Pilot Study On The Value of Echocardiography Combined With Lung Ultrasound In The Diagnosis And Treatment of COVID-19 Pneumonia

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Abstract

Background: This study aimed to investigate the relationship between echocardiography results and lung ultrasound score (LUS) in coronavirus diseases 2019 (COVID-19) pneumonia patients and to evaluate the impact of their combined application in the diagnosis and treatment of COVID-19 pneumonia.

Methods: Hospitalized COVID-19 pneumonia patients who underwent lung ultrasound and echocardiography daily were included in this study. Patients with tricuspid regurgitation within 3 days of admission were enrolled, and the correlation and differences between their pulmonary artery pressure (PAP) and LUS on days 3, 8, and 13 were compared. The inner diameter of the pulmonary artery root and the size of the atria and ventricles were also observed.

Results: Pulmonary artery pressure within 3 days (on day 3, 8 and 13) of admission was positively correlated with LUS ($r = 0.448, p = 0.003$; $r = 0.738, p = 0.000$; $r = 0.325, p = 0.036$). On day 8 the values of both PAP and LUS were higher than their corresponding values on days 3 and 13 ($p < 0.01$). On day 8 the positive rate for increased PAP and LUS was 92.9% (39/42) and 90.5% (38/42), respectively, and the combined positive rate for these two was 97.6% (41/42). On day 8 the inner diameters of the right atrium, right ventricle, and pulmonary artery differed significantly from their corresponding values on days 3 and 13 ($p < 0.05$).

Conclusions: PAP is positively correlated with LUS. The two should be combined for a more informative assessment of the status of recovery from COVID-19 pneumonia.

Background

On February 11, 2020, the disease caused by the severe acute respiratory syndrome coronavirus 2, which broke out in Wuhan, Hubei, China, was named coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO)^[1]. With the rapid worldwide spread of COVID-19^[2, 3], real-time reverse transcriptase polymerase chain reaction (RT-PCR) and high-resolution chest computed tomography (CT) have been increasingly unable to meet the demands of diagnosis. Many countries and regions have gradually adopted ultrasonography as the basic examination method^[4–6], especially Italy^[7]. Improvements in the diagnostic value of ultrasound for COVID-19 pneumonia are required. At present, there is some literature^[8, 9] regarding the development of combined pulmonary and cardiac ultrasound for the evaluation of patients with COVID-19 pneumonia, but the correlation between pulmonary arterial pressure and lung ultrasound score (LUS) has not been clearly reported. If the two are related, the results of one of these investigations may reflect the results of the other, thereby reducing the burden of work in a specific environment. The present study aimed to provide useful information in this regard for the diagnosis and treatment of COVID-19 pneumonia.

Methods

Study design

This study was supported by the Ministry of Science and Technology of the People's Republic of China (grant number: 2020YFC0844900). The study was approved by the Ethics Committee of Beijing You An Hospital affiliated to the Capital Medical University ([2020]020). Informed consent was obtained from all the patients. In keeping with the WHO guidelines for prevention of the spread of COVID-19, our hospital's infection prevention and control procedures were strictly followed, thus ensuring that none of the health workers involved in the study were infected with the disease.

The present study included hospitalized COVID-19 pneumonia patients (diagnosis confirmed by RT-PCR and CT) who underwent dynamic lung ultrasound and echocardiographic observation upon admission to the hospital. The combined use of the two modalities for evaluating lung lesions was assessed, and correlations between the two were calculated.

One hundred and thirty-eight patients with COVID-19 pneumonia were treated at our hospital. As per the government policy in China, such patients must be hospitalized for observation and treatment once diagnosed; therefore, the hospitalization rate of patients with COVID-19 pneumonia was 100%. The proportion of patients with tricuspid valve regurgitation increased by day 3 of admission; therefore, we selected patients in whom tricuspid regurgitation was evident within 3 days as the study subjects (42 cases). Thereafter, LUS and echocardiographic examinations were conducted daily. The mean length of stay in hospital was 15 days. Other studies, including our own previous research, suggest that the length of time between the appearance of symptoms and the most severe stage of the disease is approximately 10 days^[10, 11] and the duration between the appearance of symptoms and hospitalization is approximately 2 days. Accordingly, days 3, 8, and 13 were selected for comparisons among LUS, pulmonary arterial pressures, and atrial and ventricular diameters. General symptoms including fever, cough, dyspnea, and history of underlying heart and lung disease were recorded.

