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Independent Determinants of Predominant Emphysematics-Phenotyping in the Chest Scanner in Three Medical Training of Kinshasa: Cross Sectional Study

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ABSTRACT

Background and Objective: Chronic obstructive pulmonary disease (COPD) is predicted to be the third leading cause of death worldwide by 2020. Its diagnosis remains a challenge in developing countries such as DRC, with the use of Gold standard, spirometry, limited. Chest imaging plays an important role in orientation. The absence of local radiological data from COPD had therefore motivated this study.
The objective of this study was to define the radio-CT metric aspects of COPD in our environment and determine their association with the clinical phenotype.
Materials and Methods: Retrospective and analytical study of clinical and thoracic imaging data (radiography and CT scan), collected from the records of 120 COPD subjects followed in three Kinshasa medical trainings between January 2014 and June 2017. Fisher's test compared the results obtained. The combination of imaging data and clinical phenotype through Pearson chi-square testing, logistic regression and odds-ratio (OR). The service threshold was set at 0.05.
Results: the study population (average age of 64.52±6.82 years) was predominantly male (78.3% n=94). The main risk factors were tobacco (32.5% n=39) and domestic pollution (30.8% n=37). The consultation took place at Stage II (42.5% n=51) and Stage III of GOLD (36.7% n=44). The TDM phenotype reached mixed was (50% n=4) at stage III and (83.3% n=10) at stage IV with a 0.001. The dominant emphysematic TDM phenotype was (25% n=2) at stage III and (66.7% n=8) at stage IV with a p= 0.029.
Conclusion: This study showed that diagnosis was often delayed. Stage III and IV of COPD were associated with the predominant emphysematic and mixed-achieving TDM phenotype, while stage I and II were associated with the predominant TDM type phenotype with airway.

Keywords: COPD, Clinical and Radiological Profile, Kinshasa.

1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease characterized by generally progressive limitation of air flow; associated with a chronic inflammatory response of the respiratory tract, following chronic inhalation of harmful particles and / or gases. [1, 2]

COPD is a preventable and treatable disease. It affects adults over 40 years old and its frequency increases with age. Its prevalence is variously reported around the world. US statistics estimate it to be between 7% and 9% of the general population. In the West it would reach nearly 10% of the population. [3] In France

nearly 3.5million people are thought to be affected. [4] In Africa, its prevalence varies between 2.7% and 14%. [5] However, there is reason to believe that the incidence of this disease is generally underestimated, especially in the absence of an objective test, a comprehensive study and given its progressive nature. Similarly, global prevalence is difficult to estimate given the inaccessibility to spirometry in several regions of the globe. [6, 7] This is particularly the case in several developing countries where spirometric surveys are not always available as in DRC. This disease is the fifth leading cause of death in the world after heart attacks, strokes, community respiratory infections and tuberculosis. [1, 8, 9]

The DR Congo, our country is not spared by this pandemic of the century and some studies in the middle have already shown the existence of some risk factors for COPD, as well as the harmful role of smoking at 17.5% and 25% exposure to industrial pollutants in the city of Kinshasa. [10] Another study had shown that cardiovascular pathologies represented 17.9% of co-morbidities in patients with COPD. [11] Its diagnosis remains a challenge in developing countries, the use of standard Gold, spirometry, being limited. Chest imaging plays an important guiding role. The lack of local radiological data for COPD therefore motivated this study.

2. MATERIALS AND METHODS

2.1. Material

2.1.1. Type and study period

Retrospective and analytical study, based on the exploitation of the various records of the pneumology services, dated January 01, 2014 to June 01, 2017.

2.1.2. Study Framework

This is a multi-center study, conducted simultaneously at the Kinshasa University Clinics (CUK), the Kinshasa General Reference Hospital (HGRK), the BIAMBA Marie MUTOMBO Hospital (HBMM); all residents of Kinshasa. The choice of these institutions was justified by their respective capacities to handle COPD cases.

