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Non-invasive mechanical ventilation in severe chronic obstructive lung disease and acute respiratory failure: short- and long-term prognosis

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Abstract *Objective:* To evaluate the short- and long-term prognosis of patients with chronic obstructive lung disease (COLD) who had non-invasive mechanical ventilation (NMV) for acute respiratory failure (ARF).
Design: Retrospective study.
Setting: Two respiratory intermediate intensive care units.
Patients: Two groups of patients suffering from COLD and an ARF episode requiring mechanical ventilation. Group 1 (30 patients) was given NMV using face masks (aged 64 ± 9 years; pH $= 7.28 \pm 0.05$; $PaCO_2 = 83 \pm 18$ mmHg; $PaO_2/FIO_2 = 141 \pm 61$). Group 2 (27 patients) was composed of control patients (aged $= 65 \pm 8$ years; pH $= 7.26 \pm 0.05$; $PaCO_2 = 75 \pm 17$ mmHg; $PaO_2/FIO_2 = 167 \pm 41$) given MV using endotracheal intubation (EI) when clinical and functional conditions had further deteriorated because the medical therapy failed and NMV was not available at the time. Causes of ARF were in group 1 and 2 respectively: pneumonia in 8 (27%) and 11 (41%), acute exacerbation of COLD in 19 (63%) and 14 (52%) and pulmonary embolism in 3 (10%) and 2 (7%) patients.
Measurements and results: Success rate, mortality during stay in ICU (at 3 months and at 1 year), and the need for rehospitalization during the year following ARF were measured in this study. Group 1 showed a success rate of 74%, only 8/30 patients needing EI and conventional MV. In group 2, the weaning success was 74% (20/27 patients). The mortality for group 1 was 20% in IICU, 23% at 3 months and 30% at 1 year; and 26% for group 2 in ICU, 48% at 3 months and 63% at 1 year. Within each group 1-year mortality was greater ($p < 0.01$) in patients with pneumonia. The number of new ICU admissions during the follow-up at 1 year was 0.12 versus 0.30 in groups 1 and 2 respectively ($p < 0.05$).
Conclusion: For patients suffering from COLD who have undergone ARF, avoiding EI by early treatment with NMV is associated with better survival in comparison to patients bound to invasive MV. Pneumonia as a cause of ARF may worsen the prognosis in both groups of patients.

Key words COPD · Mask ventilation · Pneumonia · Endotracheal intubation · Intermediate intensive care unit · Positive pressure ventilation

Introduction

Acute respiratory failure (ARF) is a common and frequently fatal complication in patients with chronic obstructive lung disease (COLD) often requiring mechanical ventilation (MV) [1]. The immediate recovery rate varies from about 60% to more than 90% [2–18], and the long-term survival is quite low [7, 9, 15]. Correlates of short- and long-term outcome remain unclear. The age of the patient, the severity of COLD before the acute episode, and the duration of ventilator assistance may affect the outcome of these patients [7]. Among the causes of ARF in these patients, pneumonia generally worsens the outcome [3–5, 18, 19]. MV through endotracheal intubation (EI) or tracheostomy is associated with several complications, and there is an increasing incidence of ventilator-associated pneumonia [6, 20]. The recent development of non-invasive methods of ventilation has led to an effort to avoid the complications of invasive MV during episodes of ARF and, at the same time, to ensure a similar degree of efficacy [21–25].

Corrado et al. [26] suggested that the long-term survival of COLD patients with ARF who were non-invasively ventilated with intermittent negative pressure ventilation by means of an iron lung was better than that reported in the literature for invasively ventilated patients. To our knowledge, no data have yet been published on the long-term outcome in non-invasive mechanical ventilation (NMV) delivered with positive pressure by face or nasal mask. The need for studies comparing NMV and MV via EI has recently been advocated by Tobin [27]. Therefore, the aims of this study were: first, to determine the short- and long-term (1 year) prognosis of COLD patients with ARF treated by early NMV, and second, to compare this prognosis with that of patients in whom EI was necessary because of further deterioration in spite of medical therapy, when NMV was not available.

