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Prognostic Value of Chest CT in the Elderly Patients Admitted with COVID-19 Pneumonia

COVID-19 Pnömonisi ile Başvuran Yaşlı Hastalarda Göğüs BT Prognostik Değeri

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ABSTRACT

Aim: The late elderly, are the leading group of non-survivors infected with the coronavirus disease 2019 (COVID-19). Computed tomography (CT) imaging has been recognized as an important diagnostic method for COVID-19. This study aimed to determine the prognostic performance of CT imaging in patients above 75 years old.

Material and Methods: After meeting the inclusion and exclusion criteria 56 elderly patients, 28 male, and 28 female were included in the study. Two radiologists interpreted CT imaging and a third experienced radiologist was in charge of reviewing the data and imaging findings in the controversial and disagreement cases. The lung score was determined for each patient, and radiologic signs were also examined.

Results: The mean age of the patients was 81.4±5.0 years. Thirty-six patients survived, and 20 did not. 28 (50.0%) patients had central involvement, while 25 (44.6%) patients had diffuse involvement. Radiologic signs such as consolidation and air bronchogram were more common among non-survivors than survivors (both p=0.001). The mean lung score for the survivors was 8.75±6.21 and 13.45±6.41 for non-survivors, and the difference between the two groups was statistically significant (p=0.010). The area under the receiver operating characteristic curve for a cut-off score of 12 was 0.714 (95% CI, 0.577 to 0.827, p=0.003).

Conclusion: It seems that using lung scores can play a very important role in predicting the condition of hospitalized patients over 75 years old.

Keywords: Elderly; geriatrics; COVID-19; computed tomography; imaging; radiology.

ÖZ

Amaç: İleri yaşlılar, koronavirüs hastalığı 2019 (coronavirus disease 2019, COVID-19) ile enfekte olan ve hayatta kalamayanların önde gelen grubudur. Bilgisayarlı tomografi (BT) görüntüleme COVID-19 için önemli bir tanı yöntemi olarak kabul edilmiştir. Bu çalışmanın amacı 75 yaş üstü hastalarda BT görüntülemenin prognostik performansını belirlemektir.

Gereç ve Yöntemler: Dahil etme ve hariç tutma kriterleri karşılandıktan sonra 28 erkek 28 kadın olmak üzere 56 yaşlı hasta çalışmaya dahil edildi. İki radyolog BT görüntülerini yorumladı ve üçüncü bir deneyimli radyolog, tartışmalı ve anlaşmazlık vakalarında verileri ve görüntüleme bulgularını gözden geçirmekten sorumluydu. Her bir hasta için akciğer skoru belirlendi ve radyolojik bulgular incelendi.

Bulgular: Hastaların yaş ortalaması 81,4±5,0 yıl idi. Otuz altı hasta hayatta kaldı ve 20 hasta hayatta kalamadı. 28 (%50,0) hastada merkezi tutulum varken 25 (%44,6) hastada ise yaygın tutulum vardı. Konsolidasyon ve hava bronkogramı gibi radyolojik bulgular hayatta kalamayanlar arasında hayatta kalanlardan daha yaygındı (her iki p=0,001). Hayatta kalanlar için ortalama akciğer skoru 8,75±6,21 ve hayatta kalamayanlar için 13,45±6,41 idi ve iki grup arasındaki farklılık istatistiksel olarak anlamlıydı (p=0.010). Alıcı işlem karakteristiği eğrisi altında kalan alan 12 kesim değeri için 0,714 (%95 GA, 0,577 ile 0,827, p=0,003) idi.

Sonuç: Akciğer skorlarının kullanılmasının hastanede yatan 75 yaş üstü hastaların durumunu tahmin etmede çok önemli bir rol oynayabileceği görülmektedir.

Anahtar kelimeler: Yaşlı; geriatri; COVID-19; bilgisayarlı tomografi; görüntüleme; radyoloji.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) is characterized by viral pneumonia accompanied by clinical symptoms such as dyspnea, cough, and fever. COVID-19 is usually associated with a mild clinical course in healthy adults with no pre-existing conditions. Still, it has shown to be associated with acute severe respiratory distress syndrome and a grim clinical outcome in the elderly and those with pre-existing conditions. A retrospective study comparing the elderly with other age groups has shown that the elderly are at higher risk of being hospitalized in the intensive care unit (ICU) and dying from the disease. They also have a significantly higher pneumonia severity index (PSI) score (1). Clinicians speculate that para-clinical findings may be significantly altered in the elderly compared to others, such as laboratory test results and imaging findings observed in chest X-rays and computed tomography (CT). CT imaging has been used extensively in the diagnosis of COVID-19, and studies have proven it to be more sensitive than molecular assays in diagnosing the disease (2,3). CT imaging is also possibly associated with disease severity and can be used in the evaluation of prognosis. Bilateral multifocal involvement is associated with more severe clinical signs and symptoms, increased mortality rate, and specific imaging findings such as airspace consolidations are seen in specific periods of the disease (4).

