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# CT Examinations for COVID-19: A Systematic Review of Protocols, Radiation Dose, and Numbers Needed to Diagnose and Predict

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# CT Examinations for COVID-19: A Systematic Review of Protocols, Radiation Dose, and Numbers Needed to Diagnose and Predict

## COVID-19 진단을 위한 CT 검사: 프로토콜, 방사선량에 대한 체계적 문헌고찰 및 진단을 위한 CT 검사량

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**Purpose** Although chest CT has been discussed as a first-line test for coronavirus disease 2019 (COVID-19), little research has explored the implications of CT exposure in the population. To review chest CT protocols and radiation doses in COVID-19 publications and explore the number needed to diagnose (NND) and the number needed to predict (NNP) if CT is used as a first-line test.
**Materials and Methods** We searched nine highly cited radiology journals to identify studies discussing the CT-based diagnosis of COVID-19 pneumonia. Study-level information on the CT protocol and radiation dose was collected, and the doses were compared with each national diagnostic reference level (DRL). The NND and NNP, which depends on the test positive rate (TPR), were calculated, given a CT sensitivity of 94% (95% confidence interval [CI]: 91%–96%) and specificity of 37% (95% CI: 26%–50%), and applied to the early outbreak in Wuhan, New York, and Italy.
**Results** From 86 studies, the CT protocol and radiation dose were reported in 81 (94.2%) and 17 studies (19.8%), respectively. Low-dose chest CT was used more than twice as often as standard-dose chest CT (39.5% vs.18.6%), while the remaining studies (44.2%) did not provide relevant information. The radiation doses were lower than the national DRLs in 15 of the 17 studies (88.2%) that reported doses. The NND was 3.2 scans (95% CI: 2.2–6.0). The NNPs at TPRs of 50%, 25%, 10%, and 5% were 2.2, 3.6, 8.0, 15.5 scans, respectively. In Wuhan, 35418 (TPR, 58%; 95% CI: 27710–56755) to 44840 (TPR, 38%; 95% CI: 35161–68164) individuals were estimated to have undergone CT examinations to diagnose 17365 patients. During the early surge in New York and Italy, daily NNDs changed up to 5.4 and 10.9 times, respectively, within 10 weeks.
**Conclusion** Low-dose CT protocols were described in less than half of COVID-19 publications, and radiation doses were frequently lacking. The number of populations involved in a first-line

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diagnostic CT test could vary dynamically according to daily TPR; therefore, caution is required in future planning.

**Index terms** Coronavirus; Tomography, X-Ray Computed; Radiation Dosage; Mass Screening; Clinical Protocols

## INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has spread rapidly and swept the world, resulting in at least 165 million confirmed cases and 3.4 million global deaths as of May 21, 2021 (1). For the diagnosis of COVID-19, reverse transcription-polymerase chain reaction (RT-PCR) is the standard test (2, 3). Several guidelines, including those of the World Health Organization, the Center for Disease Control and Prevention, the American College of Radiology, and the Fleischner Society, do not recommend the use of CT examinations as a first-line test for COVID-19 because of potential false-negativity and overlapping CT features with other types of pulmonary diseases (4-7). However, RT-PCR may also yield false-negative results, and there may be limited access or availability of RT-PCR testing in resource-constrained environments, especially during the early stages of an outbreak (8, 9).

CT examinations have been discussed as a first-line test because of their high sensitivity for COVID-19 (8-12). Indeed, CT scans were performed in 88.7% of confirmed COVID-19 patients in the early outbreak in China and were temporarily introduced as the first diagnostic tool in Hubei (10). In addition, a screening strategy with both CT and RT-PCR was also suggested to maximize early diagnosis because early detection, isolation, and quarantine of patients with COVID-19 are required to block its transmission and reduce mortality (12-18). Prior discussions have mainly focused on the diagnostic accuracy of CT, but the impact of CT exposure on large populations has remained under-discussed. One of the major concerns is that the first-line diagnostic use of chest CT scans for COVID-19 would be accompanied by mass population exposure to ionizing radiation. Medical imaging involves a relatively small amount of radiation, but even this minimal degree of radiation may be harmful, especially for pediatric patients given their longer life expectancy and high susceptibility to radiation (19-22). This study aimed to review the chest CT protocols and radiation doses described in COVID-19 publications and to explore the number needed to diagnose (NND) and the number needed to predict (NNP) if CT scans are used as first-line tests.

## MATERIALS AND METHODS

This systematic review article was performed and reported in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This study was conducted with COVID-19 publications, therefore was deemed exempt by the Seoul National University Hospital Institutional Review Board, and informed consent was not necessary.

## SEARCH STRATEGY

We searched COVID-19 publications between January 2020 and January 2021 from the following top seven highly cited radiology journals according to the impact factor of Journal Citation Reports 2020: Radiology; Investigative Radiology; Journal of the American College of Radiology; European Radiology; Korean Journal of Radiology; American Journal of Roentgenology; and European Journal of Radiology. We also added Radiology: Cardiothoracic Imaging and Pediatric Radiology to the literature search. The search was conducted on January 10, 2021, with the following search terms: (CT OR computed tomography) AND (coronavirus OR COVID-19 OR 2019-nCoV OR SARS-COV-2) on the journal websites.

## ELIGIBILITY CRITERIA FOR STUDY SELECTION

We reviewed all the searched publications regardless of the study type. The inclusion criteria were as follows: studies 1) including patients confirmed or suspected of COVID-19, and 2) discussing the CT features of COVID-19 pneumonia. We applied the following exclusion criteria: studies dealing with 1) CT features of COVID-19 other than pneumonia (e.g., pulmonary thromboembolism) or 2) state-of-the-art radiologic techniques (e.g., studies with artificial intelligence, radiomics-based studies).

