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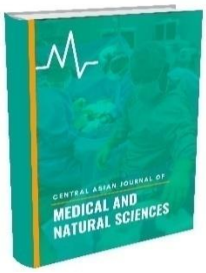

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Advantages of Ultrasound Diagnosis of Pulmonary Pathology in COVID-19 Compared to Computed Tomography

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Key words: chest computed tomography, lung ultrasound, COVID-19 pneumonia, sensitivity, specificity, diagnostic accuracy.

Abstract: Ultrasound examination (US) of the lungs demonstrates high diagnostic value in the evaluation of lung diseases.

Purpose of the study. To determine the diagnostic accuracy of lung ultrasound versus computed tomography (CT) of the chest in diagnosing lung changes in COVID-19.

Materials and methods. A retrospective study was conducted in 45 patients (28 men) aged 37 to 90 years who underwent polypositional ultrasound with an assessment of 14 zones. Echograms of the lungs were compared with CT data on the prevalence of the process and the nature of structural changes. The diagnostic accuracy, sensitivity and specificity of ultrasound compared with the results of CT were determined, and 95% confidence intervals (CI) were calculated. Results. In 44 patients (98%), CT revealed pathological changes in both lungs and had subpleural localization; in 30 cases, the inflammation was limited only to the subpleural sections, in 14 cases, the changes spread to the central sections, while ultrasound revealed changes at a lesion depth of no more than 4 cm. 13-14 zones - CT of the 3rd-4th degree. The sensitivity of ultrasound in detecting lung changes of various nature was > 92%. The highest sensitivity of 97.9% (95% CI: 92.8-99.8%) was determined for small consolidations against the background of interstitial changes (grade 1a+, 1b+), which corresponded to the "cobblestone pavement" on CT. The specificity depended on the nature of the changes and varied from 46.7 to 70.0%. Diagnostic accuracy was > 81%, peaking at 90.6% (95% CI: 85.6–94.2%) for moderate interstitial changes (grade 1a) consistent with ground glass (type 1) CT.

Conclusion. The sensitivity of ultrasound in detecting lung changes in COVID-19 is over 90%. The limitations of ultrasound are the inability to clearly determine the prevalence of the process and to identify centrally located zones of changes in the lung tissue.

The spread of the SARS-CoV-2 coronavirus, which causes the disease COVID-19. started at the end of December 2019. The focus of infection was the Chinese city of Wuhan. In a few months, the disease has spread to more than 210 countries around the world. On March 11, 2020, the World Health Organization declared an outbreak. caused by the new coronavirus. Pandemic [1]. The incubation period for COVID-19 ranges from 1 to 14 days, with most people developing symptoms between 3-7 days: the longest incubation period can be up to 24 days. The clinical severity of COYID-19 varies greatly, from asymptomatic to fatal [1-4].

The "gold standard" for diagnosing SARS-CoV-2 is the detection of viral RNA in a nasopharyngeal swab using polymerase chain reaction (PCR).

Many authors have repeatedly noted the importance of radiodiagnosis in the detection and monitoring of lung damage in COVID-19 [5–8]. Computed tomography (CT) of the lungs is highly sensitive in detecting pathological changes in the lungs in a new coronavirus infection, therefore, to confirm the disease COVID-19 has become the main diagnostic tool that is used in combination with clinical symptoms and epidemiological history data [9,10].

According to Fang Y. et al. [11]. in diagnosing COVID-19, the sensitivity of CT (98%) was significantly higher than that of PCR (71%).

However, this imaging method cannot be used in a hospital ward, and in some clinics in China. Europe and Russia began to use ultrasound examination (ultrasound) of the lungs as an alternative imaging method [12-16].

Ultrasound of the lungs demonstrates a high diagnostic value in the evaluation of various lung diseases and is superior in sensitivity and specificity to X-ray examination of the chest organs [17].

Several recommendations have been published since the start of the pandemic. explaining how best to use lung ultrasound to detect changes characteristic of COVID-19 [18-20]. However, little information is available in determining the diagnostic value of ultrasound in COVID-19 versus chest CT.

Objective: To determine the diagnostic accuracy of lung ultrasound versus chest CT in diagnosing lung changes in COVID-19.

MATERIALS AND METHODS

From March 21 to May 25, 2020, 460 patients were treated in the newly opened infectious diseases department. CT of the chest organs was performed in 397 patients with suspected COVID-19, ultrasound of the lungs and pleural cavities was performed in 77 patients.

