

Different recovery from respiratory failure and functional changes after lung cancer surgery depending on the extent of resection, the influence of COPD

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Abstract

BACKGROUND

Lung cancer is recognized to be the main cause of cancer death worldwide and it is closely associated with cigarette smoking and chronic obstructive pulmonary disease (COPD). Only about 15% of patients affected by lung cancer are suitable for surgery and the clinical postoperative outcomes are variable.

We aim to investigate the variables that affect post-surgery complications .

METHODS

A sample of 65 COPD patients who underwent surgery for lung cancer was retrospectively studied about respiratory function and arterial gasanalysis .Data were collected before and after surgery.

A subgroups comparative analysis was performed between group who underwent lobectomy vs group who underwent sub-lobar resection represented by either wedge or segmentectomy.

RESULTS

The overall data were: mean age 71.5, hospitalization time 7.8 days, pack-year 34, body mass index (BMI) 25.4, chronic obstructive pulmonary disease(COPD) assessment test (CAT) mean value was 16.5, forced expiratory one second volume (FEV1) at baseline 1.6 l corresponding to 73.6% of predicted.

The mean age was 71.5, males/females rate 35/30

The prevalent stage was IA and prevalent histotype was adenocarcinoma.

Among the variables affecting the long lasting oxygen therapy (24 hours a day) only the type of surgery along with presence of COPD showed a significant impact.

The relationship between the type of surgery and the lasting of oxygen therapy after surgery showed that lobectomy was 90% more likely to be associated with long lasting oxygen therapy than sub-lobar resection ($p < 0.0005$). Abnormal CAT questionnaire > 10 was also associated with greater risk of long lasting daily oxygen therapy($p < 0.04$).

The subgroups were comparable for age and pack-year , and for PaO₂, FEV 1 and FVC at baseline. A significant difference was observed in terms of hospitalization time ($p < 0.03$) that was longer in group of lobectomy and PaO₂ post-surgery ($p < 0.04$).

Changes between pre and post surgery about the main functional parameters FEV1 and FVC revealed a greater reduction of the above in the group who underwent lobectomy ($p < 0.001$) compared with group treated with sub-lobar resection.

The recovery from lung failure was higher in group with sublobar resection at 3 month check.

CONCLUSIONS

All patients affected by lung cancer who undergo surgery report lung failure of different intensity depending on the type of surgery.

COPD itself could influence the outcome, too. A greater negative variations of functional parameters after surgery is found in group who undergo lobectomy.

Introduction

Lung cancer it is the leading cause of cancer death worldwide. It is classified as non small cell that includes squamous, adenocarcinoma, large cell and small cell lung cancer. All histotypes are often associated with COPD .

The latter is defined as an inflammatory bronchial chronic condition characterized by airflow limitation that is not fully reversible and it is usually caused by exposure to noxious particles or gases predominantly cigarette smoking, though other exposures such as biomass fuels are an important cause. It is the major cause of morbidity and mortality worldwide. It is frequently a comorbidity in lung cancer patients.

The relationships between inflammation, airflow limitation , and lung cancer are known but not fully clarified(1)

By far the main avoidable cause of both COPD and lung cancer is tobacco smoke which contains several chemicals more than 5,000 identified , including tobacco-specific carcinogens such as nitrosamines, nitric oxide, benzopyrene.

By contrast smoking cessation is recognized to be the main tool to improve by itself the prognosis of the diseases and lung function(2).

Lung failure is a possible complication of both diseases and it often occurs after surgery(3)

Lung cancer and COPD are often associated share the same initial pathogenesis (4)

Lung cancer survival has reached partial improvements in the last few decades. Poor outcomes are linked to late clinical presentation, yet early diagnosis can be challenging as lung cancer symptoms are common and non-specific.

Furthermore it is vital in assessing lung cancer risk to look carefully at lifestyle factors and past medical history

The aim of our study is to investigate the effects of the type of surgery in lung cancer patients on lung failure development to determine the variables influencing long lasting oxygen therapy meaning oxygen

for 24 hours a daily and to detect the functional and respiratory changes after surgery comparing the two subgroups.

