Influence of early pulmonary rehabilitation on transcutaneously measured oxygen saturation and carbon-dioxide pressure values after lung cancer surgery: an observational pilot study

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AIMS: *The aim of our study was to evaluate the influence of early pulmonary rehabilitation treatment on values of oxygen saturation and transcutaneous pCO_2 in lung cancer patients after surgery.*
MATERIAL AND METHODS: *The observational pilot study included 41 patients (25 males and 16 females) who underwent lung resection for lung cancer. Further parameters were continuously measured for 12 hours over 7 days period: oxygen saturation (SpO_2), transcutaneous pCO2 ($TpCO_2$), desaturation time (DT) and hypercapnia time (HT).*
RESULTS: *Significantly lower values of SpO2 were found at day 3 compared to days 1 and 2 ($p<0.05$ on both occasions), at day 4 compared to days 1 and 2 ($p<0.01$ and $p<0.05$ respectively), at day 6 compared to day 2 ($p<0.05$), and at day 7 compared to day 2 ($p<0.05$). There are, significant negative correlations between mean values of SpO_2 and $TpCO_2$ on days 1, 3, 4 and 5 ($R= -0.535$, $p<0.01$ on day 1; $R=-0.477$, $R= -0.365$, and $R= -327$ on days 3, 4, and 5, respectively all $p<0.05$).*
CONCLUSION: *Pulmonary rehabilitation administered to the lung cancer patients in early postoperative stage significant lowered SpO_2 values in study group. Our preliminary findings stressed out importance and positive effects of early pulmonary rehabilitation on oxygen saturation values in lung cancer patients after surgery.*

KEY WORDS: Blood gases, Lung cancer surgery, Pulmonary rehabilitation

Introduction

Lung cancer is emerging oncological medical condition and is considered to affect different aspects of patient's quality of life. Improvement in medicine along with

introducment of novel medical treatments, prolonged surviving rates in these patients. However, it is important to underline that for lung cancer patients both before and after surgical intervention, they suffer different degree of pulmonary dysfunctions. Previous studies have demonstrated the effectiveness of pulmonary rehabilitation (PR) in patients with lung cancer [1-3]. The justification of such rehabilitation treatment refers to the fact that it reduces possible complications and influence oxygen transport and thus gas exchange improvement [1,2]. Further it was stressed out that PR particularly in patients with chronic obstructive pulmonary disease

(COPD) improves exercise tolerance, respiratory muscle functions and ultimately quality of life [4]. Nagarajan et al., stated the importance of respiratory physiotherapy by the fact that even one day of chest physiotherapy compared to routine nursing care reduces atelectasis rate and length of hospital stay [5]. Findings from the study of Kim et al., suggested that PR is beneficial in improvement of reduced forced vital capacity (FEV) in patients after lung resection [6], while Qiao et al., highlighted the fact that PR in lung cancer patients reduces surgical morbidity [7].

The aim of our study was to evaluate the influence of early pulmonary rehabilitation treatment on values of oxygen saturation and transcutaneous pCO_2 in lung cancer patients after surgery.

Methods

The observational pilot study included 41 patients (25 males and 16 females) who underwent lung resection for lung cancer. Prior to surgery spirometry, reversibility test where appropriate, diffusion capacity of lungs for carbon monoxide (DLCo) and arterial blood gas measurement were performed in order to detect patients with COPD and hypoxemia and/or hypercapnia and to estimate perioperative risk for respiratory complications.

Spirometry was performed by commercial Lilly-pneumotachometer (MasterScreen Pneumo®, Viasys Healthcare, Germany) according to joint American Thoracic Society/European Respiratory Society standards [8]. In patients with initial FEV_1/FVC ratio less than 0.7 reversibility test was performed. After spirometry we applied 4 puffs of combined ipratorpium-bromide and fenoterole in single meter-dose inhaler (Berodual® N, Boehringer Ingleheim Pharma GMBH & Co, Germany) via spacer (Aerochamber, Forest Laboratories Inc, USA), which gave cumulative dose of 200 mcg and 80 mcg of fenoterol and ipratropium-bromide, respectively. Post bronchodilator spirometry was performed 30 minutes after application of last doze of fenoterol and ipratropium-bromide combination. Patients who had post bronchodilator value of FEV_1/FVC ratio less than 0.7 and positive history were considered to have COPD.

