testing preference where the most frequent reason for preferring home-based testing was "sleeping in one's own bed" (4, 5).

We also found that PAP adherence did not differ by PAP initiation strategy, consistent with clinical trial results (6, 7). This is reassuring given concerns that durable medical equipment support for home-based initiation in the real world is lower than what has been provided in clinical trials. However, we did find that adherence was significantly lower among patients who had PAP initiated in a manner discordant with their personal preference. Specifically, patients who preferred laboratory-based initiation but received home autotitration had the lowest PAP usage. A preference for in-laboratory titration may identify a subset of patients who need higher levels of support to optimize PAP adherence. Unfortunately, we did not collect information about health literacy or self-efficacy to directly test this hypothesis.

The results of this study reflect the preferences of patients initiating treatment from an academic sleep medicine clinic. Therefore, the findings may not be generalizable to other patient populations. Furthermore, because patients were recruited into this study, there may be selection biases in who agreed to participate. In addition, this study was conducted before the global coronavirus disease (COVID-19) pandemic, which may lead to changes in how both patients and clinicians weigh the benefits and risks of in-laboratory titration studies (8).

Over the last decade, there has been an increasing call toward a sleep healthcare delivery system that encourages patient engagement and incorporates patient values in clinical decision-making (9). Our findings suggest that patient preference should play an important role in selecting a strategy for PAP initiation. Not only does such a strategy hold true to the values of patient-centered care, but our data suggest it may lead to better treatment outcomes. Future research should prospectively assess whether OSA treatment approaches that explicitly incorporate patient preference lead to improved clinical outcomes.

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References

1 Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *J Clin Sleep Med* 2019;15:301–334.
2 Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med* 2019;15:335–343.
3 Skomro RP, Gjevre J, Reid J, McNab B, Ghosh S, Stiles M, *et al*. Outcomes of home-based diagnosis and treatment of obstructive sleep apnea. *Chest* 2010;138:257–263.
4 Garg N, Rolle AJ, Lee TA, Prasad B. Home-based diagnosis of obstructive sleep apnea in an urban population. *J Clin Sleep Med* 2014;10:879–885.
5 Safadi A, Etzioni T, Fliss D, Pillar G, Shapira C. The effect of the transition to home monitoring for the diagnosis of OSAS on test availability, waiting time, patients' satisfaction, and outcome in a large health provider system. *Sleep Disord* 2014;2014:418246.
6 Rosen CL, Auckley D, Benca R, Foldvary-Schaefer N, Iber C, Kapur V, *et al*. A multisite randomized trial of portable sleep studies and positive airway pressure autotitration versus laboratory-based polysomnography for the diagnosis and treatment of obstructive sleep apnea: the HomePAP study. *Sleep (Basel)* 2012;35:757–767.
7 Berry RB, Hill G, Thompson L, McLaurin V. Portable monitoring and autotitration versus polysomnography for the diagnosis and treatment of sleep apnea. *Sleep* 2008;31:1423–1431.
8 American Academy of Sleep Medicine. Summary of CDC recommendations relevant for sleep practices during COVID-19. Darien, IL: AASM; 2021 [updated 2021 Jan 18; accessed 2021 Jan 25]. Available from: https://aasm.org/covid-19-resources/covid-19-mitigation-strategies-sleep-clinics-labs.
9 Hilbert J, Yaggi HK. Patient-centered care in obstructive sleep apnea: a vision for the future. *Sleep Med Rev* 2018;37:138–147.

Masking the 6-Minute Walking Test in the COVID-19 Era

The pandemic due to the coronavirus disease (COVID-19) has changed every aspect of life. Different measures have been implemented in pulmonary function test laboratories to ensure patient and staff safety (1–6); however, there are technical aspects that need to be clarified. One of these is whether face mask use affects the distance a subject can walk during the 6-minute walking test (6-MWT) as well as the oxygen saturation (Sp_{O_2}), heart rate (HR), dyspnea, and fatigue. The aim of this study was to investigate whether two types of face mask modified the walking distance during the 6-MWT among survivors of COVID-19.

