Chest CT Scan Findings in Children with COVID-19: A Systematic Review

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ABSTRACT

Objectives. To gather, summarize, and appraise the available evidence on: 1) the accuracy of chest CT scan in diagnosing COVID-19 among children, and 2) the characteristic chest CT scan findings associated with COVID-19 pneumonia in children.

Methods. We comprehensively searched databases (MEDLINE, COCHRANE), clinical trial registries, bibliographic lists of selected studies, and unpublished data for relevant studies. Guide questions from the Painless Evidence Based Medicine and the National Institutes of Health Quality Assessment Tools were used to assess study quality.

Results. A poor quality study showed 86.0% (95% CI 73.8, 93.0) sensitivity and 75.9% (95% CI 67.1, 83.0) specificity of chest CT scan in diagnosing COVID-19 in children. Thirty-nine observational studies describing chest CT scan in children with COVID-19 showed abnormal findings in 717 of 1028 study subjects. Common chest CT scan findings in this population include: 1) ground glass opacities, patchy shadows, and consolidation, 2) lower lobe involvement, and 3) unilateral lung lesions.

Conclusion. Studies which investigate the accuracy of chest CT scan in the diagnosis of COVID-19 in children are limited by heterogeneous populations and small sample sizes. While chest CT scan findings such as patchy shadows, ground glass opacities, and consolidation are common in children with COVID-19, these may be similar to the imaging findings of other respiratory viral illnesses.

Keywords: COVID-19, children, computed tomography, ct scan, imaging

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INTRODUCTION

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), a virus which originated from China which then spread across countries causing a pandemic, primarily affects the respiratory system. Even though this infection mainly affects adults, cases of children with the disease have also been reported, and the numbers continue to rise.[1,2] Children most commonly present with fever and cough, which may also be frequent symptoms of other common childhood viral illnesses. Similarly, the laboratory findings cannot definitely differentiate these etiologies, making the diagnosis of COVID-19 a challenge.[2]

Nucleic acid testing by reverse transcriptase-polymerase chain reaction (RT-PCR) continues to be recognized as the gold standard for the diagnosis of coronavirus-19 disease (COVID-19). Results, however, may take longer to be

released since turnover is limited by the availability of test kits, laboratory capacity, and the number of trained personnel. In addition, the test sensitivity may be suboptimal; detection rates range from 50.0-72.0% in nasal swab samples.[3,4] Thus, the role of chest imaging in the work-up for COVID-19 has been explored.[3,5,6]

Chest computed tomography scan (CT scan) is an advanced form of imaging which uses x-rays to form a detailed image of the lungs and other structures of interest. An advantage of this diagnostic test is the immediate availability of the image for analysis after the procedure. Some studies report that in patients with normal chest radiographic findings, chest CT scan may reveal subtle abnormal changes.[5] In a study by Fang et al., it was reported that in patients who were positive for COVID-19, chest CT scan has a higher sensitivity than RT-PCR (98.0% versus 71.0%, p<0.001) in the detection of COVID-19 among adult patients at initial presentation. The patients who had an initial negative RT-PCR but with abnormal chest CT scan findings eventually became positive during their admission.[7] During the first few weeks of the outbreak, the National Health and Health Commission of China included chest CT scan in the clinical criteria for the diagnosis of COVID-19.[6] Thus, this diagnostic modality may play an important role in the early detection and consequently, in the prompt isolation of COVID-19 cases.

An International Expert Consensus on chest imaging in pediatric COVID-19 patients by Foust et al., divides chest CT scan findings into four categories: typical, atypical, indeterminate, and negative. This classification aims to standardize the reporting of the chest CT scan results of COVID-19 patients.[8] The aspects in the chest CT scan which should be evaluated include: 1) distribution pattern of the lung lesion (subpleural/peripheral or central, lung lobe involved), 2) quantity and range of the lung pathology (multifocal vs unifocal, number of lobes affected), 3) density of the lung lesion (ground glass opacities or consolidation), 4) shape and interface of the lung lesion (patchy, cone-shaped, subsegmental/segmental), 5) internal features in the lesion (crazy-paving sign, thickening of small vessels, air bronchograms), and 6) adjacent structures changes (thickening and/or shifting of pleura).[9]

The most common chest CT scan feature in adults with COVID-19 is ground-glass opacities with bilateral peripheral distribution.[10] Other findings described are ground-glass opacities with consolidation, air bronchograms, interlobular septal thickening, and crazy-paving pattern.[11] Few evidence is available if these findings are consistent with pediatric COVID-19. Also, these imaging findings were found to overlap with those detected in other coronaviruses such as SARS-CoV and MERS-CoV, as well as in other infections such as Influenza A, Influenza B, and *Mycoplasma*.[8,12]

MATERIALS AND METHODS

Criteria for Considering Studies in the Review

Type of Studies

Observational studies (cohort, case-control, cross-sectional, and case series) were included in this review. Case reports were excluded.

Types of Participants

Studies of children (age 0-18 years old) diagnosed with COVID-19 through RT-PCR, were considered for inclusion. These patients may have any co-morbidities, and any disease severity.

Types of Diagnostic Tests and Reference Standard

Studies which used chest CT scan, with or without contrast enhancement, with any slice thickness, were considered for inclusion. Studies which used other imaging modalities such as chest X-ray and reported the imaging findings as one were not included.

Reference Standard

The reference standard used was reverse transcriptase-polymerase chain reaction (RT-PCR) of SARS-COV2 of any respiratory sample (oropharyngeal swab, nasopharyngeal swab, throat swab). Studies which used antibody tests (IgG, IgM) were excluded.

Types of Outcome Measures

The primary outcome of this study included the sensitivity and specificity of chest CT scan in diagnosing COVID-19 in children. This study also looked into the common chest CT scan findings based on 1. the lung lobe involved, 2. the distribution of lung lesions (unilateral vs. bilateral), and 3. density and pattern of lung lesions, and 4. other associated findings such as pleural effusion, pneumothorax, lymphadenopathy, etc. These outcomes were not part of the eligibility criteria.

Search Methods for Identification of Studies

A thorough electronic search through online databases (PubMed, COCHRANE), clinical trial registries (clinicaltrials.gov, Chinese Clinical trial Registry, EU Clinical Trials Register, Republic of Kore-Clinical Research Information Service, and NIPH Clinical Trials Search), as well as unpublished journals (chinaxiv.org, medrRix.org) was done to identify eligible studies. Medical subject heading and free-text terms were used in every database searched to identify the study intervention and population as indicated. There was no date, language, or study design restriction in the search. Search terms applied included: ("Coronavirus Infections"[Mesh] OR "Coronavirus"[Mesh] OR coronavirus OR novel coronavirus OR NCOV OR "COVID-19" [Supplementary Concept] OR covid19 OR covid 19 OR

covid-19 OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept] OR severe acute respiratory syndrome coronavirus 2 OR SARS2 OR SARS 2 OR SARS COV2 OR SARS COV 2 OR SARS-COV-2) AND ("chest tomography"[Mesh] OR "CT" "chest radiograph" OR "radiograph" OR imaging OR "chest imaging" OR "CT scan" OR "Chest CT scan") AND ("children"[Mesh] OR "pedia" OR "pediatric" OR "child").

Searching Other Sources

Other published journals and researches were also manually searched to look for possible relevant studies. A free-hand search inside and outside the identified electronic databases was done.

Data Collection and Analysis

Outcomes of the initial search were browsed through titles and abstracts to exclude duplicates and insignificant studies. The primary investigator and the co-investigator independently scanned, selected, and reviewed the studies. Incongruences between the two reviewers were resolved by consulting a third party.

Data Extraction and Management

The following data were extracted from each study included in this review:

- Source: study ID by the review authors, citation, contact details
- Eligibility: confirmation of eligibility for review or reason for exclusion
- Methods: study design, total study duration, other concerns about bias
- Participants: total number, setting, age, sex, country, co-morbidity, socio-demographics, ethnicity, date of study
- Diagnostic Tests: type of test used and specifications, reference test, specimen used for testing
- Outcomes: outcomes and time points collected and reported; for each outcome of interest: outcome definition
- Results: number of participants who underwent the test of interest, number of participants with positive and negative result, number of participants per specific imaging finding

Assessment of Risk Bias in Included Studies

The authors of this study independently assessed each of the included studies for the risk of bias using the Guide Questions from Painless Evidence Based Medicine and the National Institutes of Health Quality Assessment Tools. Any difference in the assessment was resolved through discussion or with the help of a third party.

Measures of Effect

Studies used continuous outcomes and dichotomous outcomes (positive or negative chest CT scan results). A description of the chest CT scan findings were also reported. The sensitivity and specificity, as well as positive predictive value and negative predictive value were calculated from data from the studies. The pooled proportions of the imaging findings were also generated using the OpenMeta[analyst] application. A 95% confidence interval was used for all values.

Assessment of Heterogeneity

The chi-squared, as well as the I-squared tests, were applied to assess the heterogeneity of the studies. A statistically significant heterogeneity is considered with a p-value of <0.1, or a cut off point of 50%, respectively.

Data Synthesis

Qualitative synthesis of data was performed in narrative writing. Forest plots were generated for outcomes that can be quantitatively pooled using the OpenMeta[analyst] application.

RESULTS

Results of the Search

A total of 422 journals (243 from MEDLINE through PubMed, 23 from COCHRANE, 50 from clinicaltrials.gov, 100 from medRxiv.org, 6 from journal references) were screened and reviewed. After initial screening of titles and abstracts and removal of duplicates, 382 studies were excluded. Full text articles of 40 studies were retrieved and assessed for eligibility. One study which used antibody tests as reference standard was excluded, thus, a final total of 39 studies were included for analysis.