Methods

From 2019 to 2020 65 patients were retrospectively analyzed who underwent thoracic surgery for lung cancer. This is a monocentric study based on the collaborations between thoracic surgeons and pulmonologists.

The age and demographic data were recorded as well as functional data, types of surgery, tumor staging, hospitalization time.

Patients underwent lung resection by different approach, some had lobectomy by thoracotomy and some others underwent sub-lobar resection by mini-thoracotomy .

All patients performed spirometry before and after surgery with detection of post-bronhodilator values, an arterial blood sample was also done with hemogasanalysis that was performed at baseline, soon after surgery and at three month check(GEM 3000 device) . The COPD assessment test was also applied and it was considered positive in case of score>10 according to GOLD guidelines.

The spirometry was performed by body plethysmography (Jaeger system masterscreen, Germany) as follows: briefly, flow and dynamic volumes were measured by the pneumotacographic method and volumes and resistances by the plethysmographic method. Data considered were post-bronchodilator Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV1), recorded as liters and percentage of predicted. The time for post-bronchodilation was 25 minutes obtained by salbutamol 400 µg. The techniques followed the American Thoracic Society and European Respiratory Society task force guidelines(5).

sub-analysis included a group who underwent lobectomy(25) and group with sub-lobar resection (40)

The study was approved by S.Andrea-Sapienza Ethic Committee, and a consent form was obtained by each patient.

Statistical Method And Analysis

The normality of the data was assessed by the Kolmogorov-Smirnov test and values were expressed as mean and standard deviation (SD) or median and interquartile range, as appropriate. A sub-analysis was performed to compare subgroup of patients as described previously.

For this purpose Mann-Whitney test or Fisher's test was applied as appropriate and significance p level was set at <0.05

A logistic regression analysis was performed to correlate functional data and type of surgery with long-time oxygen therapy. Subsets of patients depending on type of surgery and their association with different grade of lung failure was detected by contingency table test and odds ratio calculation.

A one way ANOVA test was eventually performed for repeated measurements to compare the changes in respiratory function before and after surgery between groups.

All data were acquired by SPSS version 24.0(USA)

Results

Overall data revealed 40 wedge resections and 25 lobectomies.

The prevalent stage was IA2 and prevalent histotype was adenocarcinoma

At baseline table 1 displays the following

The mean age was 71.5 ± 7 , males/females rate 35/30

Mean pack years 34 ± 11.3

Hospitalization time was 7.8 ± 2.5 , mMRC 1.3 ± 0.7 , BMI 25.4 ± 3.3 , CAT 16.5 ± 7.1

FEV1 I 1.68 ± 0.77 and FEV1 percentage 73.6 ± 27.5 , FVC 2.5 ± 0.9 , TLC 5.1 ± 1.3 .

No significant bleeding or complications due to surgery technique were observed.

Patients are still alive except for 4 patients who died of whom 3 underwent lobectomy and 1 underwent wedge resection.

In Table 2 a logistic regression analysis revealed the following

Only the type of resection and COPD affected significantly the dependent variable consisting of long lasting oxygen therapy ($p < 0.04$ and $p < 0.03$).

Table 3 contingency table with determination of odds ratio of the relationship between patients treated with sub-lobar resection(group 0) versus patients treated with lobectomy (group 1)with the need of high intensity oxygen therapy showed a significant association of lobectomy with higher risk of long lasting oxygen supply($p < 0.005$) and a greater high risk for patients with CAT mean value major than 10 ($p < 0.04$)

Table 4

Differences between group 0 and group 1 were significant about hospitalization time($p < 0.03$) with a longer time in patients treated by lobectomy, comparable for COPD ,age and pack-year. A significant difference in PaO₂ value was also observed($p < 0.03$) post-surgery and at 3 month check.

In group 0 (sub-lobar resection) 60% of patients gave up oxygen after 3 months from surgery, compared with 45% in group 1.

Table 5

Differences of changes of the main functional parameters before and after surgery comparing the two subgroups ,group 0 sub-lobar resection and group 1 lobectomy. A greater lost of functional values was observed in the second group and the difference was significant for both FEV 1 and FVC ($p<0.001$).

Figure 1 and 2 depict the differences in variations among groups highlighting a higher reduction post-surgery of values in group 1 who underwent lobectomy.

