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Research Article

Stereological Analysis of Volume of Pulmonary Parenchymal Damages in Chest CT Scans of Patients with COVID-19 Pneumonia

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Abstract

Purpose: To analyze volumetric quantities of the most frequent features of chest CT scans in patients with COVID-19 pneumonia by stereological methods.

Materials and Methods: Chest CT scans of 29 patients confirmed with COVID-19 whose ages were from 27 to 66 was retrospectively evaluated. Lung images were obtained using computed tomography device with the patient in the supine position at full inspiration, without administration of contrast medium. The total lung volumes, volumes and volume ratios of ground glass opacities without and with consolidation and intraparenchymal pulmonary vessels were estimated by stereological methods. SPSS 26 was used to process the data. Results were expressed as means ± SD and percentages.

Results: Volumetric analyses showed that the mean of total lung volume in patients infected with 2019 novel coronavirus was 4352·06 ± 1324·45 cm^3. The mean volumes of ground glass opacity without and with consolidation, intraparenchymal pulmonary vessels and intact remaining parenchyma in both lungs were 696·29 ± 397·44 cm^3, 888·18 ± 510·05 cm^3, 345·66 ± 135·83 cm^3, and 3118·21 ± 1355·82 cm^3 and their volume ratios were 17·27 ± 10·45 %, 22·18 ± 13·53 %, 7.84 ± 1.56 %, and 69.98 ± 13.15 % respectively.

Conclusion: It was concluded that the volumes and volume ratios of ground glass opacity without and with consolidation and intraparenchymal pulmonary vessels and intact remaining parenchyma of COVID-19 pneumonia could be estimated practically on CT scans using stereological methods.

Keywords: Humans; COVID-19; Lung volume; Tomography; X-Ray computed; Stereology

Abbreviations

CT: Computed Tomography; COVID-19: Coronavirus Disease 2019; SD: Standard Deviation; SPSS: Statistical Package for the Social Sciences

Introduction

On December 31, 2019, several cases of pneumonia of unknown etiology were reported to World Health Organization WHO from Wuhan city, Hubei Province of china [1]. A novel coronavirus, which was named 2019-nCoV, was identified as the cause of these pneumonia cases in Wuhan. The presence of 2019-nCoV in lower respiratory tract specimens of patients was discovered by Reverse-Transcription Polymerase Chain Reaction (RT-PCR) [2,3].

This disease was named COVID-19 by WHO, which is the acronym of "coronavirus disease 2019". The virus that causes COVID-19 was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses, because it was very similar to the one that caused the SARS outbreak (SARS-CoVs) [4].

Coronaviruses are a large family of single strand positive RNA (+ssRNA) viruses, belonging to order Nidovirales, family Coronaviridae, and subfamily Orthocoronavirinae that produce diseases ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome emerged in 2012 and Severe Acute Respiratory Syndrome (SARS-CoV) emerged in 2002 [5].

COVID-19 infection has not been previously recognized in humans and is extremely contagious. COVID-19 spread rapidly around China and all countries throughout the world and this condition was determined a Public Health Emergency of International Concern (PHEIC) on January 30, 2020 by WHO. Symptoms of 2019-nCoV diseases include fever and respiratory infection, and radiologic abnormality, among these clinical features, radiologic features are particularly important for diagnosing and management of COVID-19 pneumonia [6,7].

An initial analysis of the clinical features of the admitted patients in Wuhan with laboratory-confirmed 2019-nCoV confirmed that all patients had bilateral abnormal lung opacities on chest CT scans [8].

The volume of biological structures can be estimated by combining sectional radiological imaging techniques with the Cavalieri principle of volume estimation as described previously [9-11]. Volume and volume fraction of a component within a reference volume can be calculated to be close as possible as to reality using stereological

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methods [12].

Our study aimed to evaluate volumetric quantities of the most frequent features of Spiral CT scans of the thorax in 29 patients infected with 2019 novel coronavirus by applying stereological methods. We believe this information is valuable for physicians and clinical groups to manage COVID-19 patients.