2.1.3. Different conventional X-ray machines used

Were used the Hitachi model ZU-L3TY (year 2011), Siemens iconos R 100 (year 2006) and Allengers (year 2008) respectively at CUK, HMBM and HGRK. The acquisition settings were 60 to 75 KV / 22mAs for the front RTS shot and 90 to 110 KV / 28 mAs for the profile shot. Automatic development with cassette decoding by an AGFA laser CXR 35® preceded the archiving of images on CD with embedded reading software (I-viewer®).

2.2 Methods

2.2.1 Variable methods of interest

Sociodemographic Variables (Sex, Age), Epidemiological data (Concept of tobacco use, exposure to domestic and industrial pollutants, comorbidity), Clinical data (Cough, dyspnea, sputum) and paraclinical data were collected.

2.2.2. Statistical analysis

The entry of compac-branded computer data and statistical calculations were made using EPI INFO version 7.0 and IBM SPSS 23.0 software on Windows 10. The data were represented by proportions (%) or absolute frequencies for quantitative variables and averages; deviation-types with their extremes for qualitative variables. The Pearson chi-square test was used to compare proportions, and the student test was used to compare average ages. The univariate risk was assessed with a 95% confidence interval by odds-ratio or odds-ratio using the contingency table and the Manteel Haenszel test with the Yates correction if necessary. The value of $p<0.05$ was considered a threshold of statistical significance.

3. RESULTS

3.1. General characteristics of the study population

Care Among all patients (n=120), 63.3% (n=76), 23.3% (n=28) and 16.3% (n=16) were treated respectively at CUK, HGHK and HBMM. Smoking (32.5% n=39), Exposure to Domestic Pollution (30.8% n=37), Exposure to Occupational Pollution (30.37) 5.8% n=.7), and the after-effects of pulmonary tuberculosis (7.5% n=9) were, respectively, the risk factors for COPD observed in this study. Respiratory functional explorations characterize the study population based on the staging of COPD progression (the stage of VEMS alteration): the proportions of stage II and III being the most frequent around 80% of the series. All patients were assessed by chest x-ray. All X-ray shots of the front chest and profile were of very good quality. Radiographic manifestations of the thorax were dominated by pulmonary distension (Table 1).

Table 1. General characteristics of the study population

Variable of Interest	n=120 (%)
Care	
Univesity Clinical of Kinshasa	76(63.3)
General hospital of Kinshasa	28(23.3)
Biamba Marie Mutombo Hospital	16(16.3)
Risque factors	
Smoking	39(32.5)
Domestic Pollution	37 (30.8)
Occupational Pollution	7 (5.8)
TBC Sequelae	9 (7.5)
Severity of COPD	
Stage I	3(2.5)
Stage II	51(42.5)
Stage III	44(36.7)
Stage IV	22(18.3)
Face chest x-ray lesions	
Pulmonary distension	96 (80.0)
Pulmonary Hypertension	62 (51.7)
Bronchial parietal thickness in rail	73 (60.8)
Emphysema Bubbles	56 (46.7)
Sword Sheath	48 (40.0)
Expiratory Trapping	8 (6.7)
Bronchial Parietal Ring Thicken	6 (5.0)

3.2. Association between aging and covariate

The proportions of aging varied unevenly and very significantly (P<0.001) between men and women. Aging was observed in all women followed by men with aging and men without aging, as shown in Figure 1.

