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META-ANALYSIS

Association of chest CT severity score with mortality of COVID-19 patients: a systematic review and meta-analysis

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Abstract

Purpose Chest computed tomography (CT) is a high-sensitivity diagnostic tool for depicting interstitial pneumonia and may lay a critical role in the evaluation of the severity and extent of pulmonary involvement. In this study, we aimed to evaluate the association of chest CT severity score (CT-SS) with the mortality of COVID-19 patients using systematic review and meta-analysis.

Methods Web of Science, PubMed, Embase, Scopus, and Google Scholar were used to search for primary articles. The meta-analysis was performed using the random-effects model, and odds ratios (ORs) with 95% confidence intervals (95%CIs) were calculated as the effect sizes.

Results This meta-analysis retrieved a total number of 7106 COVID-19 patients. The pooled estimate for the association of CT-SS with mortality of COVID-19 patients was calculated as 1.244 (95% CI 1.157–1.337). The pooled estimate for the association of CT-SS with an optimal cutoff and mortality of COVID-19 patients was calculated as 7.124 (95% CI 5.307–9.563). There was no publication bias in the results of included studies. Radiologist experiences and study locations were not potential sources of between-study heterogeneity (both $P > 0.2$). The shapes of Begg's funnel plots seemed symmetrical for studies evaluating the association of CT-SS with/without the optimal cutoffs and mortality of COVID-19 patients (Begg's test $P = 0.945$ and 0.356, respectively).

Conclusions The results of this study point to an association between CT-SS and mortality of COVID-19 patients. The odds of mortality for COVID-19 patients could be accurately predicted using an optimal CT-SS cutoff in visual scoring of lung involvement.

Keywords COVID-19 · Computed tomography · Mortality · CT · CT severity score · Pneumonia

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Abbreviations

COVID-19	Coronavirus disease 2019
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
CT-SS	Chest CT severity score
CT	Computed tomography
CI	Confidence interval
RT-PCR	Reverse-transcriptase polymerase chain reaction
OR	Odds ratio
HR	Hazard ratio

Introduction

Since the outbreak of the COVID-19 pandemic at the end of 2019, a total of 5,414,769 deaths had been reported all over the world [1]. Symptoms of this new infectious disease include fever, respiratory illness, lymphopenia, and pneumonia of unknown etiology [2–7]. The severity of pneumonia caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) could explain the high mortality of the infected subjects [8]. Given the mortality rate of COVID-19, it is very important to find predictors of poor prognosis to properly deal with COVID-19 patients. Early identification of patients at higher risk of death would help to recognize the patients with a higher need for intensive care. Improvement of the patient's management and their outcomes would be the main results of this clinical decision-making optimization [9].

However, the reverse-transcriptase polymerase chain reaction (RT-PCR) test is the main standard of reference for confirming COVID-19, CT is used as a fundamental complementary diagnostic approach [8]. Chest computed tomography (CT) is a high-sensitivity diagnostic tool for depicting interstitial pneumonia [10] and may lay a critical role in the evaluation of the severity and extent of pulmonary involvement. Bilateral multiple lobar ground-glass opacity and consolidation were the main chest CT findings on admission [11, 12]. Other chest CT manifestations include crazy-paving patterns, multi-lobar involvement, and increasing lung consolidations with disease progress [12].

CT severity score (CT-SS) is the suggested index to evaluate the severity of pulmonary involvement. In several studies, it was reported that there were significantly higher CT-SS magnitudes in deceased patients as compared to survivors. A significant correlation between CT-SS and mortality of the COVID-19 patients was also observed. Therefore, the extent of the lung lesions in early CT images after symptom onset could be considered as a potential predictor of patient mortality.

To our knowledge, a dedicated systematic review and meta-analysis study has not yet been performed for the assessment of the prognostic value of CT-SS to predict mortality in COVID-19 patients. In this study, we aimed to evaluate the association of CT-SS with mortality of COVID-19 patients using systematic review and meta-analysis.

Materials and methods

Protocol of the systematic review and meta-analysis

This systematic review was performed following a predefined protocol and reported in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) checklist [13]. The study was approved by the local Medical Ethical Committee (approved number. IR.ABADANUMS.REC.1400.087).

Information sources and search strategies

Web of Science, PubMed, Embase, Scopus, and Google Scholar were used to search for primary articles evaluating the association of CT-SS with mortality of COVID-19 patients. These databases were searched between December 2019 and August 2021. We used the following MeSH and non-MeSH terms:

"COVID-19", "SARS-CoV-2", "2019 Novel Coronavirus", "2019-nCoV", "Wuhan virus", "severe acute respiratory syndrome coronavirus 2", "coronavirus disease 2019" in conjunction with "CT", "computed tomography", "Chest computed tomography", "Chest CT", "X-Ray CT Scan", "X-Ray CAT Scan", "CT scan", "CAT scan", "Mortality", "Death", "decease*", "died", and "dead. Boolean operators (NOT, AND, OR) were also used in succession. The references of the included studies were also screened for other possible additional publications. Case reports, editorials, commentaries, and opinions were not included in the meta-analysis.