Chest CT was performed as a standard method for diagnosing and monitoring the dynamics of the process. Ultrasound of the lungs and pleural cavities was additionally performed in patients with clinical signs of respiratory failure, who could be performed polypositional examination.

To compare the capabilities of CT and ultrasound in diagnosing lung changes in the new coronavirus infection COVID-19, the results of studies of 45 patients were retrospectively analyzed.

Criteria for inclusion in the study:

- a positive test result for SARS-CoV-2. performed using PCR;
- availability of CT data of the lungs:

- availability of lung ultrasound data with an assessment of 14 zones:
- time between chest CT and lung ultrasound < 48 hours.

Among the diseased were 28 (62%) men and 17 (38%) women aged 37 to 90 years: mean age 58.5 = 16.2 years. The time interval between the onset of the disease and hospitalization was from 2 to 19 days, with an average of 7 days. CT and ultrasound were performed on the 2nd-24th day from the onset of the disease, on average, on the 10th day.

Chest CT scan was performed in the "red zone" of the infectious case using a Philips Ingenuity CT tomograph (Philips, the Netherlands).

The optimal variant of the organization of the office was used, when the trained medical staff of the intensive care unit, without the help of an X-ray laboratory assistant, laid down and positioned the patient for examination. In such a situation, the paramedical staff and the CT doctor worked in a clean, “green zone”. All CT examinations were performed in any position convenient for the patient: on the back and lying on the stomach (prone position). If the patient lying on his back showed a decrease in saturation 0, up to 80-84%, the respiratory rate was more than 20 per minute. then the CT examination was performed lying on the stomach (prone position).

All lung ultrasounds were performed in the "red zone" of the infectious diseases department; at the time of the study, the doctor who conducted the study did not have information about the CT results. While working in the “red zone”, they used personal protective equipment recommended by the M3 of the Russian Federation.

Ultrasound was performed on a medium class device ESAOTE MyLab 70 (ESAOTE, Italy). To assess the deep-lying parts of the lung, a high-resolution convex (abdominal) probe with an ultrasound frequency of 2.5-5.0 MHz was used. for a more detailed study of subpleural changes in the lung, a linear sensor with a frequency of 7.5–10 MHz was used. Depending on the severity of the patient's condition, the study was performed in the supine, sitting and prone position (prone position), using the intercostal spaces as an acoustic window.

To detect lung changes in COVID-19, a special U31 I-protocol was used with an assessment of 14 lung zones [20].

Table 1. Ultrasound protocol for assessing 14 zones of the lungs and the correspondence of the zones of examination with ultrasound to the segments of the lungs with CT

Rib cage				Ultrasound	CT
side	surface	designation	zone	compliance with the lungs	(lung segments)
	Front	R1	front upper	upper lobe in front	S3
		R2	anterior lower	middle lobe in front	S5
	Lateral	R3	middle top	upper lobe lateral	S4
Right		R4	middle lower	lower lobe lateral	S2 (1-2-3)
		R5	rear upper	upper lobe behind	S6
	Rear	R6	rear middle	lower sections of the upper lobe and upper sections of the lower lobe at the back	S6
		R7	rear lower	lower parts of the lower lobe from behind	S9-10
	Front	L1	front upper	upper lobe in front	S3

		L2	anterior lower	reed segments in front	S5
Left	Lateral	L3 L4 L5	middle top middle bottom back top	upper lobe lateral lower lobe lateral upper lobe posterior	S2-3 S8 S3
	Rear	L6	rear middle	lower sections of the upper lobe and upper sections of the lower lobe at the back	S6
		L7	rear lower	lower parts of the lower lobe from behind	S9-10

During ultrasonic testing of the lungs, the transducer was positioned in accordance with the BLUE protocol (Fig. 1).

The presented ultrasound technique for examining the lungs - Bedside Lung Ultrasound in Emergency (BLUE protocol) - urgent sonography of the lungs in acute respiratory failure was proposed by Lichtenstein D.A. and Meziere G.A. in 2008 [17], then used by other specialists in ultrasound diagnostics [13, 20].

All ultrasound results obtained were analyzed according to the following criteria:

- state of the pleural line:
- the presence of A-lines;
- the number of V-links;
- presence and volume of lung tissue consolidation:
- the presence or absence of free fluid in the pleural cavities.