Methods

Subjects over 18 years of age who were hospitalized for pneumonia due to a polymerase chain reaction–confirmed diagnosis of COVID-19 who were at least 30 days from discharge were invited to participate; those who could not walk were excluded from the study. It was decided at random (according to a table of random numbers)

Table 1. General characteristics of individuals

	Surgical (*n* = 36)	N95 (*n* = 41)
Age, y	45.9 ± 11.7	43.3 ± 12.3
Sex, M, *n* (%)	23 (64)	26 (63)
Weight, kg	76.2 ± 11.6	78.5 ± 13.5
Height, cm	164.1 ± 6.8	164 ± 7.7
BMI, kg·m^2	28.2 ± 3.6	29.1 ± 4.4
Overweight or obese, *n* (%)	31 (86.1)	37 (90)
High blood pressure, *n* (%)	4 (11.1)	5 (12.2)
Heart disease, *n* (%)	1 (2.8)	1 (2.4)
Diabetes, *n* (%)	4 (11.1)	6 (14.6)
Gastritis or GERD, *n* (%)	1 (2.8)	3 (7.3)
Tobacco smoker, *n* (%)	2 (5.6)	7 (17.1)
Asthma, *n* (%)	1 (2.8)	1 (2.4)
COPD, *n* (%)	1 (2.8)	0

Definition of abbreviations: BMI = body mass index; COPD = chronic obstructive pulmonary disease; GERD = gastroesophageal reflux disease; SD = standard deviation.
Data are expressed in mean ± SD (minimum to maximum) unless otherwise specified. All parameters, $P > 0.05$. Anthropometric comparisons were made between the surgical and N95 face mask groups (Student's *t* test or Mann-Whitney *U* test). The χ^2 test was used for categorical variables

whether the subject was entered to the surgical or N95 face mask group and whether the first walk was done with or without a face mask. The following two types of face masks were used: the surgical type, which is a pleated spunbond/melt-blown/spunbond nonwoven fabric made from 100% polypropylene (Mds Medical Dress Supplier) and the folding N95 particle face mask, which is made of polypropylene and 3M polyester (model 9010, 3M).

All participants performed two 6-MWTs according to American Thoracic Society/European Respiratory Society standards, with a recovery time of 30 minutes between the two 6-MWTs (7).

The National Institute of Respiratory Diseases "Ismael Cosío Villegas" in México City science and bioethics committee approved the study (C16–20), and participants signed the informed consent form. Anthropometric data are presented as means and standard deviations or as number and percentage; Student's *t* tests, Mann-Whitney *U* tests, and χ^2 tests were used to compare groups. Analysis of variance was used to analyze the results of the 6-MWT with or without the face mask, and Spearman's correlation coefficient (r_{sp}) and concordance correlation coefficient (CCC) were used to search for associations. Multivariable linear regression analysis was performed to investigate whether the difference walked in meters between both 6-MWTs (with and without face mask [dependent variable]) was predicted by some variables selected by their potential influence in the outcome, such as using or not using the face mask, the type of face mask, the presence of desaturation, the degree of dyspnea and fatigue (10-grade Borg Scale) (8), overweight or obese status, and tobacco use (independent variables). The Enright and colleagues' reference equation, adjusted for body mass index, was used to calculate the percentage predicted for the 6-MWT (9).

Results

We included 77 individuals aged 44 (±12) years, with 49 (64%) men. Table 1 shows their general characteristics; 41 (53%) subjects were assigned to the N95 face mask group. Without wearing the face mask, 43 (56%) subjects had a decrease in Sp_{O_2} of >4%, with 29 (67%) of them experiencing a desaturation event of an Sp_{O_2} ≤88% during the 6-MWT. No differences were observed in the meters walked, Sp_{O_2}, HR, dyspnea, or fatigue, between tests with or without the face mask (surgical or N95) (Table 2).

