CHEST RADIOLOGY

COVID-19 pneumonia: computer-aided quantification of healthy lung parenchyma, emphysema, ground glass and consolidation on chest computed tomography (CT)

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Abstract

Objective To calculate by means of a computer-aided tool the volumes of healthy residual lung parenchyma, of emphysema, of ground glass opacity (GGO) and of consolidation on chest computed tomography (CT) in patients with suspected viral pneumonia by COVID-19.

Materials and methods This study included 116 patients that for suspected COVID-19 infection were subjected to the reverse transcription real-time fluorescence polymerase chain reaction (RT-PCR) test. A computer-aided tool was used to calculate on chest CT images healthy residual lung parenchyma, emphysema, GGO and consolidation volumes for both right and left lung. Expert radiologists, in consensus, assessed the CT images using a structured report and attributed a radiological severity score at the disease pulmonary involvement using a scale of five levels. Nonparametric test was performed to assess differences statistically significant among groups.

Results GGO was the most represented feature in suspected CT by COVID-19 infection; it is present in 102/109 (93.6%) patients with a volume percentage value of 19.50% and a median value of 0.64 L, while the emphysema and consolidation volumes were low (0.01 L and 0.03 L, respectively). Among quantified volume, only GGO volume had a difference statistically significant between the group of patients with suspected versus non-suspected CT for COVID-19 ($p < < 0.01$). There were differences statistically significant among the groups based on radiological severity score in terms of healthy residual parenchyma volume, of GGO volume and of consolidations volume ($p < < 0.001$).

Conclusion We demonstrated that, using a computer-aided tool, the COVID-19 pneumonia was mirrored with a percentage median value of GGO of 19.50% and that only GGO volume had a difference significant between the patients with suspected or non-suspected CT for COVID-19 infection.

Keywords COVID-19 · Tomography · X-ray computed · Computer tool · Volume quantification

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Abbreviations

AI	Artificial intelligence
COVID-19	Coronavirus disease 19CT = Computed tomography
GGO	Ground glass opacity
MERS	Middle East respiratory syndrome
RT-PCR	Reverse transcription real-time fluorescence polymerase chain reaction
SARS	Severe acute respiratory syndrome
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

Introduction

The novel coronavirus that was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses caused a pneumonia outbreak worldwide [1–4]. The disease caused by the virus, named coronavirus disease (COVID-19), can be spread through human-to-human contact.

In Italy, the geographical distribution of the infection was uneven, with the northern regions that face disproportionately higher numbers of contagions and deaths compared with the central and southern regions [5]. To support Italian radiologists in becoming familiar with COVID-19 imaging features, the Italian Society of Medical and Interventional Radiology (SIRM) established a dedicated page on the SIRM Web site with an Italian collection of COVID-19 examinations and provided operational procedures to help radiology units in the daily management of COVID-19 patients [5].

The estimation of the incubation period mean value was of 5.2 days, which allows air travelers to spread the disease globally [6, 7]. Evidence shows that virus transmission can occur during the incubation period in asymptomatic patients. The COVID-19 diagnosis is confirmed by the positive results of the nucleic acid amplification test of the respiratory tract or blood specimens using reverse transcription real-time fluorescence polymerase chain reaction (RT-PCR).

In the context of the COVID-19 pandemic, there is a scrupulous need for ready-to-use resources for data acquisition, the computerized tool and artificial intelligence (AI) algorithms to speed up the search for effective and safe treatments. The progressive integration of AI-based solutions in healthcare is already changing established paradigms in the entire healthcare ecosystem, leveraging the progressive digitalization of medical data. In particular, diagnostic and decision support systems developed for medical imaging are the first successful examples of innovation for health. Radiomics and AI-based methods have led to diagnostic applications that accelerate image acquisition, preprocessing, annotation and interpretation, offering an "augmentation" of the radiologists, rather than their unrealistic substitution. In particular, the application of AI in medical imaging has improved the assessment, diagnosis and early detection of neurodegenerative diseases and heart diseases, with specifically high impact on breast and lung cancer.

Medical imaging has been efficiently applied for diagnostics and management of COVID-19 pneumonia. Mainly, computed tomography (CT) examination has been used extensively in China and now worldwide to evaluate the grade and the extension of the viral pneumonia by COVID-19 and in the follow-up, also based on AI algorithms [8–12]. The most Italian hospitals are employing chest X-ray as the first-line method, with faster results comparing with those of RT-PCR, especially by using portable X-ray units which reduce the movement of patients and so minimizing the risk of cross-infection [10].

