BMJ Open Respiratory Research

Assessment of lung hyperinflation in occupational chronic obstructive pulmonary disease: a multicentric cross-sectional study

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To cite: de Broucker V, Andujar P, Wardyn P-M, *et al*. Assessment of lung hyperinflation in occupational chronic obstructive pulmonary disease: a multicentric cross-sectional study. *BMJ Open Respir Res* 2023;**10**:e001846. doi:10.1136/bmjresp-2023-001846

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjresp-2023-001846).

Received 23 May 2023
Accepted 8 September 2023

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ABSTRACT

Occupational exposure is associated with elevated morbidity and lower quality of life in patients with chronic obstructive pulmonary disease (COPD). Static hyperinflation is an independent risk factor for all-cause mortality in COPD and for COPD exacerbation. In a multicentre, cross-sectional study (BPROFETIO), we sought to analyse the relationship between static hyperinflation and occupational exposure in patients with COPD with or without occupational exposure.

Material and methods An overall 'whole working life' cumulative exposure index was calculated for occupational patients with COPD. Spirometry indices and lung volumes were measured according to the 2005 American Thoracic Society/European Respiratory Society guidelines.

Results After adjustment for age, sex, height, body mass index, smoking and coexposure, the analysis for each occupational hazard showed a higher risk for hyperinflation and FEV_1 decline or progression of COPD or GOLD stage for patients with COPD exposed to non-metallic inorganic dusts.

Conclusion Occupational exposures should be more investigated in clinical practice and studies as they contribute to the COPD heterogeneity and are associated for some with the development of a static hyperinflation; a condition that is known to have a negative impact on quality of life and survival.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Static hyperinflation is an independent risk factor for all-cause mortality in chronic obstructive pulmonary disease (COPD) and for COPD exacerbation.

WHAT THIS STUDY ADDS

⇒ In this study (BPROFETIO), we sought to analyse the relationship between static hyperinflation and occupational exposure in patients with COPD with or without occupational exposure. The analysis showed a higher risk for hyperinflation and FEV_1 decline or progression of COPD or GOLD stage for patients with COPD exposed to non-metallic inorganic dusts.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Occupational exposures should be more investigated in clinical practice and studies as they are associated for some with the development of a static hyperinflation.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable, treatable respiratory disease characterised by persistent respiratory symptoms associated with airflow limitation. COPD is currently the third-leading cause of death worldwide.[1]

In Europe, the estimated prevalence of COPD is 12.4%.[2] Tobacco smoking is the main risk factor for COPD[3 4]: the attributable risk is over 80%.[5] Other risk factors include a history of lung infections in childhood, preterm birth, intrauterine growth restriction, alpha-1-antitrypsin deficiency, poor socioeconomic conditions, nutritional factors and air pollution.[3 6–12] Recently, Yang *et al* reported that 15% of the COPD-associated disability-adjusted life-years were attributable to occupational exposure in a non-smoker population.[13] Occupational exposure is also involved in the pathogenesis of COPD. The estimated fraction of the COPD risk attributable to occupational exposure ranges from 10% to 18% in smokers and 31% in non-smokers.[14] The main categories of respiratory exposure characterised to date are organic and inorganic dust, gases, vapours and fumes.[6] Epidemiological studies have identified several occupational sectors or activities causal related to COPD: the mining industry, the construction industry, metal foundries, the iron and steel industry, the textile industry, the cereal industry (silo workers), dairy farming and pig farming.[8] The main causes of occupational COPD are crystalline silica, coal dust, cotton dust, cereal dust and endotoxins. Occupational sectors

or activities that are possibly or probably associated with COPD include the cement industry, cement handling, woodworking, welding, metalworking and diesel exhaust fume exposure.[8]

COPD impairs quality of life; this is notably due to limited exercise tolerance, which has been linked to lung static and dynamic hyperinflation.[15] In fact, small airway disease can lead to expiratory flow limitation, gas trapping within the lung, dynamic hyperinflation and thus decreased inspiratory capacity. It has been shown that static hyperinflation (quantified as the ratio between the residual volume (RV) and the total lung capacity (TLC) is an independent risk factor for all-cause mortality in COPD[16] and for COPD exacerbation.[17 18]

To the best of our knowledge, there are few functional data on static hyperinflation in the setting of occupational COPD (in this manuscript, we use the term 'occupational COPD' for COPD whose most likely origin is occupational exposure). In a multicentre, cross-sectional study (BPROFETIO), we sought to analyse the relationship between static hyperinflation and occupational exposure in people with COPD.