Characteristics of Included Studies

Diagnostic Accuracy of Chest CT scan

Only one study reported the accuracy of chest CT scan in diagnosing COVID-19 in children.[13] This study was done in Wuhan, China and was published last April 2020.

This single-center retrospective study by Ma et al. included children <16 years old suspected to have COVID-19 due to social or family history of exposure, admitted from January 21 to February 14, 2020. It compared the chest CT scan findings in children who tested positive versus those who tested negative for SARS-CoV-2 on RT-PCR. The timing of RT-PCR specimen collection and chest CT scan were not reported. Findings of this study included the density and location of the lung lesions, as well as the presence of pleural fluid and/ or lymphadenopathy.[13] (Table 1)

Common Chest CT Scan Findings

Thirty-nine studies which characterize chest CT scan findings in pediatric patients with COVID-19 were included in this review. The literature search yielded 11 case series[14-24], 1 multicenter prospective cohort study[25], and 27 retrospective cohort reviews[13,26-51]. These studies were published online from January to July 2020.

Table 1. Characteristics of Included Studies

No.	Title/Author	Study design	Country	Population	Age	Outcomes	Timing of Chest CT scan	Type of CT Scan
1	***Clinical analysis of 25 COVID-19 infections in children*** Bai K et al. April 2020 [28]	Multi-center retrospective cohort study	Chongqing, China	25 children with laboratory-confirmed 2091 nCoV infection by RT PCR admitted from 4 designated hospitals in Chongqing from January 19 to March 12, 2020 14 males, 11 females	0.6-17 years (mean 11.0 years)	Clinical data and epidemiologic history	not stated	not stated
2	***The early experiences of a single Italian emergency department treating COVID-19 in children*** Brisca G, et al. [26]	Single center retrospective cohort study	Italy	24 patients admitted to the emergency department at IRCSS Gaslini Children's Hospital, Genoa, Italy from February 24 to April 16, 2020 11 males, 13 females	14 days to 18 years	Clinical data and course	not stated	Non-contrast chest CT scan
3	***Clinical characteristics of 5 COVID-19 cases with non-respiratory symptoms as the first manifestation in children*** Cai X et al. May 2020 [14]	Case Series	Wuhan, China	5 patients with non-respiratory symptoms as the first manifestation, later confirmed to have COVID-19 from January 23 to February 20, 2020 at the Wuhan Children's Hospital 4 males, 1 female	2 months - 5.6 years	Clinical features of COVID-19 with non-respiratory symptoms as first manifestation	Day 2-9 of symptom onset	not stated
4	***Asymptomatic SARS-CoV-2 infection in children: a clinical analysis of 20 cases*** Chen, Jun et al. May 2020 [29]	Single center retrospective cohort study	Shenzhen, China	20 cases admitted to the Shenzhen Third People's Hospital from January 20 to March 4, 2020 7 males, 13 females	8 months - 4 years	Main clinical manifestations, course of disease, treatment	after admission	High resolution chest CT scan
5	***Clinical features of pediatric patients with COVID-19: a report of two family cluster cases*** Ji Li-Na et al. March 2020 [15]	Case Series	Beijing, China	2 pediatric cases admitted January 25, 2020 and February 3, 2020 at Beijing Tsinghua Changgung Hospital 2 males	9-15 years	Epidemiological features, physical examinations, laboratory studies, and clinical outcome	not stated	Unenhanced chest CT scan
6	***CT image features analysis of 15 cases of novel coronavirus infection in children*** Kai Feng et al. [30]	Single-center retrospective cohort study	Shenzhen, China	15 cases of new coronavirus infection in children diagnosed by Shenzhen Center for Disease Control and Prevention from January 16, 2020 to February 6, 2020 75 males, 10 females	4-14 years	Chest CT examination, clinical data	with fever: when they visit a doctor; asymptomatic: during the initial RT-PCR; then 3-5 days after admission	Unenhanced chest CT scan with Toshiba 64-slice spiral CT 135 kV, pitch 0.8, matrix 512 x 512, FOV 320 mm x 320 mm, slice thickness 5.0 mm, slice distance 5.0 mm
7	***Computed tomography of the lungs in novel coronavirus (COVID-19) infection*** Lai W. et al. March 2020 [16]	Case Series	Guangdong, China	2 children diagnosed with COVID-19 2 males	12-16 years	Clinical and chest CT features	Initial and repeat after 4,13,17 days	Unenhanced chest CT scan

Table 1. Characteristics of Included Studies *(continued)*

No.	Title/Author	Study design	Country	Population	Age	Outcomes	Timing of Chest CT scan	Type of CT Scan
8	***Early CT findings of Coronavirus Disease 2019 (COVID-19) in asymptomatic children: A single center experience*** Lan L. et al. March 2020 [17]	Case series	Wuhan, China	All pediatric patients diagnosed with COVID-19 and who underwent CT scan in Zhongnan Hospital of Wuhan University from January 20 to February 28, 2020 2 males, 2 females	7-13 years	Clinical and CT features	on admission	CT scan 120kV, 100-150 mA, slice thickness 1 mm, lung window -700, window width 1500 HU
9	***Radiographic and Clinical Features of Children with Coronavirus Disease (COVID-19) Pneumonia*** Li Bo et al. April 2020 [31]	Single-center retrospective cohort study	Hubei, China	22 patients 12 males, 10 females	mean age 6 years	Clinical data, physical examination, laboratory data, radiographic features	not stated	Non-enhanced Chest CT Scan using a 16-row multi-detector CT scanner (Siemens Somatom), 120 kVp, 140 mA, 5 mm collimation, 1.35:1 pitch
10	***Clinical and CT features of the COVID19 infection: comparison among four different age groups*** Li, W. et al July 2020 [32]	Single center retrospective cohort study	China	patients with chest CT examination and positive RT PCR from January 17 to February 21, 2020 at the Fifth Affiliated Hospital of Sun Yat-sen University 5 males, 1 female	mean 5 years	Clinical and chest CT features	not stated	Non-enhanced chest CT scan
11	***Chest computed tomography in children with COVID-19 respiratory infection*** Li, Wei et al. [18]	Case Series	Zhuhai, China	5 children who tested positive on a reverse transcriptase- polymerase chain reaction for COVID-19 during the period January 28 to February 8, 2020 4 males, 1 female	10 months-6 years	Clinical history, laboratory findings, and chest CT imaging	2-9 days after admission/ onset of symptoms; 5-7 days after initial CT scan	Non-enhanced chest CT scan
12	***Chest CT imaging characteristics of COVID-19 pneumonia in preschool children: a retrospective study*** Li Yang et al. [33]	Multi-center retrospective cohort study	Hubei, China	8 preschool children with laboratory-confirmed COVID-19 from 2 hospitals from January 26 to February 20, 2020 3 males, 5 females	1-5 years (median 2.5 years)	Clinical, initial chest CT imaging data	At the time of admission	Plain CT scan using multi-detector CT scanner, thickness of the slices 1 mm, interslice gap 1 mm matrix 512 mm x 512 mm, tube voltage 80 kV, current 200 mA, pitch 0.813/HP 65.0 and dose length product 36-51 mGycm
13	***Clinical and CT imaging features of the COVID-19 pneumonia: Focus on pregnant women and children*** Liu Huanhuan et al. [19]	Case Series	Hubei, China	4 children with laboratory-confirmed and clinically-diagnosed COVID-19 pneumonia 2 males, 2 females	2 months - 9 years	Clinical and chest CT imaging data	Median of 2 days from onset of symptoms	Non-enhanced chest CT examination, 64 section multidetector CT scanner 120kV, automatic tube current (120-380) mA, thickness 507 mm, slice interval 5 mm, rotation speed 0.5s, helical pitch 1:0875:1 or 1.375:1