Several radiological organizations do not recommend CT as a primary diagnostic tool for COVID-19 viral infection [13–17]. However, the diagnosis of viral pneumonia based on chest CT may be used to recommend patient isolation. Further, chest CT has an important role in the management of patients with suspected SARSCoV-2 infection, identifying patients with severe lung involvement of viral pneumonia at CT; this could direct the clinician versus an anticipation of mild invasive ventilation that has been demonstrated effective in reducing severity of pneumonia [18–27]. The main CT characteristics reported in the recent literature and individuated in patients affected by COVID-19 pneumonia were ground-glass opacity (GGO), consolidation, reticulation/thickened interlobular septa, nodules and lesion distribution in left, right or bilateral lungs [17–19].

We analyzed the chest CT images performed at the time of admission of 116 patients with suspected SARS-CoV-2 infection in order to calculate automatically by post-processing automatic tool the volume of healthy lung parenchyma, emphysema volume, GGO and consolidation volume. Endpoint of the study is also to identify the CT patterns linked and correlate with the severity of the COVID-19 viral infection.

Materials and methods

Patient characteristics

Institutional review board of "Bergamo Est" waived written informed consent for this retrospective study considering the COVID-19 emergency. The cohort was composed of 116 patients (32 women and 77 men; 68.8 years of mean age; range, 29–93 years) subjected to the nucleic acid amplification test of the respiratory tract or blood specimens using reverse transcription real-time fluorescence polymerase chain reaction test, between February 23, 2020, and March 5, 2020. The RT-PCR test was executed in the clinical laboratory of ASST Bergamo Est (Seriate, Italy).

CT technique

Chest CT scan was acquired at the time of patient admission in hospital with a 128 slice CT scanner (Ingenuity of Philips, Amsterdam, The Netherlands). CT examinations were performed with the patient in the supine position in breath hold during an inspiration using a standard dose protocol, without contrast intravenous injection. The scanning range was from the apex to the base of the lungs. The tube voltage and the

current tube were 120 kV and 100–200 mA, respectively. All data were reconstructed with 0.6–1.0 mm increment. The matrix was 512×512 mm^2. Images were reconstructed using a sharp reconstruction kernel for parenchyma and viewed at window settings optimized for the assessment of the lung parenchyma (window width, 1600 HU; window level, 600 H.U).

Post-processing with thoracic VCAR software

DICOM data were transferred into a PACS workstation (AW SERVER 3.2 ext 3.0, of GE Healthcare, Chicago, Illinois, USA), and CT images were evaluated using a clinically available artificial intelligence computer tool, the Thoracic VCAR software (GE Healthcare, Chicago, Illinois, USA) in order to evaluate thoracic disease.

The software has the CE certification to document emphysema. The software provides automatic segmentation of the lungs and automatic segmentation and tracking of the airway tree. It provides the classification of voxels based on Hounsfield Units and a color-coded display of the segmented regions. We analyzed the CT scans by pre-setting a threshold value of Hounsfield Units in order to obtain a quantification for both lungs of emphysema ($-1024/-977$; blue) [20], of healthy residual lung parenchyma ($-977/-703$; yellow) [21, 22], of GGO ($-703/-368$; pink) and of consolidation ($-100/5$; red) [21, 23–25] (Fig. 1). Chest CT evaluation using this computer tool was done on 116/134 (86.6%)

patients because the software in 18 cases was not able to provide automatically quantification of thoracic disease.

Radiologist analysis

Radiologists attributed to each lung looking the CT images at the pulmonary involvement by disease a severity score using a scale of five levels (none, mild: $\leq 25\%$ of involvement, moderate: 26–50% of involvement, severe: 51–75% of involvement and critic involvement: 76–100%). An overall radiological severity score was obtained summing the scores for each lung and then considering a mild severity a score ≤ 2, moderate 3–4, severe 5–6 and critic 7–8. Two radiologists with more than 10 years of thoracic-imaging analysis experience evaluated the severity of images in a double-blind manner. Another, more experienced, radiologist resolved any disagreement between the two radiologists.

