Chest computed tomography (CT) features in children with reverse transcription-polymerase chain reaction (RT-PCR)-confirmed COVID-19: A systematic review

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Summary
To describe the chest CT features reported in children with confirmed COVID-19 infection, published in English literature. A systematic review was completed on PubMed, Embase and Scopus databases on the 1st of June 2020 using the PICO strategy. The NIH Quality Assessment Tool was used to assess the quality of the selected articles. The systematic review was evaluated by Case Series Studies and the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA). The extracted data were assessed and compared with those reported in the adult population. Seventy-two articles were retrieved from the database search and screened by the title, abstract and keywords. Eleven articles were deemed eligible for full-text assessment. Nine articles were included for the data extraction and in the final analysis. Chest CT features in children with COVID-19 differ from those in adults. ‘Ground-glass opacities’ (GGOs) are the most commonly described abnormalities, but closely followed by a combination of GGO and consolidation, not usual in adults. Children tend to have a more variable involvement than the subpleural and posterior and basal topography described in adults. Interlobular thickening and air bronchogram found in adults with COVID-19 are not frequent in children. Pulmonary embolism reported in up to 30% of adults has not been yet reported in children. Original articles describing chest CT features in children with COVID-19 in the English literature are limited to small populations of Chinese children. Chest CT imaging features are very diverse across the selected studies and globally different from those reported in adults. Data from children of different countries would provide a more comprehensive description of chest CT features in children with COVID-19.

Key words: children; computerized tomography; COVID-19; epidemiology; SARS-CoV-2; systematic review.

Introduction
On December 2019, several cases of severe respiratory distress provoked by viral pneumonia were reported in Wuhan, China. The respiratory syndrome was caused by a coronavirus, named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), which was isolated from nasopharyngeal swabs, and confirmed by reverse transcription-polymerase chain reaction (RT-PCR). The syndrome was eventually named coronavirus disease 2019 or COVID-19. Thereupon, the number of new COVID-19 cases rapidly increased in China, and the disease subsequently spread to several western countries. On the 11th of March 2020, COVID-19 was
declared a pandemic by the World Health Organization (WHO). Through the worldwide dissemination of COVID-19, an interactive site providing real-time global cases and trends of COVID-19 cases and related deaths was established by the Centre for Systems Science and Engineering at Johns Hopkins University, Baltimore, Maryland, USA. From the early days of the outbreak, COVID-19 appeared to have a limited impact on children, with only a small number of symptomatic and severe cases compared to the adult population. Most of the children affected by COVID-19 were part of family clusters. Some cases of vertical transmission from SARS-CoV-2-infected mothers to newborns were also reported.

In a recent systematic review carried out by Ludvigsson et al. focusing on the epidemiologic features of children with confirmed COVID-19, the vast majority of patients had a complete recovery in one to two weeks. In the most extensive published series of paediatric patients with COVID-19, including 2143 Chinese children, 95% were asymptomatic or showed mild-to-moderate symptoms. In Shenzhen, China, SARS-CoV-2 reported infection prevalence in children under ten years was 7.4%, similar to that of the general population (7.9%). Only 5.4% of infected children had severe symptoms, and critical cases were reported in 0.6% of cases.

Other series supported that the number of severe and critical cases in children was significantly less numerous than those observed in adults. Nevertheless, it was reported that a limited number of children deteriorated in a few days presenting dyspnoea, lymphocyte and platelet count decrease, cyanosis, and abnormal transaminase or creatine kinase. Cases of acute respiratory distress syndrome (ARDS), septic shock, multiple organ failure (MOF) and dysregulation in the coagulation cascade in children were also reported. Clinical deterioration was reported as more likely for paediatric patients with chronic medical illness. The risk of a mild-to-severe acute respiratory syndrome in the context of COVID-19 in paediatric population might be increased in patients on anticancer treatment.

To date, medical literature in English has reported three fatalities in children positive for COVID-19, but the direct relationship with viral infection was controversial. All these three fatal cases in children occurred in China.

Epidemiological data of COVID-19 in children need to be interpreted with caution because some published series or isolated case reports during the early spread included children with a clinical diagnosis of SARS-CoV-2 infection without confirmation by RT-PCR.

Different studies highlight the role of chest CT in the rapid diagnosis of COVID-19, describing some specific lesions and spatial patterns in COVID-19 patients.

Ai et al. using RT-PCR as a gold standard reported that chest CT had a sensitivity of 97%, a specificity of 25% and an accuracy of 68% in the diagnosis of COVID-19. Because RT-PCR sensitivity has been reported to be as low as 70%, chest CT has been used as a screening tool and to monitor treatment in many institutions around the world during the early worldwide spread of SARS-CoV-2.

Although CT studies on patients with COVID-19 included a variable number of children and adolescents, studies focusing on COVID-19 infection in children are limited and performed in small populations.

