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Original Article

Effect of demographic factors on CT findings and prognostic implications of imaging in COVID-19 participants: A multicenter study

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Abstract

Introduction: Studies show that chest computed tomography (CT) findings in patients with COVID-19 may differ among different populations, which could be attributed to demographic differences. The present study is done to provide evidence regarding the effect of demographic factors on imaging findings.

Methods: This retrospective study involved 202 participants with COVID-19. The participants underwent CT imaging before hospitalization or on the first day of admission. Two expert radiologists determined each patient's radiologic signs and symptoms.

Results: by comparing dead participants and survivors, airspace consolidation, air Bronchogram, and posterior segment involvement were commonly seen in passing participants. Lung score and mean number of involved segments were higher in passing participants. Participants over 75 were less likely to have lymphadenopathy, septal thickening, and sub-pleural transparent lines. The area under the curve was 0.706 (95% CI: 0.631-0.782), higher among women older than 75.

Conclusion: Although demographic features generally do not affect common imaging findings in COVID-19 participants, the prognostic significance of chest CT imaging may differ based on gender and age.

Introduction

Severe-acute-respiratory-syndrome-related coronavirus (SARS-CoV-2), a highly contagious disease, has rapidly spread to over 212 countries worldwide.it is closely related to bat SARS-like coronavirus but from a separate clade.[1] The virus can be transmitted from human to human through respiratory droplets, contact, and even fecal-oral transmission. Due to its impressive transmission speed, the current outbreak of the novel coronavirus is expected to surpass previous beta-coronavirus outbreaks of the 21st century, including SARS-CoV and Middle East respiratory syndrome-related coronavirus (MERS-CoV), and become a public health crisis.[2]

The major structures of SARS-CoV-2 that contribute to tissue damage include the spike surface glycoprotein, small envelope protein, matrix protein, and nucleocapsid protein.[3] The spike surface glycoprotein binds to host receptors through the receptor-binding domains of angiotensin-converting enzyme-2 (ACE2), identified in numerous human organs, including pulmonary interstitial tissue.[4] Respiratory tract infection manifests from mild pneumonia to acute respiratory distress syndrome and multiple organ failure, leading to death.[5]

The standard method for detecting SARS-CoV-2 infection is the polymerase chain reaction (PCR) method applied to respiratory tract samples; however, due to the low sensitivity of RT-PCR at initial presentation and some intrinsic limitations, several studies have suggested using imaging modalities such as computed tomography (CT) as a better method of screening those with respiratory symptoms. Evidence suggests that this modality could be used to estimate disease severity and predict the prognosis of interstitial pneumonia in participants with a high degree of suspicion for SARS-CoV-2 infection.[6-8] Although the widespread use of CT imaging in detecting COVID-19 initially showed promising results, inconsistencies in involvement patterns reported in different studies and the rise in estimated false-negative cases have led scholars to

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rethink the role of CT imaging in diagnosing the disease.[9,10]

One of the most essential inconsistencies is the varying results in different populations with different demographic outcomes, such as studies reporting more pronounced involvement in male-elderly populations. Clinical studies on laboratory results and treatment measures report the same.[11,12] This study was performed to better understand whether CT imaging results differ between sexes or age groups and whether the predictive value of CT imaging remains solid among other demographics.

Methods

Participants

The present retrospective study was performed on consecutive participants presenting to three emergency departments of tertiary medical or educational centers affiliated with two different universities of medical sciences. All participants presenting with signs and symptoms of COVID-19 infection and positive for SARS-CoV-2 on PCR who underwent CT imaging were included in this study. Based on Institutional guidelines, CT imaging was only performed for participants considered for hospitalization. Exclusion criteria were the presence of underlying pulmonary conditions (such as tuberculosis, concomitant bacterial pneumonia on admission (proven by the culture of lavage specimens), silicosis, idiopathic fibrosis, history of lung carcinoma of any kind, or those with metastatic malignancies) and pregnancy.

