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The role of CT in prognosis prediction in COVID-19 patients

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Abstract

Introduction: The purpose of the present study was to summarize and evaluate previously published scientific studies examining whether computed tomography (CT) of the thorax can predict the COVID-19 prognosis. The aim is to clarify whether CT can predict the COVID-19 prognosis, and also if a CT examination can predict whether the patient will be admitted to the intensive care unit (ICU) or not.

Methods: Traditional digital literature searches were performed in the Medline, Pubmed and Embase databases. Subsequent back- and forward citation-based searches were then conducted. A total of 17 studies were included according to preset inclusion and exclusion criteria.

Results: All 17 included articles were retrospective studies. The mean number of patients included was 219 (range: 28-901). Overall, the studies showed that CT-findings of abnormalities in the lung tissue may provide a possible COVID-19 prognosis determination. A total of 11 studies used a quantitative scoring system to evaluate the lung images. Based on the percentage of lung involvement, the ICU patients had a higher score compared with patients not admitted to the ICU. The pathology type with the highest predictive value was crazy paving pattern followed by vascular enlargement and air bronchogram. Pleural effusion and pleural thickening can help estimating the prognosis according to some of the studies.

Conclusion: The present study shows that CT can contribute to early diagnosis and predict the prognosis when using scoring systems or qualitative assessment of certain radiologic features which are more prevalent in critically ill COVID-19 patients.

Introduction

Reliable diagnostics of COVID-19 were essential during the pandemic outbreak in December 2019. COVID-19 is a transmittable respiratory infectious disease that spreads rapidly and is caused by the acute respiratory virus SARS-CoV-2[1]. The symptoms vary from patient to patient, of which the most common include fever, cough, fatigue and shortness of breath, whereas less common are sore throat, headache, hemoptysis, confusion and tightness in the chest. Some patients are asymptomatic despite the viral infection[2]. The virus can cause acute respiratory distress syndrome and multiorgan failure, requiring respiratory support and intensive care[3]. The rapid spread of the virus and potentially severe prognosis indicate the importance of early identification of at-risk patients to begin treatment as early as possible, thus preventing complications arising from delayed treatment[3].

PCR has been the most used test for detecting the COVID-19 virus due to its efficiency, sensitivity and reliability[2,4]. Due to PCR test kit scarcity in the beginning of the pandemic, radiological examinations, X-rays, ultrasound, and computed tomography (CT), were assessed as alternative methods.

However, conventional chest X-ray has neither sufficient sensitivity nor specificity for COVID-19 and could neither confirm, nor exclude COVID-19[3,4]. In addition, performing an optimal x-ray exam is challenging for COVID-19 patients as they may be unable to stand or take full inspiration. A higher diaphragm level as a result of inadequate inspiration can give the illusion of ground glass opacities (GGO), and reduce the sensitivity of other significant findings, such as pleural fluid and consolidations. Moreover, in early stages of COVID-19 the X-ray may be normal.

CT thorax plays a significant role in examining COVID-19 because it can help monitor how the disease develops and evaluate the effects of treatment[4]. Typical findings from CT are GGO with peripheral distribution, consolidations and affection of several lung lobes, and crazy paving pattern as a sign of interstitial affection[5]. GGO are densifications that do not obliterate the architecture of the lung, whereas consolidations are consolidated densification where the densification obliterates the architecture of the lung. This means that vessels and bronchial walls cannot be separated from the opacities[5].

Although CT has higher sensitivity compared to conventional X-ray, the disadvantage is the higher radiation dose. In order to achieve an optimal balance between radiation dose and image quality, one must use the right exposure parameters. CT is sensitive for detecting COVID-19 but does not achieve adequate specificity for other acute interstitial pneumonia, likely producing similar findings. As the time from symptom onset to CT findings can vary between 3-20 days, normal images may be the outcome if the CT examination is performed shortly after the onset of symptoms[5].

The COVID-19 pandemic put intense pressure on hospitals and intensive care units (ICU). For a period, the number of patients in ICUs exceeded the available equipment, and healthcare personnel had to make choices of which patients should receive treatment[6]. If CT proves beneficial in predicting the prognosis of COVID-19, treatments can be initiated in an earlier stage of the disease, lessening the burden on hospitals and healthcare workers.