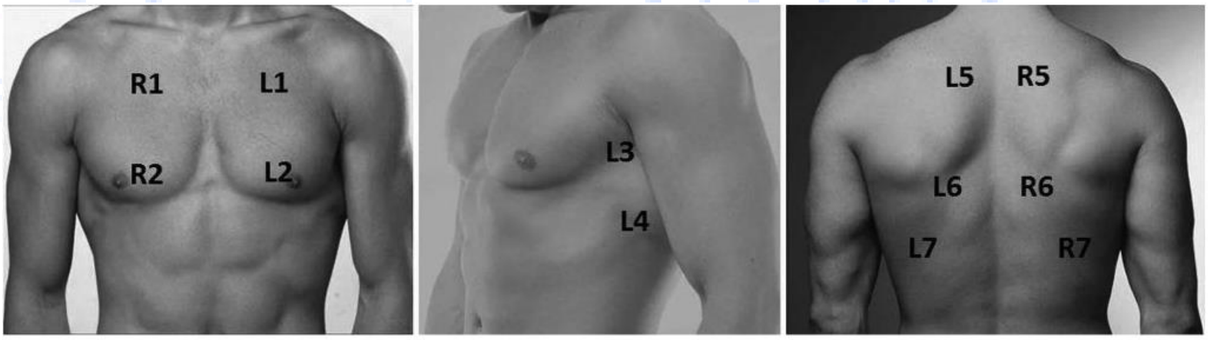

Fig. 1. The layout of the sensor during ultrasound examination of the lungs using the BLUE protocol

***Note**. When examining zones R3 and R4, the location of the sensor is identical to L3 and L4.*

According to the RACM consensus statement (version 2) on lung ultrasound in COVID-19 [20], the data obtained were evaluated taking into account the nature and degree of lung damage, where:

- 0: lung tissue is not changed;
- 1a: moderate interstitial changes:
- 16: pronounced interstitial changes:
- 1a+ or 1b+: small consolidations against the background of interstitial changes:
- 2 or 2+: extended consolidation;
- 3: extensive consolidation (segmental or equity).

All changes revealed by ultrasound of the lungs. were compared with changes detected by CT. taking into account the localization of the inflammatory process and the nature of structural changes in the lung tissue.

CT data were assessed according to approved criteria for the severity of pneumonia, where CT 0 — no lung injury; CT 1 - mild degree (less than 25% of the parenchyma is involved); CT 2 — moderate (from 25 to 50% of the parenchyma affected); CT 3 — severe (from 50 to 75% affected): CT 4 — critical (diffuse involvement of the lung parenchyma over 75%) [21]. Additionally, densitometric parameters of pathological changes in the lungs were measured with CT.

Statistical analysis of data The diagnostic accuracy, sensitivity and specificity of ultrasound compared with CT results were determined. 95% confidence intervals (CI) were calculated [22]. Statistical data analysis was performed using the statistical package MedCalc v. 16.8.4.

RESULTS

Comparison of the number of affected areas by ultrasound with the volume of the lesion by CT

In our study, in 1 patient (2%) with a positive PCR for SARS-CoV-2, inflammatory changes in the lungs were not detected either by CT. not by ultrasound. On ultrasound, his lung tissue was not changed, the pleural line was thin and even. A-lines were traced. B-lines were single. With increasing severity of CT. according to ultrasound. there was a trend towards an increase in the number of affected areas: from 10 areas at CT 1 to 14 areas at CT 4 (Table 2).

In 44 patients (98%), CT showed pathological changes in both lungs and had subpleural localization. Pathological changes only in the lower lobes of both lungs were observed in 3 cases (7%). An isolated lesion of only the upper lobes was noted in 1 case (2%). At the same time, in 30 (68%) cases, inflammation was limited only to the subpleural regions, and in 14 (32%) cases, changes were noted to spread to the central regions of the lungs. Ultrasound showed no changes in the basal parts of the lungs.

Table 2. Distribution of patients depending on the volume of inflammatory changes in the lungs

CT		US	
volume of inflammatory changes in the lungs, % (severity of CT scan)	number of patients, n (% of the total number - 45)	average number of lesions, n (% of the number of areas examined -14)	number of patients, n (% of the total number - 45)
O(CTO)	1(2)	-	1(2)
<25 (CT 1)	7(15)	10(71)	8(18)
25-50 (CT 2)	12(27)	11 (79)	8(18)
50-75 (CT 3)	22 (49)	13(93)	25 (55)
> 75 (CT 4)	3(7)	14(100)	3(7)

Comparison of the nature of the affected areas on ultrasound with the nature of changes on CT

Of particular interest in the study was a comparison of the nature of the affected areas according to ultrasound data with CT data.

