Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Respiratory Physiology & Neurobiology 288 (2021) 103644

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

Short communication

Pulmonary function and functional capacity in COVID-19 survivors with persistent dyspnoea

Arturo Cortés-Telles [a,*], Stephanie López-Romero [b], Esperanza Figueroa-Hurtado [a], Yuri Noemi Pou-Aguilar [a], Alyson W. Wong [c,d], Kathryn M. Milne [c,d], Christopher J. Ryerson [c,d], Jordan A. Guenette [d,e]

[a] Respiratory and Thoracic Surgery Unit. Hospital Regional de Alta Especialidad de la Peninsula de Yucatan, Calle 7 por 20 y 22 Num. 433, Fraccionamiento Altabrisa, Mérida, Yucatán, 97130, Mexico
[b] Internal Medicine Department. Hospital Regional de Alta Especialidad de la Peninsula de Yucatan, Calle 7 por 20 y 22 Num. 433, Fraccionamiento Altabrisa, Mérida, Yucatán, 97130, Mexico
[c] Department of Medicine, The University of British Columbia, 2775 Laurel Street, Vancouver, British Columbia, V5Z 1M9, Canada
[d] Centre for Heart Lung Innovation, Providence Health Care Research Institute, The University of British Columbia and St. Paul's Hospital, 166-1081 Burrard Street, Vancouver, British Columbia, V6Z 1Y6, Canada
[e] Department of Physical Therapy, The University of British Columbia, 2177 Wesbrook Mall, Vancouver, British Columbia, V6T 1Z3, Canada

ARTICLE INFO

Keywords:
Breathlessness
SARS-CoV-2
6-Minute walk test
Persistent symptoms

ABSTRACT

The purpose of this study was to examine the physiological mechanisms of persistent dyspnoea in COVID-19 survivors. Non-critical patients (n = 186) with varying degrees of COVID-19 severity reported persistent symptoms using a standardized questionnaire and underwent pulmonary function and 6-minute walk testing between 30 and 90 days following the onset of acute COVID-19 symptoms. Patients were divided into those with (n = 70) and without (n = 116) persistent dyspnoea. Patients with persistent dyspnoea had significantly lower FVC ($p = 0.03$), FEV_1 ($p = 0.04$), D_{LCO} ($p = 0.01$), 6-minute walk distance (% predicted, $p = 0.03$), and end-exercise oxygen saturation ($p < 0.001$), and higher Borg 0-10 ratings of dyspnoea and fatigue (both $p < 0.001$) compared to patients without persistent dyspnoea. We have shown that dyspnoea is a common persistent symptom across varying degrees of initial COVID-19 severity. Patients with persistent dyspnoea had greater restriction on spirometry, lower D_{LCO}, reduced functional capacity, and increased exertional desaturation and symptoms. This suggests that there is a true physiological mechanism that may explain persistent dyspnoea after COVID-19.

1. Introduction

Emerging research shows a burden of chronic symptoms and reduced quality of life in coronavirus disease 2019 (COVID-19) survivors (Carfi et al., 2020; Wong et al., 2020). Approximately half of patients recovering from COVID-19 report chronic dyspnoea 2–3 months after infection (Carfi et al., 2020; Garrigues et al., 2020; Wong et al., 2020). Dyspnoea is an independent predictor of morbidity and mortality in the general population and is associated with reduced functional capacity and adverse health-related quality-of-life (Laviolette et al., 2014). This complex and multidimensional symptom can result in a downward spiral of activity avoidance, deconditioning, and ultimately the inability to perform basic activities of daily living (Moxham and Jolley, 2009). Whether COVID-19 survivors with persistent dyspnoea ultimately enter this downward spiral is unknown. More research is needed to understand the mechanisms of persistent dyspnoea in survivors of COVID-19 in order to improve patient management following infection.