During the onset of the COVID-19 pandemic, many studies examined the applications of CT scans. For example, among studies that analyzed possible determinants of the development of severe illness, Koch et al. demonstrated that atherosclerosis could lead to significant lung impairment and respiratory failure and that CT thorax can be applied to assess the amount of calcium in the aorta to determine the risk of respiratory failure and death[3]. Furthermore, studies have shown that atherosclerosis may increase the risk of thrombus formation and myocardial damage in COVID-19 infection[7]. Another study demonstrated that patients with a higher proportion of adipose tissue have a higher risk of intensive care admission and respiratory support than patients with normal proportions of adipose tissue[8]. There is also evidence that CT thorax can contribute to the measurement of epicardial adipose tissue, which can also be a risk factor and thus determine the likelihood of hospitalization and death[9].

A comprehensive review published one year after the onset of the pandemic, found that CT is efficient in assessing the severity, determining the need for hospitalization or respiratory support, and in predicting possible outcomes[10]. However, Garg et al. argued in their review that CT should be discouraged and used judiciously in COVID-19 cases, with exceptions for patients with comorbidities, severe illness and treatment determination. Despite the cautions against excessive CT use, it was evident that COVID-19 patients almost always exhibited lung abnormalities that could be classified and indicate the severity of the disease[11].

Based on recent findings[12], it appears that CT has contributed to more than just diagnostics. Because it is crucial to identify high-risk patients early, the present review aims to identify the utility of CT in assessing a patient's prognosis for COVID-19 disease. It summarizes and evaluates previous studies that have investigated whether CT-thorax can predict the prognosis of COVID-19 and determines if it can predict whether the patient will be admitted to intensive care or not.

Methods

Three steps of computerized searches were conducted to identify scientific articles relevant to the subject: an explorative non-systematic pilot search, the main traditional systematic searches, and the final improving citation-based searches (Figure 1).

Initially, to get an idea of the scope of the subject literature and identify possible terms for subsequent systematic searches, unstructured *pilot searches* were conducted in Google Scholar and PubMed.