Materials and Methods

Patients

The inclusion criteria of this retrospective case series study were patients with confirmed 2019-nCoV, in which the 2019-nCoV infections was confirmed by real-time RT-PCR on throat swab specimens and negative test patients were excluded from the study. The 29 patients in our study population were 11 women and 18 men whose age ranged from 27 to 66 years who had admitted to two designated hospitals in Qom from March 2020 to April 2020. The Ethic Commission of Qom University of Medical Sciences approved this study (IR.MUQ.REC.1399.019). To prevent any possible break of secrecy, there was no connection between the patients and the researchers.

Image acquisition

Lung images were obtained with CT Scanners (Siemens' SOMATOM Scope 16 Slice and NeuViz 16 Essence 16 slice) with the patient in the supine position during the inspiration phase of respiration, without administration of contrast medium. Spiral CT scan images of the thorax were obtained from pulmonary apex to the diaphragm using 7 mm slice width, 130 Kv, 100 mAs parameters for NeuViz 16 Essence 16 slice CT scanner and 5 mm slice width, 110 Kv, 70 mAs parameters for Siemens' SOMATOM Scope CT scanner.

Data collection

The total volume of lungs, volumes and volume ratios of ground glass opacity without and with consolidation, intraparenchymal pulmonary vessels, and intact remaining parenchyma were estimated by applying the point's grid on series of serial sections of the spiral CT scans.

Volume estimation with cavalieri principle

The point's grid, which is composed of crosses with area (1·61 cm^2), was overlaid randomly to cover the entire area of the lung sectional images and the numbers of intersections (i.e. upper right corner of the crosses) hitting the sectional images of the lung were counted on consecutive spiral CT scan images (Figure 1).

To estimate the volume of the lungs, the following formula was applied:

$$V=T.a/p.\Sigma P$$

Where "T" is the section thickness of consecutive sections "a/p" is area per point of point's grid, and "ΣP" is the total number of points hitting the lung transects [13].

Volume fraction

The volume fraction of a component within a reference volume is a simple and very widely used parameter in biomedical science [14-16]. Thus, it is used to express the proportion of a phase or component within the whole structure. The volume fraction of a X phase within a Y reference volume is expressed as follows:

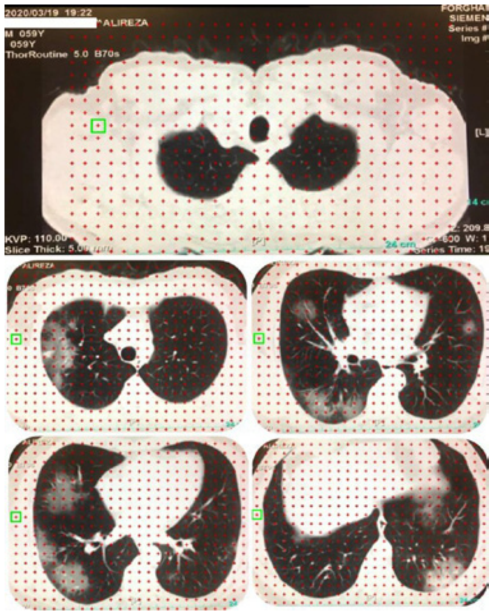

Figure 1: A point's grid superimposed on images of the thoracic CT scans of a 59-year-old man infected with COVID-19 pneumonia.

Vv (X,Y) = (Volume of X phase in Y reference space)/(Volume of Y reference space)

Where "Vv (X,Y)" indicates volume fraction of "X" phase within the "Y" reference volume. Using this method, "Vv" (ground glass opacity without consolidation, total lung volume), "Vv" (ground glass opacity without consolidation, total lung volume) and "Vv" (intraparenchymal pulmonary vessels, total lung volume) can be estimated. Volume fraction ranges from 0 to 1 and is often expressed as a percentage [16].

In the light of the above information, the same points counted for the volume estimation were also used for the estimation of volume fraction of individual ground glass opacity without and with consolidation and intraparenchymal pulmonary vessels within the lung using the following formula:

Vv (Structure, total lung) = (ΣP Structure)/(ΣP total lung)

Where "ΣP Structure" the number of points was superimposed the profiles of the ground glass opacity without and with consolidation and intraparenchymal pulmonary vessels and "ΣP total lung" was the number of points superimposed the total lung. The total volume of the structures was obtained using multiplying the volume fraction by the total lung volume.

V(structure)=Vv (structure).V (total lung)

Calculation of Coefficient Error (CE) for the cavalieri method

The coefficient error of stereological estimations was determined using the formula reported by Gundersen and Jensen [12].