Discussion

Patients are often concerned about the prospect of using oxygen therapy postoperatively, and this factor may affect their choice about lung cancer treatment.

Our study showed important findings concerning the need of oxygen therapy after surgery and pointed out what variables could be associated with the clinical outcome .

Notably we found that patients who needed long-lasting oxygen therapy meaning a oxygen supply for more than 12 hours a day, were mainly those who underwent lobectomy compared with sub-lobar resection . Part of studied population recovered from lung failure and improved their condition. Notably a higher percentage of patients who gave up oxygen therapy was found in the group who underwent wedge resection. The CAT questionnaire major than 10 was also associated with a higher risk of high intensity oxygen therapy meaning that concurrent COPD exacerbation may influence the post-surgery consequences. The recovery at 3 month after surgery was larger in group 0 than in group who underwent lobectomy.

The presence of COPD was indeed a factor affecting lung failure development and was more present in group high oxygen intensity.

COPD and smoking habit are frequently associated with lung cancer and worsen their-self prognosis since smoking is a common risk factor affecting both diseases (4).

COPD and lung cancer have a common origin sharing inflammation as main associated feature(4).

For NSCLC, surgical resection is the standard treatment for stage I-II disease; patients with IB or II disease are being offered adjuvant chemotherapy. Some patients with a stage IIIA tumor are operable but often receive pre- or post-operative radiation and/or chemotherapy(6). Depending on their extent, pulmonary resections lead to permanent loss of pulmonary function. In healthy people, resections up to a pneumonectomy are remarkably well tolerated.

Consistently with the literature our findings suggest that COPD could influence the respiratory failure development but the extension of the removed parenchyma influence even more the functional values decrease and as a consequence it influences the outcome(7).

Indeed, we found a major change in FEV1 and FVC in patients who underwent lobectomy as well as a worse hospitalization time. The risk of respiratory failure precludes lung surgery in many patients with severe chronic obstructive pulmonary disease. It is generally agreed that a minimum value of forced expiratory volume in 1 second (FEV1) is required preoperatively (2 l before pneumonectomy and 1.5 l in case of lobectomy, respectively). Variable cutoff values of FEV1(ranging from 35% to 80%) have been arbitrarily chosen to assess the severity of COPD and to predict the risk for pulmonary complications. By using receiver-operating characteristic analysis, Licker et coll confirmed that the best cutoff value of FEV1 for predicting respiratory complications was 60% (7)

Our data showed a mean baseline value of FEV1 of 73% of predicted that was considered enough for surgery exceeding the risk value of 60%. It is largely agreed that the extent of pulmonary resection, age and impairment of cardiopulmonary function such as COPD, cardiovascular disorders have to be considered independent factors of operative deaths whereas pulmonary morbidity was mainly influenced by the degree of preoperative functional lung impairment (8)

We found that COPD irrespective of FEV1 value itself influences the post-operative outcome.

We know that the maximal oxygen uptake along with the extent of lung tissue resection are independent predictors of postoperative complications (9). The presence of COPD is not an absolute contraindication to surgery as we know from the literature since lobectomy for cancer can be performed successfully also in selected patients with chronic obstructive pulmonary disease(10). However the grade of airflow limitation and concurrent cardiovascular abnormalities are associated with an increased morbidity although mortality is unchanged(11,12). A PaCO₂ alteration along with FEV1 early decrease may be observed ,mainly among patients who died after surgery(13,14,15). In our study lung failure without hypercapnia was found but without influencing the survival. The present study compares patients with lobectomy with patients with sub-lobar resection showing a worse oxygenation in the group undergoing more extensive resection consistently with similar studies (16,17). Predictors of complications may include age ,gender, history of smoking, type of resection aside from FEV1 value (18,19,20). In our analysis unlike age that did not influence the outcome COPD comorbidity influences lung failure development . Our population was mainly former smokers and pack-year did not affect significantly lung failure occurrence.