We included prospective or retrospective cohort studies and case-control studies, but not case reports, case series, letters, editorial comments, abstracts, review articles, guidelines, or consensus statements. As an exception, case reports and series in pediatric patients were included given these patients' susceptibility to radiation. The full-text articles were assessed for eligibility independently by two authors (J.H.L. and S.H.Y. with 8 and 15 years of experience in thoracic radiology, respectively). Any discrepancy was resolved by consensus.

## DATA EXTRACTION

The following items were extracted from the eligible articles using a standardized spreadsheet in Microsoft Excel 2016 (Microsoft Corp., Redmond, WA, USA): study characteristics (publication year, authors, title, abstract, number of patients with CT scans), study population characteristics (age, nationality, whether pediatric patients were included, CT indications, studies with only baseline or both baseline and follow-up CT, and number of CT scans per patient), CT examination information (multichannel CT machine, tube voltage, tube current, reconstructed slice thickness, pitch, and use of contrast media), and radiation dose information (low-dose or standard-dose chest CT, volume CT dose index [CTDIvol], dose-length product [DLP], and effective dose).

## DATA SYNTHESIS AND STATISTICAL ANALYSIS

The study-level CT protocol and radiation dose from individual studies were collected and numerically described, and the doses were compared with each national diagnostic reference level (DRL).

CT scans satisfying at least one of the following criteria were designated as low-dose chest CT: 1) a low-dose protocol was clearly mentioned in the manuscript, 2) a tube voltage $\leq$ 100 kVp was applied, or 3) a tube current lower than 150 mAs with a tube voltage of 120 kVp was used (23, 24). In contrast, chest CT protocols meeting the following criteria were regarded as standard-dose chest CT: 1) a standard dose protocol was clearly mentioned in the manuscript, or 2) the above conditions of the low-dose chest CT were not met.

To explore the magnitude of mass population CT exposure in the COVID-19 pandemic, the NND and NNP were calculated depending on test positive rate (TPR) using the following equation (25):

NND = 1/(sensitivity + specificity - 1)

NNP = 1/(positive predictive value + negative predictive value - 1) = 1/{(sensitivity × TPR)/(sensitivity × TPR + [1 - specificity] × [1 - TPR]) + (specificity × [1 - TPR])/(specificity × [1 - TPR] + [1 - sensitivity] × TPR) - 1}

The TPR was defined as the proportion of confirmed patients among those tested using RT-PCR. We utilized the CT sensitivity of 94% (95% confidence interval [CI]: 91%–96%) and the specificity of 37% (95% CI: 26%–50%) from a meta-analysis (26). The calculated NNPs were plotted according to TPRs of 0%–100%, and we specified NNPs at TPRs of 50%, 25%, 10%, and 5%, respectively.

We applied the equation of NNP to estimate the number of total CT examinations during the early outbreak in Wuhan, Hubei Province, China, where chest CT scans were temporarily used as the first-line diagnostic tool with clinic-epidemiological information according to the fifth edition of the Chinese National Health Commission published on February 4, 2020 (27). The number of confirmed patients based on RT-PCR tests and clinically diagnosed patients based on CT scans was obtained from the published article's supplemental material (28). These materials specified the number of those in the age groups of under 20, 20–39, 40–59, and 60 or older until March 8, 2020. We referred to the RT-PCR positivity rate of 38% in Wuhan from the literature (29). NNP was analyzed in the following two scenarios: test positivity using RT-PCR only, 38%; test positivity using RT-PCR or clinical diagnosis, 58% (38% + 20%; the latter rate was calculated from the supplemental material) (28). Since clinically diagnosed cases were defined as patients with pneumonia showing the typical imaging findings of COVID-19, preferentially CT scans, in the guidelines (27, 30, 31), we assumed that all of these patients had CT scans (28). In addition, we analyzed the change of NNPs according to daily TPRs in the early COVID-19 outbreak in New York State (from March 8 to May 17, 2020) and Italy (from March 2 to May 11, 2020) (32, 33), because of their resource-constrained environments and high community disease burden (7).

