidence of infection expressed as episodes per 1,000 patient-days underestimates that expressed as episodes per 1,000 ventilator-days by about 40%. In addition, considering days at risk or ventilator-days at risk additionally underestimates rates by about 20%. These differences may be of paramount importance while comparison of nosocomial infection rates, including VAP, does actually support benchmarking between units and hospitals [8, 13, 16] and has been recently incorporated into the process of quality management in many institutions [21].

Risk adjustment to publicly compare outcomes across healthcare providers constitutes one of the major challenges of today's highly charged, competitive medical environment.

Conclusions

We raise a flag of concern not only for the comparison of infection rates among hospitals but also for the "the risks of risk assessment" as raised by Iezzoni [9]. Accordingly, clinicians and hospital management in charge of patient-care policies should be aware of how to read and compare nosocomial infection rates and to become familiar with the underlying concepts of infection control and its potential role for prevention. Failure to recognize these issues will lead to biased comparisons and compromise meaningful benchmarking between healthcare institutions.

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References

1. Fagon JY, Chastre J, Vuagnat A, Trouillet JL, Novara A, Gibert C (1996) Nosocomial pneumonia and mortality among patients in intensive care units. JAMA 275:866–869
2. Heyland DK, Cook DJ, Griffith L, Keenan, SP, Brun-Buisson C (1999) The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient. The Canadian Critical Trials Group. Am J Respir Crit Care Med 159:1249–1256
3. Vincent JL, Bihari DJ, Suter PM, Bruining, HA, White J, Nicolas-Chanoin MH, Wolff M, Spencer RC, Hemmer M (1995) The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) study. JAMA 274:639–644

4. Cook DJ, Walter SD, Cook RJ, Griffith LE, Guyatt GH, Leasa D, Jaeschke RZ, Brun-Buisson C (1998) Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. Ann Intern Med 129:433–440
5. Kollef MH (1999) Epidemiology and risk factors for nosocomial pneumonia. Emphasis on prevention. Clin Chest Med 20:653–670
6. Chastre J, Fagon JY (2002) Ventilator-associated pneumonia. Am J Respir Crit Care Med 165:867–903
7. Eggimann P, Pittet D (2001) Infection control in the ICU. Chest 120:2059–2093
8. National Nosocomial Infections Surveillance (NNIS) system report. Data summary from January 1992-June 2001 (2002) Am J Infect Control 29:404–421
9. Iezzoni LI (1997) The risks of risk adjustment. JAMA 278:1600–1607
10. Eggimann P, Harbarth S, Constantin MN, Touveneau S, Chevrolet JC, Pittet D (2000) Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. Lancet 355:1864–1868
11. Garner JS, Jarvis WR, Emori TG, Toran TC, Hughes JM (1988) CDC definitions for nosocomial infections. Am J Infect Control 16:128–140
12. American Thoracic Society (1995) Hospital acquired pneumonia in adults: diagnosis, assessment of severity, initial antimicrobial therapy and preventive strategies. A consensus statement. Am J Respir Crit Care Med 153:1711–1725
13. Haley RW, Culver DH, White JW, Morgan WM, Emori TG, Munn VP, Hooton TM (1985) The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. Am J Epidemiol 121:182–205
14. Pittet D, Hugonnet S, Harbarth S, Mourouga P, Sauvan V, Touveneau S, Perneger TV, and the members of the Infection Control Programme (2000) Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. Lancet 356:1307–1312
15. Joint Commission on Accreditation of Health Care Organizations (JCAHO) (2002) Comprehensive Accreditation Manual for Hospitals. Hospital Accreditation Standards (HAS).http://www.jcaho.org/standards_frm.html
16. Richards C, Emori TG. Edwards J, Fridkin S, Tolson J, Gaynes R (2002) Characteristics of hospitals and infection control professionals participating in the National Nosocomial Infections Surveillance System 1999. Am J Infect Control 29:400–403
17. Pittet D, Harbarth S (1998) What techniques for diagnosis of ventilator-associated pneumonia? Lancet 352:83–84
18. Grossman RF, Fein A (2000) Evidence-based assessment of diagnostic tests for ventilator-associated pneumonia: executive summary. Chest 117 [Suppl 2]:177S–181S
19. Fagon JY, Chastre J, Wolff M, Gervais C, Parer-Aubas S, Stephan F, Similowski T, Mercat A, Diehl JL, Sollet JP, Tenaillon A (2000) Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. Ann Intern Med 132:621–630
20. Sax H, Pittet D, and the Swiss-NOSO Network (2002) Interhospital differences in nosocomial infection rates–importance of case-mix adjustment. Arch Intern Med 162:2437–2442
21. Cook D (2000) Ventilator associated pneumonia: perspectives on the burden of illness. Intensive Care Med 26 [Suppl 1]:S31–S37