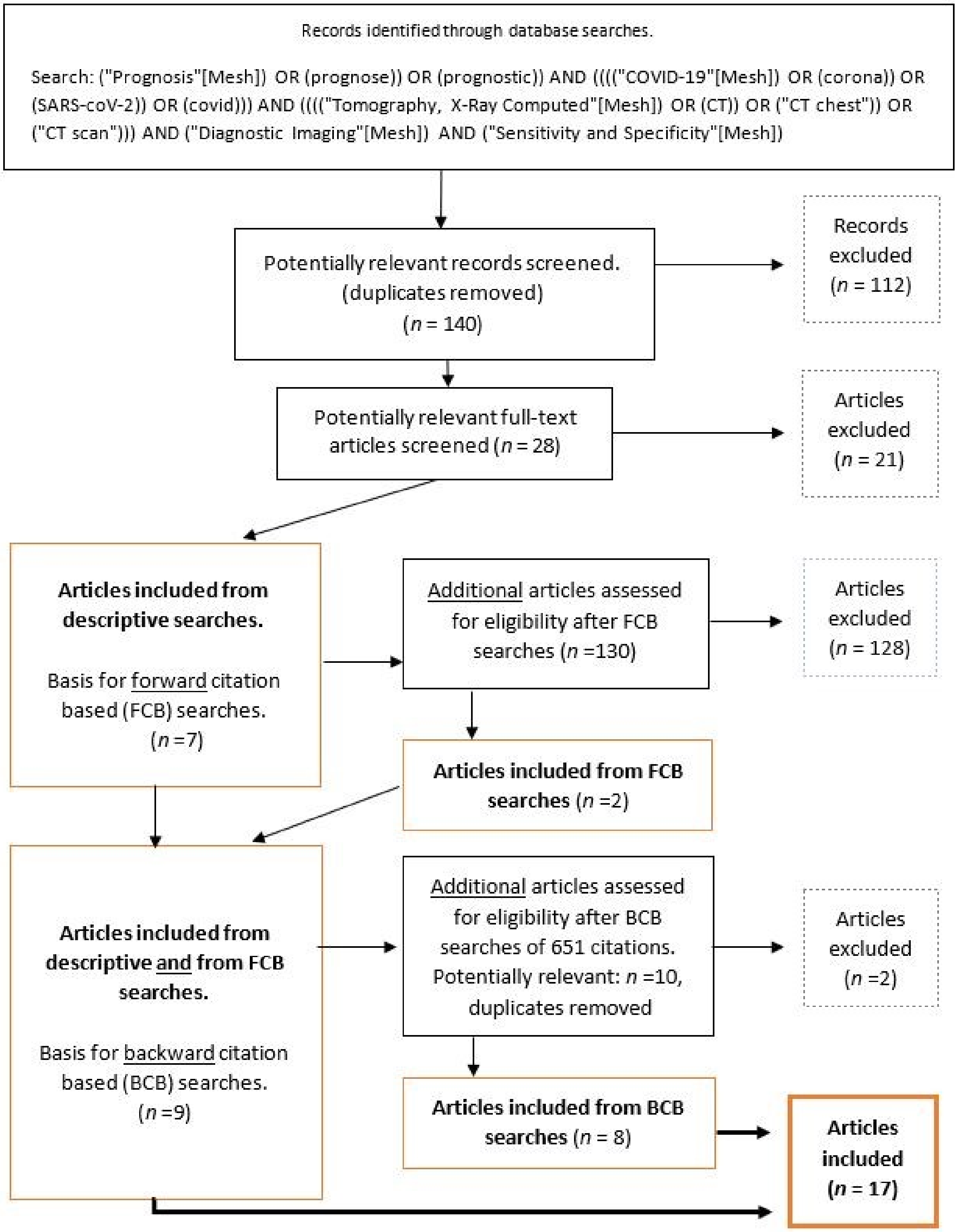

Figure 1. Prisma flow diagram

Then the main, *traditional descriptive step of searches* was conducted in PubMed, Medline and Embase to identify all relevant published articles in these databases. In the first round of this step, the search query included sets and combinations of single search terms only: "COVID-19", "CT", "prognosis", "diagnostic imaging" and "sensitivity and specificity", as well as possible synonyms to these words (Table 1).

Nevertheless, in order to reduce the risk of missing relevant articles, medical subject headings (MeSH) and Emtree were added to the search query in the second round. For example, "COVID-19" was chosen from the MeSH catalogue before terms such as "corona" "covid" and "SARS-CoV-2" were added to the query. The list of MeSH and Emtree terms differs somewhat, however, the meaning of the words is the same (e.g., the MeSH word was "COVID-19", whereas the Emtree was "coronavirus disease 2019"). The Boolean operators "OR" and "AND" were used to combine search terms, while "NOT" was avoided to further reduce the chance of losing relevant articles. The searches were performed in March 2023. A set of inclusion and exclusion criteria guided the process of selecting articles (Table 2).

Table 1. Search strategies and findings from traditional, descriptive searches (Search step #1)

#	Search	Articles identified	Potentially relevant articles	Articles included
PubMed				
1	(("Prognosis"[Mesh]) OR (prognostic)) OR (prognose))	2,063,544	n.a.	**n.a.**
2	((("COVID-19"[Mesh]) OR (corona)) OR ("sars cov-2")) OR (covid)	355,651	n.a.	**n.a.**
3	((("Tomography, X-Ray Computed"[Mesh]) OR (CT)) OR ("CT scan")) OR ("CT chest")	840,386	n.a.	**n.a.**
4	"Diagnostic Imaging"[Mesh]	2,896,143	n.a.	**n.a.**
5	"Sensitivity and Specificity"[Mesh]	644,885	n.a.	**n.a.**
	1 AND 2 AND 3 AND 4 AND 5	72	21	**4**
MedLine				
1	(MH "Prognosis+") OR (prognose) OR (prognostic)	2,052,073	n.a.	**n.a.**
2	(MH "Covid-19") OR (corona) OR (SARS-CoV-2) OR (Covid)	348,170	n.a.	**n.a.**
3	(MH "Tomography, X-Ray Computed+") OR (CT) OR (CT chest) OR (CT scan)	912,896	n.a.	**n.a.**
4	(MH "Diagnostic imaging+")	2,890,219	n.a.	**n.a.**
5	(MH "Sensitivity and specificity+")	643,910	n.a.	**n.a.**
	1 AND 2 AND 3 AND 4 AND 5	69	7	**7**
Embase				
1	´x-ray computed tomography`/exp ´CT´ ´CT chest´ ´CT scan´	1,073,698	n.a.	**n.a.**
2	´prognosis´/exp ´prognose´´prognostic´	1,146,684	n.a.	**n.a.**
3	´coronavirus disease 2019´/exp ´corona´´covid´´sars cov 2´	406,189	n.a.	**n.a.**
4	´diagnostic imaging´/exp	252,863	n.a.	**n.a.**
5	´sensitivity and specificity´/exp	462,083		
	1 AND 2 AND 3 AND 4 AND 5	3	1	**0**
TOTAL articles identified from traditional searches:				**11**

