A low-dose chest CT protocol for the diagnosis of COVID-19 pneumonia: a prospective study

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Abstract

Purpose The increasing trend of chest CT utilization during the COVID-19 pandemic necessitates novel protocols with reduced dose and maintained diagnostic accuracy. We aimed to investigate the diagnostic accuracy of 30-mAs chest CT protocol in comparison with a 150-mAs standard-dose routine protocol for imaging of COVID-19 pneumonia.

Methods Upon IRB approval, consecutive laboratory-confirmed positive COVID-19 patients aged 50 years or older who were referred for chest CT scan and had same-day normal CXR were invited to participate in this prospective study. First, a standard-dose chest CT scan (150 mAs) was performed. Only if typical COVID-19 pneumonia features were identified, then a low-dose CT (30 mAs) was done immediately. Diagnostic accuracy of low-dose and standard-dose CT in the detection of typical COVID-19 pneumonia features were compared.

Results Twenty patients with a mean age of 64.20 ± 13.8 were enrolled in the study. There was excellent intrareader agreement in detecting typical findings of COVID-19 pneumonia between low-dose and standard-dose (intraclass correlation coefficient [ICC] = 0.98–0.99, P values < 0.001 all readers). The mean effective dose values in standard- and low-dose groups were 6.60 ± 1.47 and 1.80 ± 0.42 mSv, respectively. Also, absolute cancer risk per mean cumulative effective dose values obtained from the standard- and low-dose CT examinations were 2.71 × 10⁻⁴ and 0.74 × 10⁻⁴, respectively.

Conclusions According to our study, it was found that proposed low-dose CT chest protocol is reliable in detecting COVID-19 pneumonia in daily practice with significant reduction in radiation dose and estimated cancer risk.

Keywords COVID-19 pneumonia · Computed tomography · Diagnosis · Low-dose · Cancer risk

Introduction

The outbreak of Coronavirus Disease 19 (COVID-19) was first reported in Wuhan, China, in December 2019. Shortly after, the disease was extended as a pandemic affecting 203 countries and territories with the number of confirmed cases surpassing 17 million globally as of July 31, 2020 [1]. The current rapid spread and surge in deaths during the COVID-19 pandemic can be altered by early detection, timely intervention, and public health measurements [2].

Although real-time reverse transcriptase polymerase chain reaction (RT-PCR) remains the standard diagnostic reference of COVID-19, many limitations such as high false-negative rate, limited availability, and delay in confirmation may exist [3]. More specifically, the World Health Organization and Centers for Disease Control recommends viral testing (including PCR) as the method for the identification and laboratory confirmation of COVID-19 cases. Despite high analytical
sensitivity and near-perfect specificity, test sensitivity in clinical practice may be adversely affected by some variables, including adequacy of specimen, specimen type, specimen handling, and stage of infection in which the specimen is acquired [4, 5]. False-negative RT-PCR tests have been reported in patients with CT findings of COVID-19 who eventually tested positive with serial sampling [6]. On the other hand, CT abnormalities might predate RT-PCR positivity in symptomatic patients and in those without symptoms who subsequently test positive by RT-PCR [7].

Chest X-ray (CXR) is not a sensitive tool to detect viral pneumonia [8]. However, it has been shown that chest computed tomography (CT) scan plays a key role in the detection of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia [9–11]. More recent studies have suggested that CT scan can not only demonstrate the course of the disease and the severity of involvement but also is able to predict the prognosis [12–14]. Although current guidelines do not recommend CT as a screening tool [15], the widespread availability, high sensitivity, and short test-to-result time interval suggest that many cases with suspicious clinical or equivocal laboratory data will benefit from chest CT scan for the diagnosis of COVID-19 pneumonia, particularly where RT-PCR kits are limited or not easily accessible. Patients at higher risk for complication, those with comorbidities, not responding to supportive treatment, and presenting with acute clinical deterioration are among the groups that benefit imaging the most [16].

The increasing trend of chest CT scan utilization during the COVID-19 pandemic raises the concern about the radiation burden of the population [17], both in patients and health care workers. It is widely accepted that ionizing radiation increases the lifetime likelihood of developing cancer [18]. Most recently, Sakane et al., based on a study on 209 patients, concluded that standard-dose chest CT results in chromosome aberrations and DNA double-strand break, while no detrimental effect on human DNA by low-dose chest CT was detected [19]. Accordingly, the principle of ALARA (as low as reasonably achievable) suggested by the International Commission of Radiological Protection (ICRP) should be followed in the daily practice of radiology, even in the setting of pandemic events [20].