Eligibility criteria

The inclusion criteria for the meta-analysis were as follows: (a) studies on patients with laboratory-confirmed COVID-19 disease; (b) studies on patients with CT examination on admission/ after triage; (c) studies that have reported the association of CT-SS with mortality of COVID-19 patients using OR; (d) studies in which CT-SS scores have been determined based on the visual assessment of the extent of lung involvements in initial CT images; and (e) original research with any type of study designs. Exclusion criteria were: (a) The full texts of studies were not available; (b) studies that have reported the association of CT-SS with mortality of COVID-19 patients using hazard ratio (HR); and (c) studies in which necessary parameters for OR calculation did not exist.

Study selection and data collection process

Data extraction was carried out independently by two reviewers (NN and HS). In case of disagreement, the consensus was reached by discussing it with a third reviewer

(SSZ). The first author of the selected articles, publication year, country, age average, sample size, the gender ratio of males, OR for the association of CT-SS with mortality of COVID-19 patients, the total number of deceased and survivors, and other related information were extracted from the studies that have been provided for the meta-analysis process. The characteristics of included studies are presented in Table 1.

Assessment of quality of studies

The Newcastle–Ottawa Scale (NOS) was used to assess the quality and risk of bias of the included studies. The NOS tool determines the quality of a case–control study according to selection (0–4 points), comparability (0–2 points), and exposure (0–3 points) definitions. The studies were categorized as good quality if they scored ≥ 7 points, fair quality if they scored 5–6 points, and poor quality if they scored < 5 points. The assessment of study quality was independently conducted by two investigators (HS and NN) and any discrepancy was resolved through discussion.

Summary measures and synthesis of results

Data analysis was performed using Stata version 11.0 (Stata Corporation, College Station, TX, USA). ORs were used for the analysis of a pooled effect size. In this study, the association between CT-SS (exposure) and mortality of COVID-19 patients (outcome) was evaluated. The OR represents the odds of mortality for COVID-19 patients with CT-SS > the considered threshold in each study, compared to the odds of mortality for COVID-19 patients with CT-SS < the threshold. Since we have a ratio of mortality probability in patients with CT-SS > the threshold to mortality probability in patients with CT-SS < the threshold, the range of scores in each study do not affect the results. Therefore, the difference between scoring systems has no role in calculating OR and has not been considered.

For included and pooled studies, data were presented as ORs with 95% CIs. Between-studies heterogeneity was evaluated using Cochran's Q test and the Inconsistency index (I^2) test.

$I^2 > 50\%$ was considered as the apparent heterogeneity between the studies and the random-effects model (Der Simonian and Laird method) was adopted. For those analyses with $I^2 < 50\%$, the fixed-effect model (Mantel–Haenszel model) was used. For evaluation of publication bias among studies, a visual inspection of the generated funnel plot was employed.

Results

Study selection

Figure 1 shows the flowchart of the study selections in the systematic review processes. A total of 7463 records were identified in the initial literature search. After removing duplicate studies, 3302 studies were screened based on title and abstract. Of the 3302 records, 3162 publications were excluded after the first screening. Because of data presentation in HR and the insufficient data for calculation of OR and 95% CI two papers were excluded. Based on inclusion criteria, 28 studies (which are detailed in Table 1) were included in the meta-analytical processes that reported the association of CT-SS with mortality of COVID-19 patients.

Characteristics and quality of the included studies

The characteristics of the included studies are presented in Table 1. The first author, publication year, country, age average, sample size, the gender ratio of males, and the method of image interpretation of the included articles are presented in the table. This meta-analysis retrieved a total number of 7106 COVID-19 patients.

The quality of studies were assessed using the NOS tool for case–control studies and the results are shown in Table 1. The scores were as follows: 9/9 score [2 studies (7%)]; 8/9 score [2 studies (7%)]; and 7/9 score [24 study (86%)]. The cases and controls could be compared for only four studies based on the design or analysis controlled for age or other confounding variables. All studies were categorized as good quality (scores of ≥ 7). Therefore, quality of the included studies were not the source of heterogeneity among the studies.

Risk of bias within studies

The p value obtained from the χ^2 test of heterogeneity could be used to determine the presence of heterogeneity between studies. The heterogeneity is significant when there is a low p value. The p value obtained from the χ^2 test of heterogeneity were 0.008 and < 0.0001 for studies evaluating the association of CT-SS with mortality of COVID-19 patients and studies predicting mortality of COVID-19 patients using the optimal CT-SS cutoffs, respectively. Moreover, the I^2 test for studies evaluating the association of CT-SS with mortality of COVID-19 patients and studies predicting mortality of COVID-19 patients using the optimal CT-SS cutoffs were calculated as 65.5 and 63.4%, respectively. Therefore, the