MATERIAL AND METHODS

Population and study design

All patients with COPD with a postbronchodilator obstructive ventilatory disorder (as assessed by pulmonary function tests (PFTs)) were recruited between 1 July 2010 and 31 January 2016, in six tertiary hospitals in France (in the cities of Bordeaux, Caen, Créteil, Le Havre, Lille and Nancy) (online supplemental appendix 1). As one of the primary objectives of the BPROFETIO study was to monitor the occupational exposure of people with COPD in the general population, we included prevalent and incident cases of COPD aged 40–80. The participants were recruited by the hospitals'occupational physicians, pulmonologists and PFT department or through smoking cessation programmes.

The following exclusion criteria were applied: age under 40 or over 80; COPD exacerbation during the last month; a diagnosis of bronchial dilatation before the age of 40; a history of bronchiectasis, alpha-1-antitrypsin deficiency or asthma (except asthma in childhood) and insufficient clinical or occupational data.

Participants in the study were divided into an 'occupational COPD' group (people with COPD who had at least one occupational exposure, identified by questionnaire during a face-to-face interview with an occupational physician, as a definite or probable risk factor for COPD, irrespective of their smoking status) and a 'non-occupational COPD' group (people with COPD but no occupational exposures known to be a risk factor for this disorder during their working life).

For each participant, we recorded the sex, age, height, weight, medical history and smoking history (to obtain tobacco consumption in pack-years (PY)). With regard to smoking status, the participants were classified as never-smokers (PY=0), former smokers (having given up smoking for at least 1 year) or current smokers (including former smokers having given up smoking for less than a year at the time of the study).

Patient and public involvement

Patients were not involved.

Assessment of occupational exposure

For each study participant, an occupational physician collected occupational data during a face-to-face interview, via a standardised questionnaire. The questionnaire was based on occupational activities considered in the literature to be certainly or probably associated with a risk of developing COPD. The study participant was asked to report all his/her jobs. For each job, the participant was asked to report the employer, the corresponding period and the working conditions (tasks performed at the workstation, conditions in the workplace, the personal protective equipment provided or not, and proximity to other workstations). Periods of inactivity were specified (unemployment, invalidity leave, work stoppages, parental leave and retirement).

Specific questionnaires were also administered to gain data on the following activities: crop farming, animal husbandry, milk production, wood milling, construction, cement production, smelting, diesel exhaust fume exposure, metallurgy, mining/quarrying, steel or metal milling, welding fume exposure and textile dust exposure (see online supplemental appendix 2).

For each workstation, occupational exposure hazards were grouped into six groups: (1) organic dusts (wood, cereals, fodder, textiles, animals, moulds, animal excrement and other organic dusts), (2) inorganic, non-metallic dusts (asbestos, mineral wools, cement, crystalline silica, coal, coke, bitumen, asphalt and tars), (3) inorganic metallic dusts (steel, aluminium, cadmium, chromium, copper, iron, cast iron, nickel, lead and titanium), (4) non-specific inorganic dusts (building sites), (5) vapours/mists/liquid aerosols (strong acids, organic solvents, varnish, paint, mineral oils and cutting fluids) and (6) fumes (diesel exhaust fumes, welding fumes, bitumen, asphalt and tar fumes).

For each workstation and exposure reported by the study participant, an occupational expert assigned the probability, intensity and frequency of exposure according to a French national consensus statement. The probability of exposure was classified as possible (level 1), probable (level 2) or certain (level 3). The intensity of exposure was classified as low (level 1), medium (level 2) or high (level 3). The frequency of exposure was classified as sporadic (level 1), regular (level 2) or continuous (level 3).

