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Computed Tomography scanning in patients with COVID-19: artificial intelligence analysis of lesions volume and outcome

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Abstract. – OBJECTIVE: The aim of this study was to summarize the computed tomography (CT) chest scanning results of COVID-19 patients, and to assess the value of artificial intelligence (AI) dynamics and quantitative analysis of lesion volume change for the evaluation of the disease outcome.

PATIENTS AND METHODS: First chest CT and reexamination imaging data of 84 patients diagnosed with COVID-19 who were treated at Jiangshan Hospital of Guiyang, Guizhou Province from February 4, 2020, to February 22, 2020, were retrospectively analyzed. Distribution, location, and nature of lesions were analyzed according to the characteristics of CT imaging and COVID-19 diagnosis and treatment guidelines. Based on the results of the analysis, patients were divided into the group without abnormal pulmonary imaging, the early group, the rapid progression group, and the dissipation group. AI software was used to dynamically measure the lesion volume in the first examination and in the cases with more than two reexaminations.

RESULTS: There were statistically significant differences in the age of patients between the groups (p<0.01). The first chest CT examination of the lung without abnormal imaging findings mainly occurred in young adults. Early and rapid progression was more common in the elderly, with a median age of 56 years. The ratio of the lesion to the total lung volume was 3.7 (1.4, 5.3) ml 0.1%, 15.4 (4.5, 36.8) ml 0.3%, 115.0 (44.5, 183.3) ml 3.33%, 32.6 (8.7, 98.0) ml 1.22% in the non-imaging group, early group, rapid progression group, and dissipation group, respectively. Pairwise comparison between the four groups was statistically significant (p<0.001). AI measured the total volume of pneumonia lesions and the proportion of the total volume of pneumonia lesions to predict the receiver operating characteristic (ROC) curve from early development to rapid progression, with a sensitivity of 92.10%, 96.83%, specificity of 100%, 80.56%, and the area under the curve of 0.789.

CONCLUSIONS: Accurate measurement of lesion volume and volume changes by AI technology is helpful in assessing the severity and development trend of the disease. The increase in the lesion volume proportion indicates that the disease has entered a rapid progression period and is aggravated.

Key Words:
COVID-19, CT manifestations, Artificial intelligence, Proportion of lesion volume.

Introduction

Since it was found in Wuhan, China, in December 2019, COVID-19 has been rampant all over the world[1,2]. It is caused by the newly discovered highly infectious positive-strand RNA virus of genus β and mainly manifests as a lower respiratory tract inflammation[2]. In China, the epidemic has been controlled within a short time. All confirmed (170) and suspected cases in Guizhou Province were treated in the General Mountain Hospital of Guizhou Province. Our hospital is fortunate to participate in the epidemic prevention, control, and treatment initiatives, and has some experience and ideas in the application of computed tomography (CT) diagnosis and artificial intelligence (AI) technology. At present, the ninth edition of the diagnostic and therapeutic specifications for the imaging manifestations of the disease has been published[3], but there are only a few studies[3,4] that focus on the progress of imaging technologies in COVID-19 patients. This study retrospectively analyzed and summarized the imaging data that were obtained from the initial CT scan and multiple reexaminations of patients with clinically confirmed COVID-19, further strengthening the understanding of the imaging manifestations of COVID-19. AI technology was used to quantita-

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tively analyze the volume change of the lesions and to objectively evaluate the severity and progression of the disease. The results of our study may help to improve the efficiency of clinical diagnosis and treatment of COVID-19 patients.

Patients and Methods

Imaging data of 84 patients with COVID-19, diagnosed at Guizhou Jiangjunshan Hospital from February 4, 2020, to February 22, 2020, were analyzed retrospectively.

This study was approved by the Ethics Committee of Guizhou Orthopedic Hospital and the written informed consents were obtained from patients (Approval No.: 20200301A, 20200302A).

Inclusion Criteria

- In line with the "Diagnosis and Treatment Plan for novel coronavirus Pneumonia (Tentative Ninth Edition)[3]".
- Nucleic acid positive, with clear contact history.
- In addition to the first CT examination, at least two or more reexaminations were performed, with CT interval ≥ two days, and included in AI dynamic analysis.