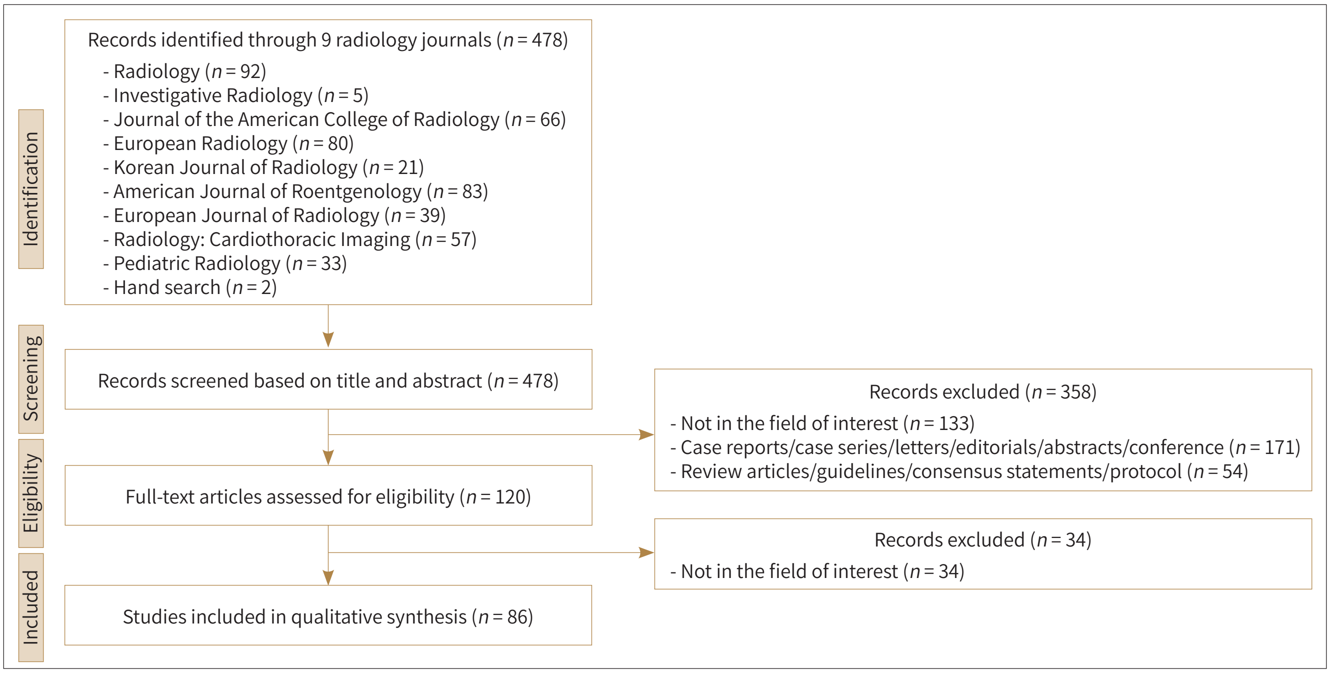
The NNDs and NNPs were calculated and the extent of mass population CT exposure was estimated using R version 4.0.0 (R Foundation for Statistical Computing, Vienna, Austria).

# RESULTS

## LITERATURE SEARCH

From the initial literature search identifying 476 publications, 86 studies were finally included in the qualitative analysis (Fig. 1) (11-16, 34-113).

Fig. 1. Flow diagram of the literature search.




## BASELINE STUDY CHARACTERISTICS

The baseline information of the 86 studies included in this study is presented in Table 1. The median number of patients was 85.5 (range, 4–4824) with an age range of 3 hours to 101 years. In 11 studies (12.8%; 11 of 86), a total of 332 pediatric patients were included (median number, 8; range, 2–201) (13, 41, 47, 64, 68, 85, 90-92, 96, 100). Of the 11 studies, six studies included only pediatric patients (41, 85, 90-92, 96).

The studies were most commonly reported from China (66.3%; 57 of 86), and other countries included Italy (7.0%; 6 of 86), France (4.7%; 4 of 86), Iran (3.5%; 3 of 86), the United States (2.3%; 2 of 86), Germany (2.3%; 2 of 86), Belgium (2.3%; 2 of 86), Republic of Korea (1.2%; 1 of 86), Switzerland (1.2%; 1 of 86), Japan (1.2%; 1 of 86), India (1.2%; 1 of 86). Six studies included two or more countries (7.0%; 6 of 86).

Chest CT scans were performed routinely for COVID-19 patients confirmed with RT-PCR (69.8%; 60 of 86). In 20 studies, CT was performed to screen patients with clinically suspected COVID-19 (23.3%; 20 of 86), and six studies (7.0%; 6 of 86) had specific indications for chest CT imaging (evaluation for comorbidities or complications associated with COVID-19, $n = 5$; chest radiographs that provided negative or uncertain findings, $n = 1$).

The baseline CT results were preferentially analyzed in the included studies (65.1%; 56 of 86), and both baseline and follow-up CT results were included in the remainder (34.9%; 30 of 86). Regarding the number of CT scans, 14858 patients, 267 patients, and 447 patients had one, two, and three or more CT examinations, respectively.

## REPORTED CT PROTOCOLS AND RADIATION DOSES

Eighty-one studies described the specific CT protocols used in their studies (94.2%; 81 of 86) (Table 1). For these 81 studies, a multichannel ≥ 16-channel CT machine (91.4%; 74 of 81),

Table 1. Baseline Information, Reported CT Protocols, and Radiation Doses of the 86 Studies on COVID-19

| | *n* (%) |
|---|---|
| Median number of patients (range) | 85.5 (4–4824) |
| Age (range) | 3 hours–101 years |
| Pediatric patients | |
| Inclusion | 11 (12.8) |
| Not inclusion | 39 (45.3) |
| Unknown | 36 (41.9) |
| CT indications | |
| Routine examination in patients confirmed with COVID-19 | 60 (69.8) |
| For screening in patients with clinical suspicion for COVID-19 | 20 (23.3)* |
| Specific reasons in patients confirmed with COVID-19† | 6 (7.0)* |
| Unknown | 1 (1.2) |
| Inclusion of only baseline CT results | 56 (65.1) |
| Inclusion of baseline and follow-up CT results | 30 (34.9) |
| Number of CT examinations per a patient | |
| Single | 14858 in 55 studies |
| Two | 261 in 10 studies |
| Three or more | 447 in 7 studies |
| Unknown | 17 studies |
| Number of studies reporting CT protocol | 81 (94.2) |
| Type of CT examinations | |
| Low-dose chest CT | 34 (39.5)‡ |
| Standard-dose chest CT | 16 (18.6)‡ |
| Unknown | 38 (44.2) |
| Multichannel CT machine | |
| ≥ 16-channel | 74 (91.4) |
| < 16-channel | 1 (1.2) |
| ≥ 16-channel or < 16-channel | 1 (1.2) |
| Unknown | 5 (6.2) |
| Tube voltage (range, 80–140 kVp) | |
| 120 kVp or higher | 53 (65.4) |
| Inclusion of 100 kVp or lower | 16 (19.8) |
| Unknown | 12 (14.8) |
| Number of studies reporting tube current | |
| Automatic exposure control | 35 (43.2) |
| mAs or mA | 30 (37.0) |
| Unknown | 16 (19.8) |
| Slice thickness, mm (range, 0.5–8) | |
| ≤ 3 | 67 (82.7) |
| > 3 | 3 (3.7) |
| ≤ 3 or > 3 | 7 (8.7) |
| Unknown | 4 (4.9) |
| Pitch (range, 0.75–1.8) | |
| ≤ 1 | 7 (8.6) |

