Αποδιδόμενη θνητότητα της νοσοκομειακής πνευμονίας: μύθος ή πραγματικότητα;

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Οι κοινωνικοοικονομικές επιπτώσεις των νοσοκομειακών λοιμώξεων: νοσηρότητα, θνητότητα, κόστος και πρόληψη

- 2 εκατομμύρια νοσοκομειακές λοιμώξεις/έτος στις ΗΠΑ

- Παράταση της ημερών νοσηλείας: ουρολοιμώξεις 1-4, χειρουργικές λοιμώξεις 7-8.2, λοιμώξεις της αιματικής ροής 7-21, πνευμονία 6.8-30
- Αδρή θνητότητα: λοιμώξεις της αιματικής ροής 23.8-50%, πνευμονία 14.8-71%
- Αποδιδόμενη θνητότητα: λοιμώξεις της αιματικής ροής 16.3-35%, πνευμονία 6.8-30%
- Κόστος: ουρολοιμώξεις 558-593 $, χειρουργικές λοιμώξεις 2,734 $, λοιμώξεις της αιματικής ροής 3,061-40,000 $, πνευμονία 4,047 $

- «Ακόμη και ένα ελάχιστα αποτελεσματικό πρόγραμμα ελέγχου των λοιμώξεων δικαιολογεί το κόστος του»

Jarvis WR. Infect Control Hosp Epidemiol 1996

Το κλινικό και οικονομικό κόστος της νοσοκομειακής πνευμονίας

- Συστηματική ανάλυση των μελετών που δημοσιεύθηκαν μετά το 1990
- 10-20% των ασθενών που υποβάλλονται σε μηχανικό αερισμό για >48 ώρες θα αναπτύξουν VAP
- Η πιθανότητα θανάτου είναι διπλάσια
- Ο επιπλέον χρόνος νοσηλείας των ασθενών με VAP είναι 6.10 ημέρες
- Επιπλέον κόστος 10,019 $

  Safdar N, et al. Crit Care Med 2005
- Οι χειρουργικοί ασθενείς που αναπτύσσουν σήψη και πνευμονία έχουν μέση διάρκεια νοσηλείας 23.7 ήμερες, επιπλέον κόστος 80,000 $ και θνητότητα 27.9% ενώ με σήψη και χωρίς πνευμονία, 10,3 ημέρες, 30,800 $ και 18.7% αντίστοιχα

  Eber MR, et al. Arch Intern Med 2010
- Αύξηση του χρόνου νοσηλείας: 10 ημέρες. Επιπλέον κόστος 40,000 $

  Al-Tawfiq JA, Abed MS. Am J Infect Control 2010

Οι νοσοκομειακές λοιμώξεις αυξάνουν τη θνητότητα των ασθενών στη ΜΕΘ;

«Αν και δεν έχει αποδειχθεί πειστικά μια ευθεία σχέση ανάμεσα στις νοσοκομειακές λοιμώξεις και στη θνητότητα στη ΜΕΘ, είναι πιθανό να συμπεράνει κανείς ότι οι νοσοκομειακές λοιμώξεις αυξάνουν τον κίνδυνο θανάτου των ασθενών που βρίσκονται σε κρίσιμη κατάσταση.

Μια πιο ακριβής ανάλυση δείχνει ότι:

1.Η επίδραση στη θνητότητα είναι πολύ πιθανή για την πνευμονία, αμφίβολη για τη βακτηριαιμία και αβέβαιη για τις ουρολοιμώξεις

2.Ο κίνδυνος αυξάνει με τη διάρκεια παραμονής στη ΜΕΘ

3.Η μικροβιακή αιτιολογία τροποποιεί τον κίνδυνο

4.Η επίδραση είναι πιο ισχυρή στους λιγότερο βαριά ασθενείς, πιθανά επειδή η βαρύτητα της υποκείμενης νόσου παραμένει ο πιο ισχυρός παράγοντας»

Fagon JY, et al. Infect Control Hosp Epidemiol 1994

Ποια είναι η (αδρή) θνητότητα της VAP;

- Η όψιμη VAP εμφανίζει θνητότητα 65%

  Kollef MH, et al. Chest 1995
- Η θνητότητα είναι 45.5%

  Ibrahim EH, et al. Chest 2001
- Είναι 50%

  Warren DK, et al. Crit Care Med 2003
- Είναι 41%

  Karhu J, et al. Acta anaesthesiol Scand 2011
- Είναι 15% και 23% στις 14 και 28 ημέρες αντίστοιχα

  Wiskinrchen DE, et al. Surg Infect (Larchmt) 2011

Intensive Care Med. 2002 Feb;28(2):154-63. Epub 2002 Jan 16.

Mortality associated with late-onset pneumonia in the intensive care unit: results of a multi-center cohort study.

Moine P, Timsit JF, De Lassence A, Troché G, Fosse JP, Alberti C, Cohen Y; OUTCOMEREA study group.

Département d'Anesthésie Réanimation, CHU de Bicêtre, 78 rue du Général Leclerc, 94275 Le Kremlin Bicêtre cedex, France. pierre.moine1@fnac.net

"Inappropriately treated LOP remained significantly associated with an increased risk of mortality (HR=1.69, 95% CI 1.08-2.65, p=0.022), whereas appropriately treated LOP did not (HR=1.44, 95% CI 0.75-2.76, p=0.27).

In addition to severity scores, the underlying medical conditions and the evolution of severity within the first 4 days in ICU, late-onset pneumonia independently contribute to ICU patient mortality when empirical antibiotic treatment is not immediately appropriate"

Η θνητότητα των πολλαπλών επεισοδίων ανεπαρκώς θεραπευμένης VAP

- Αναδρομική μελέτη σε 82 ασθενείς με πολλαπλά επεισόδια VAP
- Σύνολο επεισοδίων: 200
- Συχνότερα παθογόνα: *Acinetobacter spp, Stenotrophomonas maltophilia, Alcaligenes xylosoxidans*
- Θνητότητα:

  3.6% χωρίς επεισόδιο VAP

  8.8% με ένα επεισόδιο VAP

  45% με περισσότερα επεισόδια VAP
- Τα πολλαπλά επεισόδια σχετίζονται με μεγαλύτερο διάστημα νοσηλείας στη ΜΕΘ (p=0.007) και μηχανικού αερισμού (p=0.005)

Mueller EW, et al. J Trauma 2005

Πως ορίζεται η αποδιδόμενη (ή αποδοτέα) θνητότητα;

Ως αποδιδόμενη θνητότητα ορίζεται η διαφορά που προκύπτει αν από τη συνολική θνητότητα αφαιρεθεί η θνητότητα που αντιστοιχεί στην υποκείμενη νόσο

Η απόλυτη αποδιδόμενη θνητότητα της VAP/HAP είναι η διαφορά μεταξύ της ολικής θνητότητας στον πληθυσμό της μελέτης, μείον τη θνητότητα του πληθυσμού των ασθενών χωρίς VAP/HAP

Μια άλλη έκφραση της αποδιδόμενης θνητότητας μπορεί να γίνει μέσω της διαίρεσης των OR θνητότητας σε ένα πληθυσμό με VAP/HAP δια του ίδιου OR σε αντίστοιχο πληθυσμό χωρίς VAP/HAP

Muscedere JG, et al. Clin Infect Dis 2010

Πόση είναι η αποδιδόμενη θνητότητα της νοσοκομειακής πνευμονίας;

- Είναι 42.8%, αν η πνευμονία οφείλεται σε *P. aeruginosa* ή *Acinetobacter spp.*
  Fagon JY, et al. Am J Med 1993
- Είναι 15-27%
  Pittet D. Schweiz Med Wochenschr 1994
- Είναι 16.2% αν ο ασθενής λαμβάνει κατάλληλη αντιμικροβιακή αγωγή και 24.7%, αν λαμβάνει ακατάλληλη
  Alvarez –Lerma F. Intensive Care Med 1996
- Είναι περίπου 40%, αν οφείλεται σε *P. aeruginosa*
  Brewer SC, et al. Chest 1996
- Είναι 26-28% μετά από νοσηλεία για βαριά CAP
  Leroy O, et al. J Crit Care 1999
- Είναι 13.3%
  Ibrahim EH, et al. Chest 2001
- Μετά από ταύτιση των ασθενών με VAP με εκείνους χωρίς, συμπεραίνεται ότι η VAP αποτελεί ανεξάρτητο παράγοντα κινδύνου θανάτου (OR 2.1, 95% CI, 1.2-3.1, p=0.008)
  Bercault N, Boulain T. Crit Care Med 2001
- Είναι 16%
  Warren DK, et al. Crit Care Med 2003
- Είναι 30.3-35%
  Rosenthal VD, et al. Am J Infect Control 2003
  Rosenthal VD, et al. Am J Infect Control 2005
- Είναι 18.5% και δεν επηρεάζεται χορήγηση της κατάλληλης αντιμικροβιακής αγωγής
  Valles J, et al. Intensive Care Med 2007
- Είναι 40% αν το αίτιο είναι ο MRSA
  Meyer E, et al. Eur J Med Res 2010
- Είναι 32% για τη μικροβιολογικά διαγνωσμένη πνευμονία
  Burgmann H, et al. Intensive Care Med 2010

Πόση είναι η αποδιδόμενη θνητότητα της νοσοκομειακής πνευμονίας;

- Η αποδιδόμενη θνητότητα είναι 7.3- 7.7%

  Schumacher M, et al. Methods Inf Med 2007 - Huqonnet S, et al. Infect Control Hosp Epidemiol 2004
- Υπολογίζεται σε 8.1%
- Είναι μεγαλύτερη σε χειρουργικούς ασθενείς , σε όσους δεν έχουν πολύ υψηλό SAPS και έχουν πολυοργανική ανεπάρκεια
- Επηρεάζεται από τον χρόνο εμφάνισης της VAP αλλά όχι από τα πολυανθεκτικά παθογόνα!