Table 2. Inclusion and exclusion criteria

Inclusion Criteria
Studies reporting original data
Studies written in English
Studies published after 31.12.2020
Studies examining CT thorax
Studies describing COVID-19 patients' prognosis
Studies with scoring system or radiological findings
Studies discussing ICU
Exclusion criteria
Studies of deep learning and/ or AI
Studies comparing low-dose CT with standard CT-protocol
Studies of COVID-19 and pregnancy
Studies aiming at developing a scoring system
Studies focused specifically on children
Studies with focus on image post-processing
Studies with follow-up CT after COVID-19 diagnosis
Studies including cancer patients
Studies reporting the effect of COVID-19 vaccines
Mortality studies
Studies reporting COVID-19 discovered on CT-scans performed for other clinical indications

Articles were initially screened and deemed potentially relevant based on an examination of their title and abstracts. Subsequently, potentially relevant articles were examined in full text for eligibility according to the above-mentioned criteria (Table 2). After excluding duplicate articles, the traditional descriptive search step resulted in an initial set of seven articles (Table 1). Screening of titles and abstracts, and the selection of full text articles was performed by two reviewers.

In order to further reduce the chance of missing relevant information, forward and backward citation-based searches[13] were conducted on the initial set of seven articles, respectively.

Articles that had cited articles in the set of the seven initially included studies were first assessed for eligibility (forward citation-based search), resulting in two relevant articles. Then a scan of eligible studies in the reference lists in the same initial set of seven articles (backward citation-based search) retrieved another eight articles. In total, the citation-based searches retrieved 10 articles, resulting in a set of 17 finally included.

Data extraction was performed by three reviewers. Data were extracted on study characteristics (year, country, patient population, inclusion and exclusion criteria, prognosis prediction approaches, number of observers, methodology), outcome measures and results related to the research question (CT-scanning protocols used, scorings systems and findings with predictive value).

A critical appraisal checklist from Joanna Briggs Institute (JBI) [14] was used to assess the quality of the reviewed studies by examining the extent to which the risk factors for bias in its design, conduct and analysis was addressed. The JBI quality score gave a value out of ten points, with higher scores indicating higher quality.

Results

Characteristics of included studies

A total of 140 articles were identified from the searches of three databases, after removing the duplicates. Out of these, 17 studies, which met the inclusion criteria, were included in the final analysis (Figure 1). Four studies were reported from Italy[15-18], three from Türkiye[19-21], three from Iran[22-24], two from Germany[25,26], and one from Poland[27], Japan[28], China[29], India[30] and Qatar[31].

All the included studies were retrospective studies, which analyzed the prognostic value of CT in patients with COVID-19 infection. One of them was two centers study[19] and the rest were single center studies.

The CT images were assessed independently by two radiologists who were blind to the clinical and laboratory data and a third radiologist made the final decision when inter-observational disagreement occurred, except for one study where CT images were analyzed by five radiologists[19] and two studies which don't provide any information about the observers who performed the image interpretation[25,26]. The radiologists had at least 5 years' experience in nine studies[16,18,20,23,24,27,28,30,31], at least 10 years in three studies[17,29,32] and at least 20 years in three studies[19,21,22].

The JBI quality scores were above 8 out of a possible 10 points except for one study with a score of 6 (Table 3.)

Patient population

These 17 studies included a total of 3717 patients and the sample size varied between 28 and 901 participants. All the patients included in the studies had a respiratory infection and had been diagnosed with COVID-19 using a PCR test.

Most of the patients were adults, of the seven studies[19,21,22,24,28,29,31] that provided the patient age interval only two[21,22] included children too. The mean age in most of the studies was between 60 and 70 with the lowest mean age 45 and the highest 68.

None of the studies excluded patients with extrapulmonary underlying diseases/comorbidities, such as hypertension, diabetes, heart disease or kidney disease. However, several studies excluded patients with other lung diseases[17,20,22,27,31] such as tuberculosis[22,27,31], pulmonary fibrosis[22,27], sarcoidosis[31], interstitial lung disease[17,27], pleural effusion[17], COPD[17,27], pneumonia[31] and lung cancer or malignancies[27,31].

The total number patients who needed treatment in the intensive care unit was 397 (the mean age was 72 years) and 135 of the patients included in the studies died.

