The Resting Pulmonary Hyperinflation: A Determinant of the MMRC Dyspnea Scale in COPD Patients in a Real-Life Cohort?

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On behalf of the Palomb project

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Introduction

- The degree of dyspnea is an important and valid factor in the assessment of COPD severity, as its severity is related to poor prognosis, but its determinants remain poorly understood.
- Dyspnea and hyperinflation are closely interrelated with daily-living activities. However, hyperinflation cut-off values are both ill-defined and non-standardized
- We hypothesized that increased RV, FRC, TLC, RV/TLC and FRC/TLC ratio and reduced IC and IC/TLC ratio would be associated with higher dyspnea.

Objective

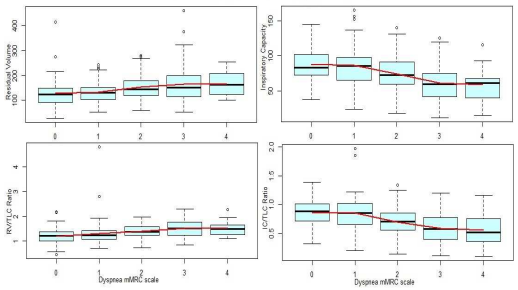
- The aim of our study was to analyze the determinants that could be associated with higher dyspnea mMRC score in COPD patients.

Methods

- The degree Diagnosis of COPD in patients was made by pulmonologists using spirometry with post-bronchodilator $\frac{FEV_1}{FVC}$ <70%.
- The following variables were collected: age, gender, BMI, FEV_1, RV, IC, TLC, FRC, mMRC, comorbidities and frequency of exacerbations.
- We used the LASSO method (least absolute shrinkage and selection operator), a machine learning regression analysis method to build the models and assessed their predictive performance.

Results (1)

Box Plot for IC, RV, IC/TLC and RV/TLC ratio by mMRC scale



Results (2)

Summary of the characteristics of COPD patients (1,973) according to Dyspnea grade mMRC

Subjects characteristics, n (%) or mean(SD) Variable names	Data in all patients	dyspnea mMRC « 0 » n=221	dyspnea mMRC « 1 » n=571	dyspnea mMRC « 2 » n=627	dyspnea mMRC « 3 » n=425	dyspnea mMRC « 4 » n=106	P Value
Males, n (%)	1289(65.33)	166(75.11)	369(64.62)	401(63.96)	265(62.35)	71(66.98)	0.0193
Age, yrs. mean(SD)	66.1 (10.98)	62.9 (10.2)	63.3 (10.4)	66.2 (10.8)	69.4 (10.6)	73.1 (10.7)	<0.0001
BMI, (kg/m^2), mean(SD)	26.69 (10.8)	26.05 (5.08)	26.3 (5.48)	27.2 (17.11)	26.55 (6.27)	27.59 (7.57)	0.4502
<21 (underweight), n (%)	331(16.78)	32 (14.47)	93 (16.3)	107 (17.07)	76 (17.8)	20 (18.87)	
[21-26[(normal), n (%)	683(34.62)	86 (38.9)	196 (34.3)	216 (34.45)	147 (34.6)	28 (26.42)	
[26-29[(overweight), n (%)	396(20.07)	49 (22.17)	129 (22.6)	117 (18.66)	77 (18.12)	19 (17.92)	0.3322
≥29 (obese), n (%)	563(28.54)	54 (24.43)	153 (26.8)	187 (29.82)	125 (29.41)	39 (36.79)	
FEV1, % pred, Mean (SD)	58.11 (19.5)	71.7 (16.7)	65.5 (15.9)	56.11 (17.7)	48.2 (18.7)	40.5 (20.1)	0.4504
Chronic cough, n (%)	1124(56.97)	97(43.9)	273(47.8)	383(61.08)	288(67.7)	74(69.81)	<0.0001
Chronic sputum, n (%)	795(40.3)	71 (32.13)	174 (30.47)	270 (43.06)	216 (50.82)	57 (53.77)	<0.0001
Current smokers, n (%)	793(40.2)	107 (48.42)	238 (41.68)	253 (40.35)	159 (37.41)	30 (28.3)	0.0064
0-1 exacerbation, n (%)	1427(72.33)	183(82.8)	465(81.4)	464(74)	243(57.1)	56(52.8)	<0.0001
≥ 2 exacerbations, n (%)	546(27.67)	38(17.2)	106(18.6)	163(26)	182(42.9)	50(47.2)	<0.0001
Pulmonary rehabilitation, n (%)	157(8)	4(1.8)	18(3.15)	50(7.9)	62(14.6)	23(21.7)	<0.0001
Smoking cessation, n (%)	155(7.8)	15(6.8)	52(9.1)	44(7.02)	37(8.7)	6(5.6)	0.5087
Hyperinflation (RV/TLC≥130%), n (%)	1167(59.14)	79(35.75)	277(48.51)	402(64.11)	313(73.65)	80(75.47)	<0.0001