Furthermore, it has been suggested CT imaging may have distinct characteristics in pediatric patients, with more uncommon radiologic signs observed, such as a tree in bud formation, collapse, nodular opacities, and predominance of central lesions, in contrast to peripheral lesions (5). In contrast to pediatric patients, a rather small number of studies have focused on CT imaging in older adults, especially the late elderly (those who are older than 65 years old), who are at an increased risk of severe complications. Most studies are composed of cases in their 40s and 50s (6). Particular attention should be given to CT imaging in the late elderly, as it may act as a prognostic marker to provide early provision, and prompt early provision of more serious medical interventions, such as hospitalization in ICU wards, early intubation, early initiation of anti-viral medication, etc. (7). This is of clinical significance as the already existing evidence may not be entirely generalizable for the elderly population as a limited number of studies include large groups of the elderly (8). In the current study, we aimed to evaluate the diagnostic and prognostic value of CT imaging on admission for late elderly (aging more than 75) patients.

MATERIAL AND METHODS

The present retrospective study was conducted on late elderly patients admitted to medical, and educational centers at Urmia University of Medical Sciences between February 1st and July 10th, 2020. All of the included patients were initially managed by attending specialist physicians and then had CT imaging. Age and other demographic information of the patients were collected via the health information system of the institutions and electronic medical records of individuals. In cases of disagreement between the information, patients or their representatives were contacted for more information. All patients included in the study were followed until a definite clinical outcome. Inclusion criteria of patients consisted of those ages above 75 years old, who were diagnosed with COVID-19. Exclusion criteria consisted of those individuals with concomitant infections, heart failure on presentation, patients with pre-existing lung disease such as tuberculosis and idiopathic fibrosis, those individuals who had a CT scan performed on late days of admission, or those with CT images not taken in our centers.

Molecular Assay

Polymerase chain reaction (PCR) was performed to detect if patients were indeed infected with the virus. Specimens obtained from the nasopharynx and oropharynx, based on guidelines by the World Health Organization (WHO), were used to detect the virus. Taqman® Premix TAKARA diagnostic kits (TaKaRa, Dalian, China) were used. All patients underwent molecular assay on the first day of admission, and if needed, secondary molecular assay tests were performed if necessary. All of the patients included had positive PCR results.

CT Imaging Protocol

Patients underwent an imaging protocol based on the WHO guidelines and recommendations provided by the Ministry of Health and Education of the country where the study was performed (9). CT imaging was done with (multi-slice and multi-detector), 256-slice Siemens SOMATOM (Hannover, Germany) and (multi-slice and multi-detector), 256-slice Toshiba Alexion (Tokyo, Japan) machines based on the following technical specifications: low dose mode, automatic tube current modulation with a voltage of 120 kVp, axial and sagittal images, matrix size of 512×512, increment and thickness of 1.5 mm.

Interpretation of Imaging Findings

Interpretation of imaging findings was done separately by two board-certified radiologists with 12 and 2 years of experience in cardiothoracic imaging. The radiologists were not aware of the clinical diagnosis or outcome of the patients. In cases of disagreement, a third experienced radiologist was in charge of reviewing the data and imaging findings. A checklist was provided based on the recommendations by the Radiological Society of North America (RSNA), and Kanne et al (10,11). Lung score was defined and estimated based on the article by Francone et al. (4,10-12). As mentioned in the previous publications, lung score was determined based on the following: 0: no involvement seen, 1: less than 5% involvement in the affected lobe, 2: 6-25% involvement in the affected lobe, 3: 26-50% involvement in the affected lobe, 4: 51-75% involvement in the affected lobe, and 5: involvement more than 75% of the affected lobe. Based on the same publications, two cut-off (8 and 12) scores were determined to categorize the patients (13). These cut-offs are based on the anatomic properties of the human lung, and the fact that involvement equal to two or three complete lobes (hence the cut-off of 8 or 12, respectively) is considered as moderate to severe involvement (14).