Table 1 Characteristics and quality of included studies

Study	Publication year	Country	Sample size (*N*)	Age (mean ± SD)	Male (*N*)	Image interpretation	Quality score
Abdollahi I et al. [14]	2021	Iran	742	56.59 ± 14.88	451 (60.8%)	Five lobes were visually scored as: 0, no involvement; 1, less than 5% involvement; 2, 5–25% involvement; 3, 26–49% involvement; 4, 50–75% involvement; and 5, more than 75% involvement. The total CT score was the sum of the individual lobar scores and ranged from 0 to 25	9
Angeli E et al. [15]	2021	Italy	301	69.8 ± 13.0	209 (69.4%)	Five lobes were visually scored as: 0: no involvement; 1: ≤ 25%; 2: 26–50%; 3: 51–75%; 4: 76–100% of involvement. The sum of all lobe scores yielded the final PI score ranging from 0 to 20	7
Bayrak V et al. [16]	2021	Turkey	86	71.1 ± 14.1	61 (70.9%)	Five lobes were visually scored as: 0, no involvement; 1, less than 5% involvement; 2, 5–25% involvement; 3, 26–49% involvement; 4, 50–75% involvement; and 5, more than 75% involvement. The total CT score was the sum of the individual lobar scores and ranged from 0 to 25	7
Besutti G et al. [9]	2021	Italy	866	59.8 (50.2–72.5)[a]	527 (60.85%)	The extension of pulmonary lesions was evaluated using a visual scoring system as: < 20%, 20–39%, 40–59%, and ≥ 60%	7
Cao Y et al. [17]	2020	China	101	56.6 ± 15.1	67 (66.3%)	Five lobes were visually scored as: 0, no involvement; 1, < 5% (minimal but not normal); 2, 5–25%; 3, 26–49%; 4, 50–75%; and 5, > 75%. The total CT severity score was calculated by summing the individual lobar scores and ranged from 0 to 25	7
Charpentier E et al. [18]	2021	France	210	66 ± 16	146 (69.5%)	Each of the five lung lobe extents was classified as having 0, 1, 2, 3, or 4 score when none, minimal (1–25%), mild (26–50%), moderate (51–75%), or severe (> 75%) were visually estimated, respectively. The sum of all lobe scores yielded the total severity score ranging from 0 to 20	7

Table 1 (continued)

Study	Publication year	Country	Sample size (*N*)	Age (mean ± SD)	Male (*N*)	Image interpretation	Quality score
Chon Y J et al. [19]	2020	Korea	281	61.5 (50–72)[b]	75 (26.7%)	According to the anatomical structure, both lungs were divided into 20 segments (left apicoposterior segment subdivided into the apical and posterior segments, left antero-medial basal segment subdivided into the anterior basal and medial basal segments). The lung opacity in 20 segments were visually evaluated and scored as 0 (no involvement), 1 (less than 50% involvement), and 2 (more than 50% involvements). The sum of all lobe scores yielded the total score ranging from 0 to 40	8
Dilek O et al. [20]	2021	Turkey	100	61 ± 14.85	61 (61%)	The involvement scores were categorized as: 0, 0% involvement; 1, 1–25% involvement; 2, 26–50% involvement; 3, 51–75% involvement; and 4, 76–100% involvement. The sum of all lobe scores yielded the patient score (TSS) ranging from 0 to 20	7
Guillo E et l. [8]	2020	France	214	59 ± 19	119 (56%)	The severity of COVID-19 pneumonia was graded according to the extent of ground glass opacities and consolidation on lung window CT images, as follows: minimal (less than 10% of lung parenchyma), moderate (10–25%), intermediate (25–50%), severe (50–75%), critical (50–75%)	7
Hajiahmadi S et al. [21]	2021	Iran	192	57.5 ± 1.11	114 (59.38%)	Each lung was divided into three regions (upper, middle, and lower). Each region of the lung was evaluated in terms of the percentage of involvement as: 0, no involvement; 1, less than 25%; 2, 25% to less than 50%; 3, 50% to less than 75%; and 4, 75% or greater involvement. The sum of all lobe scores yielded the total CSS ranging from 0 to 24 (diffuse interstitial involvement)	8
Isik S A et al. [22]	2021	Turkey	257	52 ± 14.62	142 (55.3%)	Five lobes were visually scored as: 0, no involvement; 1, < 5%; 2, 5–25%; 3, 25–49%; 4, 50–75%, and 5, > 75%. The sum of all lobe scores yielded the total CT severity score ranging from 0 to 25	7

Table 1 (continued)

