Original Research Article

Multidetector CTin Evaluation of Post COVID-19 Pulmonary Complications with 3D CT volumetric assessment of post COVID-19 fibrosis.

Abstract

Background: Coronavirus disease 2019 (COVID-19) disease is not just an acute infection but is a complex entity with post-infection complications and long effects especially involving the pulmonary system.The aim of this study was to assess post COVID-19 pulmonary complications using multidetector computed tomography after resolution of the acute infection and to correlate the findings with clinical manifestations.

Methods: This prospective study was carried out on 30 patientswith pulmonary manifestations after more than 3 months of previously diagnosed initial COVID-19 infection, based on clinical, laboratory and radiological findings.All patients were scanned using different multidetector Computed Tomography (CT) scanners, automated and semi-automated volumetric measurementsempowered by artificial intelligence (AI) techniqueswere used.

Results: There was significant relation between the adequate breath holding and the use of automated technique, between the percentage of lung volume loss and the need for oxygen support, andbetween the percentage of volume loss of lung by fibrosis and the degree of previous COVID -19 infection.

Conclusions: Multi-slice CT is a very useful diagnostic tool to be used in patients presented with suspected post COVID -19 pulmonary complications.3D CT volumetry could easily detect diseases that cause volume loss, including pulmonary fibrosis, which may develop in the follow-up of COVID-19. Quantitative CT (QCT) is an ideal tool for classifying post COVID-19 fibrosis.

Keywords: Multidetector Computed Tomography, COVID-19, Pulmonary Complications, Evaluation

Introduction

In December 2019, a novel coronavirus was identified to cause pneumonia in many people in the city of Wuhan in China[1, 2].

This new disease, coronavirus disease 2019 (COVID-19), was closely related to what was previously discovered in bats. COVID-19 was linked to lung pneumonia that progressed to respiratory failure in the infected people[3].

Clinical manifestations of fever, cough, or shortness of breath were observed in most patients during active infection. COVID-19 infection has a variable recovery rate. Although the majority of people would completely recover, others would suffer from long-term implications after they have recovered from the acute infection, with symptoms ranging from moderate to debilitating[4].

The World Health Organization issued laboratory testing guidelines. However, the predominant imaging modality for diagnosing COVID-19 was a chest computed tomography (CT) scan[5].

The most common CT findings of active COVID-19 pneumonia are multifocal and bilateral ground-glass opacities (GGOs) and/or consolidations in the peripheral, posterior, and lower lobes of the lungs, pleural thickenings, and pleural effusion [6].

Most patients showed residual disease at discharge. In some cases, the disease and CT findings were mild to moderate which heal completely, but severe cases may develop acute respiratory distress syndrome, pulmonary fibrosis, and subsequent lung volume loss. Also, patients with COVID-19 infection were vulnerable to bacterial or fungal infections that were detected by CT studies. Vascular complications were also encountered like acute or chronic pulmonary thrombosis that could be detected by CT pulmonary angiography[7].

Now, with the aid of state-of-art automated and semi-automated lung volumetric measurements powered by artificial intelligence (AI), using cutting-edge post-processing workstations, it was possible to quantify the degree of pulmonary fibrosis and the changes in lung capacity which hadsignificant impact on patient′s outcome regarding the need of oxygen support[8-10].

The aim of this study was to assess post COVID-19 pulmonary complications using multidetector CT after the resolution of acute infection, using lung volumetric measurements and to correlate the findings with clinical manifestations.

Patients and Methods:

This prospective study was carried out on 30 patients, who suspected clinically to have post COVID-19 pulmonary complicationswhich were confirmed by positive chest CT findings and/or RT-PCR test, after at least three months (12 weeks) from the active stage of the disease. The study was done from February 2022 to April 2023 after approval from the Ethical CommitteeTanta University Hospitals.An informed written consent was obtained from all patients.