Multiple prior studies have suggested that obtaining a low-dose chest CT scan by applying a reduced tube current results in reliable sensitivity compared with the standard-dose CT protocols in detecting intrathoracic pathologies, such as pulmonary nodules, lung masses, or parenchymal abnormalities. For example, Zhu et al. concluded that low-dose (40 or 25 mAs) helical chest CT protocol produced diagnostic image quality, thus optimally protecting patients from radiation exposure [21]. Kubo et al. reported that application of 50 mAs as tube current for the routine chest CT has comparable diagnostic performance as standard-dose of 150 mAs [22]. A recent study by Tofighi et al. has discussed the application of low-dose CT in COVID-19 pneumonia and stated that low-dose and ultralow-dose CT have a comparable efficacy in the detection of ground glass and consolidative opacities. They have suggested comparison of low-dose and conventional protocol in early stages of the disease, because in intermediate and advanced stages, the low-dose CT protocol will provide adequate image quality and diagnostic accuracy [23]. More recently published studies on applying low radiation dose chest CT scan in COVID-19 pneumonia have suggested acceptable diagnostic accuracy [17, 24], although they are all non-comparison studies. A statistically more advanced study designed based on an internal control and head-to-head comparison of pulmonary findings in COVID-19 in low- and conventional-dose CT has not been performed yet.

In this prospective study, we aimed to study the diagnostic accuracy of a 30-mAs chest CT compared with standard-dose (150 mAs) as the routine protocol for imaging of COVID-19 in patients with initial normal CXR. It has been hypothesized that a low-dose chest CT protocol would yield into a comparable diagnostic accuracy compared with standard protocol in the detection of COVID-19 pneumonia.

Methods

Patient selection

The study was performed between March 15 and 31, 2020, at the department of radiology in our institution. A total of 63 consecutive patients aged 50 years or older who were referred for a non-contrast chest CT scan and had same-day normal chest radiographs were invited to participate in this prospective study. Patients younger than 50 years old were excluded, as cancer risk related to ionizing radiation exposure is higher in younger population [22]. All patients were symptomatic with positive RT-PCR for SARS-CoV-2 infection at their first referral for the evaluation of extent and severity of COVID-19 pneumonia. The institutional review board approved the research protocol, and written informed consent was obtained from all participants.

For all patients, standard-dose chest CT scan was performed as the first step. Only if typical COVID-19 pneumonia features on the standard-protocol CT [25] were identified by the radiologist present in the workstation, the low-dose CT was done immediately after that, without moving the patient on the CT table. Ultimately, 20 patients were enrolled in the study. The research ethics board approved our research protocol (approval ID: IR.KAUMS.REC.1398.053), and written informed consent was obtained from all the patients who agreed to enroll in this study.
CT protocols

CT chest was acquired using a 16-detector CT scanner (Alexion TSX-034A, Toshiba, Japan). All patients were examined in supine position. After obtaining a routine scout view, two successive helical CT scans from the base of the neck to the liver dome with a fixed tube voltage of 120 kVp and tube currents of 150 mA as (standard protocol) and then 30 mA (low-dose protocol) were performed. From the raw data of each acquisition, contiguous 3-mm-thickness slices were reconstructed based on lung construction algorithm. The pitch factor was 1 for both protocols. No patient received intravenous contrast material. Results of the CT examination were immediately interpreted and reported to the referring clinician, who integrated the results into the clinical case management decision.

Image analysis

There were 40 series (20 standard-dose and 20 low-dose) of chest CT scans, coded randomly and anonymized by a radiologist who was not involved in reading the examinations. The images were read independently by three radiologists: reader A (H.R with 5-year experience), reader B (SMH. T with 7-year experience), and reader C (HR. T with 15-year experience). The patients’ name, date of performing CT scan, and image acquisition data (including radiation dose) were masked to blind the readers. The readers were also blinded to the CXRs and RT-PCR results.

In order to assess the clarity and visibility of typical CT findings of COVID-19 pneumonia on CT scan, the presence or absence of them was recorded using a 3-point CT finding scale (0, definitely absent; 1, equivocal; 2, definitely present). All CT images were viewed with both lung window (width, 1600 HU; level, −550 HU) and mediastinal window (width, 400 HU; level, 40 HU) settings.

Any of the followings were considered a typical finding for COVID-19 pneumonia based on the Radiological Society of North America Expert Consensus Statement [25]: peripheral ground glass opacity (GGO) with or without consolidation or visible intralobular lines (crazy paving), multifocal GGO of rounded morphology with or without consolidation or visible intralobular lines (crazy paving), and reverse halo sign or other findings of organizing pneumonia. The readers also assessed the images on mediastinal window settings for evaluation of mediastinal/hilar lymphadenopathy or pleural/pericardial effusion.

