Early View

Research letter

Value of Chest CT as COVID 19 screening tool in children

Peter JFM Merkus, Willemijn M Klein

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Authors:
1. Peter JFM Merkus MD PhD, Associate Professor, Pediatric Pulmonologist
2. Willemijn M Klein, MD, PhD, Associate Professor, Paediatric Radiologist

Affiliations:
1. Department of Paediatrics, Division of Respiratory Medicine and Allergology
   Radboud University Medical Centre, Amalia Children's Hospital, Geert Grooteplein
   Zuid 10, Nijmegen 6525GA, The Netherlands
2. Department of Radiology and Nuclear Medicine, Radboud University Medical Center,
   Amalia Children's Hospital, Geert Grooteplein Zuid 10, Nijmegen 6525GA, The
   Netherlands

Address of correspondence:

Prof Dr Peter JFM Merkus, MD PhD, Associate Professor
Pediatric Pulmonologist
Division of Respiratory Medicine and Allergology
Radboudumc Amalia Children's Hospital
P.O.Box 9101, 6500 HB Nijmegen, The Netherlands
Peter.Merkus@radboudumc.nl

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It is difficult to identify children infected with COVID 19 who have little or no respiratory symptoms. For routine clinical care in different circumstances, it is relevant to assess the COVID 19 status of patients. Routine PCR is recognized as the gold standard but can be falsely negative due to sampling errors. For diagnosing and monitoring adult COVID 19 patients, characteristic radiological lesions have been recognized [1,2] and to assess the possibility of COVID 19 infection *in adults* scheduled for surgery in whom a PCR test is negative or missing, a non-enhanced chest computed tomography (CT) scan has been proposed as an option in the Netherlands [3] because: (1) Patients may be pre-symptomatic in the incubation period of a COVID 19 infection and subsequently develop symptoms post-operatively, implying a greater risk for adverse post-operative outcomes; (2) Patients may be asymptomatic or mildly symptomatic carriers and shedders of COVID 19, and place hospital workers and other patients at risk.

It is unknown whether CT scanning has additional value as screening tool for to rule out COVID 19 infections in *children* with little or no respiratory symptoms or with negative or missing PCR test results. It would require very convincing evidence to justify the introduction of ionizing radiation to rule out COVID 19 infection in children.

Therefore we conducted a literature search to assess what is known about the sensitivity, specificity and negative predictive value of chest CT as a screening tool to rule out COVID 19 infections in children. We searched for pubmed articles in English or with English abstracts including mesh terms: COVID and CT scan and [adults or children] published in 2020 till April 29th. This resulted in 92 papers that mostly focused on the use of CT scans in diagnosing and/or monitoring the disease or its severity [1,2] rather than ruling it out. Most studies did not include subjects with negative PCR, so the true negative rate or specificity of CT scanning could not be calculated; instead we focused on sensitivity, the ability of chest CT to recognize as many patients as possible.

Chest CT abnormalities in adult patients with proven COVID 19 with little or no respiratory symptoms

From several case series in PCR proven adult COVID 19 patients with little or minor symptoms, it is clear that chest CT abnormalities may be absent in spite of mild symptoms, with a sensitivity depending on the study varying between 44% [4], 69% [5] and 70% [6]. In one observational study, sensitivity was exceptionally high (97%); in this case series of 1014 clearly symptomatic hospitalized patients from the highly endemic Wuhan area the large majority of patients had abnormal CT scans, resulting in a sensitivity of 97% but with a specificity of 25%, implying a high false positive rate [7]. From that study it was unclear at what moment in the course of disease diagnostic tests were conducted. Chest CT in more advanced disease is associated with more abnormalities [4, 13], and especially so in selected clinical populations [8]. In those series, the positive and negative predictive values of the CT scan were 65% and 83%, respectively. Also from another study in a highly epidemic region 82% of patients with mild symptoms had chest CT abnormalities. [9] Such results may only be valid in epidemic areas with high pre-test probability for this disease, and one should not assume similar sensitivity of chest CT in a general population for screening purposes [7,8] With a prevalence of disease of about 60% as in Wuhan, the positive and negative predictive values were 65% and 83%, respectively. However, in an area with a lower or higher prevalence the positive and negative predictive values will differ (figure 1).
In summary, in a considerable percentage of adult COVID 19 patients with little or no symptoms, a chest CT may be normal. Depending on the study population the sensitivity of a chest CT to detect abnormalities in proven COVID 19 patients ranged between 44 and 97% (median: 69%).