It should be noted that in the same patient, depending on the location (anterior, lateral and posterior surfaces of the lungs), it was possible to observe changes in the structure of the lungs, both according to ultrasound and CT.

When comparing the nature of lung lesions on CT with ultrasound data, the following characteristic features were noted. So. ground-glass lung compaction, which was determined on CT as a diffuse increase in the density of lung tissue while maintaining the visibility of the walls of blood vessels and bronchi, could be clearly divided into two types.

The first type is a less intense and less dense "ground glass" - a predominantly interstitial lesion with a slight alveolar component in the form of impregnation (edema) of the lung parenchyma with a density of -765 Hounsfield Unit (HU) to -468 HU. on average -655 HU - localized in all parts of the lungs and was detected in 28 patients in 179 areas of analysis (Fig. 2a, 2b). On ultrasound, these changes corresponded to moderate interstitial changes (ultrasound grade 1a) and were characterized by the presence of scattered B-lines in one intercostal space. extending vertically from the pleural line to the entire thickness of the visualized lung tissue, in an amount of more than 3. 6-8 on average: B-lines could always be counted (Fig. 2c). Such changes were detected in 28 patients in 168 ultrasound zones (Table 3).

The second type is a more intense and dense "ground glass" - an interstitial lesion with an alveolar component with a density of -358 HU to -150 HU. on average -267 HU: alveolar infiltration with a predominant content of large molecular protein fluid (exudate) was found in 23 patients in 100 CT zones. On ultrasound, these patients had pronounced interstitial changes characterized by multiple B-lines that merged with each other, it was impossible to count their number (ultrasound gradation 16 (Fig. 2d)): such changes were detected in 23 patients in 92 ultrasound zones (Table 3).

Ground-glass lung densities seen on CT with the presence of reticular changes (cobblestones) caused by thickening of intralobular septa were detected on CT in 15 cases (98 points of analysis). With ultrasound, these changes were located in the form of subchevral small consolidations - areas of reduced airiness. rounded or irregular in shape up to 1.0 cm in size, 0.4-0.6 cm on average, against the background of interstitial changes and a fragmented pleural line (ultrasound gradation 1a+ or 16+ (Fig. 3f)): such changes were detected in 16 cases in all parts of the lungs in 96 analysis zones (Table 3).

On CT, a combination of ground glass lung compaction and consolidation, which was defined as areas of higher density than ground glass (from -80 to + 100 HU, on average +23 HU) with no visualization of vessels against the background of consolidation , noted in 18 cases at 88 points. On ultrasound, extended consolidation was located in the form of a heterogeneous zone of reduced airiness more than 1.0 cm thick located along the visceral pleura, often observed in combination with interstitial changes (ultrasound gradation 2 or 2+): such changes were noted in 21 patients in 84 zones.

Table 3. Comparison of the nature of lung changes and the number of affected areas according to ultrasound data with computed tomography data

CT			US			US		
The nature of the changes	number of patients *n**	number of affected areas	nature of change	number of patients *n**	number of affected areas	sensitivity, % (95% CI)	specificity, % (95% CI)	diagnostic accuracy, % (95% CI)
The first type of "frosted glass"	28	179	1a (moderate interstitial changes)	28	168	93 9 (89,3-^96,9)	63,6 (40,7-82,8)	90,6 (85,6-94,2)
The second type of "frosted glass"	23	100	16 (pronounced interstitial changes)	23	92	92 (84,8-96,5)	70 (45,7-88,1)	88,3 (81,8-93,5)
"Cobblestone Pavement"	15	98	1a+ or 16+ (minor consolidation against the background of interstitial changes)	16	96	97 9 (92,8-^99,8)	53,9 (33,4-73,4)	88,71 (81,8-93,7)
Frosted Glass and Consolidation	18	88	2 or 2+ (extended consolidation)	21	84	95,5 (88,8-98,8)	46,7 (28,3-65,7)	83,1 (75-89,3)
Extensive consolidation	11	51	3 (extensive consolidation)	11	48	94,1 (83,7-98,8)	56 (34,9-75,6)	81,6 (71-89,6)