Lastly, for each participant and each of the six exposure groups, an overall cumulative exposure index (CEI) was calculated for the whole working life, using the following equation: duration of exposure

(years)×probability×intensity×frequency. For each participant, we have added up all the CEIs applied to his exposures.

Pulmonary function tests

The participants' PFT data had to contain all the following indices: forced vital capacity (FVC), forced expiratory volume in the first second (FEV_1), the FEV_1 to FVC ratio (FEV_1/FVC), TLC and RV. Spirometry indices and lung volumes were measured by body plethysmography and/or helium dilution, according to the 2005 American Thoracic Society/European Respiratory Society guidelines.[19 20] Predicted values were calculated by applying the European Respiratory Society equations.[21]

All study participants had an obstructive ventilatory disorder, as defined by an FEV_1/FVC ratio below 70% postbronchodilator. We used the Global Initiative for Chronic Obstructive Lung Disease (GOLD)[22] to define the four severity stages: stage I (mild): $FEV_1 \geq 80\%$ of the predicted value; stage II (moderate): $50\% \leq FEV_1 < 80\%$ of the predicted value, stage III (severe): $30\% \leq FEV_1 < 50\%$ of the predicted value; stage IV (very severe): $FEV_1 < 30\%$ of the predicted value. Lastly, static pulmonary hyperinflation was defined as an RV/TLC ratio greater than the upper limit of normal (defined as the theoretical value+1.65×residual SD).[23]

Statistical analyses

Statistical analyses were performed with SAS software (V.9.4, SAS Institute. Continuous (quantitative) variables were expressed as the median (IQR). Discontinuous (qualitative) variables were expressed as the frequency (percentage). Intergroup comparisons (ie, occupational COPD vs non-occupational COPD) were performed with a non-parametric Wilcoxon test for quantitative variables and a χ^2 test for qualitative variables.

For each of the six occupational respiratory hazards, the CEIs of each participant were divided into three categories: 'no exposure' if not exposed to the nuisance, 'low exposure' for a below-median CEI and 'high exposure' for an above-median CEI. Logistic regressions were used to study the bivariate relationships between the outcomes (the severity of airway obstruction and the static pulmonary hyperinflation) and each occupational respiratory exposure (giving a crude OR (95% CI)). Multivariate analyses were adjusted for age, sex, height, body mass index (BMI), smoking (pack-years) and coexposures (dummy variable). The subject is considered to have a coexposure if among the five other specific exposure groups at least one is classified as 'high exposure'. For example, for the non-metallic inorganic group, a subject is considered to have a coexposure if he is also exposed with a 'high exposure' to organic dusts or inorganic metallic dusts or non-specific inorganic dusts or vapours/mists/liquid aerosols or fumes.

RESULTS

Initially 922 subjects were included, 638 in the occupational COPD group and 284 in the non-occupational COPD group. We excluded 194 subjects because they did not have a static volume measurement (n=129 and n=65, respectively). There was no statistically significant difference between included and excluded patients for group (ie, occupational COPD vs non-occupational COPD), FVC, FEV_1 and FEV_1/FVC. The excluded group was significantly younger ((66.8 (60.7–73.1), p<0.001) and had significantly more women (n=58 (29.9%), p=0.005) and more ex-smokers (n=130 (67.0%), p<0.001) than the included group (table 1).

The occupational and non-occupational COPD groups were similar in terms of age, BMI, smoking habits and tobacco consumption (table 1). The proportion of women was higher in the non-occupational COPD group than in the occupational COPD group (49.3% vs 8.9%, respectively; p<0.001).

The total career length and the PFT indices (expressed as % predicted) were not significantly different between the occupational and non-occupational COPD groups (table 1). The proportion of subjects with hyperinflation was slightly but not significantly higher in the occupational COPD group (table 2). The GOLD stages did not differ between the two groups (table 2).