Study	Publication year	Country	Sample size (*N*)	Age (mean ± SD)	Male (*N*)	Image interpretation	Quality score
Kazemi M A et al.[12]	2020	Iran	91	58.04 ± 16.5	57 (62.6%)	Five lobes were visually scored as: 0, non-involvement; 1, less than 5% involvement; 2, 5–25% involvement; 3, 26–49% involvement; 4, 50–75% involvement; and 5, > 75% involvements. The sum of all lobe scores yielded the total CT-score ranging from 0 to 25	7
Khosravi B, et al. [23]	2021	Iran	121	60 ± 16	67(55.37%)	Each lung was divided into upper, lower, and middle zones (six zones). Six zones were visually scored as: 0: no involvement, 1: 1–25% involved, 2: 26–50% involved, 3: 51–75% involved, 4: 76–100% involved. The sum of all zone scores yielded the final CT severity score (CSS) ranging from 0 to 24	7
Kimura-Sandoval Y et al. [24]	2021	Mexico	166	50 ± 14	100 (60.2%)	Five lobes were visually scored as: 0, no involvement; 1, ≤ 25%; 2, 26–50%; 3, 51–75%; 4, 76–100% of involvement. The sum of all lobe scores yielded the final PI score ranging from 0 to 20	7
Li H et al. [25]	2021	China	147	66 (57–72)[a]	83 (54%)	Each lung was divided into upper, lower, and middle zones (six zones). Six zones were visually scored as: score 0, 0%; score 1, less than 25% involvement; score 2, 25% to less than 50%; score 3, 50% to less than 75%; and score 4, 75% or higher. The sum of all zone scores yielded the total severity score ranging from 0 to 24	7
Li K et al. [26]	2020	China	102	57 (45–70)[a]	59 (58%)	Five lobes were visually scored as: 0, no involvement; 1, < 5% involvement; 2, 5–25% involvement; 3, 26–49% involvement; 4, 50–75% involvement; 5, > 75% involvement. The sum of all lobe scores yielded the total severity score ranging from 0 to 25	7
Li K et al. [27]	2020	China	83	45.5 ± 12.3	44 (53.0%)	Five lobes were visually scored as: 0, 0% involvement; 1, less than 5% involvement; 2, 5% to 25% involvement; 3, 26% to 49% involvement; 4, 50% to 75% involvement; and 5, greater than 75% involvement. The sum of all lobe scores yielded the total possible score ranging from 0 to 25	7

Table 1 (continued)

Study	Publication year	Country	Sample size (*N*)	Age (mean ± SD)	Male (*N*)	Image interpretation	Quality score
Li Y et al. [28]	2020	China	46	71.1 ± 8.5	65 (66.3%)	The severity of each lung lobe (left upper/lower lobe and right upper/middle/lower lobe) was scored as: 0, 0%; 1, 1–25%; 2, 26–50%; 3, 51–75%; and 4, 76–100%. The sum of all lobe scores yielded the total cumulative score ranging from 0 to 60	7
Lieveld A et al. [29]	2021	Netherlands	741	62.1 ± 17.2	417 (56.3%)	Five lobes were visually scored, every CT with a CO-RADS of 3 or higher was graded according to the CTSS. The sum of all lobe scores yielded the total CTSS ranging from 0 to 25	9
Mirza-Aghazadeh-Attari M et al. [30]	2020	Iran	50	65.4 ± 16.77	27 (54%)	Lung score was determined based on the following: 0, no involvement; 1, less than 5% of involvement; 2, 6–25% involvement; 3, 26–50% involvement; 4, 51–75%involvement; and 5, involvement more than 75%	7
Mohamed I A I et al. [31]	2021	Egypt	164	44.3 ± 16.5	86 (52.44%)	Five lobes were visually scored as: 0, no involvement; 1, < 5% involvement; 2, 5–25% involvement; 3, 25–50% involvement; 4, 50–75% involvement; and 5, > 75% involvement, then multiplied by 5 to calculate the overall severity score	7
Raoufi M et al. [11]	2020	Iran	380	53.62 ± 16.66	251 (66.1%)	Five lobes were visually scored as: 0, no involvement; 1, < 5%; 2, 5–25%; 3, 25–49%; 4, 50–75%, and 5, > 75%. The sum of all lobe scores yielded the total CTSS ranging from 0 to 25	7
Ruch Y et al. [32]	2020	France	572	66.0 ± 16.0	343 (60.0%)	The CT images were classified as: normal CT (no lesion), minimal (0–10%), moderate (11–25%), important (26–50%), severe (51–75%), and critical (> 75%). The patients were divided into three subgroups (25%, 26–50%, and > 50%) to simplify the analysis	7
Salahshour F et al. [33]	2020	Iran	739	49.2 ± 17.2	419 (56.7%)	Five lobes were visually reviewed for GGO and consolidation and scored from 0 to 5 for each pattern as: 0, no involvement; 1, ≤ 5%; 2, 6–25%; 3, 26–50%, 4, 51–75%; and 5, ≥ 76%. Total PI score (ranged from 0 to 35) was calculated as: sum of total GGO scores and total consolidation scores or sum of GGO and consolidation score of all five lobes	7

Table 1 (continued)