Table 1. Characteristics of Included Studies *(continued)*

No.	Title/Author	Study design	Country	Population	Age	Outcomes	Timing of Chest CT scan	Type of CT Scan
14	***High-Resolution Computed Tomography Manifestations of 5 Pediatric Patients With 2019 Novel Coronavirus*** Liu Mengqi et al. [20]	Case Series	Chongqing, China	5 cases of pediatric patients with 2019 novel coronavirus 4 males, 1 female	7 months - 13 years	Clinical and chest CT features	Initial and follow-up 5-13 days after admission/ treatment	Unenhanced chest high resolution CT scan
15	***Detection of COVID-19 in Children in Early January 2020 in Wuhan, China*** Liu W. et al. March 2020 [21]	Case Series	Wuhan, China	6 patients detected with SARS-CoV-2 from January 2 to January 8 2 males, 4 females	1 – 7 years (median 3 years)	Clinical data and CT findings	Not stated	Not stated
16	***SARS-CoV-2 infection in children*** Lu X. et al. March 2020 [34]	Cohort	Wuhan, China	171 children with confirmed SARS CoV infection from January 28 to February 26 104 males, 67 females	1 day - 15 years (median 6.7 years)	Epidemiologic characteristics, clinical features, radiologic findings	Not stated	Not stated
17	***Clinical characteristics and radiologic features of children infected with the 2019 novel coronavirus*** Lu Y. et al. May 2020 [22]	Case Series	Guangzhou, China	9 children infected with the 2019-nCoV from January 22 to February 9, 2020 admitted to Guangzhou Women and Children's Medical Center 5 males, 4 females	2 months - 5 years	Clinical characteristics and radiologic features	Not stated	64 section spiral CT system 120 kV tube 87 voltage, 50e70 mA tube current 0.5 s/rot bulb rotation 88 speed, and 0.2 mm slice thickness.
18	***A single-center, retrospective study of COVID-19 features in children: a descriptive investigation*** Ma Hujing et al. [13]	Single- center retrospective cohort study	Wuhan, China	158 children 16 years of age and under who had a family or social history of COVID-19 exposure, recruited from January 21-February 14, 2020 28 males, 22 females	0.9-7 years old	Demographic information, clinical symptoms, laboratory result, outcome data Chest CT without IV contrast features	Not stated	Chest CT without intravenous contrast was performed on all patients using a Siemens SOMATOM Definition AS128 or GE Optima CT 660 with a 1-mm or 0.625-mm slice thickness
19	***Clinical features of children with SARS-CoV-2 infection: an analysis of 115 cases*** Ma Yao-Ling et al. March 2020 [35]	Single-center retrospective cohort study	Wuhan, China	115 cases of outpatient diagnosis and emergency diagnosis of COVID-19 73 males, 42 females	51 days - 15 years old	Epidemiological contact, clinical symptoms, laboratory tests, and chest CT imaging findings of the lungs	Not stated	Not stated
20	***Clinical and radiological characteristics of pediatric patients with COVID-19: focus on imaging findings*** Mohammadi A. et al. June 2020 [36]	Single- center retrospective cohort study	Urmia, Iran	27 pediatric patients with COVID-19 pneumonia between January 23 to March 25, 2020 10 males, 17 females	mean 4.7 years	clinical and radiologic findings of pediatric patients with COVID-19 pneumonia	initial day of hospitalization	Siemens SOMATOM, Toshiba Alexion: low dose mode, automatic tube current modulation with a voltage of 120 kVp, matrix size of 512 × 512, increment and thickness of 1.5–2 mm

Table 1. Characteristics of Included Studies *(continued)*

No.	Title/Author	Study design	Country	Population	Age	Outcomes	Timing of Chest CT scan	Type of CT Scan
21	***Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study*** Qiu H. et al. March 2020 [37]	Multi-center retrospective cohort study	Zhejiang, China	36 children infected with SARS CoV infection from January 17 to March 1, 2020 in 3 hospitals in Zhejiang, China 23 males, 13 females	1-16 years old	Epidemiologic data and clinical features	Not stated	Not stated
22	***Novel coronavirus infection in children outside of Wuhan, China*** Shen Q et al. March 2020 [38]	Single-center retrospective cohort study	Hunan, China	9 hospitalized patients diagnosed with COVID-19 between January 8 to February 19, 2020 3 males, 6 females	1-12 years (median 8 years)	Epidemiological, clinical, laboratory, and radiologic characteristics	Not stated	Not stated
23	***Pediatric coronavirus disease 2019 (COVID-19): An insight from west of Iran*** Soltani J et al. May 2020 [25]	Multi-center prospective cohort study	Iran	30 children diagnosed as probable or confirmed COVID-19 cases from March 1 to April 15, 2020 in Hamadan and Kurdistan province 14 males, 16 females	1 day - 15 years (mean 6, median 5.5 years)	Clinical, laboratory, radiological characteristics	Not stated	Not stated
24	***CT features of coronavirus disease (COVID-19) in 30 pediatric patients*** Steinberger S et al. May 2020 [40]	Multi-center retrospective cohort study	China	30 pediatric patients with laboratory confirmed COVID-19 who were at six centers in China from January 23, 2020 to February 8, 2020 15 males, 15 females	10 months-18 years (median 10 years)	Clinical characteristics and CT features	Not stated, 11 had follow-up CT scan	Non-contrast chest CT scan, slice thickness of 1-5 mm
25	***Clinical features of pediatric patients with coronavirus disease*** Song, Wenliang et al. April 2020 [39]	Single-center retrospective cohort study	Xiangyang City, Hubei, China	16 children diagnosed with COVID-19 at Central Hospital of Xiangyang City between January 31, 2020 and March 17, 2020	11.5 months-14 years (median 8.5 years)	Clinical features, laboratory testing and imaging	on the day or 1 day after the RT-PCR	Not stated
26	***Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study*** Sun D et al. [41]	Single-center retrospective cohort study	Wuhan, China	8 severely or critically ill patients with COVID-19 who were treated at the Intensive Care Unit, Wuhan Children's Hospital from January 24 to February 24, 2020 6 males, 2 females	2 months - 15 years	Clinical characteristics and chest imaging results	Not stated	Not stated
27	***SARS-CoV2 infection in infants under 1 year of age in Wuhan City, China*** Sun D et al. June 2020 [42]	Single- center retrospective cohort study	Wuhan, China	36 infants with SARS-CoV-2 infection in Wuhan Children's Hospital from January 26 to March 22, 2020 22 males, 14 females	2-12 months (mean 6.43 months)	Clinical features, chest imaging findings, laboratory test results, and clinical outcomes	Not stated	Not stated

Table 1. Characteristics of Included Studies *(continued)*

No.	Title/Author	Study design	Country	Population	Age	Outcomes	Timing of Chest CT scan	Type of CT Scan
28	***Epidemiological and clinical characteristics of 10 children with Coronavirus Disease 2019 in Changsha, China*** Tan Y et al. April 2020 [43]	Single-center retrospective cohort study	Changsha, China	10 children with confirmed COVID-19 from January 27 to March 10,2020 in the First Affiliated Hospital of Hunan Normal University 3 males, 7 females	1-12 years (mean 7 years)	Epidemiological and demographic information, signs and symptoms on admission, laboratory results, coinfection, CT findings, treatment and outcome	Not stated	Not stated
29	***A retrospective study of the clinical characteristics of COVID-19 infection in 26 children*** Tang A et al. March 2020 [44]	Single-center retrospective cohort study	Shenzhen, China	26 cases of children (>1 year old and <14 years old) In the Third People's Hospital of Shenzhen from January 16 to February 8, 2020 9 males, 17 females	1-13 years	Clinical manifestations, laboratory results, chest CT, treatment methods and outcomes	Not stated	Not stated
30	***Clinical analysis of 31 cases of 2019 new coronavirus infection in children from six provinces (autonomous regions) in northern China*** Wang D et al. [45]	Multi-center retrospective cohort study	Shaanxi, Ningxia, Hebei, Henan, and Shandong provinces, China	30 cases of children with 2019-nCoV infection in 21 hospitals from January 25 to February 21, 2020 15 males, 15 females	6 months - 17 years old	Clinical manifestations, laboratory examination, imaging examinations, and treatment	Not stated	Not stated
31	***Epidemiological and Clinical Characteristics of Children with Coronavirus Disease 2019*** Wu Q et al. [46]	Multi-center retrospective cohort study	China	74 pediatric cases admitted to 2 hospitals from January 20 to February 27, 2020 44 males, 30 females	Median of 6 years	Baseline information, clinical manifestations, laboratory and radiologic findings, treatment, and outcome	Not stated	Not stated
32	***Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults*** Xia W et al. [47]	Single-center retrospective cohort study	Wuhan, China	20 pediatric inpatients with COVID-19 infection from January 23 to February 8, 2020 13 males, 7 females	1 day - 14 days (median 2 years and 1.5 months)	Clinical and laboratory data, chest CT findings	Initial, Advanced, Critical, Recovery	Non-contrast chest CT studies were performed on SOMATOM Definition AS 128 unit with the following parameters 120 Kv, 100 to 150 mA, 0.5 mm collimation, and 1:1 Pitch
33	***A follow-up study of children infected with SARS-CoV2 from Western China*** Xu H et al. [48]	Multi-center retrospective cohort study	4 provinces in Western China	32 children confirmed with SARS-CoV-2 infection between January 24 and February 12, 2020 17 males, 15 females	mean 10 years	History of exposure, demographic characteristics, laboratory findings, radiologic findings and clinical outcomes	Not stated	Not stated

Table 1. Characteristics of Included Studies *(continued)*

No.	Title/Author	Study design	Country	Population	Age	Outcomes	Timing of Chest CT scan	Type of CT Scan
34	***The clinical and epidemiological features and hints of 82 confirmed COVID-19 pediatric cases age 0-16 in Wuhan, China*** Yu H et al. [49]	Single-center retrospective cohort study	Wuhan, China	82 children infected with COVID-19, on February 1-20, 2020 at Wuhan Children's Hospital 51 males, 31 females	3 days - 16 years	Symptoms, laboratory results, chest radiography and CT findings	Not stated	Not stated
35	***Clinical Characteristics of 34 Children with Coronavirus Disease-2019 in the West of China*** Zhang C et al. [50]	Multi-center retrospective cohort study	China	34 admitted children with laboratory-confirmed SARS-CoV-2 from 4 hospitals during January 1 to February 23, 2020 14 males, 20 females	1-144 months (media 33 months)	Demographic information, medical and exposure history, CT scan, therapeutic information	Not stated	Not stated
36	***Clinical Characteristics of Children with Coronavirus Disease 2019 in Hubei, China*** Zheng F et al. [23]	Multi-center retrospective cohort study	Wuhan, China	24 children aged 1 month -14 years admitted to hospitals with COVID-19 between February 1 to February 10, 2020	1 month - 14 years (media 3 years)	Clinical and laboratory data, radiological characteristics, treatments and outcomes	On admission	Not stated
37	***Chest CT findings and clinical features of coronavirus disease 2019 in children*** Zhong, Zheng et al. [51]	Single- center retrospective cohort study	Hunan province, China	Laboratory confirmed pediatric COVID-19 patients 4 males, 5 females	3 months - 12 years	Clinical history, laboratory results, and epidemiological characteristics, CT scan results	Same day as being diagnosed and on follow-up (2-3 days after treatment)	Not stated
38	***Clinical features and chest CT manifestations of 2019 coronavirus in infants*** Zhou Y et al. [52]	Single-center retrospective cohort study	Shenzhen, China	9 infants (0-3 years old) patients diagnosed with COVID-19 from January 20 to February 10,2020 4 males, 5 females	0-3 years (median age 1 year)	Clinical data and chest CT data	Same day or 1 day after the throat swab	64-slice spiral CT scan: tube voltage 80-120 kV, FOV 200 x 200 mm, reconstruction layer thickness 0.8 mm
39	***Clinical characteristics of a case series of children with coronavirus disease 2019*** Zhu Li et al. March 2020 [24]	Case Series	Jiangsu, China	10 children aged from 1 to 18 years with confirmed COVID-19 from 3 designated hospitals in 3 cities of Jiangsu province 5 males, 5 females	1 year 7 months - 17 years	Demographic, epidemiological, and clinical data	On admission	Not stated