Table 1. Baseline Information, Reported CT Protocols, and Radiation Doses of the 86 Studies on COVID-19 (Continued)

| | *n* (%) |
|---|---|
| > 1 | 12 (14.8) |
| ≤ 1 or > 1 | 10 (12.4) |
| Unknown | 52 (64.2) |
| Use of contrast media | |
| Non-contrast enhancement | 47 (58) |
| Contrast enhancement | 1 (1.2) |
| Contrast or non-contrast enhancement | 7 (8.7) |
| Unknown | 26 (32.1) |

*In one study, the indication for initial chest CT was a high clinical suspicion for COVID-19 in the setting of a high pretest probability or comorbidities associated with severe illness from COVID-19.
†Evaluation for comorbidities or complications associated with COVID-19 (*n* = 5), chest radiographs provided negative or uncertain findings (*n* = 1).
‡Both low-dose and standard-dose CT scans were used in two studies.
COVID-19 = coronavirus disease 2019

Table 2. Reported Radiation Doses in 17 Studies on COVID-19

| Study | Country | CTDIvol (mGy) | DLP (mGy*cm) | Effective Dose (mSv) |
|---|---|---|---|---|
| Schalekamp et al. (15) | Germany | - | Range of mean value, 40–140 [350] | - |
| Herpe et al. (97) | France | - | Mean, 160 ± 40 (range, 80–400) [475] | - |
| De Smet et al. (94) | Belgium | - | Median, 520 (range, 310–906) [400] | 7.6 [5.6] |
| Pan et al. (98) | China | Mean, 8.4 ± 2.0 (range, 5.2–12.6) [15] | - | - |
| Liu et al. (70) | China | 6.2 [15] | 208.45 [470] | 2.9 [6.58] |
| Wu et al. (75) | China | - | 454.7 [470] | - |
| Liu et al. (40) | China | Mean, 4.1 ± 0.9 (range, 2.3–5.8) [15] | - | - |
| Booz et al. (46) | Europe + the United States | Mean, 5.3 ± 1.4 (range, 2.5–7.9) [17] | Mean, 182.4 ± 34.2 (range, 76.6–286.1) [610] | - |
| Hu et al. (52) | China | Mean, 2.37 ± 1.11 [15] | Mean, 93.9 ± 45.6 [470] | Mean, 2.0 ± 0.7 [6.58] |
| Tabatabaei et al. (58) | Iran | Mean, 5.1 (range, 3.8–7.8) [12] | - | - |
| Falaschi et al. (50) | Italy | Mean, 8.9 ± 1.6 (< 90 Kg)<br>Mean, 15.1 ± 2.4 (> 90 Kg) [15] | Mean, 334.2 ± 33.8 (< 90 Kg)<br>Mean, 557.6 ± 62.6 (> 90 Kg) [570] | - |
| Dangis et al. (102) | Belgium | Mean, 1.27 ± 0.59 | Mean, 39.9 ± 17.8 [400] | Mean, 0.6 ± 0.3 [5.6] |
| Tabatabaei et al. (109) | Iran | Mean, 4.9 (range, 3.9–7.8) [12] | - | - |
| Chen et al. (100) | China | - | - | Range, 2.8–3.5 (adult)<br>Range, 0.8–1.2 (child) [6.58] |
| Moradi et al. (106) | Iran | Range, 2.3–8.4 [12] | - | - |
| Inui et al. (105) | Japan | - | - | < 2.8 [7.14] |
| Wen et al. (110) | China | Mean, 9.3 ± 4.1 [15] | Mean, 314.0 ± 152.8 [470] | - |

Numbers in square brackets: national diagnostic reference levels in each study.
COVID-19 = coronavirus disease 2019, CTDIvol = volume CT dose index, DLP = dose-length product

tube voltage of 120 kVp or higher (65.4%; 53 of 81), automatic tube current modulation (43.2%; 35 of 81), and pitch > 1 (14.8%; 12 of 81) were preferentially used. Images were frequently reconstructed and reviewed with a slice-thickness of 3 mm or thinner (82.7%; 67 of 81). In the majority of studies, CT examinations were performed without intravenous contrast media (58%; 47 of 81). Although eight studies reported CT examinations with intravenous contrast media (9.9%; 8 of 81), information on how many CT phases were obtained could not be identified.

Of 86 studies, low-dose and standard-dose chest CT examinations were performed in 34 studies (39.5%; 34 of 86) and 16 studies (18.6%; 16 of 86), respectively. Both low-dose and standard-dose CT scans were used in two studies. However, the type of CT examinations could not be determined in 38 studies (44.2%; 38 of 86).

Only 17 studies (19.8%; 17 of 86) reported radiation doses in terms of CTDIvol ($n$ = 11), DLP ($n$ = 10), or effective dose ($n$ = 6) (15, 40, 46, 50, 52, 58, 70, 75, 94, 97, 98, 100, 102, 105, 106, 109, 110). None of the studies contained size-specific dose estimates. The corresponding information is tabulated in Table 2. In 15 of these 17 studies, the mean radiation dose was lower than the national DRL (88.2%; 15 of 17). One study reported a similar radiation dose to the national DRL (5.9%; 1 of 17) (50), and the remaining study reported a radiation dose larger than their DRL (5.9%; 1 of 17) (94). Of the 11 studies handling pediatric patients, the radiation dose was reported in only one study, with an effective dose of 0.8 to 1.2 mSv (100).