Statistical analysis

To evaluate the inter-reader agreement among the three radiologists for each lobe, kappa (κ) test was used. Intraclass coefficient correlation (ICC) was used to assess the inter-reader agreement by comparing the total score in both low-dose and standard-dose. To evaluate the intrareader agreement between the low-dose and standard-dose, κ values were obtained for each lobe and each radiologist. ICC was then used to assess the intrareader agreement in evaluation of total lung score between the low-dose and standard-dose.

All κ and ICC values were interpreted as proposed in the literature [26, 27]. A κ value lower than 0.20 indicated poor agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, good agreement; and 0.81–1.00, excellent agreement. An ICC below 0.50 indicated poor agreement, between 0.50 and 0.75 moderate, between 0.75 and 0.90 good, and above 0.90 excellent. The results were considered statistically significant when P value < 0.05.

Effective radiation dose and cancer risk estimation

The effective dose values (mSv) of chest CT scan examinations were calculated by multiplying dose-length product (DLP) with conversion coefficients (0.016 mSv/mGy·cm) presented by Huda et al. [28], with DLP values extracted from the patients’ information.

In the present study, the cancer absolute risks following standard-dose and low-dose CT scan examinations were estimated in accordance with the risk model presented in ICRP Publication 103 [29]. Absolute risk is defined as the probability that a person of disease-free at a specific age will develop the cancer disease later following radiation exposure to a risk factor. To calculate the cancer risk, mean effective dose values obtained from standard-dose and low-dose CT scan examinations were multiplied by the risk coefficient (0.041 Sv⁻¹).

Results

A total of 20 patients were enrolled in the study, consisting of 7 females and 13 males, aged between 50 and 99 years (mean age of 64 ± 13.8). The mean body mass index was 26.5 ± 3.5 kg/m².
Imaging findings

The mean total lung scores calculated for readers A, B, and C in low-dose CT protocol were $5.60 \pm 3.2$, $6.40 \pm 3.0$, and $6.20 \pm 2.6$, respectively. The total scores for readers A, B, and C in standard-dose CT protocol were $5.80 \pm 3.2$, $6.45 \pm 3.0$, and $6.20 \pm 2.7$, respectively. No chest CT was reported as normal without lung parenchymal abnormalities by the three readers.

Inter-reader agreement was assessed for both low-dose and standard-dose in each lobe using $\kappa$ value (Table 1). Inter-reader agreements in evaluation of total involvement score were assessed for both low-dose and standard-dose measurements (Table 1). There is excellent inter-reader agreement based on ICC values in both low-dose and standard-dose measurements, 0.84 and 0.81, respectively.

Intrareader agreements were assessed between low-dose and standard-dose using $\kappa$, and $P$ values were calculated for each lobe (Table 2). The highest agreements between low-dose and standard-dose were seen in RUL, RML, and LUL with all $\kappa$ values ranging from 0.91 to 1.00 among all readers ($P$ value < 0.001 all) (Fig. 1a,b). The lowest agreement was seen in RLL with $\kappa$ ranging from 0.67 to 0.86 ($P$ value < 0.001 all) (Figs. 2a,b and 3a,b).

ICC was used to assess intrareader agreement between the low-dose and standard-dose in calculation of the total score of lung involvement (Table 2). All readers have high ICC (0.98–0.99) with a statistically significant confidence interval in calculation of total lung score between low-dose and standard-dose ($P$ values < 0.001 for all readers).

| Lobe   | Kappa (κ) | $P$ value for $\kappa$ | ICC [confidence interval] total lung score | $P$ value for ICC |
|--------|-----------|------------------------|-------------------------------------------|-------------------|
| Standard-dose | RUL | 0.63 | $<0.001$ | 0.81 [0.66–0.91] | $<0.001$ |
|         | RML | 0.45 | $<0.001$ | | |
|         | RLL | 0.45 | $<0.001$ | | |
|         | LUL | 0.53 | $<0.001$ | | |
|         | LLL | 0.67 | $<0.001$ | | |
| Low-dose | RUL | 0.54 | $<0.001$ | 0.84 [0.70–0.93] | $<0.001$ |
|         | RML | 0.46 | $<0.001$ | | |
|         | RLL | 0.51 | $<0.001$ | | |
|         | LUL | 0.54 | $<0.001$ | | |
|         | LLL | 0.67 | $<0.001$ | | |