Lung ultrasound

Rouby^[12] proposed to divide a unilateral lung into six zones for examination. In the present study, with the anterior and posterior axillary lines as the boundaries, the lung was divided into three zones: anterior, lateral, and posterior (Fig. 1). Each zone was further divided into the upper and lower parts. In the examination, the worst sign of each zone was considered as the final judgment sign of the zone, and the results were recorded as the following four basic types (Fig. 2): type N: the ultrasonographic features were line signs of ≤ 2 independent B lines, indicating good lung inflation; type B1: the ultrasonographic features were multiple B lines, with an interval of approximately 7 mm between the B lines (B7 lines); type B2: the ultrasonographic features were multiple B lines, and the interval between B lines was ≤ 3 mm (B3 lines); and type C: the ultrasonographic features were hepatization or fragmentation sign of the lung tissue, with dynamic bronchial inflation sign, with or without a small amount of pleural effusion, indicating consolidation of the lung. The scoring of lung ultrasonography was based on the above four types as: N = 0, B1 = 1, B2 = 2, and C = 3. All patients underwent lung ultrasonographic examination, and

the sum of the scores of the 12 zones was recorded. All lung ultrasound images were obtained by two experienced sonologists.

Echocardiography

All the patients underwent echocardiographic examinations daily. Routine parasternal, apical, and other cardiac section scans were performed. The European Society of Cardiology and the European Respiratory Society (ESC-ERS) guidelines specify the diagnosis of pulmonary hypertension (PH), the screening criteria for estimating of PH mainly based on tricuspid regurgitation peak velocity and systolic artery pressure^[13, 14]. Left atrial volume (LAV), left ventricular volume (LVV) and right atrial volume (RAV) were estimated using the disc summation algorithm (Simpson's technique) from a biplanar approach from the apical four chamber^[15, 16]. The pulmonary artery root diameter (PA), right ventricular base diameter (RV-b) and right ventricular internal dimension (RVID) were recorded.

Statistical analysis

The sample size was sufficient for this study. SPSS 26.0 statistical software was used for data analysis. Continuous data were expressed as means $\pm$ the standard deviation. Non-parametric tests were used to assess data that were not normally distributed. The Mann–Whitney U test was used for comparisons of two independent samples. The Kruskal–Wallis test was used for testing multiple independent samples. Pearson's correlational analysis was used to assess correlations between LUS and pulmonary artery pressures. The analysis of variance (ANOVA) was used to analyze the differential distribution of data among more than two groups (LAV), with subsequent *post hoc* corrections for multiple comparisons. A *p* value < 0.05 was deemed statistically significant.

Results

Forty-two patients were included in the cohort, 24 males and 18 females, with an average age of 47.8 ± 10.8 years. Extracorporeal membrane oxygenation support was provided in one case, ventilator support was provided in three cases, and oxygen masks were provided in nine cases. No patients had a history of heart disease or chronic respiratory disease. Their general characteristics, clinical features, and relevant medical history are shown in Table 1.

Table 1
Patients' (n = 42) general characteristics, symptoms,
and relevant medical history.

Characteristics	Patients (42 cases)
Sex(M/F)	24(18)
Age(y)	47.8±10.8
Fever	36(85.7%)
Cough	34(80.9%)
Dyspnea	36(85.7%)
Myalgia	37(88.1%)
Diarrhea	16(38.1%)
Heart disease history	0
Chronic lung disease history	0

LUS and pulmonary arterial pressures in the 42 COVID-19 pneumonia patients on days 3, 8, and 13 differed significantly as the disease progressed. The two parameters were positively correlated within 3 days of admission, and the correlation was higher in patients with more severe disease ($r = 0.448$, $p = 0.003$; $r = 0.738$, $p = 0.000$; $r = 0.325$, $p = 0.036$) (Fig. 1).

LUS directly reflected the degree of lung disease, whereas pulmonary arterial pressure was an indirect indicator of lung disease. Increased pulmonary arterial pressure can directly cause dilation of the pulmonary artery trunk with the corresponding enlargement of the right ventricle and right atrium, and lead to the exacerbation of tricuspid regurgitation. One such patient is shown in Fig. 2, which illustrates the relationships between pulmonary artery changes and tricuspid regurgitation on days 3, 8, and 13. There were significant differences in the LUS of the 42 COVID-19 pneumonia patients within 3 days. Differences in the inner diameters of the atria, ventricles, and pulmonary artery are shown in Tables 2 and 3.

Tables 2. Overall differences in LUS, pulmonary arterial pressure, and atrial diameter on days 3, 8, 13.