Comorbidities associated with COPD according to mMRC dyspnea scale

Dyspnea grade Vs comorbidities, n (%)	dyspnea mMRC « 0 » n=221	dyspnea mMRC « 1 » n=571	dyspnea mMRC « 2 » n=627	dyspnea mMRC « 3 » n=425	dyspnea mMRC « 4 » n=106	P Value
Hypertension, 734(37.2)	75(33.9)	167(29.2)	248(39.5)	171(40.23)	59(55.6)	<0.0001
Dyslipidemia, 446(22.6)	47(21.26)	106(18.56)	123(19.61)	128(30.11)	34(32.07)	<0.0001
Ischemic cardiopathy, 353(17.9)	30(13.57)	76(13.3)	100(15.94)	105(24.7)	36(33.96)	<0.0001
Apnea Syndrome, 340(17.23)	59(26.69)	112(19.61)	80(12.75)	67(15.76)	19(17.92)	<0.0001
Anxiety, 318(16.1)	10(4.52)	55(9.63)	92(14.67)	114(26.82)	47(44.33)	<0.0001
Cancer, All causes, 318(16.1)	35(15.83)	88(15.41)	104(16.58)	70(16.47)	17(16.03)	0.9852
Depression, 282(14.3)	22(9.95)	58(10.15)	78(12.44)	89(20.94)	33(31.13)	<0.0001
Diabetes, 250(12.67)	32(14.47)	51(8.93)	76(12.12)	69(16.23)	19(17.92)	0.0037
Arythmia, 241(12.2)	20(9.04)	52(9.1)	81(12.91)	61(14.35)	25(23.58)	0.0002
Asthma, 207(10.49)	17(7.69)	58(10.15)	60(9.56)	56(13.17)	11(10.37)	0.2169
Left heart failure, 100(5.07)	3(1.35)	17(2.97)	26(4.14)	32(7.52)	20(18.86)	<0.0001
Bronchiectasis, 92(4.66)	6(2.71)	12(2.1)	42(6.69)	27(6.35)	5(4.71)	0.0009
Patients with presence of cardiovascular comorbidities, 1087(55.1)	109(49.32)	262(45.88)	353(56.3)	269(63.29)	78(73.58)	<0.0001

- 1,158 patients were considered to have higher dyspnea. Dyspnea was more frequent in women and overweight patients and also correlated with the number of exacerbations.
- Dyspnea was higher in patients with presence of cardiovascular comorbidities (60.45%), and more precisely in hypertensive patients (41.28%) and ischemic cardiopathy (20.81%). Dyspnea was also frequent in patients with presence of anxiety (21.85%).

Results (3)

Variables in three dyspnea models

Variables	Higher dyspnea (mMRC grade ≥1)	Higher dyspnea (mMRC grade ≥2)	Higher dyspnea (mMRC grade ≥3)	Higher dyspnea (mMRC grade ≥4)
FEV_1 (% pred.)	2.937[1.920 - 4.493]	3.716[2.863 - 4.822]	4.304[3.306 - 5.604]	4.660[2.968- 7.317]
Anxiety	4.098[2.128 - 7.894]	2.520[1.827 - 3.475]	2.478[1.822 - 3.371]	3.656[2.269- 5.891]
Age	1.630[1.221 - 2.175]	1.807[1.457 - 2.240]	2.271[1.785 - 2.889]	2.858[1.757- 4.649]
Cough	1.715[1.291 - 2.278]	1.944[1.573 - 2.403]	1.607[1.257 - 2.053]	----------
Hyperinflation	1.717[1.261 - 2.337]	1.687[1.347 - 2.112]	1.340[1.016 - 1.768]	----------
Gender (Women vs. Men)	0.566[0.405 - 0.791]	0.719[0.572 - 0.905]	0.766[0.592 - 0.992]	----------
BMI	1.763[1.288 - 2.414]	1.339[1.069 - 1.676]	----------	----------
Apnea Syndrome	0.684[0.474 - 0.986]	0.722[0.540 - 0.963]	----------	----------
Ischemic cardiopathy	----------	1.634[1.222 - 2.183]	1.901[1.418 - 2.547]	----------
exacerbations	----------	1.413[1.101 - 1.813]	1.842[1.433 - 2.366]	----------
Depression	----------	----------	1.674[1.198 - 2.340]	2.017[1.193 - 3.409]
Hypertension	----------	1.526[1.218 - 1.912]	----------	1.622[1.049 - 2.507]
Bronchiectasis	----------	1.842[1.031 - 3.292]	----------	----------
Dyslipidemia	----------	----------	1.814[1.380 - 2.385]	----------
Asthma	----------	----------	1.449[1.007 - 2.086]	----------
Left heart failure	----------	----------	----------	3.354[1.840 - 6.113]

- We performed a sensitivity analysis for higher dyspnea with three different cut-offs: mMRC scale ≥ 2; mMRC scale ≥ 3 and mMRC scale ≥ 4.
- The increase in the mMRC threshold (2; 3 and 4) implies a slight increase in the odds ratio of the severity of FEV1 (≤50%) (3.7; 4.3 and 4.6).

Conclusions

- Irrespective of cut-offs set to define higher dyspnea groups, our results suggested that dyspnea is related not only to FEV_1 but also to gender, exacerbations, comorbidities and hyperinflation, revealing that the hyperinflation defined by IC/TLC ratio was a better determinant of the mMRC dyspnea scale in comparison to both RV/TLC and FRC/TLC ratio.
- These results illustrate the clinical heterogeneity of COPD patients in real life.

Disclosure

Dr. Molimard report personal fees from Bordeaux university during the conduct study, other from Novartis , MundiPharma and GSK, outside the submitted work.
Dr. Raherison reports grants from Bordeaux University Foundation , during the conduct of the study; personal fees from: Astra Zeneca, Chiesi, ALK, Boehringer Ingelheim, Glaxo SmithKline, Mundi Pharma and Novartis, outside the submitted work.

ATS INTERNATIONAL CONFERENCE May 17-May 22, 2019 dallas tx ATS international conference, May 17- May 22, 2019 Dallas ATS INTERNATIONAL CONFERENCE May 17-May 22, 2019 dallas tx