| Lobe   | Kappa (κ) | $P$ value for $\kappa$ | ICC [confidence interval] total lung score | $P$ value for ICC |
|--------|-----------|------------------------|-------------------------------------------|-------------------|
| Reader A | RUL | 1.00 | $<0.001$ | 0.98 [0.96–0.99] | $<0.001$ |
|         | RML | 0.91 | $<0.001$ | | |
|         | RLL | 0.86 | $<0.001$ | | |
|         | LUL | 1.00 | $<0.001$ | | |
|         | LLL | 0.80 | $<0.001$ | | |
| Reader B | RUL | 1.00 | $<0.001$ | 0.99 [0.98–0.99] | $<0.001$ |
|         | RML | 1.00 | $<0.001$ | | |
|         | RLL | 0.81 | $<0.001$ | | |
|         | LUL | 1.00 | $<0.001$ | | |
|         | LLL | 0.73 | $<0.001$ | | |
| Reader C | RUL | 0.81 | $<0.001$ | 0.98 [0.95–0.99] | $<0.001$ |
|         | RML | 1.00 | $<0.001$ | | |
|         | RLL | 0.67 | $<0.001$ | | |
|         | LUL | 0.92 | $<0.001$ | | |
|         | LLL | 0.89 | $<0.001$ | | |

*RUL* right upper lobe, *RML* right middle lobe, *RLL* right lower lobe, *LUL* left upper lobe, *LLL* left lower lobe, *ICC* intraclass correlation coefficient
Effective radiation dose and cancer risk estimation

The mean volume computed tomography dose index (CTDIvol) values in standard- and low-dose groups were 13.115 ± 2.48 and 3.505 ± 0.83 mGy, respectively (P value < 0.001). The mean DLP values were 412.810 ± 91.68 and 112.230 ± 26.55 mGy·cm in standard- and low-dose groups, respectively.

The mean effective dose values in standard- and low-dose groups were 6.60 ± 1.47 and 1.80 ± 0.42 mSv, respectively. Absolute cancer risk per mean cumulative effective dose values obtained from the standard- and low-dose CT examinations were $2.71 \times 10^{-4}$ and $0.74 \times 10^{-4}$, respectively (Table 3).

Discussion

Although recent studies have reported that chest CT has high sensitivity in the detection of COVID-19 pneumonia [9–11], characteristic radiologic features should be present in chest CT of the patients, and the utilization of CT is still limited in the era of COVID-19 pandemic. Current American College of Radiology (ACR) guidelines state that CT should not be used as a first-line test to screen and diagnosis of COVID-19 pneumonia [15] with nonspecific appearance of COVID-19 pneumonia on CT, associated radiation exposure and issues related to infection control after using the imaging equipment, being among the major reasons. Nevertheless, chest CT may be used in hospitalized symptomatic patients with relevant indications. An updated CT imaging algorithm seems warranted in each radiology department to maximize radiation protection and achieve the ALARA radiation dose.

Medical imaging remains as one of the major sources of radiation exposure in the USA. It has been proven that upward trending of radiation increases the risk of malignancies [30]. Number and dose of CT studies are one of the largest sources of imaging exposure. It is critical to make the maximum...
efforts to utilize CT examinations with reduced radiation dose without harm to diagnostic accuracy.

The purpose of our study was to determine whether it is scientifically logical to accept a 30-mAs chest CT protocol as an available routine protocol for COVID-19 pneumonia, a pandemic condition which may necessitate multiple CT imaging for detection of suspicious indeterminate cases (e.g., negative RT-PCR with high clinical suspicion or definite history of exposure) and worsening of clinical findings in the course of disease. Our results show that there is no significant difference between the low-dose and standard-dose CT images in diagnosing radiographically normal laboratory-confirmed COVID-19 pneumonia cases, with excellent agreement rate among the readers. We showed that recently described typical findings to suggest COVID-19 pneumonia on chest CT can be evaluated appropriately using a low-dose CT protocol (Figs. 1a,b, 2a,b, and 3a,b). In the same line, final diagnosis of COVID-19 pneumonia on low-dose CT chest was not affected in any of our twenty patients who had a confirmed positive RT-PCR test. Of note, in our study the mean CTDIvol, DLP, effective patients’ dose, and estimated cancer risk were reduced by more than 73% without sacrificing the diagnostic accuracy of the disease. Chest CT scanning parameters applied for the diagnosis of COVID-19 pneumonia in multiple recent studies have been summarized in Table 4.

