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# Prophylactic use of noninvasive ventilation in patients undergoing lung resectional surgery

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## KEYWORDS

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## Summary

**Question of the study:** We studied whether prophylactic use of noninvasive pressure support ventilation (NIPSV) administered pre- and postoperatively may reduce the postoperative pulmonary function impairment.

**Patients and methods:** Prospective randomized clinical trial. Thirty-nine patients with a preoperative FEV<sub>1</sub> < 70% of the predicted value scheduled for elective lobectomy related to lung cancer were enrolled. Seven patients were excluded after enrollment. Patients were required to follow standard treatment without (control group, *n* = 18) or with NIPSV (study group, *n* = 14) during 7 days at home before surgery, and during 3 days postoperatively. Primary outcome variable was the changes on arterial blood gases on room air.

**Results:** Two hours after surgery, PaO<sub>2</sub>, FVC and FEV<sub>1</sub> values were significantly better in the NIPSV group. On day 1, 2 and 3, PaO<sub>2</sub> was significantly improved in the NIPSV group. Also on day 1, FVC and FEV<sub>1</sub> improved significantly in the NIPSV group. The hospital stay was significantly longer in the control group than in the study group (*p* = 0.04). The incidence of major atelectasis was 14.2% in the NIPSV group and 38.9% in the no-NIPSV group (*p* = 0.15).

**Abbreviations:** CPAP, continuous positive airway pressure; EPAP, expiratory positive airway pressure; FEV<sub>1</sub>, forced expiratory volume in 1 s; FVC, forced vital capacity; ICU, intensive care unit; IPAP, inspiratory positive airway pressure; PaCO<sub>2</sub>, arterial carbon dioxide tension; PaO<sub>2</sub>, arterial oxygen tension; Paw, airway pressure; SD, standard deviation; NIPSV, noninvasive pressure support ventilation

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*Answer to the question:* Prophylactic use of NIPSV in a pre- and postoperative manner significantly reduces pulmonary dysfunction after lung resection. As a result, recovery of preoperative respiratory function is accelerated.

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## Introduction

Lung resectional surgery is often complicated by significant pulmonary dysfunction that persists for a few days after surgery.<sup>1-3</sup> Alteration of ventilatory function is multifactorial; reflex inhibition of the phrenic nerve, anesthesia, chest pain, closure of distal airways and the loss of functioning parenchyma, all contribute to these changes.<sup>2,3</sup> This pulmonary function impairment may lead to postoperative pulmonary complications such as sputum retention, atelectasis, pneumonia and respiratory failure with prolonged mechanical ventilation.<sup>4</sup> Furthermore, it has been suggested that an increased risk of postoperative pulmonary dysfunction is associated with a preoperative forced expiratory volume in 1 s (FEV<sub>1</sub>) or forced vital capacity (FVC) of less than 70% of the predicted value.<sup>5</sup> Continuous positive airway pressure (CPAP) administered by full face or nasal mask in the postoperative phase can restore functional residual capacity to preoperative values,<sup>6</sup> improve oxygenation,<sup>7</sup> and spare inspiratory muscles.<sup>8</sup> Although CPAP seems to be more effective than routine chest physiotherapy,<sup>9</sup> its benefits are unfortunately not sustained, and functional residual capacity deteriorates a few minutes after interruption of CPAP.<sup>6</sup> Noninvasive pressure support ventilation (NIPSV) is a recognized treatment for acute hypercapnic and hypoxemic acute respiratory failure.<sup>10,11</sup> In comparison to CPAP, relatively high inspiratory pressure is used with NIPSV. As a result, NIPSV may improve the distribution of ventilation by recruiting zones of alveolar collapse.<sup>12</sup> Also, NIPSV minimizes the work of breathing.<sup>8</sup> Although the postoperative preventive use of NIPSV may improve oxygenation in nonhypercapnic patients,<sup>13-15</sup> prophylactic NIPSV therapy used pre- and postoperatively in patients with severe preoperative pulmonary function impairment submitted to elective lung resection has never been studied. In this randomized-controlled study, we tested if the perioperative prophylactic use of NIPSV promoted better recovery of arterial blood gases and pulmonary function after lung resectional surgery.

