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Original Research

The Effects of Smoking in Patients in the Intensive Care Unit During the COVID-19 Pandemic

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Abstract

Objectives: In this study, we aimed to see the effects of smoking prevalence, the length of stay regarding the usage of cigarettes, and the effects on the mortality of COVID-19 in our Intensive Care Unit (ICU).

Methods: This is a retrospective single-centered study that was done in the ICU on patients with COVID-19 between 16th of March and 16th of May in 2020. The demographic data, comorbidity status, the units they were accepted from, clinical symptoms, respiratory support, prevalence of smoking, length of stay in the ICU, and mortalities of the patients were recorded. There were two groups: Smoker and non-smoker. There were 1100 COVID-19 patients and 150 of these were treated in ICU unit. 95 patient's data were accessed. Statistical analyses were performed with the Scientific Package for the Social Science (version 21.0; SPSS Inc.).

Results: There were 69.4% non-smoker and 35.8% smoker, and 5.3% of the smoker did smoke before (Table 1). The average age of the patients in smoker group was less than nonsmoker. The incidence of chronic obstructive pulmonary disease was higher in smokers (Table 2). The most common symptom was cough and it was 82% in nonsmoker group and 76.5% in smoker group (Table 3). In both groups, respiratory support was provided by İMV (Table 4). There was no relationship between two groups according to age (p=0.044) and gender of patients (p:0.062) (Table 2). The length of ICU stay was 7.6 days for smoking patients in the ICU and 9.3 days for non-users. While the mortality was 52.9% for smokers, it was 39.3% for non-smokers. No statistical correlation was found between smoking status, length of stay in ICU, and survival (Fig. 1). Smoking is blamed among the factors that cause this aggressive process, which can progress to respiratory failure and result in mortality in COVID-19 disease.

Conclusion: Some studies also claim that smoking can be protective. There is still no clarity on this issue. It was concluded that smoking has no effect on the duration of ICU stay and mortality in patients treated in the ICU with respiratory failure due to COVID-19 pneumonia.

Keywords: COVID-19, ICU, mortality, smoking

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Responsible for severe pneumonia which was first seen in China's city, Wuhan, in December 2019 and spread all around the world, the name of the pathogen was determined by the International Committee on Taxonomy of Viruses as the severe acute respiratory syndrome coronavirus-2 (SARS CoV-2).[1] This pneumonia was named Coronavirus Disease 2019 (COVID-19) by the World Health Organization.[2]

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Smoking is still the secondary reason for the deaths in the world and it is expected to reach a rate of 9 million deaths in 2030.[3] Epidemiological studies show that the usage of cigarettes is an important risk factor for cardiovascular diseases (CAD), chronic obstructive pulmonary disease (COPD), and lung cancer.[4-6] The usage of cigarettes is detrimental to the immune system. Not only it has negative effects on the response to infections but it also makes people more susceptible to infectious diseases.[7] People who smoke compared to people who do not smoke get infected by influenza twice as much and have more severe symptoms. It has also been shown that the mortality of people was higher with people who used tobacco during middle-east respiratory syndrome coronavirus epidemic that occurred in previous years.[8,9] Toxins that result in immune disorder are nicotine, carbon monoxide, and acrolein reactive oxidant materials.[10] Because serum antioxidant concentrations such as folate, C, and E vitamins have been found low on chronic smokers which strengthened the idea of cigarette harm on the oxidant defense system.[11,12]

There are many speculative studies on the effects of smoking cigarettes on COVID-19 patients. Even though the usage of cigarettes is in a high prevalent in China, the number of people who have been diagnosed with COVID-19 who are also smokers was not as high as expected[13] It is possible to see that smoking and COVID-19 do not have a strong connection and in the two studies that have been done, and it is observed that COVID-19 was in a low prevalence on patients who use tobacco products.[14] However, another study indicated, that usage of tobacco products is one of the risk factors of the disease progression.[15] In this study, we aimed to see the effects of smoking on the length of stay and the mortality rates in our COVID-19 patients treated in the Intensive Care Unit (ICU).

Methods

This study was a retrospective and single-center study, including our COVID-19 patients admitted to the ICU between the 16th of March and 16th of May of 2020 after obtaining an approval letter from the local ethics committee of our hospital, dated June 02, 2020, numbered 2810. Patients were eligible for the study when they were diagnosed with COVID-19 and aged over 18 years old. Insufficient data were exclusion criteria.