A growing body of literature indicates the presence of racial and ethnic disparities in COVID-19-related infections and hospitalizations (Mackey et al., 2020; Ogedegbe et al., 2020). A recent systematic review concluded that Hispanic populations experience a disproportionate burden of severe COVID-19 and have increased mortality (Mackey et al., 2020). Racial and ethnic disparities may be at least partly attributable to the higher rates of comorbidities that worsen COVID-19 outcomes. Mexico has a high prevalence of chronic non-communicable diseases (Parra-Rodriguez et al., 2020), with diabetes, obesity, and the presence

* Corresponding author.
E-mail address: dr_morenheim@hotmail.com (A. Cortés-Telles).

https://doi.org/10.1016/j.resp.2021.103644
Received 23 December 2020; Received in revised form 3 February 2021; Accepted 24 February 2021
Available online 27 February 2021

of more than one comorbidity all being independently associated with laboratory-confirmed COVID-19, need for hospitalization, and adverse outcomes (Giannouchos et al., 2020). Unfortunately, there is limited data on persistent COVID-19 symptoms, and particularly dyspnoea, in this population. Understanding differences in pulmonary function, comorbidities, and functional capacity between those with and without persistent dyspnoea may provide insight into the mechanisms of this symptom in individuals who are susceptible to the negative lasting effects of COVID-19. Accordingly, the purpose of this study was to compare spirometry, diffusing capacity of the lungs for carbon monoxide (D_{LCO}), and 6-minute walk distance (6MWD) in Mexican survivors of COVID-19 with and without persistent dyspnoea. We hypothesized that COVID-19 patients with persistent dyspnoea would have lower forced vital capacity (FVC), D_{LCO}, and 6MWD compared to patients without persistent dyspnoea, suggesting a physiologic driver of this persistent symptom.

2. Material and methods

This study received ethical approval (#2020-024) from the Hospital Regional de Alta Especialidad de la Peninsula de Yucatan and all patients provided written informed consent. Non-critically ill patients who tested positive for SARS-CoV-2 based on real-time reverse transcriptase-polymerase chain reaction on nasal swabs were identified from hospital records and subsequently contacted to participate. COVID-19 severity was classified as mild (ambulatory without hypoxemia), moderate (ambulatory but requiring supplemental O_2 of $\leq$5 L/min), or severe (hospitalized with O_2 >5 L/min and in the prone position for at least 12 h per day but without invasive mechanical ventilation). Follow-up testing occurred between 30 and 90 days after the onset of acute COVID-19 symptoms. Following the administration of a standardized questionnaire to determine the presence or absence of persistent symptoms (see list in Table 1) (Carfi et al., 2020), participants completed spirometry, D_{LCO}, and a 6-minute walk test (6MWT) according to recommended guidelines (Holland et al., 2014; MacIntyre et al., 2005; Miller et al., 2005) with data being expressed relative to predicted values (Enright and Sherrill, 1998; Hankinson et al., 1999; Stanojevic et al., 2017). Spirometry and D_{LCO} were performed using calibrated equipment (Ultima PF™ Pulmonary Function System, Medical Graphics, UK or Easy One Pro®, ndd Medical Technologies, Switzerland). Peripheral oxygen saturation via finger oximetry (Masimo RAD 5; Masimo Corporation, USA) was measured throughout the 6MWT. Independent t-tests and Fisher's Exact test were used where appropriate to compare groups with and without persistent dyspnoea and fatigue. A p-value <0.05 was considered statistically significant. Data are presented as mean ± SD unless otherwise specified.