In adults with COVID-19, chest CT abnormalities might appear before clinical symptoms, and be disproportionately severe. Chest CT abnormalities can be found in patients with negative RT-PCR. On the contrary, a variable proportion of symptomatic children with COVID-19 may have a negative chest CT.

Besides, in the early studies published in Chinese and assessed in a systematic review by Duan et al., Chinese children with COVID-19 exhibited specific imaging features on chest CT, different from those described in adults.

The scope of the present systematic review is to analyse the recent studies that appeared in the English literature focusing on the chest CT features at diagnosis in children with RT-PCR-confirmed COVID-19.

Methods

The systematic review was performed by a panel of board-certified radiologists at the ‘Reine Fabiola’ Children’s University Hospital (Brussels, Belgium), ‘Istituto Ortopedico Rizzoli’ (Bologna, Italy) and Auckland District Health Board (Auckland, New Zealand)/Hospital Vithas Nueve de Octubre (Valencia, Spain). The systematic review field of search was determined using the PICO strategy, as detailed below. PubMed, Scopus and Embase databases were used to search for relevant articles related to computed tomography, COVID-19/SARS-CoV-2 infection in children from the 1st of January 2020 to the 1st of June 2020. The first search was performed on the 24th of April 2020. Considering the fast throughput of publications on COVID-19 chest imaging, the search was repeated on the 1st of June 2020.

PICO strategy

To correctly select the terms in the different databases, the PICO strategy was used. The following PICO question was used to query the different databases:

Population – Children (0–16 years) with a diagnosis of COVID-19 (RT-PCR)
Intervention – Children with chest CT
Comparison – Features of appearances with adult features on chest CT
Outcome – Diagnosis/detection and description of specific signs at diagnosis

Eligibility criteria

The articles were selected for full-text analysis based on the title, abstract and keywords.

- The main scope of the study stated in the title and abstract had to be the assessment of CT features in children (0–16 years).
- Only original articles were considered (single-case reports, review articles, editorials, letters to editors, commentaries and opinion articles were excluded).
- Only articles written in English were included to be able to accurately extract data.
- The population must have been confirmed positive for SARS-CoV-2 by RT-PCR testing (if this criterium was not specified in the abstract, a targeted search in the full text was performed).
- The article had to be accepted for publication in a peer-reviewed journal indexed on PubMed, Scopus or Embase at the date of the search.

The articles matching all the following criteria were deemed eligible for full-text reading.

Article search

The article search and selection were performed by consensus by two different radiologists (PS and MPAG) in the PubMed, Scopus and Embase databases.

The details of the search string and the number of retrieved items are detailed in Appendix 1.

Data extraction and synthesis

Data extraction was independently performed by a fourth author (ADL) and collected in an Excel worksheet. Data inserted in the Excel worksheet were independently checked by another author (MP). A hand-search was planned by looking up the references section of the articles eligible for the full-text analysis or previous systematic reviews.

For each selected study, the following data were extracted:

- Prospective or retrospective study
- Country of the population enrolled
- Period of enrolment
- Monocentric/multicentric study
- Number of children included in the study
- Sex ratio
- Mean age and age range of enrolled patients
- Clinical data: symptomatic/asymptomatic
- Presence/absence of findings on CT
- Distribution of findings (unilateral/bilateral)
- Parenchymal lesions (ground-glass opacities, patchy opacities, specify)
- Prevalent overall involvement (diffuse, central, subpleural)
- Prevalent pattern for each type of lesion (i.e. right/left, superior lobes, inferior lobes, middle lobe, lingula)

Systematic review of quality assessment

The systematic review evaluation was carried out and assessed according to the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA) by an independent Author who was implied in the manuscript writing (GB).27

Selected article quality assessment

The NIH Quality Assessment Tool was used to assess the quality of the selected articles by two authors (GB and AB).

Statistical analysis

The extracted data were encoded in a comparative table. An analysis of the results providing the cumulative data with the range of values found across the different studies was performed.

A meta-analysis was planned to evaluate the relationship of different imaging features with demographic and clinical data in the case that the homogeneity of data would be adequate for the statistical analysis.27

Results

Selected articles

Titles and abstracts were identified from publications from the 1st of January 2020 to the 1st of June 2020, using MEDLINE (16 items), Scopus (25 articles) and Embase (56 articles). The search was performed by one of the authors (PS) on the 24th of April 2020. The results were rechecked with the same search strings on the 1st of June 2020 independently by two authors (PS and MPAG), to make sure no recent entries were missed in the analysis.

A hand-search was performed in the references section of each selected article. After duplicate removal, 73 articles were included in the process of selection by title, abstract and keywords.

Eleven articles matched the selection criteria and were selected for the full-text assessment. One of the articles was excluded after reading the full text (high-resolution CT study, including both adults and children, with lack of specific information for the comparative assessment). Another article was excluded by
consensus, because the chest CT features were limited to the presence/absence of abnormalities on CT, along with the unilateral/bilateral involvement, with no other quantitative data.

