ORIGINAL

Age and gender-associated radiological findings in COVID-19 infection

Hallazgos radiológicos asociados a la edad y al sexo en la infección por COVID-19

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Abstract

Objectives: At present, the novel coronavirus disease 2019 (COVID-19) pandemic is the most important infectious disease worldwide. Due to false positives and false negatives of PCR results in the diagnosis of coronavirus infection, Computed Tomography (CT) is especially important in the initial diagnosis and assessment of the intensity of COVID-19 infection. According to the stage and intensity of COVID-19 infection chest CT scan findings display different features. Although men, women, and different age groups may be equally affected, different epidemiological studies have shown differences in gender and age in intensity and mortality. Although there are many studies on radiological findings in COVID-19 infection, however limited literature reviews have been stated on the relationship between age and gender with radiological finding. Methods: This reviews summarized studies that evaluated the association age and gender with radiologic CT fndings.

Results: In general, the findings of these studies show that different age and gender groups have different characteristics which can role in primary diagnosis, facilitate the classification of the initial prognosis in COVID-19 pneumonia.

Conclusions: As an indicator for outcome, treatment, determining the intensity of the disease as well as the prognosis, nevertheless studies with higher sample sizes and multicenter are required.

Keywords: COVID-19, Ct scan findings, age, gender.

Resumen

Objetivos: En la actualidad, la pandemia de la nueva enfermedad por coronavirus 2019 (COVID-19) es la enfermedad infecciosa más importante a nivel mundial. Debido a los falsos positivos y falsos negativos de los resultados de la PCR en el diagnóstico de la infección por coronavirus, la Tomografía Computarizada (TC) es especialmente importante en el diagnóstico inicial y la evaluación de la intensidad de la infección por COVID-19. Según el estadio y la intensidad de la infección por COVID-19, los hallazgos de la TC torácica presentan características diferentes. Aunque los hombres, las mujeres y los diferentes grupos de edad pueden estar igualmente afectados, diferentes estudios epidemiológicos han mostrado diferencias de género y edad en la intensidad y la mortalidad. Aunque hay muchos estudios sobre los hallazgos radiológicos en la infección por COVID-19, sin embargo se han establecido revisiones bibliográficas limitadas sobre la relación entre la edad y el género con el hallazgo radiológico. Métodos: Esta revisión resume los estudios que evaluaron la asociación entre la edad y el género con los hallazgos radiológicos de la TC.

Resultados: En general, los hallazgos de estos estudios muestran que los diferentes grupos de edad y género tienen características diferentes que pueden jugar un papel en el diagnóstico primario, facilitando la clasificación del pronóstico inicial en la neumonía por COVID-19.

Conclusiones: Como indicador del resultado, del tratamiento, determinando la intensidad de la enfermedad así como el pronóstico, no obstante se requieren estudios con mayor tamaño de muestra y multicéntricos.

Palabras clave: COVID-19, hallazgos de la tomografía computarizada, edad, género.

Introduction

At present, the novel coronavirus disease 2019 (COVID-19) p pandemic is the most important infectious disease worldwide and causing the death of 5,484,439 people until January 06, 2022[1].The virus is transmitted through airborne droplets, air, and physical contact from person to person. The incubation period of this disease differs between 2 to 7 days (average 4 days) and can even last up to 24 days[2]. The range clinical finding of COVID-19 are wide, from no symptoms to fever, acute respiratory distress syndrome, multiple organ failure, and death[3]. The most important common symptom of COVID-19 is fever, dry cough and tiredness. Symptoms of this condition might comprise of shortness of breath or difficulty breathing, muscle aches, chills, sore throat, runny nose, headache, or chest pain[4]. Although the clinical signs are mild in more than 80% of patients, however risk factors advanced age and comorbidity (eg. diabetes mellitus, high blood pressure, heart disease, chronic kidney failure and tumor linked with increase admission to intensive care unit (ICU), need mechanical ventilation, and death or critical states of the disease especially acute respiratory distress syndrome[5,6]. Therefore, early isolation and diagnosis and timely treatment can be effective in reducing mortality[7].