Moreover, all chest CT examinations were reviewed using a structured report realized by Italian Society of Medical Radiology and Interventional Radiology (SIRM, Milan, Italy) in collaboration with the Exprivia Healthcare Company (Bari, Italy) [26]. The presence of GGO and consolidation was assessed in order to define their localization (unilateral and bilateral), axial distribution (diffuse, predominantly peripheral, mainly central, declivous, antideclivous), distribution on the cranio-caudal plane (diffuse, multifocal/patching, prevalent in the upper lobes, prevalent in the lower lobes, gravitational) and their site.
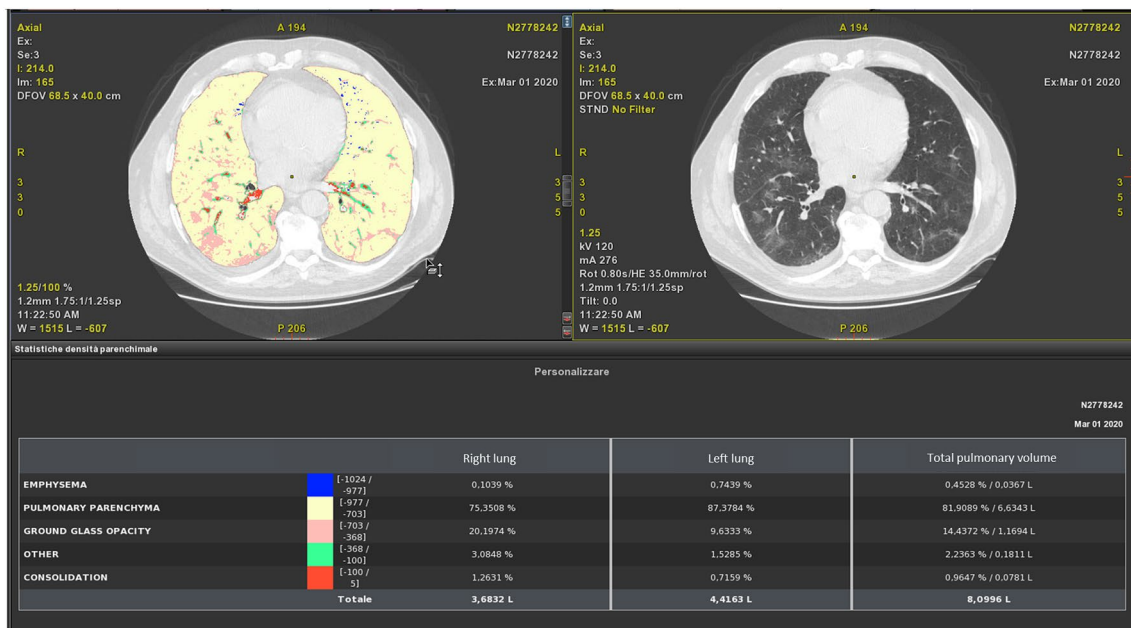

		Right lung	Left lung	Total pulmonary volume
EMPHYSEMA	[-1024 / -977]	0,1039 %	0,7439 %	0,4528 % / 0,0367 L
PULMONARY PARENCHYMA	[-977 / -703]	75,3508 %	87,3784 %	81,9089 % / 6,6343 L
GROUND GLASS OPACITY	[-703 / -368]	20,1974 %	9,6333 %	14,4372 % / 1,1694 L
OTHER	[-368 / -100]	3,0848 %	1,5285 %	2,2363 % / 0,1811 L
CONSOLIDATION	[-100 / 5]	1,2631 %	0,7159 %	0,9647 % / 0,0781 L
	Totale	3,6832 L	4,4163 L	8,0996 L

Fig. 1 Example of lung volumes calculated by computer-aided tool on CT images by pre-setting a threshold value of Hounsfield Units and a color in order to obtain a segmentation of both lungs and a quantitative evaluation of emphysema ($-1024/-977$; blue), Healthy lung parenchyma ($-977/-$s703; yellow), GGO ($-703/-368$; pink), consolidation ($-100/5$; red) and other ($-368/-100$; green)

Statistical analysis

Continuous data were expressed in terms of median value and range. Mann–Whitney test was performed to verify differences statistically significant between groups of continuous variables. Kruskal–Wallis test and chi-square test with Yates correction were used to assess statistically significant differences between percentage values.

p value < 0.05 was considered statistically significant for all tests.