  Nquile-Makao M, et al. Intensive Care Med 2010
- Ανάλυση των στοιχείων της βάσης δεδομένων OUTCOMEREA
- Διάρκεια: 1997-2008. Αριθμός ασθενών: 4,479
- Η αποδιδόμενη θνητότητα είναι 1% στις 30 ημέρες και 1.5 % στις 60 ημέρες

  Bekaert M, et al. Am J Respir Crit Care Med 2011
- Η αποδιδόμενη θνητότητα είναι 6-9% (3-17% ανάλογα με την ομάδα)

  Timsit JF, et al. Curr Opin Crit Care 2011 – Melsen WG, et al. Crit Care Med 2011

Am J Epidemiol. 1989 Jun;129(6):1258-67.

Hospital-acquired pneumonia. Attributable mortality and morbidity.

Leu HS, Kaiser DL, Mori M, Woolson RF, Wenzel RP.

Hospital Epidemiology, Chang Gung Memorial Hospital, Taipei, Taiwan.

Abstract

A total of 1,001 consecutive episodes of nosocomial pneumonia in 901 patients was identified by routine surveillance at the University of Virginia Medical Center between 1979 and 1983 (8.6 episodes/1,000 admissions). When only initial episodes were examined, 890 patients comprised the study sample. The overall case fatality rate was 30%. Stepwise logistic regression indicated that time from admission to pneumonia (p = 0.0006), age (p less than 0.0001), prior use of mechanical ventilation (p = 0.0032), and neoplastic disease (p = 0.0062) were associated with mortality. Multiple regression analysis indicated that the factors associated with increased length of hospitalization included posttracheostomy status (p = 0.0001), prior mechanical ventilation (p = 0.0001), immunosuppressive or leukopenic status (p = 0.0009), nasogastric intubation (p = 0.0003), and prior bacteremia (p = 0.0127). A sampled, individually matched cohort study (n = 74 pairs) was conducted to determine the proportion of mortality in cases that was attributable to infections (33%) and to determine excess hospital stay (seven days) among the patients with nosocomial pneumonia. Excess stay was statistically significant (p less than 0.0001), but proportional mortality was only marginally significant (p = 0.0892). Our findings suggest that nosocomial pneumonia accounts for approximately 33% of the crude mortality and contributes significantly to the economic burden associated with prolonged hospitalization.

Cancer. 1992 Jun 1;69(11):2653-62.

Nosocomial pneumonia in patients having bone marrow transplant. Attributable mortality and risk factors.

Pannuti C, Gingrich R, Pfaller MA, Kao C, Wenzel RP.

Division of General Medicine, Clinical Epidemiology, and Health Services Research, University of Iowa College of Medicine, Iowa City.

Abstract

The authors performed a matched historic cohort study to determine the attributable mortality and risk factors for nosocomial pneumonia in bone marrow transplant (BMT) recipients. All patients with nosocomial pneumonia at a university tertiary care center were identified by a prospective surveillance system between 1980 and 1988. Control patients were selected from the population of BMT patients. The crude mortality for 55 patients with nosocomial pneumonia was 74.5% (95% confidence interval [CI95], 63% to 86%). The excess or attributable mortality was 61.8% (CI95, 43.7% to 80%). Aspergillus species represented the most frequent etiologic agent in this series, causing 20 of the 55 (36%) episodes. The attributable mortality of Aspergillus species pneumonia alone was 85% (CI95, 58.6% to 100%). For death in the hospital, the risk ratio for all 55 case patients relative to control patients was 9.5 (CI95, 4.1 to 22.1). To evaluate several risk factors simultaneously, a multiple logistic regression analysis using a conditional likelihood method was performed. A mathematical model with three variables best predicted nosocomial pneumonia in our patients: the occurrence of other nosocomial infections before the diagnosis of pneumonia, allogeneic BMT, and the use of methotrexate. The presence of other nosocomial infections before the diagnosis of pneumonia remained a significant independent risk factor, with an odds ratio of 13.27 (CI95, 2.51 to 70.2) after adjustment for the use of methotrexate and allogeneic BMT. Most importantly, effective methods for preventing nosocomial pneumonias in BMT recipients will have an enormous effect on crude mortality.

Incidence, Etiology, and Outcome of Nosocomial Pneumonia in Mechanically Ventilated Patients*

Chest 1991;100:439-44

Jordi Rello M.D., Ph.D.;† Elisabet Quintana, M.D.;† Vicenç Ausina, M.D., Ph.D.;‡ Joan Castella, M.D., Ph.D.;§ Marina Luquin, Ph.D.;‡ Alvar Net, M.D., Ph.D.;† and Guillem Prats, M.D., Ph.D.‡

"Ventilator-associated pneumonia does not appear to increase fatality in critically ill patients with a high mortality rate (38 percent); however, it significantly prolongs the length of stay in the ICU for survivors"

Table 2—*Pneumonia Acquired during MV: Characteristics of 264 Patients Studied**

Variable	Whole Group (n = 264)	Without NP (n = 206)	With NP (n = 58)
Age, yr	46.4 ± 1.3	45.7 ± 1.6	49.8 ± 1.9
Male/female	174/90	126/80	48/10
Shock on admission	11 (4)	11 (5)	0
Pneumonia on admission	25 (9)	22 (10)	3 (5)
COPD	50 (19)	40 (19)	10 (17)
Coma	63 (24)	44 (21)	19 (33)
ARDS	11 (4)	9 (4)	2 (3)
Bronchoaspiration	12 (4)	10 (4)	2 (3)
Corticosteroid use	36 (13)	23 (11)	13 (22)
Neoplasia associated	25 (9)	17 (8)	8 (14)
Immunodepression	11 (4)	6 (3)	5 (8)
Renal failure	15 (5)	9 (4)	6 (10)
Prior trauma	66 (25)	46 (22)	20 (34)
Prior surgery	143 (54)	104 (50)	39 (67)
Mortality	101 (38)	77 (37)	24 (42)

*NP = nosocomial pneumonia. Values in parentheses are percentages.

"These observations may indicate that host factors and underlying diseases in critically ill patients are more important determinants of outcome than the organism responsible for pneumonia or treatment given"

J Rello, et al. Chest 1991

Η VAP έχει μηδενική αποδιδόμενη θνητότητα;

- Προοπτική μελέτη σε πολυδύναμη ΜΕΘ
- Αυστηρά κριτήρια διάγνωσης της VAP. Μικροβιολογική διάγνωση με τη χρήση PSB
- Αντιστοίχηση 1:1 με ασθενείς ελέγχου με την ίδια διάγνωση, τις ίδιες ενδείξεις μηχανικού αερισμού, ηλικία, φύλλο, score APACHE II κατά την εισαγωγή, ημέρες μηχανικού αερισμού πριν την έναρξη της VAP, χρόνο επιλογής των ατόμων ελέγχου
- Η θνητότητα ήταν ίδια: 40% vs. 38.8%
- Η διάρκεια μηχανικού αερισμού και παραμονής στη ΜΕΘ ήταν μεγαλύτερη στους ασθενείς με VAP
- Η ανάπτυξη VAP δεν αύξησε τη θνητότητα!

Papazian L, et al. Am J Respir Crit Care Med 1996

Anesthesiology. 2001 Apr;94(4):554-60.

Is ventilator-associated pneumonia an independent risk factor for death?

Bregeon F, Ciais V, Carret V, Gregoire R, Saux P, Gainnier M, Thirion X, Drancourt M, Auffray JP, Papazian L.

Laboratoire de Physiopathologie Respiratoire, Université de la Méditerranée, France.