Diagnosis of COVID-19

çFast and precise diagnosis of COVID-19 is essential to detect and manage infected individuals, track contact, epidemiological identification, and make general health decisions[8]. COVID-19 can be diagnosed by clinical diagnostics and molecular tests[9]. Clinical diagnostics such as symptoms, laboratory indicators are not limited to SARS-CoV-2 infection, and totally of them might be suspected of having COVID-19, nevertheless it does not show conclusive confirmation[10]. Molecular reverse-transcription polymerase chain reaction (RT-PCR) is the definite and golden standard diagnostic test for recognition of RNA virus in nasal or throat swab SARS-CoV-2 infected patients, but have low sensitivity[11]. Nevertheless, this method may have false-negative results because of improper sampling time relative to infection, inappropriate sampling method, insufficient preservation of specimens, and technical limitations[12]. On the other hand, false-positives might happen lead to technical errors, specially contamination during the manual RT-PCR method. Subsequently, RT-PCR alone cannot be a reliable, independent, and exclusive test for screening people suspected of having COVID-19[13]. Therefore, negative results do not indicate that a person does not have COVID-19 infection and CT scans should be used in addition to PCR testing to screen and diagnose COVID-19 infection[14].

COVID-19 infection according to age and gender

Currently, epidemiological statistics show that age, gender and type of underlying disease are high risk factors for COVID-19 disease. Related risk factors, underlying diseases, and biological differences that differ with gender and age may lead to in outcomes COVID-19 infection specially mortality[15,16]. Also susceptibility COVID-19 varies due to biological differences at different ages and between gender. Mortality from COVID-19 increases dramatically in older ages, with very few deaths demonstrated under the age of 50. Therefore, the age and gender pattern of infections in combination with the age and gender composition of the population is essential to describe the difference between COVID-19 transmission and mortality worldwide[17]. Elderly is known as a risk factor compared to young and middle-aged people, which is mostly due to reduced immunity due to weakness and higher prevalence of chronic diseases in the elderly population[18]. Another important factor in the difference in COVID-19 mortality is gender, in which there are many gender differences and men are at higher risk than women, which may be related to gender hormones such as testosterone and estrogen, so that the immune response and the presence of other risk factors, for example diabetes, hypertension and cardiovascular disease that affects men more than women[19,42]. In general, the detected COVID-19 positive cases are high, especially in people between 35 and 65 years old. This group, which comprises mainly of the elderly population, accounts for 50% of the confirmed positive cases, indicating that the infection does not only affect the elderly. COVID-19 is more common in men aged 55 to 80 than in women, but more positive cases have been seen in women aged 15 to 55 and over 80[19]. In general, the mortality rate is higher among men for all age groups. Male and older patients with more comorbidities have an unfavorable survival outcome[20]. The immune system plays an important role in preventing various viruses, including COVID-19. The human's natural immune system adapts from the embryonic to the neonatal stage, matures from adolescence to adulthood, changes during pregnancy, and decreases in old age[21]. These changes in the immune system have a higher risk of complications in infants, pregnant women and the elderly. Numerous factors role in discriminating the immune system based on gender and age[22]. Changes in the level / number of immunoglobulins, CD4 and CD8 cells, B cells, T cells in men and women may cause changes in COVID-19 cases and death. Overall age and gender differences in COVID-19 infection can be effective as a prognostic factor in determining survival outcome, prevention and treatment[23].

CT findings and COVID-19

Chest CT scanning is convenient, fast with higher sensitivity than RT-PCR which used for early diagnosis and evaluation intensity COVID-19 infection[24]. Numerous studies have shown specific features of lung CT images in patients with COVID-19, which is a reliable source for diagnosis[25]. The CT intensity score index was calculated according the amount of lobar involvement (0:0%; 1, <5%; 2:5-25%; 3:26-50%; 4:51-75%; 5, >75%; range 0-5; total score 0-25)[26]. Based on the stage and intensity of COVID-19 infection chest CT scan findings display different features and could contain several bilateral ground-glass opacities in the peripheral lower lung zones[27]. The ground glass opacities (GGO), consolidation, septal thickening mostly with the subpleural lungs or bronchovascular bundles or diffusely in the whole lungs reported as CT characteristic features of COVID-19[28]. Although men, women, and different age groups may be equally affected, different epidemiological studies have shown differences in gender and age in intensity and mortality. Many studies on radiological findings in infection have been done[29,43-45]. Although there are many studies on radiological findings in COVID-19 infection, however limited literatures have been shown the relationship between age and sex with radiological finding and most of the available studies have compared the COVID-19 disease between children and adults without age group[30]. This reviews summarized studies that evaluated the association age and sex with radiologic CT fndings.