Molecular assay

PCR was done for specimens obtained from the nasopharynx and oropharynx, which were based on guidelines issued by the WHO. Taqman® Premix TAKARA diagnostic kits (TaKaRa, Dalian, China) were used for participants. All participants underwent molecular assay on the first day of admission, and if needed, secondary molecular assay tests were conducted in the wake of a negative PCR result but high suspicion of infection. During our study, the Delta subtype of COVID-19 was the most prevalent.

Imaging protocol

All participants underwent imaging based on the latest institutional guidelines adapted from the World Health Organization and the Radiologic Society of North America.[1] All imaging was performed by two Siemens SOMATOM (Hannover, Germany) scanners on the admission day in the emergency department, with the following technical specifications: participants were set in the recumbent position with both arms located over the head; 1-mm slice thickness in increments of up to 10 mm from the lung apices through the superior margin of the hemidiaphragm, with the patient being instructed to do a deep inspiration; tube voltage was set at 120 kV; tube current time set at 50–100 mAs, and pitch set at 0.8–1.5. Parenchymal window settings were set for all participants to a range of window levels and a window width of 500. All imaging was archived in a picture archiving and communications system, and the scanner did image reconstruction automatically. No contrast media was injected.

Imaging findings

Two board-certified radiologists with at least five years of experience interpreted radiologic findings . The radiologists observed the images simultaneously, and in case of disagreement, the opinion of another radiologist with more than ten years of experience was demanded. A checklist is an interpretation with the following items:

- Location of the lesions regarding being unilateral or bilateral, involving the superior or inferior segments of the lungs, and number of lesions (single, multiple, or diffuse involvement)
- Imaging signs such as ground-glass opacities, airspace consolidation, air-bronchogram, halo sign, reverse halo sign, nodules, cavities, the reticulonodular pattern of involvement, bronchial wall and septal wall thickening, the tree in bud sign, the existence of pleural effusion or thickening, lymphadenopathies, and bronchiectasis
- The situation of individual lesions in posterior or anterior segments of the lungs
- Number of involved lobes and the lobes involved (right upper lobe, right middle lobe, right lower lobe, left upper lobe and left lower lobe.
- Lung score was calculated based on previous studies.[7,13-15]

Statistical analysis

The statistical analysis was conducted using SPSS version 23.0.0 in Chicago, Illinois, US. Quantitative data were presented as mean and standard deviation, while qualitative data were presented as frequency. The Smirnov-Kolmogorov test was used to test the normality of distributions. The chi-square test compared qualitative variables; the independent T-test and Mann-Whitney U compared mean results. The receiver operating characteristic curve showed the diagnostic ability of binary classifiers. The chi-square test determined the relationship between categorical variables. Mann-Whitney U tested distribution shapes. Independent T-test compared means of two groups. The frequency procedure in SPSS computes summary statistics for one variable. All statistical tests were two-sided, and a P value of ≤ 0.05 was considered statistically significant with a 95% confidence interval (CI).

Ethical considerations

The local ethics committee approved the study. The ethics committee deemed written informed consent unnecessary as the study was retrospective, and no individual data of participants were disclosed. However, every patient

included in the study had signed a consent form to have their data used in a non-interventional study.

Results

The study included 202 participants, with 87 females and 115 males. Among males, 29 had diabetes, 31 had hypertension, 11 had ischemic heart disease, and 4 had chronic renal failure. Among females, 21 had diabetes, 41 had hypertension, 5 had ischemic heart disease, and 3 had chronic renal failure. The difference between the two groups in terms of each condition alone and all combined conditions was insignificant ($P > 0.1$ in all cases).

The study included individuals with an average age of 67.1 ± 16.9, and there was no significant difference in age between male and female participants. Out of all the participants, 140 survived, and 62 died due to the disease, with no significant difference in mortality between male and female participants. Of those who died, 38 were male, and 24 were female, but the difference was insignificant. Additionally, 69.4% of the deaths were in participants over 65, and 48.4% were over 75. The study analyzed three demographic subgroups: survivors vs. non-survivors, male vs. female participants under 75 years old vs. those over 75 (Table 1).