Study	Publication year	Country	Sample size (*N*)	Age (mean ± SD)	Male (*N*)	Image interpretation	Quality score
Salvatore C et al. [34]	2021	Italy	103	61.0 (23.0–91.0)[c]	59 (60.20%)	For each lung, CT pulmonary involvement was determined using a radiological severity visual score as: none (0%), mild (1–25%), moderate (26–50%), severe (51–75%) and critic (76–100%) involvement. The sum of all lobe scores yielded an overall radiological severity visual score ranging from 0 to 16: none (0), mild (1–4), moderate (5–8), severe (9–12) and critic (13–16)	7
Tabatabaei S M H et al. [35]	2020	Iran	90	44.2 ± 5.9 and 44.3 ± 5.9 for non-survivors and survivors, respectively	54 (60%)	Five lobes were visually scored as: 0, no involvement; 1, 1–25% involvement; 2, 26–50% involvement; 3, 51–75% involvement; 4, 76–100% involvement. The sum of all lobe scores yielded the total CT severity score ranging from 0 to 20	7
Yuan M et al. [2]	2020	China	27	60 (47–69)[a]	12 (44.44%)	Each lung was divided into upper, lower, and middle zones (six zones). Six zones were visually scored as: 0, normal; 1, < 25% abnormality; 2, 25–50% abnormality; 3, 50–75% abnormality; and 4, > 75% abnormality. The four-point scale of the lung parenchyma distribution was then multiplied by the radiologic scale. The sum of all zone scores yielded a final total cumulative score ranging from 0 to 72	7
Zhou S, et al.[36]	2020	China	134	48 (38–61)[a] and 68 (59–76)[a] for survivors and non-survivors, respectively	85 (63.43%)	Five lobes were visually scored as: 0, no lesions; 1, 1–5% involvement; 2, ≤ 25% involvement; 3, 26–50% involvement; 4, 51–75% involvement; 5, 76–100% involvement. The sum of all lobe scores yielded the total CT score ranging from 0 to 25	7

[a]Median (IQR)

[b]Median (25th–75th percentile)

[c]Median (range)

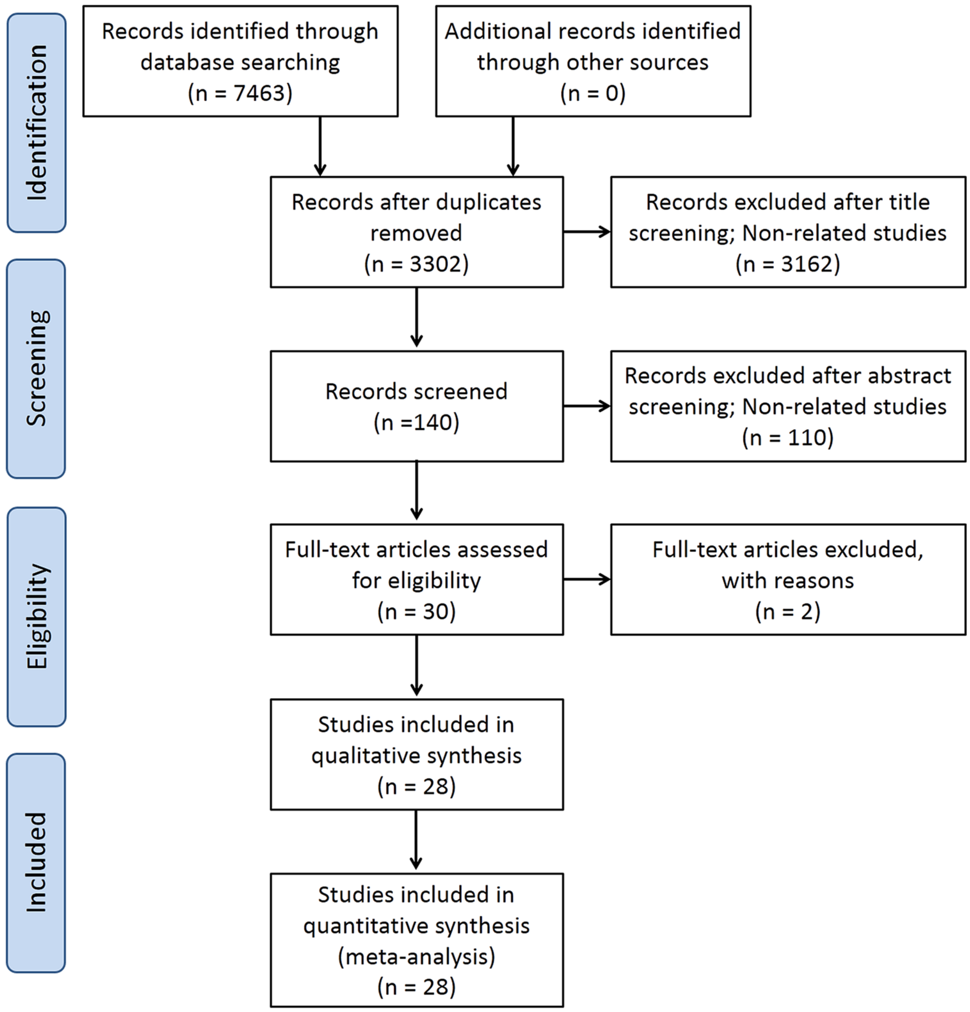


Fig. 1 Search strategy for systematic review. Twenty-eight included studies fulfilled the inclusion/exclusion criteria