Figure 1 shows the association ($r_{sp} = 0.90$, $P < 0.001$) and agreement (CCC = 0.94) between the 6-MWT with and without the face mask. The mean difference between the two walks was −0.65 (±28) m, as shown in Figure 1B; the 95% limit of agreement was −55 to 54 m. In 12 (16%) subjects, the difference between walks was >30 m, which was considered the minimum clinically significant limit (MCSL) for changes in the 6-MWT (7). The multivariable analysis showed that this difference was independent of the type of face mask used ($P = 0.74$), presence of desaturation ($P = 0.63$), degree of dyspnea before ($P = 0.75$) and after ($P = 0.5$) the 6-MWT, obesity ($P = 0.89$), and tobacco use ($P = 0.93$).

When the analysis was conducted according to the type of face mask used during the walk, distances walked with or without face mask were very similar, as follows: with the surgical type face mask, $r_{sp} = 0.91$ ($P < 0.001$), CCC = 0.94, mean of the differences = −1.36 (±28.7) and 95% confidence interval = −57.7 to 55 m, whereas with the N95 face mask, $r_{sp} = 0.93$ ($P < 0.001$), CCC = 0.94, mean of the differences = −0.02 (±27.2), and 95% confidence interval = −53.4 to 53.3 m.

Discussion

The main finding of this study is that the mean difference in the 6-MWD when using either a surgical or N95 face mask compared with not wearing a face mask was −0.65 m, with a broad 95% limit of agreement; 84% of the subjects had agreement within MCSL (±30 m).

The 6-MWT aims to measure the distance that a subject can walk during 6 minutes in a 30-m corridor (7, 10–12). It is indicated in the diagnosis, prognosis, and monitoring of individuals with chronic lung diseases (13–15). Although its importance is based on the analysis of the effects of the treatment on the meters walked in 6 minutes, the 6-MWT also allows for measuring the functional status through other parameters, such as the Sp_{O_2}, HR, dyspnea, fatigue, and blood pressure (7, 13).

Recently, some authors have suggested the usefulness of the 6-MWT in the initial diagnosis of COVID-19 (16), for early discrimination of mild from severe cases; however, there are concerns about the likely transmission of COVID-19 via the air to healthcare personnel and individuals with other chronic lung diseases who attend pulmonary function test laboratories (17, 18). Therefore, new preventive measures have been proposed, one of which is the use of face mask to reduce the risk of infection (16).

Traditionally, the 6-MWT is performed without a face mask, and the use of a face piece that covers the mouth and nostrils can increase the CO_2 concentrations to 3.0% (±0.5%), especially in subjects performing low-intensity exercise (19, 20). In this sense, using an N95 respirator may be associated with increased breathing effort, sensation of suffocation, and altered results during the 6-MWT. As far as we know, there is only one study that has evaluated the use of a surgical face mask during the 6-MWT (21); these authors found no difference in the meters walked ($P = 0.99$) in healthy subjects, and the only significant difference was in the degree of dyspnea ($P < 0.001$).

Table 2. 6-MWT differences with or without a surgical or N95 face mask

	Surgical Facemask ($n = 36$)		N95 Facemask ($n = 41$)	
	With Face Mask	Without Face Mask	With Face Mask	Without Face Mask
6-MWD, m	516.2 ± 77.8	517.6 ± 90.6	535.5 ± 78.9	537 ± 73.6
6-MWD, % of predicted	86.7 ± 18.8	86.5 ± 16.5	88.6 ± 17	88.5 ± 17.2
Basal Sp_{O_2}, %	92.4 ± 1.6	93 ± 1.9	93 ± 1.6	93 ± 1.8
Lowest Sp_{O_2}, %	88.2 ± 3.2	88.3 ± 3.5	87.8 ± 3.9	87.5 ± 4.1
Final Sp_{O_2}, %	90.3 ± 3.5	90.5 ± 3.7	89.4 ± 4.3	89.4 ± 4.3
1-min Sp_{O_2}, %	92.6 ± 2.8	93.1 ± 2.1	91.8 ± 3.3	92.1 ± 2.9
3-min Sp_{O_2}, %	93.3 ± 1.8	93.5 ± 1.6	94 ± 1.5	93.6 ± 1.7
Basal HR, bpm	83 ± 12	83 ± 12	82 ± 13	82 ± 14
Highest HR, bpm	122 ± 15	123 ± 16	124 ± 16	123 ± 13
Final HR, bpm	114 ± 19	116 ± 18	121 ± 17	118 ± 17
1-min HR, bpm	98.1 ± 17.6	95.7 ± 16.7	101.1 ± 17.6	100.8 ± 18.5
3-min HR, bpm	91.5 ± 14.2	91.6 ± 15.5	92.6 ± 14.2	92.4 ± 14.7
Dyspnea basal score	0.2 ± 0.7	0.3 ± 0.7	0.3 ± 0.4	0.3 ± 0.6
Dyspnea final score	1.2 ± 1.2	1.0 ± 1.1	1.8 ± 1.5	1.2 ± 1.4
Dyspnea 1-min score	1 ± 1.1	0.9 ± 1	1.3 ± 1.2	1 ± 1.2
Dyspnea 3-min score	0.6 ± 0.8	0.5 ± 0.8	0.7 ± 0.7	0.5 ± 0.7
Fatigue basal score	0.6 ± 1.0	0.6 ± 1.3	0.6 ± 1.0	0.6 ± 1.0
Fatigue final score	1.8 ± 2.2	1.8 ± 1.2	2.4 ± 2.0	2.3 ± 2.0
Fatigue 1-min score	1.6 ± 1.9	1.7 ± 2.1	2.1 ± 1.5	1.8 ± 1.7
Fatigue 3-min score	1.1 ± 1.8	1.1 ± 1.9	1.3 ± 1.2	1.3 ± 1.4