The most common imaging finding among our participants was ground-glass opacities, which were seen in 187 participants (92.6%), followed by airspace consolidation, which was seen in 81 participants (40.1%). The most common pattern of involvement was bilateral, multifocal, and peripheral involvement, which was seen in 169 (83.7%), 138 (68.3%), and 172 (85.1%) participants, respectively. The most common lung lobes involved were the right lower and left lower lung lobes, which were involved in 162 and 159 participants (70.3% and 67.3%, respectively) (Table 2).

The radiologic signs and patterns of involvement were similar in both genders. However, non-survivors had a higher incidence of airspace consolidation, air bronchogram, and posterior segment involvement. These participants also had higher lung scores and more lobe involvement (Table 3). The study found that participants over 75 with COVID-19 had a higher rate of diffuse involvement with a higher rate of anterior segment distribution but a lower rate of lymphadenopathy, septal thickening, and sub-pleural transparent lines. These participants also had less multifocal involvement. Although they had a significantly higher number of involved lobes, their lung score was not notably different from other age groups.

The lung score was compared among six age groups, and it was found that there was a significant difference among the age groups ($P = 0.02$). This difference was due to the variation between the age groups of 71-80, 41-50, and 51-60. However, no significant difference was observed in other subgroups (Table 4).

Figure 1 demonstrates the ROC analysis for lung score and mortality. The area under the curve was 0.706 (0.631-0.782, 95% CI). Figure 2 shows the ROC analysis for lung score and mortality between the two sexes. The area under

Table 1. Demographic information.

	Number	Age
All participants	202	67.1 ± 16.9
Male	115	64.6 ± 12.7
Female	87	69.6 ± 21.1

Table 2. Radiologic signs and patterns of involvement of the patients are included

Radiologic signs	Frequency	Pattern of involvement	Frequency
Ground glass opacities	187 (92.6%)	Unilateral	26 (12.9%)
Airspace consolidation	81 (40.1%)	Unifocal	22 (10.9%)
Septal thickening	54 (26.7%)	Bilateral	169 (83.7%)
Air bronchogram	65 (32.2%)	Diffuse	47 (23.3%)
Crazy paving	45 (22.3%)	Multifocal	138 (68.3%)
Sub-pleural transparent line	41 (20.3%)	Posterior	157 (77.7%)
Reversed halo sign	3 (1.5%)	Central	70 (34.7%)
Peribronchovascular involvement	26 (12.9%)	Peripheral	172 (85.1%)
Atelectasis	14 (6.9%)	Anterior	60 (29.7%)
Cavitation	2 (1.0%)	RUL	140 (69.3%)
Lymphadenopathy	28 (13.9%)	RLL	162 (80.1%)
Halo sign	1 (0.5%)	RML	142 (70.2%)
Reticulonodular lesions	7 (3.5%)	LLL	159 (78.7%)
Nodular opacities	19 (9.4%)	LUL	136 (67.3%)
Tree in bud signs	1 (0.5%)	Mean Number of lung lobes involved	3.6 ± 1.4
Bronchiectasis	11 (5.4%)	Mean lung score	11.475 ± 6.42
Pleural effusions	31 (15.3%)	Median lung score	12.0

Table 3. Comparison of radiologic signs, involvement pattern, and lung scores in different demographic groups

