The Relationship Between Balance Disorders and Lung Involvement in COVID-19 Patients

COVID-19 Hastalarında Görülen Denge Bozuklukları ile Akciğer Tutulumu Arasındaki İlişki

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ABSTRACT

Introduction: *To better understand COVID-19 and prevent the spread of the disease, symptoms associated with COVID-19 should be known. The list of symptoms of COVID-19 is expanding. This study aimed to examine the relation between balance disorders and radiologically detected lung involvement seen in COVID-19 patients.*

Materials and Methods: *This cross-sectional study was conducted in Cerrahpaşa School of Medicine Hospital and Cerrahpaşa Medicine Faculty between July 2021 to June 2022. The study included 174 COVID-19 patients with pulmonary involvement (Group 1) and 174 COVID-19 patients without pulmonary involvement (Group 2). Balance disorders of the patients within one month after the diagnosis of COVID-19 were questioned with a self-reported questionnaire made over the phone. The incidence of balance disorders, type of balance disorder, onset time, duration, and severity were questioned.*

Results: *Balance disorders were detected in 67 (19.3%) of the patients. Dizziness was detected in 60 (89.55%) of these patients, and vertigo was detected in seven (10.45%) of them. The number of patients with balance disorders was 49 (28.2%) in Group 1 and 18 (10.3%) in Group 2. The frequency of balance disorders was significantly higher in Group 1 (p= 0.001). Vertigo was detected in in (3.4%) and dizziness in 43 patients (24.7%) in Group 1, and vertigo was detected in one patient (0.6%) and dizziness in 17 patients (9.8%) in Group 2. The frequency of dizziness was significantly higher in Group 1 (p= 0.001). Balance disorders were significantly longer and more severe in Group 1 (p= 0.048, p= 0.029, respectively).*

Conclusion: *Balance disorders can be a symptom of COVID-19, and they may be more frequent, more serious, and longer lasting in patients with pulmonary involvement.*

Key Words: *COVID-19; Dizziness; Vestibular diseases; Vertigo; SARS-CoV-2*

ÖZ

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Giriş: COVID-19'u daha iyi anlamak ve hastalığın yayılmasının önlenmesi için COVID-19 ile ilişkili semptomlar bilinmelidir. COVID-19 semptom listesi giderek genişlemektedir. Bu çalışma, COVID-19 hastalarında görülen denge bozuklukları ile radyolojik olarak saptanan akciğer tutulumu arasındaki ilişkiyi incelemeyi amaçlamaktadır.

Materyal ve Metod: Bu kesitsel çalışma, Temmuz 2021 ile Haziran 2022 tarihleri arasında Cerrahpaşa Tıp Fakültesi Hastanesi ve Eyüpsultan Devlet Hastanesinde yürütülmüştür. Çalışmaya akciğer tutulumu olan 174 COVID-19 hastası (Grup 1) ve akciğer tutulumu olmayan 174 COVID-19 hastası (Grup 2) dahil edilmiştir. Hastaların COVID-19 tanısından sonraki bir ay içerisindeki denge bozuklukları, telefon üzerinden yapılan öz bildirimli anketle sorgulanmıştır. Denge bozukluklarının görülme sıklığı, denge bozukluğunun türü, başlangıç zamanı, süresi ve şiddeti sorgulanmıştır.

Bulgular: Hastaların 67'sinde (%19.3) denge bozuklukları saptandı. Bu hastaların 60'ında (%89.55) dizziness, yedisinde (%10.45) vertigo saptandı. Denge bozukluğu olan hasta sayısı Grup 1'de 49 (%28.2) ve Grup 2'de 18 (%10.3) idi. Denge bozukluklarının sıklığı Grup 1'de anlamlı olarak yüksekti (p= 0.001). Grup 1'de altı hastada (%3.4) vertigo, 43 hastada (%24.7) dizziness, Grup 2'de bir hastada (%0.6) vertigo ve 17 hastada (%9.8) dizziness tespit edildi. Dizziness sıklığı Grup 1'de anlamlı olarak daha yüksekti (p= 0.001). Denge bozuklukları Grup 1'de anlamlı olarak daha uzun süreli ve daha şiddetliydi (sırasıyla; p= 0.048, p= 0.029).