Table 3. Study characteristics

Study	Patients	Exclusion criteria*	Prognose	JBI score
Aminzadeh et al[22]	n=201 mean age 55,4±17,6 (13-97)	Non-covid pulmonary diseases,	-intubation/ICU 18,5% -mortality 11,9%	9
Angeli et al[15]	n=301 mean age 69,8±13	Non-covid pulmonary diseases	-ICU 15,9% -mortality 30,5%	10
Baysal et al[19]	n=405 mean age 52 (36-65)	History of trauma	-ICU 9,63% -mortality 6,9%	9
Buttner et al[25]	n=28 mean age 61 (49-72)		-ICU 64,2%	8
Colombi et al[16]	n=236 mean age 68 (66-70)	Negative CT-findings	-ICU 54,2%	6
Hajiahmadie t al[23]	n=192 mean age 57,5±1,1	Asymptomatic	-ICU 18,8% -mortality 5,2%	9
Hosse et al[26]	n=265 mean age 68 (56-27)		-ICU 51,7%	8
Leonardi et al[17]	n=189 mean age 61 (53-70)	Coexisting pulmonary and pleural diseases	-ICU/intubation 14,3%	8
Nair et al[31]	n=67 mean age 45 (24-75)	Pre-existing lung diseases or lung metastasis	-ICU 34,3% -mortality 4,5%	8
Parry et al[30]	n=89 mean age 49,1±14,1		-ICU 22,5%	8
Pence et al[20]	n=901 mean age 56,9	Age under 18 Suboptimal image quality Chemotherapy and/or radiotherapy History of lung mass and/or lobectomy	-ICU 21% -mortality 12,4%	8
Rorat at al[27]	n=61 mean age 62,5 (50-80)	Pulmonary disease (cancer, tuberculosis, fibrosis, obstructive disease) Poor image quality	-ICU 16,4%	8
Salaffi et al[18]	n=165 mean age 61,5±12,5		-ICU 18,2%	10
Sun et al[29]	n=84 mean age 46 (20-79)	Negative findings Artifacts	-ICU 27,4	10
Tabatabaei et al[24]	n=120 mean age 54,9±17		-ICU 9,2% -mortality 10,8%	8
Tekcan Sanli et al[21]	n=231 mean age 48,1±15,6 (5-94)		-ICU 8,7%	8
Yamada et al[28]	n=69 mean age 58,7(47-72)	History of lung resection	-intubation 72,5%	10

*All studies mentioned either positive PCR and a CT-thorax examination as an inclusion criterion or lack of such as an exclusion criterion.

CT scanning protocols

In the studies that mentioned the workflow and timing, CT was performed on an average 4.3 days (between 1–7 days) after symptom onset[30], within 12 hours after clinical evaluation and laboratory test results[16] or few hours after admission[17].

In all studies the CT-examinations were performed at full inspiration with the patient in supine position and without administration of intravenous contrast agent except for patients with pulmonary embolism suspicion.

The CT scanning protocols are relatively similar in the included studies considering the presence of scanners from different manufacturers (often mentioned models were GE Light-speed VCT, Canon Aquilion Prime, Siemens Healthineers and Siemens Somatom) and the wide range of technological advances (16-slice scanners are mostly used[15-17,19,20,22,23,28-30], but also 64-slice[27], 128-slice[19], 256-slice[28], 640-slice[31] and 192 dual-energy CT (DECT) [20]).

The use of a low-dose protocol was specifically mentioned in some of the studies[16,20,21,24-26] and some of them reported radiation dose reduction factors as the use of iterative reconstruction[18,20,25,26], and body weight adjusted tube voltage[16,19,30,31]. The most used tube voltage was 120kV[17,18,22-24,27-29], followed by 100kV as standard setting[25,26] or as alternative for patients with body weight under 80kg[16,19,30,31], while only two studies reported higher voltages (130kV in overweight patients[16] of 140kV as standard setting[21]). There was observed quite large variation in the tube current settings. The pitch was high (1-1.15) in all studies that reported the value of this parameter[16,17,21,22,28,30,31].

Only three studies reported radiation doses, the average CT dose index volume (CTDIvol) was 4.9 mGy[24], 11.21 mGy[28] and 3.45 mGy in patients with a body weight under 80kg[19] and 5.6 mGy in patients with a body weight over 80kg[19]. There was reported an average dose length product (DLP) of 525,54 mGycm[28] and effective doses of 1.4mSv and 2.7mSv in patients with body weight under and over 80kV respectively[19], or 1mSv in all patients[25].