Definitions

Ground-glass opacity is a radiological finding in computed

Table 1: Volumetric analyses of lungs, ground glass opacity without and with consolidation and intraparenchymal pulmonary vessels in patients with COVID-19 pneumonia.

Variables	N	Minimum	Maximum	Mean	Std· Deviation
Right lung					
Ground glass opacity without consolidation volume (cm³)	29	10·12	836·69	386·88	232·22
Ground glass opacity with consolidation volume (cm³)	29	10·12	1089·73	513·21	328·89
Intraparenchymal pulmonary vessel volume (cm³)	29	73·10	376·74	189·07	84·86
Total lung volume (cm³)	29	1568·80	4083·38	2461·75	758·36
Coefficient of error	116	0	0.07	0.022	0.017
Left lung					
Ground glass opacity without consolidation volume (cm³)	29	17·99	768·74	309·41	224·46
Ground glass opacity with consolidation volume (cm³)	29	23·62	971·97	374·97	281·32
Intraparenchymal pulmonary vessel volume (cm³)	29	52·86	269·90	156·59	60·41
Total lung volume (cm³)	29	1113·34	3280·43	1890·31	595·71
Coefficient of error	116	0·00	0·09	0·027	0·020
Both lungs					
Ground glass opacity without consolidation volume (cm³)	29	231·67	1501·33	696·29	397·44
Ground glass opacity with consolidation volume (cm³)	29	231·67	1929·80	888·18	510·05
Intraparenchymal pulmonary vessel volume (cm³)	29	125·95	646·64	345·66	135·83
Intact remaining parenchyma volume (cm³)	29	1189·82	6527·12	3118·21	1355·82
Total lung volume (cm³)	29	2873·33	7363·81	4352·06	1324·45

tomography consisting of a hazy opacity that does not obscure the underlying bronchial structures or pulmonary vessels. Consolidation was defined as homogeneous opacification of the parenchyma obscuring the underlying vessels and airways [17].

Statistical analysis

All calculations and other related data were acquired as a worksheet using Microsoft Excel. After the primary setup and providing of the formulae, the point counts and formulae were entered for each subject and the final data gained automatically. SPSS version 26 was used to process the data. Results were expressed as means ± SD and percentages.

Results

According to the results of volumetric analyses on spiral CT scans, the means of total lung volume in right, left and both lungs were 2461·7 ± 758·36 cm³, 1890·31 ± 595·71 cm³, and 4352·06 ± 1324·45 cm³ respectively. The mean volumes of ground glass opacity without and with consolidation and intraparenchymal pulmonary vessels in right lung were 386·88 ± 232·22 cm³, 513·21 ± 328·89 cm³, and 189·07 ± 84·86 cm³ respectively and in left lung were 309·41 ± 224·46 cm³, 374·97 ± 281·32 cm³, and 156·59 ± 60·41 cm³ respectively. The mean volumes of ground glass opacity without and with consolidation, intraparenchymal pulmonary vessels, and intact remaining parenchyma in both lungs were 696·29 ± 397·44 cm³, 888·18 ± 510·05 cm³, 345·66 ± 135·83 cm³, and 3118·21 ± 1355·82 cm³ respectively (Table 1).

To our study, it was observed that the means of volume Ratio of ground glass opacity without and with consolidation and intraparenchymal pulmonary vessels in right lung to total both lung volumes were 9·79 ± 6·26 %, 13·02 ± 8·71 %, and 4·27 ± 1·06 % respectively and in left lung to total both lung volumes were 7·47 ± 5·58 %, 9·16 ± 7·09 %, and 3·57 ± 0·89 % respectively. The means of volume Ratio of ground glass opacity without and with consolidation, intraparenchymal pulmonary vessels, and Intact remaining parenchyma in both lungs to total both lung volumes were 17·27 ± 10·45 %, 22·18 ± 13·53 %, 7.84 ± 1.56 %, and 69.98 ± 13.15 % respectively (Table 2).