Criteria	Over 75 years old			Gender			Death		
	No	Yes	*P*	Female	Male	*P*	No	Yes	*P*
Ground glass opacities	108 (91.5%)	79 (94%)	0.5	83 (95.4%)	104 (90.4%)	0.2	31 (93.6%)	56 (90.3%)	0.9
Airspace consolidation	48 (40.7%)	33 (39.3%)	0.8	34 (39.1%)	47 (40.9%)	0.8	45 (32.1%)	36 (58.1%)	0.01
Septal thickening	44 (37.3%)	10 (11.9%)	0.0001	28 (32.2%)	26 (22.6%)	0.13	37 (26.4%)	17 (27.4%)	0.8
Crazy Paving	29 (24.6%)	16 (19%)	0.3	19 (21.8%)	26 (22.9%)	1	26 (18.6%)	19 (30.6%)	0.06
Air bronchogram	37 (31.4%)	28 (33.3%)	0.8	28 (32.2.%)	37 (32.2.%)	1	29 (20.7%)	36 (58.1%)	0.001
Sub-pleural transparent line	36 (30.5%)	5 (12.2%)	0.0001	17 (19.5%)	24 (20.9%)	0.8	32 (22.9%)	9 (14.5%)	0.19
Halo sing	1 (0.8%)	0 (0.0%)	0.9	1 (1.1%)	0 (0.0%)	0.4	1 (0.7%)	0 (0.0%)	1
Reversed halo sign	3 (2.5%)	0 (0.0%)	0.2	1 (1.1%)	2 (1.7%)	1	3 (2.1%)	0 (0.0%)	0.5
Nodular opacities	15 (12.7%)	4 (4.8%)	0.08	9 (10.3%)	10 (8.7%)	0.8	15 (10.7%)	4 (6.5%)	0.4
Reticulonodular pattern of involvement	5 (4.2%)	2 (2.4%)	0.7	3 (3.4%)	4 (3.5%)	1	6 (4.3%)	1 (1.6%)	0.6
Tree-in-bud appearance	1 (0.8%)	0 (0.0%)	1	0 (0.0%)	1 (0.9%)	1	1 (0.7%)	0 (0.0%)	1
Atelectasis	11 (9.3%)	3 (3.6%)	0.16	7 (8.0%)	7 (6.1%)	0.5	11 (7.9%)	3 (4.8%)	0.5
Peribronchovascular	20 (16.9%)	6 (23.1%)	0.054	13 (14.9%)	13 (11.3%)	0.5	17 (12.1%)	9 (14.5%)	0.6
Bronchiectasis	9 (7.6%)	2 (2.4%)	0.12	3 (3.4%)	8 (7.0%)	0.3	8 (5.7%)	3 (4.8%)	1
Cavitation	1 (0.8%)	1 (1.2%)	1	1 (1.1%)	1 (0.9%)	1	2 (1.4%)	0 (0.0%)	1
Pattern of involvement									
Unilateral	13 (11%)	13 (15.5%)	0.3	9 (10.3%)	17 (14.8%)	0.4	20 (14.3%)	6 (9.7%)	0.4
Unifocal	12 (10.2%)	10 (11.9%)	0.8	7 (8%)	15 (13%)	0.3	13 (9.3%)	9 (14.5%)	0.3
Peripheral segments	96 (81.4%)	76 (90.5%)	0.1	75 (86.2%)	97 (84.3%)	0.8	120 (85.7%)	52 (83.9%)	0.8
Anterior segments	27 (22.9%)	33 (39.3%)	0.013	28 (32.2%)	32 (27.8%)	0.5	37 (26.4%)	23 (37.1%)	0.1
Bilateral	103 (87.3%)	66 (78.6%)	0.12	76 (87.6%)	93 (80.9%)	0.2	113 (80.7%)	56 (90.3%)	0.1
Multifocal	94 (79.7%)	44 (52.4%)	0.001	61 (70.1%)	77 (67.0%)	0.6	93 (66.4%)	45 (72.6%)	0.4
Central	40 (33.9%)	30 (35.7%)	0.881	33 (37.9%)	37 (32.2%)	0.4	40 (28.6%)	30 (48.4%)	0.01
Diffuse	20 (21.5%)	27 (37.5%)	0.03	23 (32.4%)	24 (25.5%)	0.3	35 (27.8%)	12 (30.8%)	0.8
Posterior segments	85 (72.0%)	72 (85.7%)	0.02	67 (77.0%)	90 (78.3%)	0.8	103 (73.6%)	54 (87.1%)	0.04
Lymphadenopathy	22 (18.6%)	6 (7.1%)	0.023	13 (14.9%)	15 (13.0%)	0.8	20 (14.3%)	8 (12.9%)	1
Pleural effusion	20 (16.9%)	11 (13.3%)	0.55	16 (18.4%)	15 (13.0%)	0.3	17 (54.8%)	14 (22.6%)	0.08
Number of lung lobes involved	3.9±1.3	3.2±1.5	0.01	3.7±1.3	3.5±1.5	0.3	4.2±1.0	3.3±1.5	0.0001
Mean lung score	12.0±6.1	10.6±6.7	0.1	11.6±6.5	11.3±6.2	0.7	10.0±6.1	14.7±5.8	0.0001

