COMPARISON OF ARTIFICIAL INTELLIGENCE-BASED CHEST CT EMPHYSEMA QUANTIFICATION TO PULMONARY FUNCTION TESTS

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ABSTRACT:

Background: *Chronic obstructive pulmonary disease is caused by small-airway disease and emphysema. Although pulmonary function tests (PFT) measure airflow obstruction, they can't differentiate between airflow limitation and emphysema. Computed Tomography (CT) can be used to identify patients with emphysema. AI-based algorithms are convenient for pattern recognition on chest CT images and emphysema quantification.*

Aim of the work: *To evaluate an artificial intelligence-based prototype algorithm for quantification of emphysema on chest CT compared with PFT.*

Patients and Methods*: This cross-sectional study was carried at radiodiagnosis department Ain Shams university hospitals. A total of 35 patients who underwent both chest CT and PFT within 6 months were retrospectively included. The spirometry based Tiffeneau index (TI; which is the ratio of forced expiratory volume in the first second to forced vital capacity) was used to identify emphysema severity; a value of <0.7 was considered to imply airway obstruction. Lung volume analysis was calculated using local artificial intelligence-based 3D reconstruction software and emphysema was quantified using attenuation-based threshold of (-950 HU). Percentage of Low attenuation area (LAA %) was reflected by automated calculation of Goddard score. Emphysema quantification was compared to TI using the using Pearson's method.*

Results: *The mean TI for all patients was 0.77 ± 0.22. The mean percentages of emphysema (LAA%) 20.54% ± 21.8%. AI-based emphysema quantification showed good correlation with TI (p < 0.001). Conclusion: AI-based, automated emphysema quantification either with Goddard score or LAA % shows good correlation with TI, possibly contributing to an image-based diagnosis, COPD categorization, follow-up, and treatment strategies planning.*

Key words: *emphysema, low-attenuation area, lung analysis, quantitative computed tomography, artificial intelligence.*

INTRODUCTION:

In terms of morbidity and death, chronic obstructive pulmonary disease (COPD) is one of the most prevalent diseases in the world. COPD is defined as chronic, progressive airflow limitation that is not completely reversible, associated with a range of pathologic alterations in the lungs with significant extrapulmonary effects, caused by the chronic inflammation and architectural changes. The two factors contributing to the chronic airflow obstruction are emphysema and small-airway disease (obstructive bronchiolitis). The relative contributions of these two factors differ greatly from patient to patient. The existence and degree of each element may have an impact on the clinical presentation, illness severity, prognosis, and therapeutic response. Chronic overinflation of the terminal bronchioles and thinning of bronchial walls are characteristics of emphysema[1].

The Tiffeneau index (TI) (FEV1/FVC) and other spirometric measurements used in pulmonary function testing are commonly used to diagnose COPD. These measurements are recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD). The diagnosis of COPD is confirmed if the forced expiratory volume in one second to forced vital capacity ratio (FEV1/FVC) is less than 0.7[2].

By evaluating the low-attenuation volume (LAV) of the lung, quantitative computed tomography (QCT) can also be used to assess the pathologic evolution of emphysema[3]

Emphysema can be measured with the use of chest computed tomography (CT). Additionally, this extra information might help to maximize the advantages and cost-effectiveness of CT screening. Emphysema patients can be identified with CT, and COPD patients can have their COPD progression tracked. CT densitometry is established on the percentage of voxels below -950 HU since this parameter have the best link with microscopic and macroscopic emphysema findings. The limitation of airflow is measured by pulmonary function tests, but they cannot distinguish between airway obstruction and emphysematous damage. On the other hand, CT enables for the separation between emphysematous destruction and airway obstruction and offers in vivo information regarding pathological alterations[4].

Radiology is quickly embracing artificial intelligence (AI), and tasks like emphysema quantification and pattern detection on chest CT images may be well suited for AI-based systems[3].

AIM OF WORK:

To compare emphysema quantification on chest CT to pulmonary function tests using a prototype method based on artificial intelligence.

PATIENTS AND METHODS:

A cross sectional study that included 35 patients with clinical suspicion of COPD, who underwent Pulmonary function testing in the department of Chest diseases at Ain Shams University Hospitals and then referred to the Radiodiagnosis Department for chest HRCT examination. 35 patients were included in the study.

