Use of lung ultrasound in COVID-19: comparison with ultra-high-resolution computed tomography among 29 patients at "D. Cotugno" hospital, Naples, Italy

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SUMMARY

Ultra-High-Resolution Computed Tomography (U-HR-CT) is the reference imaging technique for pneumonia in the new coronavirus disease (COVID-19). Pulmonary Ultrasound (LUS) could be a valid diagnostic alternative for the imaging of COVID-19. Our study aimed to investigate the clinical performance of LUS in the initial evaluation of pneumonia in COVID-19 patients, compared to standard U-HR-CT.
Among 29 patients with confirmed COVID-19, all U-HR-CT hallmarks showed an excellent concordance with LUS findings according to Cohen coefficient. In our experience, LUS is a viable alternative to U-HR-CT, with the advantages of being radiation-free, flexible, cost-effective, and reasonably reducing nosocomial transmission risks because performed at bed-side.

Keywords: COVID-19, SARS CoV-2, ultra-high-resolution computed tomography, pulmonary ultrasound, diagnosis.

INTRODUCTION

A new strain of Coronavirus, called SARS CoV-2, is causing a worldwide epidemic of a new disease called COVID-19 [1]. With increasing numbers of patients presenting with possible coronavirus disease (COVID-19), an efficient approach to patients' assessment is needed to conserve resources and to limit risks of in-hospital transmission. The role of imaging, particularly of Ultra-High-Resolution Computed Tomography (U-HR-CT) as complementary to Reverse Transcription–Polymerase Chain Reaction (RT-PCR) in the screening or diagnosis of COVID-19 pneumonia, has been subject of debate: indeed, U-HR-CT has high sensitivity and is usually readily available. Conversely, RT-PCR has a variable turnaround times, ranging from hours to days [2-5]. Furthermore, in some healthcare settings, RT-PCR may be not available because of lack of testing kits and reagents. Besides its complementary role in the COVID-19 diagnosis, U-HR-CT is useful in the monitoring of the disease evolutions, too.
Interesting are the studies concerning the use of Lung Ultrasound (LUS). LUS is an alternative imaging approach for the COVID 19 diagnosis and, compared to CT, has the advantage of being performed at the patient's bed-side, such reducing the risk of contaminating the environment and limiting the number of healthcare workers ex-

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posed during transport and radiological procedures. Moreover, it is less expensive of U-HR-CT and can be repeated frequently for monitoring the disease not exposing patients to ionizing radiation [6-8].

For these reasons, LUS is gaining growing popularity as a possible complementary tool for the diagnosis of pulmonary diseases [9-11]. However, guidelines on COVID-19 pneumonia diagnosis and management do not include specific recommendations about LUS [9, 12-14].

Our study aims to investigate the radiological performance of LUS in the initial assessment of pneumonia in COVID-19, compared to standard U-HR-CT.

PATIENTS AND METHODS

We performed an observational prospective study comparing the initial radiological assessment of pneumonia among confirmed COVID-19 patients using both LUS and U-HR-CT.

The study has been performed within two Medical Divisions at "D. Cotugno" Hospital in Naples, Southern Italy. "D. Cotugno" hospital is a large mono-specialistic Infectious Diseases hospital, that has been progressively dedicated to the care of suspected and confirmed COVID-19 patients since the end of February 2020. The hospital has a Radiology Unit open on 24 h basis, entirely dedicated to COVID-19 patients during the outbreak period.

The study period started from April 1, 2020, as the portable Ultrasound echography become available. Last patient was included on April 16, 2020.

We included in the study 29 consecutively patients admitted from the two selected Medical Divisions at "D. Cotugno" Hospital", with COVID-19 confirmed diagnosis, and with a U-HR-CT performed at hospital admission.

Radiological methods

In all patients included in the study, U-HR-CT and LUS were performed at admission.

We evaluated ultra-high-resolution CT (U-HR-CT) images of COVID-19 pneumonia to analyse the imaging characteristics in detail. U-HR-CT has both a detector element and X-ray tube focus size smaller than those in conventional CT. The CT images where reconstructed with a 512x512 matrix size, 120 KV, 200 mAs field of view (FOV), window width 1500 HU (range 1100/2000 HU) and window level - 600 HU (range 500/900 HU). Expert radiologist team analysed the U-HR-CT images using a workstation with a 1 K monitor (TCMS Aquilon Toshiba 64 slice, U-HR-CT) that provided multi-planar reconstruction images promptly. The radiologists consensually evaluated the distribution and hallmarks (Ground-Glass Opacity [GGO], consolidation, crazy paving) of the lung opacities, and the presence of local lung volume loss. The "crazy paving pattern" is characterized by the reticular interlobular septa thickening within the patchy GGO.

In the study period, all patients underwent to a LUS in the same day of U-HR-CT, before the performance of U-HR-CT. Radiologist who described the U-HR-CT were not informed about LUS findings.