Classification of chest CT results in COVID-19 patients by gender and age

In the Alper Karacan et al study in Turkey the ground-glass opacity and consolidation, the tree-in-bud pattern, the halo signs, the thin reticular pattern and crazy-paving pattern were the most common CT scan fndings in age groups under 20 years of age, 20-29 age group, 30-39 years, 60-79 years and over 80 years respectively. Also in men centrilobular nodules, airway changes, and tree-in-bud pattern were considerably greater compared with women. They concluded that due to the high prevalence of radiological findings in the elderly and men, therefore, the prognosis of the disease plays an important role in these groups[31]. Another study by Behnaz Moradi et al. in Iran reported that peripheral distribution was more frequently in men >60 years than, while women >60 years demonstrated peribronchovascular distribution pattern. Also in men <60 years' anterior distribution of opacities more frequently than with women. In term of CT-scores women <60 years have been shown significantly lower intensity scores which is associated with predicting poor prognosis[32].

The study by Selçuk Parlak et al. examined the effect of age on CT scan features and the intensity of COVID-19 disease. Their results showed that ground-glass opacity was the most common CT scan features in all age groups. CT scan findings including consolidations, crazy-paving patterns, air bronchograms and the number of lesions were higher frequency in older patients than other age groups. Also the upper lobe and right middle lobe were more involved in older patients. Overall, they concluded that these CT scan findings observed in older patients are associated with as an indicator for worse outcomes[33].

Huanhuan Liu et al study in China evaluated that GGO and consolidation were the typical CT scan finding in non-pregnant adults and the pregnant women respectively, while children shown mild pulmonary involvement with a focal GGO or consolidation[34].

Dangis et al showed that CT intensity scores were significantly higher in men with a tendency to bilateral lung involvement. The difference in the score of lung involvement was more noticeable in the advanced and peak stages of the disease[35].

In a study by Wang et al. in China surveyed the relationship different CT findings in three age groups. The results of this study presented that in the elderly, more lobes as well as more subpleural lesions were affected and also on the other hand in term of crazy paving sign, bronchodilatation and pleural thickening a significant difference was observed between Group 1&2, Group 2&3 with more frequently in the elderly group. They concluded that determining the radiological characteristics of patients based on age will be useful in the primary definitive diagnosis COVID-19[36]. Ammar Mosa et al in Iraq showed that there is a noteworthy relationship between male gender and enhancing age between CT intensity scores[37].

A study by Abdelwahab et al indicated that in terms of gender distribution, consolidation of CT scan findings was significantly more common in women than men, while other radiological patterns, distribution of radiological abnormalities, and CT intensity score in both there was no statistically significant difference between the gender groups[38].

The study of Qianbiao Gu et al. in China demonstrated that although there is no statistically significant relationship between gender distribution in radiological characteristics of patients, but thickened interlobular, honeycomb pattern and nodular infiltration there were significant differences between younger and elderly group patients. Also there was also a statistically noteworthy relationship between patient CT score and age[39].

A study by Chao Jin and colleagues showed that there are significant differences between pattern-categories CT

scan with age. As the age increases, the scoring pattern of CT scan findings increases and the older patients show diffuse alveolar damage pattern. Also in this study most men indicated multifocal lesions with a peripheral distribution predominantly in the middle to lower lung zones and GGO or consolidation, or interlobular septal thickening pattern. They concluded that classification of the CT pattern along with clinical features such as age could facilitate the classification of the initial prognosis in COVID-19 pneumonia[40].

The study by Russell et al. exhibited that there was no statistically significant difference in age and gender distribution in different categories of radiological abnormalities from mild to severe, however, the frequency of multifocal and bilateral findings was higher in women than men, but this was not statistically significant. They concluded that neither age nor gender had a statistically significant effect on the intensity or type of CT scan findings[41]. **Table I** presented studies which compare CT findings of COVID-19 infection in different gender and age.

Table I: Summary of studies conducted from compare CT findings of COVID-19 infection in different gender and age.

