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ORIGINAL ARTICLE

Lung and respiratory muscle function at discharge from a respiratory intensive care unit

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ABSTRACT: ***Lung and respiratory muscle function at discharge from a respiratory intensive care unit. M. Vitacca, L. Bianchi, L. Barbano, N. Ambrosino.***

Background. **The purpose of this prospective observational study was to describe lung and respiratory muscle function at Respiratory Intensive Care Unit (RICU) discharge after a severe exacerbation of Chronic Obstructive Pulmonary Disease (COPD).**

Methods. **The study was conducted in 42 consecutive COPD patients in whom arterial blood gases, dynamic and static lung volumes, maximal inspiratory pressure (MIP) were assessed at discharge from the RICU and compared with values measured 6 months previously when they were in a stable state. The same measurements were performed at 6-month interval in 42 comparable stable COPD patients not requiring any hospitalisation for at least 6 months used as controls.**

Results. **24% of patients in the study group were discharged with hypercapnia whereas they were normocapnic before the acute episode. Compared to prior to exacerbation, patients of study group showed a significant worsening in mean values of $PaCO_2$ (p=0.005), MIP (p=0.005) and FEV_1 (p=0.041). Predefined criteria of worsening in $PaCO_2$, MIP and FEV_1 were observed in 47%, 33% and 28% of patients in study respectively. Neither lung nor respiratory muscle function in last stable state did predict post RICU functional worsening. In a period of 6 months controls showed no change in the studied parameters.**

Conclusions. **After a severe acute exacerbation requiring admission to a RICU and immediately before discharge 1) a large proportion of COPD patients still show preserved lung and respiratory muscle function 2) more than one third of them would require further care and rehabilitative attempts to restore functional derangements.** ***Monaldi Arch Chest Dis 2005; 63: 3, 142-148.***

Keywords: Acute exacerbations of COPD, respiratory failure, respiratory muscles, lung function.

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of death, a major medical and an increasing economic problem [1]. Acute exacerbations of COPD requiring hospitalisation are associated with substantial mortality rates [2, 3] which increases further among those patients requiring admission to an Intensive Care Unit (ICU) [4, 5]. Compared to patients who do not need admission to an ICU, these patients suffer from more severe chronic disease with predominantly irreversible airway obstruction when in their stable condition [6], and show a trend towards a progressive increase in $PaCO_2$ in the two years preceding admission [7].

It has been shown recently that frequency of exacerbations contributes to long-term decline in the lung function of patients with moderate to severe COPD [8] and that recovery from a decline of peak expiratory flow rate after a COPD exacerbation may be very slow [9]. Previous admissions to hospital before an acute exacerbation, a low FEV_1 and the under-prescription of Long Term Oxygen Therapy (LTOT) are independently associated with a high risk of admission for COPD exacerbation [10] while a severe underlying lung disease, greater frequency and severity of exacerbations were associated with a greater rate of treatment failure [11]. Criteria to discharge patients from a Respiratory Intensive Care Unit (RICU) following severe episodes of COPD exacerbation are usually based on clinical and arterial blood gases stability; nothing was known about lung and respiratory muscle function immediately before this discharge. Therefore we conducted an observational prospective study to evaluate lung and respiratory muscle function immediately before discharge after a severe exacerbation of COPD leading to admission to a RICU. Furthermore we have evaluated whether any functional measurement in the previous stable state might have predicted such changes.

Methods

The investigative protocol was conducted according to the declaration of Helsinki. Informed consent for personal data treatment for routinary and scientific use was obtained by every patient upon admission into our department. The ethical committee of Fondazione S. Maugeri approved the present study.

Patients

A prospective, observational study was carried out on patients known to be affected with COPD according to the American Thoracic Society (ATS) criteria [2] based on the clinical history, physical examination, chest X-ray and, previous pulmonary function tests. Forty-two consecutive COPD patients whose physiological data in stable state were available, discharged since 1st January 1995 to 1st January 1996, from the RICU of Gussago, Salvatore Maugeri Foundation, were studied. The RICU of Gussago is a unit of a Rehabilitation Institution, which is a referral rehabilitation and chronic care centre for a large geographic area in Northern Italy. Among others, difficult- to wean tracheostomised patients are also admitted to this Institution to undergo a progressive discontinuation of mechanical ventilation programme or to be discharged to a home programme of long-term ventilatory assistance if liberation from the ventilator fails [12]. In addition patients undergoing episodes of acute on chronic respiratory failure are admitted to be treated by non-invasive positive pressure ventilation (NPPV) [13].