## Methods

### Patients

This investigation was approved by our institution's Ethics Committee. Written consent was obtained from all participants after they were fully informed of the nature, characteristics, aims, and potential risks of the study.

All patients with preoperative FEV<sub>1</sub> < 70% of the predicted value and scheduled for elective lobectomy related to lung cancer between January 2001 and January 2004 were initially considered as potential candidates. Patients were excluded if one or more of these conditions occurred: (1) incisions other than posterolateral thoracotomy, (2) minor pulmonary resection such as open lung biopsies, (3)

exploratory thoracotomy (no parenchymal resection), (4) pneumonectomy, (5) previous treatment with NIPSV or CPAP, (6) postoperative hemodynamic instability (ventricular dysrhythmia and myocardial ischemia or infarction) or acute respiratory failure that required endotracheal mechanical ventilation, (7) pregnancy, (8) mental retardation or other severe cognitive disorders, and inability to provide informed consent. Standard anesthetic procedures were used in all patients. These techniques have been described elsewhere in the literature.<sup>16</sup> Surgical techniques were those of standard pulmonary resection. After surgery, the patients were placed in the surgical intensive care unit (ICU) for at least 4 days. During this period of time, all patients received a thoracic epidural analgesia with continuous infusion of ropivacaine 0.2% combined with sufentanil (1 or 0.5 µg/ml if age was over 70 years). An infusion started 1 h before the end of surgery at a rate of 6 ml/h, and was adjusted thereafter according to the visual analog scale.

### Study design

This study was designed as a randomized, controlled, and parallel trial. Seven days prior surgery, enrolled patients visited our outpatient pulmonary clinic. Vital signs were measured and patients were randomly assigned to standard treatment without (Control Group) or with NIPSV (Study Group). Randomization was achieved using sealed envelopes with the order of distribution determined by computer generated randomized numbers. Patients in both groups were required to follow the treatment during 7 days at home before surgery, and during 3 days postoperatively.

### Standard treatment

All patients of both groups received all therapeutic measures necessary to provide optimal care for the patient and systematically: aerosolized terbutaline (10 mg/24 h) and ipratropium bromure (1 mg/24 h), oral ambroxol (60 mg/24 h) and chest physiotherapy. Chest physiotherapy was performed with the same regimen during the preoperative period at home and during the postoperative phase. At home, a private physiotherapist contacted by the principal investigator had in charge the patient. Chest physiotherapy was performed twice a day at 10 am and 2 pm. Patients were instructed to take four to five maximal inspirations and then to cough heartily every 3 min during 15 min. Furthermore, patients carried out deep breathing exercises taking 20 maximal inspirations and 20 maximal expirations with the aid of a deep breathing exerciser (Triflo, Chesebrough-Pond's Inc.).

### NIPSV

Ventilation was provided via an industrial facial mask (Mirage<sup>®</sup>, Resmed, Sidney, Australia). NIPSV was provided with a pressure-preset ventilator (VPAP ST3<sup>®</sup>, Resmed, Sidney, Australia) in the spontaneous mode. This device

maintained pressure at two preset levels, an inspiratory positive airway pressure (IPAP) and an expiratory positive airway pressure (EPAP). The IPAP level was maintained for at least 0.1 s and could not exceed 2 s. The ventilator cycled to EPAP when the patient inspiratory flow decreased below a threshold level. If an expiratory effort was detected or if inspiratory period was held for more than 2 s, the device automatically switched from IPAP to EPAP. NIPSV was initiated in our outpatient pulmonary clinic 7 days prior surgery. IPAP was initially set at 8 cmH<sub>2</sub>O and then was increased until the maximal level tolerated by the patient was reached. EPAP was set at 2–4 cmH<sub>2</sub>O. Patients were acclimatized to NIPSV during a 1 h period under the supervision of one of the investigators. During this training trial, pulse oximetry was recorded and arterial blood gases were obtained. Preoperatively, patients were required to perform NIPSV at least five 1-h period per day. Postoperatively, the same NIPSV regimen was required with the exception of the first 2 h following surgery during which the patients were not wearing NIPSV. Throughout the study, the inspired concentration of oxygen with NIPSV was 0.21. Patients' adherence to NIPSV at home was determined by the ventilator timer and checked by the same manner in the ICU.