Among patients with COPD, the preoperative pulmonary status appears to affect the quality of life and the possibility of complications is reversed by bronchodilators and smoking cessation (21,22,23). The type of approach seems to influence the outcome, too. Indeed, the video assisted thoracoscopy (VATS) approach has a significantly lower rate of complications compared with thoracotomy (28% vs 45%, p = 0.04) with a lower hospitalization time (24).Our approach consisted of either mini-thoracotomy or lateral muscle sparing thoracotomy suitable for different extensive resection. Further consideration is that the

interdisciplinary cooperation notably between pulmonologist and thoracic surgeon allows to better manage the patient affected by lung cancer as demonstrated by previous studies (25) Greater loss of function in the sense of a decrease of FEV1 and FVC was observed in patients treated with lobectomy leading to a greater lung failure percentage and longer hospitalization time. A recovery from lung failure after three months along with a lower hospitalization time was observed notably in patients treated with sub-lobar resection.

Conclusions

Our study highlights the influence of COPD and extent of lung parenchyma resection on respiratory failure development. To our knowledge there are no published reports about the comparison between patients treated with sub-lobar resection and patients treated with lobectomy in terms of functional changes and differences about lung failure development. The majority of patients treated with a more conservative surgery recovered quickly in comparison with patients more extensively treated. COPD was the main comorbidity able to affect the outcome along with the type of surgery.

The changes of functional parameters was notably observed in cases treated with lobectomy. Considering the results we advise a screening of high risk patients to find an early diagnosis in order to promote a sparing parenchyma resection considering equal oncological radicality to reduce post-operative complications. Our study represents a basis for future new prospective studies to confirm our results.

Abbreviations

FEV1 Forced one second expiratory Volume

FVC Forced Vital Capacity

COPD Chronic Obstructive Pulmonary Disease

VATS Video-assisted thoracoscopy

CAT COPD Assessment Test

mMRC modified medical Research Council dyspnea test

NSCLC Non small cell lung cancer

Declarations

[Ethics Approval and Consent](#)

The study was approved by the S.Andrea Hospital-Sapienza University Ethic Committee and a consent form was provided by each patient.

Consent form for publication

A consent form approved by our Institution was provided by each patient.

Availability of data

The data acquired will not be shared because the population is still under control in a long follow up

Funding

Nothing to declare.

Authors' contributions

All authors contributed to the drafting and conception of the manuscript.

Aldo Pezzuto, Massimo Ciccozzi and Beatrice Trabalza Marinucci in addition performed the analysis of data.

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Tables

Table 1 Demographic data

	Mean	SD
Age	71.5	7
Males/females	35/30	
Hospitalization	7.8	2.5
Pack-year	34.0	11.3
mMRC	1.30	0.70
BMI	25.4	3.3
CAT	16.5	7.1
FEV1 l	1.68	0.77
FEV1 perc	73.6	27.5

Baseline data

Table 2

Dependent variable long- lasting oxygen therapy

	OR	CI	p
Age	0.9	0.83-1.1	0.9
FEV1	1.0	0.9-1.0	0.9
FEV1 %	0.9	0.94-1.0	0.9
FVC	1.1	0.9-1.08	0.1
Lobectomy	2.8	0.7-3.2	0.04
TLC	1.0	0.9-1.0	0.6
Smoke history	0.7	0.1-4.9	0.7
COPD	2.1	0.6-2.9	0.03

Logistic multi-regression analysis

Odds ratio and confidence interval

Table 3

Relationship :type of surgery and CAT>10 vs long-lasting oxygen therapy

Sub-lobar vs lobectomy	OR 0.1 (95%CI 0.03-0.38)	p <0.0005
Segmentectomy or wedge Lobectomy	12/40 oxygen >1400 l 20/25 oxygen >1,400 l	24/30 <1,400l 5/25 <1,400l
CAT questionnaire>10	OR 2.8 (0.51-9.5)	p<0.04

Contingency tables with Odds ratio determination

Table 4

Difference between group 0 (sub-lobar resection) and 1(lobectomy)

	Group 0	Group 1	p
Age	73(68-75)	74(67-76)	0.8
Hospitalization	6(4.5-8)	9(7-12)	0.03
Pack-year	35.0(30-40)	40(35-40)	0.07
FEV 1 basal liters	1.75(1.62-1.85)	1.79(1.60-1.81)	0.10
COPD perc patien	56	52	0.10
PaO2 pre mmHg	65.7(61-70.5)	62.58(58.1-61.2)	0.12
PaO2 post	60.6(58.1-62.3)	54.6 (51.5-59.5)	0.03