Prognosis prediction approaches

While some of the studies focused solely on quantifying the radiological features using different scorings systems[15,19,20,22,27,31], some of the studies performed both subjective image evaluation to find pathology types with the high predictive value and quantitative measurements[16-18,21,23-26,28,29] and only one study used only qualitative image assessment[30]

Common findings and their predictive value

The studies which used subjective assessment alone or combined with quantitative scoring stated that they use Fleischner Society nomenclature recomendations[16-18,21,23-26,28-30]

A wide span of findings has been described across the studies included for review (Table 4). With regards to the type of pathology, GGO and consolidation were the dominant abnormalities in all patients[16-18,21,23-26,28,29].

Table 4. Overview of the CT-scanning protocols used, scorings systems and findings with predictive value

Study	Protocol	Scoring system	Findings with predictive value
Aminzadeh et al[22]	120kV	-Total lung involvement (TLI) score based on % involvement in each lobe -Modified TLI score- based on sum of lobe scores multiplied with the number of segments in each lobe.	No difference in prognostic value between TLI and modified TLI score
Angeli et al[15]	-only reconstruction parameters	Pulmonary involvement (PI) Pulmonary consolidation (PC) Scores based on percent, manuelt	PI significant PC-not significant
Baysal et al[19]	100 or 120kV-based on weight CTDIvol 3.45mGy <80kg 5.6mGy >80kg Eff dose 1.4 and 2.7mSv	Zonal CT Visual Score (ZCVS) Lungs divided in zones, score based on % involvement in each zone.	
Buttner et al[25]	Low dose, 100kV IR Eff dose<1mSv	Lung involvement-subjective estimation and semiquantitative (%)	Semi-quantitative measurement better than subjective.
Colombi et al[16]	Low dose 110kV og 130kV-vekt	-software-based quantification of well aerated lung (WAL) -visual assessment	-diffuse pattern -nr of involved lobes
Hajiahmadiet al[23]	120kV	-Computed tomography severity score (CSS)semi-quantitative, scores degree of involvement	CSS pred value The distribution of the lesions was not shown to be associated with a poor prognosis
Hosse et al[26]	Low dose, 100kV IR	-Manuelt GGO - consolidations (%) -Semi-quantitative measurement (SSQ)	SSQ better than subj.
Leonardi et al[17]	120kV	-analyzed typical features -quantitative assessment, semiautomatic bordering of affected tissue, %affected lung	-GGO+consolidation -crazy paving -bronchial wall thickening -air bronchogram -bronchial distortion -vascular enlargement -central+peripheral distribution -limph node involvement

Nair et al[31]	100-120kV	-visual coronary calcification score (V-CACS) -CT severity score (CTSS) - based on % parenchymal opacification in 20 regions	
Parry et al[30]	100-120kV	-Subj assessment	crazy paving pattern, consolidation with air bronchogram and segmental or subsegmental vessel enlargement
Pence et al[20]	Low dose IR	-semi quantitative scores based on % involvement in each lobe -clinical score -combined score (radiological and clinical)	
Rorat at al[27]	120kV	-Quantitative modeling with Thoracic VCAR software (GE Healthcare, Chicago, IL, USA) -percentages of ground-glass opacity volume, consolidation volume and emphysema volume in both lungs. -total lesion calculation was also performed	-number of lobes involved -bilateral involvement not significant -crazy paving pattern not significant -mixed peripheral and central distribution
Salaffi et al[18]	DE 120kV IR	-Subj assessment -CT severity scoring system	-distribution not significant -consolidation -crazy paving pattern -interlobular septal thickening -bronchial wall thickening not significant -air bronchogram -pleural effusion -pleural thickening not significant -vascular dilatation -lymphadenectasis
Sun et al[29]	120kV	-software Pulmonary Infection Assisted Diagnosis. -total lesion score -GGO score (%) -consolidation score (%)	-nr of lobes involved -mixed peripheral and central distribution -crazy paving -air bronchogram -lymphadenopathy not significant -pleural effusion not significant -total lesion score demonstrated best predictive performance
Tabatabaei et al[24]	Low dose 120kV CTDIvol4.9	-Subj assessment -percentage of lung involvement	-bilateral lung disease not significant Predominant GGO -central involvement %involvement

			-crazy paving - -air bronchograms -pleural effusion not significant
Tekcan Sanli et al[21]	Low dose 140kV	-subj assessment -percentage of lung involvement	-distribution not significant -crazy pavement pattern -nr of affected lobes -total nr of lesions -% of affected lung parenchyma -vascular enlargement -lobar consolidation -mediastinal lymphadenopathy -pleural effusion -pleural thickening -air bronchogram
Yamada et al[28]	120kV DLP525mGcm CTDIvol11.21	-Quantitative analysis of percentage of the total volume affected -Opacification pattern classification: peripheral, multifocal and diffuse pattern	Diffuse pattern-highest risk Subj noninferior to quantitative analysis.