## Measurements

Resting daytime blood gases (Ciba-Corning 288 blood gas analyzer, Medfield, MA, USA) were obtained from the radial artery with the patient breathing room air pre- and postoperatively in both groups. In the study group and on room air, arterial blood gases were systematically performed before NIPSV sessions pre- and postoperatively.

Preoperatively, static lung volumes were determined by a constant-volume whole body plethysmograph (Jaeger Masterscreen Body, Wuerzburg, Germany) and, FEV<sub>1</sub> and FVC were measured with a pneumotachograph (Jaeger Masterscreen Body, Wuerzburg, Germany). Postoperatively, FVC and FEV<sub>1</sub> were also recorded using a spirometer (Hycos & Aulas, Buckingham, England). Pre- and postoperatively, pulmonary function was measured in the sitting position by the same technician blind as to patient randomization. Preoperatively, arterial blood gases and pulmonary function were systematically assessed as patients were randomized and after 7 days of treatment at home. Postoperatively the same parameters were measured on operative day (2 h after surgery), and at 10 am on day 1, day 2, and day 3. Pain and dyspnea scores, heart rate, respiratory rate, arterial blood pressure, opioid consumption were recorded by nurses on the surgical ICU every 4 h postoperatively. In both groups, chest X-rays obtained 2 h after surgery and, at 9 am on the first, second and third postoperative days were assessed by 2 radiologists (BP and AC) who were blinded to the patient's randomization. Lobar or supralobar atelectasis requiring a fiberoptic bronchoscopy have been recorded. Duration of in-hospital stay was also recorded.

## Statistical analysis

The primary outcome variable was the changes in arterial blood gases on room air. Secondary outcomes were changes in lung function, the rate of postoperative lobar or

supralobar atelectasis and duration of in-hospital stay. Results are reported as mean  $\pm$  SD. For the between-groups comparison and for comparison at different times, a repeated analysis of variance (ANOVA) was used. If a significant difference was noted, pairwise comparisons were performed by the Student–Newman–Keuls test to account for multiple comparisons. *p*-Values at 0.05 or less were considered to be statistically significant.

## Results

Between January 2001 and January 2004, 300 patients have been scheduled for elective lobectomy related to lung cancer. Among them, 39 patients were enrolled in the study. Seven patients were excluded after enrollment. One patient in the control group was excluded for immediate postoperative acute respiratory failure related to total pneumothorax, which has required invasive mechanical ventilation. Six patients in the study group were excluded (3 for pneumonectomy and 3 for minor pulmonary resection). The two groups were similar with regard to age, body mass index, preoperative pulmonary function and arterial blood gases, duration of surgery, duration of lung deflation, and opioid consumption during surgery and during the first 72 h postoperatively (Table 1). Although, 7 of 14 patients in the study group were current smokers just before surgery as compared to 9 of 18 in the control group, the patients in the study group smoked significantly much more than the control group, respectively, 80  $\pm$  11 (mean  $\pm$  SD) packets year versus 59  $\pm$  5 packets year (*p* = 0.04).

Patients' compliance to NIPSV was 4  $\pm$  1 h/day preoperatively at home and 5  $\pm$  1 h/day postoperatively. The average inspiratory pressure support level was 12.6  $\pm$  1.2 cmH<sub>2</sub>O and the average expiratory pressure level was 2.9  $\pm$  0.7 cmH<sub>2</sub>O.