Study protocol

Study group. During the exacerbation, patients had been treated either by NPPV (11 patients, 26%), or by invasive mechanical ventilation through tracheotomy, requiring prolonged weaning (23 patients, 55%) or medical therapy alone (8 patients,19%). Criteria for NPPV or invasive mechanical ventilation have been described elsewhere [13, 14]. Upon admission all patients of study group had shown severe Acute Physiology and Chronic Health Evaluation (APACHE) II scores (15±4). Mean RICU stay was 10±5 days in the 11 patients treated with NPPV, 17±5 days in the 23 difficult-to wean tracheostomized patients and 9±5 days in the 8 patients treated only with medical therapy. The 23 patients transferred to our RICU from ICUs of other Hospitals were defined as difficult-to-wean after some weaning attempts failed and tracheostomy was performed. The time elapsed from intubation to tracheostomy ranged from 4 to 11 days. Time from intubation to RICU admission ranged from 10 to 45 days. Weaning modalities were spontaneous breathing trial or decreasing levels of inspiratory pressure support as described elsewhere [12].

All patients ventilated non-invasively underwent pressure support ventilation through a nasal or face mask according to previously described criteria [15]. In these patients, the weaning process consisted of increased periods of discontinuation of NPPV and spontaneous breathing. Patients were considered successfully weaned when they were able to tolerate at least 48 consecutive hours of spontaneous breathing without signs of poor tolerance [12, 15].

Standard medical therapy included: a) antibiotics according to empirical decision of doctors in charge, and then adjusted according to sputum culture, b) i.v. steroids were used for 4±6 days, thereafter, oral administration of 25 mg/die of prednisone with scalar reduction according to symptoms, and final administration of inhaled steroids were prescribed c) inhaled long and short term bronchodilators d) oxygen able to maintain SaO_2 > 92% < 96%.

Admission to a general ICU as first step of care rather than to our RICU was guided by location problems, disease severity, or availability of beds.

Control Group. Among all patients affected with COPD with a comparable functional impairment that attended the out-patient clinics (ambulatory or day hospital patients) we have retrospectively selected 42 patients whose functional data was available for a period of at least 6 months.

Diagnosis of COPD, age, weight, chronic drugs treatment, lung function and arterial blood gases in stable state had to be comparable between the two groups.

In their stable state, all patients of both groups were taking standard medical therapy, including beta2-agonists, ant cholinergic agents and diuretics, if needed. Table 1 shows the anthropometric, demographic and historical clinical characteristics of patients in study and of controls. All the studied patients of both groups were regularly followed by our hospital with ambulatory visits.

Exclusion criteria were: Episodes of acute exacerbations requiring mechanical ventilation either invasive or non-invasive during the six months preceding the study, concomitant neurological diseases, cancer, psychiatric problems, and lack of consensus.

Study trial. Figure 1 shows the study trial. Among the 110 admissions to our RICU during the study period, 83 were due to exacerbations of COPD. 24 out of these 83 patients (29%) had been treated

Table 1. - Anthropometrics, demographics, lung function and clinical characteristics of patients in study and controls

	Study	Controls
N°	42	42
Age, y	64±8	65±8
Weight, Kg	67±18	68±13
Smokers n° (%)	4 (9.5%)	6 (14%)
Ex smokers n° (%)	37 (88%)	34 (80%)
pH	7.39±0.04	7.40±0.03
PaO_2, mmHg	54±10	58±12
$PaCO_2$, mmHg	52±9	48±10
FEV_1, % pred	36±17	36±12
TLC, % pred	161±42	149±46
RV, % pred	180±54	161±45
MIP, cm H_2O	41±20	49±16
LTOT, n, (%)	37 (88)	25(60)
Home mechanical ventilation, n, (%)	6 (14)	5 (12)

Abbreviations: PaO_2 = arterial oxygen tension; $PaCO_2$ = arterial carbon dioxide tension; FEV_1 = forced expiratory volume at first second; TLC = total lung capacity; RV = residual volume; MIP = maximal inspiratory pressure LTOT = long term oxygen therapy.