Methods

Patients

We retrospectively studied 57 COLD patients, as defined according to ATS criteria [28], with chronic respiratory insufficiency and who had been treated in our institutions. The two departments (Montescano and Gussago) are both part of the same Research Institution (Clinica del Lavoro Foundation, Pavia). Doctors and nurses work interchangeably in both hospitals, and the medical guidelines are common to both; therefore, treatment was identical for the entire patient population.

The patients under study were all hypoxemic, hypercapnic and on long-term oxygen therapy. Each had undergone exacerbations of the disease and required MV. MV was instituted when patients showed rapid deterioration in neurological status (Glasgow Coma Scale < 9) [29], acute onset of severe hypercapnia ($PaCO_2 > 65$ mmHg), acute decrease in pH (< 7.34), tachypnoea, and/or abdominal paradox.

Patients were divided into two groups according to the non-invasive MV (group 1: 30 patients; 21 male; ages 64 ± 9 years) or invasive MV (group 2: 27 patients; 18 male; ages 65 ± 8 years) approach.

Patients in group 1 were admitted to our intermediate intensive care units (IICUs) where they were submitted to NMV with either pressure support (NPSV: 18 patients) or intermittent positive pressure ventilation in assist/control mode (NIPPV: 12 patients) by means of a face mask (Crystalcone, Harol, UK) as previously described [24]. NMV was considered successful when patients reached levels of $pH > 7.35$ in spontaneous breathing without further worsening in neurological signs and with improvement in signs of respiratory muscle distress [30] for at least 48 h. Unsuccessful therapy was defined as either the need of EI according to the judgment of the physicians in charge or the occurrence of death during NMV.

Group 2 was composed of control patients who had undergone EI and conventional MV. These patients were chosen from those who, in the 2 years preceding the IICU institution in our hospitals, had been treated with standard medical therapy because NMV was not available at the time. In spite of medical therapy, the clinical and physiological status of these patients worsened (inability to maintain a $pH > 7.26$ on oxygen therapy able to obtain a $SaO_2 > 90\%$ [31]), and they were transferred to an ICU functionally linked to our institutions and mechanically ventilated through EI. In both groups, MV was added to standard i.v. medical therapy (aminophylline, steroids, B_2 agonists, antibiotics when required) and O_2 therapy.

Patients with coexisting medical conditions such as uncontrolled coronary heart disease, malignancies, any other condition that might influence long-term prognosis, or patients who were enclosed in a home mechanical ventilation program during the year following the ARF episode were excluded.

Measurements

We reviewed the following clinical and functional data at the beginning of the acute episode requiring MV: success rate and duration of MV, ICU and intrahospital deaths, 3 and 12 month follow-up for survival and hospitalization needs (ICU and respiratory departments, respectively). The last data of spirometry and blood gas analysis were available before ARF episodes were recorded when the patients were in stable state. The first data of lung function were also recorded in a clinically stable state after the ARF episode. Clinical stability was defined as stable hemodynamics, no change in medical and oxygen therapy, and no history of exacerbation in the 3 weeks previous to the measurement.

Dynamic lung volumes were evaluated by means of a water spirometer (Biomedin, Padova, Italy) with the patient in a sitting position. The predicted values were based on Quanjer [32]. An automated analyzer (Radiometer ABL 500, Copenhagen, Denmark) was used to measure arterial blood gases (ABG) from radial artery.