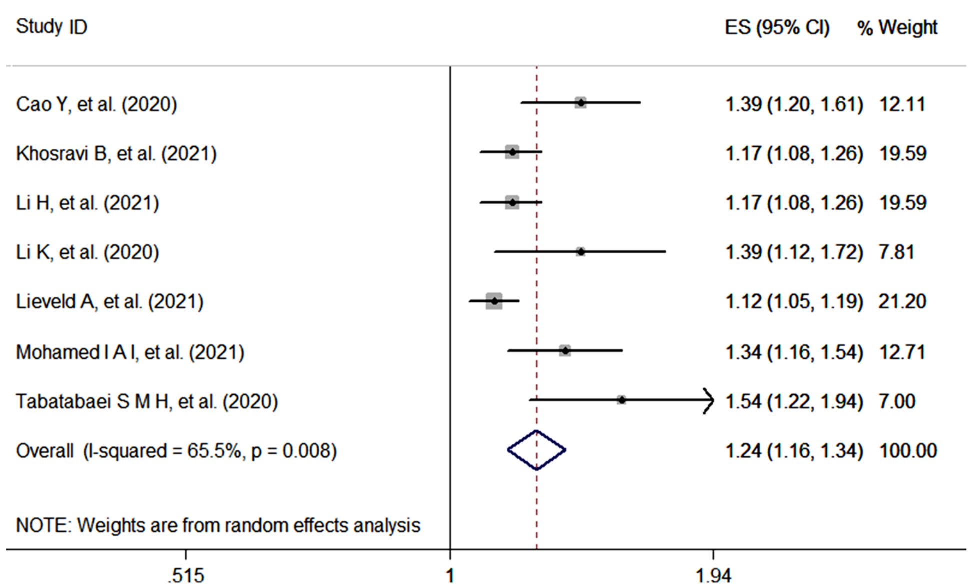


Fig. 2 Forest plot of 7 included studies. In this plot, pooled data evaluating the association of CT-SS with mortality of COVID-19 patients have been demonstrated under the random-effects model. The pooled estimate for ORs was calculated as 1.244 (95% CI 1.157–1.337)

random-effects model of the meta-analysis was applied for evaluating the associations of both CT-SSs with mortality of COVID-19 patients.

Synthesis of results

The forest plot for the included studies reporting the association of CT-SS with mortality of COVID-19 patients is presented in Fig. 2. In addition to the effect sizes (in OR) and 95% CIs of the studies, the overall effect size and its 95% CI have also been presented in this plot. The pooled estimate for the association of CT-SS with mortality of COVID-19 patients was calculated as 1.244 (95% CI 1.157–1.337). The pooled estimate is significant.

The forest plot for the included studies predicting mortality of COVID-19 patients using the optimal CT-SS cutoffs is presented in Fig. 3. In addition to the effect sizes (in OR) and 95% CI magnitudes of the studies, the overall effect size and its 95% CI have also been presented in this plot. The pooled estimate for the association of CT-SS with an optimal cutoff and mortality of COVID-19 patients was calculated as 7.124 (95% CI 5.307–9.563). The pooled estimate is significant.

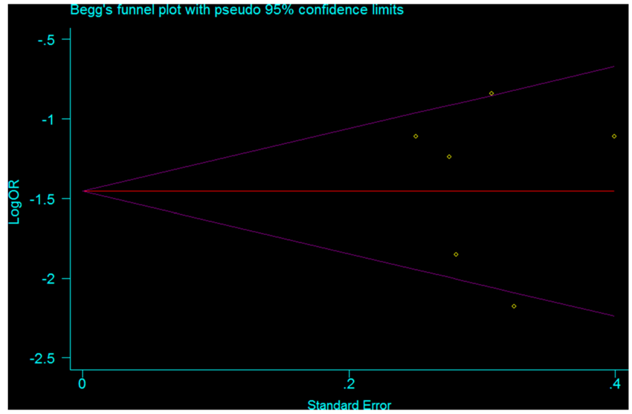
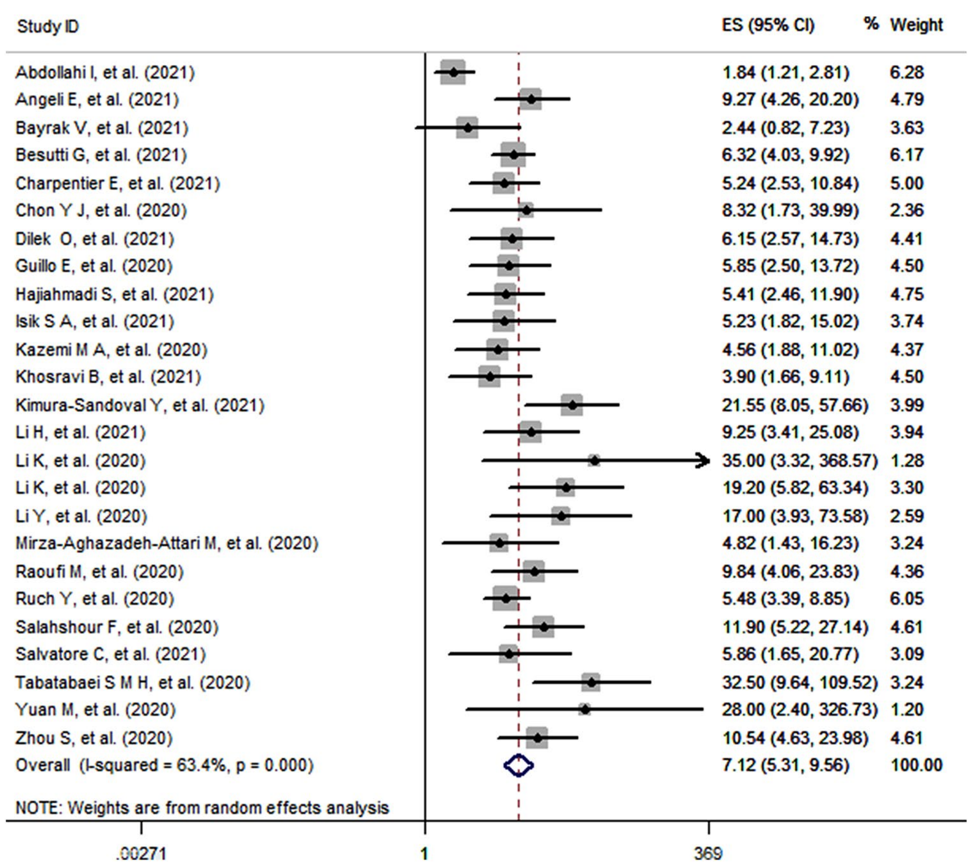