Exclusion Criteria

- The image quality is not enough for evaluation.
- Incomplete clinical data (For example, missing imaging examination results).

Inspection Method

The 16-row uCT510 scanner (United Imaging, Shanghai, China) was used. The patient was placed in the supine position, with the head advanced, hands up, and a single breath holding. The scanning range was from the chest entrance to the lung bottom.

Scanning parameters

The tube voltage was 120 KV, and the tube current adopted automatic adjustment output technology; Pitch 1.03-1.22, collimator width 0.625-1.3 mm, matrix 512×512, field of vision 350 mm×350 mm, reconstructed by standard algorithm, with a reconstruction layer thickness of 1.0-1.5 mm and layer spacing of 1.0-1.5 mm.

CT image analysis

The film was read independently by two experienced radiologists, and consensus was reached through consultation in case of disagreement. According to the study by Jin et al[4] CT imaging classifies the disease in five temporal stages, namely super early stage, early stage, rapid progression stage, consolidation stage and the dissipation stage. The characteristics of staging are mainly combined with clinical manifestations[5]. Ultra-early stages refer to having been exposed to the virus-polluted environment for 1-2 weeks without any clinical manifestation, negative laboratory examination, positive throat swab examination, and basically missing CT examination. Early stage refers to 1-3 days after the appearance of clinical manifestations (fever, cough, dry cough, etc.), the pathological mechanism is alveolar septal capillary dilation, hyperemia, alveolar cavity fluid exudation and interlobular edema, which is characterized by single or scattered multiple patchy or clustered ground-glass opacities (GGOs), separated by honeycomb-like or grid-like thickened interlobular septa. Rapid progression refers to the appearance of clinical manifestations at about 3-7 days. This stage is characterized by the cellular exudates, further aggravation of the alveolae and interstitial and large area of lighter consolidation. Bronchial inflation sign can be seen. The consolidation stage refers to the clinical symptoms at 7-14 days and is associated with the alveolar fibrin exudates and subsiding interstitial capillary congestion. CT shows consolidation with a smaller range than in the previous stage. The dissipated stage is within 2-3 weeks after the appearance of clinical symptoms, and the scope of the disease is further reduced. The CT manifestations are consolidation, strip shadow, grid thickening of interlobular septa, thickening and twisting of bronchial wall into strip shape and a little patchy consolidation shadow[5,6].

AI quantitative measurement

AI was used to dynamically evaluate the changes in the disease. The Airigin 3D Pro software developed by Shanghai Xinjian Medical Technology Co., Ltd. (Shanghai, China) was used to measure the volume of lesions and manually calculate the proportion of the volume of lesions in the whole lung in 30 cases with more than three CT examinations and imaging data with a review interval of more than or equal to two days. While the focus is automatically segmented by software, there is also an option of manually outlining the area of the lesion to ensure the accuracy of the volume measurement. Briefly, the total volume

and proportion of the lesions can be calculated for each CT examination. The dynamic analysis of the lesions can be divided into three stages: early, progressive and dissipation stage. Based on the AI measurement, the proportion of the lesion volume in the progressive stage is larger than that in the early stage, and the proportion of the lesion volume in the recovery stage is smaller.

Statistical Analysis

SPSS 26.1 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 8.0 (La Jolla, CA, USA) statistical analysis software were used. The measurement data that do not conform to the normal distribution are expressed by M (Q1, Q3), and the Kruskal-Wallis' rank sum test is used for the comparison of the four periods. The counting data is expressed in the number of cases. Since the expected value is less than 5 in each stage group, Fisher's exact probability method is compared in four periods. The dynamic change trend of the volume ratio of pneumonia focus was displayed by using a line chart. Sensitivity, specificity, and area under the curve (AUC) were used to predict the rapid progression of the focus by analyzing the volume of pneumonia focus and the proportion of the volume of pneumonia focus with the receiver operating characteristic (ROC) curve. $p<0.05$ is statistically significant.

Results

In this study, imaging data of 84 COVID-19 patients with confirmed epidemiological history, 40 males and 44 females, aged from 2 to 84 years, with an average age of 44 years, met the inclusion criteria of the study. The median age of initial CT imaging staging is statistically significant ($p<0.01$). There were no significant differences in the gender of patients between the groups ($p>0.05$) (Table I).