DLCo was measured using single-breath method by commercial equipment (MasterScreen Diffusion®, Viasys Healthcare, Germany) according to joint American Thoracic Society/European Respiratory Society standards [9]. Cut-off point of 80% of predicted value was used as a lower limit of normality for DLCo, for reason that patients with lower values of DLCo have increased risk for perioperative respiratory complications [10]. In patients with initial FEV_1/FVC ratio less than 0.7 diffusion was measured after reversibility testing.

Arterial blood samples were taken and handled according to International Federation of Clinical Chemistry Standards [11]. Arterial blood gases and pH values are measured by commercial blood gas analyzer (ABL 5, Radiometer, Denmark). Only patients with normal values of blood gases while breathing ambient air were included. For pO_2 we used normal values given by Sorbini et al., while for pCO_2 we used cut-off point for upper limit of normality of 6.7 kPa [12,13].

After surgery, all patients were treated in surgical intensive care unit (ICU) for seven days according to standard postoperative protocol which included application of oxygen where needed, adequate medications, supportive treatment and postoperative respiratory rehabilitation (breathing exercises, aerosol inhalation of bronchodilatators and exercises for chest and shoulders area mobilization). Patients which developed significant surgical or pulmonary complication were excluded from the study, as well as the patients who required prolonged mechanical ventilation after surgery or developed sustained respiratory failure that required reintubation and mechanical ventilation during the observed period. Included study patients were extubated immediately after surgery and were breathing spontaneously without assistance of any kind, except for supplemental oxygen where needed, throughout the stay in the ICU, and were discharged from ICU on eighth postoperative day.

During the stay in ICU, oxygen saturation (SpO_2), transcutaneous pCO_2 ($TpCO_2$), desaturation time (DT) and hypercapnia time (HT) were continuously measured for 12 hours every day by commercial monitor (Sentec Digital Monitoring System, SenTec AG, Switzerland). Significant desaturation value was set on monitor at 90%, and significant $TpCO_2$ value at 6.7 KPA.

STATISTICAL ANALYSIS

Categorical data were presented as numbers and percents (%), while continuous data were expressed as mean values (MV) and standard deviation (SD). Differences between genders for observed parameters were analyzed by t-test for independent samples and Mann-Whitney test. Differences of mean values for study parameters were analyzed by t-test for paired samples. Wilcoxon test for paired samples was used to evaluate statistical difference in frequencies of patients regarding desaturation and hypercapnia. Pearson's correlation coefficient was used for statistical evaluation between SpO_2 and $TpCO_2$. Differences were declared to be significant when p value was <0.05.

Results

We included 41 patients who underwent lung resection for bronchial cancer at the Clinic for Thoracic Surgery, Clinical Center of Serbia, Belgrade, Serbia. In total 3 patients were excluded from the study, of which two that developed surgical complication (one with pneumotho-

Parameter	Males	Females	p
Age, years	62.44±6.59	57.37±7.90	<0.05[a]
COPD, N/(%)	10/(60)	2/(12.5)	=0.01[b]
FVC, % of predicted	101.40±17.76	107.56±12.76	>0.05[a]
FEV1, % of predicted	87.08±16.48	97.31±15,02	<0.05[a]
DLCo, % of predicted	77.12±15.35	73.44±14.95	>0.05[a]
pH	7.42±0.03	7.41±0.03	>0.05[a]
pCO$_2$, kPa	5.39±0.60	5.38±0.60	>0.05[a]
pO$_2$, kPa	10.82±1.17	11.46±1.44	>0.05[a]
SpO$_2$, %	95.82±1.83	96.17±1.36	>0.05[a]

All values are expressed as MV±SD unless otherwise indicated. [a]t-test for independent samples; [b]Mann-Whitney test.

rax and other with empyema), and one due to the pneumonia that led to sustained respiratory failure which was treated with non-invasive ventilation during observed period in the ICU.