Other common findings were halo sign, crazy paving pattern, bronchial wall thickening, air bronchogram, bronchial distortion, vascular enlargement centrilobular nodules, septal thickening, perilobular opacities, reticular pattern, architectural distortion, subpleural bands, traction bronchiectasis.

While GGO is the most common finding in COVID-19 patients[16-18,21,23-26,28,29] it did not show predictive value in any of the included studies unless it appears together with consolidation; consolidation alone did not show predictive value in any the studies either. The pathology type with the highest predictive value was crazy paving pattern which was shown to be conclusive in all studies which mention it[17,18,21,24,29,30] except for one study which found it non significant[27]. Vascular enlargement[17,18,21,30] and air bronchogram[17,18,21,24,29,30] has also been documented to have predictive value in several studies. Pleural effusion and pleural thickening can help estimating the prognosis according to some of the studies[18,21]; however, other studies did not find these features useful as predicting tools[24,29]. There was no consensus among the studies regarding the predictive value of bronchial thickening[17,18] and lymph node involvement[17,18,29]. Extrapulmonary findings like pericardial effusion[18] and splenomegaly[24] were also shown to have predictive value.

In numerous studies, the readers assessed the presence, pattern, location, distribution of parenchymal abnormalities[16-18,21,23,24,27,28,30]. Mixed peripheral and central distribution was shown to indicate a poor prognosis[17,27,29,30] and also a diffuse pattern was associated with higher probability of subsequently required ICU care[16,28] while other studies found that distribution was not significant for the prognosis[21,23].

Quantitative assessment and scoring systems
The majority of the studies used a quantitative measurements or scoring systems.

The extent of lung involvement on CT was an approach shown to be effective in multiple studies regardless of the variety of measurement methods employed. While some of the studies used the percentage of affected pulmonary parenchyma[24-29] or software-based quantification of the percentage of well-aerated lung (WAL) [16], other used more complicated scoring systems. When using numerical scores, the imaging of the lungs was divided into three[18], four[22], five[15,20], six[19,22,23] or even 20 regions[31] where each region received a numerical score based on the percentage of lung involvement and these numbers where summated to get a total score. In some studies, the assessment and scoring of lung involvement were performed manually, while in others[16,17,27,29], various types of software were utilized to evaluate the extent of lung involvement.

Several studies used two or more scores in their calculations and the scores were either compared to see which was best suited[15,16,18,20,22] or used in combination to strengthen the probability of the most correct prognostic prediction[16,18].

The use of combined score based on percentual involvement and the nature of involvement (GGO vs consolidation ratio) was not show to increase the predictive value[18], and neither pulmonary consolidation scores based on percent affected tissue[15] had a significant impact on the prognostic.

A study which evaluated the predictive value of both semi quantitative CT-score based on % involvement in each lobe, clinical score, and combined score (based on CT and clinical score) demonstrated quite similar sensitivity for those three scores (the CT-score had slightly higher sensitivity than the clinical score and equal sensitivity with the combined score). The CT-score had higher specificity than clinical score, but the specificity of the combined score was highest[20]. Another study with a quite similar approach evaluated the predictive value of both CT severity score (CT-SS)-based on % parenchymal opacification in 20 regions, visual coronary calcification score V-CACS and a combination of those two and showed higher sensitivity of CT-SS compared to both V-CACS and combined score. The CT-SS had higher specificity than V-CACS, while the specificity of the combined score was highest[31].

The predictive value of the quantitative methods was found to be slightly superior to subjective assessment of pulmonary involvement[16,25,26]; however, one study found subjective assessment non-inferior to quantitative analysis[28]. Both visual assessment of the extent of lung involvement and software-based quantification of the well-aerated lung (WAL) were independent predictors of ICU admission or death in patients with COVID-19[16].

Certain studies which employed a scoring system could also state in their results the cut-off values[18,19,27,31] that could make admission to the ICU more probable. However, some of the studies which confirmed the potential role of quantitative analysis of chest CT performed in predicting the patient outcome recommended an evaluation of radiological data integrated with clinical and laboratory parameters in order to significantly enhance the predictive power[15,17,18,27].