In this study, AI was used to analyze the imaging data of 30 patients who underwent more than three CT examinations for the first time. Among them, 3 patients had no obvious imaging findings after nine examinations. However, AI also gave the volume of the lesions and calculated the proportion of the lesions. There were 13 cases in the early stage, 23 cases in the rapid progression stage, and 48 cases in the dissipation stage. A total of 93 CT examinations were performed. The total volume and proportion of lesions in the non-imaging group, early stage, rapid progression stage, and dissipation stage were significantly different among the four groups ($p<0.01$) (Table II).

In 30 patients with more than three reexaminations, the total volume of pneumonia and the proportion of the total volume of pneumonia were measured by AI. The total volume was 37 ml, accounting for 1.13%. When used as the cut-off value, this total volume predicted rapid progression of pneumonia, with a sensitivity of 92.10% and 96.83% respectively, and specificity distribution of 100% and 86.56%, as demonstrated by the ROC curve. The area under the curve was 0.789 (Figure 1). Figure 2 shows CT images and an AI-derived three-dimensional modeling diagram, measuring the volume of each lesion in the same patient as in Figure 2, in the early (Figure 2 A, D), progressive (Figure 2 B, E), and dissipation (Figure 2 C, F) stages.

Discussion

The imaging staging of COVID-19 can be divided into super early stage, early stage, rapid

Table I. Basic information of COVID-19 patients in different imaging stages.

Stages	n	Age (years)	Gender	
		M, 95% CI	Male	Female
No imaging manifestation	26	30.7 (25.2, 36.2)	11	15
Early stage	22	42.6 (34.6, 50.6)	13	9
Rapid progress period	32	47.6 (41.3, 54.0)	12	20
Dissipating	4	56.0 (39.7, 72.3)	3	1
Z/χ^2		5,124.942[a]	3.829[b]	
p		<0.001	0.293	

[a]Kruskal-Wallis' rank sum test Z value; [b]Fisher's exact probability Chi-square value.

Table II. Analysis of dynamic chest CT images of COVID-19 patients in different stages.

Stage	n	Lesion volume [ml, M (Q1, Q3)]			Lesion volume ratio [%, M (Q1, Q3)]			Lung volume [ml, M (Q1, Q3)]		
		Left lung	Right lung	Total volume of lesion	Left lung	Right lung	Total volume ratio of lesions	Left lung	Right lung	Total lung volume
No performance	9	2.0 (0.6, 4.1)	0.8 (0.7, 2.6)	3.7 (1.4, 5.3)	0.1 (0.0, 0.2)	0.0 (0.0, 0.2)	0.1 (0.1, 0.3)	1,922.2 (1,304.3, 2,373.5)	2,458.9 (1,383.4, 2,701.5)	4,301.7 (2,354.7, 4,903.9)
Early stage	13	8.1 (3.9, 14.2)	4.5 (1.0, 25.1)	15.4 (4.5, 36.8)	0.3 (0.3, 1.0)	0.3 (0.1, 1.1)	0.3 (0.1, 1.0)	2,373.3 (1,483.5, 2,800.8)	2,443.9 (1,712.2, 2,759.1)	5,056.4 (3,222.0, 5,292.8)
Rapid progress period	23	31.4 (18.5, 75.4)	71.3 (18.9, 120.2)	115.0 (44.5, 183.3)	2.2 (0.7, 6.1)	4.4 (1.1, 1.0)	3.3 (1.2, 8.6)	1,445.8 (1,284.2, 1,750.8)	1,619.4 (1,441.5, 1,864.4)	3,132.0 (2,785.5, 3,725.7)
Dissipating	48	11.6 (3.0, 37.7)	24.5 (1.9, 73.0)	32.6 (8.7, 98.0)	0.81 (0.1, 2.7)	1.2 (0.1, 3.6)	0.9 (0.2, 2.9)	1,571.7 (1,357.3, 2,378.6)	1,858.0 (1,607.6, 2,537.7)	3,603.9 (3,069.1, 4,850.8)
Z		21.489	21.109	26.543	17.907	20.171	22.585	6.105	8.536	6.388
p		.000	.000	<.001	.000	.000	<.001	.107	.036	.094

*CRAO: central retinal artery occlusion; BRAO: Branch retinal artery occlusion; dw-MRI: Diffusion-weighted.