Abstract

BACKGROUND: Ventilator-associated pneumonia (VAP) has been implicitly accused of increasing mortality. However, it is not certain that pneumonia is responsible for death or whether fatal outcome is caused by other risk factors for death that exist before the onset of pneumonia. The aim of this study was to evaluate the attributable mortality caused by VAP by performing a matched-paired, case-control study between patients who died and patients who were discharged from the intensive care unit after more than 48 h of mechanical ventilation.

METHODS: During the study period, 135 consecutive deaths were included in the case group. Case-control matching criteria were as follows: (1) diagnosis on admission that corresponded to 1 of 11 predefined diagnostic groups; (2) age difference within 10 yr; (3) sex; (4) admission within 1 yr; (5) APACHE II score within 7 points; (6) ventilation of control patients for at least as long as the cases. Precise clinical, radiologic, and microbiologic definitions were used to identify VAP.

RESULTS: Analysis was performed on 108 pairs that were matched with 91% of success. There were 39 patients (36.1%) who developed VAP in each group. Multivariate analysis showed that renal failure, bone marrow failure, and treatment with corticosteroids but not VAP were independent risk factors for death. There was no difference observed between cases and controls concerning the clinical and microbiologic diagnostic criteria for pneumonia.

CONCLUSION: Ventilator-associated pneumonia does not appear to be an independent risk factor for death.

The Attributable Morbidity and Mortality of Ventilator-Associated Pneumonia in the Critically Ill Patient

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To evaluate the attributable morbidity and mortality of ventilator-associated pneumonia (VAP) in intensive care unit (ICU) patients, we conducted a prospective, matched cohort study. Patients expected to be ventilated for > 48 h were prospectively followed for the development of VAP. To determine the excess ICU stay and mortality attributable to VAP, we matched patients with VAP to patients who did not develop clinically suspected pneumonia. We also conducted sensitivity analyses to examine the effect of different populations, onset of pneumonia, diagnostic criteria, causative organisms, and adequacy of empiric treatment on the outcome of VAP. One hundred and seventy-seven patients developed VAP. As compared with matched patients who did not develop VAP, patients with VAP stayed in the ICU for 4.3 d (95% confidence interval [CI]: 1.5 to 7.0 d) longer and had a trend toward an increase in risk of death (absolute risk increase: 5.8%; 95% CI: −2.4 to 14.0 d; relative risk (RR) increase: 32.3%; 95% CI: −20.6 to 85.1%). The attributable ICU length of stay was longer for medical than for surgical patients (6.5 versus 0.7 d, $p < 0.004$), and for patients infected with "high risk" organisms as compared with "low risk" organisms (9.1 d versus 2.9 d). The attributable mortality was higher for medical patients than for surgical patients (RR increase of 65% versus −27.3%, $p = 0.04$). Results were similar for three different VAP diagnostic criteria. We conclude that VAP prolongs ICU length of stay and may increase the risk of death in critically ill patients. The attributable risk of VAP appears to vary with patient population and infecting organism. **Heyland DK, Cook DJ, Griffith L, Keenan SP, Brun-Buisson C, for the Canadian Critical Care Trials Group. The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient.**

AM J RESPIR CRIT CARE MED 1999;159:1249–1256.

J Crit Care. 2008 Mar;23(1):5-10.

The impact of ventilator-associated pneumonia on the Canadian health care system.

Muscedere JG, Martin CM, Heyland DK.

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Abstract

INTRODUCTION: Ventilator-associated pneumonia (VAP) is a cause of morbidity and mortality in critically ill patients. It is associated with increased health care costs and duration of mechanical ventilation. Using published data and information from public health care providers, we sought to determine the impact of VAP on the Canadian health care system.

METHODS: Ventilator-associated pneumonia incidence, attributable mortality, and intensive care unit (ICU) utilization/resource data were obtained through Canadian published and institutional data. Ontario case cost methodology was used for the cost of a critical care bed which is CAN dollars 2396 per day, excluding treatment costs. Antibiotic acquisition costs for Ontario were used. Physician reimbursement rates were obtained from the provincial ministries of health. Ventilator-associated pneumonia data, ICU resource data, and costs were combined to determine the impact of VAP.

RESULTS: For the Canadian health care system; ICU utilization is 217 episodes per 100000 population and 1150 days of mechanical ventilation per 100000. The incidence of VAP is 10.6 cases per 1000 ventilator days (95% CI, 5.1-16.1). Ventilator-associated pneumonia increases ICU length of stay 4.3 days (95% CI, 1.5-7.0 days) per episode. The attributable mortality of VAP is 5.8% (95% CI, -2.4 to 14). The number of cases of VAP is estimated to be approximately 4000 cases per year (95% CI, 1900-6100). This results in 230 deaths per year with the lower and upper confidence intervals ranging from 0 to 580. Ventilator-associated pneumonia accounts for approximately 17000 ICU days per year or around 2% of all ICU days in Canada. The cost to the health care system is CAN dollars 46 million (possible range, dollars 10 million to 82 million) per year.

CONCLUSION: The impact of VAP on the Canadian health care system is considerable. Eradication of this preventable nosocomial infection would save lives and conserve scarce health care resources.

Am J Respir Crit Care Med. 1996 Jan;153(1):343-9.

Pneumonia in intubated trauma patients. Microbiology and outcomes.

Baker AM, Meredith JW, Haponik EF.

Department of Medicine, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina, USA.

Abstract

To describe the epidemiology of nosocomial pneumonia in trauma patients and its impact on outcome, we performed a retrospective case-control analysis. Quantitative bronchoscopic cultures were collected from 62 intubated patients with suspected pneumonia. Patients with proven pneumonia had higher abdominal injury scores. Those with bronchoscopy-negative pneumonitis were older. Age and injury severity were used to match two controls to each case. The incidence of pneumonia was 5.8% Streptococci and Hemophilus were common pathogens, but gram-negative rods were isolated more frequently after lengthier intubation. Polymicrobial infections were common. There were no serious complications of bronchoscopy, and culture results often led to antibiotic therapy. No excess mortality could be attributed to pneumonia. Patients with pneumonia and those with bronchoscopy-negative pneumonitis required prolonged care compared with others ($p < 0.05$). Patients with pneumonia did not receive excess ventilation or hospitalization but incurred hospital charges 1.5 times higher than controls ($p = 0.04$). Pneumonia was confirmed in less than half of those suspected of having it on the basis of clinical findings. When severity of injury was considered, pneumonia was associated with neither increased mortality nor increased hospital care, but the clinical features suggesting respiratory infection identified trauma patients requiring prolonged hospitalization and incurring higher costs.

Η επίδραση της VAP στη θνητότητα των πολυτραυματιών

- Προοπτική ελεγχόμενη μελέτη σε πολυτραυματίες με κρανιοεγκεφαλική κάκωση και χορήγηση SDD
- Διάρκεια μελέτης: 6 έτη
- 324 διαδοχικοί ασθενείς με διάρκεια μηχ. αερισμού >48 ώρες
- Ταύτιση ασθενών για: ηλικία, Glasgow scale, κλίμακα βαρύτητας τραύματος, APACHE II, διάρκεια μηχ. αερισμού
- SDD σε όλους (με συστηματική συνχορήγηση κεφαζολίνης)
- Ανάλυση σε 58 ζεύγη
- Μεγαλύτερη διάρκεια νοσηλείας των ασθενών με VAP
- Παρόμοια θνητότητα

Leone M, et al. Crit Care Med 2002

Am Rev Respir Dis. 1986 Jul;134(1):12-6.

Incidence, site, and outcome of infections in patients with the adult respiratory distress syndrome.

Seidenfeld JJ, Pohl DF, Bell RC, Harris GD, Johanson WG Jr.

Abstract

Bacterial infection in the adult respiratory distress syndrome (ARDS) is associated with the occurrence of multiple organ failures and death. We studied 108 infections in 129 patients with ARDS and evaluated the organisms responsible, the body sites involved, and the outcomes of therapy. Gram-negative bacilli represented 57% of the microbial pathogens and gram-positive cocci 36%. Only 7% of infections were caused by other organisms (fungi, viruses, Pneumocystis, Legionella). Gram-negative organisms were more common in the lung, abdomen, and pleura. Bacteremia was more common in abdominal infections (11 of 17, 67%) than in infections at other sites (18 of 65, 28%), (p less than 0.01); ;9 patients were bacteremic from clinically undetected sites. Ten of 17 (59%) patients with abdominal infections survived compared with 7 of 56 (13%) patients with lung infections (p less than 0.001). A retrospective review of in vitro organism susceptibility and the antibiotics administered revealed that the patients who received adequate antibiotic therapy did not have a higher survival rate (20 of 69, 29%) than those who received inadequate antibiotic therapy (3 of 13, 23%). These data suggest that further investigation of infections in patients with ARDS is required and that emphasis should be placed on pathogenesis, prevention, and host responses.