Age, COPD frequency, preoperative values of pulmonary function tests, arterial blood gases values, and type of surgery performed are presented in Table I. There are non significant differences in observed parameters between genders, except for the age that was significantly lower in females (p<0.05), and significantly lower frequency of COPD (p=0.01), and higher preoperative FEV[1] values (p<0.05) in females.

Seven-day trend and differences in values of SpO[2], DT, TpCO$_2$ and HT by day are presented in Graph 1. While we didn't found any significant difference in day to day mean values of TpCO[2], DT and HT, significantly lower values of SpO$_2$ were found at day 3 compared to days 1 and 2 (p<0.05 on both occasions), at day 4 compared to days 1 and 2 (p<0.01 and p<0.05 respectively), at day 6 compared to day 2 (p<0.05), and at day 7 compared to day 2 (p<0.05). We didn't find any significant difference in frequencies of patients who had either desaturation or hypercapnia during monitoring (Fig. 2).

Correlations between SpO$_2$ and TpCO$_2$ parameters are presented in Graph 3. There are, significant negative correlations between mean values of SpO$_2$ and TpCO$_2$ on
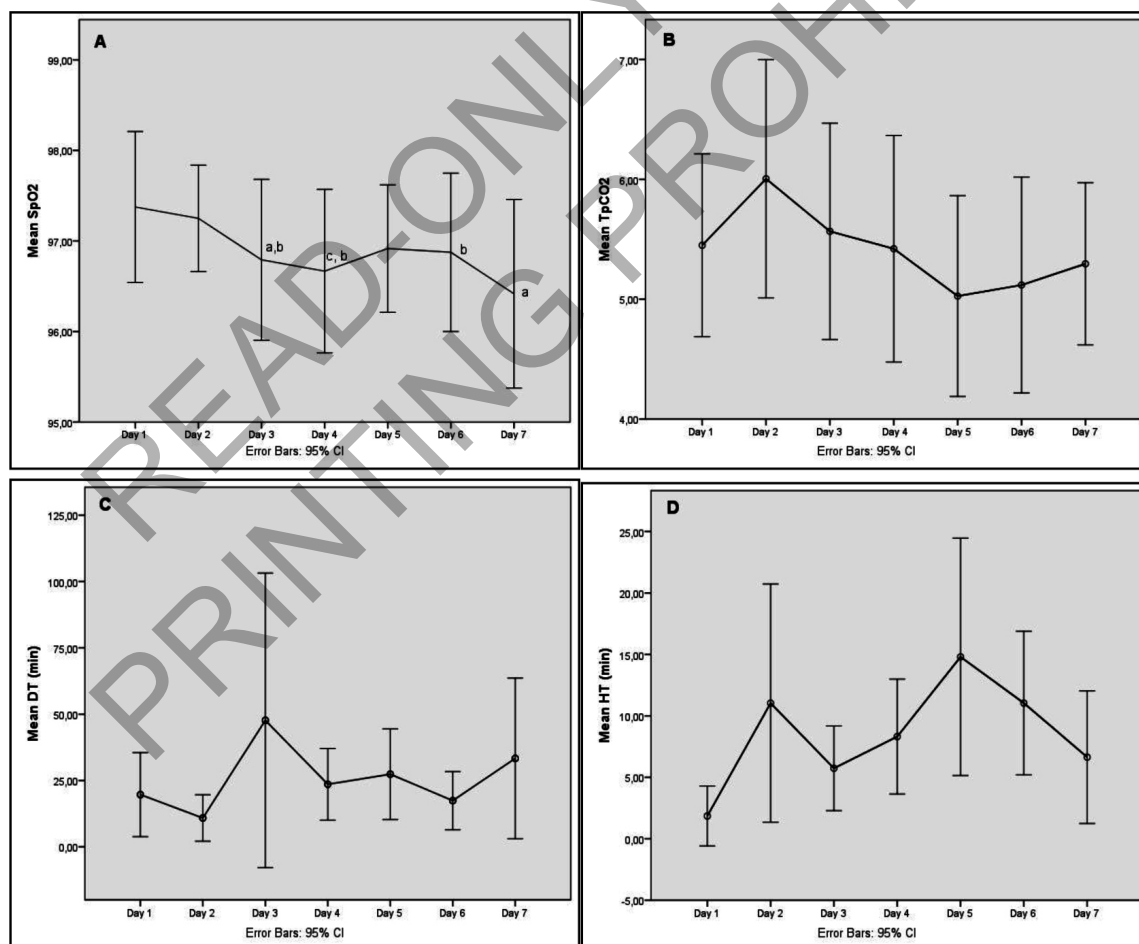