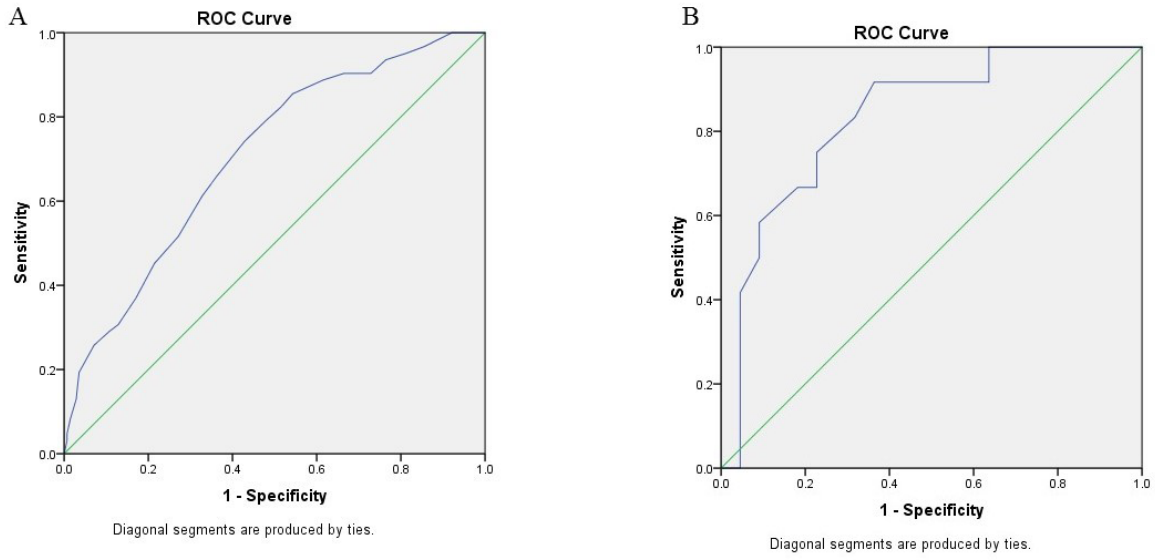

Figure 1. (A) ROC curve depicting the relation between lung score and mortality in all patients included in the study. (B) ROC curve showing the relation between lung score and mortality in female patients older than 75

Table 4. Comparison of lung score among different age groups

Age groups		Mean difference (first-second)	Sig.
1	2	-3.5190	.075
	3	-3.1790	.089
	4	-1.5048	.387
	5	1.2410	.449
	6	-1.5798	.334
2	1	3.5190	.075
	3	.3400	.857
	4	2.0143	.255
	5	4.7600*	.005
	6	1.9392	.244
3	1	3.1790	.089
	2	-.3400	.857
	4	1.6743	.311
	5	4.4200*	.005
	6	1.5992	.299
4	1	1.5048	.387
	2	-2.0143	.255
	3	-1.6743	.311
	5	2.7457*	.049
	6	-.0751	.957
5	1	-1.2410	.449
	2	-4.7600*	.005
	3	-4.4200*	.005
	4	-2.7457*	.049
	6	-2.8208*	.025
6	1	1.5798	.334
	2	-1.9392	.244
	3	-1.5992	.299
	4	.0751	.957
	5	2.8208*	.025

Note: Groups are defined as follows: 1: under 45, 2: 45-55, 3: 55-65, 4: 66-75, 5: 76-85, 6: over 85- differences marked by an asterisk are statistically significant)

the curve was 0.722 (0.669-0.875, 95% CI) for females and 0.666 (0.563-0.770, 95% CI) for males. It also shows the ROC curve based on age groups. As seen, lung score has an area under the curve of 0.749 (0.639-0.859, 95% CI) in those above 75 and an AUC of 0.719 (0.625-0.813, 95% CI) in those above 65 years old. The highest AUC belonged to female participants over 75 years old (0.833: 0.692-0.975, 95% CI) (Figure 1). Figure 3 presents samples of imaging findings (Supplementary file).