All analyses were performed using IBM SPSS Statistics 24 (IBM, USA).

Results

CT and RT-PCR performance results

The patients' characteristics are reported in Table 1.

Median value of temporal difference between RT-PCR tests execution and CT scan was 0.18 days $\pm$ 2.0 days. CT

Table 1 Demographic characteristics of 116 patients with suspected coronavirus disease (COVID-19) at CT scan

	Patients with suspected CT for COVID-19 (N. 109)		Patients with non-suspected CT for COVID-19 (N. 7)		p value
Age (y)					
Median	69.3		68.9		> 0.05
Range	29–93		46–85		
Sex, no. (%) of patients	Tot	%	Tot	%	p value
Male	77	70.6	3	42.9	> 0.05
Female	32	29.4	4	57.1	

Note p value was evaluated for continuous variable by Mann–Whitney test and by chi-square test with Yates correction for categorical ones. The *p* values reported in bold were considered significant

was suspected for COVID-19 viral pneumonia in 109 of 116 (94.0%) patients, while COVID-19 was diagnosed at RT-PCR in 90 of the 116 (77.6%) patients.

CT volumes analysis

No differences of the value of volumes between right and left lung were identified (p value > 0.05 at Mann–Whitney test).

GGO was the most represented characteristic in suspected CT by COVID-19 (Table 2), it was present in 102/109 (93.6%) patients. GGO percentage volume was 19.50% with a median value of 0.64 L, statistically superior (p value $<< 0.01$ at Mann–Whitney test) with respect to the other volumes (emphysema volume (0.01 L) and consolidation volume (0.03 L)).

GGOs were predominantly bilateral in 89/102 (87.3%) patients with involvement in multiple lobes in 77/102 (75.5%) patients, distribution peripheral in 82/102 (80.4%) patients and multifocal/patching in 69/102 (67.7%) patients. Consolidations were found in 78/109 (71.6%) patients, predominantly bilateral in 68/78 (87.2%) patients, with involvement in multiple lobes in 53/78 (67.9%) patients, distribution peripheral in 67/78 (85.9%) patients and segmental in 33/78 (42.3%) patients.

Among quantified volumes, only GGO had a difference statistically significant between patients with suspected CT and non-suspected CT for COVID-19 (p value $<< 0.01$ at Mann–Whitney test, Table 2).

In Table 3, the percentage values of volumes of healthy residual lung parenchyma, emphysema, GGO and consolidations are reported considering the patients grouped for pneumonia radiological severity score.

Volume median values of healthy residual lung parenchyma were, respectively, of 93.8%, 91.1%, 77.8%, 66.0% and 60.0% for none, mild, moderate, severe and critical radiological score.

Volume median values of GGO were, respectively, of 4.1%, 6.6%, 16.0%, 26.8% and 31.2% for none, mild, moderate, severe and critical radiological score.

Table 2 Volume measurements on 116 patients with suspected coronavirus disease (COVID-19) at CT scan

CT volume measurements	Patients with suspected CT for COVID-19 (N. 109)		Patients with non-suspected CT for COVID-19 (N. 7)		p value
	Median value [L/%]	Range [L/%]	Median value [L/%]	Range [L/%]	p value
Healthy lung parenchyma	2.69/74.38	5.01/72.40	4.19/90.86	2.43/14.1	**<< 0.01**
Emphysema parenchyma	0.01/1.12	0.82/21.10	0.01/1.33	0.15/4.80	> 0.05
GGO	0.64/19.50	1.63/56.50	0.21/5.67	0.25/10.80	**<< 0.01**
Consolidation	0.03/1.06	0.08/2.70	0.03/0.70	0.03/0.6	> 0.05
Total volume	3.80	3.90	4.55	2.20	> 0.05

Note *p* value was evaluated for continuous variable by Mann–Whitney test and by chi-square test with Yates correction for categorical ones. The *p* values reported in bold were considered significant. % = percentage values of volumes with respect to the lung total volume

Table 3 Percentage values of volumes of healthy lung parenchyma, emphysema, GGOs and consolidations with respect to total lung volume considering the patients grouped based on pneumonia severity score