Study Population:

Inclusion criteria:

The study included Patients referred to the Chest Department, Ain Shams University Hospitals for clinical suspicion of COPD undergoing Pulmonary function tests who were referred to the radiology Department for Non-Contrast CT Chest. Patients, with clinical suspicion of COPD, complain of chronic and/or progressive dyspnea, cough, and sputum production. Patients may also have wheezing and chest tightness with no sex predilection.

Exclusion criteria:

Patients with contraindications to undergo spirometry:

- Hemodynamic instability.
- Recent myocardial infarction or acute coronary syndrome.
- Respiratory infection, a recent pneumo-thorax, or a pulmonary embolism.

- A growing or large (>6 cm) aneurysm of the thoracic, abdominal aorta.
- Retinal detachment.

***Patients with contraindication to radiation exposure;* pregnant[5].**

Ethical Considerations:

The study was approved by the Research Ethics committee of Ain shams University Hospitals. The cases were retrieved from our PACS, with the patient's consent waived being a retrospective study.

Study Tools and procedures:

Lung functions: Spirometry was used to quantify FEV1, FEV1/FVC ratio. The pulmonary function laboratory of the chest department of Ain Shams University hospital uses a VIASYS FLOWSCREEN Spirometer.

The highest readings were recorded and represented as percentages of the projected value after being completed in triplicate. The examination was conducted in accordance with the American Thoracic Society's recommendations.

Airways obstruction was determined to be FEV1 less than 80% predicted and a post-bronchodilator FEV1/FVC (TI) of 0.70 or below. Four categories of patients were created using GOLD 2023 based on their severity[6].

Imaging protocol:

Since the investigation was conducted without the use of intravenous or oral contrast, no specific preparation was required. The patient was lying supine with his arms up above his head.

CT machine: high-speed, Machine used: General Electric (GE) version bright speed CT, multirotational 16 director with rotation time = 0.5 seconds. Slice thickness used was 0.625-1.25 mm with tube voltage of 120 KV and tube current 250 mAs, Collimation: 1.5-3 mm.

Technique:

The patients were scanned cranio-caudally, starting from above the lung apices till below the lowest costophrenic angle. the patients were instructed to inhale and hold their breaths in full inspiration for the entire scan time.

Image processing:

Multiplanar reformatted images were obtained. All images were displayed with lung window '1500 width/600 level' for interpretation.

CT lung analysis:

The analysis was performed using our local Fujifilm 3D synapse software.

1. CT volumetry, which is automatically calculated volume of each lung.
2. CT densitometry: It involves the automated red coloring of the low attenuation areas (LAAs), which are defined as locations with Hounsfield unit (HU) density less than -950. (Fig. 1).
3. Goddard score calculation: It involves calculating the percentage of LAA per surface area and determining the severity level using a specific scoring system, as given in Table 1. Three zones were identified in each lung: the upper zone, which ran from the apices to the level of the aortic arch; the mid zone, which ran to the level of the carina; and the lower zone, which ran to the level of the diaphragm. (Fig. 2).

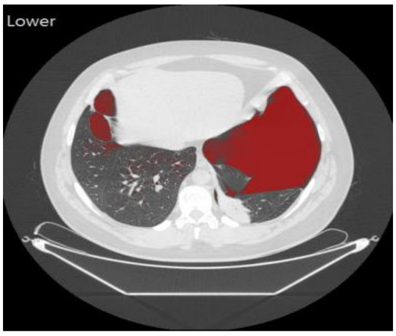


Figure (1): Computed tomography densitometry showing lower zonal low-attenuation area (LAA) less than −950 HU marked by red coloring.

Table (1): Illustrating the Goddard score per lung zone[7]

Percentage of LAA	Score	Grading
0-5	0	Normal = 0
5-25	1	
25-50	2	Mild =1-7
50-75	3	Moderate = 8-15
75-100	4	Severe = 16-24

The final Goddard grade is determined by adding the scores corresponding to the percentages of low-attenuation zones in the top, middle, and lower zones of the right and left lungs.

Data Management and Analysis:

The collected data was revised, coded, tabulated, and introduced to a PC using Statistical package for Social Science (SPSS 25). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

Descriptive statistics:

1. Mean, Standard deviation (± SD) and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data.
2. Frequency and percentage of non-numerical data.

Analytical statistics:

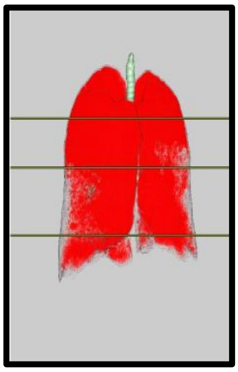
Chi-Square test was used to examine the relationship between two qualitative variables.