Thirty-six studies were conducted in China, two in Iran[25,35], and one in Italy[26]. The sample sizes of the cohort studies range from 6 to 171[13,26-51]; the case series discussed 2 to 27 cases[14-24]. (Table 1)

Nine out of the 39 studies described the chest CT scan findings on admission to the hospital[16,17,20,23,24,28,32,35,46]; three studies had the chest CT scan done on the same day or a day after the swab test[38,50,51]. Studies by Cai X et al.[14] and Li W et al.[31] discussed the characteristics of chest CT scan at 2-9 days from admission or from symptom onset. Liu H et al.[19] examined the findings of chest CT scan done with a median of 2 days from onset of symptoms. The rest of the studies did not report the timing of the chest CT scan.

In terms of establishing the diagnosis of COVID-19, all 39 studies used the RT-PCR assay of oropharyngeal, nasopharyngeal, or throat swab in detecting SARS-CoV-2 RNA.

Unenhanced chest CT scans were used in 18 studies[13,15-20,22,26,19-32,35,39,46,51]. The rest of the studies did not specify the type of chest CT scan done.

The studies involved children who tested positive for COVID-19 RT-PCR seen as inpatients or as outpatients. The ages of the patients included in the studies range from 1 day to 18 years. Most studies reported the clinical characteristics, laboratory results, and imaging findings of the study subjects. Of the 39 studies, 33 reported on the density and pattern of the lung lesion. The study by Dan et al., however, only stated that imaging findings included thin scattered patches, multiple patchy or scattered ground glass opacity, increased short strip or patchy density, patchy blurry shadows and cord-like dense shadows, but did not break down the numbers of each finding.[40] To describe the location and distribution of the lung pathology, a total of 30 studies classified the findings as bilateral or unilateral. Of these, three studies reported only unilateral findings, four reported only bilateral findings, and 23 studies reported both. There were a total of 14 studies which recorded the lung lobe involved.

Critical Appraisal

Study on Diagnostic Accuracy of Chest CT scan

Guide questions from the Painless Evidence-Based Medicine Book on Evaluation of Articles on Diagnosis[52] were used to critically appraise the quality of the study by Ma et al. The reference standard used by Ma et al. was RT-PCR[13], as what is used as the gold standard in the diagnosis of COVID-19 worldwide. The timing of the test, however, was not reported. It was not specifically indicated whether the outcome assessors for both chest CT scan and RT-PCR were blinded from the result of the other test. The time interval of the release of the two test results was not provided. In the analysis of the said study, a positive CT scan result only required one abnormal CT scan finding whether or not it was typical of COVID-19 pneumonia. This may potentially be a source of bias since a particular chest CT scan lesion may not be consistent with COVID-19, thus, should not be labelled as a positive CT scan result. This study was thus assessed to have poor quality.

Studies on Common Chest CT Scan Findings

The National Institutes of Health Quality Assessment Tools for Case Series was used in appraising the quality of the retrieved journals.[53] After screening, 11 of the 39 included studies were assessed to have good quality, 22 were of fair quality, and the remaining six have poor quality. The description of the intervention (in this case, chest CT scan) as to the timing and type used, the definition of outcome measures in terms of the specific aspects on the chest CT scan to be examined, and the standardization of reporting of results, were the common areas identified to be of poor quality. Since most of the studies included study subjects from the same area in China, it is possible that a number of patients may have been reported in more than one study included in our review. (Table 2)

Diagnostic Outcomes

Diagnostic Accuracy of Chest CT scan

Based on the study of Ma et al.[13], the sensitivity of chest CT scan in diagnosing COVID-19 is at 86.0% (95% CI 73.8, 93.0), specificity of 75.9% (95% CI 67.1, 83.0), positive predictive value of 62.3% (95% CI 50.5, 72.8), and negative predictive value of 92.1% (95% CI 72.1, 84.7).

Common Chest CT Scan Findings

Of the 39 included studies, a total of 1028 patients under-went chest CT scan. Three-hundred eleven (30.3%) of these cases had no abnormal findings despite a positive test for COVID-19. Using the OpenMeta[analyst] application, the pooled sensitivity of chest CT scan in diagnosing COVID-19 is 69.4% (95% CI 62.5, 76.3 I^2=89.89%). (Figure 1)

Thirteen studies reported findings involving the lower lobe. The pooled proportions of lower lobe involvement is 45.8% (95% CI 38.8,97.5, I^2=0). Eleven studies reported findings involving the upper lobe. The pooled proportions of upper lobe involvement is 33.6% (95% CI, 21.8, 45.3, I^2=62.11%). Only five studies reported findings involving the middle lobe. The pooled proportions of middle lobe involvement is 16.5% (95% CI 3.1, 29.9, I^2= 71.54%). (Figure 2)

The pooled proportions from 26 studies of unilateral lung involvement is 33.1% (95% CI 26.5,39.7, I^2=68.02%). On the other hand, 27 studies reported bilateral lung lesions, with pooled proportions of bilateral lung involvement at 31.2% (95% CI 23.5, 38.8), I^2=85.15%). (Figure 3)

In the studies which reported the density of the lesion, the common findings reported were patchy shadows, ground glass opacities, and consolidation. Patchy shadows were reported in seven studies. Pooling the data from these studies

shows that the proportion of patchy shadows is 43.8% (95% CI 19.6, 67.9, I^2= 92.66%).Thirty-two studies reported the presence of ground glass opacities in the chest CT scan of children with COVID-19. Pooling these data gives a pooled proportion of 43.1% (95% CI 34.5, 51.6, I^2=87.14%). Fifteen studies reported the presence of consolidation. The pooled proportions of consolidation is 26.2% (95% CI 1.61, 36.3, I^2=85.13%). Seven studies also reported the number of patients with both ground glass opacities and consolidation. The pooled proportion of these findings is 6.4% (95% CI 0.9, 11.9, I^2=0). (Figure 4). Other patterns reported include fine mesh shadows, "enhanced lung texture", white lung, and halo sign. (Table 3)

Pleural effusion was reported in 16 studies, with a pooled proportion of 1.6% (95% CI 0.5, 2.7, I^2=0). Halo sign was reported in eight studies with a pooled proportion of 15.5% (95% CI 5.8, 25.2, I^2=75.09) (Figure 5). No cases of pneumothorax were recorded. Other reported findings on the CT scan are as follows: air bronchogram, pleural thickening, crazy paving sign, reverse halo sign, interstitial abnormalities, and lymphadenopathy.

It is worthwhile to note that the studies included children who manifested with a wide spectrum of clinical severity of COVID-19. Only three of the 19 studies which included asymptomatic patients described their findings separately from patients who presented with COVID

