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Prolongation of Hospital Stay and Extra Costs due to Ventilator-Associated Pneumonia in an Intensive Care Unit

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A prospective cohort study was performed to determine the prolongation of stay and the extra costs incurred due to the occurrence of ventilator-associated pneumonia in intensive care unit patients. Over a 16-month period a sample of 270 consecutive adult patients from a large university anesthesiological intensive care unit requiring ventilation therapy for more than 24 hours was analyzed. A matching procedure using multiple control patients without pneumonia per infected patient (= case) was employed. Of 78 cases 21 (26.9 %) died and were excluded from the matching procedure as well as 23 (29.5 %) for whom suitable controls could not be found. The maximum number of controls per case was five. The mean added stay was calculated to be 10.13 days and the extra costs attributable to the prolongation of stay were 14,253 German Marks (US$ 8,800) per patient, demonstrating considerable added stay and costs due to ventilator-associated pneumonia acquired during intensive care. However, it should be taken into account that the calculations for excess stay and costs are based on a subset of rather ill patients and thus cannot generally apply to all ventilated patients and that cases were excluded which could not be matched.

Nosocomial infections are an important medical problem, one consequence of which is prolonged and often severe morbidity with an increased hospital stay. Nosocomial pneumonia is the third most common infection acquired in hospitals and contributes considerably to the additional hospital stay and costs, thereby representing an important economic factor (1). This is especially true in the case of ventilator-associated pneumonia since the risk of acquiring pneumonia during ventilation is substantially higher than in other patient populations (2).

There are many studies emphasizing the influence of nosocomial infections on the duration of hospitalization and the resulting costs (1, 3–14). However, the methods used to estimate the extra stay vary considerably. In some studies the results were obtained by the physicians' estimate method whereby an independent physician-epidemiologist, who was not involved in infection surveillance or treatment of the patients, reviewed the medical records and other relevant clinical information and judged whether the continued hospital stay should be attributed to nosocomial infection. The results of this usually retrospective method depend largely upon the subjective assessment of the physician leading to an underestimation of the extra hospital stay (5–7, 12). Another method is the direct comparison of the total hospital stay of all infected and non-infected patients (6, 11). This procedure results in an overestimation of the added hospitalization because it does not consider the duration of stay of the infected patient prior to the onset of nosocomial infection. Furthermore, the risk factors for nosocomial infections frequently also predispose to a longer hospital stay, which leads to groups not being directly comparable.

To reduce the effects of potential confounding factors such as underlying diseases or age it is necessary to match infected patients with similar control patients who did not experience a nosocomial infection during hospitalization and who had the same chance as the infected patients of developing pneumonia, i.e. their average hospital stay was at least as long as the hospital stay prior to onset of nosocomial infection in the infected patient.

To the best of our knowledge there are no data in the literature on the effect of nosocomial pneu-

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monia on the length of hospitalization in the high-risk group of ventilated intensive care unit (ICU) patients. Compared to previous studies, we used a methodologically improved matching procedure with a variable number of multiple control subjects for each of the infected patients, considering the time spent in the ICU prior to onset of infection as a matching criterion. In addition, to avoid the influence of potential confounding factors such as underlying and concomitant diseases, we focused on a special patient population according to predefined inclusion criteria, resulting in a study group which was as homogeneous as possible.

Patients and Methods

Patients. From June 1988 to September 1989, 270 consecutive ventilated patients from a typical large university hospital anesthesiological ICU were prospectively included in the study. Patients were selected using the following criteria: 1) duration of ventilation more than 24 hours, and 2) one of the following underlying conditions as the reason for ventilation therapy: severe head injury, polytrauma, chronic lung disease, heart failure.

All 270 patients, i.e. the patients who subsequently developed pneumonia (= cases) *and* those who did not (= controls), were monitored daily from the day of admission to the ICU until discharge from the ICU to another ward or until death, by a physician who was not involved in the treatment of the patients. The following dates were recorded: time of admission to the ICU, time of onset of pneumonia, and time of discharge from the ICU or time of death, respectively.