In 11 patients, ultrasound revealed the presence of extensive consolidation occupying a segment or lobe of the lung. The lung was of reduced echogenicity. comparable to the echogenicity of the liver tissue. In the affected lung, there was a symptom of "air bronchogram" and the presence of blood flow (US gradation 3). At the same time, linear hyperechoic signals of various lengths were noted in the hypoechoic consolidation, radially diverging towards the periphery and branching at an acute angle, or successively arranged chains of short hyperechoic signals interspersed with short hypoechoic areas. These changes occurred when ultrasonic waves were reflected from inflammatory exudate in the lumen of the bronchial tree. The most pronounced and denser (consolidated) changes were found in the posterior sections of the lungs, both by CT and ultrasound.

The nature of the changes obtained by ultrasound was fully consistent with the nature of the changes by CT (extensive consolidation), but the prevalence of the detected changes in the lungs by CT and ultrasound in 3 patients did not coincide: with ultrasound, a depth of lung damage up to 4 cm was noted, and with CT, the changes were distance of 10 cm or more (Fig. 3a.b).

DISCUSSION

Due to its high sensitivity, CT is currently the imaging modality of choice for diagnosing and monitoring patients with COVID-19. However, chest CT can be difficult for critically ill patients with respiratory and hemodynamic compromise.

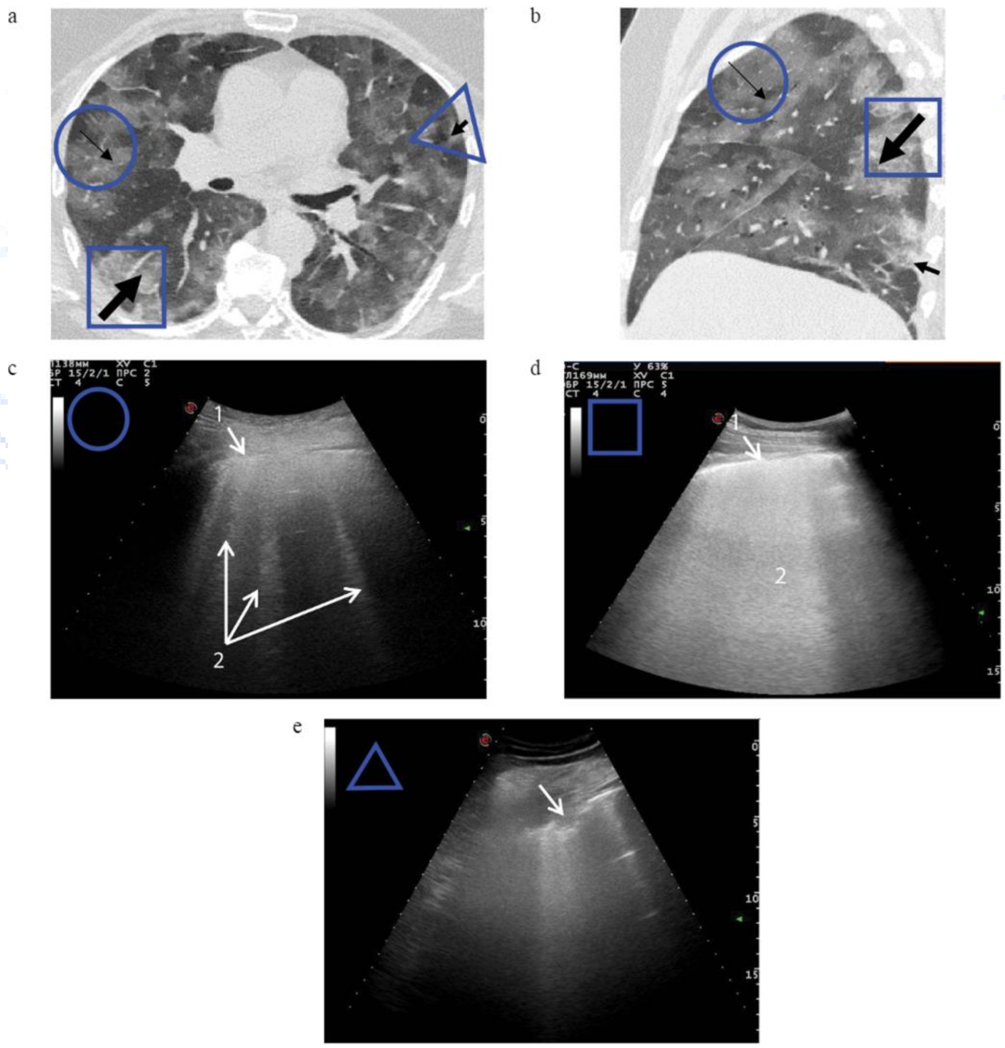

Fig. 2. Computed tomography and echograms of the lungs of a 62-year-old man with COVID-19