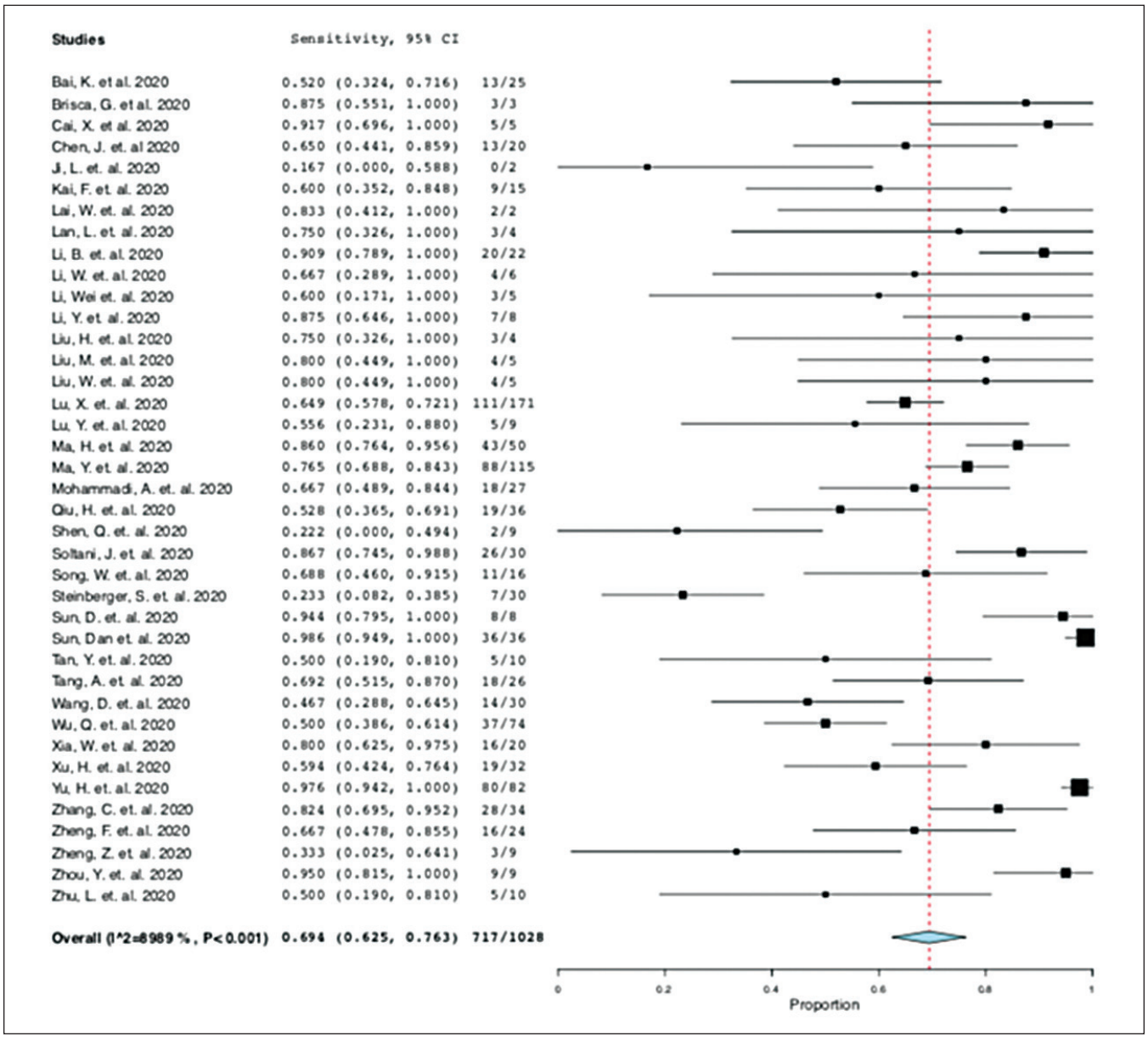


Figure 1. Pooled proportions of sensitivity of chest CT scan in children with COVID-19.

symptoms. All asymptomatic patients with an RT-PCR positive for SARS-CoV-2 in the study of Steinberger et al.[39] had normal chest CT scan. In the study of Xu H. et al.[47], on the other hand, 45.0% (5/11) of the children were found to have abnormal chest CT scan findings. Chen et al.[29], who only included patients who were asymptomatic, reported that 13 out of the 20 included patients had abnormal chest CT findings. Both the studies of Xu, et al. and Chen et al., however, did not characterize the CT scan findings of this group of patients.

Recommendations from Other Guidelines

The Interim Guidelines by the Philippine Pediatric Society and Pediatric Infectious Disease Society of the Philippines on the Screening, Assessment, and Clinical Management of Pediatric patients with suspected or confirmed COVID-19 does not recommend its use as an initial diagnostic test in children with COVID-19.[54]

An International Expert Consensus on Chest Imaging in Pediatric COVID-19 recommends doing a chest CT scan in the following situations: 1) in patients with mild

Table 2. Critical Appraisal of Studies on the Common Chest CT Scan Findings in Children with COVID-19

Study	1	2	3	4	5	6	7	8	9	Quality
Bai K et al.	Y	Y	CD	Y	N	N	N	Y	Y	Fair
Brisca G et al.	Y	Y	CD	Y	N	N	N	N	N	Poor
Cai X et al.	Y	Y	CD	Y	Y	N	N	N	Y	Fair
Chen J et al.	Y	Y	CD	Y	N	N	Y	NA	N	Fair
Hameed S et al.	Y	Y	CD	Y	Y	Y	N	N	N	Fair
Ji L et al.	Y	N	CD	Y	N	Y	N	NA	Y	Fair
Kai F et al.	Y	Y	CD	Y	Y	Y	Y	NA	Y	Good
Lai W et al.	N	N	CD	Y	N	N	Y	N	Y	Poor
Lan L et al.	Y	Y	CD	Y	Y	Y	Y	Y	Y	Good
Li B et al.	Y	Y	CD	Y	Y	Y	Y	Y	Y	Good
Li W et al.	Y	Y	CD	Y	Y	Y	N	Y	Y	Good
Li Wei et al.	Y	Y	CD	Y	N	N	Y	NA	Y	Fair
Li Y et al.	Y	Y	CD	Y	Y	Y	Y	NA	Y	Good
Liu H et al.	Y	Y	CD	N	Y	Y	Y	NA	Y	Fair
Liu M et al.	Y	Y	CD	Y	Y	N	Y	NA	Y	Fair
Liu W et al.	N	Y	CD	Y	N	N	Y	NA	N	Poor
Lu X et al.	Y	Y	CD	Y	N	Y	N	N	Y	Fair
Lu Y et al.	Y	Y	CD	Y	Y	N	Y	NA	Y	Fair
Ma H et al.	Y	Y	CD	Y	Y	Y	Y	Y	Y	Good
Ma Y et al.	Y	Y	CD	Y	N	N	N	NA	N	Poor
Mohammadi A et al.	Y	Y	CD	Y	Y	Y	Y	Y	Y	Good
Qiu H et al.	Y	Y	CD	Y	N	N	Y	NA	N	Fair
Shen Q et al.	Y	Y	CD	Y	N	N	Y	NA	Y	Fair
Soltani J et al.	Y	Y	CD	Y	N	Y	N	Y	Y	Fair
Song W et al.	Y	Y	CD	Y	N	Y	Y	NA	Y	Fair
Steinberger S et al.	Y	Y	CD	Y	Y	Y	Y	Y	Y	Good
Sun D et al.	Y	Y	CD	Y	Y	N	N	NA	Y	Fair
Sun D et al.	Y	Y	CD	Y	N	N	N	NA	N	Poor
Tan Y et al.	Y	Y	CD	Y	N	Y	N	NA	Y	Fair
Tang A et al.	Y	N	CD	Y	N	Y	N	Y	Y	Fair
Wang D et al.	Y	Y	CD	Y	N	N	Y	NA	Y	Fair
Wu Q et al.	Y	Y	CD	Y	N	N	N	Y	Y	Fair
Xia W et al.	Y	Y	CD	Y	Y	Y	Y	NA	Y	Good
Xu H et al.	Y	Y	CD	Y	N	N	N	Y	Y	Fair
Yu H et al.	Y	Y	CD	Y	N	N	N	Y	Y	Fair
Zhang C et al.	Y	Y	CD	Y	N	Y	Y	Y	Y	Fair
Zheng F et al.	Y	Y	CD	Y	N	N	N	NA	Y	Fair
Zheng Z et al.	Y	Y	CD	Y	Y	Y	Y	NA	Y	Good
Zhou Y et al.	Y	Y	Y	CD	Y	Y	Y	NA	Y	Good
Zhu L et al.	Y	Y	CD	Y	N	N	N	NA	N	Poor

**National Institutes of Health Quality Assessment Tools*

Table 3. Summary Table of the Common Chest CT Scan Findings in Children with COVID-19

Chest CT Scan Aspect	No. of Studies	Total No. of Patients	Pooled Proportions
Lobe Involvement			
Upper Lobe	11	63/173	33.6% (95% CI 0.218, 0.453)
Middle Lobe	5	17/103	16.5% (95% CI 0.031, 0.299)
Lower Lobe	13	86/187	45.8% (95% CI 0.388, 0.975)
Laterality			
Unilateral	26	207/683	33.1% (95% CI 0.265, 0.397)
Bilateral	27	199/735	45.8% (95% CI 0.235, 0.388)
Pattern/Density of the Lesion			
Patchy Shadows	7	95/246	43.8% (95% CI 0.196, 0.679)
Ground Glass Opacities	32	281/799	43.1% (95% CI 0.345, 0.516)
Consolidation	15	68/296	26.2% (95% CI 0.161, 0.363)
Ground Glass Opacities with Consolidation	7	8/70	6.4% (95% CI 0.009, 0.119)
Other Findings			
Pleural Effusion	16	16/516	1.6% (95% CI 0.005, 0.027)
Halo Sign	8	23/141	15.5% (95% CI 0.058, 0.252)

symptoms who have an underlying comorbidity, is in an immunocompromised state, or if with worsening respiratory symptoms, 2) may be considered in a child with moderate to severe clinical features in a non-resource constrained setting if it will affect clinical decisions, 4) may be considered as an initial diagnostic in a child with moderate to severe clinical features in a resource constrained setting (no available laboratory test or if with a slow turnaround time). It also stated that chest imaging is not generally indicated as a screening tool for symptomatic or asymptomatic pediatric patients with suspected COVID-19 infection.[8]

DISCUSSION

Studies which directly compare the results of chest CT scan and RT-PCR in children suspected to have COVID-19 are still limited. The study by Ma et al.[13] showed that its sensitivity is at 86.0% (95% CI 73.8, 93.0) while the pooled sensitivities of the 39 studies included in this review gave a sensitivity of 69.4% (95% CI 62.5, 76.3 I^2=89.89%). This is similar to the findings of a rapid review by Meng et al. which found that the sensitivity of chest CT scan using RT-PCR as the reference standard is lower in children at 66.0% (95% CI, 0.15–1.00, I^2=96.74%) from seven