Correlation analysis (using Pearson's method):

To assess the strength of association between two quantitative variables. The correlation coefficient denoted symbolically "r" defines the strength (magnitude) and direction (positive or negative) of the linear relationship between two variables.

- r= 0-0.19 is regarded as very weak correlation
- r=0.2-0.39 as weak correlation
- r=0.40-0.59 as moderate correlation
- r=0.6-0.79 as strong correlation
- r= 0.8-1 as very strong correlation

Kappa statistics to compute the measure of agreement between two investigational methods.



Total score	10 (Moderate)

Goddard score:

Right lung	Area(cm^2)	LAA(%)	Score
Upper	141.5	74.7	3
Middle	187.9	32.0	2
Lower	182.9	16.8	1

Left lung	Area(cm^2)	LAA(%)	Score
Upper	117.0	46.7	2
Middle	144.4	18.6	1
Lower	106.3	18.0	1

Figure (2): A case with automatic red coloring of the low-attenuation area (LAA) smaller than 950 HU from a CT densitometry scan. The three zones of each lung were the upper zone, the mid zone, and the lower zone. Goddard score computation is shown in the table that is connected to the image. In this patient, the spirometric data classified as GOLD III/IV were associated with the Goddard score of 10, which is considered to be moderate.

RESULTS:

Our study was performed on 35 patients with clinical suspicion of COPD. The mean age of the study population was 50.23 ± 14.66 years (range 17-80 years). Totally, 22 patients were males, representing (62.9%) of the study sample.

Lung Function Parameters:

In the overall population, mean FVC low limit of normal (LLN) was 2.85 ± 0.7, mean FVC % was 66.32 ± 28.89, mean of the FEV1% was 60.13 ± 31.91, mean TI was 0.77 ± 0.22.

Pathologic TI was found in 22 patients, all of them gave pathological Goddard score (100%), whereas 13 patients showed physiologic TI, only 8 of them (61.5 %) showed normal Goddard score. Table 2 provides an overview of the PFT results.

Table (2): PFT Results of Study Participants

	Mean ± SD	Median (IQR)	Range
FVC LL	2.85 ± 0.7	2.8 (2.55 - 3.18)	(1.56 - 4.54)
FVC A2	2.47 ± 1.19	2.35 (1.5 - 3.2)	(0.78 - 6.76)
FVC%	66.32 ± 28.89	67 (43 - 86)	(2.42 - 129.4)
FEV1%	60.13 ± 31.91	62 (32.8 - 84.6)	(14 - 131.1)
FEV1/FVC %	77.31 ± 22.3	81 (59 - 98)	(43 - 123)
MMEF	44.82 ± 39.43	27.7 (13 - 71)	(5 - 143.8)
CT total Lung volume ml	4319.53 ± 1573.07	4568 (3248.5 - 4994.4)	(1331.3 - 8450)
Total LAA %	20.54 ± 21.8	9.6 (3 - 31.43)	(0.1 - 70.3)

Totally, 13 (37.14%) patients were categorized to be grade I (mild) by the Goddard score, with four of them (30.77%) showing normal PFT, two of them (15.38%) showing mild obstructive pattern by PFT (GOLD I), four of them (30.77%) had moderate obstructive pattern by PFT (GOLD II), while three of them (23.08%) had severe obstructive pattern on PFTs (GOLD III/IV)

Eight (22.86%) patients were grade II (moderate) by the Goddard score, with one of them (12.5%) showed normal PFT, two of them (25%) showed moderate obstructive pattern by PFTs (GOLD II) and five (62.5%) cases showed severe obstructive pattern on PFTs (GOLD III/IV).

Six (17.14%) patients were considered grade III by the Goddard score, with one of them (16.67%) showed moderate obstructive pattern by PFTs (GOLD II) and five (83.33%) cases showed severe obstructive pattern on PFTs (GOLD III/IV).

Finally, 8 (22.86%) cases were found to be normal by the Goddard score, with all of them (100%) showed normal PFT. (Figure 3).