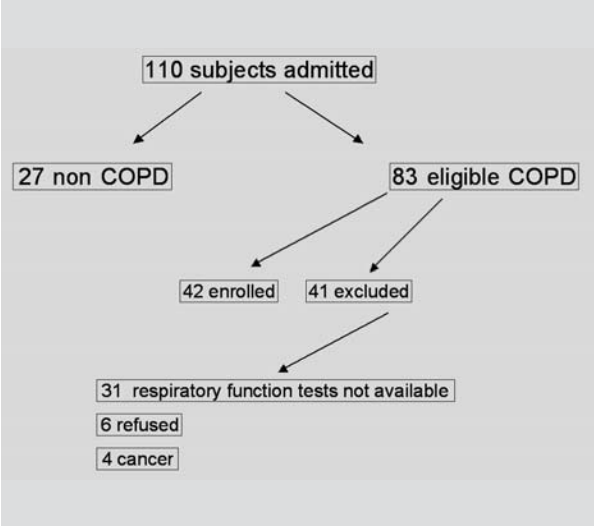

Fig. 1. - Study trial profile.

with NPPV whereas 49 (59%) were tracheostomised difficult-to wean patients and 10 (12%) were treated with medical therapy only. 11 out of these 83 COPD patients (13%) died during RICU stay, therefore 72 COPD patients were discharged alive. 30 out of 72 COPD patients discharged, were excluded from the study due to the following reasons: cancer: 4, lack of consensus: 6, lack of stable state data: 20. 42 patients (11 treated with mask ventilation, 23 difficult- to wean patients and 8 treated with medical therapy only) entered the study.

All patients were discharged from RICU to a rehabilitative ward with the following criteria: all patients were free from their exacerbation without any change in systemic drug therapy for at least 6±3 days (range 3 to 13 days).

They were able to maintain spontaneous breathing for more than 48 consecutive hours without changes in Arterial Blood Gases (ABG) or clinical signs of respiratory distress. NPPV was allowed for patients who used it before admission in RICU.

Measurements

The following parameters were recorded: anthropometrics, previous history of mechanical ventilation (% of either invasive or non-invasive), RICU and Hospital length of stay, location after RICU discharge.

Physiologic measures

Dynamic and static lung volumes were measured by means of a constant volume body plethysmograph (CAD-NET system 1085, Medical Graphic Corp, St. Paul MN USA), according to ERS guidelines [16], the predicted values of Quanjer were used [17].

Arterial blood gases were assessed by means of an automated analyzer (ABL 300 Radiometer, Copenhagen, Denmark) on blood samples drawn from the radial artery while patients breathed room air.

Maximal inspiratory pressure (MIP) was assessed at the level of Functional Residual Capacity (FRC), using a respiratory module system (Medical Graphic Corp, St. Paul MN USA). Patients performed a minimum of three maneuvers with at least a 1-minute interval between efforts until two acceptable values not differing from each other by more than 5% were obtained [18]. The highest value was recorded. Predicted values were according to *Bruschi et al.* [19]. Despite the possibility of underestimating results due to a leakage of air around the cannula and resistance created by the cannula itself, in tracheostomised patients spirometry and respiratory muscle function were evaluated through a mouthpiece with the simultaneous closure of the external hole of a fenestrated and uncuffed cannula.

In study patients available measurement in stable state 5-to 6 months before exacerbation were recorded and compared with measurements performed at discharge from the RICU. In controls, comparisons between measurements performed at the 6 month intervals free from exacerbation, were made. All this retrospective data was performed by the same technician in our department, where the study was carried out.

Statistical analysis

Results are given as mean±SD. All tests and p value are two fold. Parametric variables were analyzed by unpaired or paired t tests as these are appropriate to test the baseline differences between and within groups. ANOVA was used to evaluate differences in the changes overtime between the groups. A post hoc analysis was added when necessary.