The US machine was equipped with convex probe multifrequency (3.5-5 MHz and 3-8 MHz), linear probe (9-12 MHz), transducers of different frequencies, with standard presets for the organ of interest (VERSANA ACTIVE - GE). Most US examinations are performed with the patient in the supine position, start at the anterior and anterolateral chest wall (second intercostal space at mid clavicular line and at fourth or fifth intercostal space at the midaxillary line), posterior part of the lung and pleura may be scanned with patient in upright position, sagittal plane provides "bat sign", longitudinal scans used for fracture detection [14, 15]. The duration of the ultrasound scan for each lung sector (anterior, medial and posterior) was 4-5 minutes; the total time needed to complete the entire lung examination was 12-15 minutes.

The abnormal increase in lung water associated with a reduction of air in the alveoli causes loss of fluid into the pulmonary interstitium and alveolar spaces (edema-interstitium lung diseases and acute alveolar-interstitial syndrome: these pathological changes are demonstrable on ultrasound as multiple vertical hyperechoic artifacts originate at the pleural line and extend to the edge of the US screen, called "B-line". The B-lines are a type of reverberation artifact secondary to reflection of sound waves at the interlobular septa. Thickened B lines may fuse together to form coalescent B lines (white lung). B lines represent the LUS finding equivalent to peripheral lung ground glass opacities (GGO) seen in U-HR-CT (ARDS) [12-15].

Study variables

For all included patients, demographical, epidemiological, clinical, radiological and laboratory data were collected consulting the electronic clinical database. In particular, U-HR-CT hallmarks were compared with LUS pattern. We selected as key finding the presence of GGO at U-HR-CT and the presence of multiple B-lines at LUS.

Bias

In order to reduce the risk of bias, no previous communications about radiological findings occurred from LUS operator and U-HR-CT team. The LUS were performed by a single operator, who is an Infectious Diseases specialist Medical Doctor with specific and certified experience for this imaging method. U-HR-CT were performed by a radiologist team.

Statistical methods

Descriptive statistics were performed to describe the study population, and to analyse demographical, epidemiological, clinical, radiological and laboratory data. We used for comparisons the Student t-test for unpaired variables. The χ^2 test (or Fisher's exact test) was used for categorical variables. A *p*-value <0.05 was considered to be statistically significant.

The statistical correlation between U-HR-CT and LUS findings has been calculated by Cohen's k coefficient: k<0.2 = poor concordance; k: 0.2-0.4 = modest concordance; k: 0.41-0.61 = moderate concordance; k: 0.61-0.80 = good concordance; K>0.80 = excellent concordance. The statistical analysis has been performed with Stat Calc software, version 9.3.

RESULTS

The demographic, biochemical and clinical data are summarized in Table 1. Our COVID-19 study population is constituted predominantly by male patients (26/29, 90%), of median age 60 (range 34-79). Twenty-four of the twenty-nine patients enrolled had comorbidities, 62% (15/24 patients) had arterial hypertension as concomitant disease. Upon admission, 26/29 (90%) patients presented with fever, 15/29 (52%) with cough and 8/29 (28%) with dyspnoea. Twenty-three patients (79%) needed respiratory assistance.

All patients have at U-HR-CT multiple bilateral lesion in the lungs, 80% of patients had ground-glass opacity in both lungs, 18/29 (62/%) patients show consolidation in lung left and 20/29 (69%) show consolidation in lung right. 5/29 (17%) patients in lung left and 5/29 (17%) in lung right show "crazy-paving pattern". Table 2 summarizes the U-HR-CT characteristics of the patients: there is no statistically significant difference in the involvement of the lung lobes.

All patients showed abnormal lung ultrasound findings, including multiple B-lines and consolidation. All patients had at US multiple B-lines in both lungs. Consolidation was represented in posterior-basal region of left lung in 26/29 (90%) patients and in right lung in 23/29 (80%), in ante-

Table 1 - Demographic characteristics of the 29 enrolled patients at baseline.

Enrolled patients	29
Gender - female - male	 3/29 (10 %) 26/29 (90%)
Age (median, range)	60 (34-79)
Smoking	6/29 (21%)
Comorbidity - hypertension - diabetes mellitus - bronchial asthma	24/29 (84) % 15/24 (62%) 5/24 (21%) 4/24 (17%)
Clinical characteristics at hospital admission: - fever (n, %) - cough (n, %) - dyspnoea (n, %) - arthralgias (n, %) - conjunctivitis (n, %)	 26/29 (90%) 15/29 (52%) 8/29 (28%) 4/29 (14%) 2/29 (7%)
Oxygen therapy	23/29 (79%)
White cell count (/μl) median±SD	6728,26±2229,41
Lymphocyte count (/μl) median±SD	1090,43±424,31
C reactive protein –CRP (mg/dl) median±SD	3,6±5,75

Table 2 - U-HR-CT characteristics of the 29 enrolled patients at baseline.

	U-HR-CT		
	Left Lung	*Right Lung*	*p value*
GGO	23/29 (80%)	23/29 (80%)	–
Consolidation	18/29 (62%)	20/29 (69%)	0.5806
Crazy-paving pattern	5/29 (17%)	5/29 (17%)	–

Table 3 - LUS characteristics of the 29 enrolled patients at baseline.