CT image abnormalities in children with proven COVID 19 with little or no respiratory symptoms

In children the course of the disease in general is milder than in adults. Both symptomatic and asymptomatic children with known contact with persons having confirmed or suspected COVID 19 infection (n=1391) were evaluated in a Chinese cohort [10]. COVID 19 was confirmed through PCR in 171/1391 (12.3%) children. Of these 171, CT abnormalities consistent with (any) viral pneumonia were found in 111, implying a sensitivity of 65%. In 27 (16% of 171) infected children there were no symptoms nor abnormalities on CT images and

in 33 infected children (19%) only an upper respiratory tract infection was observed. Hence, in about 35% of proven pediatric COVID 19 patients, CT images were normal. In a retrospective study on clinical data and chest CT of 15 children diagnosed with COVID 19 infection, 10 of whom were asymptomatic, 6 (40%) children showed no lesions on chest CT [11]. In a case series of 5 young COVID 19 positive children, 4 were asymptomatic patients; of these 50% had some minor abnormalities on CT scan, 50% had normal CT images [12]. Of 13 hospitalized children with mild to severe COVID disease, 6 (46%) had no abnormalities on CT scan [15, Tan] and out of 115 pediatric clinical patients infected with COVID, 24% had no abnormalities on CT scan [16, Ma].

In summary, in pediatric COVID 19 positive patients with little or only minor upper airway symptoms, a chest CT may be normal in 35-50% of cases. Hence, depending on the study, the reported sensitivities of CT scanning to detect abnormalities in pediatric COVID 19 patients range between 50 and 74%, (median value of 60 %).

Discussion

A screening test should accurately identify diseased and non-diseased individuals. An ideal screening test is affordable, safe and patient-friendly, and highly sensitive (high probability of detecting disease) and highly specific (high probability that those without the disease will screen negative) with high positive and negative predictive values.

Studies in asymptomatic adults and children are scarce. In adult studies, chest CT can be normal in a considerable percentage of symptomatic COVID 19 patients. The median (range) sensitivity of finding chest CT abnormalities was 69% (44-97)% in COVID 19 proven (mildly) symptomatic adult patients. According to 5 pediatric studies, normal chest CT has been reported in a large percentage of children with asymptomatic or mild COVID 19 disease. The median (range) sensitivity of finding CT image abnormalities was only 60% (40 - 74)% in COVID 19 proven pediatric patients.

This implies an unacceptable percentage of false negative cases, creating a false sense of safety for health care personnel while exposing the child to potentially harming ionizing radiation, that will not contribute to a better outcome for the child.

CT scanning should always be carefully considered in children due to the potential harm that ionizing radiation may cause [15]. A routine chest CT in case of any viral pneumonia in

children is rarely performed, except for cases suspected of unexplained symptoms or complications that could need a change in therapy.

With the information currently available and considering the PCR as gold standard for the diagnosis COVID 19, a negative chest CT scan does not rule out COVID 19 lung disease in at least a third of the pediatric COVID patients tested positive and who have little or no respiratory symptoms. Therefore, we consider CT scanning of the chest not suitable as a screening tool to rule out COVID 19 in pediatric patients with little or no symptoms.

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Figure 1. Based on the Wuhan data of adult patients [7], Positive Predicted Value (PPV) and Negative Predictive Value (NPV) can be calculated. This figure illustrates that the positive and negative predictive values highly depend on the prevalence of disease in the study population.

PPV and NPV of CT depend on disease prevalence