3. Results

This study included 186 COVID-19 patients with non-critical illness. There was no difference in the time of experimental testing relative to the onset of COVID-19 symptoms comparing those with and without dyspnoea (59 ± 13 vs. 60 ± 14 days, respectively). Table 1 shows anthropometric data, comorbidities, persistent symptoms, pulmonary function, and 6MWT data for the entire group and in those with and without persistent dyspnoea. Persistent dyspnoea occurred in 38 % of patients, which was the second most common persistent symptom after fatigue (67 %). The percentage of patients with mild, moderate, and severe COVID-19 (see Table 2 for descriptive characteristics of severity subgroups) was 27, 14, and 59 %, respectively, with a relatively similar distribution in the dyspnoea (21, 23, and 56 %, respectively) and non-dyspnoea groups (31, 9, and 60 %, respectively). The dyspnoea and non-dyspnoea groups had similar age, sex, height, mass, body mass index, and frequency of comorbidities. Patients with persistent dyspnoea were more likely to experience persistent fatigue, chest pain, and anosmia/ageusia compared to their non-dyspnoea counterparts (all $p < 0.05$). Pulmonary function data shows that patients with persistent dyspnoea had significantly lower FVC ($p = 0.03$), forced expiratory volume in 1 s ($p = 0.04$), and D_{LCO} ($p = 0.01$), with 47 % having a restrictive ventilatory pattern compared to 33 % in the non-dyspnoea group. Patients with persistent dyspnoea also had lower %-predicted 6MWD ($p = 0.03$) and end-exercise oxygen saturation during the 6MWT ($p < 0.001$) compared to non-dyspnoea patients. Borg 0-10 ratings of dyspnoea and fatigue at the end of the 6MWT were significantly higher in those with persistent dyspnoea compared to those without (both $p < 0.001$). A secondary analysis was performed to compare those with and without persistent fatigue given the high prevalence of this symptom (Table 3). There were no statistically significant differences in pulmonary function or 6MWD between fatigue groups, although the group with persistent fatigue had higher Borg 0-10 ratings for dyspnoea and fatigue during the 6MWT (both $p < 0.01$) and were more likely to experience persistent dyspnoea ($p < 0.001$), myalgias ($p < 0.001$), and rhinitis ($p < 0.05$) compared to the group without persistent fatigue.

Table 1
Participant Characteristics.

	Overall (n = 186)	Dyspnoea (n = 70)	Non-Dyspnoea (n = 116)
Age, years	47 ± 13	48 ± 14	47 ± 13
Sex, %male	61	61	61
Height, cm	159 ± 11	159 ± 13	159 ± 10
Mass, kg	81 ± 20	79 ± 18	82 ± 20
BMI, kg/m^2	31.8 ± 6.7	31.2 ± 6.2	32.2 ± 6.9
Smoking history, %	20	21	20
Disease severity, n (mild, moderate, severe)	51, 26, 109	15, 16, 39	36, 10, 70
Comorbidities			
Obesity, %	52	49	53
Hypertension, %	20	13	24
Diabetes, %	16	14	16
Other, %	8	6	9
COVID-19 Symptoms			
Fatigue on effort, %	67	84‡	57
Dyspnoea, %	38	100‡	0
Myalgias, %	32	31	32
Cough, %	30	39	25
Chest Pain, %	30	43†	22
Sore throat, %	17	23	13
Sputum Production, %	17	20	15
Diaphoresis, %	17	17	17
Headache, %	15	19	13
Rhinitis, %	15	19	13
Telogen Effluvium, %	11	9	12
Anosmia/Ageusia, %	11	20†	6
Dermatological symptoms, %	12	10	13
Wheezing, %	7	9	6
Conjunctivitis, %	4	6	3
Diarrhea, %	3	6	2
Pulmonary Function			
FVC, %predicted	83 ± 18	80 ± 18*	85 ± 18
FEV_1, %predicted	88 ± 18	84 ± 18*	90 ± 18
FEV_1/FVC, %	85 ± 8	85 ± 6	85 ± 9
FEF_{25-75}, %predicted	108 ± 35	104 ± 32	110 ± 37
D_{LCO}, % predicted	99 ± 27	92 ± 28*	104 ± 25
V_A, % predicted	93 ± 16	91 ± 19	94 ± 14
6-Minute Walk Test			
Distance, m	450 ± 104	438 ± 103	457 ± 105
Distance, % predicted	83 ± 19	79 ± 18*	85 ± 20
Peak Heart Rate, bpm	110 ± 18	113 ± 19	108 ± 17
End-exercise SpO_2, %	95 ± 3	94 ± 4‡	96 ± 2
Peak Dyspnoea, Borg 0–10	2.1 ± 1.4	2.7 ± 1.4‡	1.8 ± 1.3
Peak Fatigue, Borg 0–10	1.9 ± 1.8	2.7 ± 2.2‡	1.4 ± 1.3

BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; FEF_{25-75}, forced expiratory flow between 25–75% of FVC; D_{LCO}, diffusion capacity of the lungs for carbon monoxide; V_A, alveolar volume; SpO_2, peripheral oxygen saturation. *p < 0.05, †p < 0.01, ‡p < 0.001 between dyspnoea and non-dyspnoea groups. Other comorbidities included metabolic syndrome, hypothyroidism, pulmonary hypertension, cancer, asthma, HIV, tuberculosis, and schizophrenia.

Table 2
Participant Characteristics.

	Mild (n = 51)	Moderate (n = 26)	Severe (n = 109)
Age, years	42 ± 11	54 ± 12	48 ± 14
Sex, %male	53	50	68
Height, cm	161 ± 11	158 ± 12	158 ± 12
Mass, kg	77 ± 18	79 ± 12	83 ± 21
BMI, kg/m^2	29.8 ± 6.7	31.7 ± 4.7	32.8 ± 6.9
Smoking history, %	29	31	14
Comorbidities			
Obesity, %	39	46	59
Hypertension, %	10	12	27
Diabetes, %	6	8	22
Other, %	6	12	7
COVID-19 Symptoms			
Fatigue on effort, %	59	73	70
Dyspnoea, %	29	62	36
Myalgias, %	31	38	30
Cough, %	31	38	28
Chest Pain, %	18	38	34
Sore throat, %	12	19	18
Sputum Production, %	12	19	18
Diaphoresis, %	18	19	17
Headache, %	18	4	17
Rhinitis, %	18	12	15
Telogen Effluvium, %	18	15	6
Anosmia/Ageusia, %	12	15	10
Dermatological symptoms, %	12	8	13
Wheezing, %	2	0	11
Conjunctivitis, %	0	12	5
Diarrhea, %	4	4	3
Pulmonary Function			
FVC, %predicted	94 ± 13	84 ± 14	78 ± 19
FEV_1, %predicted	96 ± 14	89 ± 16	84 ± 19
FEV_1/FVC, %	83 ± 5	83 ± 5	86 ± 9
FEF_{25-75}, %predicted	104 ± 34	107 ± 35	110 ± 35
D_{LCO}, % predicted	112 ± 21	107 ± 26	89 ± 26
V_A, % predicted	99 ± 15	95 ± 11	88 ± 17
6-Minute Walk Test			
Distance, m	493 ± 74	428 ± 97	436 ± 111
Distance, % predicted	83 ± 13	82 ± 19	83 ± 21
Peak Heart Rate, bpm	110 ± 16	117 ± 17	109 ± 19
End-exercise SpO_2, %	97 ± 2	94 ± 3	95 ± 3
Peak Dyspnoea, Borg 0–10	1.9 ± 1.1	2.5 ± 1.1	2.1 ± 1.6
Peak Fatigue, Borg 0–10	2.2 ± 1.5	3.4 ± 2.0	1.5 ± 1.7

BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; FEF_{25-75}, forced expiratory flow between 25–75% of FVC; D_{LCO}, diffusion capacity of the lungs for carbon monoxide; V_A, alveolar volume; SpO_2, peripheral oxygen saturation. Other comorbidities included metabolic syndrome, hypothyroidism, pulmonary hypertension, cancer, asthma, HIV, tuberculosis, and schizophrenia.