Multicenter Prospective Study of Ventilator-Associated Pneumonia During Acute Respiratory Distress Syndrome

Incidence, Prognosis, and Risk Factors

Am J Respir Crit Care Med Vol 161. pp 1942–1948, 2000

PHILIPPE MARKOWICZ, MICHEL WOLFF, KAMEL DJEDAÏNI, YVES COHEN, JEAN CHASTRE, CHRISTOPHE DELCLAUX, JACQUES MERRER, BERNARD HERMAN, BENOIT VEBER, ALAIN FONTAINE, DIDIER DREYFUSS and the ARDS Study Group

COMPARISON OF PATIENTS WITH AND WITHOUT VENTILATOR-ASSOCIATED PNEUMONIA: CLINICAL CHARACTERISTICS AT THE ONSET OF ACUTE RESPIRATORY DISTRESS SYNDROME AND OUTCOME

	With VAP ($n = 49$)	Without VAP ($n = 85$)	p Value
Temperature, °C	38.1	38.3	0.7
White blood cells/mm^3	13,085 ± 7,380	13,172 ± 7,775	0.9
SAPS II	45 ± 13	47 ± 16	0.4
OSF	2.6 ± 1.1	2.6 ± 1.1	0.2
Antibiotic treatment	45 (92)	75 (88)	0.6
Broad-spectrum antibiotics	42 (86)	70 (82)	0.8
Pa_{O_2}/FI_{O_2} ratio	113 ± 40	118 ± 40	0.4
Pa_{CO_2}, mm Hg	49 ± 13.7	47 ± 19	0.8
Plateau pressure, cm H_2O	26.5 ± 4.8	25.6 ± 4.5	0.3
ARDS etiology			
Extrapulmonary infection	5 (10)	13 (15)	
Pulmonary infection	27 (55)	45 (53)	
Drug overdose	7 (14)	10 (12)	
Other*	5 (10)	10 (12)	
> 1 Etiology	5 (10)	7 (8)	
Mortality	28 (57)	50 (59)	0.8

Crit Care Med. 2009 Oct;37(10):2709-18.

Ventilator-associated pneumonia and mortality: a systematic review of observational studies.

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Abstract

OBJECTIVE: To determine the attributable mortality of ventilator-associated pneumonia in a systematic review and meta-analysis of observational studies. Ventilator-associated pneumonia is generally believed to increase the mortality of patients. This notion is predominantly based on the results of observational studies.

DATA SOURCE: We performed a systematic search strategy using PubMed, Web of Science, and Embase from their inception through February 2007. In addition, a reference and related article search was performed.

STUDY SELECTION: Studies were included if they reported mortality rates of patients with and without ventilator-associated pneumonia.

DATA EXTRACTION AND SYNTHESIS Fifty-two studies with a total of 17,347 patients met the inclusion criteria. Pooling of all studies resulted in relative risk of 1.27 (95% Confidence Interval = 1.15-1.39), but heterogeneity was considerable (I2 statistic = 69%). The origin of heterogeneity could not be explained by differences in study design, study quality, and diagnostic approach. However, heterogeneity was limited for studies investigating only trauma patients (I2 = 1.3%) or patients with acute respiratory distress syndrome (I2 = 0%), with estimated relative risk of 1.09 (95% Confidence Interval = 0.87-1.37) among trauma patients and 0.86 (95% Confidence Interval = 0.72-1.04) among patients with acute respiratory distress syndrome.

CONCLUSIONS: There is no evidence of attributable mortality due to ventilator-associated pneumonia in patients with trauma or acute respiratory distress syndrome. However, in other nonspecified patient groups, there is evidence for attributable mortality due to ventilator-associated pneumonia, but this could not be quantified due to heterogeneity in study results. More detailed studies, allowing subgroup analyses, are needed to determine the attributable mortality of ventilator-associated pneumonia in these patient populations.

Research

Determinants and impact of multidrug antibiotic resistance in pathogens causing ventilator-associated-pneumonia

Pieter O Depuydt[1], Dominique M Vandijck[1], Maarten A Bekaert[2], Johan M Decruyenaere[1], Stijn I Blot[3], Dirk P Vogelaers[3] and Dominique D Benoit[1]

Critical Care 2008, v12, No6

Introduction The idea that multidrug resistance (MDR) to antibiotics in pathogens causing ventilator-associated pneumonia (VAP) is an independent risk factor for adverse outcome is still debated. We aimed to identify the determinants of MDR versus non-MDR microbial aetiology in VAP and assessed whether MDR versus non-MDR VAP was independently associated with increased 30-day mortality.

Methods We performed a retrospective analysis of a prospectively registered cohort of adult patients with microbiologically confirmed VAP, diagnosed at a university hospital intensive care unit during a three-year period. Determinants of MDR as compared with non-MDR microbial aetiology and impact of MDR versus non-MDR aetiology on mortality were investigated using multivariate logistic and competing risk regression analysis.

Results MDR pathogens were involved in 52 of 192 episodes of VAP (27%): methicillin-resistant *Staphylococcus aureus* in 12 (6%), extended-spectrum β-lactamase producing *Enterobacteriaceae* in 28 (15%), MDR *Pseudomonas aeruginosa* and other non-fermenting pathogens in 12 (6%). Multivariable logistic regression identified the Charlson index of comorbidity (odds ratio (OR) = 1.38, 95% confidence interval (CI) = 1.08 to 1.75, p = 0.01) and previous exposure to more than two different antibiotic classes (OR = 5.11, 95% CI = 1.38 to 18.89, p = 0.01) as predictors of MDR aetiology. Thirty-day mortality after VAP diagnosis caused by MDR versus non-MDR was 37% and 20% (p = 0.02), respectively. A multivariate competing risk regression analysis showed that renal replacement therapy before VAP (standardised hazard ratio (SHR) = 2.69, 95% CI = 1.47 to 4.94, p = 0.01), the Charlson index of comorbidity (SHR = 1.21, 95% CI = 1.03 to 1.41, p = 0.03) and septic shock on admission to the intensive care unit (SHR = 1.86, 95% CI = 1.03 to 3.35, p = 0.03), but not MDR aetiology of VAP, were independent predictors of mortality.

Conclusions The risk of MDR pathogens causing VAP was mainly determined by comorbidity and prior exposure to more than two antibiotics. The increased mortality of VAP caused by MDR as compared with non-MDR pathogens was explained by more severe comorbidity and organ failure before VAP.

Epidemiology and Outcomes of Ventilator-Associated Pneumonia in a Large US Database*

Jordi Rello, MD; Daniel A. Ollendorf, MPH; Gerry Oster, PhD; Montserrat Vera-Llonch, MD, MPH; Lisa Bellm, MIM; Rebecca Redman, MD; Marin H. Kollef, MD, FCCP; for the VAP Outcomes Scientific Advisory Group†

Objectives: To evaluate risk factors for ventilator-associated pneumonia (VAP), as well as its influence on in-hospital mortality, resource utilization, and hospital charges.
Design: Retrospective matched cohort study using data from a large US inpatient database.
Patients: Patients admitted to an ICU between January 1998 and June 1999 who received mechanical ventilation for > 24 h.
Measurements: Risk factors for VAP were examined using crude and adjusted odds ratios (AORs). Cases of VAP were matched on duration of mechanical ventilation, severity of illness on admission (predicted mortality), type of admission (medical, surgical, trauma), and age with up to three control subjects. Mortality, resource utilization, and billed hospital charges were then compared between cases and control subjects.
Results: Of the 9,080 patients meeting study entry criteria, VAP developed in 842 patients (9.3%). The mean interval between intubation, admission to the ICU, hospital admission, and the identification of VAP was 3.3 days, 4.5 days, and 5.4 days, respectively. Identified independent risk factors for the development of VAP were male gender, trauma admission, and intermediate deciles of underlying illness severity (on admission) [AOR, 1.58, 1.75, and 1.47 to 1.70, respectively]. Patients with VAP were matched with 2,243 control subjects without VAP. Hospital mortality did not differ significantly between cases and matched control subjects (30.5% vs 30.4%, $p = 0.713$). Nevertheless, patients with VAP had a significantly longer duration of mechanical ventilation (14.3 ± 15.5 days vs 4.7 ± 7.0 days, $p < 0.001$), ICU stay (11.7 ± 11.0 days vs 5.6 ± 6.1 days, $p < 0.001$), and hospital stay (25.5 ± 22.8 days vs 14.0 ± 14.6 days, $p < 0.001$). Development of VAP was also associated with an increase of > $40,000 in mean hospital charges per patient ($104,983 ± $91,080 vs $63,689 ± $75,030, $p < 0.001$).
Conclusions: This retrospective matched cohort study, the largest of its kind, demonstrates that VAP is a common nosocomial infection that is associated with poor clinical and economic outcomes. While strategies to prevent the occurrence of VAP may not reduce mortality, they may yield other important benefits to patients, their families, and hospital systems. *(CHEST 2002; 122:2115–2121)*