Eight articles\textsuperscript{19,21,24,31,33,34} were included for the final analysis. A ninth article\textsuperscript{13} was hand-selected from the references section of the review article by Duan et al.\textsuperscript{20} This article was attentively read, and references compared, with the aim to minimize overlapping. The article extracted from their references did not appear in our original search and was not included in their analysis.

The selection process is summarized in Figure 1, using the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA) flow chart.\textsuperscript{27}

The data extracted from the nine articles considered for the final analysis are detailed in Table 1.

**Cumulative results and quantitative trends (the detailed data are available in Table 1)**

The total number of patients from the different series was 166 (94 males, 72 females). The average age of patients in the studies ranged from 2.6 to 10 years. Children with symptoms ranged from 20% to 100%. A normal CT was reported in up to 50% of the cases (0–77%).

The extension of involvement was not specified in three\textsuperscript{23,33,35} of the nine selected articles. Unilateral involvement ranged from 25% to 42.9%, while bilateral involvement ranged from 57.1% to 75% in five studies.

Parenchymal distribution was described as diffuse in up to 41% (0–41%), central in up to 12.5% (0–12.5%), subpleural (peripheral) distribution ranged from 12.5% to 100%, and peribronchial distribution was reported in up to 28.6% (0–28.6%).

Ground-glass opacities (GGOs) with no associated findings were seen in 12.5–100% of the cases. GGO with consolidation ranged from 14% to 87.5%. Consolidation ranged from 0% to 50% in the different series.

Other findings reported were bronchitis changes or bronchopneumonia, nodules, ‘mesh shadows’, bronchial wall thickening, ‘crazy paving’ appearance, ‘halo sign’, ‘reverse halo sign’, parenchymal bands, interstitial involvement, pleural effusion and ‘white lung’.

Six of the studies\textsuperscript{21–23,31,33} reported the topographic predominance of abnormalities, four concluded this was lower lobes, one upper lobes, and one the same (see Table 1).

The National Institutes of Health (NIH) Quality Assessment Tool was applied to assess the quality of the selected articles (Table 2). The PRISMA assessment of

![Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram shows the study selection process. Embase is a product of Elsevier. WHO = World Health Organization. Adapted from Moher et al. (https://doi.org/10.1371/journal.pmed.1000097) ©2009, under terms of Creative Commons Attribution 4.0 International Licence (creativecommons.org/licenses/by/4.0/legalcode).](image-url)
| Article | Retrospective Study | Country | Enrolment beginning | Enrolment end | Type of Study | Number of Patients | Sex Ratio (F/M) | Mean Age (years) | Symptomatic patients (%) | Normal chest CT (%) | Unilateral or bilateral involvement (%) | Chest CT Features (location) | Consolidations (% of patients) | Other chest CT features of patients | Predominant topography of other chest CT features (location) |
|---------|---------------------|---------|--------------------|--------------|---------------|-------------------|-----------------|-------------------|-----------------------|------------------|-----------------------------------|---------------------------|---------------------------|-----------------------------|-----------------------------------|
| Li et al. | Retrospective Study | China | 23rd of January | 20th of February | Multicentric | 8                | 5:3             | 2.6               | 87.5%                  | 30%              | 25%                                | 25%                       | Diffuse (12.5%); Central (0.1%); Lobar (0%); Subpleural (10%); Peribronchial (0%) | GGO with consolidation (14.3%) | Predominant topography (50%); Predominant topography of remaining lung (0%) |
| Xia et al. | Retrospective Study | China | 23rd of January | 8th of February | Monocentric | 20               | 7:13            | 10.12             | 65%                    | 50%              | 0%                                | 0%                        | Diffuse (0%); Central (0%); Lobar (50%); Subpleural (0%); Peribronchial (0%) | GGO with consolidation (14.3%) | Predominant topography (50%); Predominant topography of remaining lung (0%) |
| Chen et al. | Retrospective Study | China | 16th of January | 14th of February | Monocentric | 14               | 4.5             | 8.5               | 35%                    | 0%              | 10%                                | 10%                       | Diffuse (0%); Central (0%); Lobar (50%); Subpleural (0%); Peribronchial (0%) | GGO with consolidation (14.3%) | Predominant topography (50%); Predominant topography of remaining lung (0%) |
| Li et al. | Retrospective Study | China | 22nd of January | 3rd of February | Monocentric | 9                | 3:6             | 3.5               | 78%                    | 0%              | 0%                                | 0%                        | Diffuse (0%); Central (0%); Lobar (50%); Subpleural (0%); Peribronchial (0%) | GGO with consolidation (14.3%) | Predominant topography (50%); Predominant topography of remaining lung (0%) |
| Lu et al. | Retrospective Study | China | 28th of January | 8th of February | Monocentric | 50               | 1:4             | 8                 | 3%                     | 0%              | 0%                                | 0%                        | Diffuse (0%); Central (0%); Lobar (50%); Subpleural (0%); Peribronchial (0%) | GGO with consolidation (14.3%) | Predominant topography (50%); Predominant topography of remaining lung (0%) |
| Sun et al. | Retrospective Study | China | 24th of January | 24th of February | Monocentric | 50               | 1:4             | 8                 | 3%                     | 0%              | 0%                                | 0%                        | Diffuse (0%); Central (0%); Lobar (50%); Subpleural (0%); Peribronchial (0%) | GGO with consolidation (14.3%) | Predominant topography (50%); Predominant topography of remaining lung (0%) |
| Ma et al. | Retrospective Study | China | 21st of January | 23rd of January | Monocentric | 30               | 1:5             | 10                | 3%                     | 0%              | 0%                                | 0%                        | Diffuse (0%); Central (0%); Lobar (50%); Subpleural (0%); Peribronchial (0%) | GGO with consolidation (14.3%) | Predominant topography (50%); Predominant topography of remaining lung (0%) |
| Steinberger et al. | Retrospective Study | China | 31st of January | 23rd of January | Monocentric | 50               | 1:4             | 8                 | 3%                     | 0%              | 0%                                | 0%                        | Diffuse (0%); Central (0%); Lobar (50%); Subpleural (0%); Peribronchial (0%) | GGO with consolidation (14.3%) | Predominant topography (50%); Predominant topography of remaining lung (0%) |
the quality of the present systematic review is presented in Figure 1.