The durations of exposure and the CEIs for the various occupational hazards are summarised in table 3. After adjustment for age, sex, height, BMI, smoking (in pack-years) and coexposure to other types of exposure, we found a higher risk of hyperinflation and of severe COPD (GOLD 3 or 4 vs GOLD 1 or 2) in subjects exposed to non-metallic inorganic dusts (low and high exposure combined) compared with unexposed subjects ($OR_{adjusted}$=2.33 (95% CI 1.29 to 4.23) for hyperinflation and $OR_{adjusted}$=1.67 (95% CI 1.00 to 2.79) for COPD severity). We found no significant increase in the risk of COPD or hyperinflation for other occupational exposures. The analysis for each occupational hazard (divided in three categories: no exposure/low exposure/high exposure) showed a higher risk of hyperinflation only for people with COPD exposed to non-metallic inorganic dusts and a higher risk of more severe COPD (table 4). Moreover, comparison of the medians of the RV/TLC ratio shows significant differences between levels of exposure to non-metallic inorganic dusts (median RV/TLC (observed/predicted)=133.3 (95% CI 115.3 to 156.5) in the unexposed group, 140.6 (95% CI 124.3 to 167.01) in the low exposure group and 133.01 (95% CI 110.3 to 148.9) in the high exposure group; p=0.0184). In the adjusted model, smoking (in pack-years and including non-smokers) was a significant contributor to static hyperinflation and COPD severity. We did not find any interaction between smoking and occupational exposure with regard to their effects on hyperinflation.

DISCUSSION

Our results highlighted an elevated risk of static hyperinflation in the non-metallic inorganic dusts COPD group,

Table 1 Demographic and pulmonary characteristics of the study participants

	Overall study population	Occupational COPD	Non-occupational COPD	P value
	n=728	n=509	n=219	0.590*
Age (years)	64 (57–70)	64 (56–71)	64 (58–69)	0.699†
≥40 and <50	57 (7.8)	41 (8.1)	16 (7.3)	
≥50 and <60	199 (27.3)	137 (26.9)	62 (28.3)	
≥60 and <70	280 (38.5)	191 (37.5)	89 (40.6)	
≥70	192 (26.4)	140 (27.5)	52 (23.7)	
Sex (male)	579 (79.5)	468 (91.9)	111 (50.7)	**<0.001**†
Height (cm)	170 (163–175)	171 (166–175)	166 (159–173)	**<0.001***
Weight (kg)	75 (62–87)	77 (64–88))	70(58-83)	**<0.001***
BMI (kg/m^2)	25.8 (22.2–29.7)	26.1 (22.4–29.9)	25.1 (21.8–29.3)	0.057*
Smoking (PY)	40 (26–56)	39 (26–57)	40 (23–54)	0.668*
Smoking Status				
Current smoker	330 (45.3)	229 (45.0)	101 (46.1)	0.487†
Ex-smoker	373 (51.2)	265 (52.1)	108 (49.3)	
Never-smoker	25 (3.4)	15 (3.0)	10 (4.6)	
PY≤15,	58 (8.2)	43 (8.7)	15 (7.2)	0.716†
15<PY≤30	168 (23.9)	120 (24.3)	48 (23.0)	
30<PY≤45	200 (28.5)	134 (27.1)	66 (31.6)	
45<PY≤60	133 (18.9)	92 (18.6)	41 (19.6)	
PY≥60	144 (20.5)	105 (21.3)	39 (18.7)	
Total working time (years)	39 (34–43)	39 (34–44)	37 (31–42)	**0.006***
Duration of exposure (years)	–	29 (13–37)	–	–
Pulmonary function test indices (% predicted)				
FVC	79.3 (63.2–95.8)	77.7 (63.0–94.2)	82.2 (64.4–97.1)	0.243*
FEV_1	52.6 (37.9–69.1)	52.5 (37.9–68.1)	53.0 (37.9–71.4)	0.800*
FEV_1/FVC	0.72 (0.59–0.82)	0.72 (0.58–0.81)	0.71 (0.60–0.82)	0.920*
TLC	109.3 (96.5–121.0)	108.8 (95.7–120.7)	110.4 (98.6–122.2)	0.205*
RV	149.0 (121.1–188.7)	148.3 (121.0–187.8)	150.8 (121.3–190.7)	0.865*
RV/TLC	134.5 (115.8–157.8)	134.9 (117.0–157.7)	132.9 (115.2–158.3)	0.850*