Regarding to the pre- and postoperative periods and as compared to the control group, the use of NIPSV significantly improved the overall evolution of the arterial blood gas values measured on room air (pH (*p* = 0.0003), arterial carbon dioxide tension (PaCO<sub>2</sub>) (*p* = 0.04), arterial oxygen tension (PaO<sub>2</sub>) (*p* = 0.0006)), FVC (*p* = 0.03) and FEV<sub>1</sub> (*p* = 0.02). Before surgery and as compared to the control group, arterial blood gases measured on room air improved significantly after 7 days of treatment with NIPSV. Furthermore, a trend to improve FVC and FEV<sub>1</sub> was observed with NIPSV preoperatively in the study group. Two hours after surgery and before NIPSV, as compared to the preoperative values, arterial blood gases on room air, FVC and FEV<sub>1</sub> significantly worsened in both groups. However, the values of PaO<sub>2</sub>, FVC and FEV<sub>1</sub> remained at a significant higher level in the study group. Subsequently, arterial blood gas values and pulmonary function parameters progressively returned to preoperative values. The effect of NIPSV on arterial blood gases, FVC and FEV<sub>1</sub> are presented in Figs. 1 and 2. PaO<sub>2</sub> values were significantly greater in the study group than the control group at the four postoperative time points. FVC and FEV<sub>1</sub> values were also significantly increased in the study group, respectively, on the first and third postoperative days and on the postoperative day 1.

The development of postoperative chest X-ray lobar or supralobar atelectasis has been assessed with an excellent concordancy between the two radiologists (*K* = 0.832).

**Table 1** Preoperative characteristics of patients.

	Control group (n = 18) Mean $\pm$ SD	Study group (n = 14) Mean $\pm$ SD	p-Value*
Age (years)	63 $\pm$ 3	64 $\pm$ 2	0.6
Body mass index (kg/m <sup>2</sup> )	24 $\pm$ 1	25 $\pm$ 1	0.6
Arterial blood gases (room air)			
pH	7.42 $\pm$ 0.01	7.42 $\pm$ 0.01	0.8
PaO <sub>2</sub> (mmHg)	74.1 $\pm$ 1.6	75.0 $\pm$ 1.7	0.7
PaCO <sub>2</sub> (mmHg)	39.1 $\pm$ 0.9	39.5 $\pm$ 0.9	0.8
Pulmonary function testing			
FVC (% pred)	84.9 $\pm$ 18.8	88.4 $\pm$ 15.4	0.5
FEV <sub>1</sub> (% pred)	53.7 $\pm$ 10.0	54.9 $\pm$ 9.2	0.7
PEFR (% pred)	53.6 $\pm$ 15.0	55.5 $\pm$ 12.2	0.7
Duration of surgery (min)	149 $\pm$ 15	158 $\pm$ 15	0.6
Duration of one lung deflation (min)	121 $\pm$ 11	110 $\pm$ 10	0.5
Opioid consumption ( $\mu$ g)			
During surgery	115 $\pm$ 23	90 $\pm$ 9	0.4
During the first 72 h postoperatively	32.9 $\pm$ 5.8	32.2 $\pm$ 5.9	0.5

PaCO<sub>2</sub> = arterial carbon dioxide tension; PaO<sub>2</sub> = arterial oxygen tension; FVC = forced vital capacity; FEV<sub>1</sub> = forced expiratory volume in 1 s; PEFR = peak expiratory flow rate; % pred = percentage of the predicted value.

\*p-Values refer to between-group comparisons.

In the control group, five of the 18 patients (27.7%) had an atelectatic consolidation on the first postoperative day, this figure increasing to 7 of 18 on the third postoperative day (38.9%). In the study group, two of 14 patients (14.2%) got an atelectasis on the second postoperative day. The difference between the two groups was not significant ( $p = 0.15$ ).

NIPSV was mostly well tolerated. No patient died and no complications, such as nasal abrasion, aspiration, gastric distension or hemodynamic derangement were observed. The incidence of supraventricular dysrhythmia and the duration of thoracic drainage were not different between the two groups.