Discussion

To the best of our knowledge, this is the first systematic review of the English literature focusing on the features of chest CT findings in paediatric patients with COVID-19.

Because of the low morbidity and anecdotic mortality of COVID-19 in the paediatric population, only a limited number of studies have reported the chest CT features of COVID-19 in children.\textsuperscript{20}

A recent systematic review of chest CT features of COVID-19 in paediatric patients published on the 1st of April 2020 by Duan et al.,\textsuperscript{20} reviewed the early data available in six series of children published in Chinese (total = 208 children)\textsuperscript{35–40} and one in English\textsuperscript{24} (including 20 children), and 12 case reports\textsuperscript{5,12,41–50} (total = 17 children). All these series included Chinese children. In this systematic review, many children with symptoms had no abnormalities on chest CT.

Overall, in their analysis, in children with COVID-19 and abnormal chest CT the ground-glass opacities (GGOs) seemed more localized and dense and with less lobular involvement compared to the adult population.\textsuperscript{20,37} GGO in children seemed to predominantly involve the peripheral and posterior lungs.\textsuperscript{20,36,37}

Consolidations, GGOs with patchy areas of consolidation and interlobular septa thickening were also observed in paediatric patients.\textsuperscript{24,35,37,38} Cases of global consolidation, presenting as a ‘white lung’, were sporadic.\textsuperscript{13,37} Pleural effusion was not a rare finding in children with COVID-19.\textsuperscript{13,37,40} Additionally, no cases of lymphadenopathy were reported.

The present systematic review eventually includes eight recent series of paediatric patients (166 patients), all including Chinese children. The series by Xia et al.\textsuperscript{24} (already included in the review by Duan et al.,\textsuperscript{20}) with 20 patients, was also considered in our review, given it was published in English.

All the studies assessed children that were enrolled retrospectively, in a short time frame, mostly from late January to late February (one of the series gathered information up to mid-March), mostly in monocentric studies. Five of the series were published in late April, two in March, and two of them, including the largest one (with 50 patients) in May.

Noticeably, the nine selected studies included patients of paediatric age with low average ages, four studies reporting average ages well below eight years (below the age of 5). One of the studies by Xia et al.\textsuperscript{24} has a median age of 2.2 years, also affecting predominantly young children.

The average age of the different populations and the presence of symptoms do not seem to correlate when comparing the various series, suggesting a possible selection bias. Also, the percentage of patients with normal CT was very variable between the different studies, without any correlations with age, sex prevalence and the presence of symptoms.

In case of the presence of abnormalities on chest CT, the alterations seemed more frequently bilateral. Bilateral versus unilateral involvement was reported in six\textsuperscript{13,19,21,22,23,24,24,34} of the nine selected articles. Bilateral involvement ranged from 57.1% to 75%, and unilateral involvement ranged from 25% to 42.9%.

