

Nosocomial pneumonia in the intensive care unit of a Brazilian university hospital: An analysis of the time span from admission to disease onset

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Background: In addition to controversies as to the definition of nosocomial pneumonia (NP) because of the lack of a widely accepted diagnostic standard, there has been no agreement concerning the time span from hospital admission to disease onset. This study aims at both estimating the time span, in hours, from admission to the occurrence of suspected NP and investigating risk factors that might influence this time span.

Methods: This is a cohort study, and subjects were patients with nosocomial infection acquired in the intensive care unit of Edgard Santos University Hospital (HUPES/ICU) in Salvador, Brazil, from January 1995 to December 1997. Patients were observed from admission to 48 hours after discharge from the intensive care unit. The time span from admission to occurrence of suspected NP, the reason for admission, patient's origin, history of surgery, general anesthesia, mechanical ventilation, and use of antibiotic were analyzed and given a multivariate analysis using Cox regression model.

Results: Among 246 patients with nosocomial infection, 198 (80.5%) were suspected cases of NP, whereas 48 patients (19.5%) were not classified as such. The mean time, in hours, for the NP-free time span was 85.1 ± 3.5 hours, and the median time was 72 hours when estimated by Kaplan-Meier method. Patients admitted from surgical heart procedures who had been given general anesthesia, mechanical ventilation, and antibiotics showed statistically significant shorter mean time spans from admission to NP occurrence when compared with the other patients. Age ≥ 50 years, use of mechanical ventilation, and use of antibiotics were associated with NP.

Conclusions: Our finding for the estimated mean NP-free time span at the HUPES/ICU is somewhat in accordance with the literature (48 to 72 hours). Patients at HUPES/ICU might be considered as showing early NP, because they were diagnosed before the 5th day after admission. Preventive measures to NP should be reviewed and intensified at the HUPES/ICU, especially as related to mechanical ventilation. (Am J Infect Control 2004;32:209-14.)

INTRODUCTION

The intensive care unit (ICU), a primary component of modern hospital care, is a high-technology complex unit for critically ill patients who depend on life support systems.¹ However, as an environment, the ICU also puts patients at risk for the development of nosocomial infection (NI). The risk is associated primarily with patient's condition, infectious agents, invasive and immunosuppressive procedures, and ICU environment.^{1,2}

Patients in ICUs have NI rates that are 5 to 10 times greater than those on general wards.³ Pneumonia has been considered the most common infection in ICUs,²⁻⁵ with morbidity and mortality rates so substantial that it has been deemed the most serious infection acquired in the hospital environment.⁶ Nosocomial pneumonia (NP) is a lower respiratory tract infection not present or incubating at the time of patient's admission to the hospital.^{1,6-8} Risk factors for NP may be grouped into (1) host factors (intrinsic), comprising conditions that favor colonization and aspiration, and (2) those factors (extrinsic) related to long ICU stay, previous exposure to antimicrobials and other drugs, invasive procedures, and exposure to contaminated equipment, devices, hands, individuals, air, water, and solutions.⁹

Because there is no well-accepted gold standard for diagnosis, the definition of NP is controversial.⁹ Frequently the criteria for diagnosis have included clinical signs and symptoms in combination with radiologic evidence and laboratory results.⁶ In addition,

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there has been no agreement concerning the time span from admission to disease onset as a diagnostic criterion. Despite the difficulty in specifying the time duration for determining whether pneumonia is nosocomial or community acquired, a 48- to 72-hour interval between admission and symptom onset has been often used.^{10,11} The American Thoracic Society defines hospital-acquired pneumonia as “occurring at or more than 48 hours after admission.”¹²

This study aims at both estimating the time span, in hours, from admission to the occurrence of suspected NP and investigating risk factors that might influence this time span in patients with NI acquired in the ICU of Edgard Santos University Hospital (HUPES/ICU) in Salvador, Brazil, from January 1995 to December 1997.