Discussion

In this study, we focus on the imaging characteristics of different demographic groups of participants with coronavirus. Since the beginning of the pandemic, mortality trends have favored younger female individuals. At the same time, most deceased have been elderly males with pre-existing conditions such as renal failure, cerebrovascular disease, diabetes, and hypertension.[16] The culprit for this disparity is poorly understood. Still, recent in vitro studies suggest that the difference could be caused by a variable expression of cell surface receptors, such as ACE2.[17] Other epidemiologic studies relate this discrepancy to the higher number of pre-existing conditions in male participants, their increased risk of acquiring the virus due to social and occupational status, or other issues relating to seeking timely medical services.[18]

Since the beginning of the pandemic, CT imaging has gained a role in the early diagnosis and triage of participants. It has even been considered a prognostic marker in some clinical guidelines.[19] Highlighting the importance and relevance of this imaging method, it is essential to understand if significant variations exist among imaging results of different genders and age groups, especially elderly males who are the most susceptible to severe disease complications.[20] A review and meta-analysis of CT scans in COVID-19 patients found that this imaging technique is crucial for diagnosing the disease. The study identified CT features such as ground glass opacity, consolidations, and bilateral involvement that are common in COVID-19 patients but not in other types of pneumonia; the presence of consolidations and pleural effusions is associated with more severe disease,[21] which was totally in concordance with our study. One such study focused on this issue was held by Moradi et al on 74 male and 41 female participants. They showed that those with a poor prognosis were older, had more co-morbidities, and were significantly more likely to be males ($P=0.016$). They also suggested that imaging signs other than peripheral distribution had no significant difference between the two genders, irrespective of age. However, when participants older than 60 were compared, imaging signs such as anterior involvement and peribronchovascular distribution differed among the two genders. They also suggested that a lung score was a better predictor of mortality in women than men (AUC of 0.96 compared to 0.73).[22] Although we were not also able to observe any differences among sexes (not even peripheral distribution), this insignificance stayed stable when considering only the elderly participants (over 65 years old and 75 years old). We also find a significant difference among the lung scores of participants dying or surviving the disease. Still, the AUC of the lung score in any given situation regarding age and sex did not reach that of Moradi et al. Furthermore, Moradi et al showed a significant correlation between age and lung score, a finding which we did not witness in our data. These differences could arise from differences in the study population and methodology. In this study, we only included hospitalized participants, while Moradi et al included inpatients and outpatients. Because of this, they may have included some participants with mild disease