Fig. 1: Seven-day trend and differences in mean values by day of SpO$_2$, TpCO$_2$, DT, and HT. **A)** Mean SpO2 values by day; **B)** Mean TpCO$_2$ values by day; **C)** Mean DT values by day; **D)** Mean HT values by day. Paired sample t-test: Ap<0.05 vs day 1; Bp<0.05 vs day 2; Cp<0.01 vs day 1.
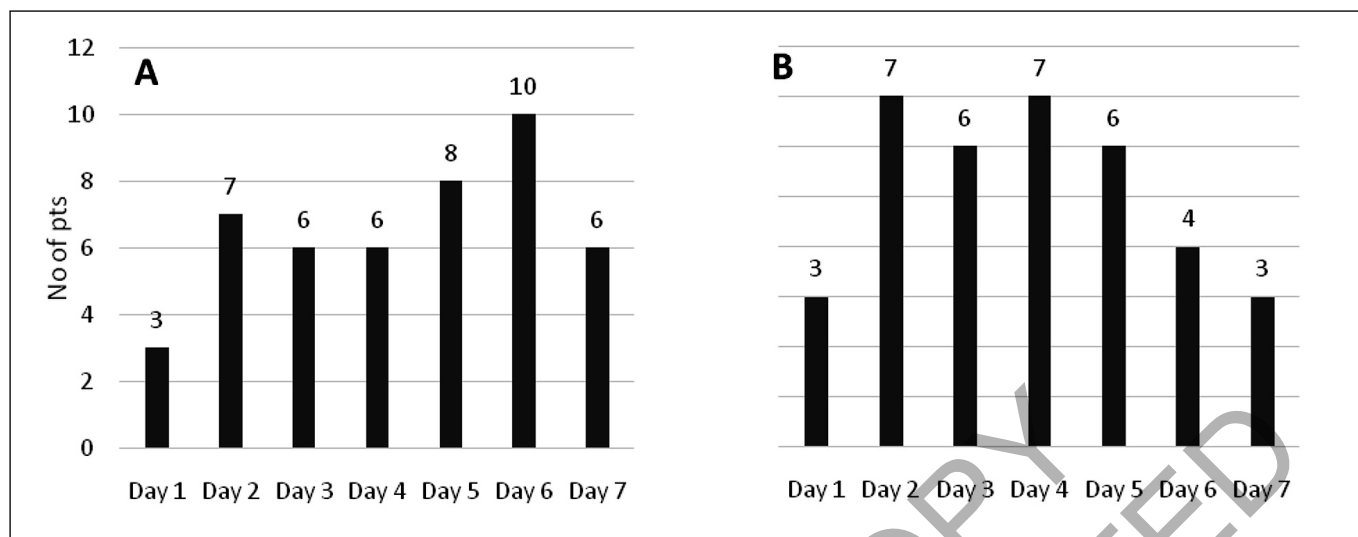
Fig. 2: Number of patients with oxygen desaturation and hypercapnia by day. **A)** Patients with oxygen desaturation; **B)** Patients with hypercapnia. Wilcoxon signed rank test: A, B p>0.05)

days 1, 3, 4 and 5 (R= -0.535, p<0.01 on day 1; R= -0.477, R = -0.365, and R= -327 on days 3, 4, and 5, respectively all p<0.05). We didn't find any significant correlation between mean SpO_2 and $TpCO_2$ values on days 2, 6, and 7 (p>0.05) (Fig. 3).

Discussion

In the study we have noticed that mean age for the diagnosis of lung cancer was around 60 years of life that is in line with previous reports [14]. However, other studies suggested higher age [15]. Further, we have noticed that females are significantly younger at the time of diagnosis and treatment induction. These findings are as well in line with previous reports [14,16] Lower COPD frequency in females might be explained to the certain degree by the fact that such condition increases with age [17], and our findings imply that female patients with lung cancer were younger.