Exclusion criteria were patients during active COVID-19 infection, presented earlier than 3 months after acute COVID-19 infection, previous history of chronic interstitial lung and/or pleural disease, acute dyspnea who were unable to hold their breath to avoid severe respiratory motion artifacts which could degrade the quality of CT images and pregnant females.

All patients were subjected to: history taking, laboratory investigationsrevision and radiological imaging through non-contrast enhanced multi-slice chest CT,contrast-enhanced chest CT (CT pulmonary angiography in clinically indicated patients).

Image acquisition

All patients were scanned using different multidetector CT scanners installed including 16,128& 320 slices scanners, were examined in a supine position. Non-ionic contrast media was injected through a peripherally inserted IV cannula using a dual head- powered automatic injector followed by saline flushing. Helical CT acquisition in cranio-caudal direction was initiated after IV contrast arrival into main pulmonary artery which was detected automatically through bolus tracking method with manual drawing of ROI at main pulmonary artery with trigger threshold set at 80HU.

Image reconstruction

The obtained CT images, Coronal and sagittal reformatted images were reconstructed at thin slices (0.5-0.625mm) thickness with 50% overlap using a sharp reconstruction filter. 3D volume-rendered images were obtained for both lungs for visual assessment of the lung volume, thereafter with slice thickness of 1 mm and 0.5 mm interval, after which axial MIP cuts of pulmonary arterial tree was generated together with oblique coronal and sagittal MIP images of both pulmonary branches.

Image post processing and data analysis

The reconstructed images were transferred to dedicated workstations for post processing using Advantage Workstation 4.6, GE Health care, USA and VitreaFx, Vital Images, USA workstations.Images were interpreted by radiologists in chest radiology for the detection of pulmonary abnormalities and/ or acute or chronic pulmonary emboli or thrombi.

Automated and semi-automated lung volumetric measurements powered by artificial intelligence techniques were used to calculate: the total lung volume and volume of lung fibrosis with the calculation of its percentage in relation to obtained total lung volume.We have performed quantitative chest CT analysis by using a dedicated post processing software. Before segmentation, attenuation value < −1000 HU was used to exclude tracheal air from the analysis. Quantification was performed on naive acquisition using a lung window with a width of 1500 HU and a level of −600 HU. The software automatically calculated the following parameters: healthy parenchyma, GGOs, consolidation, fibrotic alterations (including fibrotic stripes and subpleural lines) using an adaptive mean based on grayscale, expressed in milliliters, also the total lung volume was reported in milliliters. Then the percentage of compromised lung volume is calculated in relation to the total lung volume.

Semi-automated techniques included manual adjustment of traced lung borders (were needed in 24 out of the 30 cases) to insure accurate volume measurements.

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). The Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative parametric data were presented as mean and standard deviation (SD). Quantitative non-parametric data were presented as median and interquartile range (IQR). Qualitative variables were presented as frequency and percentage (%).

Results:

Total number of cases was 30; 19 (63.3%) were males and 11 (36.7%) were females. The mean age of these patients 58.13± 16.34 SD. Patients′ coexisting comorbidities and special habits; 18 (60 %) were smokers while the remaining 12 (40%) cases were not. The most common comorbidity was hypertension in 14 (46.7%) cases then diabetes in 11 (36.7%) cases, followed by cardiac diseases in 9 (30%) cases then asthma in 2 (6.7%) cases. Cough was the most common symptom in 86% of the cases followed by dyspnea in 60%, fever in 43.3%, fatigue in 43.3%, sputum production in 36.7% then myalgia in 20% as of cases. 25 cases were admitted by moderate to severe infection. Moderate infection who needed hospital admission (with oxygen saturation≥94%) in 13(43.3%) cases and severe infection (with oxygen saturation<94%) in 12 (40%) cases. Only 5 (16.7%) cases had mild infection with no hospital admission. Patients who had severity score calculation with findings consistent with mild severity in 3 (10 %) cases, and with moderate severity in 10 (33.3%) cases, while the highest group was with severe score in17 (56.67 %) cases. Table1