Statistical Analysis

Statistical analysis was done by SPSS v.23.0 (IBM Inc. Chicago, USA) and MedCalc v.19.3.0 (MedCalc Software Ltd, Ostend, Belgium). The normality assumption was determined using the Kolmogorov-Smirnov test. Categorical variables were presented as numbers and percentages. Mean±standard deviation was used to present

numeric data. Independent samples t, chi-square, and Fisher's exact tests were used to compare findings between the groups. The receiver operating characteristic (ROC) curve was drawn, and the area under the curve (AUC) was determined. An AUC of 1 to 0.9 was considered to have an excellent predictive value, 0.9 to 0.8 to have a good value, and 0.8 to 0.7 was considered to have a fair diagnostic value. The sensitivity and specificity were determined for each lung score cut-off, and the Youden index was calculated based on these cut-offs.

Ethical Considerations

This study was approved by the local ethics committee of the Urmia University of Medical Sciences in which it was performed (IR.UMSU.REC.1399.029). All COVID-19 patients were asked to sign a written informed consent note before hospitalization, and patients were selected from among these cases. The study complied with the latest update of the Helsinki declaration.

RESULTS

A total of 56 patients were included in the study, of which 36 survived the disease, and 20 died. The mean age of the patients included in the study was 81.4±5.0 years. Of all of the patients, 28 (50%) were male, and the rest were female. The mean age of the groups of patients dying from the condition was 83.4±4.8 and was 80.6±4.9 in those surviving the condition. The difference was statistically significant (p=0.045). There were 20 (55.6%) females and 16 (44.4%) male patients in the surviving group, and 8 (40%) females and 12 (60%) males in the other. The difference between the two groups was not statistically significant (p=0.265). The median time between imaging and onset of symptoms was 3 (range, 1-5) days in the surviving group and 3 (range, 1-5) days in non-survivors with the difference being non-significant (p=0.800). The median period of hospitalization was 7 (range, 4-11) days for survivors and 7.3 days (range, 4-13) for non-survivors with the difference not being significant (p=0.203).

The clinical signs and symptoms of patients being included in the study are summarized in Table 1. The pre-existing conditions of the patients are summarized in Table 2.

Most patients had involvement in the upper and lower lobes of the lungs, with every patient except one having peripheral involvement. Figure 1 demonstrates some of the imaging findings. 28 (50.0%) patients had central involvement, while 25 (44.6%) patients had diffuse involvement. Imaging findings are presented in Table 3.

The lung score was calculated for both groups of patients. In patients dying from COVID-19, the mean lung score was 8.75±6.21 for whom survived and 13.45±6.41 for non-survivors. The difference between the two groups was significant (p=0.010). The odds ratio of not surviving COVID-19 in patients whose lung score was more than 8 in comparison to those whose lung score was equal to or

Table 1. Clinical signs and symptoms of the patients

Symptom	n (%)
Fever	12 (21.4%)
Cough	28 (50.0%)
Dyspnea	40 (71.4%)
Malaise	1 (1.8%)
Irritability	3 (5.4%)
Myalgia	4 (7.1%)
Soar trough	4 (7.1%)
Diarrhea	2 (3.6%)
Nausea	7 (12.5%)
Headache	2 (3.6%)
Chest pain	4 (7.1%)
Cyanosis	1 (1.8%)

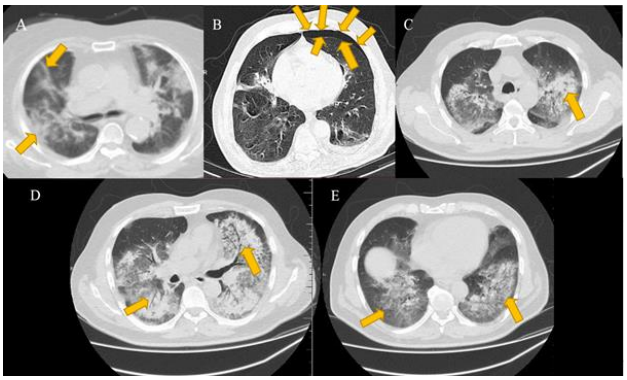

Figure 1. A) Axial HRCT of a 76 years old woman with a lung score of 12 revealed patchy ground-glass opacities in the right upper and right middle lobes (Yellow arrows denote the lesions). Ground glass lesions are also seen in the contralateral lobe. **B)** Axial HRCT of a 56 years old male with a lung score of 13 shows a pleural edge line due to pneumothorax in the left hemithorax (Yellow arrows delineate the contour of the line). **C)** HRCT of an 80 years old man, lung score of 18 with bilateral ground-glass opacities and left upper lobe alveolar consolidation. **D)** HRCT of an 82-year-old man, lung score of 23 with bilateral right and left ground-glass opacities, and alveolar consolidation with air-bronchogram. **E)** HRCT of a 78 years old man, lung score of 18 with bilateral right and left lower lobe ground-glass opacities.