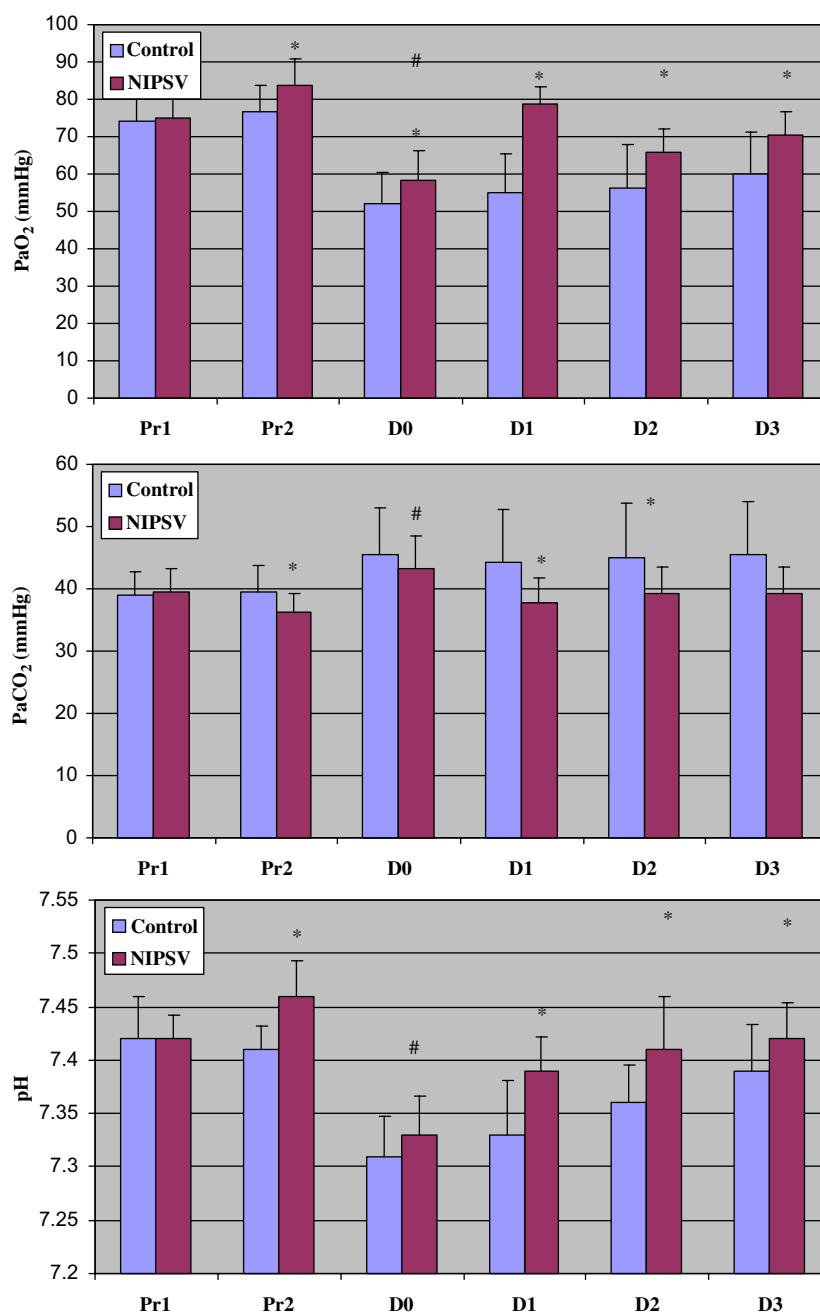
The hospital stay was significantly longer in the control group (19  $\pm$  3 days) than in the study group (12  $\pm$  1 days,  $p = 0.04$ ).

## Discussion

This study demonstrates that preventive NIPSV therapy used pre- and postoperatively in patients with a preoperative FEV<sub>1</sub> < 70% of the predicted value submitted to elective lung resection improves the overall perioperative evolution of arterial blood gas values and pulmonary function parameters. We show that the preoperative use of NIPSV may reduce the immediate postoperative hypoxemia and pulmonary function impairment developed after such a surgery. Our results also demonstrate that the prophylactic use of NIPSV during the first 72 h postoperatively leads to quicker recovery of preoperative arterial blood gas values and spirometric volumes. In our study, although the incidence of postoperative atelectatic consolidation is not significantly different, the prophylactic use of NIPSV decreases the length of in-hospital stay.