Fig. 4 Funnel plot for 7 included studies. For interpretation of any publication bias among studies, a visual inspection of the generated funnel plot was employed. The funnel plot seemed symmetrical in shape ($P = 0.941$) demonstrating the absence of publication bias in the results of included studies evaluating the association of CT-SS and mortality of COVID-19 patients. In this plot, the X and Y axes represent ORs and standard errors, respectively

Risk of bias across studies

In Fig. 4, the funnel plot seemed symmetrical in shape ($P = 0.941$) demonstrating the absence of publication bias

Fig. 3 Forest plot of 25 included studies. In this plot, pooled data evaluating the association of CT-SS with an optimal cutoff and mortality of COVID-19 patients were demonstrated under the random-effects model. The pooled estimate for ORs was calculated as 7.124 (95% CI 5.307–9.563)



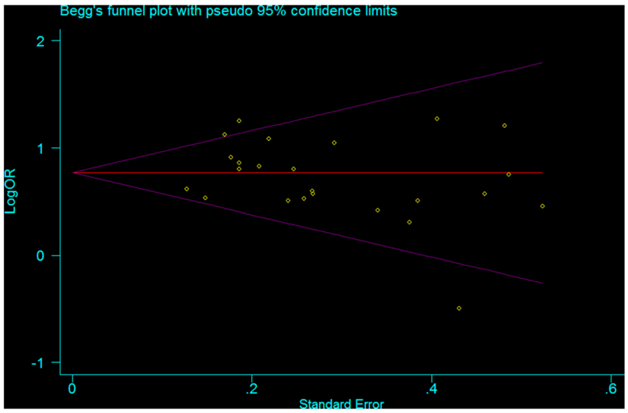


Fig. 5 Funnel plot for 25 included studies. For interpretation of any publication bias among studies, a visual inspection of the generated funnel plot was employed. The funnel plot seemed symmetrical in shape ($P = 0.941$) demonstrating the absence of publication bias in the results of included studies evaluating the association of CT-SS with an optimal cutoff and mortality of COVID-19 patients. In this plot, the X and Y axes represent ORs and standard errors, respectively

in the results of included studies evaluating the association of CT-SS and mortality of COVID-19 patients.

In Fig. 5, the shape of the Begg's funnel plot seemed symmetrical ($P = 0.365$) which indicates the absence of publication bias in the results of included studies predicting mortality of COVID-19 patients using the optimal CT-SS cutoffs.

To explore the possible source of between-study heterogeneity, meta-regression analysis was conducted on radiologist experiences. Results showed that radiologist experiences did not affect the prognostic value of CT-SS to predict mortality in COVID-19 patients ($P = 0.404$). In subgroup analysis, study locations were also investigated to evaluate another possible source of heterogeneity among the studies. The test for subgroup differences indicated that there is no statistically significant subgroup effect ($P = 0.229$, analysis not presented), suggesting that study location does not modify the prognostic value of CT-SS to predict mortality in COVID-19 patients.

Discussion

In the last 2 years, countless infections and deaths were reported due to the outbreak of the COVID-19 pandemic. Effective management and treatment of the infected subjects might be possible by understanding the mechanism of severe/critical conditions and identification of their imaging and clinical features [37–39]. Radiological and clinical features of COVID-19 pneumonia have been investigated in several case series [40, 41]. Radiological manifestations of COVID-19 lesions resemble those of SARS and MERS pneumonia, which may be related to their similar pathogenesis [42].