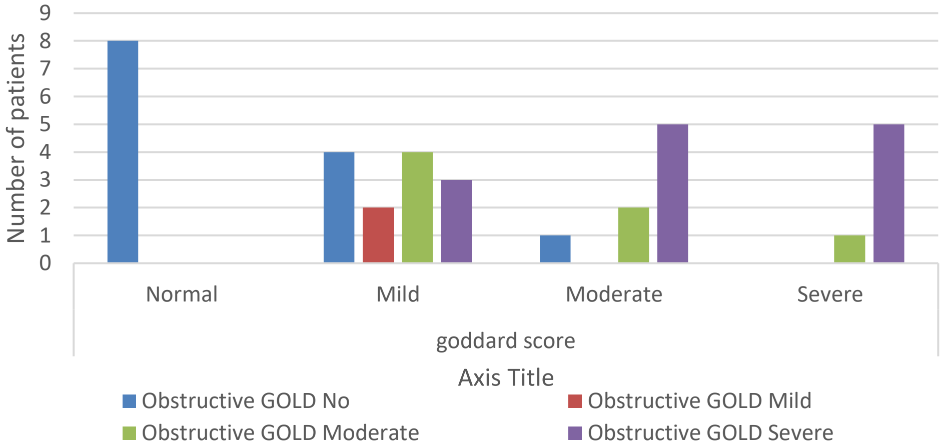


Figure 3: GOLD scoring by Pulmonary function tests plotted against the corresponding Goddard score by automated emphysema quantification.

Comparing the artificial intelligence based calculated Goddard score to the GOLD classification of the PFTs showed significant correlation (P< 0.001)

Emphysema quantification mediated by AI demonstrated a statistically significant correlation with TI, p value less than 0.001. Therefore, higher percentage of the lung being afflicted by emphysema is related with a decline in lung function, which can be meaningfully predicted by the AI system used here.

An inverse relationship was observed between the Tiffeneau (TI) by PFT with the total percentage LAA (P< 0.001) (Table 3).

Figure (4) shows the scatterplot of the relationship between TI and total LAA %

Table (3) Correlation between total the LAA % and TI

		T1
Total LAA %	Spearman Correlation Coefficient	0.712
	p value	<0.001
	sig.	S

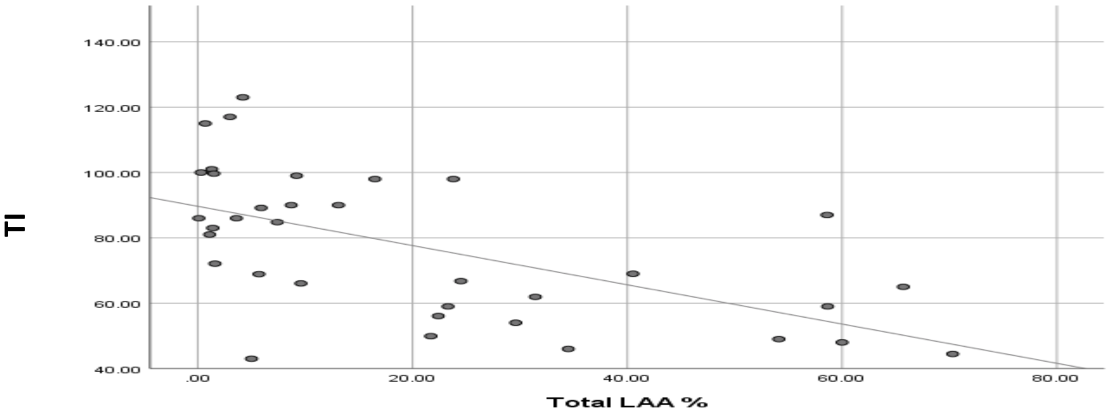


Figure (4): Correlation between the TI and the LAA %

Ct lung Volume and total LAA % was automatically calculated with mean CT lung volume 4319.53 ± 1573.07 and median 4568 (3248.5 - 4994.4). Mean LAA % calculated was 20.54 % ± 21.8 % (Table 4).