## NND, NNP, AND THE ESTIMATED AMOUNT OF CT EXPOSURE

Plots of NND and NNP depending on TPR is shown in Fig. 2. Since the sensitivity and spec-

Fig. 2. Plots demonstrate (A) the NND according to the CT sensitivity and specificity, and (B) the NNP according to the CT sensitivity, specificity, and test positive rate of RT-PCR. Dotted lines represent 95% confidence intervals.
COVID-19 = coronavirus disease 2019, NND = number needed to diagnose, NNP = number needed to predict, RT-PCR = reverse transcription-polymerase chain reaction

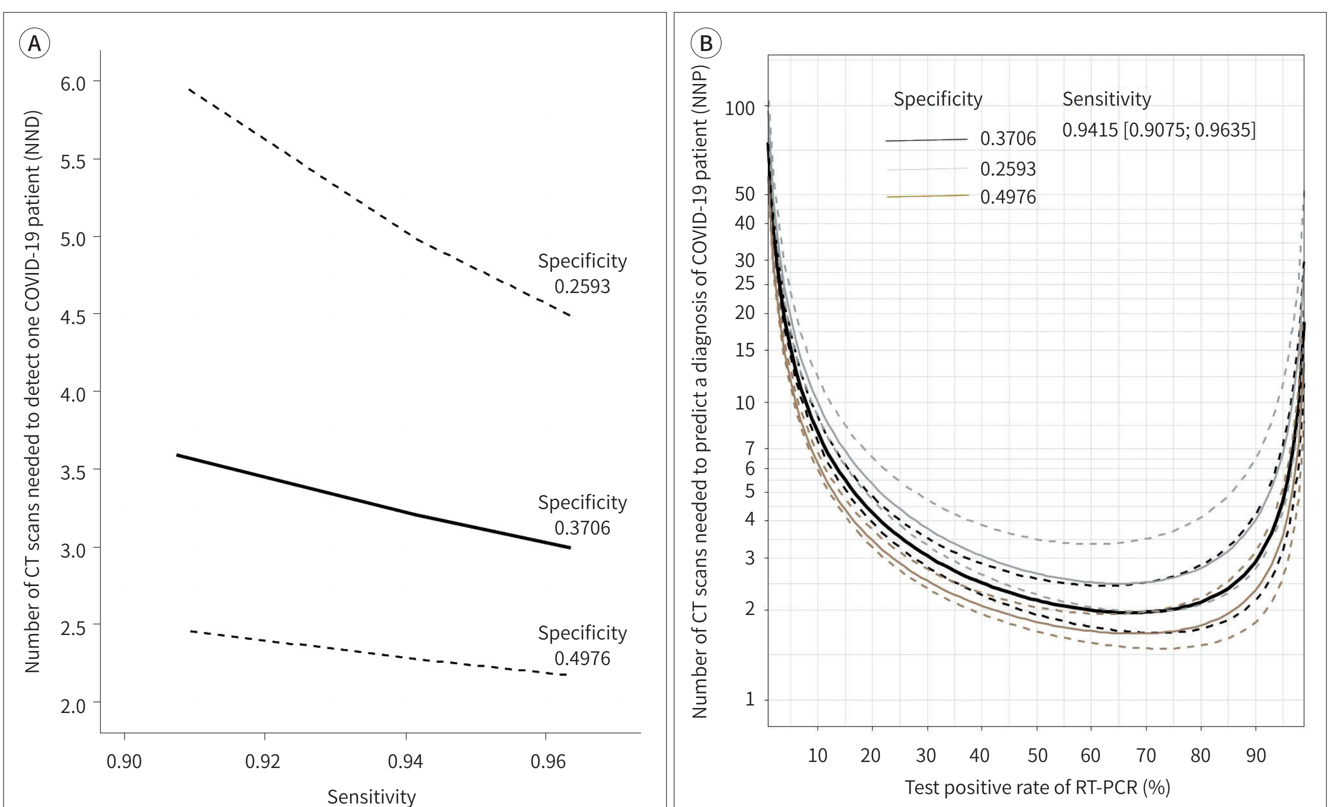


Table 3. Number of CT Scans Needed to Clinically Diagnose COVID-19 according to the Age Distribution in Wuhan, China

| Age (Years) | Number of Clinically-Diagnosed COVID-19 Patients | Test Positive Rate of 58%* | Test Positive Rate of 38%* |
|---|---|---|---|
| Total | 17365 | 35418 (27710–56755) | 44840 (35161–68164) |
| 0–19 | 344 | 702 (549–1124) | 888 (697–1350) |
| 20–39 | 3700 | 7547 (5904–12093) | 9554 (7492–14524) |
| 40–59 | 6919 | 14112 (11041–22614) | 17866 (14010–27160) |
| ≥ 60 | 6402 | 13058 (10216–20924) | 16531 (12963–25130) |

95% CIs are in bracket. CT sensitivity of 0.94 (95% CI: 0.91–0.96) and a CT specificity of 0.37 (95% CI: 0.26–0.50) for COVID-19 are applied.
*Test positive rates of 58% and 38% were assumed based on the positive rate of reverse transcription-polymerase chain reaction or clinical diagnosis and reverse transcription-polymerase chain reaction, respectively.
CI = confidence interval, COVID-19 = coronavirus disease 2019

Table 4. Estimates of the NNP for COVID-19 according to the Daily TPR of COVID-19 in New York State and Italy