Table 1: Distribution of the studied cases according to demographic data, comorbidities history, current presenting symptoms, clinical severity of COVID pneumonia during active infection and CT severity scoring system of initial chest CT during active COVID-19 pneumonia

		Number	Percentage (%)
Sex	**Male**	19	63.3
	Female	11	36.7
Age (Years)		58.13 ± 16.34	
Comorbiditieshistory			
Smoking		18	60
Not smoking		12	40
Hypertension		14	46.7
Diabetes		11	36.7
Cardiac diseases		9	30
Asthma		2	6.7
Current presenting symptoms			
Cough		26	86.7
Dyspnea		18	60.0
Fever		13	43.3
Fatigue		13	43.3
Sputum		11	36.7
Myalgia		6	20.0
Clinical severity of COVID pneumonia during active infection			
Mild (no admission)		5	16.7
Moderate (Oxygen saturation ≥94%)		13	43.3
Severe (Oxygen saturation <94%)		12	40.0
Total number of cases		30	100
CT Severity score			
Mild (<8)		3	10%
Moderate (8-15)		10	33.3%
Severe (>15-25)		17	56.67%

Data are presented as number (%) or mean ± SD.

The most common radiological finding detected was fibrosis in (56.7%)of cases, followed by pulmonary consolidation in (53.3%)of cases, cavitary lesion in (30%)of cases, pleural effusion in (23.33%) of cases, ground glass opacities in (13.3%)of cases, pericardial effusion in (6.67%)of cases, bronchopleural fistula in (3.3%)of cases , emphysema in (6.7%)of cases, pulmonary nodules in (10%)of cases, pulmonary embolism in (6.7%)of cases, pulmonary hypertension in (3.3%)of cases and other findings in (3.3%)of cases. Table 2

Table 2: Distribution of the studied cases according to post COVID pulmonary complicationsdetected by CT

	Number	%
Fibrosis	17	56.7
Consolidation	16	53.3

Cavitary lesion	9	30.0
Pleural effusion	7	23.3
Ground glass	4	13.3
Nodules	3	10.0
Pericardial effusion	2	6.7
Emphysema	2	6.7
Pulmonary embolism	2	6.7
Bronchopleural fistula	1	3.3
Pulmonary hypertension	1	3.3
Others (occluded coronary stent)	1	3.3

There was significant relation between the adequate breath holding and the use of automated technique, between the percentage of lung volume loss and the need for oxygen support, between the percentage of volume loss of lung by fibrosis and the degree of previous COVID -19 infection and between the percentage of lung volume loss and the need for oxygen support. Table3

Table 3: Relation between ability of artificial intelligence to detect post COVID-19 complications and inadequate breath holding during CT scan

(n = 30)	**Detection by artificial intelligence**				**^{FE}p**
	Automated (n = 6)		**Semi-Automated (n = 24)**		
	No.	**%**	**No.**	**%**	
Dyspnea	1	16.7	17	70.8	0.026*

Data are presented as number (%). p: P value for comparing between Automated and Semi-Automated. *: Statistically significant at P ≤ 0.05.

There was a statistically significant relation between the percentage of lung volume loss and the need for oxygen support.(Table 4, figure 1)

Table 4: Relation between the percentage of compromised lung volume by fibrosis and the need of oxygen support

	Need of oxygen support for			**p**
	No need (n = 4)	**Received oxygen (n = 9)**	**Intubation (n = 4)**	
Percentage of diseased lung volume	3.89 ± 1.42	17.29 ± 9.35	59.86 ± 8.77	**0.001***
Sig.bet.Grps	**p_1=0.032*, p_2<0.001*, p_3=0.032***			

SD: Standard deviation, p: p value for comparing between the different categories, p1: p value for comparing between No need and Received oxygen, p2: p value for comparing between No need and Intubation
p3: p value for comparing between Received oxygen and Intubation, *: Statistically significant at $p \leq 0.05$.