The causes of exacerbations were recorded in the hospital registers and defined for this study as follows. First pneumonia, as defined by the presence of lung infiltrates on chest radiography, combined with any three from the list of fever, positive blood cultures, leukocytosis, or potential pathogenic bacterial cultures from sputa. The second was exacerbation of COLD: excessive dyspnoea and/or bronchial hypersecretion associated with no obvious cause for respiratory deterioration (in particular, absence of lung

Table 1 Last functional stable-state characteristics before exacerbation

	pH	PaO_2/FIO_2	$PaCO_2$ (mmHg)	FVC (% pred)	FEV1 (% pred)
Group 1 ($n = 30$)	7.36 ± 0.02	233 ± 75	55 ± 4	36 ± 19	25 ± 14
Group 2 ($n = 27$)	7.39 ± 0.04	290 ± 67	51 ± 14	45 ± 19	27 ± 12

infiltrates on chest radiography). The third cause of exacerbation was pulmonary embolism when confirmed by perfusion lung scan. Information on hospitalization and survival were obtained by interviews with caregivers or with ICU physicians during hospital visits to our outpatient division.

Statistical analysis

Baseline data of the two groups were compared using an unpaired *t*-test. To evaluate the main factors influencing survival, the patients were divided according to ventilation modalities (invasive vs non-invasive) and presence of pneumonia. All patients were compared for success rate using: a χ^2 Fisher test to assess different mortality between the two groups, and a survival-stratified analysis divided all patients for the presence or absence of pneumonia. The rate of survivors across groups with presence and absence of lung infiltrates was calculated. The contribution of each stratum was first calculated and then combined to form the overall test statistic. A *p*-value < 0.05 was considered statistically significant.

Results

The last stable-state functional characteristics before the ARF episode of all patients under study are shown in Table 1. There were no significant differences between the two groups with respect to severity of the underlying disease. The causes of ARF requiring MV were acute exacerbations of COLD without signs of lung infiltrates: 19 (63%) and 14 (52%) in groups 1 and 2, respectively; pneumonia: 8 (27%) and 11 (41%); pulmonary embolism: 3 (10%) and 2 (7%). These differences were not significant.

The functional characteristics of the two groups at the beginning of the acute episode are shown in Table 2. At the moment of EI, 50–65 min after ARF, the ABGs of patients in group 2 had further deteriorated as assessed by a mean pH of 7.23 ± 0.06 and a mean $PaCO_2$ of 92 ± 15 mmHg.

Success and survival

Patients in group 1 showed a success rate of 74% (22/30), [62% (5/8) with pneumonia and 77% (17/22) without lung infiltrates] avoiding EI and conventional

Table 2 Baseline anthropometric and functional characteristics

	Baseline		
	Group 1 ($n = 30$)	*P*	Group 2 ($n = 27$)
Age	64 ± 9	NS	65 ± 8
pH	7.28 ± 0.05	NS	7.26 ± 0.05
$PaCO_2$ (mmHg)	83 ± 18	NS	75 ± 17
PaO_2/FIO_2	141 ± 61	NS	167 ± 41
Respiratory rate (act/min)	33 ± 8	NS	32 ± 6

MV. The duration of NMV in group 1 was 2.6 ± 2 days (range: 4–11 days) in comparison to MV performed with EI, which lasted 19 ± 10 days (range: 2–84 days). Patients in group 1 remained in our ICUs for 10 ± 8 days; patients in group 2 remained in the ICU for 24 ± 12 days. The actuarial survival curves of the two groups are shown in Fig. 1. The IICU and ICU death rate was 20% (6 patients) and 26% (7 patients) for groups 1 and 2, respectively. Of the eight patients in group 1 in whom NMV had failed, two patients with pulmonary embolism died during NMV, four died after EI and MV (three due to MOFS, one due to sepsis), and two were successfully weaned from MV (one with a long-term tracheostomy) and were alive after a 1-year follow-up. One was not weaned and was discharged with home nocturnal MV by tracheostomy. Tracheostomy was performed in 6% of the patients in group 1.

All patients in group 2 surviving to ICU (20/27 patients: 74%) were successfully weaned [5 (18.5%) with long-term tracheostomy]. In all cases, tracheostomy had been performed due to prolonged EI, none being removed. Four patients in group 2 died in the ICU due to MOFs, two patients died due to pulmonary embolism and one patient died of sepsis.