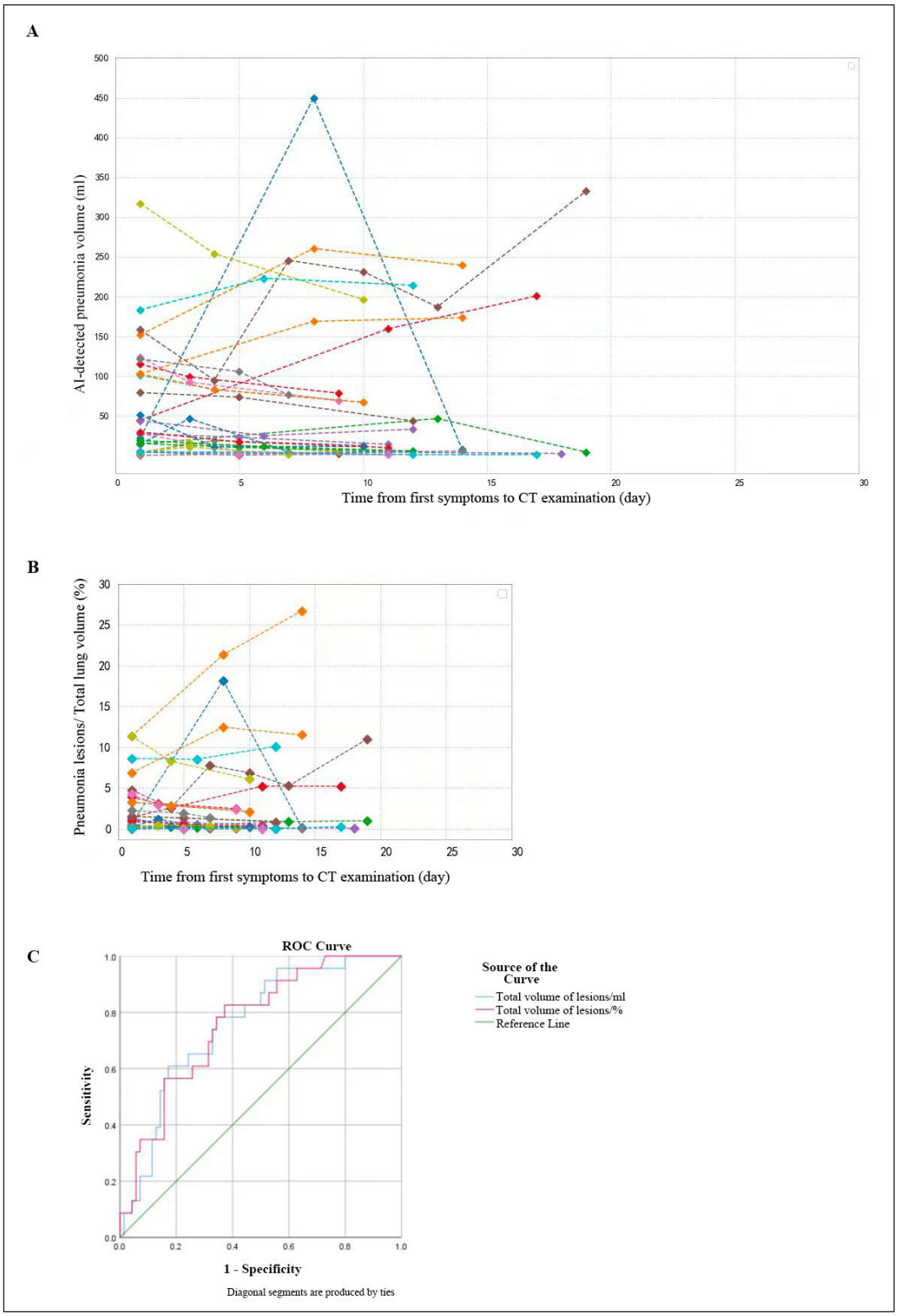

Figure 1. Measurement of dynamic changes in COVID-19 patients with different imaging stages and ROC plot of pneumonia development into rapid progression. **A**, Sequential measurement of the dynamics of pneumonia lesions as a percentage of total lung volume from the time of first symptoms to CT examination. **B**, Sequential measurement of dynamic change of the ratio of pneumonic focus to total lung volume with the time from the first symptom to CT examination. **C**, The total volume of pneumonia lesions measured by AI and the total volume of pneumonia lesions were compared with the ROC curve of predicting the rapid progression of pneumonia.