The diagnosis of pneumonia was based upon the broadly accepted definitions for nosocomial infections of the Centers for Disease Control (15). Accordingly, the diagnosis had to fulfill one of the following criteria:

1. rales or dullness to percussion on physical examination of the chest *and* any of the following: a) new onset of production of purulent sputum or a change in the character of sputum, b) isolation of an organism from blood cultures, c) isolation of a pathogen from the specimen obtained by bronchoalveolar lavage, bronchial brushing or biopsy;
2. chest radiograph showing new or progressive infiltrate, consolidation, cavitation or pleural effusion *and* any of the following: a)–c) as above, d) isolation of a virus or detection of viral antigen in respiratory secretions, e) a diagnostic single antibody titer (IgM) or fourfold increase in paired serum samples (IgG) for a pathogen, f) histopathologic evidence of pneumonia.

Methods. To estimate the extra costs incurred due to ventilator-associated pneumonia, the prolongation of ICU stay was determined using a matching procedure with a variable number of multiple corresponding control patients who did not acquire pneumonia for each of the infected patients (= cases) (16, 17). Each case was matched to one or more control subjects on the basis of four variables considered to be potential confounding factors as follows: 1) case and controls had to have the same underlying condition as the reason for ventilation therapy; 2) age of the case and controls had to be matched within ten years to consider the potential effect of age; 3) control patients had to be ventilated at least as long as the case prior to the onset of pneumonia since the duration of ventilation therapy both indicates the severity of illness and constitutes a risk factor for the development of pneumonia; 4) the time the control patients were subjected to the risk of acquiring nosocomial infections generally, i.e. the duration of ICU stay, had to be at least as long as the time spent by the infected patient in the ICU until onset of pneumonia.

Patients who died were excluded from the analysis. It is still a methodologically unresolved problem as to how to consider death since it does not seem appropriate to use the time of death as the time of discharge thereby putting patients who died in the same category as discharged patients, although this has been done in other studies (3, 7). Assuming nosocomial infection increases the risk of mortality and death occurs shortly after the onset of nosocomial infection, it can be concluded that nosocomial infections shorten the duration of hospital stay. The duration of excess hospital stay would thus be underestimated.

To utilize the pool of appropriate controls as far as possible, a matching procedure with a variable number of multiple control patients per infected patient was employed. First, a pool of suitable comparison subjects was established according to the aforementioned matching criteria for the "most difficult" case, i.e. the case hardest to find a match for because of relatively late onset of pneumonia. Subsequently, the patient with the least difference in age was selected as control from the pool of possible control subjects and the remaining controls were returned to the pool. For a case which remained without control in this first matching procedure the added length of stay could not be determined. The procedure was repeated ten times so that up to ten controls could have been assigned to each case. The procedure was carried out automatically by means of a computer programme written in SAS (Statistical Analysis System) by one of the authors (G.S.). The added duration of stay was calculated by subtracting the mean duration of stay of all controls for a given case from the duration of stay of that case. The additional costs were calculated by multiplying the average number of extra days of all cases by the ICU rate of 1,407 German Marks (US$ 869) per day at the University Hospital of Freiburg because using more accurate estimations of itemized costs is very difficult to perform.

Results

Overall, 270 consecutive patients were included in the study. The mean age and standard deviation (SD) was 44.0 ± 21.9 years; 196 (72.6 %) patients were male, 74 (27.4 %) were female. Ventilation support was necessary in 130 (48.2 %) patients because of severe head injury, in 81 (30.0 %) because of polytrauma, in 37 (13.7 %)

because of chronic lung disease, and in 22 (8.1 %) because of heart failure. Seventy-eight (28.9 %) patients acquired pneumonia and 45 (16.7 %) patients died during their ICU stay. The mortality rate in the group of patients with pneumonia was 26.9 % (n = 21) and in the control group 12.5 % (n = 24). The higher mortality rate in the group of patients with pneumonia is probably due to this infectious complication, but it is also possible that this difference occurred by chance. As expected, pneumonia rates were highest in trauma patients: 33.8 % (n = 44) in patients with severe head injury and 29.6 % (n = 24) in the polytrauma group. Of 37 patients with chronic lung disease, 2 (5.4 %) developed pneumonia; no patient with chronic heart failure acquired pneumonia.

For the matching analysis, 21 of the 78 patients (cases) had to be excluded because of death. Twenty-three of the remaining 57 cases could not be matched to control subjects. The remaining 34 cases entered the matching process. Twenty-four of the 192 patients without pneumonia died and were therefore excluded from the analysis. Of the remaining 168 uninfected patients, 69 control patients were selected. The maximum number of controls for each infected patient was five.