Volumes grouped considering pneumonia radiological severity score		Healthy lung parenchyma (%)	Emphysema (%)	GGO (%)	Consolidation (%)
None	Median	93.75	0.15	4.10	0.55
	Minimum	8810	0.00	3.30	0.50
	Maximum	95.20	4.80	5.80	1.10
Mild	Median	91.05	0.20	6.60	0.70
	Minimum	67.90	0.00	2.90	0.20
	Maximum	95.60	1.40	25.70	1.20
Moderate	Median	77.75	0.50	15.95	0.90
	Minimum	46.00	0.00	5.20	0.40
	Maximum	93.60	21.10	44.90	2.20
Severe	Median	66.00	0.40	26.80	1.30
	Minimum	50.20	0.00	12.70	0.60
	Maximum	83.60	5.40	40.20	2.10
Critical	Median	59.55	0.20	31.15	1.55
	Minimum	23.20	0.00	28.00	0.80
	Maximum	66.40	4.20	59.40	2.90
Total	Median	77.80	0.30	16.10	0.90
	Minimum	23.20	0.00	2.90	0.20
	Maximum	95.60	21.10	59.40	2.90

Volume median values of consolidations were, respectively, of 0.6%, 0.7%, 0.9%, 1.3% and 1.60% for none, mild, moderate, severe and critical radiological score.

There were differences statistically significant among the groups based on radiological severity score in terms of healthy residual parenchyma volume, of GGO volume and of consolidations volume with a p value $<< 0.001$ at Kruskal–Wallis test (Fig. 2).

Discussion and conclusions

Several recent publications have described CT imaging features of COVID-19, the evolution of these features over time and the performance of radiologists in order to distinguish COVID-19 from other viral infections [8, 11, 27–31]. These studies reported that COVID-19 often produces a CT pattern resembling organizing pneumonia, notably peripheral ground-glass opacities and nodular or mass-like GGO that are often bilateral and involvement in multiple lobe.

Numerous artificial intelligence software applications have recently been proposed for the recognition of lung lesions from COVID-19 on chest CT examination, many of which are Chinese [32–34]. However, these tools are not recognized as medical devices because CE marking is absent. Furthermore, they have been tested on thousands of cases of COVID-19 but not equally on as many cases of non-COVID-19 coronavirus, affecting their ability to make a differential diagnosis. In this context, the role of artificial
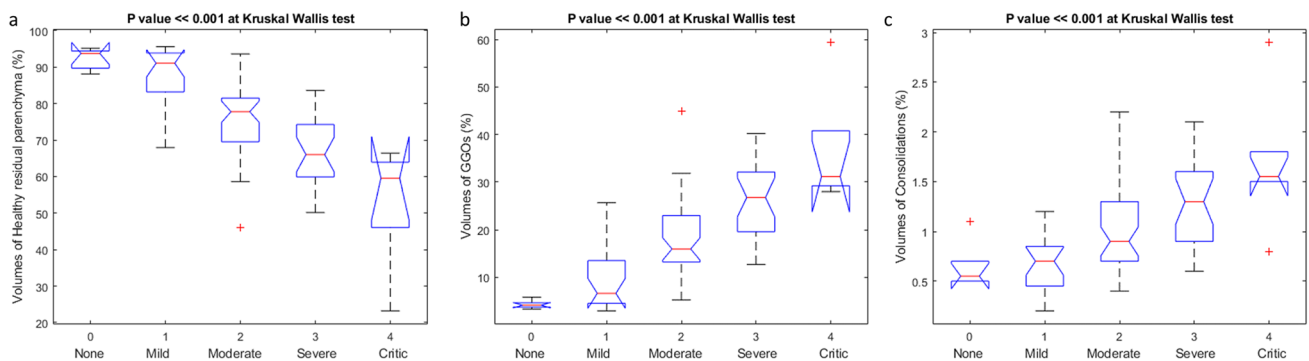

Fig. 2 Box plot of volumes of healthy lung parenchyma (**a**), GGOs (**b**) and consolidations (**c**) with respect to total lung volume considering the patients grouped based on radiological pneumonia severity score (none, mild, moderate, severe, critic)

intelligence remains limited to the numerical quantization of the lesions and their distribution. Therefore, the aid of these artificial intelligence software is limited in experimental protocols to evaluate the therapies effectiveness or to compare several CT examinations in search of findings that can anticipate the outcome of the disease and the prognosis.