The predictive models were developed using stepwise discriminant analysis. Multiple stepwise correlations were performed among all data recorded in stable state to predict post RICU functional worsening. To use the parametric discriminant analysis and correlation tests, the variables found to be non parametric were logarithmically transformed. A p value < 0.05 was considered as statistically significant.

For the purposes of the study a worsening in lung and respiratory muscle function was defined as follows: an increase in $PaCO_2$ and a decrease in PaO_2 greater than 5 mmHg respectively to overcome the level of variability of our blood gases analyzer; a decrease in MIP (cm H_2O) greater than 75^{th} percentile of the whole worsening showed by our patients (> 6.5 cm H_2O); a decrease in FEV_1 (ml) greater than the 75^{th} percentile of the whole worsening showed by patients (> 95 ml). Frequency distributions were analysed with χ^2 test.

Results

Comparison of groups

Table 1 shows anthropometric, demographic and historical clinical characteristics of study patients and controls. The patients in two groups were comparable for age, weight, lung and respiratory muscle function, use of long term oxygen therapy (LTOT) or home mechanical ventilation. Among study patients on domiciliary mechanical

ventilation, 5 patients were ventilated by mask and 1 patient through tracheostomy. All controls on domiciliary mechanical ventilation were ventilated by mask.

Causes of acute respiratory failure

In 23 tracheotomised difficult-to-wean patients the causes of acute hypercapnic respiratory failure were pneumonia in 6, exacerbation of COPD without any other evident cause in 17 patients respectively. In 19 patients treated in our RICU during their exacerbation with standard medical therapy plus NPPV (11 patients) or with medical therapy alone (8 patients), the cause of acute hypercapnic respiratory failure was pneumonia in 5 patients, exacerbation of COPD without pneumonia in 14 cases. Their level of severity upon admission to our RICU as assessed by means of APACHE II score was 15±4. Standard medical therapy included antibiotics (100%), systemic steroids (72% of patients), inhaled bronchodilators (100%), and oxygen (100%).

Independent of modality of delivery, either invasive or non-invasive, duration of mechanical ventilation, was 3 to 49 days. Mechanical ventilation had been withdrawn between 4 and 15 days before discharge and physiological evaluation.

At the moment of evaluation at discharge from RICU, all patients were free from their exacerbation without any change in drug therapy for at least 7±3 days (range 3 to 14 days). In 3 out of 23 patients tracheostomy was closed before the RICU discharge. The hospital stay was 13±10 days for patients admitted only in RICU and 26±10 days for patients who experimented ICU assistance before RICU admission.

One patient in the study group died 3 months before discharge while no patients in the control group died during the 6-month period of observation.

Physiological measurements

Pre and post exacerbation values of the physiological measurements in patients in study and changes over time in controls are shown as mean values in table 2 and as individual data for MIP, FEV_1 and $PaCO_2$ in figure 2. 24% of patients were discharged from RICU with hypercapnia whereas they were normocapnic before the acute episode. Compared to prior to exacerbation, at discharge from RICU, only the study group demonstrated a statistically significant mean increase in $PaCO_2$ (by 5.5±7.9 and 0.04±3.9 mmHg in study and control group respectively), decrease in MIP (by 8.9±14.5 and 0.8±3.1 cmH_2O) and decrease in FEV_1 (by 129±257 and 54±129 ml) (table 2). According to our criteria of worsening in $PaCO_2$, MIP and FEV_1 (see Methods) were observed in 20 (47%), 14 (33%) and 12 (28%) of patients of study group respectively.

In a period of 6 months no significant change in mean values of the studied parameters was found in controls. Predefined criteria of worsening in $PaCO_2$, MIP and FEV_1 were observed in 4 (10%), 7 (17%) and 9 (21%) of the controls respectively.