Η επίδραση της SDD στον κίνδυνο ανάπτυξης VAP και στη θνητότητα

- «Παρά τη σημαντική μείωση των λοιμώξεων με τη χρήση της SDD, οι περισσότερες μελέτες δεν έδειξαν μείωση των ποσοστών θνητότητας»

  Quinio B, et al. Ann Fr Anesth Reanim 1994
- Ανασκόπηση 16/21 μελετών της Αγγλόφωνης βιβλιογραφίας 1982-1992
- Η SDD μείωσε τη συνολική επίπτωση της πνευμονίας και της τραχειοβρογχίτιδας στους ασθενείς της ΜΕΘ αλλά δεν είχε αποτέλεσμα στη νοσοκομειακή θνητότητα

  Kollef MH. Chest 1994
- Ανασκόπηση 36 μελετών με 6,914 ασθενείς
- Η προφυλακτική χρήση τοπικών αντιβιοτικών μειώνει τις αναπνευστικές λοιμώξεις αλλά όχι τη συνολική θνητότητα

  Liberati A, et al. Cxochrane Database Syst Rev 2009

Η αποτελεσματική πρόληψη της VAP με SDD μειώνει τη θνητότητα;

- Μετα-ανάλυση των τυχαιοποιημένων ελεγχόμενων μελετών σε MEDLINE, Embase και Cochrane Library
- Ανάλυση 28 δημοσιεύσεων
- Η SDD με αντισηπτικά μείωσε τη συχνότητα της VAP κατά 27% και η SDD με αντιβιοτικά κατά 36%
- Καμιά από τις δύο μεθόδους δεν έδειξε στατιστικά σημαντική επίδραση στη θνητότητα!

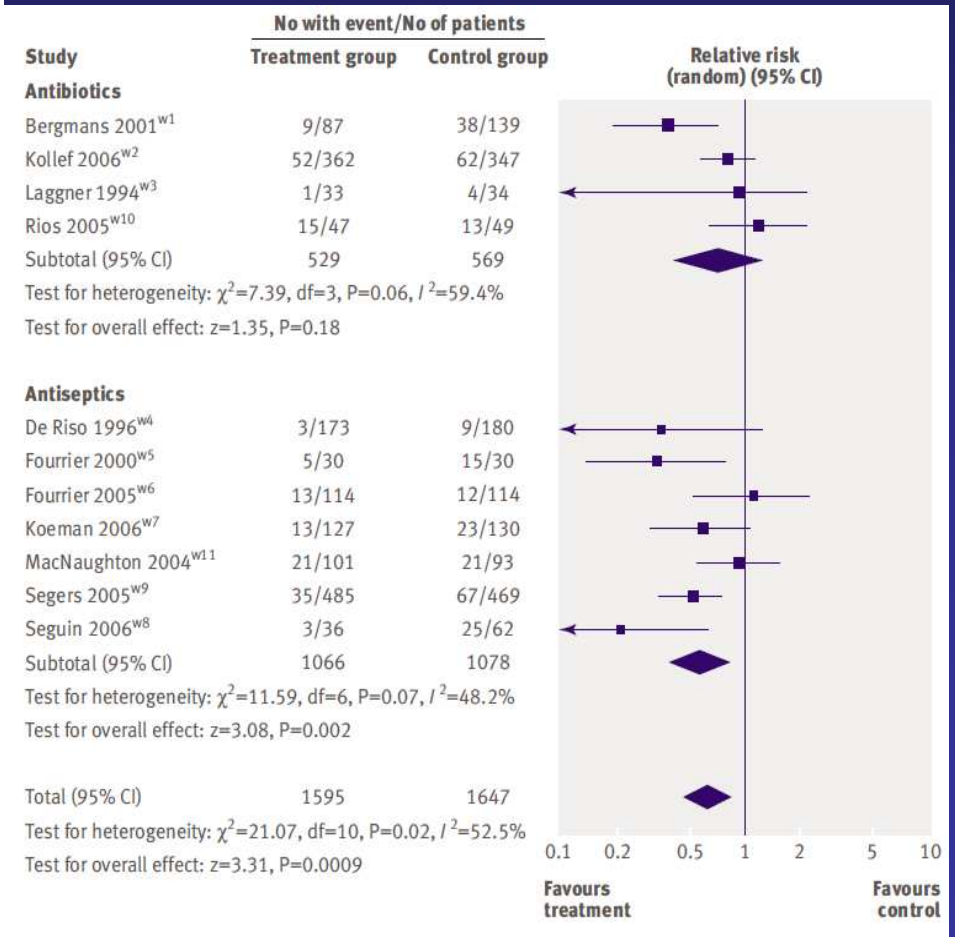
Pileggi C, et al. Crit Care 2011

Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis

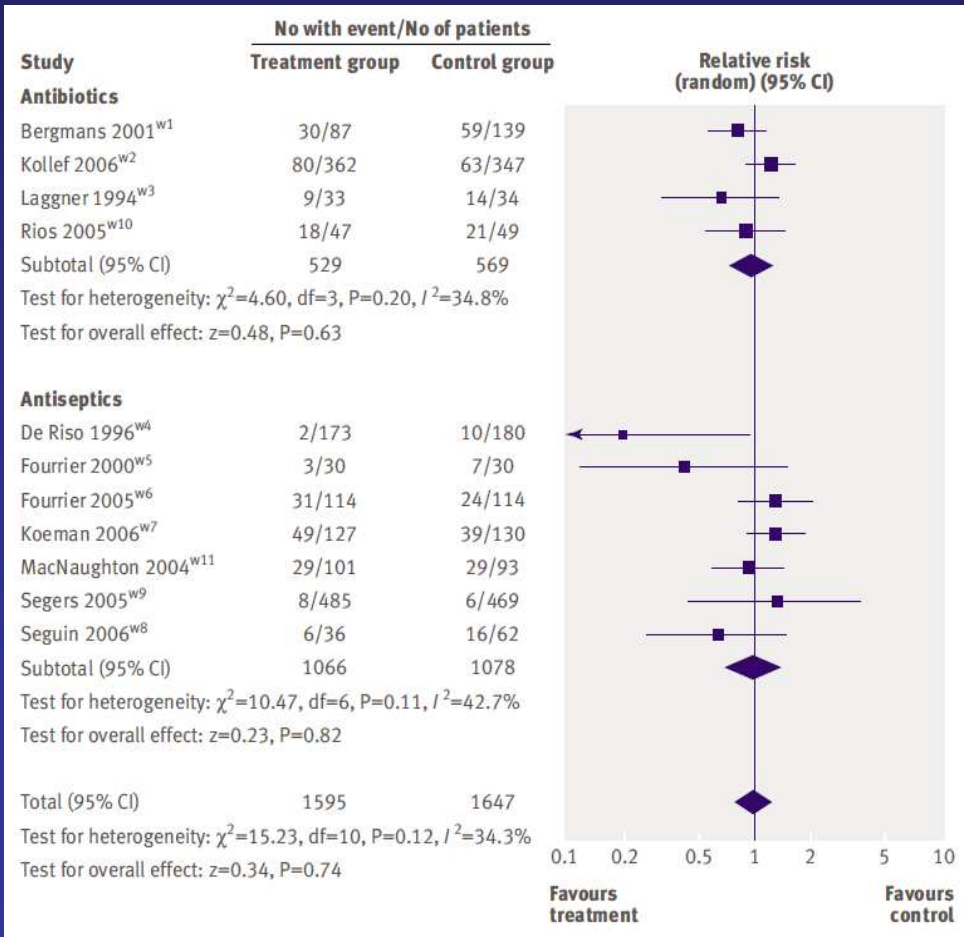
BMJ 2007Apr 28;334(7599):889

Ee Yuee Chan, nurse educator,[1] Annie Ruest, infectious diseases consultant,[2] Maureen O Meade, associate professor,[3] Deborah J Cook, professor[3]

Η επίδραση της προφυλακτικής στοματικής απολύμανσης στον κίνδυνο ανάπτυξης VAP



Η επίδραση της προφυλακτικής στοματικής απολύμανσης στην συνολική θνητότητα



Prevention of Gram-Negative Bacillary Pneumonia Using Polymyxin Aerosol as Prophylaxis

II. EFFECT ON THE INCIDENCE OF PNEUMONIA IN SERIOUSLY ILL PATIENTS

JAMES M. KLICK, GARY C. DU MOULIN, JOHN HEDLEY-WHYTE, DANIEL TERES, LEONARD S. BUSHNELL, and DAVID S. FEINGOLD

ABSTRACT All 744 patients admitted to a Respiratory-Surgical Intensive Care Unit (RSICU) were included in a prospective study of the effects of a polymyxin (2.5 mg/kg body wt/day in six divided doses) or a placebo aerosol sprayed into the posterior pharynx and tracheal tube (if present), during 11 alternating 2-mo treatment cycles. The incidence of upper airway colonization in the RSICU with *Pseudomonas aeruginosa* was 1.6% during the polymyxin treatment cycles (total 374 patients) and 9.7% during the placebo cycles (370 patients) ($\chi^2 = 23.2$, $P < 0.01$). 3 patients in the RSICU acquired *Pseudomonas* pneumonia, as defined by independent "blinded" assessors, during the polymyxin cycles while 17 acquired a *Pseudomonas* pneumonia during the placebo cycles ($\chi^2 = 10.2$, $P < 0.01$). The overall mortality was similar in both placebo and polymyxin-treated groups (12.2 vs. 12.0%). Systemic antibiotic usage was similar in the different cycles; 49% of patients in the placebo and 53% in the polymyxin-treated groups received systemic antibiotics while in the RSICU.