In adults, a bilateral involvement was reported more frequently in patients with COVID-19 infection, when compared with patients with other viral infections, and with a higher rate in severe and critical cases.\textsuperscript{31}

Regarding the parenchymal distribution, in the selected articles, the tendency to the peripheral distribution of abnormalities already reported in the review by Duan et al.\textsuperscript{20} was the predominant feature observed in the study by Lu et al.,\textsuperscript{33} Li et al.,\textsuperscript{22} Xia et al.\textsuperscript{24} Ma et al.,\textsuperscript{31} and Steinberger et al.\textsuperscript{34} In the series by Chen et al.\textsuperscript{19} and Li et al.,\textsuperscript{21} this peripheral distribution was found only in more or less half of the cases (51.7% and 45%, respectively). Only in the series by Li et al.,\textsuperscript{23} the peripheral distribution was relatively infrequent, reported as 12.5%. Central distribution was still uncommon, described in two of the series, by Li et al.\textsuperscript{21} in 5% of the cases and by Li et al.\textsuperscript{23} in 12.5% of the cases. In these same two series,\textsuperscript{21,23} diffuse involvement was described, ranging from 25% to 41%. A concentration of peribronchial abnormalities was reported in three studies,\textsuperscript{19,21,23} in up to 28.6% of the cases in the studies by Li et al.\textsuperscript{21} and Chen et al.\textsuperscript{19} These data are in keeping with what was observed in adults, exhibiting a variable distribution of the parenchymal abnormalities.\textsuperscript{20}

In our review, GGOs were the most characteristic alterations in COVID-19 patients, even in the paediatric age. The areas of GGO were seen to be mainly isolated (not associated with consolidation) in eight out of the nine studies\textsuperscript{13,19,21,22,24,31,33,34} ranging from 12.5% to 100% of the cases. GGOs with areas of consolidation were also frequently reported in five series\textsuperscript{13,19,21,23,31,34} ranging from 14% in the series by Steinberger et al.\textsuperscript{34} to up to 87% in the series by Sun et al.\textsuperscript{12} Ma et al.\textsuperscript{31} reported local (37%) and bilateral (21%) ‘patchy shadowing’ (i.e. consolidation) in the group of children with positive CT findings in their series, with no specification of whether this was found in combination with GGO, which they described in 67% of the patients in the same group. However, the rate of combination of GGO with consolidations was not specified.

In adults, GGOs associated with areas of consolidation were reported with a prevalence between 19% (Ng et al.\textsuperscript{55} in a small series of 21 patients) to up to 59% (Song et al.\textsuperscript{53} in a series of 51 patients). GGO as a unique feature is the most specific type of alteration described in adults, in some series in up to 91% of patients (Wu et al.,\textsuperscript{54} in a series with 80 patients). In other adult series with 81 patients,\textsuperscript{55} the prevalence of
| Criteria                                                                 | Li et al.\(^\text{23}\) | Xia et al.\(^\text{24}\) | Chen et al.\(^\text{19}\) | Li et al.\(^\text{21}\) | Lu et al.\(^\text{33}\) | Li et al.\(^\text{22}\) | Sun et al.\(^\text{13}\) | Ma et al.\(^\text{31}\) | Steinberger et al.\(^\text{34}\) |
|------------------------------------------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Was the study question or objective clearly stated?                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     |
| Was the study population clearly and fully described, including a case definition? | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     |
| Were the cases consecutive?                                             | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     |
| Were the subjects comparable?                                           | No                      | No                      | No                      | No                      | No                      | No                      | No                      | No                      | No                      |
| Was the intervention clearly described?                                 | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      |
| Were the outcome measures clearly defined, valid, reliable and implemented consistently across all study participants? | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      |
| Was the length of follow-up adequate?                                   | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      | NA                      |
| Were the result of studies well described?                              | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     |
| Quality rating (good, fair or poor)                                     | Fair                    | Fair                    | Fair                    | Fair                    | Fair                    | Fair                    | Fair                    | Fair                    | Fair                    |
| Rater #1 MPAG                                                           |                         |                         |                         |                         |                         |                         |                         |                         |                         |
| Quality rating (good, fair or poor)                                     | Fair                    | Fair                    | Fair                    | Fair                    | Fair                    | Fair                    | Fair                    | Fair                    | Good                    |
| Rater #2 PS                                                             |                         |                         |                         |                         |                         |                         |                         |                         |                         |
| Were the results well described?                                        | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     | Yes                     |

CD, Cannot determine; NA, Not applicable; NR, Not reported.
GGO as a unique feature is also high (65%). Consolidation independently from GGO is not a dominant feature in children, described in four of the series in one of them in up to 50% of children.24–26

Concerning consolidations in adults, in a series of 1014 patients, Ai et al.15 found GGO in 46% of the patients, with half of the patients (50%) demonstrating consolidations. Interestingly, in this series, the prevalence of interlobular septal thickening was low (1%), while in other series, like the one by Song et al.,53 this was reported to be up to 75%.