Gozes et al. [34] used 2D and 3D deep learning models to explore AI tools in the CT images analysis for detection, quantification and tracking of COVID-19. A total of 106 COVID-19 chest CT scans (and 99 normal ones) were used to find potential COVID-19 CT features and to evaluate progression of the disease in patients over time. Proof of principle of diagnostic capability of deep learning methods from CT images to screen COVID-19 have been recently demonstrated by Wang et al. [34] on 1,119 CT images of pathogen-confirmed COVID-19 cases versus typical viral pneumonia. The accuracy and applicability of deep learning for screening COVID-19 by CT examinations have, however, been questioned, based on concerns of the radiologists' association and given the impact of selection bias reported in first published results. At the same time, radiomics approaches can be usefully implemented, focusing on segmentation techniques of the lung parenchyma based on region growing techniques and on other radiomics COVID-19-specific feature and their use with machine learning such as support vector machines or random forests [35–40].

In clinical practice, lung recruitment is usually considered a useful strategy [41, 42]. For this reason, it has been suggested that the condition of patients with a high percentage of potentially recruitable lung is better than that of patients with a lower percentage of potentially recruitable lung, given the presence of similar degrees of lung injury.

Several methods of disease extent quantification at chest CT have been proposed, including the extent of emphysema, pulmonary fibrosis and acute respiratory distress syndrome (ARDS) [43–46].

Grassi et al. compared different commercial software applications in the quantification of pneumonia lesions in COVID-19 infection in order to stratify the patients based on the disease severity using chest CT images. They concluded that computer-aided pneumonia quantification could be an easy and feasible way to stratify COVID-19 cases according to severity [47].

CT score of the burden of lung disease was previously reported as a risk factor for mortality in ARDS [43]. A variable combination of CT signs and their distribution affects the degree of diagnostic confidence in the diagnosis of COVID-19 infection (respectively high, intermediate and low or alternative diagnosis) but does not correlate with a statistically significant difference in the outcome prediction of patients. Therefore, the objective quantification by a post-processing automatic tool of the volumes of healthy lung parenchyma, emphysema, GGO and consolidation could be useful in the COVID-19 diagnosis and could be used to differentiate the patients with severe lung involvement.

According to recent publications, in this study we quantified using a computer tool the abnormalities visible at the chest CT images (emphysema, GGO and consolidations) and we reported that GGO was the most represented characteristic in suspected CT by COVID-19 with a percentage volume value of 19.50% and a median value of 0.64 L. Among quantified volumes, only GGO volume had a difference statistically significant between the group of patients with suspected CT and non-suspected CT for COVID-19. GGO abnormality, also in our cohort, was predominantly bilateral (87.3%), with involvement in multiple lobe (75.5%) involvement, peripheral (80.4%) and multifocal/patching (67.7%) distribution.

Moreover, we reported that no differences between right and left volume lung could be observed, while there were differences statistically significant among the groups based on radiological severity score in terms of healthy residual lung parenchyma volume, of GGO volume and of consolidations volumes.

The main limitations of the present study are as follows: the nature retrospective and monocentric of the study conducted on a cohort of symptomatic hospitalized patients from an area of high epidemiological risk and with a high pretest probability of COVID-19 infection; too small comparison group represented by the patients with CT no suspected for COVID-19 viral pneumonia; and the absence of clinical data to correlate with radiological findings. However, a future endpoint of the study is the correlation of the radiological finding and clinical one using artificial intelligence tools.

In conclusion, we demonstrated that the COVID-19 was mirrored mainly by GGO abnormality and that this had a percentage value of 19.50% with respect to the total lung volume. Moreover, we observed that only the GGO volume had a difference significant between the patients with suspected or non-suspected for COVID-19 infection. We think that analysis of CT findings using a computer tool based on different thresholding Hounsfield Units setting could be able to identify pulmonary abnormalities and lung recruitment and we believe that knowledge of the percentage of potentially recruitable lung may be important for establishing the management of COVID-19 pneumonia.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

Human and animal Rights "Bergamo Est" Institutional Review Institute (IRB) approved the study and renounced the written informed consent for this retrospective study, considering the ongoing epidemic emergency, which assessed the unidentified data and did not involve risk potential for patients.

Informed consent Consent for publication was received.

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