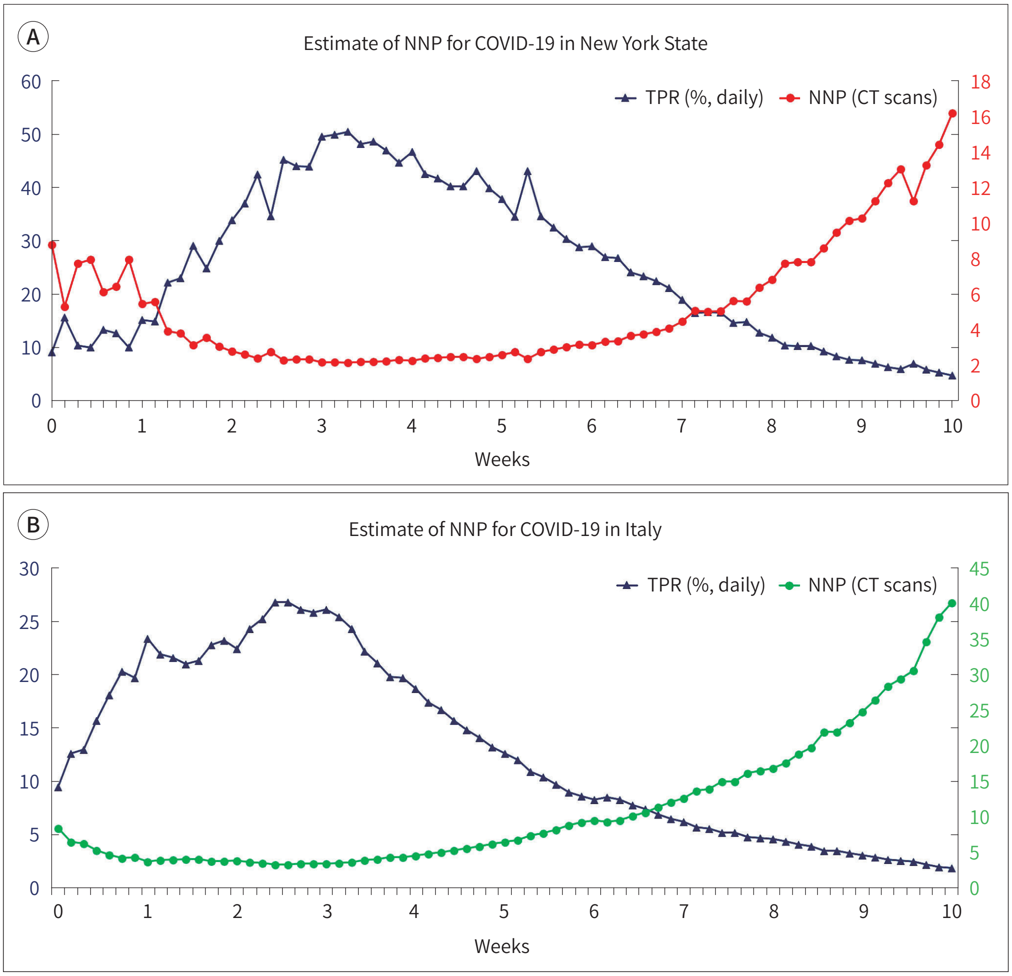
| Weeks | New York State | | Italy | |
|---|---|---|---|---|
| | TPR (%)* | NNP | TPR (%)* | NNP |
| 0 | 9.1 | 8.8 (6.5–13.1) | 9.5 | 8.4 (6.3–12.6) |
| 1 | 10.1 | 8.0 (5.9–11.9) | 19.7 | 4.4 (3.3–6.5) |
| 2 | 30.0 | 3.1 (2.4–4.6) | 23.2 | 3.8 (2.9–5.7) |
| 3 | 43.9 | 2.3 (1.8–3.6) | 25.8 | 3.5 (2.7–5.2) |
| 4 | 44.6 | 2.3 (1.8–3.6) | 19.7 | 4.4 (3.3–6.5) |
| 5 | 39.9 | 2.5 (2.0–3.8) | 13.2 | 6.2 (4.7–9.3) |
| 6 | 28.8 | 3.2 (2.5–4.8) | 8.6 | 9.3 (6.9–13.9) |
| 7 | 21.2 | 4.1 (3.1–6.1) | 6.5 | 12.1 (8.9–18.1) |
| 8 | 12.8 | 6.4 (4.8–9.6) | 4.7 | 16.5 (12.1–24.8) |
| 9 | 7.8 | 10.1 (7.5–15.2) | 3.3 | 23.3 (17.0–35.0) |
| 10 | 5.4 | 14.4 (10.6–21.6) | 2.0 | 38.1 (27.7–57.2) |

95% CIs are in bracket. CT sensitivity of 0.94 (95% CI: 0.91–0.96) and a CT specificity of 0.37 (95% CI: 0.26–0.50) for COVID-19 are applied.
*TPRs were based on the positive rate of reverse transcription-polymerase chain reaction.
CI = confidence interval, COVID-19 = coronavirus disease 2019, NNP = number needed to predict, TPR = test positive rate

ificity of CT examinations for COVID-19 are fixed as 94% and 37%, respectively, the NND was 3.2 scans as a fixed value. When 95% CIs of CT sensitivity and specificity for COVID-19 were taken into account, the NND was demonstrated to change from 2.2 to 6.0. On the other hand, the NNPs at TPRs of 50%, 25%, 10%, and 5% were 2.2 (95% CI: 1.7–3.4), 3.6 (95% CI: 1.7–5.3), 8.0 (95% CI: 6.0–12.0), 15.5 (95% CI: 11.4–23.3) scans, respectively.