In the series of cases presented by Xia et al.,24 50% of the patients demonstrated consolidation with a surrounding ‘halo’ (of subtle GGO), which is a finding reported in only 3.9% of adults.56 The series by Steinberg et al.34 describes among their findings a ‘reverse halo sign’ in with the GGO is surrounded by a ring of consolidation (in 29% of cases) and a ‘halo sign’ (also in 29% of cases). Both ‘halo sign’ and ‘reverse halo sign’ are reported as a typical finding in children with COVID-19 and preferentially located in the lower lobes.34 The presence of a ‘halo sign’ was also reported in the series by Li et al.23 (12.5%) and anecdotally by Ma et al.31

Xia et al.24 observed in their series of 20 children with COVID-19 that 80% of children with COVID-19 and positive CT showed high procalcitonin level (a marker for bacterial infection). The elevation of procalcitonin, which is not common in adults with COVID-19, may suggest the presence of bacterial coinfection in children with COVID-19.24

Six series gave detailed data about the topography of the findings. Four of those series11–23,34 described a clear predominance of the involvement of the lower lobes, similarly to reports in adults.16,17,55,57 On the contrary, in the other two series33,56 the upper lobes were more frequently or as frequently involved. These different observations suggest that in COVID-19, the spatial pattern of lung involvement in children might be less constant and not have a dominant lower lobe, lingula and middle lobe location, as reported in adults.58 Within the category of less typical CT manifestations, nodules were reported in three series (see Table 1), in up to 25% of cases. Pleural effusion was reported in one patient in the series by Ma et al.31 and in one patient in the series by Sun et al.13 The pleural effusion described by Sun et al.13 corresponds to a 10-month-old that developed intussusception and toxic shock.13

A case of ‘white lung’ was described by Sun et al.13 in a child with acute lymphoblastic leukaemia and concomitant influenza infection. Bronchial wall thickening was mentioned in two series.19,23 In the series by Li et al.,23 bronchial wall thickening was described in up to 25% of the patients, associated with bronchopneumonia. In the series by Chen et al.,19 it was found in 28.6% of cases. Bronchial wall thickening was described with lower prevalence (12%) in a series of 121 adults when compared to the prevalence observed in these paediatric series. Interestingly, air bronchogram was reported in only one of the series, by Li et al.,23 in 25% of children, whereas this was reported in two relatively large adult series to range between 47% in the series by Shi et al.55 (81 patients) and 80% in the series by Song et al.53 (51 patients).

Other findings described in children were nodules.19,24 parenchymal bands,33 crazy paving21 and fine ‘mesh shadows’24 but not homogeneously through series and in small percentages. In particular, ‘crazy paving’ appearance was described in two of the series21,34 with a prevalence of up to 29%. This is the same prevalence described in adults (29%) in the series by Wu et al.54

The fine ‘mesh shadows’ described in 20% of the cases in the series by Xia et al.24 were described in a similar percentage (22%) in the series by Song et al.53 in adults. Interstitial abnormalities are also marginally described in the series by Ma et al.31 in 7% of the cases.

Enlarged lymph nodes are mentioned in one of the series,21 with no description of the exact prevalence.

Interestingly, there are no reports of a pulmonary embolism in children with COVID-19. There is increasing evidence that pulmonary embolism is an extremely frequent CT finding in adult patients with COVID-1960,61 with an incidence as high as 30% in patients undergoing chest CT with intravenous contrast medium administration.62 The prevalence of pulmonary embolism in children is unknown even in severe cases, presumably because chest CT is performed without contrast medium administration. The role of chest CT angiography might be investigated in prospective studies, especially in the rare cases of children with clinical degradation, comorbidities or severe symptoms.

Lung viral infections common in paediatric population such as influenza virus, parainfluenza virus, respiratory syncytial virus (RSV) and adenovirus could be differentiated from COVID-19 based on specific patterns.63 However, the reliability of chest CT to diagnose a superimposed infection is unknown and challenging due to the variability of the different chest CT features.24

Hence, chest CT should be interpreted with caution in children presenting severe imaging manifestations, in the context of clinical examination and laboratory tests.24

Limitations

This study has several limitations. The small number of studies available can bias the data and the comparison with the adult populations. The selected articles were limited in terms of population size, and there was a lack of specific detailed data in some studies.

The age ranges are also diverse. This prevented us from assessing the potential associations between age and type of extension, parenchymal distribution or type of features of involvement.
Also, the COVID-19 chest CT features have only been recently described. There was heterogeneity in the type of descriptions of parenchymal involvement among series, and the different studies do not use uniform descriptions. This heterogeneity impairs the classification of patterns and excludes the possibility of performing a metaanalysis.

Further, because of the lack of clear guidelines during the early outbreak, the selection of children that should be assessed with CT was not performed based on validated criteria of appropriateness. This selection bias can explain in part some very different CT features when comparing the selected articles.

Recently, the Radiological Society of North America (RSNA) and the Fleischer Society independently comparing the selected articles.

explain in part some very different CT features when dated criteria of appropriateness. This selection bias can explain in part some very different CT features when comparing the selected articles.

