Lung ultrasound in the diagnosis and monitoring of 30 children with Coronavirus Disease 2019

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Abstract

Background: The Coronavirus Disease 2019 (COVID-19) is causing of the new global pandemic and is responsible for millions of infections and thousands of deaths in the world. The lung ultrasound is a non-invasive and easily repeatable tool and can be carried out by the pediatrician at the bedside of children with a consequent reduction in the risk of transmission of the virus. Objective: To determine whether the lung ultrasound is a useful tool in identifying the signs of lung involvement in children with COVID-19 and whether can monitor the course of the disease. Methods: The study was made in the emergency department in a tertiary level pediatric hospital. All patients with swab-confirmed COVID-19 infection were subjected a lung ultrasound within 6 hours from admission and after 96 hours. Results: Among a total of 30 children, 18 (60%) were males, 4 reported exertional dyspnea and only 1 chest pain. The mean oxygen saturation was 98.8 ± 1.0 % in ambient air in emergency department and no patient needed oxygen therapy during hospitalization. After 96 hours we had observed ultrasound abnormality al the lung ultrasound only in 20% of the children. We found a statistically significant reduction in pleural irregularities (30% vs 16.7; p: .001) and in B lines (50% vs 20%; p: .008). Conclusions: lung ultrasound is safe and useful tool in detecting lung involvement in children with COVID-19 and in monitoring these patients during the course of disease.

Introduction

Initially described in China, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, etiological agent of the Coronavirus Disease 2019 (COVID-19), rapidly spread all over the world being declared a pandemic by the World Health Organization on March 11th, 2020. Although SARS-CoV-2 caused millions of infections and thousands of deaths struggling all health systems worldwide, the impact on children has been relatively milder, with a minority of severe cases and a small number of deaths reported.[1] Despite a relatively mild acute COVID-19 in children, the Chinese approach included the routine use of chest Computed Tomography (CT) to all children with SARS-CoV-2 infection no matter the clinical situation.[2] However, many studies have proposed a clinically based classification of disease severity for pediatric COVID-19, limiting the use of CT scan to children with severe disease.[3-5] The routine use of CT scan to asymptomatic or paucysymptomatic patients can bear risks related to radiation exposure and above all can determine the increase the risk of virus diffusion due to patient displacement from visit room to X-ray room when is in hospital or moving the patient from home to hospital after the discharge.[6,7] In this context, lung ultrasound (LUS) can be a useful tool to evaluate lung involvement in children with SARS-CoV-2 infection, since COVID-19 is characterized by peripheral lung lesions easily detected by LUS.[8] However, while the role of LUS in adults with COVID-19 has been widely described and a prognostic role has been documented, its use in children is not yet established.[9-12] To date, only two small preliminary case series of Italian children with

COVID-19 have been published, while the role of LUS in the clinical follow-up of children with COVID-19 and potential implication on the use of CT scan is not yet defined.[13,14] For these reasons, we performed a prospective observational study in a pediatric COVID-19 hospital aiming to better clarify the usefulness of LUS in children with COVID-19.

Materials and Methods

We conducted an observational study analyzing LUS patterns in consecutively admitted children with COVID-19 infection in a tertiary level pediatric hospital in Rome from the 27 of March 2020 to June the 1st 2020. All patients with swab-confirmed COVID-19 infection who underwent LUS within 6 hours from admission (T0) and after 96 hours (T1) were included. Patients aged 18 years or more, those who did not underwent both LUS or with comorbidity were excluded. The severity of the disease was classified using the classification of Parri et al, based on the adapted classification of Dong et al.[15,16] The use of LUS in the evaluation of children with respiratory infection has been approved by the ethics committees of our institution. Informed consent was obtained from each parent/guardian.

Lung Ultrasound

LUS was performed with a wireless pocket device connected to a probe, which were placed in single-use plastic covers (Sonosite iViz) as described by Musolino et al.[17]

LUS was performed in patients in the sitting position, and all lung areas were scanned.[18] The two operators responsible for LUS are pediatricians with more than 5 years of experience in point of-care ultrasound.

The LUS patterns looked for were those described by Soldati et al.: pleural irregularities, subpleural consolidations, vertical artifacts, patchy areas of white lung, pleural effusions.[18]

Primary outcome

To evaluate LUS patterns at admission and during follow-up in children with COVID-19.