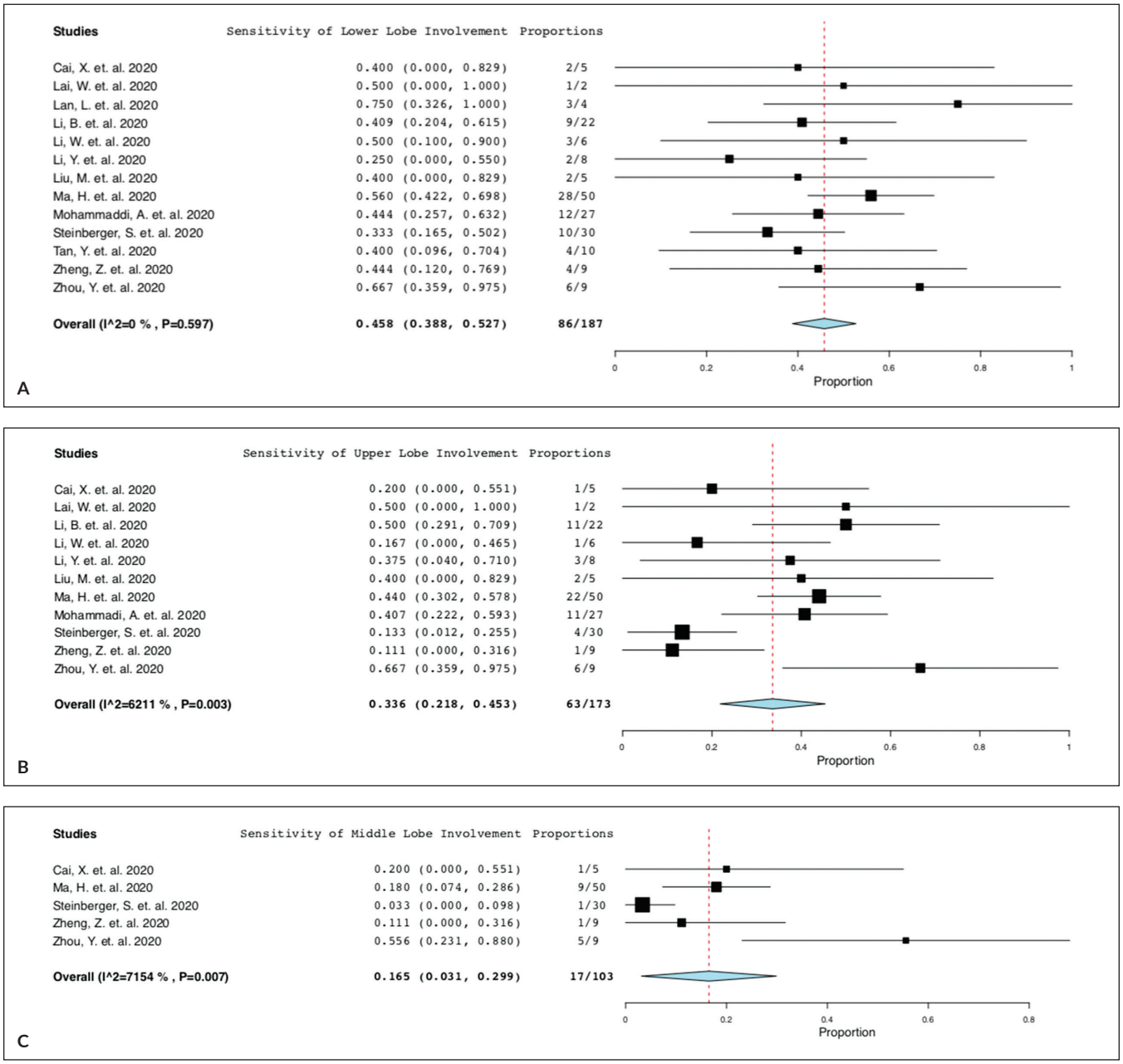
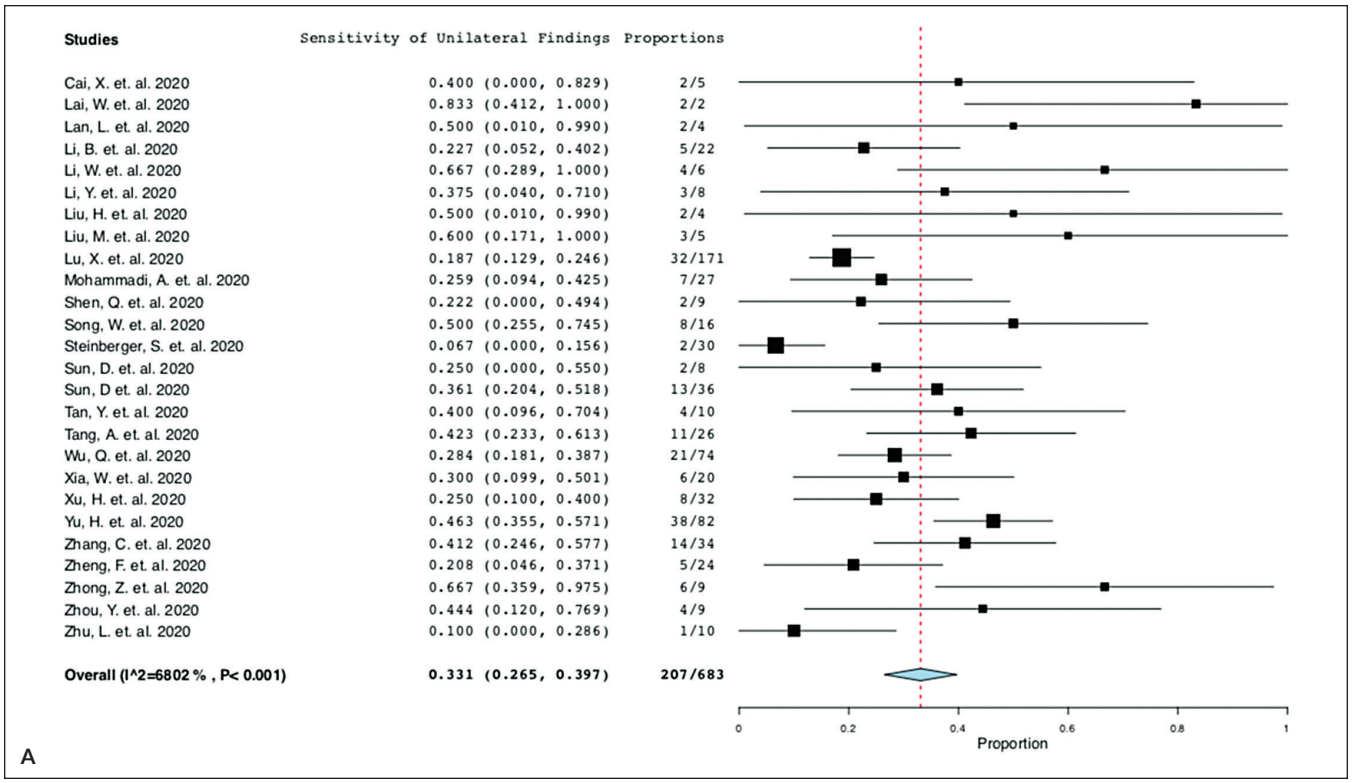


Figure 2. Pooled proportions of lobe involvement **(A)** Lower Lobe, **(B)** Middle Lobe, **(C)** Upper Lobe.