*Wilcoxon's test.
†χ2 test; the data were expressed as the n (%) or the median (IQR).
BMI, body mass index; FEV1, forced expiratory volume in first second; FVC, forced vital capacity; PY, pack-years; RV, residual volume; TLC, total lung capacity.

when compared with non-occupational COPD group. The results also highlighted an elevated risk of having GOLD 3 or 4 COPD in the subgroup exposed to non-metallic inorganic dusts. We conclude that the type of occupational exposure influences the ventilatory functional consequences (eg, static hyperinflation) for people with occupational COPD. To the best of our knowledge, this study is the first to have looked at static hyperinflation in people with occupational COPD.

Exposure to gas, dust and fumes is known to be associated with the severity of COPD and the risk of work disability.[24] Furthermore, researchers have found that occupational exposure is associated with elevated morbidity and lower quality of life in people with COPD.[25 26] It has also been reported that static hyperinflation (quantified as RV/TLC) was an independent risk factor for all-cause mortality in COPD[16 17] and was associated with an elevated risk of COPD exacerbation.[17 18] Moreover, Zeng *et al* showed that air trapping was common in smokers with normal spirometry results (2318 (31%) of the 7479 patients at risk of COPD had an RV/TLC ratio greater than the upper limit of normal)

Table 2 GOLD stages and hyperinflation in the study population

	Overall study population	Occupational COPD	Non-occupational COPD	
	n=728	n=509	n=219	P value*
GOLD				
Stage I	74 (10.2)	50 (9.8)	24 (11.0)	p=0.734
Stage II	318 (43.7)	223 (43.8)	95 (43.4)	
Stage III	248 (34.1)	178 (35.0)	70 (32.0)	
Stage IV	88 (12.1)	58 (11.4)	30 (13.7)	
Static hyperinflation	492 (67.6)	352 (69.2)	140 (63.9)	p=0.167

Data are expressed as the n (%).
*In a $\chi 2$ test; GOLD stages: stage I (mild): $FEV_1/FVC<70\%$ and $FEV_1 \geq 80\%$ of the predicted value; stage II (moderate): $FEV_1/FVC<70\%$ and $50\% \leq FEV_1<80\%$ of the predicted value; stage III (severe): $FEV_1/FVC<70\%$ and $30\% \leq FEV_1<50\%$ of the predicted value; stage IV (very severe): $FEV_1/FVC<70\%$ and $FEV_1<30\%$ of the predicted value or $FEV_1<50\%$ with chronic respiratory failure. Hyperinflation was defined as RV/TLC>upper limit of normal (residual volume (RV)/total lung capacity (TLC)).
COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

and predicted adverse respiratory outcomes and progression towards COPD.[27] We recommended measuring the lung volume in people with occupational COPD because static hyperinflation might explain (at least in part) why occupational COPD (particularly COPD caused by exposed to inorganic dusts) is more severe than non-occupational COPD.

There are many types of 'non-metallic inorganic dust'. Some (crystalline silica[28] and coal dust[29]) are already known to cause COPD in the absence of pneumoconiosis. For cement,[30] bitumen and asphalt,[31] the currently available data need to be confirmed in larger studies. However, the association between COPD or lung distension and exposure to asbestos fibres or to glass wool is controversial.[32 33] In our study, 25 people in this subgroup were exposed to asbestos fibres, 9 were exposed to mineral wools, 6 were exposed to both asbestos fibres and mineral wools; and so, 28 people were exposed to one or the other. The removal of these 28 from our analysis did not change the OR greatly that is remain all significant.