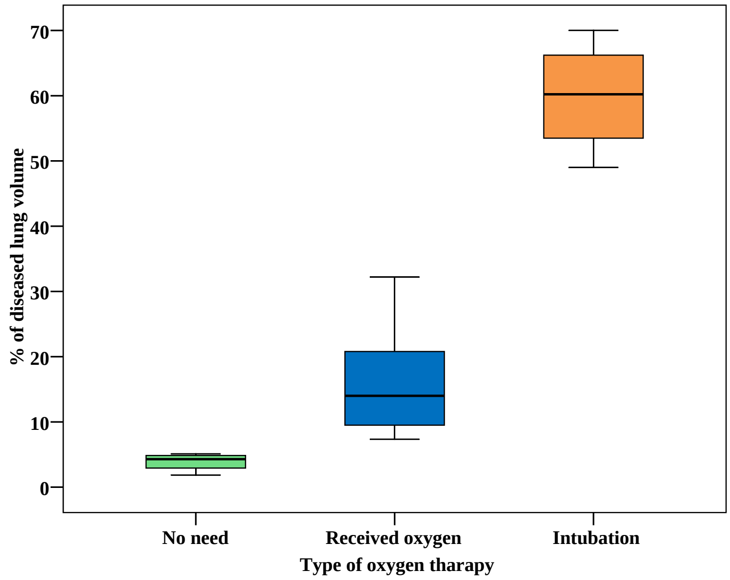

Figure 1: Box plot graph showing the relation between percentage of compromised lung volume by fibrosis and the need for oxygen support (n = 17)

There was a statistically significant relation between the percentage of volume loss of lung by fibrosis and the degree of previous COVID -19 infection. Table 5

Table 5: Relation between percentage of diseased lung volume in fibrotic cases and clinical severity of COVID -19 pneumonia during active infection

	Clinical severity of COVID pneumonia during active infection			p
	Mild (no admission) (n = 2)	Moderate ($SPO_2 \geq 94$) (n = 9)	Severe ($SPO_2 < 94$) (n = 6)	
Percentage of diseased lung volume	3.24 ± 1.93	11.29 ± 6.06	50.4 ± 16.13	**0.002***
Sig.bet.Grps	$p_1=0.042^*$, $p_2<0.001^*$, $p_3=0.018^*$			

SD: Standard deviation, p: p value for comparing between the different categories, p1: p value for comparing between, p2: p value for comparing between, p3: p value for comparing between*: Statistically significant at $p \leq 0.05$.

Case 1:

A 44-year-old heavy smoker male patient (known to have atherosclerotic coronary artery disease), presented clinically with dyspnea, cough & fatigue. His oxygen saturation was 95%

which is corrected by O2 administration through a mask. He had previous history of COVID-19 infection 4 months ago with moderate clinical severity, SpO_2 was > 94% and he needed hospital admission. His initial chest CT was assigned CO-RADS 5 score with CT severity score =19. CT severity score (CT SS) <8 is Mild, CT SS (8-15) is Moderate, CT SS (>15-25) is severe.

Final diagnosis by MSCT scan: Post COVID-19 grade IV pulmonary fibrosis with mild lung affection, so the patient needed oxygen therapy via a mask.Figure 2