Although, the postoperative preventive use of NIPSV has already been reported in patients undergoing lung resec-

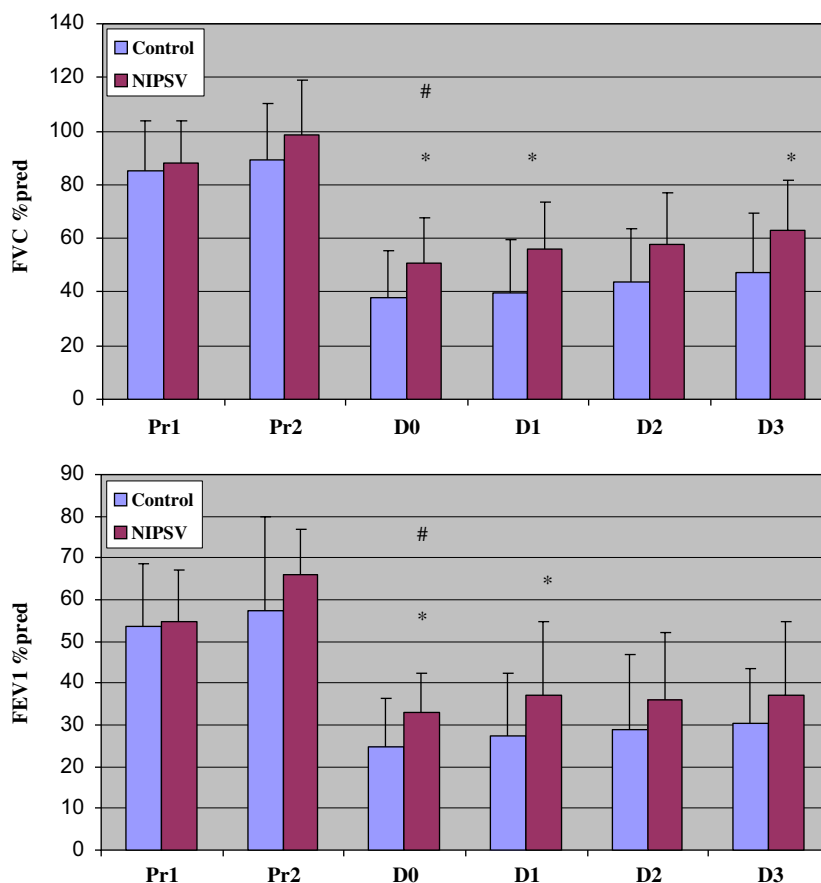
tional surgery,<sup>13</sup> in obese patients undergoing gastroplasty<sup>14</sup> or after coronary bypass grafting,<sup>15</sup> its prophylactic use in patients with a severe preoperative airflow obstruction has never been previously tested. Indeed, the patients enrolled in the studies from Aguilo et al.<sup>13</sup> and Matte et al.<sup>15</sup> had, respectively, mild preoperative airflow obstruction or normal preoperative spirometric values. In the work from Joris et al.,<sup>14</sup> preoperative pulmonary function was characterized by a restrictive syndrome. In our study, the preoperative values of FVC and FEV<sub>1</sub> were, respectively, lower than 90% and 55% of the predicted value in both groups. Patients in the study group had smoked significantly much more in the past. As a result, our study group had a stronger risk for postoperative pulmonary complications as compared to the control group.<sup>4</sup> Several hypotheses may be proposed to explain our positive results. Firstly and as compared to CPAP, the IPAP level used with NIPSV promotes lung inflation leading to alveolar recruitment. Thus, re-expansion of micro-atelectatic areas by positive pressure ventilation might explain the improvement of blood gases on room air and pulmonary function parameters.<sup>17,18</sup> Secondly, the use of a facial mask may have reduced mouth leaks induced by a sleepy state related to the residual sedative effect of the anesthetic agents, as well as of the opioid administered for postoperative analgesia. Furthermore, as it has been demonstrated, oronasal mask is better tolerated in the acute setting.<sup>19</sup> Thirdly, the "pressure boost" (IPAP-EPAP) that we used might have played a role. In our study, the average inspiratory pressure support level was 12.6  $\pm$  1.2 cmH<sub>2</sub>O and the average expiratory pressure level was 2.9  $\pm$  0.7 cmH<sub>2</sub>O. Then, the actual level of inspiratory support was 9.7 cmH<sub>2</sub>O. In a prospective randomized controlled study, Joris et al.<sup>14</sup> have investigated the effect of NIPSV on postoperative pulmonary function in obese patients after gastroplasty. In this study, the authors observed a "dose-dependent effect" of inspiratory support on the postoperative pulmonary restrictive syndrome,