Discussion

According to volumetric data emerged in our study, the mean of total lung volume was 4352·06 ± 1324·45 cm³. The mean volumes of ground glass opacity without and with consolidation, intraparenchymal pulmonary vessels, and intact remaining parenchyma within both lungs were 696·29 ± 397·44 cm³, 888·18 ± 510·05 cm³, 345·66 ± 135·83 cm³, and 3118·21 ± 1355·82 cm³ and their volume ratios were 17·27 ± 10·45 %, 22·18 ± 13·53 %, 7.84 ± 1.56 %, and 69.98 ± 13.15 % respectively. Our results indicate that volumetric quantities of the most frequent features of Spiral CT scans of the thorax in patients infected with 2019 novel coronavirus could be assessed by applying stereological methods.

Chest CT is a key factor of the diagnostic work-up for patients with suspected infection, and studies have shown some imaging findings commonly encountered in affected patients. Chest CT in patients with COVID-19 pneumonia shows ground-glass opacity with or without consolidative abnormalities. Case series have proposed that chest CT abnormalities are more likely to be bilateral [8,18].

Today, it is observed that Cavalieri Principle, an objective method of volume calculation, is often applied on images attained by radiologic studies in clinical practices [19-21]. It was perceived in many writings that images taken by CT would be valuable to reach

Table 2: Volume Ratios of ground glass opacity without and with consolidation and intraparenchymal pulmonary vessels to total lung volumes in patients with COVID-19 pneumonia (%).

Variables	N	Minimum	Maximum	Mean	Std· Deviation
Right lung					
Ground glass opacity without consolidation Ratio	29	0·00	25·00	9·79	6·26
Ground glass opacity with consolidation Ratio	29	0·00	32·00	13·02	8·71
Intraparenchymal pulmonary vessel Ratio	29	3·00	6·00	4·27	1·06
Left lung					
Ground glass opacity without consolidation Ratio	29	1·00	22·00	7·47	5·58
Ground glass opacity with consolidation Ratio	29	1·00	25·00	9·16	7·09
Intraparenchymal pulmonary vessel Ratio	29	2·00	6·00	3·57	0·89
Both lungs					
Ground glass opacity without consolidation Ratio	29	3·70	43·30	17·27	10·45
Ground glass opacity with consolidation Ratio	29	4·00	57·00	22·18	13·53
Intraparenchymal pulmonary vessel Ratio	29	4·00	11·00	7·84	1·56
Intact remaining parenchyma Ratio	29	35·00	89·00	69·98	13·15

sharper results in imaging the total lung obviously and calculations of lung diseases [22,23].

In the presented study, the mean of CE was 2.45%; it should be less than 5% [12]. This reflects the acceptability of the sectioning and the density of the points in the grid. The CE reflects the effectiveness of the applied stereological method i.e. Cavalier volume estimation. The estimation of the volume and volume fraction using the stereological approach applied in this study provides unbiased data about the volumetric quantities of the lung. The values obtained in this way are reliable and reproducible. Moreover, the stereological approach could be easily applied without altering routine radiological imaging techniques and the obtained data show little inter-observer variation [9,13,24,25].

Our study had some limitations. Firstly, our study analyzed the volumetric amounts of the most frequent features of CT scans of the thorax in patients infected with 2019 novel coronavirus pertaining to admission time and volumetric changes of the following up CT scans wasn't analyzed. Another limitation of the present study is correlation between volumetric amounts of ground glass opacity without and with consolidation, intraparenchymal pulmonary vessels, and intact remaining parenchyma and requiring of patients to oxygen therapy and mortality wasn't studied. More studies should be made to understand the efficacy of stereological methods in diagnosis and management of patients in order to decrease mortality of COVID-19 pandemic.

The radiologist plays a key role in the quick identification and early diagnosis of new cases of COVID-19, which can be of great advantage not only for the patient but also for the larger public health investigation and response systems. Images obtained by Spiral CT scan would be helpful to reach stronger results in imaging the total lung and evaluations of novel coronavirus pneumonia. Reliable quick diagnosis based on CT scans is crucial for clinicians to manage COVID-19 patients. We hope the stereological methods according to chest CT scans may help triage patients and screening patients requiring admission to ICU, oxygen therapy, and completely monitoring.

Conclusion

It was concluded that the lung volume and volume fraction of ground glass opacity, consolidation, intrapulmonary vessels, and intact remaining parenchyma of COVID-19 pneumonia could be calculated accurately and effectively using the principle of Cavalieri on CT images with this study.