Definition of abbreviations: 6-MWD = 6-minute walking distance; 6-MWT = 6-minute walking test; HR = heart rate; Sp_{O_2} = oxygen saturation measured by pulse-oximeter.
Data are presented in mean ± SD. The 1-minute and 3-minute scores correspond with measurements at 1 minute and 3 minutes after the 6-MWT. The dyspnea and fatigue scores were measured with the Borg Scale (8). The 6-MWD% predicted is the percentage predicted of the 6-MWD according to Enright and Sherrill (9). All parameters $P > 0.05$ between with and without the face mask according to the type of face mask (analysis of variance).

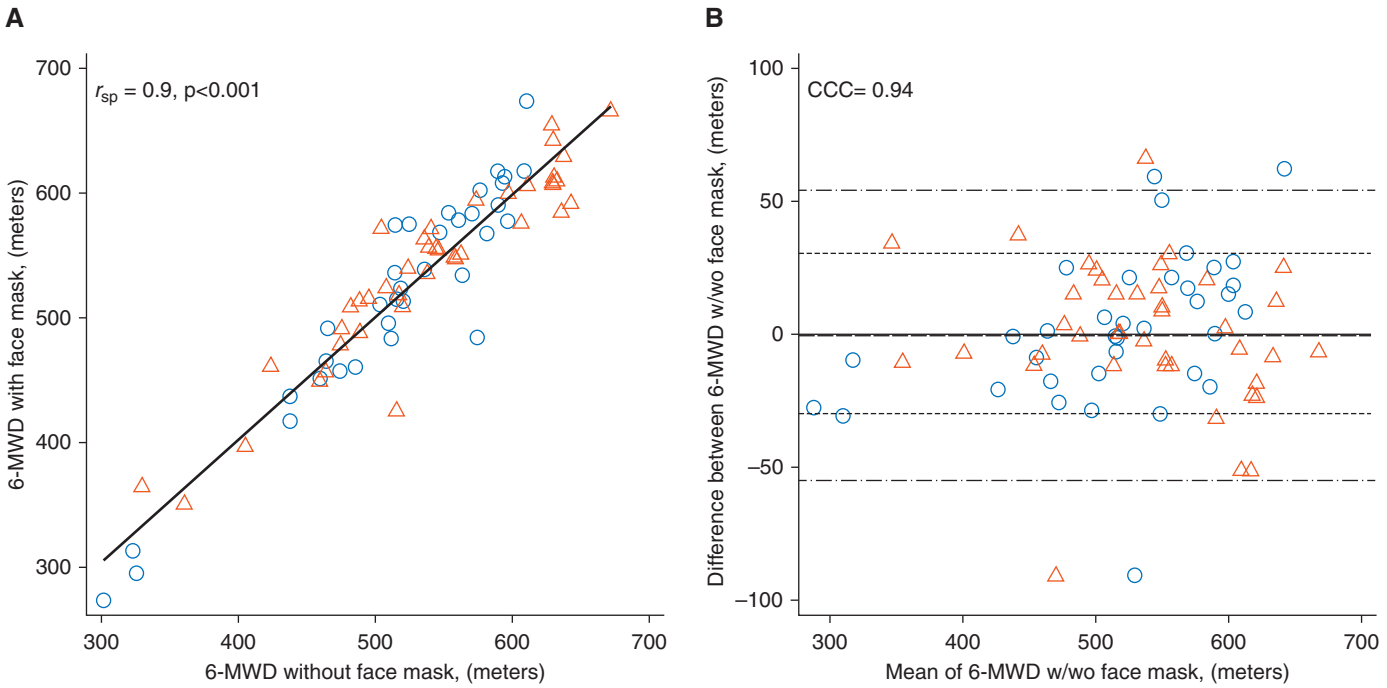

Figure 1. (*A*) Spearman correlation ($r_{sp} = 0.9$, $P < 0.001$) and (*B*) concordance correlation coefficient (CCC) between the meters walked during the 6-minute walking test (6-MWT) with and without face mask (CCC = 0.94). The small dashed lines represent the minimal clinically significant difference (±30 m) proposed in the evaluation of patients with chronic lung diseases, the dashed and dotted lines represent the 95% limits of agreement, and the large dashed lines represent the average of difference between the walking meters during the 6-MWT with and without the face mask. Open circles = surgical face mask; open triangles = N95 face mask. 6-MWD = 6-minute walking distance; w/wo = with/without.

Our study found that in 84% of the participants, the difference in meters walked was within the MCSL (±30 m) (13, 22–24), and no differences were obtained in the degree of dyspnea (25).

This study has limitations. Although this is a cohort of individuals who recovered from COVID-19, the number of participants in each group could be higher.

Conclusions

Surgical or N95-type face masks can be used during the 6-MWT, especially among those recovering from COVID-19, and the results regarding the meters walked as well as other variables, such as Sp_{O_2}, HR, and degree of dyspnea, are similar to those obtained without using a face mask.