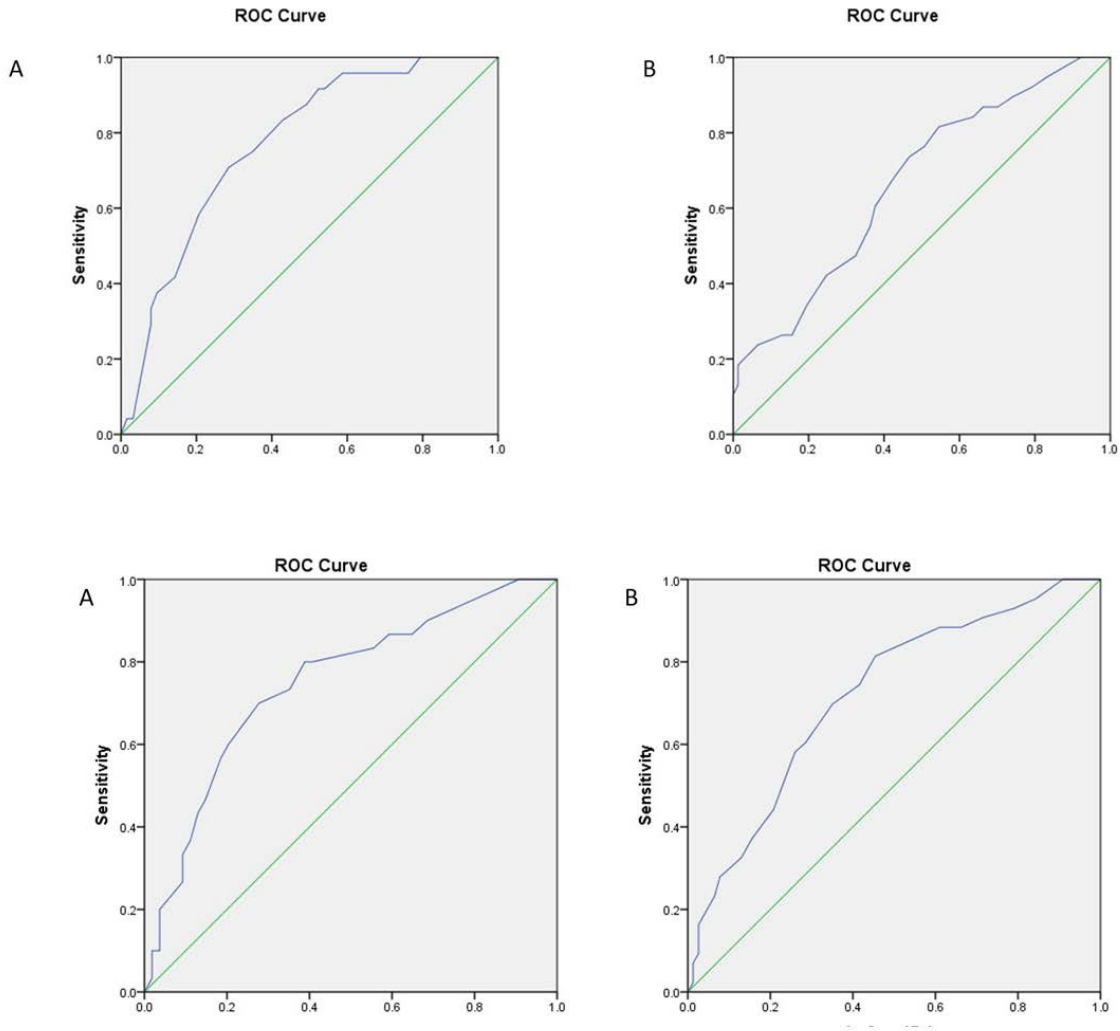

Figure 2. Up row. ROC curve depicting the relation between lung score and mortality in the two sexes. (A) Presents the ROC of women, and (B) presents the ROC curve of men, down Row. Roc curves presenting the relation between lung score and mortality in (A) patients above 75 years old and (B) patients above 65 years old

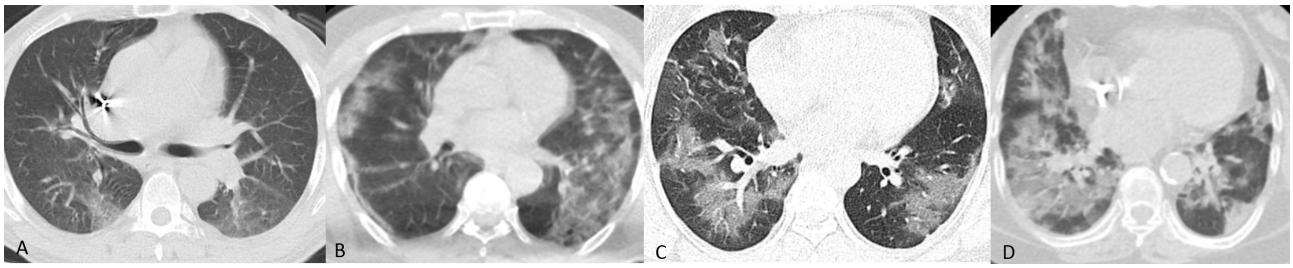

Figure 3. Different patterns of lung involvement in COVID-19. (A) Bilateral ground glass opacities located at the posterior and base of the lungs. (B) Bilateral ground glass opacities located at the peripheral segments of the lungs. The left hemithorax has involvement in the central parts of the lung. (C) Bilateral consolidation is located at the peripheral and posterior segments of the lungs, coupled with ground glass opacities at the anterior segments. Consolidations tend to happen in progressive disease. (D) Diffuse involvement of both lungs with consolidation and ground glass opacities

with scant pulmonary involvement, especially from younger ages and women, which would make their study population more heterogeneous. Furthermore, a limited number of their participants died because of the disease (30 participants out of 115), which could again account for the differences witnessed.