METHODS

A cohort (dynamic) study was carried out in HUPES/ICU. This ICU cares for critically ill adults and children requiring continuous and complex assistance within a medical and surgical clinic. The cohort included patients with NI acquired in the ICU who were followed up from admission to 48 hours after ICU discharge and transference to other wards in HUPES. Patients were considered an NI case on the basis of Brazilian NI criteria¹³ associated with those criteria set by the Centers for Disease Control⁷—that is, upon meeting one of the following requirements: (1) when at the same place in which a community infection was diagnosed, a different germ was isolated, followed by a patient’s clinical deterioration; (2) when, after 72 hours from admission, the microorganism incubation period was unknown and there was no clinical or laboratory evidence of infection on admission; or (3) when, within 72 hours from admission, the infection was associated with diagnostic and/or therapeutic procedures carried out within this time span. NP cases were diagnosed on the basis of concomitant clinical and radiologic criteria regardless of microbiologic exam results as follows:

1. Clinical criteria: dullness to percussion and auscultatory findings on pulmonary examination of fine crepitant rales, plus either (1) purulent sputum production, or (2) presence of fever $>38^{\circ}\text{C}$.
2. Radiologic criteria: chest radiograph with new or progressive infiltrates, consolidation, cavitation, or pleural effusion.

Cases of NP diagnosed within 48 hours or less after admission and those after 48 hours from discharge from the ICU were excluded from the analysis.

The Nosocomial Infection Control Service/HUPES has implemented an active, continuous, and systematic Nosocomial Infection Surveillance System since Janu-

ary 1988. Data collection consisted of reviewing the medical registers during routine visits to the ICU in search for NI among those on antibiotic therapy.

The time span in hours from admission to the occurrence of NP was used as the dependent variable in the survival analysis, representing the “failure time.” Patients who did not develop pneumonia until the end of the follow-up period were considered “censored.” The Kaplan-Meier method^{14,15} was used to estimate the NP-free time span. Age, sex, reason for ICU admission, history of surgery, general anesthesia, mechanical ventilation, and previous antibiotic use (surgical antibiotic prophylaxis) were used as independent variables. The time spans in hours until NP occurrence were described according to the study variables by using the log-rank statistical test. A multivariate analysis with semiparametric Cox regression model^{14,15} exact method¹⁵ was used.

RESULTS

Of 2183 patients admitted to the ICU between 1995 and 1997, 257 (11.8%) developed NI, which consisted of 274 occurrences. Eleven (4.3%) cases were excluded for either not meeting the NI criteria or having data inconsistencies. Among 246 NI cases (95.7%), 198 (80.5%) were considered as “failure” (NP occurring after 48 hours from admission at ICU and those diagnosed within 48 hours after ICU discharge), whereas 48 (19.5%) constituted the “censoring” data (patients without pneumonia) for survival analysis.

The Kaplan-Meier survival curve is shown in Fig 1. Mean and median NP-free time span in hours was estimated to be 85.1 and 72, respectively, which means that half of the cases remained pneumonia free for as long as 72 hours.

Table 1 shows the stratified analysis with mean and median estimates. Mechanical ventilation, general anesthesia, and previous antibiotic use were statistically significant associated with lower NP-free time span. Patients admitted to the ICU immediately after cardiac surgery showed a statistically significant lower mean NP-free time span of 79.3 hours when compared with other admission causes (99.9 hours) (Fig 2). When no surgical procedure was carried out before admission, the mean time span until NP was statistically significantly greater (100.6 hours) when compared with patients who underwent surgery (83.3 hours) (Fig 3). There is probably a correlation between surgery and mechanical ventilation, because almost all surgical patients were mechanically ventilated.

Results of the Cox proportional hazards model are shown in Table 2. It is worth noting that regardless of their lack of statistical significance, the covariables age, mechanical ventilation, and previous antibiotic use acted as accelerating factors to NP risk. Patients at 50