Table 1 shows the mean and median added stay in the ICU for the patients with pneumonia. The mean added stay for all cases included in the analysis was calculated to be 10.13 days. When we compared cases with appropriate controls with the cases who had to be excluded from the analysis because a suitable control subject could not be identified, it was found that cases without controls had a relatively late onset of pneumonia, were ventilated longer and were on average ten years older (data not shown).

Table 2: Extra costs due to the added hospital stay in ICU of patients with ventilator-associated pneumonia.

Underlying disease	Mean added stay (days)	Extra costs[a] (German Marks)
Polytrauma	15.61	21,963 (US$ 13,558)
Severe head injury	6.24	8,780 (US$ 5,420)
All patients[b]	10.13	14,253 (US$ 8,880)

[a] Costs per ICU day: 1,407 German Marks (US$ 869)
[b] Including the two patients with chronic lung disease.

Table 2 shows the additional costs associated with pneumonia due to the added stay according to the underlying diseases. Costs were calculated for the trauma patients only because the number of patients with chronic lung disease developing pneumonia was too small for analysis.

Discussion

Many studies stress the importance of nosocomial infections regarding the duration of hospital stay and the costs involved (1, 3–14). However, the various methods used in the literature to estimate the prolongation of hospital stay due to nosocomial infections in various patient groups lead to considerably varying results. In our study a matching procedure with a variable number of multiple control patients per infected patient was employed and, furthermore, since we considered the time of onset of pneumonia, an overestimation of the added length of stay should have been avoided.

Table 1: Estimated mean and median added stay in patients with ventilator-associated pneumonia according to the underlying disease.

	Number of patients[a]	Added ICU stay (days)
Statistical parameter		
Mean ± SD	34	10.13 ± 21.5
Median (quartile)[b]		5.5 (1.5, 12.4)
Underlying disease		
Polytrauma	12	15.61 ± 26.1
Severe head injury	20	6.24 ± 6.3
Chronic lung disease	2	16.20 ± 79.5

[a] Patients included in the matching analysis.
[b] 25 % and 75 % quartile.

There are several studies on the influence of pneumonia on the duration of hospital stay. The added length of hospitalization varied between 5 and 13 days (3, 4, 7, 14). The matching criteria employed in these studies, however, were different, most studies considering only the discharge diagnosis, type of surgical procedure and age, but no further risk factors. A matching procedure comparable with ours was used in only one study (14). The added length of stay in that study was 9.2 days. However, to the best of our knowledge there is no study on the influence of pneumonia on the duration of hospital stay in ventilated ICU patients.

The greatest methodological problem in most studies using a matching procedure is the limited number of patients remaining for statistical analysis. In our study only 34 (43.6 %) of 78 ventilated patients with pneumonia were entered in the matching analysis. Although the number of cases available was limited, the validity of our results is improved by the higher number of control patients (up to five) per case while other investigators used two controls at most (3).

One criticism of matching procedures is the potential confounding of the results by the exclusion of cases which could not be matched with appropriate controls with the possibility of selection bias (18). In our study 23 (29.5 %) patients with pneumonia had to be excluded because of a lack of suitable control patients. However, cases excluded seemed to be the more severely ill patients. Therefore, one can assume that exclusion of these cases from the final analysis resulted in an underestimation rather than an overestimation of the extra stay duration. A similar problem is the exclusion of patients with a fatal outcome, in our study 21 (26.9 %) patients.

In conclusion, it could be confirmed in our study that considerable extra costs (on average 14,253 German Marks (US$ 8,800) per patient) are incurred due to prolongation of ICU stay (+ 10.1 days) as a result of ventilator-associated pneumonia. However, it should be taken into account that our calculations for the excess stay and costs are based on data of a subset of rather ill patients and cannot be generally applied to all ventilated patients.

There is sufficient evidence in the literature demonstrating that the costs necessary for infection control are by far outweighed by the cost-saving resulting from a reduction in the rate of nosocomial infections (1, 8, 19, 20). It is a well known fact that a substantial proportion of all nosocomial infections (up to 70 %), constituting an irreducible minimum, cannot be prevented even with optimal hygienic measures (1). However, to keep the rate of such infections as low as possible, established infection control measures must be strictly adhered to (19).

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