Diagnosis of COVID-19 pneumonia was made using thorax computed tomography (CT) by seeing multifocal ground-glass opacity and getting oropharyngeal, nasopharyngeal polymerase chain reaction tests positive.

All the data were taken from the hospital's database. From the hospital's database, we recorded the ages, genders, body mass index (BMI), comorbidity conditions, units that they were treated in the intensive care, their complaints when they came to the hospital (fever, cough, and dyspnea), oxygen therapy methods (nasal mask, nasal high flow [NHF]), and mechanical ventilation methods – non-invasive mechanical ventilation (NIMV) and invasive mechanical ventilation (IMV) of patients. Conditions regarded to the usage of cigarettes were recorded as patients who are active smokers, patients who smoked before, and patients who do not smoke. Then, the patients were divided into two groups: Smokers (active smokers and patients who smoked before) and non-smokers.

Statistical Analysis

Statistical analyses were performed with the Scientific Package for the Social Science (version 21.0; SPSS Inc., Chicago, IL, USA). Continuous variables were given as mean±standard deviation if they were distributed normally or as median (interquartile range) if they were distributed abnormally. Qualitative variables were given as a percentage. Comparison of normally distributed data was performed by independent samples t-test. Abnormally distributed data compared with the Mann–Whitney U-test. Categorical variables were compared by the Chi-Square test. Differences were considered statistically significant for p values less than 0.05. Survival analysis has been performed by Kaplan–Meier curve.

Results

There were 1100 COVID-19 patients in our hospital and 150 of these were treated in the intensive unit. However, data from 95 patients are taken into consideration for this study. 64.2% of these patients declared that they never smoked, 5.3% of these patients smoked before, and 30.5% of the patients were active smokers (Table 1). All the conditions regarding the patient's age, gender, BMI, and comorbidity are given in Table 2. The average age of the patients who smoked was less than the patients who were non-smokers (p=0.044). There was no statistically significant difference between the groups between gender and BMI. Diagnoses of COPD were higher in the smoker patients compared to the non-smoker patients (p=0.018). A remarkable statistical difference was not seen between the two groups regarding

Table 1. Smoking habits of patients

	Number	Percentage
All patients	95	100
Non-smoker	61	64.2
Ex-smoker	5	5.3
Active smoker	29	30.5

Table 2. Demographic details and comorbidities

Parameter	All patients n=95	Non-smoker n=61	Ex and Active smoker n=34	p
Age, years, mean±standard deviation	66.24±13.53	68.1±14.6	62.7±10.7	0.044
Female patients n (%)	32.6	39.3	20.6	0.062
Body mass index, kg/m^2, mean±standard deviation	26.35±2.85	26.5±3.0	26.0±2.5	0.420
Comorbidities				
Diabetes mellitus (%)	33.7	31.1	38.2	0.483
Hypertension (%)	51.6	50.8	52.9	0.843
CAD (%)	22.1	18	29.4	0.20
COPD (%)	9.5	3.3	20.6	0.018

CAD: Cardiovascular diseases; COPD: Chronic obstructive pulmonary disease.

their comorbidity conditions (Table 2). A remarkable statistical difference was not seen between the two groups regarding the units that they were accepted to be treated and their complaints when they came to the hospital (Table 3). Between the groups, there has not been a remarkable statistical difference seen regarding the usage of IMV, NIMV, NHF, and masks (Table 4). Between the groups, there has not been a remarkable statistical difference seen regarding the length of stay in the intensive unit care and mortalities (Fig. 1). There has not been a correlation detected between the usage of cigarettes and the length of stay in the intensive care and mortalities (p=0.855) (Table 5).

Discussion

Even though for the most part the COVID-19 infection has an asymptomatic flow, it can even cause acute respiratory failure after pneumonia. This group of patients needs oxygen support treatments or mechanical ventilation support in ICUs. With treatment in ICUs and mechanical ventilation support, mortality increases. Factors that are the cause of the increase in respiratory failure which results in mortalities are being searched. Age, comorbidity, and in some data, cigarettes are some factors that cause predisposing.[16]

Since the usage of cigarettes increases the risk of cardiovas-

Table 3. ICU admission units

Parameter	All patients n=95	Non-smoker n=61	Ex and Active smoker n=34	p
Emergency department (%)	45.3	41	52.9	
Inpatient services (%)	54.7	59	47.1	
Fever (%)	32.6	34.4	29.4	0.617
Cough (%)	45.3	44.3	47.1	0.793
Dyspnea (%)	80	82	76.5	0.521