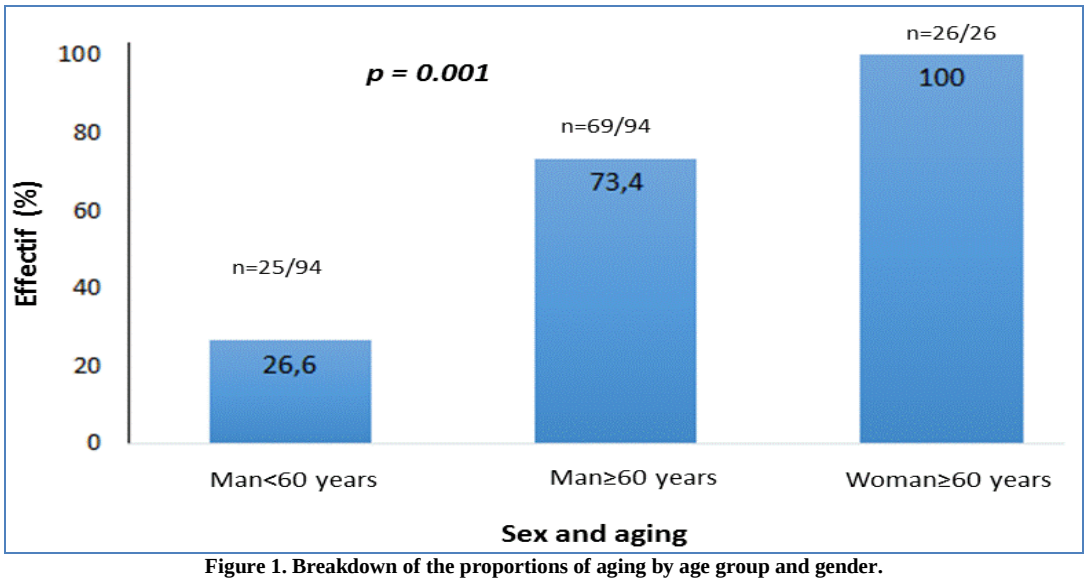

Figure 1. Breakdown of the proportions of aging by age group and gender.

3.3. Clinical and imaging characteristics between aging and youth-adult

The proportions of allergy, comorbidities and types of comorbidities were similar (P<0.05) between aging and young-adult status. There was no significant association (P>0.05) between chest distension, vessel modifications, emphysema bubble, rail images, ring images, sword sheath trachea, expiratory trappings and aging. There was no significant association (P>0.05)

between the proportions of bronchial parietal thickening, bronchial dilation, centrolular nodule, pulmonary artery dilation and aging (Table 2).

Table 2. Comparison of rates of clinical manifestations, X-ray and phenotytyping copd by chest scanner between aging and youth-adult

Variables of interest	Aging %(n)	Young adult %(n)	p
Rates of clinical manifestations			
Allergy	8.4 (8)	4 (1)	0.455
Comorbidity	27.4(26)	12(3)	0.110
Type of comorbidities			0.395
Cardiovascular Disease	15.8(15)	4(1)	
Diabetes Sweet	1.1 (1)	0 (0)	
Association Cardiovascular Disease and Diabetes Sweet	4.2(4)	0(0)	
Interstitial Pneumonia	6.3 (6)	8(2)	
X-ray			
Chest Distension	80(76)	80(20)	0.622
Pulmonary Vascular Modification	52.6 (50)	48(12)	0.680
Emphysema Bubbles	49.5(47)	9(36)	0.230
Rail image	58.9(56)	68(17)	0.409
Ring image	4.2 (4)	8 (2)	0.439
Trachea sheath	40(38)	40(10)	0.587
Expiratory Trapping	7.4 (7)	4 (1)	0.473
Phenotytyping copd by chest scanner			
Bronchial parietal epaissement	16.8(16)	24 (6)	0.411
Bronchial Dilation	14.7(14)	16(4)	0.875
Centrolobular Nodule	4.2(4)	0(0)	0.297
Pulmonary artery dilation	33.8(8)	50(4)	0.399

3.4. Interaction between aging and sex associated with covariates

3.4.1. Influence of interaction between sex and aging in the epidemiological variable

Changes in the proportions of smoking per cigarette and exposure to domestic and/or occupational pollution varied unevenly and very significantly between the groups of interactions between aging and sex, as presented in Table 3.

Cigarette smoking was higher in men with aging than in men in the young adult state than in women with aging. On the other hand, exposure to domestic and/or occupational pollution was significantly in men in the young adult state and in men with aging.