Three months after ARF, 7 patients (23%) in group 1 and 14 patients (48%) in group 2 had died; after 12 months, the percentage of death was 30% (9 patients) and 63% (18 patients) in groups 1 and 2, respectively (Fig. 1). The differences in mortality in ICU or IICU

($P < 0.03$), at 3 months ($P < 0.03$) and for the overall follow-up period were found to be statistically significant ($P < 0.005$). Causes of death in the follow-up were as follows: nine MOFs (one in group 1 and eight in group 2), two sudden deaths (in group 2), one ARF due to tracheostomy cannula obstruction (in group 2), one gastrointestinal bleeding (in group 1) and one acute heart failure (in group 1).

Comparison of lung function tests between the stable state before ARF and after the ARF episode was available for 16/24 survivors in group 1 and in 19/20 survivors in group 2. A decrease of $> 20\%$ in FEV_1 when compared to pre-ARF was observed in 12/19 (63%) in patients of group 2, but only in 1/16 (6%) patients in group 1.

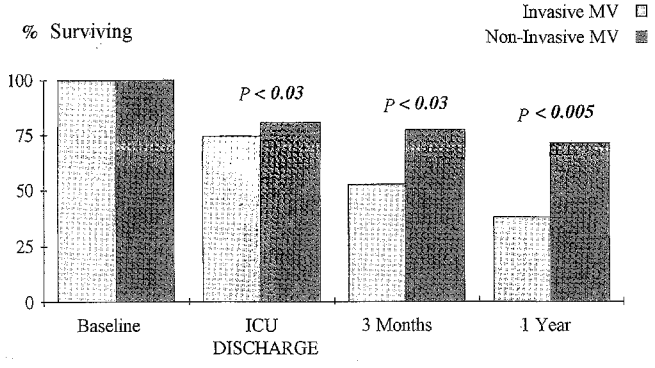


Fig. 1 Survival of patients according to modality of ventilation

Readmissions

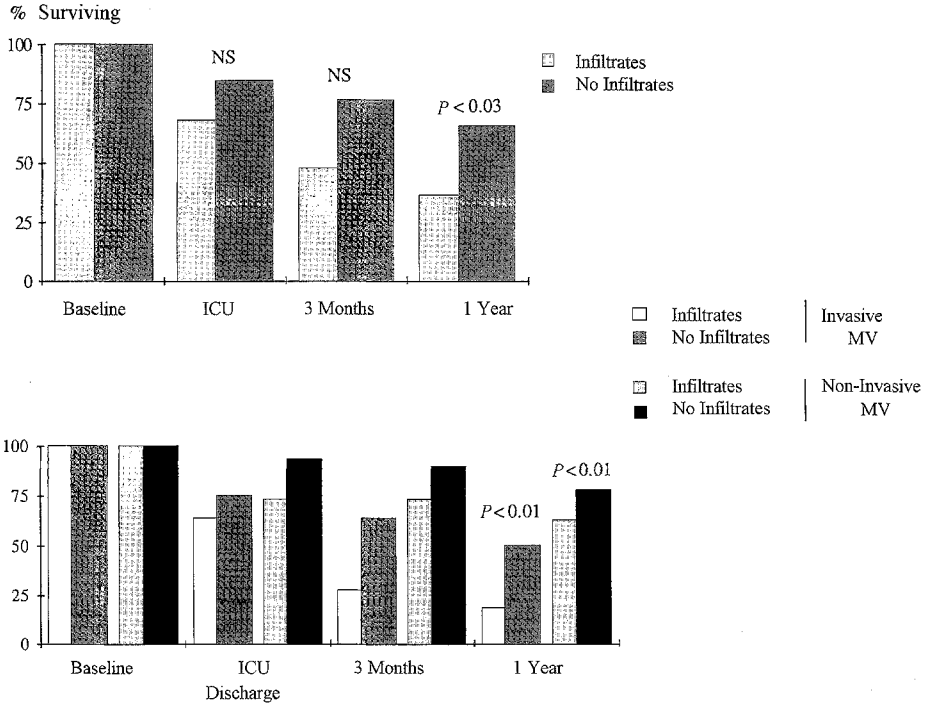
The number of post-discharge admissions into ICU following mechanical ventilation during the same follow-up period was 3 out of the 24 (0.12 patient/year) survivors in group 1 and 6 out of the 20 (0.30 patient/year) survivors of group 2 ($P < 0.05$). The number of patients requiring admission to a respiratory department for acute exacerbations was 26 (1.08 patient/year) and 21 (1.05 patient/year), respectively (NS).