Importance of pulmonary rehabilitation of lung cancer patients was pointed out in the study of Rodriguez-Larrad et al., [18], stating that such rehabilitation treatment particularly in preoperative period reduces morbidity in postoperative period and improve functional capacity. The favorable effects of preoperative pulmonary rehabilitation was stressed as well in the study of Nagarajan et al. [5], implying to the fact that it improves exercise capacity along with pulmonary function preservation after operation. This is of particular importance since advanced surgical methods along with effective chemotherapy in treatment of lung cancer patients have improved survival benefits.

The beneficial effects of pulmonary rehabilitation program that was administered to the lung cancer patients from the study in early postoperative stage was pointed out by significant changes of SpO_2 values, but without significant changes in the values of other parameters over the seven days' period. The possible explanation for reduction in oxygen saturation, and particularly significant reduction in SpO_2 values after day 3 but without significant fluctuations in other parameters ($TpCO_2$, DT and HT) might be due to the fact that pulmonary rehabilitation increases oxygen uptake, but since other parameters did not change significantly, we have assumed that pulmonary ventilation was satisfied.

Previous studies have demonstrated positive effects of pulmonary rehabilitation particularly in lung cancer patients on blood saturation and improvement of blood gas indicators [19]. The importance of pulmonary rehabilitation was stressed out as well in the study of Glattki et al., [20], where pulmonary function improvement was noticed in lung cancer patients, despite the presence of COPD or surgical treatment. Further, COPD patients with exacerbations are shown to have similar outcomes as those that does not exacerbate after pulmonary rehabilitation program [21]. However, in planning and performing pulmonary rehabilitation treatment, the exercise tolerance and FEV1 parameter should be taken into consideration, since it is still not well understood why in some cases there are discrepancies in the degree of FEV1 and exercise tolerance for patients with COPD [22]. We have demonstrated from the results of our study that even though there were non significant changes in values of oxygen desaturation and hypercapnia values, it is noticed that after third day of postoperative rehabilita-
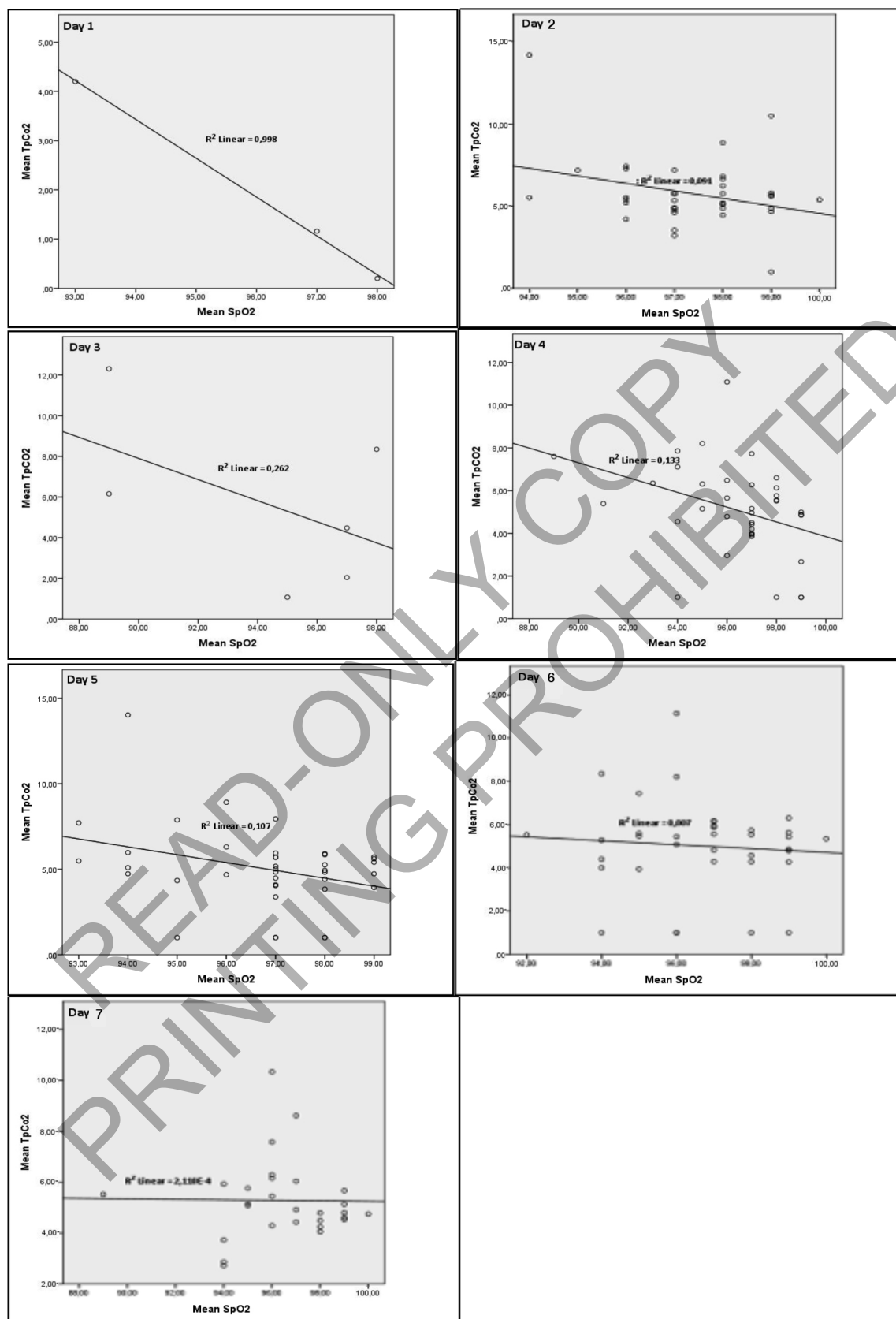
Fig. 3: Significant correlations between mean values of SpO_2 and $TpCO_2$