Sonuç: Denge bozuklukları COVID-19'un belirtisi olabilir ve bu belirti pulmoner tutulumu olan hastalarda daha sık, daha ciddi ve daha uzun süreli olabilir.

Anahtar Kelimeler: COVID-19; Dizziness; Vestibüler hastalıklar; Vertigo; SARS-CoV-2

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a systemic disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. SARS-CoV-2, which caused the first pandemic after the Spanish flu, replicates in the upper respiratory tract and then reaches the lungs via micro aspirates[2,3]. Involvement of the lungs leads to systemic disease[2].

COVID-19 patients may have the disease as an outpatient, may have a disease that is severe enough to require intensive care unit follow-up, and may die due to complications related to this disease[4]. COVID-19 may have mild to severe symptoms. Symptoms of COVID-19, which can be seen in 2-14 days after exposure to the virus, have been defined by the Centers for Disease Control and Prevention (CDC) as fever, cough, dyspnea, fatigue, myalgia, headache, smell and taste disturbance, sore throat, runny nose, nasal congestion, nausea-vomiting, and diarrhea[5]. Various symptoms outside of the CDC list may be associated with COVID-19. Some of these symptoms belong to neurological manifestations that can be seen in 30% of COVID-19 patients[6].

SARS-CoV-2 may also have neurotropic characteristics like other coronaviruses[7]. Another symptom seen in COVID-19 patients is balance disorder, which is thought to be due to the neurotropic feature of the virus similar to olfactory disorders[6,7]. The relation between balance disorders and COVID-19, which was shown for the first time in a study by Viola et al., was the subject of a limited number of studies[8]. In these studies, the relationship between balance disorders and the presence of lung involvement, which is the most important stage of COVID-19 disease, was not evaluated.

This study aimed to examine the relation between balance disorders and radiologically detected lung involvement in COVID-19 patients.

MATERIALS and METHODS

Populations, Inclusion, and Exclusion Criteria

All subjects of the current study presented to Cerrahpaşa School of Medicine Hospital and Eyüpsultan State Hospital. The outpatients with positive SARS-CoV-2 real-time polymerase chain reaction (RT-PCR) test results were included in the study. Patients with chronic diseases, neurological and psychiatric diseases, otological diseases and/or surgery, regular drug use in the last three months, smoking and alcohol use were excluded from the study.

All patients had thoracic computed tomography (CT) results registered in the hospital system.

Study Groups and Subject Size

COVID-19 patients were divided into two groups those with pulmonary involvement in thoracic CT due to COVID-19 (Group 1) and those without (Group 2).

Minimum sample number was calculated based on the study of İleri et al,[9] and it was 174 for each group (95% confidence interval and 5% tolerable error assumptions).

Lung Involvement

Thoracic CT images were obtained using the same device. The lungs were examined with high-resolution images of 1 mm section thickness. Chest CTs were classified according to the COVID-19 Reporting and Data System (CO-RADS) classification by the same radiologist[10].

Data Collection

Patients who were suitable for the study design from hospital records were reached by telephone. Balance disorders of the patients within one month after the diagnosis of COVID-19 were questioned. Dizziness and vertigo were described to the patients who said they had balance disorder, and it was determined that their complaints were compatible with which definition. Dizziness was described as disequilibrium, a sense of light-headedness, and disorientation without rotation[11]. Vertigo was defined as the sensation of motion, especially rotation, although there was no movement in the person or the environment[11].

Statistical Analysis

G*Power program was used to calculate the minimum sample size[12]. SPSS 23.0 program (IBM, USA) was used for statistical analysis. Kolmogorov-Smirnov test and Levene's test were used to analyze the normal distribution and homogeneity of data, respectively. Independent-samples t-test and Pearson Chi-Square test were used for statistical comparisons. Significance level was accepted as a p< 0.05.