Table 4. Respiratory support

Parameter	All patients n=95	Non-smoker n=61	Ex and Active smoker n=34	p
Nasal oxygen				
1st day (%)	32.6	29.5	38.2	0.384
All time (%)	44.2	42.6	47.1	0.676
High-flow nasal oxygen				
1st day (%)	15.8	19.7	8.8	0.164
All time (%)	22.1	26.2	14.7	0.194
NIMV				
1st day (%)	4.2	4.9	2.9	0.646
All time (%)	7.4	8.2	5.9	0.679
IMV				
1st day (%)	45.3	47.5	41.2	0.550
All time (%)	64.2	67.2	58.8	0.414

NIMV: Noninvasive mechanical ventilation; IMV: Invasive mechanical ventilation.

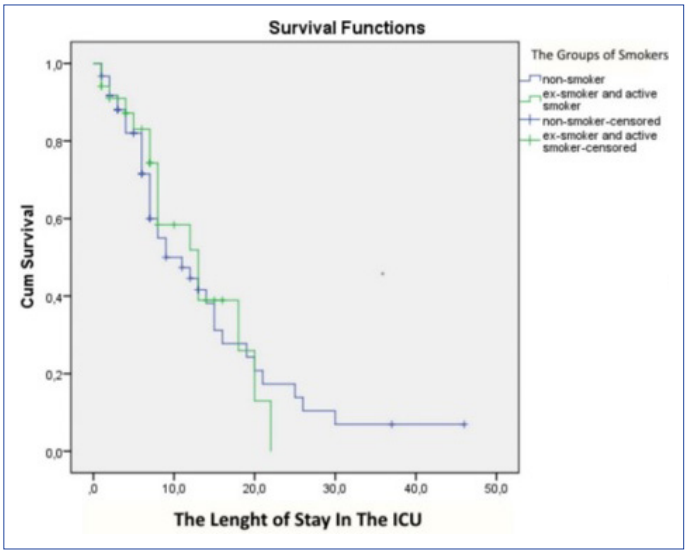

Figure 1. Survival Functions.

cular disease, cancer, and respiratory diseases, it is thought that the usage of cigarettes will increase the intensity of COVID-19 disease.[15] In this study when we consider the comorbidity of the patients, the COPD prevalence among patients who are smokers was found by 20.6% while it was 3.3% with patients who are non-smokers. In a study that was done with COPD disease, it was found that being an active smoker increases the risk of the intensity of COVID-19 disease by double.[17] Even though we did not find a statistical difference between the other comorbidities, it has been seen that hypertension, diabetes, and coronary artery disease are seen higher in patients who are smokers.

In a meta-analysis that was done in the USA, while the prevalence of using cigarettes in the community is 13.8%, it is 2.1% with patients who are hospitalized, it is as low as 1.1% with patients who are in ICUs.[18] In another compilation in China, the prevalence of smoker patients of COVID-19 was lower than expected.[19] According to the Turkish Statistical Institute (TUIK), the prevalence of the usage of tobacco is 26.5% in Turkey. According to these data, 40.1% of men and 13.3% of women are active smokers in Turkey.[20] In our study, 64.2% of these patients declared that they never smoked, 5.3% of these patients smoked before, and 30.5% of the patients were active smokers. In our study, 79.4% of smokers were men while 20.4% were women. In our study, the percentage of smokers among the patients who were hospitalized in the ICU was higher compared to the other countries and the community of Turkey. In China, the gender distribution of the COVID-19 patients was equal.[13] Despite that, in a study that was done with critical patients, it was seen that the man was affected worse than the woman.[21] According to our data, even though the percentage of smokers was higher for male patients, there was no difference between the gender distribution of smokers and non-smoker patients. However, the number of patients who are in critical condition was higher with male patients compared to women.