Study (year)	Country	Common or compare CT scan finding according gender or age group	Conclusion
Alper Karacan	Turkey	• Under 20 years: GGO and consolidation • 20-29 years: tree-in-bud pattern • 30-39 years: halo signs • 60-79 years: thin reticular pattern and crazy-paving pattern • over 80 years: crazy-paving pattern • Also in men centrilobular nodules, airway changes, and tree-in-bud pattern were considerably greater compared with women	They concluded that due to the high prevalence of radiological findings in the elderly and men, therefore, the prognosis of the disease plays an important role in these groups
Selçuk Parl	Turkey	• CT scan findings including consolidations, crazy-paving patterns, air bronchograms and the number of lesions were higher frequency in older patients compared with other age groups • the upper lobe and right middle lobe were more involved in older patients	CT scan findings observed in older patients are associated with as an indicator for worse outcomes.
Moradi	Turkey	• Peripheral distribution was more frequently in men > 60 years than, while women > 60 years demonstrated peribronchovascular distribution pattern • In men <60 years' anterior distribution of opacities more frequently than women • In term of CT-scores women < 60 years have been shown significantly lower intensity scores	Chest CT stratified by age can used for evaluation prognosis infection
Huanhuan Liu et	China	• Pregnant women: GGO • Non-pregnant adults: consolidation • Children: mild pulmonary involvement with a focal GGO or consolidation	CT can be a reliable method for primary diagnosis, evaluate the intensity and timely impact of therapeutic effects
Dangis	Belgium	• Dangis et al showed that CT intensity scores were significantly higher in men with a tendency to bilateral lung involvement.	The difference in the score of lung involvement between men and women was more noticeable in the advanced and peak stages of the disease.
Wang et al	China	• In the elderly, more lobes as well as more subpleural lesions were affected • -crazy paving sign, bronchodilatation and pleural thickening were more frequently in the elderly group.	Determining the radiological characteristics of patients based on age will be useful for the early definitive diagnosis of COVID-19.
Abdelwahab	Egypt	• Consolidation of CT scan findings was significantly more common in women than men • Other radiological patterns, distribution of radiological abnormalities, and CT intensity score in both there was no statistically significant difference between the gender groups.	---
Ammar Mosa	Iraq	• CT intensity score is higher with male and older patients.	---
Qianbiao Gu	China	• There is no statistically significant relationship in terms of gender distribution in radiological characteristics of patients • Thickened interlobular, honeycomb pattern and nodular infiltration there were noteworthy differences between younger and elderly group • A statistically significant relationship among patient CT score and age.	CT classification, especially by age, can play an important role in early diagnosis and intervention
Chao Jin	China	• There are significant differences between pattern-categories CT scan with age. • As the age increases, the scoring pattern of CT scan findings increases and the older patients show diffuse alveolar damage pattern. • Most men indicated multifocal lesions with a peripheral distribution predominantly in the middle to lower lung zones and GGO or consolidation, or interlobular septal thickening pattern	Classification of the CT pattern along with clinical features such as age could facilitate the classification of the initial prognosis in COVID-19 pneumonia
Russell	USA	• That there was no statistically significant difference in age and gender distribution in different categories of radiological abnormalities from mild to severe • The frequency of multifocal and bilateral findings was higher in women than men, but this was not statistically significant	Neither age nor gender had a statistically significant effect on the intensity or type of CT scan findings.

Conclusion

Given that CT scan have an essential impress in the diagnosis, treatment and intensity of COVID-19 disease, therefore the relationship between demographic information and other clinical findings of patients with CT scan findings is important. As mentioned, few studies have been conducted to evaluate radiological findings in terms of age and gender distribution. Overall, the findings of these studies show that the characteristics and scores of CT scans vary in different age and gender groups, however, in a number of studies, this relationship was not statistically significant. In general, the intensity and type of radiological findings were higher in the elderly compared to other groups, but these findings varied by gender in different studies. Differences in the characteristics and scores of CT scans in diverse age and gender groups can role in primary diagnosis, facilitate the classification of the initial prognosis in COVID-19 pneumonia, as an indicator for outcome, treatment, determining the intensity of the disease as well as the prognosis, nevertheless studies with higher sample sizes and multicenters are required.

Conflicto de Intereses: en este estudio no existen conflictos de interés.

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