When compared to the other 22 non tracheostomised patients, the 20 patients who performed lung and respiratory muscle evaluation with tracheostomy, did not show any statistical difference in $PaCO_2$, PaO_2, MIP and FEV_1 change. When compared to the 30 non-worsened patients, 12 patients of study group who worsened in FEV_1 (ml) showed significantly higher levels of stable state FEV_1 (1348±417 vs 853±387 ml, p=0.0001) and FVC (2022±677 vs 1705±608 ml, p=0.000).

In study group no significant differences were found when comparison between ventilated (n° 34) and non ventilated (n°8) patients was carried out. When compared to the 11 patients ventilated non invasively the 23 patients ventilated invasively showed

Table 2. - Pre and post exacerbation values of the physiological measurements in patients in study and changes over time in controls

	Before the episode	P=	After the episode	Baseline	P=	after 6 months
	Study Group			**Control**		
Subjects, n°	42		42	42		42
Weight, Kg	67±18	0.547	66±17	68±13	0.805	67±14
PaO_2, mmHg	54±10	0.227	55±8	58±12	0.345	59±12
$PaCO_2$, mmHg	52±9	**0.0051**	56±8	48±10	0.566	47±9
Ph	7.39±0.04	0.650	7.39±0.04	7.40±0.03	0.690	7.40±0.03
FEV_1 % of prd	36±17	**0.048**	29±9	36±12	0.552	35±12
FEV_1 (ml)	987±449	**0.041**	857±390	1017±461	0.467	964±444
FVC, % of prd	50±16	0.091	43±13	60±17	0.341	56±16
FVC (ml)	1790±635	0.112	1536±618	1570±661	0.201	1482±601
FEV_1/FVC%	44±11	0.320	40±10	44±12	0.462	43±12
TLC, % of prd	161±42	0.479	175±52	149±46	0.553	154±37
RV, % prd	180±54	0.091	201±63	161±45	0.356	167±43
MIP, cmH_2O	41±20	**0.0053**	32±11	49±16	0.567	48±16

Abbreviations: PaO_2 = arterial partial pressure of oxygen; $PaCO_2$ = arterial partial pressure of carbon dyoxide; FEV_1 = forced expiratory volume at first second; FVC= forced volume capacity; RV = residual volume. TLC = total lung capacity; MIP = maximal inspiratory pressure.