Multiple prior studies have confirmed that low-dose chest CT protocols have a diagnostic accuracy similar to standard-dose in spite of degraded image quality. A comprehensive study performed by Kubo et al. demonstrated that low-dose and standard-dose have statistically the same capability in detection of intrathoracic abnormalities. More specifically, their study demonstrated that low-dose chest CT (50 mAs) is as accurate as standard-dose (150 mAs) in detection of pulmonary parenchymal abnormalities (ground glass opacities, emphysema, micronodules, honeycombing, and reticular densities) and mediastinal/pleural findings (aortic aneurysm, coronary arterial calcification, pleural effusion, lymphadenopathy, and mediastinal tumors) [22]. Other studies have examined low-dose capability in CT pulmonary angiography [37]. Lung cancer screening programs with low-dose chest CT protocols have been associated with reduced mortality [38]. However, there is no current accepted low-dose protocol for routine chest CT in selected clinical scenarios, like COVID-19 pneumonia.

It is worth mentioning that we evaluated chest CT scans of 20 patients with confirmed COVID-19 infection who had normal chest radiographs. This indicates that low-dose CT was able to trace a type of disease which was radiographically hidden. It is realistically clear that more diffuse disease on chest radiographs will be even more feasible to be detected on low-dose CT protocols. The identified lesions were all typical for COVID-19 pneumonia as described in multiple prior studies, and the most common lobes involved were RLL and LLL, followed by the upper lobes, with the RML being the less involved lobe, same as the prior studies [8–13].

| Protocol type | CTDIvol (mGy) | DLP (mGy·cm) | Conversion factor (mSv/mGy·cm) | Effective dose (mSv) | Cancer absolute risk ($\times 10^{-4}$) |
|---------------|--------------|--------------|-------------------------------|---------------------|--------------------------------------|
| Standard-dose | 13.115 ± 2.48| 412.81 ± 91.68| 0.016                         | 6.60                | 2.71                                 |
| Low-dose      | 3.505 ± 0.83 | 112.23 ± 26.55| 0.016                         | 1.80                | 0.74                                 |

CTDIvol volume CT dose index, DLP dose-length product
Although there were differences in scoring lobar involvement between low-dose and standard-dose in some cases for all three radiologists (intrareader), this did not affect the final diagnosis of COVID-19 pneumonia in any case. This indicates a 100% sensitivity for low-dose chest CT scan, considering standard-dose as the gold standard test. However, a larger number of cases are required for estimating more accurate sensitivity. Of note, ethical issues in obtaining two CT scans and associated increased radiation exposure in such studies are existent challenges.

Chest CT scan is normally performed in deep inspiration with breath-hold status, but sometimes respiratory motion during the scan can blur the images. The source of some mismatches between low-dose and standard-dose CT scans was the loss of image quality due to the patient's respiratory movements so that depending on whether the motion artifact was in standard- or low-dose, this may upgrade or downgrade the diagnostic score in low-dose CT scan (Fig. 4a, b). The same concept is accurate for matching image slices between low-dose and standard-dose. Although in all of our 20 patients, the low-dose CT was done immediately after the standard-dose, and the patient did not move on the CT table; in some cases the location of the imaging slices in low-dose was not exactly the same as standard-dose. This would affect the appearance of some small lesions on the second CT scan creating a potential for interpretation mismatches. Another limitation to our study is lack of objective standard for abnormal findings. For a descriptive abnormality like GGOs, it is hard to establish a gold standard among all the readers.

### Conclusion

There was no statistically significant difference identified between the low-dose and standard-dose CT images in detecting radiographically normal laboratory-confirmed COVID-19 pneumonia. Simultaneously, the low-dose protocol in our study was associated with approximately 73% reduction in mean effective dose value and estimated cancer risk.
According to our findings, it was found that proposed low-dose CT chest protocol is reliable in detecting COVID-19 pneumonia in daily practice with a significant reduction in radiation dose and estimated cancer risk.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Main points
1. In this prospective study, there is no significant difference between the low-dose and standard-dose CT images in diagnosing radiographically normal laboratory-confirmed COVID-19 pneumonia cases, with excellent agreement rate among the readers.
2. The mean CTDIvol, DLP, effective patients’ dose, and estimated cancer risk were reduced by more than seventy-three percent in the low-dose group, without sacrificing the diagnostic accuracy of detecting COVID-19 pneumonia.
3. Although there were differences in scoring lobar involvement between the low-dose and standard-dose for the readers, this did not affect the final diagnosis of COVID-19 pneumonia in any case, indicating a 100% sensitivity for the low-dose chest CT scan, considering a standard-dose CT as the gold standard test.

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