**Figure 1** Effect of NIPSV on PaO<sub>2</sub>, PaCO<sub>2</sub> and pH (on room air). Patients had standard treatment (control group) or standard treatment plus NIPSV (NIPSV group) during 7 days at home before surgery and 3 days postoperatively. Arterial blood gases were performed preoperatively (before (Pr1) and after (Pr2) treatment) and postoperatively (2 h after surgery (D0) and on day 1, day 2 and day 3). Note that arterial blood gases were performed before NIPSV sessions in the NIPSV group. Data are mean  $\pm$  SD. \* $p < 0.05$  (control versus NIPSV groups); # $p < 0.05$  (Pr2 versus D0).

comparing NIPSV 8/4 with inspiratory and EPAP set at 8 and 4 cmH<sub>2</sub>O, respectively, versus NIPSV 12/4 set at 12 and 4 cmH<sub>2</sub>O. As a result, patients with severe preoperative pulmonary function may require a higher-pressure boost to yield a reduction of the postoperative pulmonary function impairment. In our study, lung inflation produced by a 9.7 cmH<sub>2</sub>O pressure boost might have been sufficient and not high enough to be poorly tolerated. In particular, no complications such as gastric distension, bronchus joining troubles or hemodynamic derangement has been observed.

Fourthly, NIPSV used preoperatively improved significantly the arterial blood gas values and a trend to improve the spirometric parameters was observed. As a result, the preoperative use of NIPSV may have played a role in decreasing immediate postoperative hypoxemia and pulmonary function impairment. Furthermore, we argue that the preoperative patients' training to NIPSV may have been of value in the overall postoperative improvement of these parameters. In a study designed to compare the outcome of episodes of acute exacerbation of chronic obstructive



**Figure 2** Effect of NIPSV on FVC and FEV<sub>1</sub>. For the method, see legend of Fig. 1. Data are mean ± SD. \* $p < 0.05$  (control versus NIPSV groups); # $p < 0.05$  (Pr2 versus D0).

pulmonary disease treated with NIPSV in patients with home NIPSV and in patients without home ventilatory support, Hilbert et al.<sup>20</sup> have demonstrated that previous experience with NIPSV could benefit patients in the management of acute respiratory failure.

Because of the too limited number of included patients, our study was not designed to demonstrate any potential benefit of prophylactic use of NIPSV on the incidence of postoperative pulmonary complications, however, we report a trend to reduce the incidence of lobar or supralobar atelectasis.

In our study, the hospital stay was significantly shortened by NIPSV. The quicker recovery of preoperative arterial blood gases and spirometric volumes may be an explanation. However, length of stay depends on many factors besides just the medical condition. Indeed, we cannot exclude a bias related to the facility for our patients to get earlier the institution for rehabilitation. Also, because patients and caregivers cannot be blinded to treatment group, further potential bias is impossible to eliminate.

In conclusion, prophylactic NIPSV therapy used pre-and postoperatively allows a significant reduction in the magnitude of the postoperative arterial blood gases and pulmonary function impairment in patients with a preoperative FEV<sub>1</sub> < 70% of the predicted value undergoing lung resectional surgery. As a result, recovery of preoperative respiratory function is accelerated. However, further studies are required to assess the precise impact of the

prophylactic use of NIPSV on postoperative pulmonary complications.

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