Secondary outcomes

To evaluate interobserver agreement in the evaluation of LUS patterns in children with COVID-19.

Statistical analysis

Statistical analysis was performed using the SPSS software (IBM Statistical Package for the Social Science Statistics, version 24.0, Chicago, IL). The normality of the data distribution was assessed by the Kolmogorov-Smirnov test. Values were expressed as means ± standard deviation (SD) for continuous variables, median and interquartile range (IQR) for nonparametric data, or number and percentage (%) for categorical variable. The Mann-Whitney test and Student's t test were used to compare nonparametric and normal data respectively while the $\chi 2$ was used to compare categorical variables. The rescued images were subsequently reviewed by the same operators who defined the score. Inter-observer reliability with Cohen's kappa was defined: .81 ± 1.00 excellent, .61 ± .80 good, .41 ± .60 moderate, .21 ± .40 fair, $> 0 \pm .20$ slight, and 0 absent. A p value $< .05$ was considered statistically significant.

Results

Study population

Initially, 2394 children with suspected COVID-19 infection at the first our emergency department examination underwent nasopharyngeal swab for SARS-CoV-2from the 27 of March 2020 to June the 1st2020. Of 55 children with positive swab for SARS-CoV-2, five were excluded for comorbidity: immunodeficiency (one), cerebral palsy (two), neuromuscular diseases (two). Four children were excluded because they were discharged, in six children first LUS was not performed for absence of operators while in ten patients the LUS follow up was not done. A total of 30 children were enrolled in the study (Figure 1).

Population with COVID-19

Among a total of 30 children, 18 (60%) were males with a median age of 8years and 7months (IQR 5 years and 6 months -13years and 9months). The 83.3% of patients were taken directly to our emergency department while the 16.7 % were transferred from another hospital.

Table 1 summarizes demographic and clinical findings of children with COVID-19. Most children were presented with mild disease 22 (73.3%), 7 (23.3%) had moderate disease and 1 (3.3%) had a critical presentation. No child enrolled had a severe disease. Although the distribution by sex showed a slight predominance of the male sex, the girls had a greater severity of the disease (mild disease M/F 72.7/27.3% *vs* moderate disease M/F 14.3/85.7%, p: .012).

Four (13.3%) children reported exertional dyspnea, only 1 (3.3%) chest pain but no patient had respiratory distress to clinical examination. The mean oxygen saturation was 98.8 ± 1.0 % in ambient air in our emergency department and no patient needed oxygen therapy during hospitalization.

Fever was observed in 19 (63.3%) children and had appeared three days before the visit in our emergency department. Diarrhea was reported in 3 (10%) patients but no one had vomit.

Other signs or symptoms included arthralgia 16.7%, headache 13.3% and seizure 3.3%.

Table 2 shows blood tests at base time and T1.

LUS findings

Table 3 shows main baseline (T0) LUS features of children with mild and moderate disease. Those who had moderate disease presented more B line than children with mild disease (85.7% vs 36.4% respectively; p: .03). Furthermore, in children with moderate disease, pleural irregularity and subpleural consolidations were more frequently found than in those with mild forms.

After 96 hours we had observed ultrasound abnormality al the LUS only in 20% of the children. In particular, we found a statistically significant reduction in pleural irregularities (30% *vs* 16.7; p: .001) and in B lines (50% *vs* 20%; p: .008) as showed in Table 2.

We observed a good LUS accuracy in comparison with other imaging technique (CXR/CT/MRI) to found lung abnormality (sensitivity of 90.9% and specificity of 66.6%) (Figure 2).

The inter-rater agreement was .903 with Cohen's kappa coefficient of .80.

Discussion

In this study, we prospectively addressed the role of LUS in a cohort of children with proven SARS-CoV-2 infection, evaluated in a tertiary level referral center for pediatric COVID-19. Vertical artifacts are the most common signs on LUS, while subpleural consolidations, white lung and pleural effusions are relatively rare, compared to described reports from adult with COVID-19. LUS had a 90.9% sensitivity in detecting signs of lung involvement by COVID-19. Importantly, the LUS allowed to differentiate between those with mild or moderate disease.