Baseline data

Median and interquartile range

Mann Whitney test

Table 5

Changes of FEV1 and FVC before and after surgery: comparison between group treated by sub-lobar resection G0 and group treated by lobectomy

	Mean differences G1	G0	Mean square	F	p
FEV1 l	-0.20	-0.10	0.39	86.7	<0.001
FVC l	-0.35	-0.15	0.33	31.39	<0.001

One way ANOVA test for repeated measures

Figures

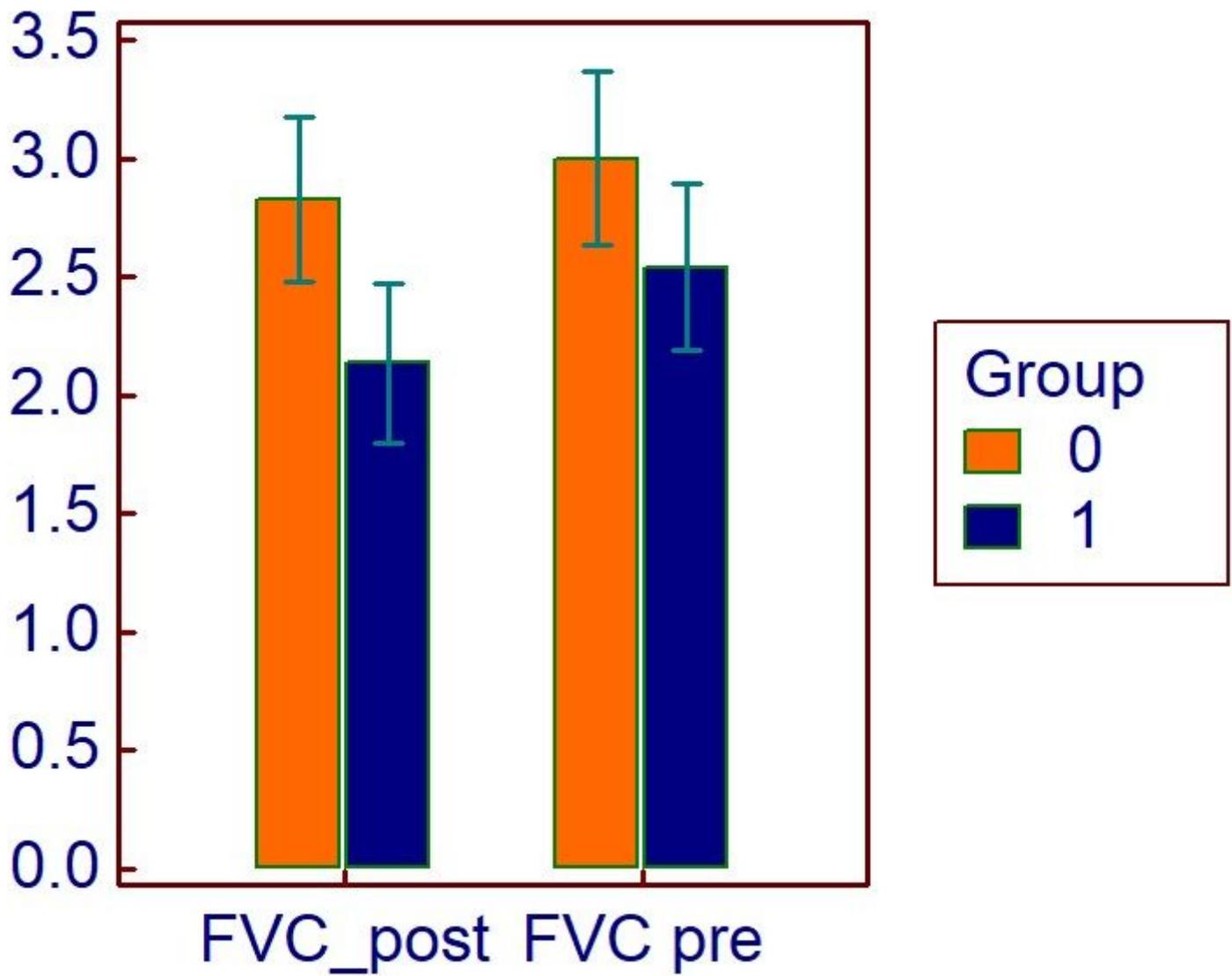


Figure 1

FVC_post FVC pre

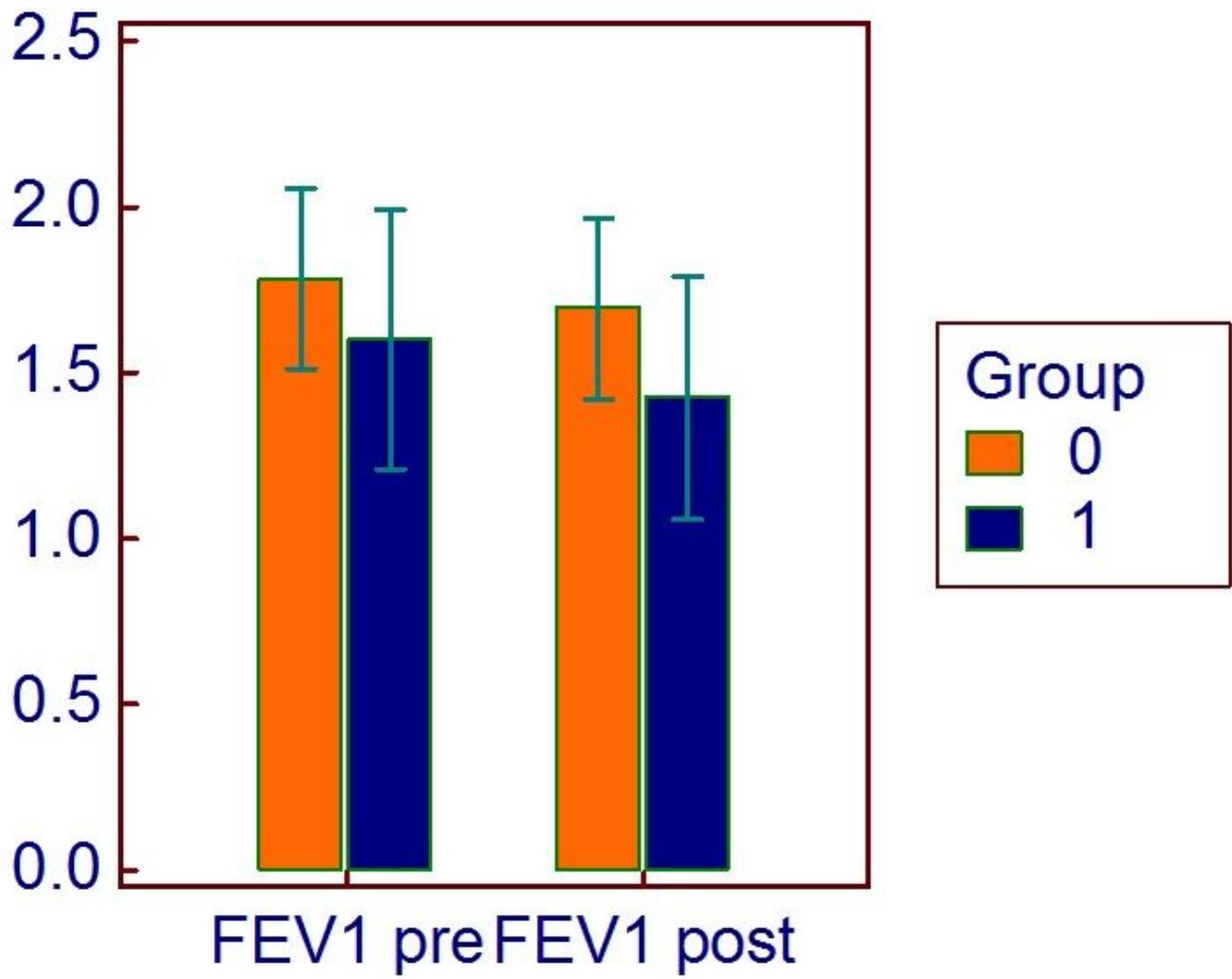


Figure 2

FEV pre FEV1 post