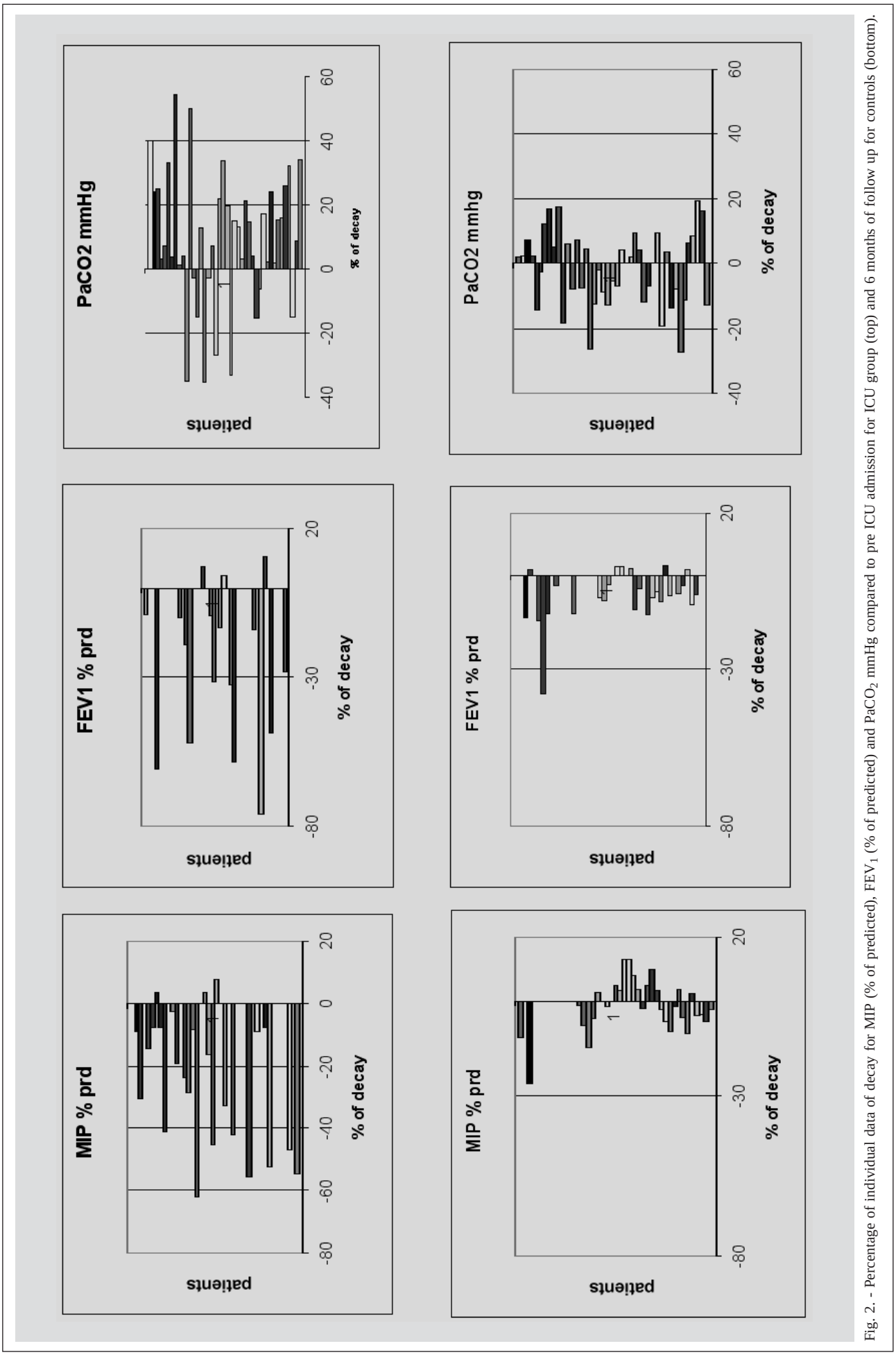

Fig. 2. - Percentage of individual data of decay for MIP (% of predicted), FEV_1 (% of predicted) and $PaCO_2$ mmHg compared to pre ICU admission for ICU group (top) and 6 months of follow up for controls (bottom).

a statistically higher increase only in residual volume (RV) (by 33±59% vs 9±20% pred, p=0.01).

No parameter assessed in stable state before the acute episode was able to discriminate patients worsening in MIP, $PaCO_2$ or FEV_1 after the acute exacerbation.

Post RICU location: 28 out 42 patients (66%) were discharged to a rehabilitative facility linked to RICU, 4 out 42 (9.5%) to a nursing home, 10 out 42 (24%) to their homes.

Discussion

After a severe acute exacerbation requiring admission to a RICU and immediately before discharge a large proportion of COPD patients still demonstrated preserved lung and respiratory muscle functions while more than one third of them would require further care and rehabilitative attempts to restore functional derangements.

The aim of our study was not to demonstrate the definitive decay in lung function after an ICU admission; in fact we have tried to convey a picture of lung function and respiratory muscle activity immediately before a RICU discharge usually based on clinical and arterial blood gases stability. Surprisingly more than 50% of patients presented no differences in lung function when compared to their pre-exacerbation data: this study could open the hypothesis to better differentiate post RICU allocation (rehabilitative, long term facilities or home) according to functional decay and subsequent expectance to restore it.