We did not find higher risk of static hyperinflation in the high-exposure group than in the low-exposure group. This trend was, however, demonstrated for each recruitment centre in the study. Several explanations are possible in our view. First, we thought that there were more coexposures in the low-exposure group but further analysis showed that they are equivalent between the low and high-exposure group. Furthermore, these coexposures were considered in our multivariate analysis. Second, it is possible that patients with a lower quality of life (due to static hyperinflation) left exposed occupations more quickly, resulting in a lower IEC for these subjects. Finally, the 'peak exposure' effect was not taken into account in our analyses and may play a role in the occurrence of diseases following inhalation of mineral particles such as crystalline silica as stated by Hoet *et al* for the decline in ventilatory function.[28]

We did not find any interaction between smoking and occupational exposure with regard to their effects on hyperinflation. In contrast, Blanc *et al* and Boggia *et al*

Table 3 Duration of occupational exposure and the CEIs in the occupationally exposed COPD group

	Exposure to at least one substance	Organic dusts	Non-metallic inorganic dusts	Metallic inorganic dusts	Non-specific inorganic dusts	Vapours/mists/ liquid aerosols	Fumes
Exposed participants (n)	509	188	289	179	157	258	281
Duration of exposure	29.0 (13.0–37.0)	9.0 (3.0–24.0)	20.0 (5.0–33.0)	18.0 (4.0.–32.0)	17.0 (4.0–35.0)	17.0 (4.0–34.0)	21.0 (5.0–34.0)
CEI (unit-years)	–	36.0 (9.0–99.0)	55.5 (18.0–150.0)	38.0 (12.0–112.0)	55.0 (18.0–163.0)	45.0 (12.0–123)	47.2 (13.5–111.0)

The data are expressed as the median (IQR).
Cumulative exposure index (CEI)=duration of exposure (years)×probability×intensity×frequency for the whole career.
COPD, chronic obstructive pulmonary disease.

Table 4 Association between the CEI and the severity of ventilatory impairment, according to the type of occupational exposure (n=728)

	GOLD III–IV (n=336) vs GOLD I–II (n=392)		Hyperinflation (n=492) vs no hyperinflation (n=236)	
	OR (95%CI)	OR adjusted (95%CI)	OR (95%CI)	OR adjusted (95%CI)
Organic dusts				
Not exposed (n=540)	Ref.	Ref.	Ref.	Ref.
Low (n=93)	1.08 (0.70 to 1.68)	1.08 (0.63 to 1.86)	1.41 (0.86 to 2.30)	1.39 (0.83 to 2.31)
High (n=95)	0.84 (0.54 to 1.30)	0.83 (0.49 to 1.42)	1.30 (0.80 to 2.10)	1.42 (0.86 to 2.34)
Non-metallic inorganic dusts				
Not exposed (n=439)	Ref.	Ref.	Ref.	Ref.
Low (n=144)	**1.87 (1.28 to 2.75)****	**2.66 (1.46 to 4.83)****	**1.85 (1.19 to 2.88)****	**3.53 (1.74 to 7.15)*****
High (n=145)	0.80 (0.54 to 1.17)	1.20 (0.69 to 2.10)	0.95 (0.64 to 1.4)	1.85 (0.99 to 3.46)
Metallic inorganic dusts				
Not exposed (n=549)	Ref.	Ref.	Ref.	Ref.
Low (n=87)	0.84 (0.53 to 1.32)	0.99 (0.47 to 2.08)	0.82 (0.51 to 1.31)	0.81 (0.48 to 1.35)
High (n=92)	0.63 (0.40 to 1.01)	0.71 (0.33 to 1.55)	0.77 (0.49 to 1.22)	0.73 (0.44 to 1.21)
Non-specific inorganic dusts				
Not exposed (n=571)	Ref.	Ref.	Ref.	Ref.
Low (n=78)	1.19 (0.74 to 1.91)	1.13 (0.49 to 2.62)	1.56 (0.90 to 2.69)	1.61 (0.88 to 2.94)
High (n=79)	0.62 (0.38 to 1.01)	0.60 (0.26 to 1.36)	1.02 (0.62 to 1.69)	1.07 (0.61 to 1.85)
Vapours/mists/liquid aerosols				
Not exposed (n=470)	Ref.	Ref.	Ref.	Ref.
Low (n=129)	1.00 (0.67 to 1.47)	1.05 (0.59 to 1.86)	1.08 (0.71 to 1.63)	1.11 (0.70 to 1.77)
High (n=129)	0.91 (0.61 to 1.34)	0.96 (0.53 to 1.75)	1.20 (0.79 to 1.84)	1.34 (0.82 to 2.19)
Fumes				
Not exposed (n=447)	Ref.	Ref.	Ref.	Ref.
Low (n=140)	1.02 (0.70 to 1.50)	0.94 (0.55 to 1.59)	0.85 (0.57 to 1.26)	0.92 (0.60 to 1.43)
High (n=141)	1.04 (0.71 to 1.52)	0.91 (0.54 to 1.56)	1.07 (0.71 to 1.61)	1.12 (0.71 to 1.77)