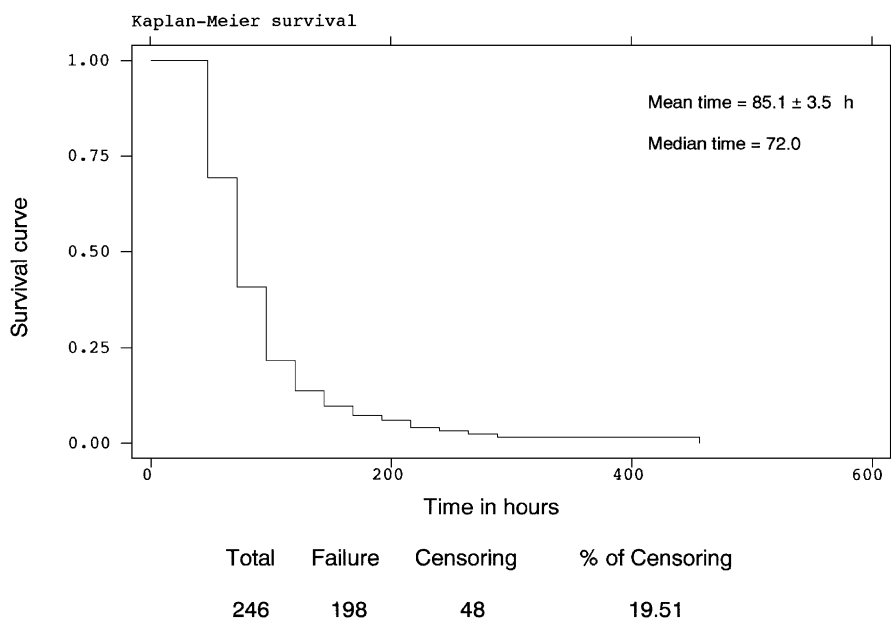


Fig 1. Survival time curve until the occurrence of nosocomial pneumonia. HUPES/ICU, 1995-1997.

Table 1. Estimated means, medians, and descriptive level (P value) of the time until nosocomial pneumonia occurrence as a function of selected variables. HUPES/ICU, 1995 through 1997

Variables	No. (N = 198)*	Mean (SE)	Median	P value†
Gender				
Male	104	83.5 (4.0)	72.0	
Female	94	86.8 (5.9)	72.0	.8331
Age				
< 50 y	70	89.5 (6.9)	72.0	
≥ 50 y	128	82.7 (3.9)	72.0	.8258
Admittance reason				
Other reasons	55	99.9 (9.4)	72.0	
Cardiac surgery	143	79.3 (3.1)	72.0	.0009
Surgery				
No	21	100.6 (12.9)	72.0	
Yes	177	83.3 (3.6)	72.0	.0001
General anesthesia				
No	22	100.4 (12.4)	96.0	
Yes	176	83.2 (3.6)	72.0	.000
Mechanical ventilation				
No	13	90.5 (12.5)	96.0	
Yes	185	78.1 (3.6)	72.0	.000
Antibiotic use				
Not previously	27	99.6 (10.6)	72.0	
Previously	171	82.8 (3.7)	72.0	.000

HUPES/ICU, Professor Edgard Santos University Hospital/Intensive Care Unit.

*Number of suspected cases with nosocomial pneumonia.

†P value based on the “log-rank” test.

years of age or older were estimated to have 1.3 times as much risk of developing NP as those under 50. Mechanically ventilated patients were 1.9 times as likely to develop NP when compared with those without

mechanical ventilation, and patients who had previously used antibiotics were 1.3 times as likely to develop NP as those who had not. The opposite was true for “origin” (from the clinic surgical unit, emergency care at the cardiovascular surgical unit and other hospital, thoracic and cardiovascular surgical unit, and pediatric care unit), which also, without statistical significance, slowed the risk (hazard ratio) of this event occurrence by 50%, when compared with patients coming from the medical clinic and infectious diseases units.

DISCUSSION

Our finding for the estimated mean NP-free time span at the HUPES/ICU is somewhat in accordance with the literature (48 to 72 hours).^{1,16-18} More than 50% of ICU-acquired pneumonia cases are diagnosed within the first 4 days after ICU admission.¹⁵ However, patients at HUPES/ICU might be considered as showing early NP, because they were diagnosed before the 5th day after admission.⁸

ICU admission immediately after thoracic and cardiovascular surgery, the history of any surgical procedure with general anesthesia, use of mechanical ventilation, and prophylactic use of antibiotics were shown to be associated with the time until occurrence of ICU-acquired pneumonia. These variables, however, are so interrelated to one another that 1 may well account for the other in determining NP-free time span.