LUS			
	Left lung	*Right lung*	*p value*
B-lines	29/29 (100%)	29/29 (100%)	–
White lung	5/29 (17%)	5/29 (17%)	–
Localization of pulmonary consolidations: - posterior-basal - anterior apical-mid thoracic - posterior-mid basal	 26/29 (90%) 28/29 (72%) 10/29 (35%)	 23/29 (80%) 14/29 (35%) 12/29 (41%)	 0.2766 0.000 0.5883

rior apical mid thoracic region in 28/29 (72%) patients in left lung and in 14/29 (35%) patients in right lung (p= 0.000), in posterior mid-basal region consolidation in 10/29 (35%) in left lung and in 14/29 (41%) patients in right lung. 5/29 (17%) patients showed "white lung" 5/29 (17%). Table 3 summarizes the ultrasound characteristics of the patients.

Table 4 shows comparison among U-HR-CT and LUS. Our data show that GGO described by U-HR-CT correlated with the presence of B-lines at LUS (Cohen's k coefficient: 0,966), there was correspondence between the presence of consolidation at U-HR-CT an the consolidation described at LUS (Cohen's k coefficient: 0,897), and the "Crazy paving" described by U-HR-CT correlated with "White lung" described by LUS (Cohen's k coefficient: 0,931). All comparisons showed an excellent concordance according to Cohen coefficient.

Table 4 - Comparison of U-HR-CT and LUS finding in 29 COVID-19 patients.

Part a - Cohen's k coefficient for the presence of interstitial impairment				
		Presence of B-lines at LUS		*Cohen's k coefficient*
		Yes	*No*	
Presence of GGO at U-HR-CT	Yes	28	0	0,966
	No	1	0	
Part b – Cohen's k coefficient for the presence of consolidation				
		Presence of consolidation at LUS		*Cohen's k coefficient*
		Yes	*No*	
Presence of consolidation at U-HR-CT	Yes	24	0	0.897
	No	1	4	
Part c - Cohen's k coefficient for the presence of advanced interstitial impairment				
		"White lung" at LUS		*Cohen's k coefficient*
		Yes	*No*	
"Crazy paving" at U-HR-CT	Yes	4	1	0.931
	No	0	24	

DISCUSSION

We performed a prospective study in order to evaluate the concordance of U-HR-CT and LUS findings in COVID-19 patients. At our knowledge this is the first real-life experience in Southern Italy on this topic.

At present, the diagnosis of COVID-19 is based on the patient's epidemiological history, clinical symptoms, chest imaging findings, and etiological evidence. COVID-19 is highly contagious, thus early detection and diagnosis are of paramount importance in order to isolate suspected and confirmed cases. Radiologic methods could be useful for obtaining a rapid diagnosis of COVID-19 pneumonia that occurs with typical lung changes to which correspond typical chest U-HR-CT imaging including multiple, peripheral, bilateral, patchy, sub-segmental, or segmental ground glass opacities and areas of consolidation, which are mostly distributed along the bronchovascular bundles and subpleural space.

View that CT reports demonstrated that most of the lesions were distributed peripherally in the lung, the examination by LUS could be a useful alternative or complementary option [16]. In fact, pulmonary ultrasound is a more manageable tool than CT for the speed of execution and costs. LUS would also simplify radiological follow-up of COVID-19 patients. In addition, it is done directly at the patient's bed, thus reducing patients' movement, and consequently reducing the spread of the infection in the hospital setting, and the number of healthcare workers exposed. On the other hand, given that the examination takes about 15 minutes, the single operator performing LUS is exposed for a longer time.

Some limits are present in this study. The sample size is small, because this study had been performed in the initial phase of COVID-19 outbreak. Moreover, our observation does not address the ability of LUS to exclude COVID-19 disease (the test sensitivity), because all included patients had confirmed infection.

Although these limits, the main remark is represented by the excellent concordance between U-HR-CT hallmarks and LUS findings. These preliminary results would be confirmed in larger studies in order to overcome the declared limits. The authors will continue to enrol patients, in order to reach a more representative study population.

In conclusion, LUS could serve as a valuable and complementary tool for the detection of lung lesions in COVID-19 pneumonia, with the advantages of being radiation-free, flexible, cost effective, and of reducing the overall nosocomial transmission risks.

Availability of data and material

Original dataset of the study is available upon request.

Authors' contributions

We declare that all authors have made substantial contributions to this paper. In particular: VI, MP, and FMF contributed to the conception and design of the study, the acquisition of data, the analysis and interpretation of data, and contributed to the drafting the article; OT, GP, GDF, RV, RP, GP, EB, contributed to the acquisition and interpretation of data, and revised critically the manuscript for important intellectual content; MC, CR, VS revised critically the manuscript for important intellectual content. All authors gave final approval of the version to be submitted.

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Conflicts of interest/competing interests

All authors declare to have no conflict of interest.

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