Table (4) The CT lung volume and the LAA %

	Mean ± SD	Median (IQR)	Range
CT total Lung volume ml	4319.53 ± 1573.07	4568 (3248.5 - 4994.4)	(1331.3 - 8450)
Total LAA %	20.54 ± 21.8	9.6 (3 - 31.43)	(0.1 - 70.3)

A strong correlation was observed between the calculated CT total lung volume with the percentage LAA with correlation coefficient of 0.71 (P< 0.001) (Fig.41). **(Table 5)**

Table (5) Correlation between the CT lung volume and the LAA %

		CT total Lung volume ml
Total LAA %	Spearman Correlation Coefficient	0.712
	p value	<0.001
	sig.	S

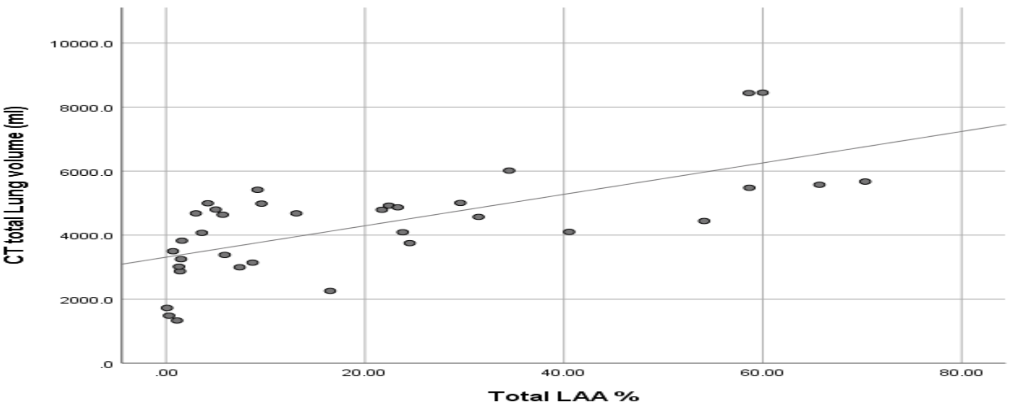


Figure (5): Correlation between the CT lung volume and the LAA %

The main zone for distribution of the emphysema was found to be the right lower zone in 25 patients (71.42 %). Followed by the Left lower zone with positive emphysema quantification score in 22 patients (62.85 %) The left upper and middle zones that showed positive emphysema quantification score in 21 patients each (60%)

The least frequent lung zones showing emphysema detected by the automated emphysema quantification was the right upper and middle zones with only 20 patients (57.14 %).

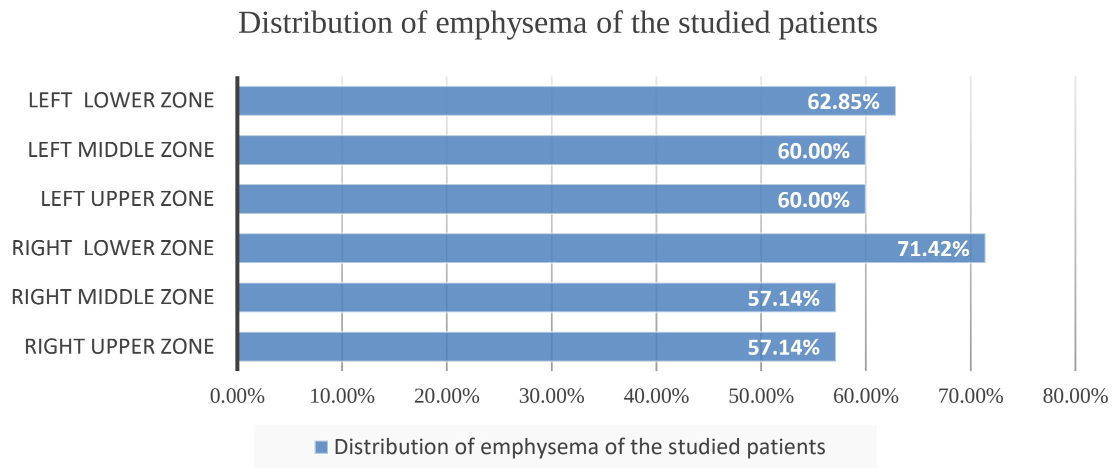


Figure (6): Distribution of emphysema of the studied patients

20 Patients (57.14 %) showed associated findings discovered on CT acquisition either pulmonary, including pulmonary nodules, atelectasis, tree in bud, bronchiectasis, mosaic attenuation, pleural effusion and ongoing inflammatory process, or extra pulmonary including: adrenal adenomas, thyroid nodules., degree of kyphoscoliosis, cardiomegaly, pericardial effusion, renal cysts, gall bladder stone and gall bladder wall calcification.