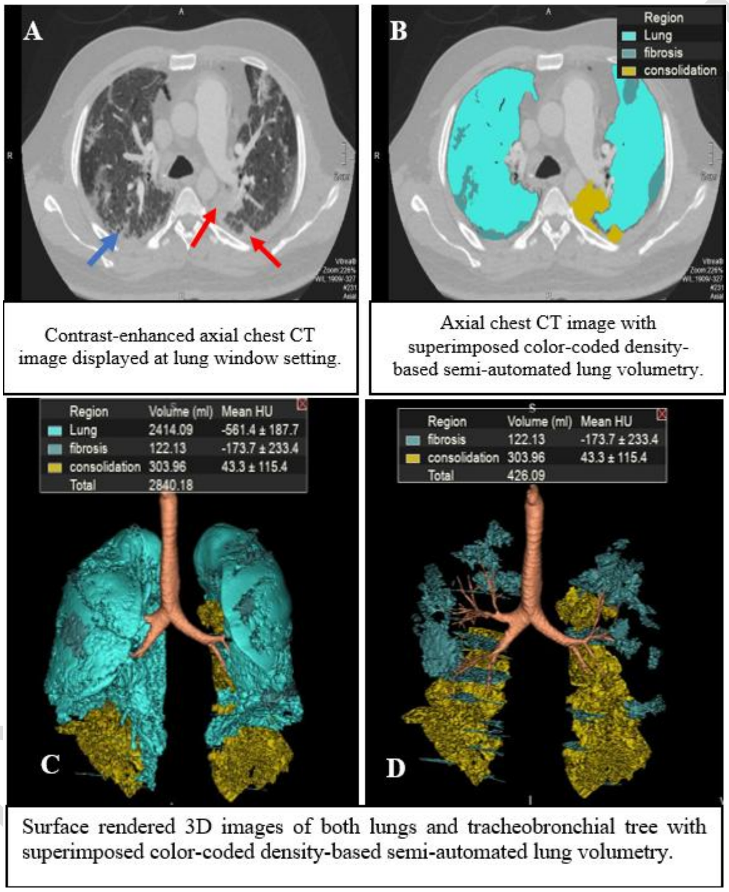

Figure 2: Shows bilateral diffuse thickening of intralobular septa together with few areas of honeycombing (blue arrow in A) and subsegmental consolidations (red arrows in A), light blue color represents normal lung parenchyma, heavy blue color represents lung fibrosis and yellow color represents consolidation (B, C&D). Detailed semi-automated volumetric lung measurements revealed total lung volume = 2840.18 ml (C) with compromised lung volume (volume of fibrosis and consolidations) = 426.09 ml (D) representing 14% of the total lung volume

Case2:

A 60-year-old male heavy smoker diabetic and hypertensive patient, presented clinically with severe dyspnea, cough & fever. His SpO_2 was 75%, thus he received high flow oxygen and needed intubation thereafter. He had previous history of COVID-19 infection about 6 months ago with severe COVID pneumonia. He was admitted on oxygen support and IV medications. His initial chest CT was assigned as CO-RADS score 5 with CT severity score was 21.CT severity score (CT SS) <8 is Mild, CT SS (8-15) is Moderate, CT SS (>15-25) is severe.

Final diagnosis by MSCT scan: Post COVID-19 grade IV pulmonary fibrosis with mild right sided pleural effusion and underlying consolidation with severe lung affection, so the patient needed high flow oxygen then intubation. Figure3