In the early outbreak in Wuhan, 35418 (TPR, 58%; 95% CI: 27710–56755) to 44840 (TPR, 38%; 95% CI: 35161–68164) individuals were estimated to have undergone CT examinations to clinically diagnose 17365 patients. By age distribution, 702 (95% CI: 549–1124) to 888 (95% CI: 697–1350) individuals under 20 years of age, 7547 (95% CI: 5904–12093) to 9554 (95% CI: 7492–14524) individuals in their 20–30s, 14112 (95% CI: 11041–22614) to 17866 (95% CI: 14010–27160) individuals in their 40–50s, and 13058 (95% CI: 10216–20924) to 16531 (95% CI: 12963–25130)

Fig. 3. NNP according to the daily TPR of COVID-19 in (A) New York State from March 8 to May 17, 2020, and (B) Italy from March 2 to May 11, 2020. The left and right Y-axes represent daily TPR and NNP, respectively. The dark-blue line with triangular symbols represents changes in the daily TPR, and the solid line with circular symbols represents changes in the NNP. The daily TPR of COVID-19 in New York State and Italy were accessed from the webpage of "New York Forward" (32) and "Our World in Data" (33).
COVID-19 = coronavirus disease 2019, NNP = number needed to predict, TPR = test positive rate




individuals in their 60s or older were estimated to have CT scans at TPRs of 58% and 38%, respectively (Table 3).

NNP changes according to daily TPR in New York State and Italy are shown in Fig. 3, and weekly NNPs are specified in Table 4. TPRs in New York State and Italy peaked to be 44.6% and 25.8% after 4 and 3 weeks since the initial surge, with corresponding NNPs of 2.3 and 3.5 scans, respectively. The lowest TPR in those areas were 5.4% and 2%, resulting in NNPs of 14.4 and 38.1, respectively. Therefore, daily NNPs changed up to 5.4 and 10.9 times within 10 weeks, respectively.

## DISCUSSION

To date, relevant guidelines have rarely contained information about the specific protocols and radiation dose of chest CT for COVID-19, although low-dose nonenhanced CT is preferably recommended (114). Indeed, a recent study reported that chest CT indications, protocols, and radiation doses for COVID-19 widely varied across different countries and healthcare sites by surveying a limited number of cases (9, 115). Concordant with this, our study also revealed similar results for COVID-19 publications. Considering the stochastic effect of ionizing radiation (19, 20, 22, 116) and the as low as reasonably achievable (ALARA) principle (117), CT examinations should be used judiciously with surveillance of protocols and radiation doses, as well as compliance with the DRL (19, 116, 118).

In this study, most COVID-19 publications in radiology journals included CT protocols, but low-dose nonenhanced CT protocols were identified in fewer than half of articles, whereas over 90% of studies used 16-channel or higher CT machines capable of performing low-dose lung cancer CT screening (119). Information on the radiation dose was frequently lacking, although the CT doses were mostly lower than corresponding DRLs when reported. A low-dose nonenhanced chest CT protocol is mostly sufficient to assess community-acquired pneumonia (120, 121), although a standard-dose CT scan with contrast medium can evaluate pulmonary embolism or necrosis within a parenchymal lesion. If chest CT is considered as the first-line diagnostic tool in the future pandemic, low-dose CT scanning and managing the radiation dose must be further addressed in relevant radiology research.

We estimated the number of people undergoing CT examinations in Wuhan, but deliberately avoided estimating the effective dose or the impact on cancer risk. The estimated number of CT examinations during 2 months (Jan-Mar 8th, 2020) approaches the number of enrolled patients in the National Lung Screening Trial over 2 years (122). This number itself can be an alarming message regarding the first-line diagnostic usage of CT scans, underscoring the need for details about managing and monitoring CT radiation exposure under the ALARA principle (117). Estimating the effective dose and cancer risk in large populations involves several assumptions, is prone to deviations in the analysis, and is affected by substantial variability in doses across sites and countries. Nevertheless, a linear-no-threshold model between radiation dose and malignancy seems applicable to the population under 20 years of age (21, 22, 116). Even in adults in their 20s or older, concerns exist about the association of thyroid, breast cancer, or hematologic malignancies with medical CT exposures (19, 123). Another point to consider is the usage of follow-up CT scans during the course of COVID-19 (42, 52, 64, 69, 80, 84, 98, 99). Indeed, 35% of studies in our study performed both baseline and follow-up CT, further increasing the radiation dose. This mass radiation dose issue should be addressed when CT is considered as a first-line diagnostic tool in the future pandemic.

The difference in NNP depending upon TPR also has implications for the use of CT scans in the future pandemic. The timely diagnosis of respiratory infections will be problematic in the earliest stages of any future pandemic as a molecular diagnostic tool requires nucleic acid sequencing of a new pathogen and may be affected by shortage or quality issues, as in Wuhan (13, 124). In the early COVID-19 outbreak in New York State and Italy, TPR rapidly rose in the earliest stage of the pandemic, as shown by the lower NNPs (Fig. 3). This is followed by a peak and then decreased TPR, accompanied by an increase in the NNP (32, 33). Thus, the early period of an outbreak is the best time window for the first-line diagnostic usage of CT scans if chest CT scans render a specific finding for a new pathogen. Subsequently, such usage of CT scans should be stopped considering the rapid increase in the NNP when TPR decreases and molecular diagnostics are widely available. Besides, efforts for increasing pretest probability before CT scanning should be considered together by triaging suspects of new infection to increase TPR (125).