In this study, we evaluated the role of LUS in the follow-up of children with COVID-19, a data not yet addressed in current literature. LUS control was performed of day 4 of disease and showed in most cases a resolution or improvement of LUS findings. The improvement in LUS was concordant with the improvement of clinical conditions and laboratory tests, suggesting that LUS can also be used in the monitoring of the disease in children with COVID-19, as also previously suggested in adults with COVID-19 (11,12) and children with other lung infections.[19]

A recent multicentric, European study described 582 children and adolescents with PCR-confirmed SARS-CoV-2 infection, with a median age of 5 years.[20] Majority of children had mild disease, including infants, and 52% of evaluated children had radiologic findings of pneumonia (47%) or acute respiratory distress syndrome (5%). Considering the widely accepted ability of LUS in detecting both pneumonia and ARDS, and the fact that majority of children have a mild disease, our study highlights the possibility of using LUS

as a routine and primary level diagnostic in children with stable clinical conditions, reserving secondary level imaging (including CT) to those with diffuse lung disease or with unstable clinical conditions, as previously hypothesized.[2]

This approach would have several benefits: first of all, would reduce radiation exposure related to the routine use of CT scan, suggested by the Chinese Study group on children with COVID-19; secondly, this approach would allow the same physicians to perform both clinical examination, blood sampling and nasopharyngeal swab, and LUS, during the first clinical examination in the emergency department, reducing the risk of exposure to SARS-CoV-2 of other operators. Third, LUS can be used multiple time and can allow close follow-up of children, potentially directly at home, reducing the pressure on critically overloaded emergency department during the peak of the pandemic.

In this study, only a limited number of children performed chest X-ray or CT scan, therefore we have not been able to compare the different technics. For ethical reasons, the routine use of CT scan for research purposes was not allowed in our Institution, and only those children with more severe disease, or in case of clinical decision of the evaluating doctor, underwent CT scan. Importantly, the use of LUS as the first examination performed in children COVID-19 has allowed to reserve the CT only in selected cases, that is, to those who presented at the first LUS a greater interstitial involvement. In addition, these patients were subjected to closer multiparametric and ultrasound monitoring during the hospitalization, performing ultrasound controls in addition to those defined by the study protocol (T0-T1). In 75% of children enrolled we performed a LUS after 10 days from the negativization of swab for SARS-CoV-2and we found in all a normalization of the lung parenchyma.

Although not showed in the results section, it is important to mention that none of the pediatricians responsible of performing LUS resulted positive to SAR-CoV-2 infection on multiple screening procedures performed within the Institution, confirming that if appropriately performed, LUS is safe also in the context of SARS-CoV-2.

Limitations

Our study has a number of limitations. First, like all ultrasound examinations, it is an operator-dependent technique and is associated to a learning curve. To minimize variability, even though the ultrasounds were performed by only two emergency pediatricians with lung ultrasound training, the rescued images were subsequently reviewed by the same operators (Cohen's kappa .80). Secondly, the ultrasound aspects described are not pathognomonic of SARS-CoV-2infection since they are artifacts also found in the course of other lung diseases (e.g. bronchiolitis). These ultrasound aspects, in fact, have a fundamental role for the pediatrician if integrated with the assessment of the child affected by SARS-CoV-2in the classification of the severity of the disease and in the programming of other laboratory and instrumental tests but do not allow the current state of our knowledge to perform diagnosis of COVID-19.

Conclusions

In conclusions, our study shows that LUS is safe and useful tool in detecting lung involvement in children with COVID-19and in monitoring these patients during the course of disease. More studies are needed to understand, on a larger number of patients, if LUS can have a prognostic role in children with COVID-19 or if children with multisystem inflammatory syndrome there are specific features that may allow the evaluating physicians in the early diagnosis of this new syndrome.

Author Contributions

REP, SC, AM: completed the data analysis, literature search, drafted the initial manuscript, reviewed and revised the manuscript.

MAB, MR, AV, PDA: collected the data, reviewed the manuscript.

MCS, AMM, PT, DB: conceived the study, completed the data interpretation and literature search.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Figure legend

Figure1 STARD diagram of flow of participants at the study

Figure 2 Computed tomography scans and lung ultrasound of a child with moderate disease at admission

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Fig 1