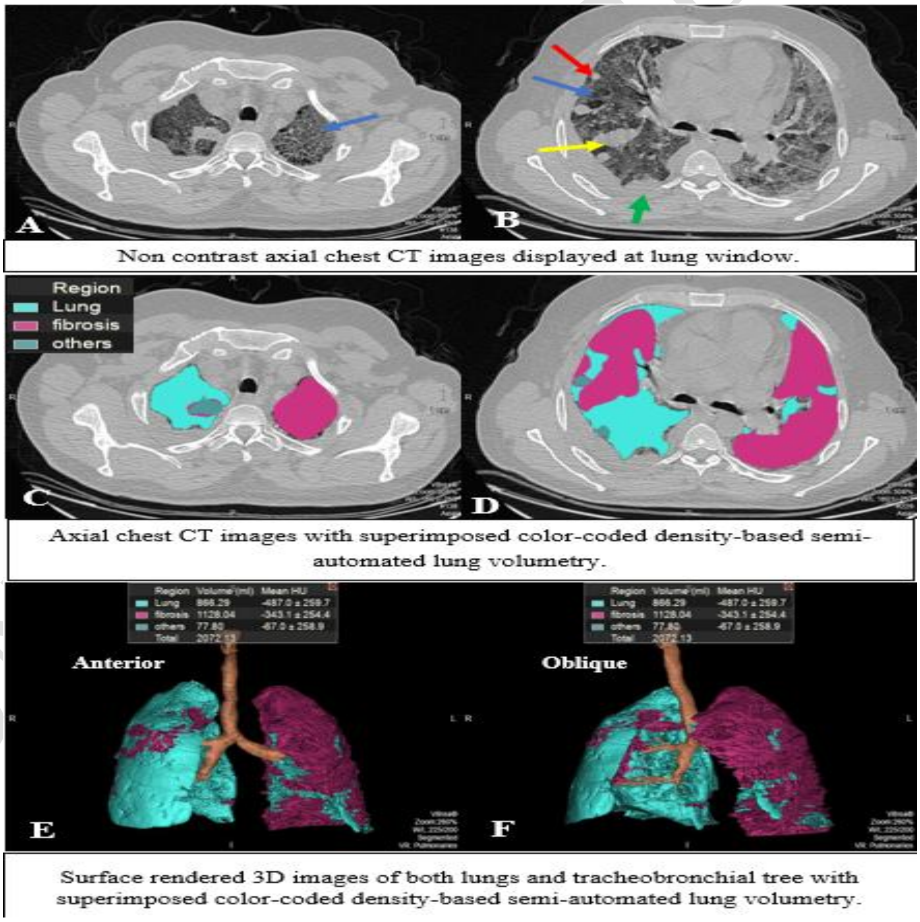

Figure 3: Shows interstitial septal thickening, peri-bronchial cuffing (blue arrows in A&B), subpleural nodules (red arrows in B), atelectatic bands, fissural thickening (yellow arrow in B), mild right sided pleural effusion with underlying consolidation (green arrow in B). Light blue color represents normal lung parenchyma, purple color

represents lung fibrosis and heavy blue color represents consolidation (C-F). Detailed semi-automated volumetric lung measurements revealed total lung volume= 2072.13 ml with compromised lung volume= 1205.84 ml (volume of fibrosis and consolidations) representing 58% of the total lung volume

Case 3:

A 44-year-old female patient, presented clinically with severe dyspnea, cough and fatigue for 5 days. Her SpO2 was 65% and laboratory tests show elevated D- Dimer and CRP. She had a history of past COVID-19 infection about 4 months earlier with mild COVID pneumonia. Her initial chest CT was assigned CO-RADS score 4 with CT severity score was 15. CT severity score (CT SS) <8 is Mild, CT SS (8-15) is Moderate, CT SS (>15-25) is severe.

Final diagnosis by MSCT scan: post COVID-19 main pulmonary artery embolism with right lower lobe basal sub-segmental consolidation. Figure 4