Lung infiltrates

Pneumonia as a cause of ARF was found in 19 out of 57 (33%) patients. No significant difference was found in either ICU admissions or in the 3-month mortality of all patients with or without pneumonia, but the overall 1-year mortality was greater ($P < 0.03$) in patients showing lung infiltrates (Fig. 2, top).

A total of 22 patients in group 1 without pneumonia showed a significantly greater 1-year survival in comparison to 16 patients in group 2 without lung infiltrates ($P < 0.01$) (Fig. 2, bottom). Eight patients in group 1 with pneumonia showed a significantly greater 1-year survival in comparison to 11 patients in group 2 with pneumonia ($P < 0.01$) (Fig. 2, bottom).

Fig. 2 Effect of lung infiltrates on survival in all patients in study (*top*) and according to modality of ventilation (*bottom*)



Discussion

This retrospective study has shown that in comparison to COLD patients given EI and invasive MV for ARF, patients avoiding severe deterioration in acidosis and EI by means of NMV have less immediate, short- (3 months), long-term (12 months) mortality rates. Pneumonia as a cause of ARF seems to worsen the outcome of both groups.

The severity of functional impairment of our COLD patients was evaluated in this study from the last stable-state lung function tests performed before ARF. The parameters recorded showed that the two groups were comparable in both incidences of severe airway obstruction and ABG showing that the patients in both groups were chronically hypoxemic and hypercapnic.

Our patients undergoing NMV showed a success rate (excluding death and EI) of 74%. This confirms results from previous studies [21–25, 33, 34]. A review of the literature from 1989 to 1993 shows that NMV in ARF episodes of COLD was 60–87% successful, the severity of ARF as assessed by $PaCO_2$ and pH being widely different among the different populations under study [21–25, 33, 34].

Our patients undergoing EI and MV showed a weaning success of 74%, a value similar to that reported by Menzies et al. [7]. Weaning success in COLD patients requiring MV for more than 21 days is reported to be 55% [35]. However, a comparison of these studies is difficult due to differences in disease severity, time and MV modalities.

The duration of NMV was less than MV through EI. Our data confirm those of Brochard et al. [21] who tested the usefulness of NPSV via a face mask to improve the course of acute exacerbations of COLD in a group of patients when compared with controls who had undergone EI. The need for ventilatory assistance was 3 ± 1 and 12 ± 11 days for the group treated with the non-invasive approach and EI, respectively. Patients in their study remained in the ICU for 7 ± 3 vs 19 ± 12 days for NMV and EI, respectively. Fernandez et al. [23] showed an ICU stay of 5 ± 2 days versus 17.3 ± 8.4 days for NPPV and EI, respectively.

The ICU mortality for COLD patients on MV has been reported to be from 22% to 54%. Data on IICU mortality of our study confirm other studies on NMV (21–25, 33, 34).

Fernandez et al. [23] showed a 6-month mortality of 8.3% in COLD patients. To our knowledge, the present study is the first to evaluate 1-year survival of COLD patients submitted to NMV by face mask for ARF. Our patients showed a 1-year mortality of 30% in comparison to 63% of our controls in group 2. The worse long-term prognosis in this selected population for whom standard medical therapy failed only suggests that performing NMV at an early stage of acute exacerbation may avoid worsening of ARF with the subsequent need of EI. What role avoiding a more severe ABG plays in the greater survival at 1 year in group 1, and what is to be ascribed to avoiding invasive MV and related complications, remains to be elucidated. It is noteworthy, however, that acidosis shown by the patients in group 2 at the moment of EI were not more severe than usual for patients who are commonly intubated in the ICU, and no more than 1 hour lapsed between the beginning of the episode and the need for EI. Furthermore, the patients in our study were comparable with regard to age, $PaCO_2$ and PaO_2/FIO_2 at the beginning of the acute episode. The patients were comparable also with regard to the severity of their underlying respiratory disease as assessed by similar values of FEV_1 measured in a stable state before ARF.