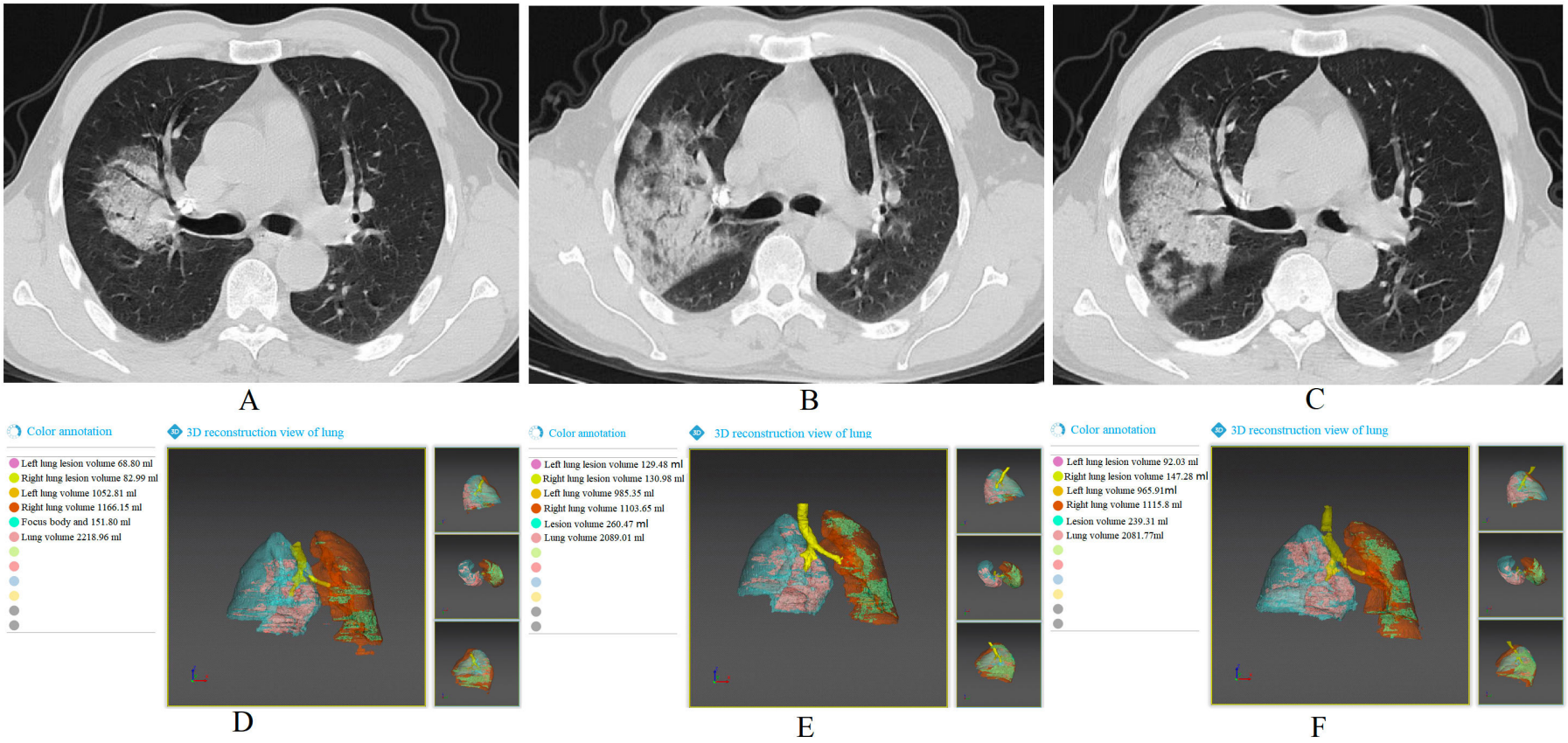

Figure 2. CT images and AI 3D-modeling in different periods of the same patient. **A-C**, Refer to the early, progressive, and dissipative CT manifestations of the same patient with COVID-19. **D-F**, Is the volume and three-dimensional reconstruction of the lung of the same patient in the early stage, progressive stage, and dissipation stage of COVID-19 AI.