Table 3. Proportion of smoking per cigarette and exposure to domestic and/or occupational pollution with the gender and aging

Group of gender interaction and aging	Cigarette smoking %(n)	Exposure to domestic and/or occupational pollution %(n)
Men with ageing	46.4(32)	20.3 (14)
Men in The Young-Adult State	24(6)	24(6)
Women with Aging	3.8(1)	65.4(17)
Value P	<0.0001	<0.0001

3.4.2. Variation in the proportions of COPD phenotypes on the scanner with the Aging-Sex Interaction Group

Only the proportions of pulmonary artery dilations, para septal emphysemas and bubble emphysema were similar ($P>0.05$) between the interaction group, between aging and the sex. On the other hand, the rate of centroobular emphysema, panlobular emphysema, predominant airway impairment, mixed impairment, predominant emphysematic impairment varied unevenly and significantly ($P<0.05$) between the group of interaction between aging and sex, as shown in Table 3.8.

This phenotyping of COPD was paradoxically on the representation of emphysema and predominant airway disease in young-adult men, while predominant emphysematics and mixed impairments specifically defined its phenotyping for men with aging. However, panlobular emphysema was characteristic of this phenotyping.

Table 4. Variation in the levels of centroobular emphysema, lobular pan-panemly emphysema with the predominant airways, Mixed achieving predominant emphysematic impairment between the interaction group, between sex and aging

Variables of interest	Men with ageing %(n)	Men to the State young-adult %(n)	Women with ageing %(n)	Value P
Centrolobular Emphysema	44.4(8)	100 (8)	0(0)	<0.001
Lobular pan-lobular emphysema	44.4 (8)	0(0)	66.7(4)	0.010
Predominant emphysematous reach	72.2(13)	12.5(1)	33.3(2)	0.013
Predominant Airway Reach	0(0)	75(6)	66.7(4)	<0.001
Mixed Reach	44.4(8)	0 (0)	0(0)	0.016

3.5. Severity Rate and Chest X-Ray

The proportions of BLCO severity were associated (P<0.05) with chest distension, pulmonary vascular modification, rail image, ring image, sword sheath trachea, expiratory trapping.

Rates of bronchial parietal thickening were similar (p=0.908) between the copd severity stage: 0% (n=0) at stage I 66.7% (n=8) at stage II, 75% (n=6) in Stage III and 66.7% (n=8) in Stage IV;

The proportions of mixed impairments were similar (p=0.169) between the severity stage of COPD: 16.7% (n=2) in stage II, 50% (n=4) in stage III and 16.72% (n=2) in stage IV;

The proportions of bronchial dilation did not vary (P=0.167) between the stages of COPD severity: 50% (n=6), stage II, 75% (n=6) in stage III and 50% (n=6) in stage IV;

The rate of centroobular emphysema was similar across the COPD severity stages (P=0.189): 50% (n=6) at stage II, 75% (n=6) in stage III and 33.3% (n=4) at stage IV.

On the other hand, the prevailing rates of emphysematic impairment, pulmonary artery dilation, panlobular emphysema, paraseptal emphysema and bubble emphysema varied unevenly and significantly (P<0.05) between the stage of COPD severity, as shown in Table 5.

Table 5. Comparison of the proportions of predominant emphysematic impairment, pulmonary artery dilations, lobular pan-led emphysema, paraseptal emphysema, bubble emphysema between the severity stage of COPD

Variables of interest	Stade II %(n)	Stade III %(n)	Stade IV %(n)	Value P
Mixed reach	16.7(2)	50(4)	83.3(10)	<0.001
Pulmonary artery dilation	50(6)	0(0)	50(6)	0.041
Pan lobular emphysema	16.7(2)	25(2)	66.7(8)	0.029
Paraseptal Emphysema	0(0)	25(2)	0(0)	0.041
Bubble Emphysema	0(0)	25(2)	0(0)	0.041

3.6. Prediction of predominant emphysematics

After adjusting for the confounding factor (aging, health system and copd severity stage) only cigarette smoking was identified as the most important, independent and highly significant determinant of predominant emphysematic COPD phenotyping in a thoracic scanner in a sub-population of 32 patients, as presented in Table 6.

For example, cigarette smoking conferred a high multivariate risk adjusted for emphysematics/phenoypages by chest scanner multiplied by 11 times.