Hyperinflation was defined as RV/TLC >upper limit of normal (residual volume (RV)/total lung capacity (TLC)).
Statistically significant ORs are given in bold type. *p<0.05; **p<0.01; ***p<0.001.
OR adjusted for age, sex, height, BMI, pack-years of smoking and coexposures.
BMI, body mass index; GOLD, Global Initiative for Chronic Obstructive Lung Disease; Ref, reference.

found a synergistic effect of tobacco/occupational exposure (although for obstructive ventilatory disorders).[5 34] Meer *et al* reported that smoking doubles the effect of mineral dust exposure on the development of chronic bronchitis.[35]

In most of the studies of a putative causal link between occupational exposure and the development of COPD, the functional endpoint was the annual decline in FEV_1. Indeed, for practical reasons, it is easier to obtain a flow-volume curve than to perform lung volume measurement; this is why very few studies (other than case reports) have measured the RV/TLC ratio in people with occupational lung disease. Bauer *et al* measured a large number of pulmonary functional indices in coal miners with pneumoconiosis and moderate bronchial obstruction. Unfortunately, to reduce data overfitting, the researchers did not include the RV/TLC ratio as a possible predictor in the clinical grade of dyspnoea—even though the miners had high mean±SD value (119.8%±25.2% predicted).[36] In a study of exposure to silica (in mining, glass/pottery industries and the building industry), Talini *et al* showed that RV and functional residual capacity (FRC) values were higher in people with conglomerate silicosis (n=4) than people with simple silicosis (the RV/TLC ratio was not reported).[37] Larsson *et al* found a significantly greater RV (p=0.049) in aluminium potroom workers than in controls but no significant difference in lung function (including the RV, TLC and closing capacity/TLC) between workers with high and low exposure to total dust or to fluorides.[38] Few literature studies used the RV/TLC ratio as the primary outcome for occupational COPD because this ratio is primarily used to assess functional lung sequelae in studies of small numbers of

patients, due to the difficulty of obtaining lung volume data in large cohorts.

Due to changes in the elasticity of the lung parenchyma and small airway disease, static hyperinflation causes gas to be trapped in the lung at rest. This static hyperinflation becomes dynamic hyperinflation, due to expiratory flow limitation and incomplete emptying of the lungs during the respiratory cycle. Hence, an increase in the respiratory rate is the only means of meeting the oxygen demand during exercise. The pathogenesis of lung hyperinflation in people with COPD has not been fully characterised but appears to be an insidious process that develops over several decades.[39 40] Small airway inflammation and loss of elastic recoil are the first two steps in the occurrence of static hyperinflation, that is, when the end-expiratory lung volume after non-forced expiration is reset to a higher volume than predicted. The increase in RV appears to be the first pulmonary function index to change.[41 42] Thereafter, FRC and TLC rise as lung compliance increases. Given the wide range of phenotypes in people with COPD and accumulation of various types of damage (eg, emphysema), the order of occurrence of these abnormalities can vary. Using multidetector CT and isolated lungs removed from people with COPD and controls, McDonough *et al* showed that narrowing and loss of terminal bronchioles preceded emphysematous destruction and can explain the elevated peripheral airway resistance observed in COPD. Unfortunately, the researchers did not report on the study participants' occupational exposures.[43]