progress stage, consolidation stage, and dissipation stage[7,8]. The ultra-early stage is often overlooked without the CT examination. Both the rapid progression stage and consolidation stage are associated with consolidations on the CT scan, making it difficult to distinguish between the images[8]. Therefore, the CT image data of 84 patients with COVID-19 in our study were divided into four groups: no abnormal imaging findings of both lungs, early stage, rapid progression stage, and the dissipation stage. CT examination is an important means to evaluate COVID-19[9]. However, it lacks specificity. At present, the diagnosis of COVID-19 is mainly based on epidemiological history, clinical manifestations, imaging manifestations, and nucleic acid detection[10]. AI has its unique advantage in quantifying the lesion volume of COVID-19. By dynamically observing lesion volume changes, the progression of the lesion can be predicted, which is helpful for clinical treatment[11].

In our study, of 84 patients with COVID-19, 26 had no abnormal imaging findings on their lung CT. The median age of this group was 31 years, indicating that the infected people without obvious CT manifestations tend to be young adults. Additionally, there was no statistically significant gender difference, which was consistent with previous literature[10,12,13]. We may speculate that the strong immune system of young adults is probably the main reason for the absence of lung lesions, but the possibility of a false positive diagnosis cannot be ruled out[7,14].

In the rapid progression stage (days 3-7 of symptomatic presentation), the scope and volume of the pathological manifestations increase[15-18]. AI technology can quantify the lung lesion volume of COVID-19 patients and may therefore help to objectively and accurately assess the condition[11,19]. Durhan et al[20] evaluated the severity of advanced novel coronavirus pneumonia through CT visual quantitative assessment and AI to provide early warning for clinically common type patients with severe disease. In this study, AI was used to carry out quantitative statistics on the patients with initial CT examinations and more than two reexaminations. It was found that the volume change of the lesions in the early, rapid progression and dissipation stages should theoretically demonstrate an upward and downward trend similar to a parabolic change. The actual time-focus overall dynamic change diagram depends on the stage of the initial examination, clinical treatment effect, individual reaction degree, and reexamination times. Most COVID-19 infections have three stages: early stage, rapid progression stage, and dissipation stage. The change in lesion volume can be seen in the parabolic-like broken line chart. The first CT examination of a few cases in the rapid progression stage showed a gradual downward trend on the time-volume change chart. In addition to calculating the volume of lesions by AI, we can also calculate the specific value of the volume change and growth of lesions from early to rapid progression[20,21].

Limitation of the Study

(1) The sample size of cases is small; (2) the inclusion criteria of AI is CT examination 3 or more times, which may exclude critical patients who have been examined once or twice, and potentially introduce a bias; (3) there is no combined data of clinical manifestations and laboratory examinations; (4) AI cannot accurately reflect the change of density when measuring the volume of the lesion, as the scope of the lesion remains unchanged, and the density may increase and decrease. The increase in density indicates the increase of exudation, and the decrease in density indicates the absorption of the lesion. Therefore, judging the progression of the disease only by the change of the lesion volume is not completely accurate; (5) the criteria for imaging grouping and staging based on the diagnosis and treatment guidelines cannot be strictly implemented, which may make our results subjective and uncontrollable; 6) some image signs, such as paving stone signs, are not clearly understood, and there is a risk of misjudgments and misinterpretation.

Conclusions

Despite certain limitations, AI technology has unique advantages in the quantification of lesion volume and dynamic accurate measurement. It can objectively evaluate the severity and predict the development trends of the disease. Further studies with large sample sizes are needed to verify the effectiveness of AI-based measurements.

Authors' Contributions

YZ conceived and designed the study, YC, LC and QZ collected data and performed data analysis. YZ wrote the draft of this manuscript. BQ edited the manuscript.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Ethics Approval
This study was approved by the Ethics Committee of Guizhou Orthopedic Hospital (Approval No.: 20200301A, 20200302A).

Conflict of Interests
The authors declare that there is no conflict of interest.

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