Concerning the association between mechanical ventilation and pneumonia, Kollef¹⁸ showed that clinical evidence appears more than 48 hours after

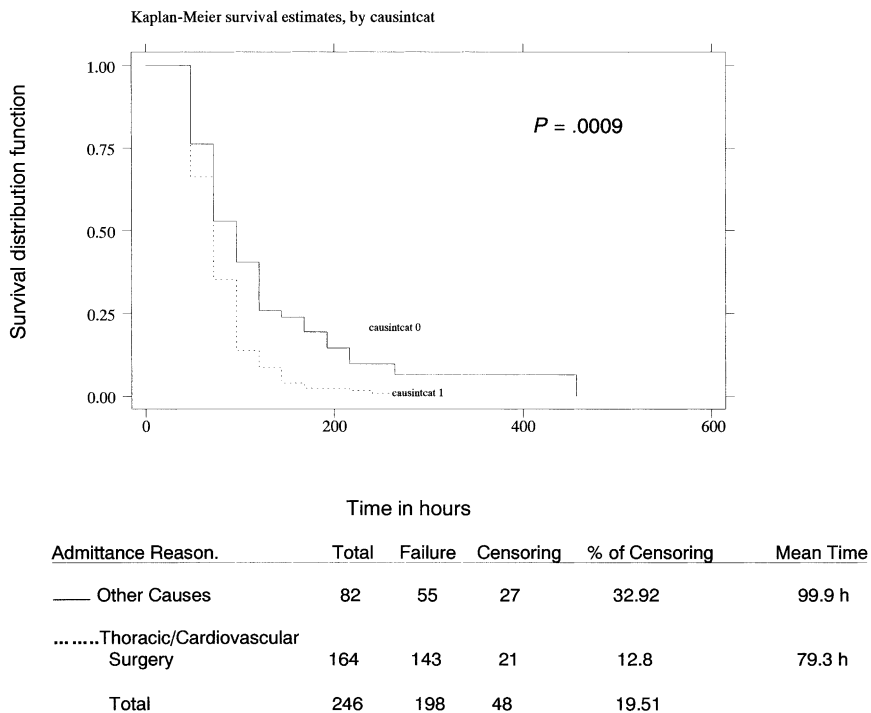


Fig 2. Comparison of the time until pneumonia occurrence according to the reason for admittance. HUPES/ICU, 1995-1997.

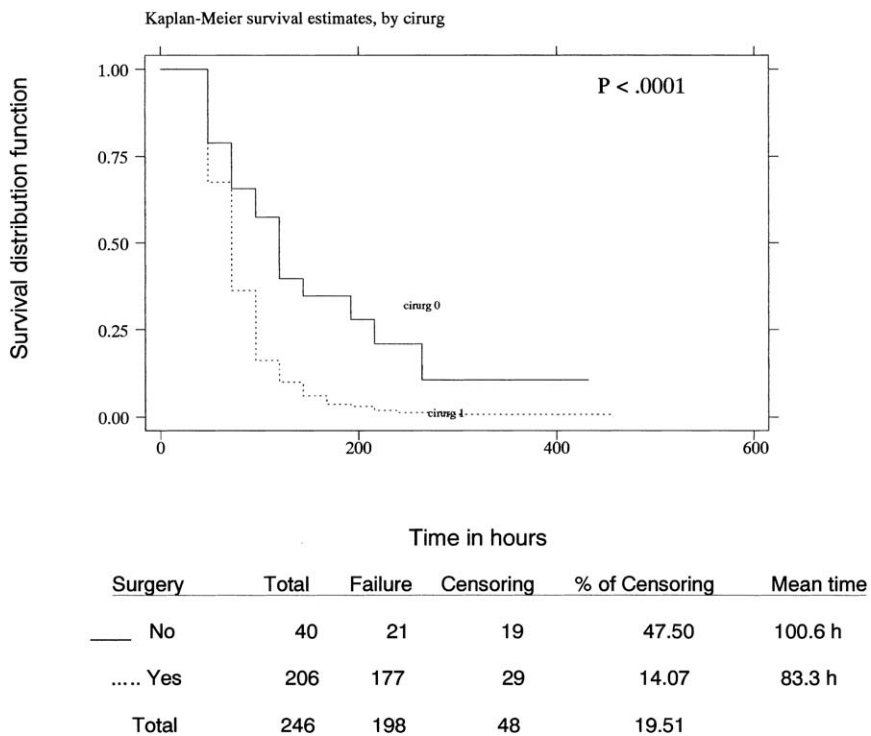


Fig 3. Comparison of the time until pneumonia occurrence according to presence or absence of surgery. HUPES/ICU, 1995-1997.