Recently, the Radiological Society of North America (RSNA) and the Fleischer Society independently stated that chest CT is not recommended as a first-line screening tool to diagnose COVID-19. Chest CT, in all age categories, is indicated for moderate-to-severe features of COVID-19, regardless of the laboratory test results. The role of chest CT in the diagnosis and follow-up of paediatric patients with mild and severe COVID-19 and investigation technique has to be elucidated.

Lastly, our systematic review only focused on articles published in English, and in groups of in Chinese children. The current literature should be updated with new evidence from large series of children with confirmed COVID-19 from other countries, ethnicity and genetic background to provide a more comprehensive description of chest CT features in children with COVID-19.

Conclusion

Chest CT features of COVID-19 infection in children differ from those in adults and can be diverse. GGO is still the most commonly described abnormality but closely followed by a combination of GGO and consolidation, which is not as usual in adults. Diffuse involvement is frequently described in children, being the subpleural pattern more prevalent in adults. Features like interlobular thickening and air bronchogram are still infrequent in children. No evidence of pulmonary embolism has been reported in children.

The presence of a ‘halo sign’, rarely described in adults positive to SARS-CoV-2, seems a typical chest CT feature of children with COVID-19.

References

1. Zhu N, Zhang D, Wang W et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020; 382: 727–33.
2. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis 2020; 20: 533–4.
3. Dong L, Tian J, He S et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn. JAMA 2020; 323: 1846–8.
4. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr 2020; 109: 1088–95.
5. Ji LN, Chao S, Wang YJ et al. Clinical features of pediatric patients with COVID-19: a report of two family cluster cases. World J Pediatr 2020; 16: 267–70.
6. Dong Y, Mo X, Hu Y et al. Epidemiology of COVID-19 among children in China. Pediatrics 2020; 145: e20200702.
7. Bi Q, Wu Y, Mei S et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. Lancet Infect Dis 2020; 20: 911–9.
8. Wang D, Hu B, Hu C et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020; 323: 1061–9.
9. Chen Z, Fu J, Shu Q et al. Diagnosis and treatment recommendation for pediatric coronavirus disease-19. Zhonghua Da Xue Xue Bao Yi Xue Ban 2020; 49: 1–8.
10. Zeng LK, Tao XW, Yuan WH, Wang J, Liu X, Liu ZS. First case of neonate infected with novel coronavirus pneumonia in China. Zhonghua Er Ke Za Zhi 2020; 58: 169–74.
11. Chen N, Zhou M, Dong X et al. Clinical and epidemiological characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020; 395: 507–13.
12. Ai T, Yang Z, Hou H et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology 2020; 296: E32–E40.
13. Cheng Z, Lu Y, Cao Q et al. Clinical features and chest CT manifestations of coronavirus disease 2019 (COVID-19) in a single-center study in Shanghai, China. AJR Am J Roentgenol 2020; 215: 121–6.
14. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol 2020; 30: 4381–9.
15. Yang Y, Yang M, Shen C et al. Evaluating the accuracy of different respiratory specimens in the laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infections. medRxiv. 2020:2020.02.11.20021493.
16. Chen A, Huang J, Liao Y et al. Differences in clinical and imaging presentation of pediatric patients with COVID-
19 in comparison with adults. \textit{Radiol Cardiothoracic Imaging} 2020; 2: e200117.

20. Duan YN, Zhu YQ, Tang LL, Qin J. CT features of novel coronavirus pneumonia (COVID-19) in children. \textit{Eur Radiol} 2020; 30: 4427–33.

21. Li B, Shen J, Li L, Yu C. Radiographic and clinical features of children with coronavirus disease (COVID-19) pneumonia. \textit{Indian Pediatr} 2020; 57: 423–6.

22. Li W, Cui H, Li K, Fang Y, Li S. Chest computed tomography in children with COVID-19 respiratory infection. \textit{Pediatr Radiol} 2020; 50: 796–9.

23. Li Y, Cao J, Zhang X, Liu G, Wu X, Wu B. Chest CT imaging characteristics of COVID-19 pneumonia in preschool children: a retrospective study. \textit{BMC Pediatr} 2020; 20: 227.

24. Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. \textit{Pediatr Pulmonol} 2020; 55: 1169–74.

25. Pan Y, Guan H, Zhou S et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019–nCoV): a study of 63 patients in Wuhan, China. \textit{Eur Radiol} 2020; 30: 3306–9.

26. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for typical 2019-nCoV pneumonia: relationship to negative RT-PCR testing. \textit{Radiology} 2020; 296: E41–E45.

27. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. \textit{BMJ} 2009; 339: b2535.

28. Schardt C, Adams MB, Owens T, Keitz S, Fontelo P. Utilization of the PICO framework to improve searching PubMed for clinical questions. \textit{BMC Med Inform Decis Mak} 2007; 7: 16.