Table 6. Independent determinants of predominant emphysematics-phenotyping in the chest scanner

Independent Variables	B	ES	Wald	AjOR (IC95%)	p
Tobacco					
Yes	2.457	0.915	7.202	11.7 (1.9-70.2)	0.007
No				1	
Age					
≥60 years	3.458	0,876	3.397	1.59 (0.89-3.89)	0.169
<60 years				1	
Constant	-1.609	0.775	4.317	1	0.038

4. DISCUSSION

This study involved a total of 120 patients with COPD with uneven distribution. The majority of copd patients were treated in the Department of Internal Medicine at university clinics compared to other COPD patients treated at HGRK and HBMM.

Indeed, the CUK has established a tertiary health level to train physicians specializing in radiodiagnosis and medical imaging. In contrast, the proportions of COPD patients were similar between HGRK and secondary health HBMM.

Approximately 40% of COPD patients were exposed to environmental pollution, 84% of whom were domestic pollution- compared to 16% occupational pollution. The socio-political and economic crisis in the DRC without access to electricity exposes the population of the city of Kinshasa to a high risk of COPD. [12, 13] In addition, the frequency of 5.8% of occupational pollution in this study was 5 times lower than that of 31.1% in the US. [14] The city of Kinshasa is today characterized by the smoke of plastics, firewood, the emanation of gas from factories and used vehicles. Worse still, the dust raised by the wind and also that of unpaved roads. The extent of exposure to smoke exhaled by relatives, friends, co-workers and other cigarette or cigar smokers were not specified in this study. Exposure to smoking and other particles induce COPD and other respiratory diseases. [15] The clinical picture of COPD described in this study was similar to that regularly reported in the Gold literature. [16] Indeed, dyspnea and chronic cough were reported in 100% of patients with COPD. These results corroborate the study of Yaccouba T et al., in Mali which showed that dyspnea had a frequency of 100% and cough at 63% in patients with COPD. [17] On the other hand, expectorations of patients with COPD were less common than dyspnea and chronic cough 95% of patients with COPD in this study. This disparity could be explained by the influence of seasonality and bacterial exacerbation. [18, 19] Characteristic of COPD according to the Literature Gold [16] was not included in our research protocol. This study highlighted the coexistence of cardiovascular pathology, diabetes mellitus, interstitial lung disease as reported in the literature of Gold [17] and a study in Kinshasa conducted by Tshiasuma. [11] The multimorbidity concept defined by the World Health Organization (WHO) as the concomitant presence of at least 2 chronic medical conditions in the same individual, [20] requires a more generalized approach to the patient through personalized (individualized) medicine. [21] Multimorbidity in COPD in poor patients, aged, tabagic, underdiagnosed and under-treated in Kinshasa hospital settings will be more vulnerable to hospitalization and mortality as reported in the literature. [22, 23] During the progression of COPD, [18] spirometry and volume flow curve defined the severity of obstructive ventilatory disorder by VEMS/CVF 0.7 and 80% in this study. As the classification of Gold by exacerbation [16] is not universally accepted, spirometry remains the most invasive, sensitive and objective tool for measuring obstructive ventilatory dysfunction despite its low specificity. [24] This study characterized certain radiographic aspect of the face and profile chest in patients with COPD. Pulmonary distension was the dominant sign on head chest x-rays during this study in 80% of cases. Bronchial parietal rail thickening came second in 60.8%, followed by HATP in 52%, emphysema bubble in 46.7% of cases. These results are similar to those of Muller NL et al. in Canada [25] who noted the prevalence of pulmonary distension (pulmonary hyperinflation) and pulmonary emphysema in COPD patients. This study shows that bronchial parietal thickening, centro-lobular emphysema and predominant emphysematous impairment is the computational expression of COPD in 68.75, 50% and 50% of cases, respectively. These results are similar to those of Fernandes L et al. in India [26] who had

shown that dominant emphysematic impairment was common in the COPD patient. Bruno H et al. in Brazil [27] also stated that dominant emphysematic impairment was most common in patients with COPD. This study defined a constellation phenotype of tracheo-bronchial, emphysematic and vascular lesions by CT circumsted chest imaging. On the other hand, other European authors have reported a predominant emphysematous phenotype from the sputum examination [28] in addition to this study, a Japanese study, a Craig J Galban et al. study, in the USA, [29] and a study Hochhegger B et al., in Brazil [30] defined the phenotype and characterized a constellation of para septal centro-lobular emphysema, panlobular, bubble, distal and proximal airways in front of interstitial and nodule infringement interfaces. COPD by chest scanner defines the variability of the extent of emphysema and signs of airway damage for the same degree of obstruction. Like Craig J Galban et al. in the USA, [29] this study also defines a Bantou phenotyping of COPD by scanner with a concurrent presence of mixed impairment (emphysematic and small airway damage that may precede emphysema).