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References

1 Wilson KC, Kaminsky DA, Michaud G, Sharma S, Nici L, Folz RJ, *et al*. Restoring pulmonary and sleep services as the COVID-19 pandemic lessens: from an Association of Pulmonary, Critical Care, and Sleep Division Directors and American Thoracic Society-coordinated Task Force. *Ann Am Thorac Soc* 2020;17:1343–1351.
2 Gochicoa-Rangel L, Torre-Bouscoulet L, Salles Rojas A, Guzmán-Valderrábano C, Silva-Cerón M, Benítez-Pérez RE, *et al*. Functional respiratory evaluation in the COVID-19 era: the role of pulmonary function test laboratories. *Rev Invest Clin* [online ahead of print] 7 May 2020; DOI: 10.24875/RIC.20000250.
3 Arce SC, Baldasaria RA, Brea Folco JC, Rodríguez Moncalvo JJ. Bioseguridad y prevención de infecciones cruzadas durante la realización de estudios de función pulmonar. *RAMR* 2020;19:25–31.
4 Yan Y, Chen H, Chen L, Cheng B, Diao P, Dong L, *et al*. Consensus of Chinese experts on protection of skin and mucous membrane barrier for health-care workers fighting against coronavirus disease 2019. *Dermatol Ther* 2020;33:e13310.
5 Sociedad Española de Neumología y Cirugía Torácica SEPAR. Recomendaciones de prevención de infección por coronavirus en las unidades de función pulmonar de los diferentes ámbitos asistenciales. SEPAR; 2020 [updated 2020 May; accessed 2020 Jun 6]. Available from: https://drive.google.com/file/d/1DQgTeca76H1VtkDg6-KhPqb-kOmVoLkl/view.
6 McGowan A, Sylvester K, Burgos F, Boros P, de Jongh F, Kendrick A, *et al*. Recommendation from ERS Group 9.1 (Respiratory function technologists /Scientists) Lung function testing during COVID-19 pandemic and beyond. European Respiratory Society; 2020 [accessed 2020 Aug 31]. Available from: https://www.ersnet.org/covid-19-guidelines-and-recommendations-directory.
7 Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, *et al*. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J* 2014;44:1428–1446.
8 Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14:377–381.
9 Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med* 1998;158:1384–1387.
10 Gochicoa-Rangel L, Mora-Romero U, Guerrero-Zúñiga S, Silva-Cerón M, Cid-Juárez S, Velázquez-Uncal M, *et al*. Prueba de caminata de 6 minutos: recomendaciones y procedimientos. *Neumol Cir Torax* 2015;74:127–136.
11 ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med* 2002;166:111–117.
12 Enright PL, McBurnie MA, Bittner V, Tracy RP, McNamara R, Arnold A, *et al*.; Cardiovascular Health Study. The 6-min walk test: a quick measure of functional status in elderly adults. *Chest* 2003;123:387–398.
13 Singh SJ, Puhan MA, Andrianopoulos V, Hernandes NA, Mitchell KE, Hill CJ, *et al*. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. *Eur Respir J* 2014;44:1447–1478.