Table 2. Past medical history of the patients

Pre-existing condition	Survivors (n=36)	Non-survivors (n=20)	p	Total (n=56)
Coronary artery disease	13 (36.1%)	6 (30%)	0.644	19 (33.9%)
Diabetes	7 (19.4%)	5 (25%)	0.737	12 (21.4%)
Hypertension	6 (16.7%)	3 (15%)	1.000	9 (16.1%)
Cerebrovascular disease	4 (11.1%)	2 (10%)	1.000	6 (10.7%)
Chronic obstructive pulmonary disease	3 (8.3%)	3 (15%)	0.655	6 (10.7%)
Chronic renal disease	2 (5.6%)	2 (10%)	0.611	4 (7.1%)
Splenectomy	1 (2.8%)	1 (5%)	1.000	2 (3.6%)
Malignancy	1 (2.8%)	0 (0%)	1.000	1 (1.8%)

Table 3. Radiological signs of the patients

	Survivors (n=36)	Non-survivors (n=20)	p	Total (n=56)
Location, n (%)				
Bilateral	29 (80.6%)	18 (90%)	0.466	47 (83.9%)
Unilateral	7 (19.4%)	2 (10%)		9 (16.1%)
Lesion type, n (%)				
Diffuse	13 (36.1%)	12 (60%)		25 (44.6%)
Multiple	17 (47.2%)	6 (30%)	0.226	23 (41.1%)
Single	6 (16.7%)	2 (10%)		8 (14.3%)
Distribution, n (%)				
Peripheral	23 (63.9%)	5 (25%)		28 (50.0%)
Central	0 (0.0%)	1 (5%)	**0.007**	1 (1.8%)
Peripheral and central	13 (36.1%)	14 (70%)		27 (48.2%)
Ground glass opacities, n (%)	35 (97.2%)	19 (95%)	1.000	54 (96.4%)
Reticular lesions, n (%)	0 (0.0%)	1 (5%)	0.357	1 (1.8%)
Consolidation, n (%)	10 (27.8%)	15 (75%)	**0.001**	25 (44.6%)
Air bronchogram, n (%)	7 (19.4%)	13 (65%)	**0.001**	20 (35.7%)
Cavity, n (%)	0 (0.0%)	1 (5%)	0.357	1 (1.8%)
Cystic lesions, n (%)	1 (2.8%)	0 (0%)	1.000	1 (1.8%)
Crazy-paving, n (%)	7 (19.4%)	3 (15%)	1.000	10 (17.9%)
Pleural effusion, n (%)	4 (11.1%)	5 (25%)	0.256	9 (16.1%)

less than 8 was 4.200 (95% CI, 1.253-14.081, p=0.020). The same was 4.278 (95% CI, 1.314-13.928, p=0.015) for a lung score of more than 12 compared to a score of 12 or less. The sensitivity and specificity of a lung score of more than 8 were 75.0%, and 58.3% respectively in the prediction of death probability (positive predictive value of 50.0% and a negative predictive value of 80.8%), and on the other hand sensitivity and specificity of lung score equal to 12 were 55.0%, and 77.8% respectively (positive predictive value equaled 57.9% and negative predictive value equaled 75.7%). The Youden index was 0.3611 and it was associated with the criterion of lung scores which were more than 8. ROC curve was drawn for the sensitivity and specificity of lung score in the prediction of death probability by COVID-19. The area under the curve was 0.714 (95% CI, 0.577 to 0.827, p=0.003), showing a fair predictive value for lung CT score (Figure 2).

Of the survivors, 26 received hydroxychloroquine, 5 received oseltamivir, 9 received Lopinavir/Ritonavir, and 26 received antibiotics. In non-survivors, 14 received hydroxychloroquine, 2 received oseltamivir, 9 received Lopinavir/Ritonavir, and 13 received antibiotics.