Like Bruno H et al. in Brazil, [27] this study reports the co-existence of the severe decrease in the number of terminal bronchioles in the emphysematous territory and the parietal thickening at the residual bronchiole level. The inflammatory reaction coupled with bronchiolar remodeling precedes emphysema. This study also characterized COPD phenotyping during aging through chest radiographic abnormalities and CT scans of the chest. In this study, the expiratory trapping defined on chest x-ray was primarily related to the female sex, while the literature shows that male sex are more prone to cigarette smoking and trapping in the developed country. [17, 27] On the other hand, this study reports the role of aging and the extent of centrolobular emphysema, lobular panbarem emphysema, predominant airway impairment, mixed impairment (including predominant emphysema and predominant airway impairment) between men and women examined at chest scans. Indeed, this study shows a particular phenotype of COPD defined paradoxically from the coexistence of emphysema at all locations and the reaching of the predominant airways in young-adult men against COPD phenotyping characterized by the coexistence of predominant emphysematic impairment, and predominant airway impairment and in men with aging as reported by the GOLD literature. [16]

The results of this study focused on the global medical movement between the role of COPD, senescence and senility. [31,32] The molecular biology of senescence allows a better understanding of physiological aging at the level of an organ such as an individual's lung to shed light on the pathophysiology of multimorbidity (COPD, cardiovascular disease, weight loss, demineralization) related to advancing age. [33] In addition, COPD has high rates of morbidity, mortality and socio-economic impact. [16, 33] Pulmonary cell senescence is also involved in pulmonary remodeling in parenchymatal and vascular reshuffling through inflammation and oxidative stress. [33] It is currently established that COPD is linked to premature aging by telomere attrition, [31, 32] (end of the chromosome with a critical role in the stability of DNA and cellular functions. [34, 35] There is a lack of cellular regeneration, a lack of tissue repair, release of mediators and tissue reshuffling during the development of COPD. [33] The latter mechanism explains the accumulation of cells either from cell renewal to replicative seed or through somatic cells under oxidative stress (oncogenic factors, cytokine signaling abnormalities through premature seed). [33] Telomere shortening is reported in the white blood cells and lung cells of COPD patients. [34, 35] It is therefore an accumulation of an alveolar epithelial senescent cell, endothelial cells and fibroblasts [35, 36] that may explain susceptibility to the emergence of COPD with short telomere in 20% of smokers, [37]

on the other hand, the exaggeration of tissue repair and inflammatory reaction processes associated with COPD could shorten telomere and induce depletion of the replicative potential of cells. [37,38]

CONCLUSION

In conclusion, this clinical-radiographic study of COPD in the urban environment of Kinshasa has almost come to the same conclusion as that reported in the literature: male volunteer predominance in the 6th decade of life; The harmful role of smoking as a predisposing risk factor; the relatively frequent association of COPD with cardiovascular disease; the existence of COPD phenomenon characterized by mixed impairments (coexistence of predominant emphysematic impairment and predominant airway impairment), bubble emphysema, lobular pan-pan emphysema, and centrolubular emphysema according to aging and male sex. However, despite the above, there are many signs to more easily recognize on simple chest x-ray beyond stage I, including pulmonary distension, bronchial parietal rail thickening and the presence of emphysema bubbles; this is even in the absence of CT and spirometry.

Conflict of interest

The authors declare no conflict of interest

Knowledge

We thank all who participated in the study.

Author's contributions

FDF, BLM, ANN and HAT designed and analyzed the statistical data for the study. MLT and JMT supervised the study. All authors have read and approved the final and revised version of the manuscript.

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