14 Miyamoto S, Nagaya N, Satoh T, Kyotani S, Sakamaki F, Fujita M, *et al*. Clinical correlates and prognostic significance of six-minute walk test in patients with primary pulmonary hypertension. Comparison with cardiopulmonary exercise testing. *Am J Respir Crit Care Med* 2000;161:487–492.
15 Lacasse Y, Goldstein R, Lasserson TJ, Martin S. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2006;(4):CD003793.
16 Mantha S, Tripuraneni SL, Roizen MF, Fleisher LA. Proposed modifications in the 6-minute walk test for potential application in patients with mild COVID-19: a step to optimize triage guidelines. *Anesth Analg* 2020;131:398–402.
17 Gautret P, Colson P, Lagier JC, Parola P, Raoult D. Does spitting in public play a role in transmitting SARS-CoV-2? *Travel Med Infect Dis* 2020;36:101759.
18 Kutter JS, Spronken MI, Fraaij PL, Fouchier RA, Herfst S. Transmission routes of respiratory viruses among humans. *Curr Opin Virol* 2018;28:142–151.
19 Smith CL, Whitelaw JL, Davies B. Carbon dioxide rebreathing in respiratory protective devices: influence of speech and work rate in full-face masks. *Ergonomics* 2013;56:781–790.
20 Williams WJ. Physiological response to alterations in [O2] and [CO2]: relevance to respiratory protective devices. *J Int Soc Respir Prot* 2010;27:27–51.
21 Person E, Lemercier C, Royer A, Reychler G. [Effect of a surgical mask on six minute walking distance]. *Rev Mal Respir* 2018;35:264–268.
22 du Bois RM, Weycker D, Albera C, Bradford WZ, Costabel U, Kartashov A, *et al*. Six-minute-walk test in idiopathic pulmonary fibrosis: test validation and minimal clinically important difference. *Am J Respir Crit Care Med* 2011;183:1231–1237.
23 Redelmeier DA, Bayoumi AM, Goldstein RS, Guyatt GH. Interpreting small differences in functional status: the Six Minute Walk test in chronic lung disease patients. *Am J Respir Crit Care Med* 1997;155:1278–1282.

24 Demeyer H, Burtin C, Hornikx M, Camillo CA, Van Remoortel H, Langer D, *et al*. The minimal important difference in physical activity in patients with COPD. *PLoS One* 2016;11:e0154587.
25 Casanova C, Celli BR, Barria P, Casas A, Cote C, de Torres JP, *et al*.; Six Minute Walk Distance Project (ALAT). The 6-min walk distance in healthy subjects: reference standards from seven countries. *Eur Respir J* 2011;37:150–156.

Alcohol Consumption and the Risk of Acute Respiratory Distress Syndrome in COVID-19

To the Editor:

During the coronavirus disease (COVID-19) pandemic it has become clear that patients with comorbidities are not only at higher risk of contracting the disease but also to develop serious complications such as acute respiratory distress syndrome (ARDS). A dose-dependent correlation between alcohol consumption and viral infections is well documented (1) and, furthermore, alcohol consumption has been shown to increase the risk of acquiring community infections (2).