RESULTS

A total of 348 patients, 207 (59.5%) males and 141 (40.5%) females, were included in the present study. Mean age of the patients was 50 + 14.646 (min= 20-max= 80) years. Demographic characteristics of the patients are given in Table 1. The groups were statistically similar in terms of sex distribution and patients' age (p= 0.445, p= 0.241, respectively) (Table 1).

Balance disorders were detected in 67 (19.3%) of the patients, vertigo was observed in 2.01% and dizziness was observed in 17.4% of the COVID-19 patients included in the study. Dizziness was detected in 60 (89.55%) of these patients, and vertigo was detected in seven (10.45%) of them (Figure 1). In the examination of the groups in terms of balance disorders, the number of patients with balance disorders was 49 (28.2%) in Group 1 and 18 (10.3%)

Table 1. Demographic characteristics of the patients		Group 1 (n= 174)	Group 2 (n= 174)	p
Parameters				
Sex	Male, n (%)	107 (61.5)	100 (57.5)	0.445*
	Female, n (%)	67 (38.5)	74 (42.5)	
Age (years)	Mean ± SD (min-max)	50.92 ± 14.818 (21-80)	49.07 ± 14.457 (21-80)	0.241^{Ý}

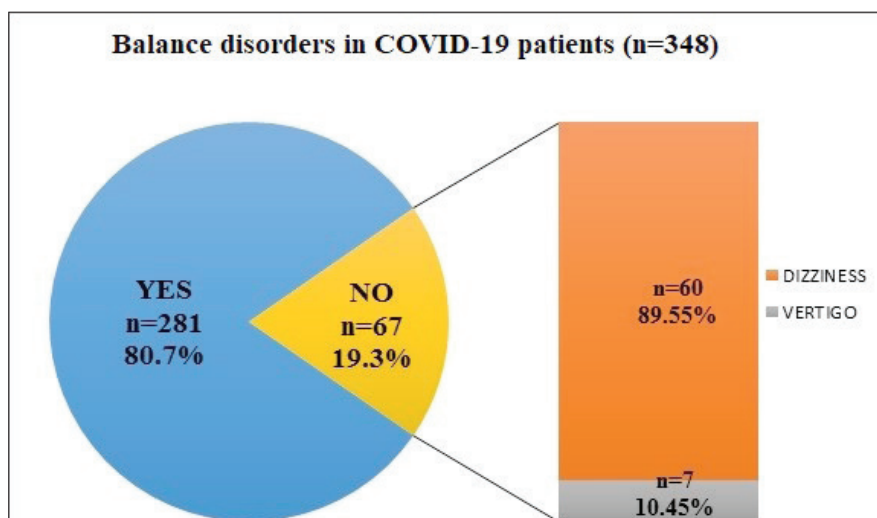*Pearson Chi-Square Test, value: 0.548; df: 1 p> 0.05
^{Ý}Independent samples t test p> 0.05

Figure 1. The incidence and types of balance disorder in COVID-19 patients.

Table 2. Evaluation of the balance disorders			
The symptom	Group 1 (n= 174) n (%)	Group 2 (n= 174) n (%)	p
Balance disorders +	49 (28.2)	18 (10.3)	0.001*
Balance disorders -	125 (71.8)	156 (89.7)	
*Pearson Chi-Square Test, value: 17.763; df: 1 p< 0.05			

in Group 2. The frequency of balance disorders was significantly higher in Group 1 compared to Group 2 (p= 0.001) (Table 2).

In the examination of the types of balance disorders in the groups, while vertigo was detected in six patients (3.4% of the patients in Group 1, 12.2% of the patients with balance disorders in Group 1) and dizziness in 43 patients (24.7% of the patients in Group 1, 87.8% of the patients with balance disorders in Group 1) in Group 1, vertigo was detected in one patient (0.6% of the patients in Group 2, 5.6% of the patients with balance disorders in Group 2) and dizziness in 17 patients (9.8% of the patients in Group 2, 94.4% of the patients

with balance disorders in Group 2) in Group 2. While no significant difference was found between the groups in terms of vertigo frequency, the frequency of dizziness was found to be significantly higher in Group 1 (p= 0.063, p= 0.001, respectively) (Table 3).