Significant correlations between mean values of SpO_2 and $TpCO_2$ (R= -0.535, p<0.01 on day 1; R= -0.477, R= -0.365, and R= -0.327 on days 3, 4, and 5, respectively, all p<0.05).

tion, there was gradual increase in oxygen desaturation followed by gradual decrease in hypercapnia values.

Given the facts above, our preliminary findings from this study stressed out importance and positive effects of early pulmonary rehabilitation on oxygen saturation values in lung cancer patients after surgery.

Riassunto

Lo scopo del nostro studio consiste nel valutare gli effetti di una riabilitazione polmonare precoce sui valori di saturazione di ossigeno e della pCO$_2$ transcutanea nei pazienti con cancro polmonare dopo l'intervento.

Lo studio pilota, di tipo osservazionale, è stato effettuato su 41 pazienti (25 uomini e 16 donne) sottoposti a resezione polmonare per carcinoma. Ulteriori parametri monitorizzati in continua per 12 ore per un periodo di 7 giorni sono stati la saturazione di ossigeno (SpO$_2$), la saturazione transcutanea della pCO2 (TpCO$_2$), il tempo di desaturazione ed il tempo di ipercapnia.

Il risultato è stato quello di rilevare valori significativamente inferiori di SpO$_2$ in terza giornata rispetto ai primi due giorni (p<0.05 in entrambe le occasioni), e in quarta giornata rispetto alla prima ed alla seconda (rispettivamente p<0.01 e p<0.05), in sesta giornata in confronto alla seconda giornata (p<0.05), ed in settima giornata rispetto alla seconda (p<0.05). Sono state rilevate significative correlazioni negative tra i valori medi di SpO$_2$ and TpCO$_2$ nei giorni 1, 3, 4 e 5 (R= -0.535, p<0.01 in prima giornata; R=-0.477, R= -0.365, and R= -327 nei giorni 3, 4, e 5, rispettivamente, e tutti p<0.05).

In conclusione la riabilitazione polmonare effettuata sui pazienti affetti da cancro polmonare nel precoce periodo postoperatorio ha comportato una significativa diminuzione dei valori di SpO$_2$ nel nostro gruppo di studio. Questi risultati preliminari hanno evidenziato l'importanza e gli effetti positivi della riabilitazione polmonare precoce sui valori di saturazione di ossigeno nei postoperatorio di pazienti affetti da cancro polmonare

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