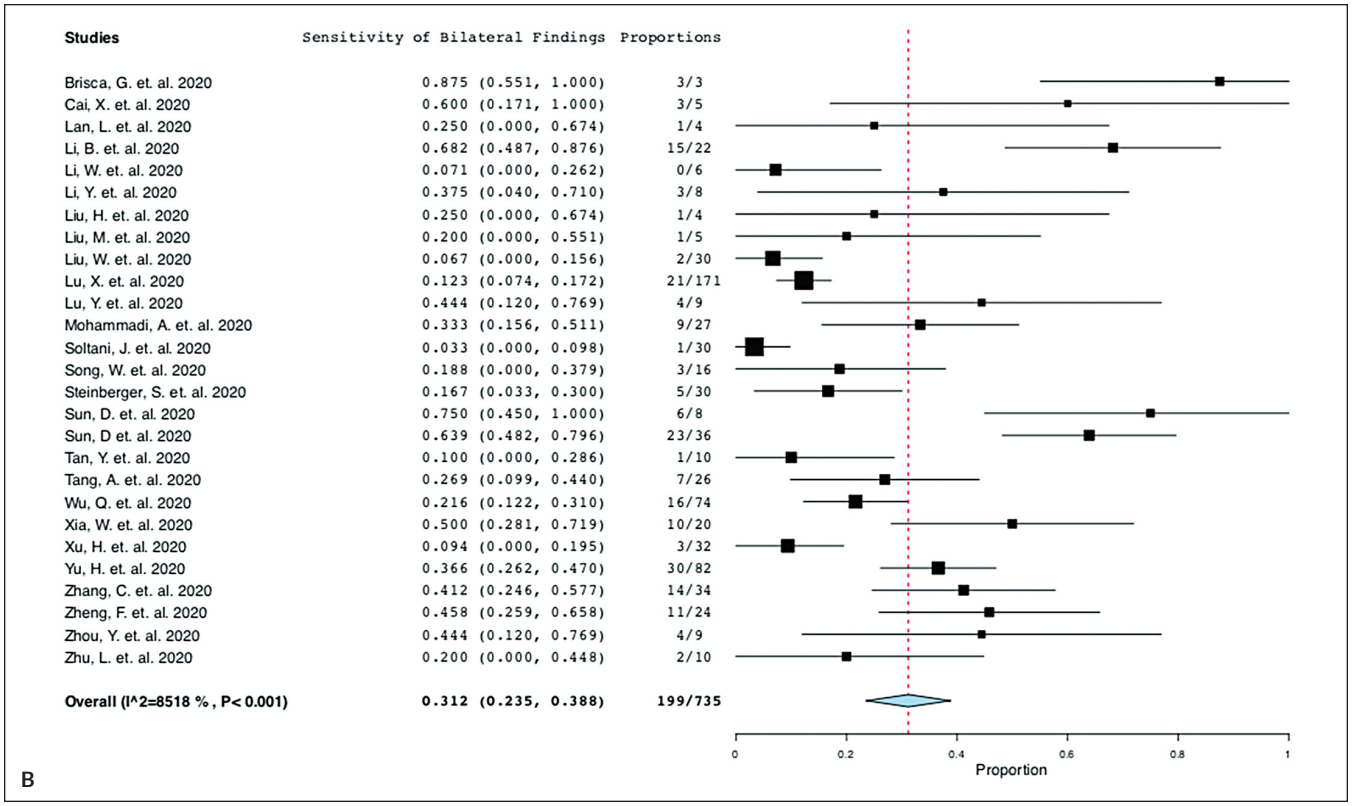
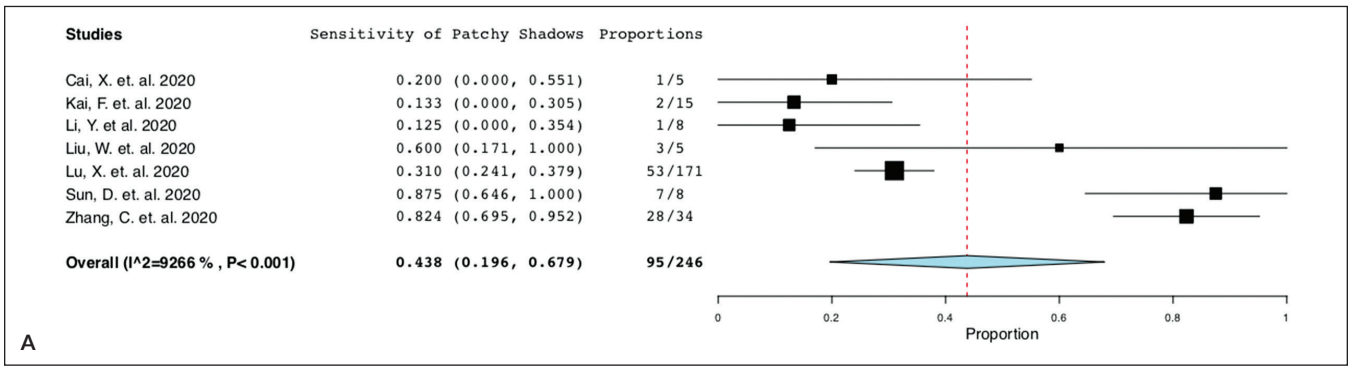


Figure 3. Pooled proportions of **(A)** Unilateral involvement, **(B)** Bilateral involvement.

studies compared with adults at 99.0% (95% CI, 0.97–1.00, I^2=85.00%) in 64 studies.[10] Another study by Shelmerdine et al. showed that only 278/432 (66.0%) children with COVID-19 had abnormal initial chest CT scan.[55]

Nonspecific and overlapping signs, symptoms, and laboratory results in childhood viral lung infections make evaluation and differentiating them a challenge. A review presented by Foust et al. on the imaging findings of recent viral epidemics such as SARS, H1N1, MERS, EVALI, and SARSCoV-2 showed that all of these viruses may present with ground glass opacities with or without consolidation on chest CT scan.[6] Diagnostic tests with high specificity are important when this difficulty is met. However, studies on the specificity, as well as positive predictive value and negative predictive value of chest CT scan in diagnosing COVID-19 in children are still lacking as of this writing.



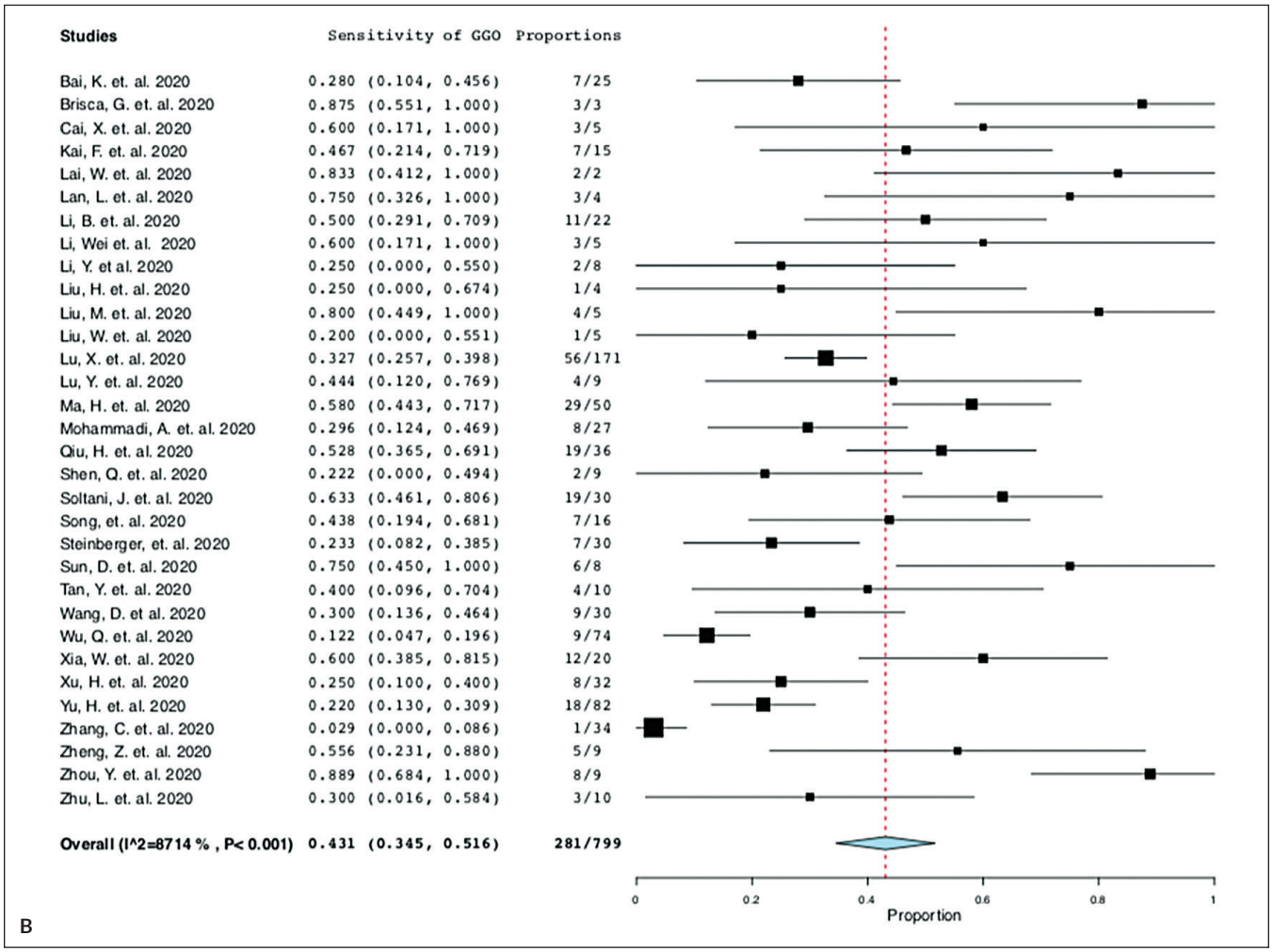


Figure 4. Pooled proportions of common chest CT scan patterns. **(A)** Patchy shadows, **(B)** Ground glass opacities.