The characteristics of balance disorders are given in Table 4. In the evaluation of the characteristics of balance disorders, balance disorders were found to be significantly longer and more severe in Group 1 compared to Group 2 (p= 0.048, p= 0.029, respectively). However, there was no significant difference between the groups in terms of symptom onset times (p= 0.557).

Table 3. Evaluation of the balance disorders			
Balance disorders	Group 1 (n= 49) n (%)	Group 2 (n= 18) n (%)	p
Vertigo	6 (3.4)	1 (0.6)	0.063*
Dizziness	43 (24.7)	17 (9.8)	0.001^{Ý}
*Fisher's Exact Test, value: 3.558; df: 1 p> 0.05. ^{Ý}Pearson Chi-Square Test, value: 13.614; df: 1 p< 0.05.			

Table 4. The characteristics of balance disorders

Balance disorders	Group 1 Mean ± SD (Median, min-max)	Group 2 Mean ± SD (Median, min-max)	p
Symptom onset time (day)	4.102 ± 4.154 (3.0-14)	4.579 ± 4.181 (3.0-15)	0.557
Symptom duration (day)	6.326 ± 4.012 (7.1-20)	4.158 ± 2.651 (3.1-10)	**0.048***
Symptom severity (0-10)	3.898 ± 1.939 (3.2-10)	3 ± 1.247 (3.2-7)	**0.029***

*Mann Whitney U test p< 0.05

DISCUSSION

Symptoms of COVID-19 are listed in the list of national and international organizations[5,13]. However, the number of symptoms associated with COVID-19 is increasing day by day. The relation of these symptoms with the lungs being affected by SARS-CoV-2 is also the subject of studies[14]. As a result of our study, we found that balance disorders seen in COVID-19 patients were significantly higher in patients with pulmonary involvement, the type of balance disorder seen with a higher rate was dizziness, and dizziness was significantly higher in patients with pulmonary involvement.

COVID-19, a pandemic infectious disease, can be asymptomatic and cause severe illness or even death[4]. COVID-19 can cause flu-like symptoms such as fever, muscle pain, fatigue, cough, and interesting symptoms belonging to various organs and systems such as headache and conjunctivitis[15]. The most common symptoms in terms of otorhinolaryngology are flu-like symptoms, odor and taste disorders. However, symptoms such as sensorineural hearing loss, facial palsy, parotitis, thyroiditis, and cervical lymphadenitis are potentially associated with COVID-19[16].

Identifying all symptoms associated with COVID-19 is crucial to ensure early detection of atypical cases and to prevent the spread of the disease. A probably unprecedented number of research groups around the world have united around one goal to study both SARS-CoV-2 and the disease it causes, COVID-19. One of the achievements of this collective effort is an ever-expanding list of COVID-19-related symptoms[17]. Like all medical specialists, otorhinolaryngologists try to detect the rare symptoms associated with COVID-19 in relation to their field. This study was designed to investigate balance disorders, which are among the rarer symptoms and whose relation with COVID-19 has not been clearly demonstrated. In addition, for the first time in the literature, we investigated the relation between balance disorders in COVID-19 patients and lung involvement due to the disease. The symptoms of COVID-19 seen in the first four weeks were defined as acute symptoms by the UK National Institute for Health and Care Excellence (NICE)[18,19]. This acute period of COVID-19 disease was examined for the presence of balance disorders with a self-reported questionnaire, similar to previous studies, in patients who were diagnosed with COVID-19 by RT-PCR test and had thoracic CT for the evaluation of COVID-19[19].