Acute exacerbations of COPD are an important cause of hospital admission, and it has been suggested that the severity of airway inflammation during exacerbations play a role in the decline of FEV_1 [20]. Little is known about lung function after a severe episode of relapse and in particular after ICU admission with or without the need of mechanical ventilation. Recently *Donaldson et al* [8] have shown that patients with moderate to severe COPD who suffered from frequent exacerbations experienced a significantly greater year decline in FEV_1 of 40 ml than patients who had infrequent exacerbations in whom FEV_1 decline was by 32 ml/year. In our study group the mean decline in FEV_1 after severe exacerbations was greater than 100 ml, a level superior to the year decline observed in frequent exacerbations of that study [8]. Nevertheless it is noteworthy that the level of severity of exacerbations in our study was greater than in that study [8]. Indeed exacerbations in our study required RICU/ICU admission with the 26% of patients presenting pneumonia as cause of Acute Respiratory Failure (ARF), whereas in the study [8] they did not. The only other study of "acute" effects of acute respiratory failure, of which we are aware, is by *Elliott et al* [21] in 13 young patients recovering from an ICU admission due to ARDS. These authors showed that the level of FVC % pred,TLC % pred, FEV_1/FVC % and FEF_{25-75}% pred had returned to the normal values within 6 months after the acute episode [21]. We have stated that patients who worsened had a significantly more stable state of FEV_1 and FVC. This observation could be explained by the higher marginal worsening reserve of patients with better functional state and that the % of functional decay in yet compromised patients may be less evident.

The mean 6 month decline in FEV_1 by 54 ml (108 ml/year) (table 2) for our control patients is superior to other recent studies of patients treated with inhaled steroids [19, 20]. *Seemungal* [9] demonstrated that recovery from a decline of lung function after COPD exacerbation may be very slow: at 35th day, the peak expiratory flow rate in 75% of cases had returned to baseline level, but on 91st day, the PEF in 7% of cases had not returned yet to baseline and in 3% of cases a further exacerbation had occurred before recovery was completed.

The role of inspiratory muscles in acute on chronic respiratory failure, has been well studied [24]. An original observation of our study was the reduction in inspiratory muscle strength in some of our patients after the severe exacerbation. To our knowledge no previous study has shown the role of exacerbation *per se* as a cause of loss of inspiratory muscle force. Maximal inspiratory pressure decreased in the 33% of the cases independent of the presence of hypercapnia. *Mc Nally* [25] suggested a high prevalence of reversible hypercapnia among patients hospitalised with exacerbations of COPD: in our study 24% of patients were discharged from RICU with hypercapnia whereas they were normocapnic before the acute episode. Stable hypercapnia has been proposed as an important negative prognostic factor for survival after discharge from ICU while "reversible" hypercapnia is associated with similar prognosis to that of COPD patients undergoing non-hypercapnic acute respiratory failure [26].

We were unable to demonstrate any clear deleterious effect of mechanical ventilation *per se* in lung function loss; nevertheless patients submitted to invasive mechanical ventilation when compared to patients ventilated non-invasively showed a statistically higher worsening in residual volume.

There were no differences in the changes of FEV_1 and MIP in patients with or without tracheotomy: therefore we are confident that the presence of tracheotomy has not influenced the measurements and the overall results of our study.

We can argue that recovery from exacerbation would not be completed at RICU discharge and further improvements in respiratory function would be expected. Lung function may require several weeks to recover after the exacerbation so that lung function measurement at a single time point can only demonstrate an acute effect on lung function. *Seemungal et al* [9] demonstrated the necessity of a long follow up with repeated measurements to describe a real time course of lung function recovery. Nevertheless our study was not aimed to demonstrate a real time course of lung function but we believe of interest the fact that not all the patients submitted to RICU are candidate to a deleterious loss (also if transient). The described picture of these kinds of patients immediately be-

fore discharge from a RICU could help physicians to differentiate post RICU allocation or rehabilitation needs decisions.

Comparison of post exacerbation lung and respiratory muscle functions with measurements taken 6 months before like in our study may be criticised. Indeed in that time interval, patients might have experienced minor episodes of worsening of COPD influencing the level of lung function before the severe exacerbation needing ICU. That is why we also evaluated a control population not experiencing an acute exacerbation. These patients did not show any substantial worsening in lung and respiratory muscle function. Therefore we are confident to ascribe to the exacerbation the worsening observed in some patients.

A limitation of our study could be the in-homogeneity of the studied groups although the necessity of mechanical ventilation was not found to be a discriminate fact for deterioration.

In conclusion, after a severe acute exacerbation requiring admission to a RICU and immediately before discharge, a large proportion of COPD patients still show preserved lung and respiratory muscle function while more than one third of them would require further care and rehabilitative attempts to restore functional derangements. The results of this study strengthen the need to better differentiate care assistance resources for post RICU patients.

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