Category	On day 3	On day 8	On day 13	p
LUS	6.1 ± 1.0	11.1 ± 1.4	7.6 ± 2.1	0.000
PAP(mm Hg)	26.5 ± 5.7	42.6 ± 8.2	31.3 ± 6.4	0.000
PA(mm)	22.8 ± 1.6	24.6 ± 1.2	23.5 ± 1.4	0.000
RAV(ml)	35.1 ± 5.7	39.3 ± 5.9	37.3 ± 5.6	0.000
RVID(mm)	36.7 ± 2.2	39.0 ± 2.2	36.0 ± 1.7	0.000
RV-b (mm)	25.7 ± 1.9	29.6 ± 2.8	26.1 ± 1.8	0.000
LAV(ml)	35.5 ± 4.4	35.7 ± 3.3	35.4 ± 3.3	0.910
LVV(ml)	95.6 ± 13.9	97.5 ± 13.8	97.3 ± 13.8	0.761

Tables 3. Differences in LUS, pulmonary artery pressure, and atrial diameter on days 3, 8, and 13

Day	LUS	PAP	PA	RAV	RVID	RV-b	LAV	LVV
	p	p	p	p	p	p	p	p
3/8	0.000	0.000	0.000	0.002	0.000	0.000	0.747	0.485
3/13	0.000	0.001	0.052	0.953	0.148	0.424	0.930	0.582
8/13	0.000	0.000	0.001	0.000	0.000	0.000	0.681	0.876

All patients exhibited an overall increase in both pulmonary arterial pressure and LUS on day 8; however, at that point in time there were four patients without any significant increase in the pulmonary arterial pressure and three without any significant increase in LUS. Comparisons of CT findings on day 8 revealed increased severity compared to day 3 in six patients, suggesting that these six patients were false negatives. In one (1/7) patient there was no substantial difference between the CT findings acquired on day 3 and those acquired on day 8, indicating a negative result in this case. There were 41/42 cases in which the two in combination were positive (Table 4).

Table 4. List of positive rates of LUS and pulmonary arterial pressure used alone or in combination.

	PAP	LUS	PAP∩LUS
Positive	39(92.9%)	38(90.5%)	41(97.6%)
Negative	3(7.1%)	4(9.5%)	1(2.4%)
Total	42	42	42

Note -Positive: the pulmonary arterial pressure was greater than 30 mm Hg in three days; LUS greater than 1.

Discussion

The assessment of pulmonary artery pressure is not singular. Right heart catheterization is an advanced method for the evaluation of pulmonary arterial pressure, but it is only used for certain patients because it is an invasive operation^[15, 17]. Abbas et al. developed an algorithm to calculate PVR of patients with pre occipital PH, but this method may lead to false-positive results^[18]. The most commonly used method in clinical practice is to calculate the maximum systolic pressure^[16, 19, 20] using the tricuspid regurgitation velocity^[21]. This method has been widely used and is based on the clear guidelines of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS); therefore, we opted to follow this method to evaluate pulmonary artery pressure in our study. However, this method requires good image quality and sufficient Doppler signal which may be disadvantageous in some settings, but the images of the 42 patients we selected all met the requirements.

In the present study, LUS was positively correlated with pulmonary arterial pressure, with the correlation becoming stronger with increasing disease severity. There are many reasons for increased pulmonary arterial pressure^[14, 22, 23]. Patients with a history of underlying cardiopulmonary disease were excluded from the present study, and the observed changes in the pulmonary arterial pressure were believed to be related to lung disease. During lung inflammation, inflammatory infiltration and alveolar exudate reduce the alveolar surface area available for diffusion, prolonging the diffusion time. Hypoxic acidosis can cause swelling of pulmonary endothelial cells and pulmonary vasospasm, leading to pulmonary hypertension^[14, 24].

The COVID-19 pneumonia outbreak and the 2003 severe acute respiratory syndrome outbreak were both caused by members of the coronavirus family. Angiotensin-converting enzyme-2 is a component of the renin-angiotensin system that protects blood vessels, and is thought to be a functional receptor for coronaviruses on epithelial cells^[25–27]. Another component of the renin-angiotensin system is angiotensin II, which causes inflammation and damage of alveolar epithelium. The lung injury associated with COVID-19 may be due to the upregulation of angiotensin II and reduced angiotensin-converting enzyme-2 levels resulting in increased pulmonary vasoconstriction. The results of the present study suggest that these factors are associated with higher LUS and higher pulmonary arterial pressure.