Discussion

The main findings of the present review of studies that have investigated whether CT-thorax can predict the prognosis of COVID-19 are that it can be used to evaluate the prognosis of COVID-19 pneumonia, stratify triage patients based on risk, and guide treatment choices. These findings support previous studies of the role of CT scans in diagnosing and managing patients with COVID-19 pneumonia10, thus adding evidence to previous indications that CT contributes to more than just diagnostics12. The importance of CT in managing COVID-19 is emphasized despite judicious advice about making reservations about using CT in these patients11.

Looking into the prognostic and therapeutic implications of CT imaging in COVID-19 naturally leads to a closer examination of the CT scanning parameters as their influence on image quality can affect both the diagnostic confidence and the prognostic utility of these examinations

CT scanning protocols

Among the CT scanning parameters, tube voltage, which has the highest influence on radiation dose (given that radiation dose is proportional with the square of kV) was quite similar across the studies. Variations in tube current are as expected due to the use of tube current modulation and variations in average weight and BMI across the countries where the studies were performed. Other approaches have been used to reduce radiation doses, such as use of dual energy, iterative or deep learning–based reconstructions for noise reduction.

The use of different CT scanning protocols, and variation in reported radiation doses might result in different image quality which in turn might influence the frequency of the reported findings. On the other side, variation in acquisition parameters is expected given the presence of many different CT scanners, and one can assume that the CT examinations nevertheless resulted in images with comparable diagnostic and prognostic value. This assumption is supported by evidence that low-dose chest CT is feasible for imaging COVID-19 patients and offers diagnostic quality comparable to that of standard thorax CT protocols[33].

A parameter that has proven to be fundamental for patient risk stratification is the timing of the CT-scan which influences the sensitivity[34]. Unfortunately, only three of the included studies provided that information.

Prognosis prediction approaches

The present review showed that extension of lung disease assessed using a quantitative method may predict the need for ICU admission in patients with COVID-19 and that several radiologic features identified during qualitative image assessment have the potential to represent prognostic imaging markers in patients with COVID-19 pneumonia. Some of the reviewed studies compared quantitative and qualitative assessment methods and there was no consensus about the superiority of either one of the methods as prognostic prediction tool.

The studies that utilized subjective assessment, either alone or in combination with quantitative scoring, reported the use of Fleischner Society nomenclature. This approach is advantageous, as standardizing the reporting of chest CT for suspected COVID-19 has been shown to enhance communication, improve the clinical significance of results, and facilitate more efficient diagnosis and prognosis prediction. [34]

The pathology types with the highest predictive value were crazy paving pattern, vascular enlargement, air bronchogram, pleural effusion and pleural thickening. In addition to estimation of lung parenchyma involvement, chest CT can provide extrapulmonary data to predict COVID-19 severity[18,21,24,34].

The present study discovered scoring systems with various complexity degree, however, the scoring systems used in the reviewed articles had quite similar sensitivity and specificity. One can therefore assume that the scoring system used in prognosis prediction in COVID-19 patients does not have to be very complex as the complexity of the assessment method can make it unpractical for daily clinical use. The most uncomplicated method was classification of the images by the opacities' pattern into peripheral, multifocal and diffuse which showed to be very effective in prognosis prediction, noninferior to quantitative assessment[28]. However, the advantage of employing scoring systems is the possibility of using cut-off values in prediction of the need of ICU care.

Limitations

The present study based on a systematic literature review shows consensus regarding the predictive value CT has for COVID-19 patients' prognosis. However, the output of the systematic literature review may be influenced by the fact that journals tend to accept studies with positive findings and reject studies that have reached other conclusions.
The study's inclusion criteria were limited to studies published in English, which is a considerable limitation since the initial outbreak was in Wuhan province in China and one can assume that there are a number of relevant studies published in Chinese.
The included studies used different number of radiologists and different experience of the interpreting radiologists, and that may induce some variability in the reported CT findings[35].
The non-exclusion of patients with some other lung diseases in some articles complicates the derivation of generalizable conclusions as chronic lung diseases may exaggerate the severity of findings on CT, leading to an overestimated prognosis for ICU admission or mortality.

Conclusion

The present literature review showed that thorax CT can be used to evaluate the prognosis of COVID-19 pneumonia, stratify triage patients based on risk, and guide treatment choices. Certain radiologic features are shown to be more prevalent in critically ill and patients and have predictive value in estimating the prognostic and qualitative assessment can therefore be a valuable predictive tool both when used alone or in addition to quantitative scoring systems. However, these findings should be evaluated together with patients' age, comorbidities, and laboratory parameters.

Statements and Declarations

Competing Interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

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