A decrease in $FEV_1 > 20\%$ in comparison to pre ARF was observed in 63% of the patients in group 2, but only in 25% of the patients of group 1. Thus, the hypothesis that conventional mechanical ventilation might produce some degree of lung injury increasing the progression of lung function deterioration may be possible. An alternative speculative explanation may be the possible avoidance of MV in patients with a previous EI. This was not confirmed in this study. In group 1, one-third (33%) of the patients and in group 2, 4/11 (36%) of the patients had died at 1-year.

Corrado et al. [26] showed that the in-hospital mortality of their patients treated by means of an iron lung was 11% and the hospital stay was 11.7 ± 7.5 days. A total of 84% of the patients had relapses ARF during the following 5 years; the overall survival rate during the first year was 82%. Their patients showed a mean stable FEV_1 of $30 \pm 11\%$ of the predicted rate, our patients a mean stable FEV_1 of $25 \pm 14\%$ of the predicted rate. Patients of Corrado et al. [26] made monthly visits to the hospital while our patients were sometimes followed up as outpatients. This fact, rather than the difference in modality of ventilation (mask ventilation vs iron lung) might explain the better 1-year survival of Corrado's patients, underlying the usefulness of a regular program of ambulatory control.

ARF causes were not different between the two groups and the better survival rate cannot be ascribed. Furthermore, 1-year mortality between the two groups was still significantly different when patients were divided according to the presence of lung infiltrates as the cause of ARF (Fig. 2).

The most common conditions leading to ARF in COLD are generally associated with some evidence of bronchial and sometimes parenchymal infection. The other most common causes are pulmonary embolism, a particularly difficult diagnosis in these patients, and left ventricular failure [36]. In our patients, the causes of ARF were considered to be pneumonia, acute exacerbations of COLD and pulmonary embolism. In a recent study, Rieves et al. [5] found pneumonia to be the cause of ARF in 42% of COLD patients undergoing EI. ARF was due to exacerbations (55%) and bronchopneumonia (40%) in COLD patients treated by Corrado et al. [26]. Nosocomial pneumonia is the second-most frequent cause of hospital-acquired infections, accounting for 15–18% of all nosocomial infections [37, 38]. COLD patients are at great risk of developing nosocomial pneumonia and ventilator-associated pneumonia [19]. The occurrence of nosocomial pneumonia requiring admission to an ICU is associated with an increased risk of fatalities [39–41].

In our study, the overall 1-year mortality was greater in patients with pneumonia in both groups, but the reasons for this are not clear. Pneumonia might have influenced the outcome; alternatively, it might have been the effect of a more severe underlying condition. In comparison with patients without pneumonia these patients showed a lower body weight (54 $\pm$ 11 vs 63 $\pm$ 18 kg), a greater long-term use of steroids (68% vs 45% of patients) and more new hospital admissions during the follow-up (90% vs 75% of patients).

Limitations of the study

Historical comparison of two different patient populations must be interpreted with caution. Owing to ethical considerations, it is difficult to propose a prospective randomized controlled study of NMV versus EI. The non-invasive approach should be initiated at an early stage of the disease more as a preventive measure to avoid EI rather than as a safe and certain means of delivering full ventilatory support [42]. For this reason, it could appear difficult to compare ICU mortality and follow-up in two different groups of patients who experienced EI or who did not. The historical group was treated within a period of time close to that of the NMV group, and we are quite confident that medical therapy was not at all different.

The retrospective analysis of data may be criticized, as it prevents further collection of information especially regarding the circumstances of the follow-up (e.g., readmission, ICU, functional deterioration data that are not available for all patients). Nevertheless, a retrospective study gives information on a "real" setting of operations in a IICU.