Many studies^[14–16, 22, 23] have investigated pulmonary arterial hypertension caused by pneumonia; however, there are no reports on the use of pulmonary arterial pressure to predict LUS. In the present study, LUS was dynamically evaluated and echocardiography was performed simultaneously. LUS increased with worsening disease and decreased with improving disease condition. Echocardiography indicated that the amount of tricuspid regurgitation increased with worsening disease condition, and the pulmonary arterial pressure and the inner diameters, volumes of the pulmonary artery, right ventricle, and right atrium also increased. All these parameters exhibited statistically significant changes, and all of them decreased with improving condition (Tables 2 and 3). These results suggest that changes in LUS and pulmonary arterial pressure can reflect lung lesions.

Hemodynamic characteristics indicate that increased pulmonary arterial pressure leads to increased right ventricular ejection resistance, which results in increased inner diameter of the right atrium, right ventricle, and pulmonary artery. Dynamic echocardiography can be used to monitor changes in pulmonary arterial pressure and the size of each chamber of the heart in real time, such that disease development can be assessed in an efficient manner. The positive correlation between pulmonary arterial pressure and LUS in the current study also indicates a tendency in LUS. There were no significant changes in left heart size during the entire course of the disease, indicating a low probability of left heart involvement, which is consistent with previous studies.

In the present study the rate of positivity for increased pulmonary arterial pressure in the 42 patients on day 8 was 92.9%. Three (3/42) patients were stable, which may be related to the compensation by pulmonary blood vessels^[12, 24]. The rate of positivity for LUS on day 8 was 90.5%, and the scores of four patients did not increase with worsening disease conditions. In conjunction with CT findings this suggests that the region of lesion exacerbation did not involve the edge of the lung, which is outside the detection range of ultrasound and is consistent with the principles of lung ultrasound. The positivity rate for the combination of the two was 97.6%, which constitutes an improvement in the accuracy of disease progression evaluation. To date there have been no comparable previous reports.

The current study had some limitations. Some patients needed to undergo oxygen therapy for dyspnea. Compared with patients who did not undergo oxygen therapy, the estimation of pulmonary arterial pressure may be biased. Since the frequency of CT examination was not as high as that of ultrasound, thus not all patients have corresponding CT data at the three study timepoints, causing a lack of basis for comparison. Fortunately, corresponding CT data were available for seven negative patients, which provided a strong basis for diagnosis. At present, many studies^[8, 9] describe the application of LUS and echocardiography in patients with COVID-19 pneumonia. The application of LUS in the literature is mainly denoted by the ultrasonic characteristics of different degrees of lung lesions; for example, B-line, white lung. Cardiac reports^[9] also focus on intensive care unit (ICU) patients. Most of the patients we evaluated were non-ICU patients. Our comprehensive evaluation of patients' lungs (bilateral lung score) may better reflect the degree of illness. The change in pulmonary hemodynamics in patients with COVID-19 pneumonia is clear; we also found the change in pulmonary arterial pressure to be a sensitive indicator at the early stage of the disease. When it is inconvenient to perform double lung scoring in patients on ventilator support, pulmonary arterial pressure can be measured to reflect the severity of lung disease. This knowledge may help to guide the management of patients with severe disease.

Conclusions

In COVID-19 pneumonia patients the pulmonary arterial pressure and LUS are positively correlated. In patients who are difficult to transfer or relocate, pulmonary arterial pressure can indirectly reflect the degree of lung lesions. The combination of the two can improve the rate of diagnosis of lung disease progression and has an important guiding role with respect to monitoring disease progression and, therefore, in making treatment decisions.

Abbreviations

COVID-19 Coronavirus disease 2019

CT Computed tomography

LUS Lung ultrasound score

RT-PCR Reverse transcriptase polymerase chain reaction

Declarations

Ethical approval and consent to participate

The study was approved by the Ethics Committee of Beijing You An Hospital affiliated to the Capital Medical University ([2020]020). The consents were signed by all patients

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Study design: JH, FM, XY, WX. Study management: JH, FM, RJ and SM. Data collection: JH, XY, W L, LD, HL,YZ and JL. Data analysis: JH, XY, YZ and SM. Data interpretation: JH and XY, Writing: JH,XY,FM. Figures: JH. All authors were involved in reviewing each manuscript draft and approving the final submitted version.

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Figures

Figure 1

Correlation between LUS and pulmonary arterial pressure in 42 patients with COVID-19 pneumonia: (a) on day 3; (b) on day 8; (c) on day 13.

Figure 2

Parameters of a 60-year-old male patient with pulmonary hypertension presented with tricuspid regurgitation on color Doppler echocardiography, and pulmonary systolic pressure was estimated on days 3 (a), 8 (b), and 13 (c) using the gradient of tricuspid regurgitation pressure. Clinical features: extracorporeal membrane oxygenation support and low fever with a stable pulse and breathing.