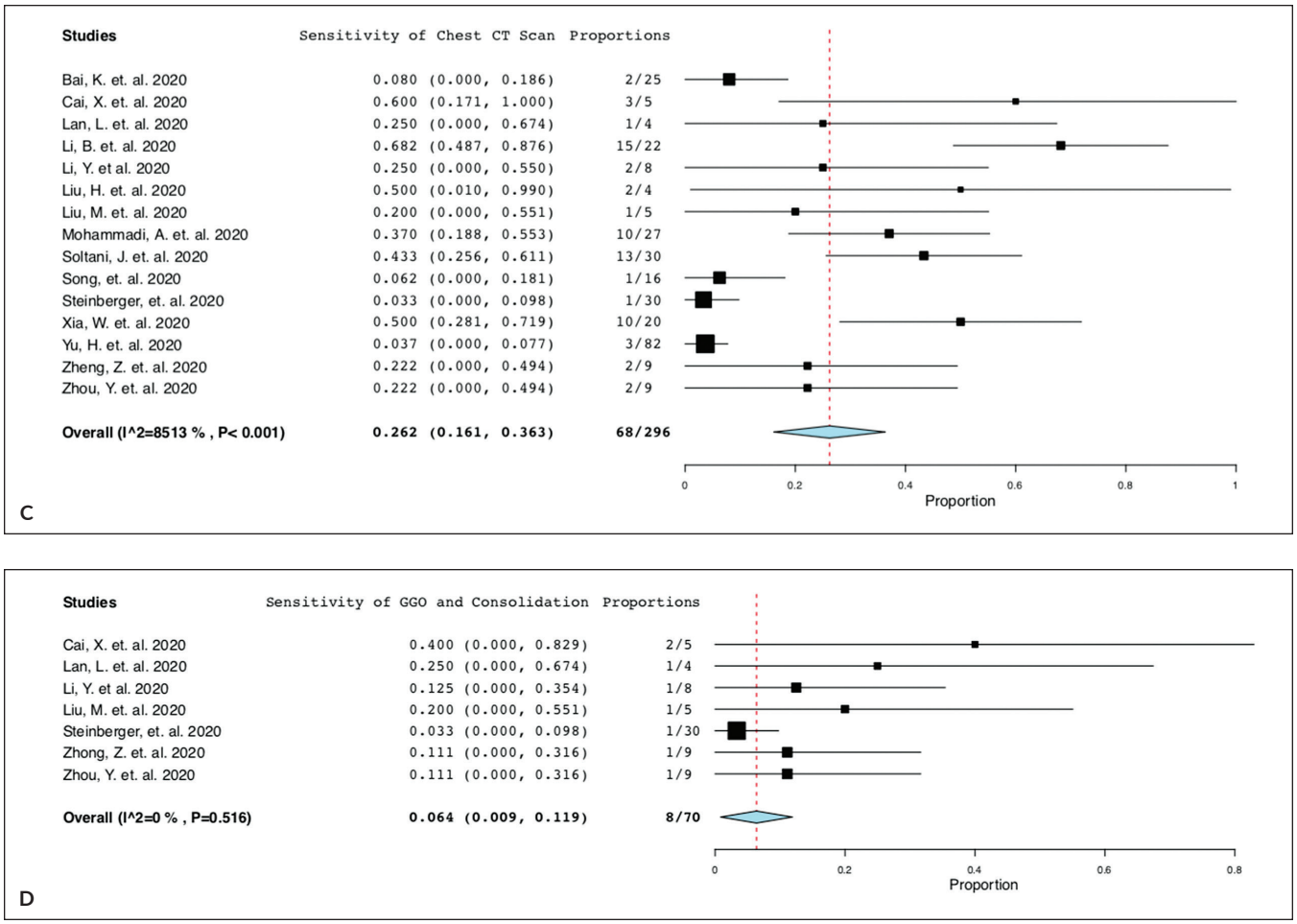


Figure 4. Pooled proportions of common chest CT scan patterns *(continued)*. **(C)** Consolidation, **(D)** Ground glass opacities and consolidation.

It is postulated that since children have a milder presentation of COVID-19, the chest imaging findings are also more subtle and are sometimes normal. In a study of 30 pediatric patients, all nine patients who were asymptomatic had normal chest CT scan results.[39] However, in a study by Chen et al. on 20 asymptomatic children with COVID-19, 13/20 (65.0%) had abnormal findings.[29] Further studies which differentiate the findings of symptomatic vs asymptomatic patients are still needed.

Similar to that of adults, the most commonly reported pattern in the chest CT scan of children is ground-glass opacities with or without consolidation, predominantly in the lower lobe. A larger percentage of lesions is found in only one lung compared to the multifocal and bilateral findings in adults.[8] The peripheral distribution seen in adults is not as commonly reported in studies in children.

Researches on chest CT scan used a wide range of terminologies used to describe CT findings. A structured reporting was already suggested by an International Expert Consensus Statement on Chest Imaging in Pediatric COVID-19 Patient Management.[8] This can standardize the language used by physicians, especially radiologists worldwide, and can help in categorizing findings associated with COVID-19 pneumonia.

More studies are still needed to make robust conclusions regarding the utility of chest CT scan in COVID-19 diagnosis, especially in the pediatric population. Aspects which may be explored, not further discussed in this review, include: differentiation of findings in symptomatic versus asymptomatic individuals, the correlation of findings with disease severity, its differences per age group and gender, and its changes as the disease progresses.

This review had several limitations. First, in most of the studies, any abnormal finding was considered a positive finding, whether typical for COVID-19 or not. This also emphasizes the need for standardized reporting as discussed. Second, included research were reports describing the pediatric cases of COVID-19 of which the chest CT scan results were only a part of. Since this was not the focus, the type of chest CT scan used were not standardized in terms

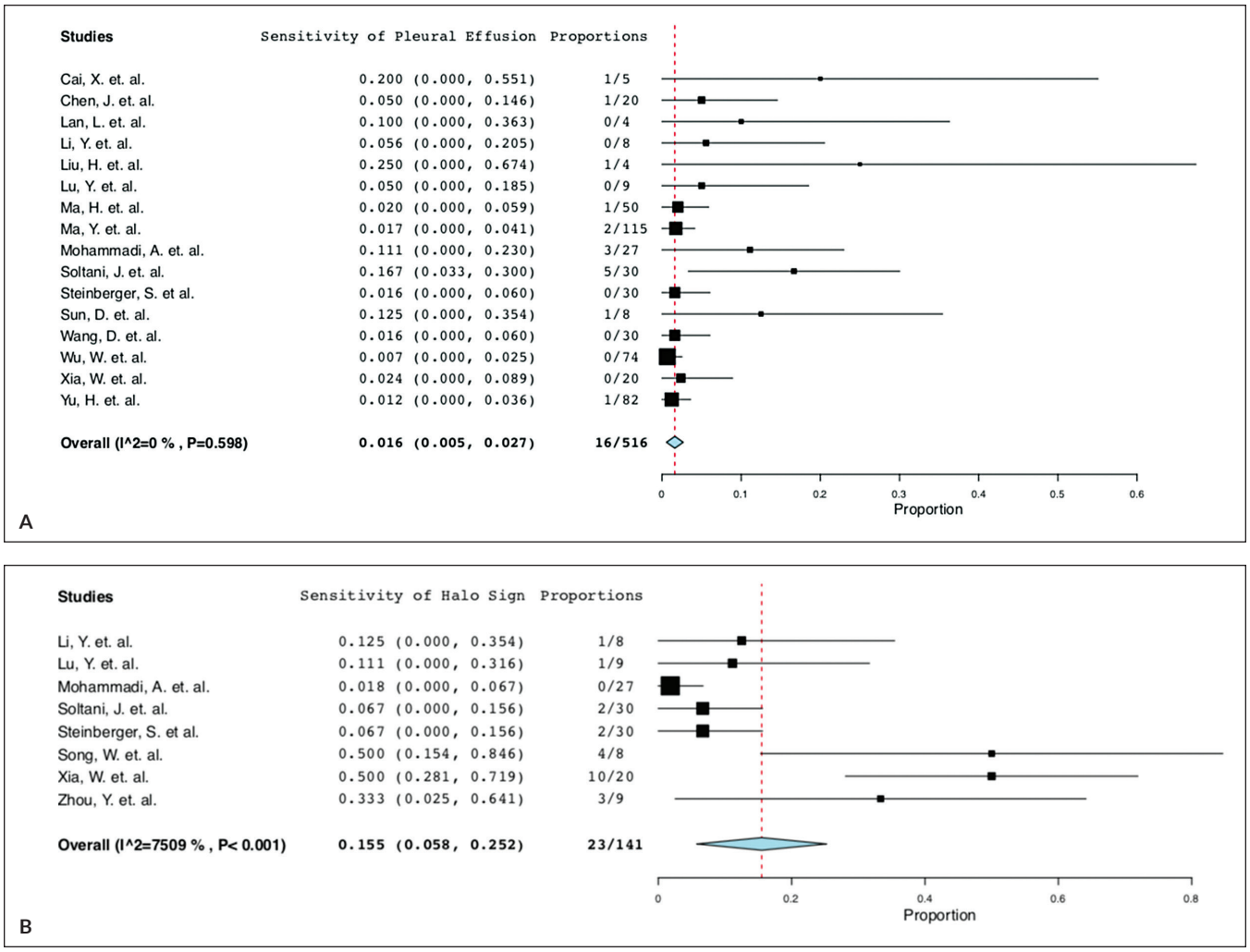


Figure 5. Pooled proportions of other findings, **(A)** Halo sign, **(B)** Pleural effusion.

of slice thickness and other settings throughout the studies. Third, samples were heterogenous and had small sample sizes with the quality of evidence being poor. Most studies were done in China so there is a possibility that one study subject may have been enrolled in more than one study. Last, the radiation exposure that comes with chest CT scan should be considered in requesting this test. Specific indications were recommended by the International Expert Consensus Statement on Chest Imaging in Pediatric COVID-19 Patient Management to identify cases to which this may be useful.

CONCLUSION

Studies which directly investigate the accuracy of chest CT scan in the diagnosis of COVID-19 pneumonia in children is very limited. There was only one study found which showed that the sensitivity of chest CT scan in diagnosing COVID-19 pneumonia in children is at 86.0% (95% CI 73.8, 93.0) while its specificity is at 75.9% % (95% CI 67.1, 83.0). This study was assessed to be of poor quality.

Based on the results of the 39 studies included in this review, the pooled sensitivity of chest CT scan in diagnosing COVID-19 is at 69.4% (95% CI 62.5, 76.3).

While chest CT scan findings such as patchy shadows, ground glass opacities, and consolidation, are common in children with COVID-19, these may be similar to the imaging findings of other respiratory viral illnesses. Presently, available studies on chest CT scan in children with COVID-19 are limited to cohort reviews and case series.

Limitations of these studies include small sample sizes and heterogenous populations with a wide spectrum of disease severity. Furthermore, there is a possibility of enrolment of the same participant/s in more than one of the included studies in our review.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

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