In conclusion, our study shows that patients with chronic obstructive lung disease who have undergone early non-invasive mechanical ventilation for acute respiratory failure, thereby avoiding endotracheal intubation, have a better survival in comparison to patients bound to endotracheal intubation because of further clinical deterioration. Pneumonia as a cause of ARF may worsen the prognosis in both groups of patients.

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References

1. Derenne JP, Fleury B, Pariente R (1988) Acute respiratory failure of chronic obstructive pulmonary disease. Am Rev Respir Dis 138: 1006–1033
2. Gracey DR, Naessens JM, Krishan I, Marsh HM (1992) Hospital and post hospital survival in patients mechanically ventilated for more than 29 days. Chest 101: 211–214
3. Stauffer JL, Fayter N, Graves B, Cromb M, Lynch JC, Goebel P (1993) Survival following mechanical ventilation for acute respiratory failure in adult men. Chest 104: 1222–1229
4. Swinburne AJ, Fedullo AJ, Bixby K, Lee DK, Wahl GW (1993) Respiratory failure in the elderly. Analysis of outcome after treatment with mechanical ventilation. Arch Intern Med 153: 1657–1662
5. Rieves RD, Bass D, Carter RR, Griffith JE, Norman JR (1993) Severe COPD and acute respiratory failure. Correlates for survival at the time of tracheal intubation. Chest 104: 854–860
6. Rello J, Ausina V, Ricart M, Castella J, Prats G (1993) Impact of previous antimicrobial therapy on the etiology and outcome of ventilator-associated pneumonia. Chest 104: 1230–1235
7. Menzies R, Gibbons W, Goldberg P (1989) Determinants of weaning and survival among patients with COLD who require MV for acute respiratory failure. Chest 95: 398–405
8. Warren PM, Flenley DC, Millar JS, Avery A (1980) Respiratory failure revisited: acute exacerbations of chronic bronchitis between 1961–1968 and 1970–1976. Lancet I: 467–471
9. Gillepsie DJ, Marsh HMM, Divertie MB, Meadows JA (1986) Clinical outcome of respiratory failure in patients requiring prolonged (> 24 hours) mechanical ventilation. Chest 90: 364–369