A general increase in the consumption of alcohol has been reported during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic (3). It has been hypothesized that patients with alcohol-related disorders are at an increased risk of COVID-19 (4). However, it remains unknown whether alcohol consumption is associated with a more severe course of COVID-19.

Methods

We conducted a cohort study to understand the association of alcohol use and ARDS development using data from ECHOVID-19 (The COVID-19 Echocardiography Study), a prospective multicenter cohort study of 215 hospitalized patients with COVID-19 recruited from eight hospitals in eastern Denmark (March 30 to June 1, 2020). All patients were included consecutively with the investigators blinded to the health status of patients before inclusion. Inclusion criteria for ECHOVID-19 were laboratory-confirmed SARS-CoV-19 infection, age $\geq$ 18 years, not admitted to an intensive care unit (ICU) at time of inclusion (patients were not excluded if later transferred to the ICU), and being capable of signing a written informed consent. Additional exclusion criteria for this substudy was an unknown history of alcohol consumption ($N = 44$).

The primary outcome was ARDS (defined according to the Berlin Criteria) (5) during hospitalization. Severe ARDS, defined as ARDS with an arterial oxygen pressure/fraction of inspired oxygen ratio $\leq$ 100 mm Hg, was a secondary outcome.

Information on alcohol consumption was obtained by a questionnaire. The exposure was defined as the continuous number of drinks of alcohol per week (12 g ethanol/drink). We used parametric and nonparametric tests to assess differences in baseline characteristics in relation to the outcome. Logistic regression models were used to test and visualize the association between alcohol consumption and the outcomes. A multivariable model was constructed to adjust for potential confounders of ARDS and severe ARDS development. The multivariable model included the variables: age, smoking status (ever-smoker vs. never-smoker), prevalent heart failure, and chronic obstructive pulmonary disease. All participants gave written informed consent, and the study was performed in accordance with the second Declaration of Helsinki and approved by the regional ethics board. The study is registered at Clinicaltrials.gov (NCT04377035).

Results

A total of 171 patients were included in the final sample. The mean age of the study sample was 69 $\pm$ 13 years and 55% were male. Baseline characteristics of patients progressing to ARDS and patients not developing ARDS are listed in Table 1. During follow-up (median, 6 d; interquartile range [IQR], 4–11) 44 patients (25.7%) developed ARDS. Of these, 22 patients (12.9%) developed severe ARDS. ARDS was not observed significantly more frequently in patients excluded from the study sample ($N = 15$ [34%]; $P = 0.27$). The comparison of self-reported alcohol consumption revealed that patients developing ARDS consumed more drinks of alcohol per week than patients free of ARDS (7.0 drinks: IQR, 5.0–20.0 vs. 3.0 drinks: IQR, 2.0–8.0; $P = 0.010$). In a univariable model, weekly alcohol consumption was associated with development of ARDS (odds ratio [OR], 1.06; 95% confidence interval [95% CI], 1.01–1.12; $P = 0.015$, per 1-drink increase) and severe ARDS (OR, 1.07; 95% CI, 1.02–1.13; $P = 0.009$) (Figure 1). The association between self-reported alcohol consumption and ARDS remained significant after multivariable adjustments (ARDS: OR, 1.05; 95% CI, 1.00–1.10; $P = 0.046$, per 1 drink increase; severe ARDS: OR, 1.07; 95% CI, 1.01–1.13; $P = 0.013$, per 1 drink increase).

Discussion

In this study, weekly alcohol consumption was associated with an increased risk of developing ARDS during hospitalization for COVID-19. Higher alcohol consumption is known to be detrimental to health, but it may also be an indicator of psychosocial and socioeconomic challenges. Currently, there does not exist published literature regarding the prognosis after COVID-19 infection according to alcohol consumption. However, before the COVID-19 pandemic, Simou and colleagues conducted a review and metanalysis investigating the association between alcohol consumption and risk of ARDS in hospitalized adults ($N = 177{,}674$) (6). The authors found that chronic high alcohol consumption significantly increased the risk

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