DISCUSSION:

The global burden of chronic obstructive pulmonary disease (COPD), which caused over 3 million deaths in 2022, is anticipated to rise during the ensuing decades due to high smoking rates and air pollution. The Global Initiative for Obstructive Lung Disease (GOLD) group revised its definition of chronic obstructive pulmonary disease (COPD) in 2023 to read as follows: "COPD, a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, expectoration, exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction [6&8].

The revised definition places more emphasis on patient characteristics, which enables us to discuss the etiology and diagnostic criteria in greater detail separately. However, the distribution of the disease process and the degree of architectural distortion in the lung parenchyma are not precisely captured by the clinical or spirometry results alone.(Mohamed et al., 2017a) [(9)].

While visual emphysema quantification requires a lot of work, multidetector CT makes it easier to characterize and quantify these morphological alterations. Emphysema quantification based on artificial intelligence has thus been a fascinating research area as it offers a means for emphysema's objective quantification. Quantitative CT may also be a very intriguing modality for detecting these pathologies in vivo because it allows for morphological categorization and visual pathology evaluation of CT images without the need for a radiologist, and it has a high degree of repeatability and reliability for follow-up.

Imaging can also be used to differentiate between pulmonary fibrosis and interstitial lung disease, which have symptoms that are similar to those of COPD. In this study, however, there was no correlation between the restrictive pattern of PFT and the LAA% estimated by automated QCT.

In their study in ***2013, Schroeder et al.*** stated that QCT has several impediments as there is considerable differences in measurement of CT lung attenuation by different types of scanner models; reconstruction algorithms; and CT protocol parameters involving size of the voxel, tube voltage (kVp), and tube current–exposure time product (mAs); these variations emphasize the necessity of several studies to identify the optimum parameters. The CT attenuation values are also influenced by changes in inspiratory and expiratory lung volumes. However, these limitations were overlooked due to the strong correlations identified in their study suggesting that differences due to these technical factors may be considered small which is consistent with our study[10]**.**

In our study, the objective was to assess an automatic AI-based prototype for quantitative emphysema assessment and lung volume analysis.

Our results suggest that AI can be successfully used to measure the increase in Low attenuation volume measured by Goddard score that relates to a decrease in TI.

Image acquisition was done with 0.625-1.25-mm image thickness and tube voltage of 120 kv in full inspiration which is consistent with the study of ***Fischer et al. in 2020*** and the recommendations of the Quantitative Imaging Biomarkers Alliance (QIBA) that suggested the use of slice thickness ≤1 mm however, this is in contrast to Mohamed et al.(2017), whose image acquisition was done after forced expiration and the meta-analysis conducted by ***Crossley et al.*** which recommends a slice thickness of 2.5–5 mm[11]**.**

Emphysema quantification was done with local 3D CT reconstruction software for lung airway analysis, Goddard score and LAA % that is calculated with threshold set at -950 HU which is consistent with many previous studies as the best cut off value for emphysema detection[11]. Yet inconsistent with others that suggested LAA-856 HU to be the most strongly associated attenuation threshold with airflow limitation in patients with COPD[10] as well as Madani et al. (12) that suggested that –960 HU or –970 HU were the best attenuation threshold correlated with microscopic and macroscopic pulmonary emphysema.

Our study also found a significant correlation between the calculated CT lung volume and the percentage of LAA, and this consistent with many previous studies[13] .

In our study there was statistically significant correlation between pulmonary functions namely TI and the LAA % and the Goddard score calculated accordingly. Which is consistent with many previous studies (Arakawa et al., 2001; Fischer et al., 2020b; Madani et al., 2001, 2006) (14-17).

It is known that clinical, pulmonary function, actual degree of parenchymal destruction, and distribution of the disease can be all considerably mismatched because of the underlying heterogenous pathogenesis which is referred to as well in the updated GOLD definition of COPD [6&18].

The forementioned heterogeneity of the disease was evident in a study in 2015 when 10.4% of patients with radiographic emphysema and clinical COPD had normal spirometry. The idea that spirometry may need to be supplemented by other manifestations of COPD became the basis of the updated GOLD guidelines (Lutchmedial et al., 2015) (19). This is consistent with our study that showed 5 patients (14%) with positively calculated Goddard score and physiological TI.

This is also. supported by autopsy studies that have shown that up to one-third of the lung can be destroyed by emphysema before respiratory function becomes impaired[20].

In our study, the most frequent lung zone showing emphysema detected by emphysema quantification was found to be the right lower zone in 25 patients (71.46%).