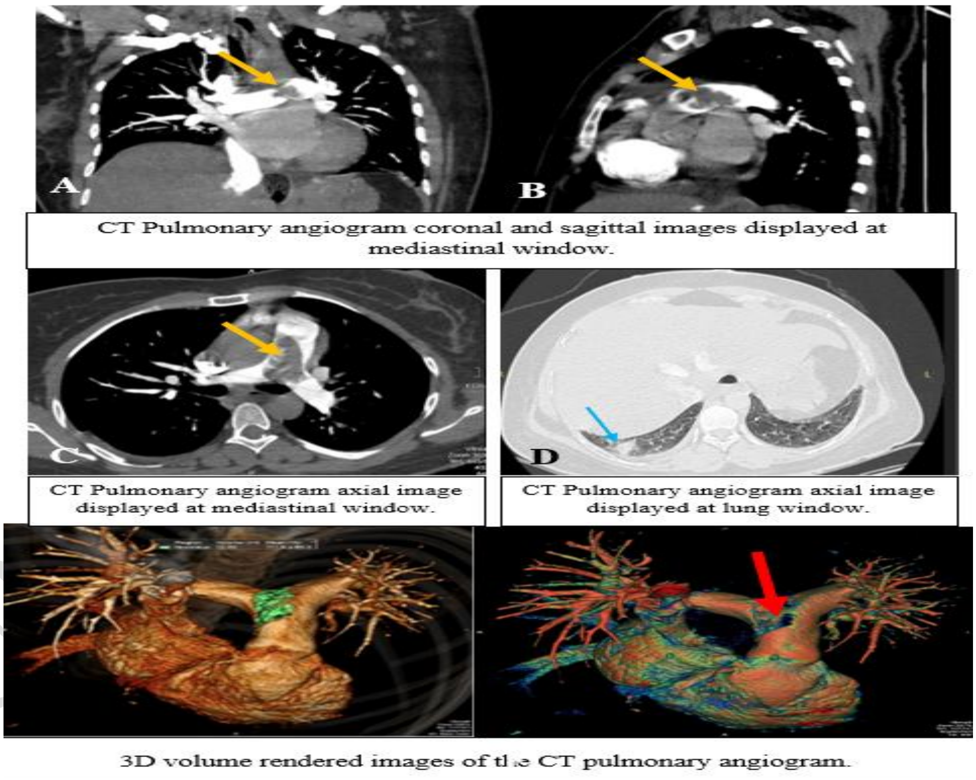

Figure 4: Shows a large hypodense filing defect (a thrombus) at main pulmonary artery reaching its bifurcation point (yellow arrow in A-C), a small subpleural sub-segmental consolidation in the posterior segment of right lower pulmonary lobe (blue arrow in D). An embolus in the main pulmonary artery which is colored in green at (E) and appears as a filling defect in (red arrow in F). Semi-automated volumetric measurement of the thrombus itself was done and it measured 12 ml

Discussion

COVID-19 pandemic has been associated with high rate of short- and long-term morbidities and mortalities with the lungs being the main organs affected by SARS-CoV-2 infection. The long-term pulmonary sequel related to COVID-19 infection was expected to rise significantly leading to an extended impact on community health and healthcare facilities[11, 12].

In our study, found that patients with previous moderate to severe infection COVID-19 pneumonia are more susceptible to develop post COVID-19 complications based on radiological and clinical findings. As after reviewing CT severity scoring of the initial CT chest study done during active infection, it was found that those with moderate infection severity (CT severity score 8-15) represented 33.3% of cases, while the highest number of cases (n= 17, 56.67%) had severe score (CT severity score >15).

Regarding the clinical severity of previous initial COVID-19 infection, 25 (83.3%) of cases were admitted by moderate to severe infection, moderate infection with oxygen saturation ≥94% (n= 13, 43.3%) and severe infection with oxygen saturation<94% (n= 12, 40%). Only 5 cases (16.7%) had mild infection with no need for admission.

Multislice chest CT showed that, the most common complication detected in the included 30 cases was fibrosis in (56.7%) of cases and ground glass opacities (GGO) were detected in (13.3 %) of the cases. This result agrees with Caruso et al.,[13] who found that 72% of the patients have fibrotic like changes at 6-month follow-up chest CT. Also, Han et al., [14] reported that, there were residual CT abnormalities at 6 months in 62% of participants. We agree also with Masclans et al., [15] who found that 76% of patients have abnormalities on high-resolution CT at 6 months after infection, and these abnormalities were typically areas of reticulation and GGO.

In our study, we could detect the following findings by multislice CT in post-COVID-19 patients presented to chest clinic; consolidations in 16(53.3%) cases, cavitary lesions in 9

(30%) cases, pleural effusion in 7(23.33%) cases and nodules in 3(10%) cases. The differentiation between bacterial and fungal pulmonary infections was difficult based on imaging alone. Some studies reported that, the presence of random nodules, "reverse halo" sign, cavitation, and concurrent sinus infection will favor the diagnosis of fungal infections, while the presence of lobar areas of consolidation, centrilobular nodules, and pleural effusion will favor the diagnosis of bacterial infections. However, cavitating bacterial pneumonias can be indistinguishable from fungal pneumonias, especially those caused by Staphylococcus aureus, Klebsiella pneumoniae, and Mycobacterium tuberculosis. The evaluation of sputum/endotracheal aspirate or bronchoalveolar lavage is necessary in many cases to arrive at the correct diagnosis [16].