10. Craven DE, Kunches LM, Kilinsky V, Lichtenberg DA, Make BJ, McCabe WR (1986) Risk factors for pneumonia and fatality in patients receiving continuous mechanical ventilation. Am Rev Respir Dis 133: 792–796
11. Sluiter HJ, Blokzijil EJ, Vandijl W et al (1972) Conservative and respirator treatment of acute respiratory insuficiency in patients with chronic obstructive lung disease. A reappraisal. Am Rev Respir Dis 105: 932–943
12. Hudson LD (1989) Survival data in patients with acute and chronic lung disease requiring mechanical ventilation. Am Rev Respir Dis 140: S19–S24
13. Nunn JF, Milledge JS, Singaraya J (1979) Survival of patients ventilated in an intensive therapy unit. BMJ 1: 1525–1527
14. Spicher JE, White DP (1987) Outcome and function following prolonged mechanical ventilation. Arch Intern Med 147: 421–425
15. Kaelin RM, Assimacopoulos A, Chevrolet JC (1987) Failure to predict six-month survival of patients with COPD requiring mechanical ventilation by analysis of simple indices. A prospective study. Chest 92: 971–978
16. Potgieter PD, Rosenthal E, Benatar SR (1985) Immediate and long-term survival in patients admitted to a respiratory ICU. Crit Care Med 13: 798–802
17. Petheram IS, Branthwaite MA (1980) Mechanical ventilation for pulmonary disease. A six year survey. Anaesthesia 35: 467–473
18. Sukulmachantra Y, Dinakara P, Williams MH (1966) Prognosis of patients with chronic obstructive pulmonary disease after hospitalization for acute ventilatory failure: a 3-year follow-up study. Am Rev Respir Dis 93: 215–222
19. Torres A, Aznar R, Gatell JM et al (1990) Incidence, risk and prognosis factors of nosocomial pneumonia in mechanically ventilated patients. Am Rev Respir Dis 142: 523–528
20. Pingleton S (1988) Complications of acute respiratory failure. Am Rev Respir Dis 137: 1463–1493
21. Brochard L, Isabey D, Piquet J et al (1990) Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. N Engl J Med 323: 1523–1530
22. Meduri GU, Abou-Shala N, Fox RC et al (1991) Non invasive face mask mechanical ventilation in patients with acute hypercapnic respiratory failure. Chest 100: 445–454
23. Fernandez R, Blanch L, Valles J, Baigorri F, Artigas A (1993) Pressure support ventilation via face mask in acute respiratory failure in hypercapnic COLD patients. Intensive Care Med 19: 456–461
24. Vitacca M, Rubini F, Foglio K, Scalvini S, Nava S, Ambrosino N (1993) Non-invasive modalities of positive pressure ventilation improve the outcome of acute exacerbations in COLD patients. Intensive Care Med 19: 450–455
25. Ambrosino N, Nava S, Rubini F (1993) Non invasive mechanical ventilation in the treatment of acute respiratory failure in chronic obstructive pulmonary disease. Monaldi Arch Chest Dis 48: 144–154
26. Corrado A, Bruscoli G, Messori A et al (1992) Iron lung treatment of subjects with COPD in acute respiratory failure. Evaluation of short and long term prognosis. Chest 101: 692–696
27. Tobin MJ (1994) Mechanical ventilation. N Engl J Med 330: 1056–1061
28. American Thoracic Society (1987) Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. Am Rev Respir Dis 136: 225–243
29. Teasdale G (1974) Assessment of coma and impaired consciousness: a practical scale. Lancet *T*: 81–83
30. NHLBI Workshop Summary (1990) Respiratory muscle fatigue: report of the respiratory muscle fatigue workshop group. Am Rev Respir Dis 142: 474–480
31. Jeffrey AA, Warren PM, Flenley DC (1992) Acute hypercapnic respiratory failure in patients with chronic obstructive lung disease: risk factors and use of guidelines for management. Thorax 47: 24–40
32. Quanjer PH (1983) Working party on "standardization of lung function test." Bull Eur Physiopathol Respir 19 [Suppl 5]: 7–10
33. Benhamou D, Girault C, Faure C, Portier F, Muir JF (1992) Nasal mask ventilation in acute respiratory failure. Experience in elderly patients. Chest 102: 912–917
34. Bott J, Carroll MP, Conway JH et al (1993) Randomized controlled trial of nasal ventilation in acute ventilatory failure due to chronic obstructive airways disease. Lancet 341: 1555–1557
35. Nava S, Rubini F, Zanotti E et al (1994) Survival and prediction of successful ventilator weaning in COPD patients requiring mechanical ventilation for more than 21 days. Eur Respir J 7: 1645–1652
36. Bone RC (1981) Acute respiratory failure and chronic obstructive lung disease: recent advances. Med Clin North Am 65: 563–578
37. Centers for Disease Control (1986) Nosocomial infection surveillance, 1984. In surveillance summaries. 35: 17–29
38. Gross PA (1987) Epidemiology of hospital-acquired pneumonia. Semin Respir Infect 2: 2–7
39. Stevens RM, Teres D, Skilman JJ, Feingold DS (1974) Pneumonia in an intensive care unit. Arch Intern Med 134: 106–111
40. Potgieter PD, Hammond JMJ (1992) Etiology and diagnosis of pneumonia requiring MICU admission. Chest 101: 199–203
41. Fagon JY, Chastre J, Hance A, Montravers P, Novara A, Gibert C (1993) Nosocomial pneumonia in ventilated patients: a cohort study evaluating attributable mortality and hospital stay. Am J Med 94: 281–287
42. Brochard L (1993). Non invasive ventilation: practical issues. Intensive Care Med 19: 431–432