Respir Care. 2005 Jul;50(7):892-8; discussion 898-9.

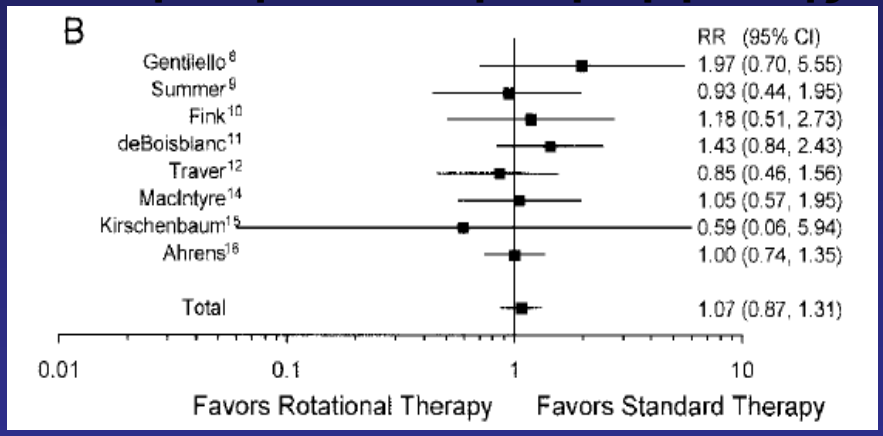
Patient positioning and ventilator-associated pneumonia.

Hess DR.

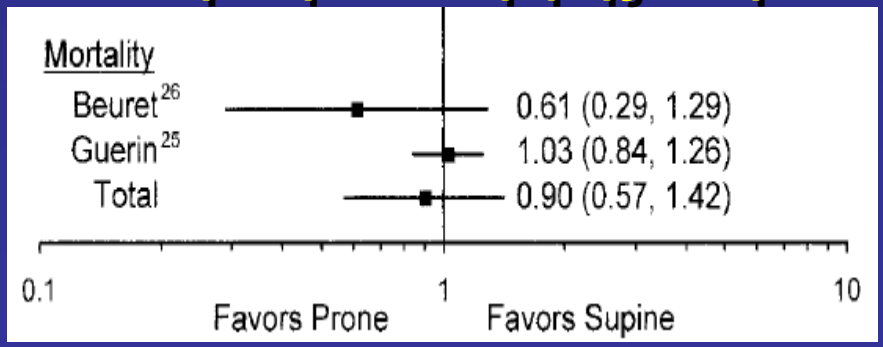
Ανασκόπηση σχετικά με τη χρήση περιστρεφόμενων κλινών, πρηνούς και ημικαθιστής θέσης για την πρόληψη της VAP

« Αν και κάθε μια από τις τεχνικές αυτές έχει δείξει ότι μειώνει τον κίνδυνο της VAP, καμία δεν έχει αποδείξει ότι επηρεάζει τη θνητότητα»

Θνητότητα και περιστροφή θέσης



Θνητότητα και πρηνής θέση



Intermittent Subglottic Secretion Drainage and Ventilator-associated Pneumonia

A Multicenter Trial

Am J Respir Crit Care Med Vol 182. pp 910–917, 2010

Jean-Claude Lacherade[1], Bernard De Jonghe[1], Pierre Guezennec[2], Karim Debbat[3], Jan Hayon[4], Antoine Monsel[1], Pascal Fangio[1], Corinne Appere de Vecchi[1], Cédric Ramaut[5], Hervé Outin[1], and Sylvie Bastuji-Garin[6]

SECONDARY OUTCOME MEASURES

	SSD (*n* = 169)	Control (*n* = 164)	*P* Value
Postextubation laryngeal dyspnea, no. (%) [95% CI]	8/79 (10.1) [4.5–19.0]	4/89 (4.5) [1.2–11.1]	0.25
Tracheostomy, no. (%) [95% CI]	25 (14.8) [9.8 to 21.1]	19 (11.6) [7.1–17.5]	0.42
Duration of MV (d), median [IQR]	8 [5–13]	7 [3–15]	0.42
Length of ICU stay (d), median [IQR]	11 [7–19]	11 [6–20]	0.33
ICU deaths, no. (%) [95% CI]	71 (42.0) [34.5–49.8]	65 (39.6) [32.1–47.6]	0.74
Hospital deaths, no. (%) [95% CI]	80 (47.3) [39.6–55.2]	84 (51.2) [43.3–59.1]	0.51

Definition of abbreviations: CI = confidential interval; ICU = intensive care unit; IQR = interquartile range; MV = mechanical ventilation; SSD = subglottic secretion drainage.

"Despite the marked decrease in the incidence of microbiologically confirmed VAP with the use of SSD in our study, secondary end points, that is, mortality, and duration of mechanical ventilation and ICU stay, were not influenced by the use of SSD"

JAMA. 2008 Aug 20;300(7):805-13.

Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: the NASCENT randomized trial.

Kollef MH, Afessa B, Anzueto A, Veremakis C, Kerr KM, Margolis BD, Craven DE, Roberts PR, Arroliga AC, Hubmayr RD, Restrepo MI, Auger WR, Schinner R; NASCENT Investigation Group.

CONTEXT: Ventilator-associated pneumonia (VAP) causes substantial morbidity. A silver-coated endotracheal tube has been designed to reduce VAP incidence by preventing bacterial colonization and biofilm formation.

OBJECTIVE: To determine whether a silver-coated endotracheal tube would reduce the incidence of microbiologically confirmed VAP.

DESIGN, SETTING, AND PARTICIPANTS: Prospective, randomized, single-blind, controlled study conducted in 54 centers in North America. A total of 9417 adult patients (> or = 18 years) were screened between 2002 and 2006. A total of 2003 patients expected to require mechanical ventilation for 24 hours or longer were randomized.

INTERVENTION: Patients were assigned to undergo intubation with 1 of 2 high-volume, low-pressure endotracheal tubes, similar except for a silver coating on the experimental tube.

MAIN OUTCOME MEASURES: Primary outcome was VAP incidence based on quantitative bronchoalveolar lavage fluid culture with 10(4) colony-forming units/mL or greater in patients intubated for 24 hours or longer. Other outcomes were VAP incidence in all intubated patients, time to VAP onset, length of intubation and duration of intensive care unit and hospital stay, mortality, and adverse events.

RESULTS: Among patients intubated for 24 hours or longer, rates of microbiologically confirmed VAP were 4.8% (37/766 patients; 95% confidence interval [CI], 3.4%-6.6%) in the group receiving the silver-coated tube and 7.5% (56/743; 95% CI, 5.7%-9.7%) (P = .03) in the group receiving the uncoated tube (all intubated patients, 3.8% [37/968; 95% CI, 2.7%-5.2%] and 5.8% [56/964; 95% CI, 4.4%-7.5%] [P = .04]), with a relative risk reduction of 35.9% (95% CI, 3.6%-69.0%; all intubated patients, 34.2% [95% CI, 1.2%-67.9%]). The silver-coated endotracheal tube was associated with delayed occurrence of VAP (P = .005). No statistically significant between-group differences were observed in durations of intubation, intensive care unit stay, and hospital stay; mortality; and frequency and severity of adverse events.

CONCLUSION: Patients receiving a silver-coated endotracheal tube had a statistically significant reduction in the incidence of VAP and delayed time to VAP occurrence compared with those receiving a similar, uncoated tube.

Surg Infect (Larchmt). 2011 Oct;12(5):373-8. Epub 2011 Sep 20.