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References

1. Deng SQ, Peng HJ. Characteristics of and Public Health Responses to the Coronavirus Disease 2019 Outbreak in China. J Clin Med. 2020; 9: E575.
2. Patel A, Jernigan DB. Initial Public Health Response and Interim Clinical Guidance for the 2019 Novel Coronavirus Outbreak - United States. 2020; 69: 140-146.
3. Zhu N, Zhang D, Wang W. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020; 382: 727-733.
4. Gorbalenya A, Baker S, Baric R. Severe acute respiratory syndrome-related coronavirus: the species and its viruses-a statement of the Coronavirus Study Group. bioRxiv. 2020.
5. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol. 2019; 17: 181-192.
6. Chen N, Zhou M, Dong X. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395: 507-513.
7. Huang C, Wang Y, Li X. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395: 497-506.
8. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. PloS one. 2020; 15: e0230548.
9. Odaci E, Sahin B, Sonmez OF. Rapid estimation of the vertebral body volume: a combination of the Cavalieri principle and computed tomography images. Eur J Radiol. 2003; 48: 316-326.
10. Sahin B, Alper T, Kokcu A, Malatyalioglu E, Kosif R. Estimation of the amniotic fluid volume using the Cavalieri method on ultrasound images. Int J Gynaecol Obstet. 2003; 82: 25-30.

11. Basoglu A, Buyukkarabacak Y, Sahin B, Kaplan S. Volumetric evaluation of the lung expansion following resection: a stereological study. Eur J Cardiothorac Surg. 2007; 31: 512-517.

12. Gundersen HJG, Jensen EB. The efficiency of systematic sampling in stereology and its prediction. J Microsc. 1987; 147: 229-263.

13. Bilgic S, Sahin B, Sonmez OF. A new approach for the estimation of intervertebral disc volume using the Cavalieri principle and computed tomography images. Clin Neurol Neurosurg. 2005; 107: 282-288.

14. Mattfeldt T, Gottfried HW, Wolter H, Schmidt V, Kestler HA, Mayer J. Classification of prostatic carcinoma with artificial neural networks using comparative genomic hybridization and quantitative stereological data. Pathol Res Pract. 2003; 199: 773-784.

15. Mattfeldt T, Trijic D, Gotffried HW, Kestler HA. Incidental carcinoma of the prostate: clinicopathological, stereological and immunohistochemical findings studied with logistic regression and self-organizing feature maps. BJU Int. 2004; 93: 284-290.

16. Cruz-Orive LM. Unbiased Stereology: Three-Dimensional Measurement in Microscopy. J Anat. 1999; 153: 157-194.

17. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology. 2008; 246: 697-722.

18. Lei J, Li J, Li X, Qi X. CT Imaging of the 2019 Novel Coronavirus (2019-nCoV) Pneumonia. Radiology. 2020; 295: 18-18.

19. Yan X, Polo Carbayo JJ, Weibel ER, Hsia CC. Variation of lung volume after fixation when measured by immersion or Cavalieri method. Am J Physiol Lung Cell Mol Physiol. 2003; 284: 242-245.

20. Markowitz ZaL, Murray and Reinhardt, Joseph. The use and benefit of stereology in choosing a CT scanning protocol for the lung. Progress in Biomedical Optics and Imaging - Proceedings of SPIE. 2005; 5747: 667-674.

21. Alkoc OA, Songur A, Eser O. Stereological and Morphometric Analysis of MRI Chiari Malformation Type-1. J Korean Neurosurg Soc. 2015; 58: 454-461.

22. Sengul AT, Sahin B, Celenk C, Basoglu A. Postoperative lung volume change depending on the resected lobe. Thorac Cardiovasc Surg. 2013; 61: 131-137.

23. Hsia CCW. Quantitative morphology of compensatory lung growth. Eur Respir Rev. 2006; 15: 148.

24. Sahin B, Emirzeoglu M, Uzun A. Unbiased estimation of the liver volume by the Cavalieri principle using magnetic resonance images. Eur J Radiol. 2003; 47: 164-170.

25. Akbas H, Sahin B, Eroglu L. Estimation of breast prosthesis volume by the Cavalieri principle using magnetic resonance images. Aesthetic Plast Surg. 2004; 28: 275-280.