The pneumonia lesions mostly involved the bilateral lungs and were located in the peripheral area of the lungs. The radiological lung injury abnormalities could be manifested on all five lobes. In the early period of virus infection, GGO without consolidation is the most common radiological sign. Consolidation is more commonly seen in severely ill subjects, which indicates that there has been a correlation between the consolidative lesions and disease severity [43, 44].

In addition to these radiological manifestations, lung lesion extension has also a relatively strong association with disease severity and patient outcome. Deceased patients had higher CT severity scores compared to survivors. Therefore, CT-SS as a prognostic factor could help to identify the high-risk patients and give physicians a better insight to manage patients with COVID-19.

In this study, we investigated the association of CT-SS with the mortality of COVID-19 patients by conducting a meta-analysis. Although there are original articles describing the association of CT-SS with mortality of COVID-19 patients and predicting mortality of COVID-19 patients using the optimal CT-SS cutoffs, no meta-analysis study has to date been carried out on this aspect. To the best of our knowledge, this report is the first meta-analysis describing the association of CT-SS with mortality of COVID-19 patients to provide appropriate clinical evidence for the prognosis of COVID-19.

In the current study, the association of CT-SS with mortality of COVID-19 patients was investigated using meta-analysis and the final pooled OR was calculated as 1.244 (95% CI 1.157–1.337). The result confirms that there is a direct relationship between CT-SS and mortality of the COVID-19 patients. For the COVID-19 patients with higher CT severity scores, there is a higher odds of mortality. The results also showed that there is no heterogeneity among the included studies. In further meta-regression and subgroup analyses, radiologist experiences and study locations were, respectively, investigated to evaluate the possible sources of heterogeneity among the studies. The results indicated that study location and radiologist experience don't modify the prognostic value of CT-SS to predict mortality in COVID-19 patients.

The time interval between the initial CT and the symptom onset might be another possible source of between-study heterogeneity. As indicated by a comprehensive meta-analysis of 9907 confirmed patients, initial normal chest CT scans after symptom onset can rapidly change and lung damages would be more pronounced in the following days [45]. The possible interaction between these time intervals and the prognostic performance of the CT-SS index cannot be investigated, because individual participant data were not available. In this study, the possible selection bias as the study limitation should be acknowledged. However, we tried to avoid any selection bias and there was no language limitation in the search strategy. There is potential for selection bias, because only published studies written in the English language were retrieved.

In this study, the prognostic efficiency of optimal CT-SS cutoffs to predict mortality of COVID-19 patients was also investigated using meta-analysis and the final pooled OR was calculated as 7.124 (95% CI 5.307–9.563). The result confirms that an optimal cutoff for CT-SS can accurately predict the prognosis of the COVID-19 patients. From the results, it could be concluded that the simple CT-SS has important clinical value and is of great significance for the diagnosis of patients who need more aggressive treatment. Thus, in addition to the typical radiological manifestations, CT-SS must be routinely included in the radiological reports for COVID-19 patients. This score could provide vital information about patient prognosis and might be potentially used to guide clinical management.

Study limitations

CT-SS as a valuable factor to predict mortality in COVID-19 patients has some limitations that must be acknowledged. A wide scoring range from 20 to 40 regions has been used for the quantification of COVID-19 pneumonia. This diversity in scoring approaches makes assessments more difficult. Therefore, CT-SS would be inherently complex and time-consuming. The similar segmented sectors of the right and left lungs have different sizes, because the right lung is larger than the left lung. For quantitative and semi-quantitative studies, these differences must be taken into account and dedicated software is required [46].

For included studies, chest CT scans were performed on all suspected individuals after triage. The interval between the onset of the symptom and the time of imaging is different for each patient. These data were not available to the authors. Therefore, the issue of time of imaging and their related implications on the scoring scheme could not be addressed.

Various scoring methods to quantify pulmonary involvement have been proposed in studies (including lung involvement by GGO or consolidations). Given that in the studies included in the meta-analysis, there are not enough results related to these scores; we cannot separately combine them and discuss their extent of lung involvement.

Conclusions

The results of this study point to an association between CT-SS and mortality of COVID-19 patients. The odds of mortality for COVID-19 patients could be accurately predicted using an optimal CT-SS cutoff in visual scoring of lung involvement.

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Author contributions SSZ: content planning, literature search and review, data collection, manuscript writing and editing, and meta-analysis. HS: content planning, literature search and review, data collection, and manuscript editing. NN: literature search and review, data collection, and manuscript editing. HK-A: project development, literature review, manuscript writing and editing, and meta-analysis. MS: literature review and manuscript editing.

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Availability of data and materials All data generated or analyzed during this study are included in the article.

Declarations

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

Ethical approval and consent to participate The study was approved by the local Medical Ethical Committee (approved number. IR.ABADANUMS.REC.1400.087).

Consent for publication Not applicable.

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