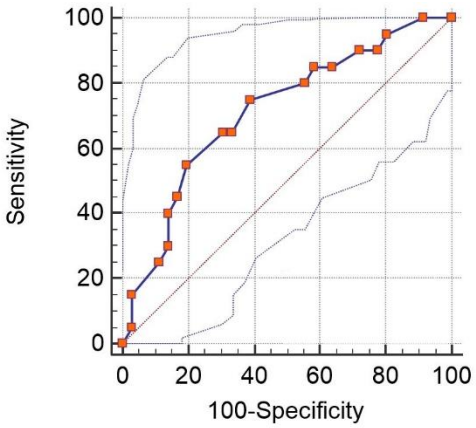

Figure 2. ROC curve for the lung score

DISCUSSION

COVID-19 presents as a viral pneumonia, compromising the ability of the respiratory system to oxygenate the blood. It also initiates an exaggerated inflammatory response, which with the medium of cytokines and interleukins, further interrupts physiologic functions of the body. Retrospective clinical studies have shown that individuals with respiratory and cardiovascular disease are in increased danger of mortality because of COVID-19, such as the elderly. A series of biomechanical changes in cells and tissues renders their functional capacities to a steep decline in instances of pathologic stress (15).

Multiple research initiatives have aimed to establish criteria to classify patients based on their probability of having severe symptoms associated with COVID-19. These criteria have consisted of past medical history, laboratory results, and imaging findings. Retrospective cohorts have shown that pre-existing conditions such as pulmonary, cardiovascular, and immune diseases increase the risk for severe disease and that in specific populations, up to almost a quarter of the population have pre-existing conditions, putting them at an increased risk of COVID-19 related complications (16). A retrospective clinical study from China enrolled 186 elderly patients with a mean age of 70.4±7.1 years and compared characteristics among the survivors and non-survivors. Non-survivors were shown to significantly have a higher rate of smoking, higher serum levels of LDH, ferritin, blood urea nitrogen, and D-dimer. The authors also studied imaging results in these groups of patients and found that non-survivors had a significantly higher rate of diffuse distribution of lesions (17).

A recent retrospective analysis performed on 63 COVID-19 patients with a mean age of 24.45±3.43 years found that patients with severe disease (defined as severe symptoms and need for hospitalization in ICUs) were associated with elevated liver enzymes, acute phase reactants, and IL-6 levels, and decreased levels of eosinophils, CD4+, CD8+, CD19+ and total lymphocyte counts (18).

All of the above studies point out significant differences among the survivors and non-survivors, but the result has

limitations in generalization to a late elderly population. Most studies have a rather small number of late elderly patients included, and even those focusing on the elderly do not include a significant number of late elderly patients. These studies also underline differences between the two groups but do not provide any means of clinical decision making based on these prognostic factors. The utilization of chest CT imaging alone or in combination with any of the following mentioned clinical criteria might be useful in detecting patients with a grim outcome.

Although evidence in this regard is scarce, this issue has significant clinical importance, as studies show mortality of up to 30 percent in patients above 70 years (19,20). Multiple descriptive studies with the mean age of the patients being included ranging between 30-50 years have shown that founding such as ground-glass opacities and consolidations being the most common lesions, with other signs such as halo sign, cavities, bronchiectasis, nodular lesions, and broncho-vascular thickening being less common (21,22). Noteworthy, none of these studies compares survivors and non-survivors, and they do not include a significant number of cases from two crucial demographic groups, the elderly and pediatric patients, who both show an increased rate of atypical findings (23). Our study faced some limitations, including the fact that we had a limited number of subjects. Furthermore, our results may not be generalizable to specific populations with a high rate of pre-existing conditions in their elderly. All of our patients had CT imaging performed before or on the first day of hospitalization. Thus CT imaging taken further in the course of the disease may not be similar in prognostic value. We also did not include asymptomatic patients, and the elderly who were not hospitalized, as diagnosing asymptomatic patients was impossible in our setting and based on institutional guidelines, all late elderly patients were hospitalized.

CONCLUSION

It seems that using lung scores can play a very important role in predicting the condition of hospitalized patients over 75 years old. However, due to the limited number of participants included in this study, designing similar studies in the future with a larger number of participants will be very helpful for the ultimate assessment.

Ethics Committee Approval: The study was approved by the Ethics Committee of Urmia University of Medical Sciences (22.04.2020, 029).

Conflict of Interest: None declared by the authors.

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