This study has several limitations. First, we searched relevant publications from specific radiology journals, not using databases such as the Embase and OVID-MEDLINE, giving rise to potential selection bias. Nevertheless, these journals are regarded as having high-quality academic reporting, and the searched publications may represent high-quality studies in radiology. Second, although the purpose of this study was to investigate CT protocols and radiation doses in COVID-19 publications, data extraction was performed solely based on descriptions in individual studies, without contacting the authors to obtain any missing or unreported data. Third, although TPR is not an equal term with disease prevalence in the strict sense, we used TPR as a proxy measure of disease prevalence. Fourth, the diagnostic accuracy of CT scans for COVID-19 for the assumption was obtained from a meta-analysis at the early pandemic (26). The accuracy of CT scans, particularly for specificity, can be improved as radiologists get experienced in interpreting infectious diseases (97). Nevertheless, considering that a molecular diagnostic tool for emerging infectious diseases is usually limited and the diagnostic use of CT can be pursued in the early pandemic as COVID-19, CT accuracy from the early pandemic result would be appropriate in the analysis. Finally, TPR, CT sensitivity and specificity for COVID-19, and the numbers of COVID-19 patients for estimating the number of CT examinations in Wuhan were derived from different studies. In addition, some of the clinically diagnosed patients in Wuhan may have been diagnosed with COVID-19 based on chest radiographs, although the imaging findings of COVID-19 are nonspecific on radiographs.

In conclusion, low-dose CT protocols for COVID-19 could be identified in fewer than half of the publications, and information on the radiation dose was frequently lacking. The first-line diagnostic use of CT scans for COVID-19 would involve a substantial amount of CT exposure for large populations, particularly at a low test positive rate. The first-line diagnostic use of chest CT in the future of the COVID-19 pandemic—and, conceivably, for future pandemics—must be discussed based on not only the diagnostic accuracy of chest CT but also ALARA principle and NNP.

## Author Contributions

Conceptualization, L.J.H., Y.S.H.; data curation, L.J.H., Y.S.H.; formal analysis, L.J.H., H.H., Y.S.H.; investigation, L.J.H., H.H., Y.S.H.; methodology, L.J.H., Y.S.H.; project administration, L.J.H., Y.S.H.; resources, L.J.H., Y.S.H.; software, L.J.H., H.H.; supervision, Y.S.H.; validation, L.J.H., H.H., Y.S.H.; visualization, L.J.H., H.H.; writing—original draft, L.J.H., Y.S.H.; and writing—review & editing, all authors.

## Conflicts of Interest

Dr. Soon Ho Yoon works in MEDICALIP Co. Ltd. as a chief medical officer outside this work. Dr. Hyungjin Kim received a research grant from Lunit Co. and holds stock in MEDICALIP Co. outside this work. Dr. Jin Mo Goo received grants from Infinitt Healthcare, Dongkook Lifescience, and LG Eletronics, outside this study. Other authors have no conflicts of interest to declare for this article.

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# COVID-19 진단을 위한 CT 검사: 프로토콜, 방사선량에 대한 체계적 문헌고찰 및 진단을 위한 CT 검사량

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**목적** Coronavirus disease 2019 (이하 COVID-19) 폐렴에서 CT를 일차 진단 검사로 사용하고자 하는 논의가 있지만, 대규모 인구에게 CT 검사를 적용했을 때의 상황을 고찰한 연구는 없었다. 본 연구에서는 COVID-19 폐렴을 다룬 연구들에서 CT 프로토콜과 방사선량을 분석하고, CT 검사가 일차 진단 검사법으로 사용될 때 필요한 CT 검사량에 대해 알아보고자 한다.

**대상과 방법** 본 연구는 9개의 인용도가 높은 영상의학과 저널에서 COVID-19 폐렴의 CT 기반 진단을 다룬 문헌들을 검색하였다. 먼저, 연구에서 제시된 CT 프로토콜, 방사선량을 조사하여, 이를 해당 국가의 diagnostic reference level과 비교하였다. 추가로, COVID-19에 대한 CT 민감도 94%, 특이도 37%를 적용하여, 우한시와 뉴욕, 이탈리아의 초기 COVID-19 outbreak에서 polymerase chain reaction (이하 PCR) 검사 양성률에 기반한 number needed to diagnose (이하 NND)와 number needed to predict (이하 NNP)를 계산하였다.

**결과** 총 86개의 연구가 검색되었고, 그중 CT 프로토콜은 81개의 연구에서(94.2%), 방사선량은 17개의 연구에서(19.8%) 보고되었다. 저선량 흉부 CT는 표준선량 흉부 CT보다 2배 많은 연구에서 활용되었다(39.5% vs. 18.6%). 방사선량을 보고한 17개의 연구들 중, 15개의 연구에서 방사선량은 해당 국가의 diagnostic reference level 수치보다 낮았다(88.2%). COVID-19에 대한 CT 민감도 94%, 특이도 37%를 적용하였을 때, NND는 3.2회 CT scans으로 나타났다. 한편, PCR 검사 양성률 50%, 25%, 10%, 5%에서의 한 명의 COVID-19 환자를 진단 위한 CT 검사량을 나타내는 NNP는 각각 2.2, 3.6, 8.0, 15.5회의 CT scans로 나타났다. 우한시에서는 최종 17365명의 COVID-19 환자를 진단하기 위하여 약 35418명에서(PCR 검사 양성률 58%) 44840명(PCR 검사 양성률 38%)의 사람들이 CT 검사를 받은 것으로 나타났다. 뉴욕시와 이탈리아의 초기 COVID-19 유행 10주간, PCR 검사 양성률에 따라 일 CT 검사량이 최대 5.4, 10.9배까지 변화하였다.

**결론** CT를 COVID-19에 대한 일차적인 진단검사로 사용할 경우, PCR 검사 양성률에 따라 CT 검사량은 변동량이 크고, 이는 추후 판데믹 상황에서 고려되어야 할 것이다.

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