Even though the specific effects of using tobacco products on being hospitalized for COVID-19 are not certain, because of all the toxins and all the chemicals in the cigarettes, it is not known how these materials have a protective effect as an immunomodulator or antiviral against COVID-19. However, it is known that nicotine prevents acute respiratory distress syndrome (ARDS) in animals and it has been shown in vitro to inhibit tumor necrosis factor (TNF) expression in the airway.[22,23]

Nicotine is an agonist of the cholinergic anti-inflammatory pathway that regulates host immune and inflammatory responses.[24] Without preventing the production of inflammatory cytokines, it prevents the production of pro-inflammatory cytokines such as TNF, interleukin (IL) 1, and IL-6.[25-28] It is found that such an effect protects against cytokine-induced diseases that cause organ damage such as sepsis and endotoxemia as well as death. "Cytokine Release Syndrome" (cytokine storm) can occur in response to infections and it will be able to progress toward ARDS which is a phenomenon characterized by increased release of pro-inflammatory cytokines.[28-31] SARS-CoV-2 can increase vascular permeability by activating the innate immune system and the release of numerous cytokines, including IL-6 and cause dyspnea and respiratory failure as a result of fluid and blood cells migrating to the alveoli.[29] IL 6 was decisive in mortality in the case series that was done with 160 COVID-19 patients and in another study that was done with 191 COVID-19 patients; it was higher in patients who died compared to patients who survived.[32,33] For this reason, the cytokine storm is a therapeutic target in clinical studies that are done with COVID-19 patients, and nicotine has effects on reducing the intensity of the cytokine storm on the immune system.

In the literature, conflicting findings regarding smoking report that smoking and nicotine downregulate angiotensin-

Table 5. ICU stay days

Parameter	All patients n=95	Non-smoker n=61	Ex and Active smoker n=34	p
ICU stay, days, mean±standard deviation	8.71±7.92	9.3±8.8	7.6±5.8	0.329

converting enzyme 2 (ACE2).[34,35] However, other studies that were published during the pandemic that showed that tobacco is raising ACE2 does not allow robust result on if nicotine or smoking has effects on ACE2.[36] For this reason, there is uncertainty if nicotine increases COVID-19 along the renin-angiotensin-aldosterone axis. It may explain, at least in part, the potential benefits of nicotine through its immunomodulatory effects and its complex interactions with the renin-angiotensin system proposed by this hypothesis. Increased violence among smokers who are hospitalized for COVID-19, or the negative consequence, may be due to these patients' sudden withdrawing of nicotine intake during hospitalization.[15]

The effects of active, ongoing smoking on the progression of COVID-19 are controversial. Lippi and Henry[37] showed that active smoking is not associated with the severity of COVID-19. In a meta-analysis study that was done on 30127 SARS-CoV-2 patients, it has been found that tobacco use is one of the risk factors for disease progression.[15]

Various comorbidities have been associated with the severity of the disease and mortality and the clinical course in COVID-19 patients.[38] Several comorbidities have been associated with the clinical course and severity of the disease as well as mortality in patients with COVID-19. Since comorbidities such as smoking-related CAD and COPD are also risk factors that increase the severity of COVID-19, the presence of these comorbidities makes it difficult to interpret the effects of nicotine. Nicotine is not expected to act as chemoprophylaxis as it does not have direct antiviral properties. Therefore, nicotine is unlikely to prevent infection and SARS-CoV-2. However, it has been suggested that the above hypothesis may be related to experiencing COVID-19 disease at a milder severity and reducing the risk of hospitalization.[15] Although it is thought that smoking may have positive effects on the process of COVID-19 disease, it may probably have negative consequences in the process of intensive care patients. This may be related to the increased risk of other diseases associated with smoking.

In our study, no difference was found between smoking and the non-smoking patient's nasal oxygen, NHF, NIMV, and IMV treatment applications. IMV application was used as high as 64%. When the complaints of the patients were compared, no difference was found between the groups, and it was seen that the patient presented with dyspnea in the foreground. When the units where the patients were admitted and evaluated, it was observed that the smoking patients were admitted from the emergency service in the foreground while the patients who were non-smokers were admitted from the COVID services. This situation may be associated with the rapid progression of COVID-19 associated with the high incidence of COPD in smoking patients. The duration of stay was found to be 7.6 days for smoking patients in the ICU and 9.3 days for non-users. While the mortality was 52.9% for smokers, it was 39.3% for non-smokers. Although it is not statistically significant, it can be thought that the intensive care stay of smokers is short while the survival is less.

The limitation of our study, its retrospective nature, and the low number of patients compared to the general population can be demonstrated. The high prevalence of COPD in smoking patients may cause hesitation in evaluating the potential positive effects of smoking.

Conclusion

As a result, no effect of smoking on intensive care stay and mortality was found in patients treated in the ICU due to respiratory failure due to COVID-19.

Disclosures

Ethics Committee Approval: The local ethics committee of Sisli Hamidiye Etfal Training and Research Hospital, Dated 02/06/2020, Numbered 2810.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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