29. National Heart L, and Blood Institute website. [Accessed May 24 2020.] Available from URL: www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools

30. Chen Z, Fan H, Cai J, et al. CT features of children with COVID-19 in 30 pediatric patients. \textit{AJR Am J Roentgenol} 2020; 215: 1–9.

31. Ma YL, Xia SY, Wang M, Zhang SM, Du WH, Chen Q. [Clinical features of children with SARS-CoV-2 infection: an analysis of 115 cases]. \textit{Zhongguo Dang Dai Er Ke Za Zhi} 2020; 22: 290–3.

32. Feng KYY, Wang XF. Analysis of CT features of 15 children with 2019 novel coronavirus infection. \textit{Zhonghua Er Ke Za Zhi} 2020; 58: E007.

33. Ma YXS, Wang M, Zhang S, Du W, Chen Q. High resolution CT features of novel coronavirus pneumonia in children. \textit{Zhonghua Fang She Xue Za Zhi} 2020; 54: E002.

34. Wang D, Ju XL, Xie F et al. Clinical analysis of 31 cases of 2019 novel coronavirus infection in children from six provinces (autonomous region) of northern China. \textit{Zhonghua Er Ke Za Zhi} 2020; 58: 269–74.

35. Zhong Z, Xie X, Huang W, Zhao W, Yu Q, Liu J. Chest CT findings and clinical features of coronavirus disease 2019 in children. \textit{Zhong Nan Da Xue Xue Bao Yi Xue Ban} 2020; 45: 236–42.

36. Zhou Y, Yang GD, Feng K et al. Clinical features and chest CT findings of coronavirus disease 2019 in infants and young children. \textit{Zhongguo Dang Dai Er Ke Za Zhi} 2020; 22: 215–20.

37. Chan JF-W, Yuan S, Kok K-H et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. \textit{Lancet} 2020; 395: 514–23.

38. Chen F, Liu ZS, Zhang FR et al. First case of severe childhood novel coronavirus pneumonia in China. \textit{Zhonghua Er Ke Za Zhi} 2020; 58: E005.

39. Cui Y, Tian M, Huang D et al. A 55-day-old female infant infected with 2019 novel coronavirus disease: presenting with pneumonia, liver injury, and heart damage. \textit{J Infect Dis} 2020; 221: 1775–81.

40. Li HILLS, Xu HB, Cheng JL. Guideline for medical imaging in auxiliary diagnosis of coronavirus disease 2019. \textit{J Med Imaging Technol} 2020; 36: 1–11.

41. Liu M, Wan X, Tu XY et al. Family cluster of child SARS-CoV-2 infections: a case report. \textit{Wuhan Da Xue Xue Bao} 2020; 41: 362–5.

42. Lou XX, Shi CX, Zhou CC, Tian YS. Three children who recovered from novel coronavirus 2019 pneumonia. \textit{J Paediatr Child Health} 2020; 56: 650–1.

43. Wang S, Guo L, Chen L et al. A case report of neonatal COVID-19 infection in China. \textit{Clin Infect Dis} 2020; 71: 853–7.

44. Zhang GX, Zhang AM, Huang L et al. Twin girls infected with SARS-CoV-2. \textit{Zhongguo Dang Dai Er Ke Za Zhi} 2020; 22: 221–5.

45. Zhang YH, Lin DJ, Xiao MF et al. [2019-novel coronavirus infection in a three-month-old baby]. \textit{Zhonghua Er Ke Za Zhi} 2020; 58: E006.

46. Zhao RSX, Xu K, Sheng J. One case report of pediatric infection with COVID-19. \textit{Zhejiang Med J} 2020; https://doi.org/10.12056/j.issn.1006-2785.2020.42.3.2020-337.

47. Sun Z, Zhang N, Li Y, Xu X. A systematic review of chest imaging findings in COVID-19. \textit{Quan Imaging Med Surg} 2020; 10: 1058–79.

48. Ng M-Y, Lee EYP, Yang J et al. Imaging profile of the COVID–19 infection: radiologic findings and literature review. \textit{Radiol Cardiothorac Imaging} 2020; 2(1): e200034.
Chest CT in children with COVID-19

Appendix 1

Literature search performed by the first author on the 24th of April 2020, repeated on the 1st of June 2020 by two authors (PS and MPAG)

MEDLINE search on the 24th of April 2020, repeated on the 1st of June 2020
"Child"[Mesh] AND "Tomography, X-Ray Computed"[Mesh] AND ("COVID-19"[All Fields] OR "COVID-2019"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019-nCoV"[All Fields] OR "SARS-CoV-2"[All Fields] OR "2019nCoV"[All Fields] OR ("Wuhan"[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields]))) AND (2019/12[PDAT] OR 2020[PDAT])
Result: 15 items

Scopus search on the 24th of April 2020, repeated on the 1st of June 2020
TITLE-ABS-KEY ("COVID-19" AND "children" OR "child" AND "CT" OR "computerised tomography")
Result: 25 items

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