a and b: computed tomograms (a — axial projection, b — reformation in the sagittal projection at the level of the right lung). Bilateral pneumonia, CT-3. In the anterior sections of both lungs, there is a low-intensity ground glass induration (thin arrow), in the posterior sections of the right lung, a high-intensity ground glass induration (thick arrow), in the subpleural parts of the left lung, an induration by type) consolidation (short arrow); c, d, e: echograms

c: gradation 1a (moderate interstitial changes), the sensor is located in the zone R1 (at the level of 3 m/r along the anterior axillary line). 1 - discontinuity of the pleural line, 2 - multiple scattered B-lines. The changes correspond to the CT picture of low-intensity ground glass compaction in the same zones, d: gradation 16 (pronounced interstitial changes), the sensor is located in the R6 zone (longitudinally the scapular line at the level of 6 m/r). 1 - thickened uneven pleural line; 2 - wide merging B-lines - "white lung". The changes correspond to the CT picture of high-intensity ground glass compaction in the same areas, e: gradation 1a-b (cortical consolidation). The arrow indicates local subpleural consolidation; the pleural line is not traced along the surface of the consolidation zone; the sensor is located in zone L3 along 5 m/'r along the midaxillary line. Against the background of moderate interstitial changes in the adjacent lung tissue, local consolidation is determined with the absence of a pleural line along the surface, which corresponds to fine consolidation on CT in the same area.

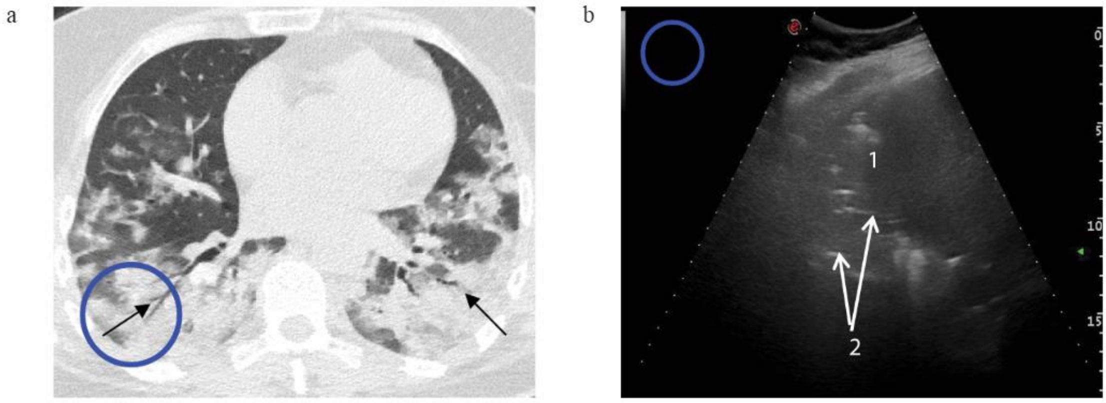

Fig. 3. Computed tomography and echogram of the lungs of a 57-year-old woman with COYID-19

a: CT scan, bilateral pneumonia — CT-2. In the posterior sections of both lungs, compaction is determined by the type of lung tissue consolidation with visualization of the bronchial lumen - a symptom of an "air" bronchogram (thin arrows).

b: echogram, grade 3. The transducer is located in zone R3 (along 7 m/'p in the midaxillary line). 1 — extensive consolidation with airborne echobronchogram, 2 — pleural line on the surface of consolidation is not visualized, which corresponds to changes in CT consolidation of the lung tissue with visualization of the bronchial lumen in the same area.

Increasingly, ultrasonography is being used to assess lung involvement in critically ill patients in the intensive care unit [23]. In these situations, ultrasound may be the best choice for critically ill patients.

Lung ultrasonography is of great importance for the diagnosis of COVID-19 due to its safety, availability, no radiation exposure, low cost, and ability to be used at the patient's bedside in the intensive care unit. The absence of exposure to ionizing radiation provides an advantage in the use of ultrasound in the treatment of COVID-19 pneumonia in pregnant women [21].