Another study was performed on 783 Italian participants, where a scoring system based on chest X-ray was used. In this system, each lung field was divided into three segments, and a score ranging from 0-3 was given to each segment. The authors of this study found that male and female participants had significantly different lung scores between 50-59 years and 70-79 years.[23] In our sample, the two genders had a marginally significant difference ($P = 0.05$), while all other age groups did not have substantial differences among female and male participants. The Italian study included inpatients, like ours, and the differences can be attributed to possible

varying guidelines of patient admission and the higher sample size of the Italian study. Noteworthy, the population of study should be of great importance in comparing the results of such a manuscript mentioned above and ours. Clinical studies demonstrate that mortality and pulmonary involvement are higher in elderly males. Thus, any population, including more such participants, will have higher lung scores and a heterogeneous population.[24]

Overall, our current knowledge regarding the role of imaging modalities in COVID-19 is growing. However, the generalizability of results attained from research initiatives remains low, since the studies are accomplished on widely different populations with different demographic features. Different treatment guidelines, which lead to the formation of pools of patients in which study subjects are recruited, further make clinical decisions prone to errors and misconceptions. Although all of the existing evidence shows tangible beneficence in the early use of CT as a diagnostic-prognostic method, radiologists and other clinicians should pay special attention to the demographic determinants of patients.[25] Furthermore, clinicians are recommended to use other possible markers, such as laboratory and pulmonary function tests, as supplements to imaging.[26] Triage guidelines or artificial intelligence models incorporating a wide array of imaging findings, lab results, and clinical signs and symptoms may be the most beneficial tool in detecting COVID-19 and determining its prognosis.[27]

Our results should be interpreted based on the limitations of our study. We included participants from a small number of centers (three centers), which could lower the diversity of the patients. Furthermore, we only included those hospitalized participants. Thus, the findings in asymptomatic individuals and those with mild disease may differ. Multicenter large-scale studies or systemic reviews focusing on the role of demographics on CT findings will be helpful.

Conclusion

Using lung scores can be a Svaluable tool in predicting the condition of hospitalized participants with COVID-19. While demographic features generally do not affect common imaging findings in participants with COVID-19, the prognostic significance of chest CT imaging may differ based on gender and age groups. Such studies aim to examine COVID-19 patients to understand the pandemic behaviors retrospectively better, look for different strains, and form more preparedness to deal with the next pandemic.

Study Highlights

What is current knowledge?

- One of the most essential inconsistencies is the variation in results across populations with different demographic characteristics, such as studies reporting more pronounced involvement
- among male-elderly populations.

What is new here?

- Demographic features generally do not affect common imaging findings in COVID-19 participants; however, the prognostic significance of chest CT may differ by gender and age.

Authors' Contribution

Conceptualization: Mohammad mirza-Aghazdeh-Attrii, Reza Rikhtegar, Afshin Mohammadi.
Data curation: Afshin Mohammadi.
Formal analysis: Mohammad mirza-Aghazdeh-Attrii, Armin Zarrintan, Zahra Babaei Aghdam.
Funding acquisition: Afshin Mohammadi.
Methodology: Mohammad mirza-Aghazdeh-Attrii.
Project administration: Mohammad mirza-Aghazdeh-Attrii.
Supervision: Mohammad mirza-Aghazdeh-Attrii.
Visualization: Seyed Ali Mousavi-Aghdas.
Writing–original draft: Ali Akhavi Milani, Mohammad khalafi, Elyad M.Ekrami.
Writing–review & editing: Ebrahim Farashi, Elyad M.Ekrami.

Competing Interests

The authors declare no conflict of interest.

Consent for Publication

All patients signed written consent notes for inclusion in potential observational studies before hospitalization.

Data Availability Statement

Requested data will be available based on reasonable request.

Ethical Approval

The local ethics committee at Urmia University of Medical Sciences approved this study (IR.UMSU.REC.1399.029).

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Supplementary File

Supplementary file contains Table S1-S3.

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