Table 2. Estimated regression coefficient, standard error, *P* value, and hazard ratio as a function of the risks of selected variables according to Cox Proportional hazards model, HUPES/ICU, 1995 through 1997

Variables	Coefficient	Standard error	<i>P</i> value	Hazard ratio (CI = 95%)
Age	0.24516	0.15824	.121	1.3 (0.937 - 1.742)
Gender	0.08764	0.15041	.560	1.1 (0.812 - 1.466)
Surgery	-0.02825	0.57448	.964	0.9 (0.315 - 3.003)
Mechanical Ventilation	0.65611	0.46130	.155	1.9 (0.780 - 4.760)
Surgical Clinic	-0.28119	0.45073	.373	0.7 (0.406 - 1.400)
EC + Other Hospital	-0.56795	0.31544	.113	0.5 (0.280 - 1.143)
TCSU + UDAP	-0.14184	0.35831	.600	0.8 (0.510 - 1.474)
Previous Antibiotics	0.28441	0.27056	.528	1.3 (0.549 - 3.215)

HUPES/ICU, Professor Edgard Santos University Hospital/Intensive Care Unit; EC, emergency care at the cardiovascular surgical unit; TCSU, thoracic and cardiovascular surgical unit; UDAP, pediatric care unit.

intubation, when cases with pneumonia because of respiratory failure were excluded.⁸ At HUPES/ICU, most of the cases (75%) using mechanical ventilation showed NP within 72 hours after ICU admission. As a whole, these cases were admitted intubated to the ICU after cardiac surgery and remained mechanically ventilated for 12 to 24 hours before extubation. Our findings are in accordance with Kelleghan,¹⁹ who found NP to occur in the time range between 24 hours or more after intubation and 72 hours after extubation.

Patients who used antibiotics prophylactically showed early NP (less than 4 days after ICU admission) when compared with those who did not. Antibiotic administration before onset of pneumonia has been linked to an increased frequency of ventilator-associated pneumonia caused by highly virulent organisms such as *Pseudomonas aeruginosa* and *Acinetobacter* species.²⁰

Although several studies have not analyzed the time span between admission and disease occurrence, they have pointed to mechanical ventilation and advanced age as important risk factors for pneumonia occurrence among ICU patients.^{9,16,21}

The time span from hospital admission to the occurrence of suspected NP turns out to be a relevant matter in that it may both answer and raise questions for further investigation, namely those related to NP diagnosis and its risk factors in ICU environments. The fact that microbiologic exams were not taken into account for NP diagnosis does not invalidate this study insofar as preventive measures may and must be taken whenever NI is suspected. It is therefore important to recommend further studies on NI in HUPES/ICU to broaden understanding of the contribution of variables herein studied and other risk factors for NP.

Increased occurrence of suspected NP (198 cases) among the study population (246 subjects) may point either to NP outbreaks during the time of the investigation or to overrepresentation because of the countless difficulties shown in the literature concerning the proper NP diagnosis. Nevertheless, the results of

this study are in accordance with those found in the literature that show that patients admitted to ICUs are especially prone to acquire NI, not only because of the specific features of this group, but also because of current diagnostic methods and treatment.

On the basis of both the estimated mean time span from hospital admission to disease onset in the HUPES/ICU and the knowledge of factors speeding disease occurrence, the Nosocomial Infection Control Center at HUPES should make all possible efforts to (1) review specific diagnostic criteria for NP by emphasizing etiologic diagnosis by means of safe techniques; (2) review NP preventive measures periodically for patients who have undergone cardiac surgery; (3) intensify NP preventive and controlling measures related to mechanical ventilation; and (4) investigate further approaches contributing to NP diagnosis and the identification of associated risk factors so that the gaps in knowledge shown by this study may be successfully bridged.

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