Despite the theoretical possibility of ultrasonic waves penetrating to great depths, there are factors that influence lung ultrasound.

1. Airiness of lung tissue. Pathological changes in the lungs that are not adjacent to the visceral pleura, in conditions of preserved airiness of the lung tissue, are difficult to assess using ultrasound. as there is a reflection of ultrasonic waves from the air in the subpleural alveoli. At the same time, in the consolidation phase with COVID-19, the contents of the alveoli are thickened due to the high content of fibrin, cellular detritus, which reduces the airiness of the lung tissue [24]. In this case, it becomes possible to scan the deep basal parts of the lung with ultrasound.

2. Bone structures (sternum, ribs). The high echo density of bone structures and their mixing during breathing make it difficult to visualize the underlying areas.

3. Soft tissue emphysema or pneumothorax. With emphysema, complete dispersion of ultrasound waves from air bubbles at the level of subcutaneous fat occurs, a continuous background of non-informative noise signals appears: with pneumothorax, multiple reverberations of the echo signal emanating from the surface of the lung are visualized due to the air environment.

4. Constitutional features of the patient (thickness and structure of subcutaneous fat). In obese patients, ultrasound waves are scattered and absorbed, which leads to their attenuation in the soft tissues of the chest wall and does not allow one to reliably examine the deep sections.

According to the ultrasound, the following symptom can be detected. indicating the presence of interstitial changes that, under the conditions of the COVID -19 pandemic, can be regarded in favor of coronavirus pneumonia: the appearance of artifacts in the form of scattered or merging B-lines is combined with a thickened intermittent pleural line.

The lack of large-scale studies of the use of ultrasound in COVID-19 and other [25] authors currently does not allow us to reliably determine the diagnostic significance of the method, which requires further research on this topic.

In the presented study, we for the first time compared structural changes in the lungs during ultrasound with CT data. During ultrasound examination, the lungs were assessed polypositionally, taking into account 14 zones.

According to our data, inflammatory changes in the lungs with COVID-19 have a peripheral subpleural location, which coincides with the literature data [8, 9], while in 68% of cases, inflammation was limited to these departments only.

There was a trend towards an increase in the number of lesions according to ultrasound data with an increase in the volume of the lesion according to CT. However, a clear staging according to ultrasound data could not be traced. So. lesions from 10 to 11 zones according to ultrasound corresponded to two degrees of severity according to CT - 1st and 2nd. and damage from 13 to 14 zones according to ultrasound - 3rd and 4th degree of severity according to CT.

Sensitivity in detecting changes in the lungs of various nature was 92% or more. The highest sensitivity - 97.9% (95% CI: 92.8-99.8%) was determined for small consolidations against the background of interstitial changes (grade 1a+ or 1b+), which corresponded to the "cobblestone pavement" according to CT data.

The specificity of ultrasound depended on the nature of the changes and varied from 46.7 to 70.0%. Diagnostic accuracy was greater than 81%, with a maximum accuracy of 90.6% for moderate interstitial changes (grade 1a) consistent with ground glass (type 1) CT.

It should be noted that in 32% of cases, the spread of changes in the central parts of the lungs was noted. At the same time, extensive consolidation was detected by ultrasound, but the prevalence of changes did not coincide with the CT data and was determined at a lesion depth of no more than 4 cm.

The limitations of the present study are the retrospective design and the lack of a sufficient number of patients without baseline lung changes, resulting in low specificity. At the same time, the sensitivity of ultrasound was at a high level, which is more significant in the conditions of mass admission of patients with COVID-19.

Large prospective studies are needed to accurately determine the diagnostic value of ultrasound in detecting lung changes in COVID-19.

CONCLUSION

Subpleural localization of changes in COVID-19 and ultrasound sensitivity of more than 90% in detecting these changes allow us to consider ultrasound as a screening method before referral to CT in conditions of mass admission of patients. The absence of ionizing radiation and the possibility of conducting research in the "red zone" gives ultrasound a number of advantages over CT. in particular in the examination of non-transportable intensive care patients, pregnant women.

At the same time, ultrasound does not make it possible to clearly separate the stages of the disease according to the prevalence of the process and to identify centrally located zones of changes in the lung tissue, for the visualization of which CT is necessary.

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