Daily multidisciplinary rounds to implement the ventilator bundle decreases ventilator-associated pneumonia in trauma patients: but does it affect outcome?

Stone ME, Snetman D, O' Neill A, Cucuzzo J, Lindner J, Ahmad S, Teperman S.

Jacobi Medical Center/Albert Einstein College of Medicine , Bronx, New York.

Abstract

Abstract Background: The incidence of ventilator-associated pneumonia (VAP) in trauma patients can be decreased with use of the ventilator bundle (VAPB). Our VAP rate remained high despite the adoption of the VAPB. To better implement the VAPB, a multidisciplinary team composed of the surgical intensive care unit (SICU) nursing staff, physician, and respiratory therapist reviewed briefly a checklist of VAPB goals for each patient before morning attending rounds. We hypothesized that such daily goal rounds (GR) focused on the VAPB would decrease the VAP rate. Methods: A pre-GR ten-month period (November 2006 to August 2007) was compared with the ten-month period (September 2007 to June 2008) with daily GRs. The occurrence of VAPs was tallied prospectively in all intubated trauma patients using the National Nosocomial Infection Surveillance criteria. Patient characteristics and outcome data were obtained from our trauma registry and medical records. Patient characteristics were similar in the 85 pre-GR patients and the 89 GR patients. Results: The number of VAPs decreased 67% in the GR patients (15 pre-GR vs. 5 GR; p=0.02); however, the all-cause mortality rate remained similar (16.5% vs. 21.3%; p=0.41). When patients were divided into those with and without VAP, there was a significant increase in mean ventilator, SICU, and hospital days in patients with VAP (p=0.01 for all). There were only two deaths among trauma patients with VAP. Conclusion: Daily multidisciplinary GRs focused on the VAPB can decrease the incidence of VAP significantly in trauma patients. Ventilator-associated pneumonia correlated with extended mean ventilator, SICU, and hospital days. Interestingly, despite a significant decrease in VAP, a decrease in the mortality rate was not observed. Given the small number of deaths in the VAP cohort, this study has insufficient statistical power to elucidate the true impact of GR intervention or VAP on the mortality rate in trauma patients.

Viewpoint

The paradox of ventilator-associated pneumonia prevention measures

Michael Klompas[1,2]

Critical Care 2009, 13:315

Randomized controlled trials of interventions to prevent ventilator-associated pneumonia

		Impact on				
	Subjects	VAP rates	Ventilator LOS	ICU LOS	Hospital LOS	Mortality
Elevation of the head of the bed						
Drakulovic, *et al.*, 1999 [5]	86	78% ↓	NS	NS	-	NS
van Nieuwenhoven, *et al.*, 2006 [46]	221	NS	NS	NS	-	NS
Oral care						
Chlorhexidine						
DeRiso, *et al.*, 1996 [40]	353	NS	NS	-	NS	80% ↓
Fourrier, *et al.*, 2000 [1]	60	68% ↓	NS	NS	-	NS
Genuit, *et al.*, 2001 [2]	95	37% ↓	NS	NS	NS	-
Houston, *et al.*, 2002 [47]	561	NS	NS	-	-	-
Fourrier, *et al.*, 2005 [48]	228	NS	NS	NS	-	NS
Koeman, *et al.*, 2006 [3]	257	NS	NS	NS	NS	NS
Segers, *et al.*, 2006 [49]	954	50% ↓	-	NS	8% ↓	NS
Tantipong, *et al.*, 2008 [50]	207	NS	-	-	-	NS
Chan, *et al.*, 2007 [4] (meta-analysis)	2,144	44% ↓	NS	NS	-	NS
Oral topical antibiotics						
Laggner, *et al.*, 1994 [51] (gentamicin)	67	NS	NS	-	-	NS
Bergmans, *et al.*, 2001 [52] (gentamicin, colistin, vancomycin)	226	57%-68% ↓	NS	NS	NS	NS
Kollef, *et al.*, 2006 [53] (iseganan)	709	NS	-	-	-	NS
Chan, *et al.*, 2007 [4] (meta-analysis)	1,098	NS	NS	NS	-	NS
de Smet, *et al.*, 2009 [31] (tobramycin, colistin, amphotericin B)	3,894	-	NS	NS	NS	14% ↓
Deep vein thrombosis prophylaxis						
Samama, *et al.*, 1999 [54]	1,102	-	-	-	-	NS
Fraisse, *et al.*, 2000 [55]	223	-	-	-	-	NS
Leizorovicz, *et al.*, 2004 [56]	3,706	-	-	-	-	NS
Mahé, *et al.*, 2005 [57]	2,474	-	-	-	-	NS
Stress ulcer prophylaxis						
Prod'hom, *et al.*, 1994 [58]	248	NS	-	-	-	NS
Bonten, *et al.*, 1995 [59]	141	NS	-	-	NS	NS
Yildizdas, *et al.*, 2002 [60]	160	NS	-	-	-	NS
Kantorova, *et al.*, 2004 [61]	287	NS	NS	NS	-	NS
Cook, *et al.*, 1996 [10] (meta-analysis)	7,218	NS	-	-	-	NS
Continuous aspiration of subglottic secretions						
Valles, *et al.*, 1995 [6]	153	37% ↓	-	NS	-	NS
Kollef, *et al.*, 1999 [62]	343	39% ↓	NS	NS	NS	NS
Smulders, *et al.*, 2002 [63]	150	75% ↓	NS	NS	NS	NS
Lorente, *et al.*, 2007 [64]	280	64% ↓	NS	NS	-	NS
Bouza, *et al.*, 2008 [39]	690	NS	NS	NS	NS	NS
Silver-coated endotracheal tubes						
Kollef, *et al.*, 2008 [8]	2,003	36% ↓	NS	NS	NS	NS

Am J Respir Crit Care Med. 1996 Jul;154(1):116-23.

Mortality of nosocomial pneumonia in ventilated patients: influence of diagnostic tools.

Timsit JF, Chevret S, Valcke J, Misset B, Renaud B, Goldstein FW, Vaury P, Carlet J.

Intensive Care Unit, Hôpital Saint Joseph, Paris, France.

Abstract

The overmortality induced by nosocomial infections, especially pneumonia in ventilated patients (VNP), is still a matter of controversy because it is difficult to know precisely the respective effects of VNP per se and both the underlying illness and the severity of the disease that indicates ICU stay. During a 3-yr period, for each patient mechanically ventilated for more than 48 h we recorded underlying illness, reason for mechanical ventilation, clinical and therapeutic data collected during the first 48 h of ventilation, and death in the ICU. Patients with suspicion of VNP (S-VNP) according to clinical, radiologic, and biologic criteria underwent bronchoscopy with protected specimen brush (PSB) and bronchoalveolar lavage culture (BAL-C). VNP was confirmed (C-VNP) if PSB > or = 10(3) cfu/ml and/or BAL-C > or = 10(4) cfu/ml. Prognostic multivariate analysis was performed introducing S-VNP and C-VNP as time-dependent covariates. Of the 387 studied patients, 112 S-VNP and 56 C-VNP were observed with overall mortality of 43% (168 patients). MacCabe, APACHE II score, shock, use of sedatives and absence of enteral nutrition were additively associated with an increased mortality as well as C-VNP (relative risk [RR]: 1.8, p = 0.007). Nevertheless, when S-VNP and C-VNP were simultaneously introduced in the Cox model, only S-VNP remained associated with increased mortality. In patients suspected of VNP, confirmation of VNP using PSB and/or BAL-C adds no prognostic information. Whether this could be explained by the lack of sensitivity of protected distal samples or the severity of underlying conditions of S-VNP patients is still an open issue. A multivariate analysis based on follow-up data during the ICU course of ventilated patients will be initiated in the near future.

REVIEW ARTICLE

Ventilator-Associated Pneumonia

Arch Intern Med. 2000;160:1926-1936

Richard Scott Morehead, MD; Simmy Jerry Pinto, MD

Ventilator-associated pneumonia is a common complication in intensive care units, occurring in 9% to 24% of patients intubated for longer than 48 hours. Because of this large disease burden and the resultant attributable morbidity and mortality, there is great interest in accurately diagnosing, treating, and preventing this complication. More severely ill patients tend to develop ventilator-associated pneumonia, and identified risk factors include prolonged mechanical ventilation, reintubation after failed extubation, and a few other clinical variables. The efficacy of diagnostic and preventive strategies is somewhat controversial. Diagnosis by invasive methods requires a considerable commitment of resources but can potentially reduce cost of care; however, mortality benefit from this approach has not been demonstrated. As such, in most institutions, ventilator-associated pneumonia is best diagnosed using traditional clinical criteria. Prompt administration of appropriate antibiotics seems to be the only intervention that alters outcome once the diagnosis is established. Several strategies seem to reduce pneumonia incidence; however, mortality and cost benefits have yet to be convincingly shown.