The relation between balance disorders and COVID-19 has been demonstrated by a limited number of previous studies[19]. Although it is not known exactly how COVID-19 causes balance disorder, hypotheses related to neurodegenerative, vascular, immune, and psychological disorders seen in COVID-19 have been suggested. Anosmia and sensorineural hearing loss seen in COVID-19 have shown that SARS-CoV-2 can cause nerve damage[19]. SARS-CoV-2 attaches to angiotensin-converting enzyme 2 (ACE-2) receptors and Transmembrane serine protease 2 (TMPRSS-2) receptors in the nasal cavity after it enters the cell and causes damage to the olfactory nerve[19,20]. In mice, ACE-2 and

TMPRSS-2 receptors have been demonstrated in the Eustachian tube, middle ear, and inner ear[21]. Through these receptors, SARS-CoV-2 can enter the vestibule and affect the vestibular nerve[19]. SARS-CoV-2 is known to cause vascular damage. Facial paralysis seen in COVID-19 has been attributed to the involvement of the vasa nervorum of the facial nerve and demyelination due to ischemia in the nerve[19,22]. Similar pathophysiology can also be seen in the vestibular nerve, and balance disorder may occur[19]. Another hypothesis is the damage that may occur in the vestibular system through the immune system[19]. Anxiety and stress seen in COVID-19 patients can lead to balance disorder[23]. It has also been suggested that prolonged bed rest may cause otolith detachment and lead to positional vertigo[8].

In a previous study, it was reported that 18.4% of the patients with COVID-19 had balance disorder, and the type of balance disorder observed was dizziness at a rate of 94.1% and acute vertigo at a rate of 5.9%[8]. Although balance disorder is relatively rare in COVID-19 disease, it can be seen as a presenting symptom (4.5%) or the only symptom (2.3%)[24]. The most observed balance disorders, vertigo and/or dizziness, in COVID-19 patients have developed within the first month after the classic symptoms of COVID-19[24]. In addition, it has been reported that the balance disorder observed was completely resolved in most of the patients. This improvement has been observed within 14 days in two-thirds of the patients who recovered completely[24].

In our study, balance disorder was observed in 19.3% of the patients. While this rate was 28.2% in patients with lung involvement, it was 10.3% in patients without lung involvement. While 2.01% of COVID-19 patients had vertigo, 17.4% had dizziness. The number of patients with a balance disorder, the number of patients with dizziness, the duration, and severity of balance disorder were found to be significantly higher in COVID-19 patients with pulmonary involvement (p< 0.05). Although the values we found in our study were similar to the study of Viola et al[8], the rate of vertigo in our study

was higher (10.45%). Viola et al. have included patients between the 30-60 days after diagnosis of COVID-19 in their study[8]. However, the patients within the first month after the diagnosis of COVID-19 were included in our study. The high vertigo rate detected in our study may be related to this.

There are some limitations of our study, which examines the balance disorders seen in COVID-19 and the relationship between the balance disorders and lung involvement seen in COVID-19 patients. The first limitation of our study is that it is a self-reported questionnaire study. It is difficult to obtain a complete vestibular assessment in COVID-19 patients due to the need for protective equipment, the need for healthcare personnel to protect themselves, and the risk of disease transmission[25]. In addition, almost all of the studies in the literature are self-reported questionnaires[19]. Another limitation is the period we examined in our study. SARS-CoV-2 has symptoms and sequelae called post-COVID syndrome that can be seen even after 12 weeks[18,19,26]. Therefore, the results of our study are the outcomes of the acute period of COVID-19 and cannot be generalized to the entire period of the disease. The last and most important limitation of our study is that all of the patients we included in our study received Favipiravir treatment, which is known to affect the audiovestibular system[27]. The balance disorders seen in patients may be related to this drug. However, the fact that all patients received favipiravir treatment does not affect the results of our comparisons between patients with and without pulmonary involvement, which was the main aim of our study.

In conclusion, balance disorders can be a symptom of COVID-19. These symptoms may be seen more frequently and may be more severe and longer lasting in patients with pulmonary involvement due to COVID-19. Considering the suspicion of SARS-CoV-2 in acute balance disorders in the COVID-19 pandemic is very important to prevent the spread of the disease.

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ETHICS COMMITTEE APPROVAL

This study was approved by İstanbul University-Cerrahpaşa Rectorate Clinical Research Ethics Committee (Date: 26.04.2022 Decision no: 367843).

CONFLICT of INTEREST

None of the authors had conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: DÇ

Analysis/Interpretation: SU

Data Collection or Processing: DÇ

Writing: DÇ, SU

Review and Correction: DC, SU

Final Approval: DÇ, SU

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