In our study pulmonary embolism was detected in 6.7% (2 out of 30). This in agreement with Ekici et al., [17] whichpulmonary embolism was detected in 23.8% of their cases. Furthermore, Bompard et al., [18] found that, the incidence of pulmonary embolism in COVID-19 patients varied between 1.9% and 35.3% in their study.

In our study, we had a case presented with chronic dyspnea and cough and was diagnosed as post COVID-19 pulmonary hypertension (PAH) by MSCT as dilated main pulmonary artery (3.8 cm) with right pulmonary artery measuring 3.3 cm and left pulmonary artery measuring 3.4 cm. This agrees with Khan et al., [18] who highlighted the possible relation of COVID-19 and PAH.

In our study, we found emphysematous changes in 2 (6.7%) cases who were previously admitted and on oxygen therapy during active infection, this agreement with Solomn et al., [19] who found new emphysematous lesions comes in 25% of symptomatic cases after 3 months of COVID-19 infection.

In our study we have performed quantitative chest CT analysis by using a dedicated post processing software. The percentage of compromised lung (CL) volume is calculated in relation to the total lung volume. In case of non-adequate or unsatisfactory automatic segmentation, the radiologists were free to manually adjust the area of lung impairment segmented by the software or adjust the lung contours. We used semi -automated techniques on about 80% of the cases as it was done mostly on those with in-adequate breath holding. There is a statistically significant correlation between dyspnea and the usage of semi-automated techniques. This may be multifactorial as most of our patients are elderly, smokers with comorbidities so they presented clinically by dyspnea.

We found out that 4 out of the 17 fibrotic cases did not need oxygen support when the median percentage of lung volume loss by fibrosis (= 4.30%). Nine out of 17 cases received oxygen when the median percentage of lung volume loss (=14%). The remaining 4 cases needed intubation when the median percentage of lung volume loss was (= 60%).There was a significant relation between the percentage of lung volume lossby fibrosis (CL%) and the need for oxygen support.

This agrees with Lanza et al., [20] who used a similar approach, found that patients who are presenting with percentage of compromised lung values in the 6–23% range are at risk for needing oxygenation therapy; values above 23% were at risk for intubation. But in our study on post COVID-19 patients we found that patients presenting with %CL values in the (7.3 - 32) % range are at increased risk for needing oxygenation therapy, whereas those with values from (49-70%) are at increased risk for intubation.

Another approach to quantitative analysis has been proposed by Huang et al., [21] who have successfully developed a commercial deep learning algorithm to quantify lung impairment.

Also, Li et al., [22] described a visual, quantitative analysis of lung damage, to the degrees of parenchymal loss, correlated with a score of clinical severity. Colombi et al., [23] have used a similar approach to predict the outcomes of COVID-19. They reported good performance of the well-aerated volume (%WAL, − 950, − 700 HU) in predicting the combined outcome of

ICU admission and death.In conclusion, the percentage of diseased lung parenchyma, namely the compromised lung volume (%CL), has shown high accuracy in predicting the need for oxygenation support and mechanical ventilation.

Limitation: Small sample size of patients who were referred from chest department with post COVID-19 complications, post COVID-19 fibrosis on whom we have done the volumetric lung measurements and assigned a new classification of the severity of lung affection depending on the volume of diseased lung.

Conclusions:

Multi-slice CT is a very useful diagnostic tool to be used in patients presented with suspected post COVID -19 pulmonary complications.Automated and semi-automated 3D CT volumetry could easily detect diseases that cause volume loss, including pulmonary fibrosis, which may develop in the follow-up of COVID-19.Quantitative CT (QCT) is an ideal tool for classifying post COVID-19 fibrosis in correlation to the need of oxygen support.

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