Our study had several strengths. First, the occupational and non-occupational COPD groups did not differ significantly in terms of age and tobacco consumption. Second, the significant expected effects of smoking were seen in our analysis. Third, occupational exposure over the whole career was evaluated by an expert in occupational diseases; this might have helped to avoid the bias of overestimation of occupational exposure often associated with self-questionnaires.[44] Lastly, our study provided lung volume data for a large number of people with occupational COPD.

Our study also had some weaknesses. First, it was not possible to perform chest CT scans to check for the presence or absence of emphysema, even though this disease is known to be related to smoking and occupational exposures. Second, we defined static hyperinflation as an RV/TLC ratio above the upper limit of normal; however, there is no international consensus on the definition of lung distension as measured by ventilatory indices.[39 45] Chuang and Lin listed other definitions of hyperinflation found in the literature (inspiratory capacity/TLC<0.25; RV/TLC≥0.4; RV/TLC>0.35 plus an increased TLC; RV/TLC>0.3 plus RV%≥120% and RV/TLC>0.35 plus a normal TLC or RV%≥120%) and correlated some of them with other functional variables assessing lung volumes in COPD subjects. The researchers found that RV%, FRC% and TLC% were highly correlated (r^2=0.59–0.74), as were RV/TLC, FRC/TLC and inspiratory capacity/TLC (r^2=0.37–0.98). We chose to use the RV/TLC ratio because several experts consider it to be a risk factor for mortality in people with COPD. In order to facilitate interstudy comparisons, the definitions of static hyperinflation should be harmonised.

In conclusion, occupational exposures should be more investigated in clinical practice and studies as they contribute to the COPD heterogeneity and are associated for some with the development of a static hyperinflation; a condition that is known to have a negative impact on quality of life and survival.

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Acknowledgements We thank the BPROFETIO members who contributed to this study. BPROFETIO members are from the following 6 French hospitals: CHU Caen (Bénédicte Clin, Marie-France Marquignon, Hervé Normand and Amèle Mouadil); CHU Bordeaux (Patrick Brochard, Chantal Rahérison and Catherine Verdun-Esquer), CH Le Havre (Antoine Gislard, Philippe Hubscher and Jean Quieffin), CHU Lille (Virginie de Broucker, Jean-Louis Edmé, Sébastien Hulo, Nadège Lepage, Annie Sobaszek), CHU Nancy (Ari Chaouat, Christophe Paris and Isabelle Thaon) and CHI Créteil (Pascal Andujar, Bruno Housset, Bernard Maitre, Jean-Claude Pairon and Elise Sergent).

Contributors PA conceived and developed the initial study protocol and discussed it with VdB, NL, J-LE and SH. J-LE developed the statistical model. VdB, NL and SH led the acquisition of hospitalisation data. J-LE ran all the analyses. VdB, P-MW, J-LE and SH wrote the initial draft. PA, NL and OLR critically reviewed the paper. VdB, P-MW, JLE and SH wrote the first draft of the revisions and PA, NL and OLR critically commented on it. All authors read and approved the final version for publication. VdB is responsible for the overall content as the guarantor.

Funding This work was supported by funds from the French Agency for Food, Environmental and Occupational Health & Safety: ANSES CRD 2009-28 to 33 grants for BPROFETIO programme.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval The study's objectives and procedures were approved by an independent ethics committee (CPP Ile de France IX, Boulogne Billancourt, France) on 28 December 2010 (reference: 2010-A00425-34). Written informed consent was obtained from all participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as online supplemental information.

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