Ventilator-Associated Pneumonia Due to *Pseudomonas Aeruginosa**

CHEST 1996; 109:1019-29

Susan Crouch Brewer, MD; Richard G. Wunderink, MD, FCCP; Carol B. Jones, RN, BSN; and Kenneth V. Leeper, Jr, MD, FCCP

"Since at least 38% of deaths can be directly attributable to the *Pseudomonas* pneumonia, improvement in therapy is needed"

But....

Table 5—*Severity of Illness in Nonsurvivors*

Cause of Death	APACHE II Day −3*	APACHE II Day 0	APACHE III Day −3*	APACHE III Day 0*	MODS Day −3*	MODS Day 0	MOFS Day −3*	MOFS Day 0*
Septic shock from VAP	25.6	28.4	87.0	116.9	2.7	5.3	1.1	2.8
Septic shock—subsequent site	19.8	21.2	63.7	72.8	3.2	3.7	1.3	1.2
Multiple organ failure	18.1	23.0	69.9	93.6	5.3†	5.7	1.7	2.7
All other	13.3†	18.7	47.0†	66.2	3.0	4.2	0	1.0

*p<0.05 between groups by ANOVA.
†Corrected p<0.05 compared with septic shock from VAP.

"Significant differences in both APACHE scores, MODS, and MOFS between patients who died of the various causes were present 3 days prior to diagnosis of VAP"

"Mortality appears to be unchanged despite the availability of more potent antibiotics and the development of more sophisticated ICU care in the last two decades"

Infect Control Hosp Epidemiol. 1998 Oct;19(10):795-7.

Mortality as an outcome in hospital-acquired pneumonia.

Rello J, Valles J.

Intensive Care Department, Hospital de Sabadell, Barcelona, Spain. jrello@siberia.chpt.es

"Attributable mortality is highly dependent on the institution of a correct initial antibiotic choice, as well as the interaction between the virulence of the pathogen responsible and host defenses.

However, survival in these patients is determined primarily by the degree of severity at the time of pneumonia diagnosis and the response to initial therapy.

As a consequence, the number of preventable deaths is likely to be much smaller than the total."

Ο υπολογισμός της αποδιδόμενης θνητότητας: Γιατί υπάρχει πρόβλημα;

- Οι υπολογισμοί από διάφορες μελέτες δίνουν ποσοστά 0-50%
- Ο ορισμός της VAP δεν είναι πάντα ακριβής (είναι μικρότερη αν ο ορισμός δεν είναι ακριβής)
- Υπάρχει μίξη περιστατικών (είναι μικρότερη σε τραυματίες)
- Η βαρύτητα της υποκείμενης νόσου (είναι μεγαλύτερη αν η υποκείμενη νόσος είναι ενδιάμεσης βαρύτητας)
- Εξαρτάται από τη βαρύτητα και τα ειδικά χαρακτηριστικά της VAP
- Οι μέθοδοι στατιστικής ανάλυσης δεν είναι πάντα οι κατάλληλοι

Timsit JF, et al. Curr Opin Crit Care 2011

Multicenter Evaluation of a Novel Surveillance Paradigm for Complications of Mechanical Ventilation

PLoS ONE, 2011

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Background: Ventilator-associated pneumonia (VAP) surveillance is time consuming, subjective, inaccurate, and inconsistently predicts outcomes. Shifting surveillance from pneumonia in particular to complications in general might circumvent the VAP definition's subjectivity and inaccuracy, facilitate electronic assessment, make interfacility comparisons more meaningful, and encourage broader prevention strategies. We therefore evaluated a novel surveillance paradigm for ventilator-associated complications (VAC) defined by sustained increases in patients' ventilator settings after a period of stable or decreasing support.

Methods: We assessed 600 mechanically ventilated medical and surgical patients from three hospitals. Each hospital contributed 100 randomly selected patients ventilated 2–7 days and 100 patients ventilated >7 days. All patients were independently assessed for VAP and for VAC. We compared incidence-density, duration of mechanical ventilation, intensive care and hospital lengths of stay, hospital mortality, and time required for surveillance for VAP and for VAC. A subset of patients with VAP and VAC were independently reviewed by a physician to determine possible etiology.

Results: Of 597 evaluable patients, 9.3% had VAP (8.8 per 1,000 ventilator days) and 23% had VAC (21.2 per 1,000 ventilator days). Compared to matched controls, both VAP and VAC prolonged days to extubation (5.8, 95% CI 4.2–8.0 and 6.0, 95% CI 5.1–7.1 respectively), days to intensive care discharge (5.7, 95% CI 4.2–7.7 and 5.0, 95% CI 4.1–5.9), and days to hospital discharge (4.7, 95% CI 2.6–7.5 and 3.0, 95% CI 2.1–4.0). VAC was associated with increased mortality (OR 2.0, 95% CI 1.3–3.2) but VAP was not (OR 1.1, 95% CI 0.5–2.4). VAC assessment was faster (mean 1.8 versus 39 minutes per patient). Both VAP and VAC events were predominantly attributable to pneumonia, pulmonary edema, ARDS, and atelectasis.

Conclusions: Screening ventilator settings for VAC captures a similar set of complications to traditional VAP surveillance but is faster, more objective, and a superior predictor of outcomes.

Πιθανά συμπεράσματα

- Η αποδιδόμενη θνητότητα της VAP/HAP φαίνεται πως είναι μικρότερη απ' όσο εμφανίζουν παλαιότερες μελέτες
- Η VAP/HAP έχει διαφορετική επίδραση στη θνητότητα και την έκβαση των ασθενών, ανάλογα με την εξέλιξη της υποκείμενης νόσου αλλά και τους ίδιους τους ασθενείς
- Ανεξάρτητα από το μέγεθος της αποδιδόμενης θνητότητας, οι οικονομικές και οικολογικές της επιπτώσεις είναι πολύ σημαντικές
- Χρειάζονται μεγάλες ομογενοποιημένες μελέτες και βελτιωμένη μεθοδολογία για την ακριβή διευκρίνηση του θέματος. Η έλλειψη μεθόδων ακριβούς διάγνωσης της VAP αποτελεί σοβαρό εμπόδιο
- Ο προσδιορισμός μόνο της θνητότητας ως κριτηρίου θεραπευτικής επιτυχίας της VAP/HAP ίσως δεν θα πρέπει να αποτελεί τον βασικό στόχο τέτοιων μελετών

Ευχαριστώ!

Η αποδιδόμενη θνητότητα και η δαπάνη πόρων που προκαλούν οι νοσοκομειακές λοιμώξεις είναι σημαντικές

- Πολυκεντρική Αυστριακή μελέτη διάρκειας 6 μηνών
- 34 ΜΕΘ, 2,392 ασθενείς
- Αποδιδόμενη θνητότητα μετά από προσαρμογή του κινδύνου:
  - 32% για την μικροβιολογικά διαγνωσμένη πνευμονία
  - 32% για μικτές λοιμώξεις
  - 26% για λοιμώξεις από CVC
- Παράταση του χρόνου νοσηλείας
- Σημαντική οικονομική επιβάρυνση

Burgmann H, et al. Intensive Care Med 2010

Ποια είναι η αποδιδόμενη θνητότητα της νοσοκομειακής πνευμονίας;

- Αναδρομική ελεγχόμενη Ελβετική μελέτη
- 106 περιπτώσεις VAP σε 452 ασθενείς υπό μηχανικό αερισμό
- Επιτυχία ταύτισης σε 97 ζεύγη
- Αποδιδόμενη θνητότητα 7.3%.
- Αποδιδόμενο κόστος ανά επεισόδιο VAP: 15,986 $.
- Αποδιδόμενος επιπλέον χρόνος νοσηλείας: 10 ημέρες

Huqonnet S, et al. Infect Control Hosp Epidemiol 2004

Η μικροβιακή πολυαντοχή αυξάνει τη θνητότητα;

- Αναδρομική μελέτη παρατήρησης διάρκειας 2.5 ετών
- Στόχος η νοσοκομειακή λοίμωξη της αιματικής ροής από πολυανθεκτικά Gram (-) βακτηρίδια (MDR-GNB)
- Ανάλυση 675 περιπτώσεων, 301 με MDR-GNB
- Αύξηση των ημερών νοσηλείας: 6.1 ημέρες
- Στην πολυπαραγοντική ανάλυση η πολυαντοχή δεν αύξησε τη θνητότητα στις 30 ημέρες
- Η χορήγηση της κατάλληλης αντιμικροβιακής αγωγής δεν σχετίσθηκε ούτε με τη θνητότητα, ούτε με την παράταση του χρόνου νοσηλείας !

Lye DC, et al. Clin Microbiol Infect 2011