Accordingly, the ability of an AI-based system to analyze image data and produce important clinical information without a radiologist contribution should thus hold significant potential for quantitative imaging approaches to provide patients with accurate diagnoses and direct treatment.

Limitations:

This retrospective study has several limitations that should be taken into consideration in the interpretation of our results. First, there was no available spirometric triggering in our CT scans, so we could not entirely ensure that imaging studies were acquired during maximum inspiration.

Specific parameters for image acquisition were used regarding CT slice thickness, tube voltage and current and emphysema threshold however multiple studies suggested different parameters which could not be all explored in our study.

Conclusion and Recommendation:

In conclusion, we found that the AI-based algorithm introduced here was able to quantify emphysema rapidly and with very strong correlation to clinical pulmonary function testing parameters which can be a reliable method for identifying the COPD phenotype of the patient , following up on the patient's condition and response to treatment as well as identifying the most affected lung lobes in planning for interventional treatment in severe cases as lung volume reduction surgery (LVRS) and bronchoscopic lung volume reduction (BLVR.). Further studies are needed to identify the best parameters for standardization of AI based emphysema quantification parameters to better the patient's follow up assessment.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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مقارنة بين القياس الكمي لانتفاخ الرئة بالتصوير المقطعي المستند إلى الذكاء الاصطناعي واختبارات وظائف الرئة

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المقدمة : يحدث مرض الانسداد الرئوى المزمن بسبب عنصرين: انسداد مجارى الهواء الصغرى وانتفاخ الرئة. على الرغم من أن اختبارات وظائف الرئة تقيس محدودية تدفق الهواء، إلا أنها غير قادرة على التمييز بين انسداد مجرى الهواء وانتفاخ الرئة. يمكن استخدام التصوير المقطعي لتحديد المرضى الذين يعانون من انتفاخ الرئة ومراقبة تقدم المرض لدى الذين يعانون من مرض الانسداد الرئوي المزمن. قد تكون الخوارزميات المستندة إلى الذكاء الاصطناعي مناسبة لمهام مثل التعرف على الأنماط على صور الأشعة المقطعية للصدر والقياس الكمي لانتفاخ الرئة.

الهدف من العمل: تقييم خوارزمية تعتمد على الذكاء الاصطناعي لتقدير كمية انتفاخ الرئة على التصوير المقطعي على الصدر مقارنة مع وظائف التنفس.

الطرق و الاشخاص المستخدمة فى الفحص : أجريت هذه الدراسة المقطعية في قسم الاشعة التشخيصية بمستشفيات جامعة عين شمس. تم تضمين ما مجموعه 35 مريضا خضعوا لكل من التصوير المقطعي للصدر وقياس وظائف التنفس خلال 6 أشهر بأثر رجعي. تم استخدام مؤشر تيفينيو القائم على قياس التنفس؛ والذي يُحسب كنسبة حجم الزفير القسري في الثانية الأولى إلى السعة الحيوية القسرية) لقياس شدة انتفاخ الرئة؛ واعتبرت قيمة أقل من 0.7 للإشارة إلى انسداد مجرى الهواء. تم حساب حجم الرئة باستخدام تقنية إعادة البناء ثلاثي الأبعاد القائم على الذكاء الاصطناعي وتم قياس كمية انتفاخ الرئة باستخدام عتبة قائمة على التوهين البالغ اقل من (-950) وحدة هاونسفيلد). انعكست النسبة المئوية لمنطقة التوهين المنخفضة في درجة جودارد. وتمت مقارنة القياس الكمي لانتفاخ الرئة ومؤشر تيفانو باستخدام طريقة بيرسون.

النتائج: وجد ان هناك علاقة عكسية بين مؤشر تيفينيو و نسبة التوهين المئويه كما وجدت علاقة عكسية بين مؤشر تيفينيو و درجة الجودارد حيث ان كلما قل مؤشر تيفانو، زادت نسبة التوهن المئوية و ارتفع نسبة الجوداردز كما وجدت علاقة طردية بين حجم الرئة المحسوب بالذكاء الاصتناعى و نسبة التوهينز

الملخص و الاستنتاج: يُظهر اهمية القياس الكمي الآلي لانتفاخ الرئة القائم على الذكاء الاصطناعي علاقته بوظائف التنفس، مما قد يساهم في التشخيص القائم على الصور، وتصنيف مرض الانسداد الرئوي المزمن، والمتابعة، وتخطيط استراتيجيات العلاج.