Table 3
Participant Characteristics.

	Fatigue (n = 125)	Non-Fatigue (n = 61)
Age, years	48 ± 13	46 ± 13
Sex, %male	62	59
Height, cm	159 ± 12	159 ± 10
Mass, kg	80 ± 19	82 ± 20
BMI, kg/m^2	31.7 ± 6.8	32.1 ± 6.3
Smoking history, %	22	18
Disease severity, n (mild, moderate, severe)	30, 19, 76	21, 7, 33
Comorbidities		
Obesity, %	51	52
Hypertension, %	21	18
Diabetes, %	22	2‡
Other, %	9	5
COVID-19 Symptoms		
Fatigue on effort, %	100‡	0
Dyspnoea, %	47‡	18
Myalgias, %	40‡	15
Cough, %	34	23
Chest Pain, %	34	21
Sore throat, %	20	10
Sputum Production, %	18	13
Diaphoresis, %	18	15
Headache, %	18	10
Rhinitis, %	19*	7
Telogen Effluvium, %	11	10
Anosmia/Ageusia, %	14	7
Dermatological symptoms, %	13	10
Wheezing, %	7	7
Conjunctivitis, %	6	2
Diarrhea, %	3	3
Pulmonary Function		
FVC, %predicted	82 ± 18	85 ± 18
FEV_1, %predicted	88 ± 18	88 ± 19
FEV_1/FVC, %	86 ± 8	83 ± 6
FEF_{25-75}, %predicted	110 ± 34	104 ± 37
D_{LCO}, % predicted	97 ± 26	105 ± 27
V_A, % predicted	92 ± 17	95 ± 15
6-Minute Walk Test		
Distance, m	443 ± 108	466 ± 95
Distance, % predicted	83 ± 20	84 ± 18
Peak Heart Rate, bpm	111 ± 19	107 ± 17
End-exercise SpO_2, %	95 ± 3	96 ± 3
Peak Dyspnoea, Borg 0–10	2.3 ± 1.5†	1.6 ± 1.0
Peak Fatigue, Borg 0–10	2.2 ± 1.9†	1.2 ± 1.2

BMI, body mass index; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; FEF_{25-75}, forced expiratory flow between 25–75% of FVC; D_{LCO}, diffusion capacity of the lungs for carbon monoxide; V_A, alveolar volume; SpO_2, peripheral oxygen saturation. *$p < 0.05$, †$p < 0.01$, ‡$p < 0.001$ between fatigue and non-fatigue groups. Other comorbidities included metabolic syndrome, hypothyroidism, pulmonary hypertension, cancer, asthma, HIV, tuberculosis, and schizophrenia.

4. Discussion

To our knowledge, this is the first study to characterize persistent symptoms, pulmonary function, and functional capacity in non-critically ill COVID-19 survivors with and without persistent dyspnoea. Describing the characteristics of these groups provides insight into the potential causes of persistent dyspnoea, which may help inform future evaluation and management of people recovering from COVID-19. Our results suggest that patients with persistent dyspnoea show greater impairments in resting and exertional pulmonary gas exchange and have greater evidence of a restrictive pattern on spirometry. The increased restrictive pattern may have contributed, at least in part, to their reduced 6MWD and greater ratings of dyspnoea and leg fatigue during the 6MWT.

The most common persistent symptom in our participants was fatigue, which is consistent with other studies (Carfì et al., 2020; Garrigues et al., 2020). Interestingly, when we compared those with and without persistent fatigue (Table 3), we do not see group differences in FVC, FEV_1, and D_{LCO}, suggesting that the underlying mechanisms of persistent dyspnoea and fatigue are different. Based on the abnormal pulmonary function observed in the present study, we speculate that COVID-19 patients with persistent dyspnoea are more likely to have greater constraints on tidal volume expansion, exertional hypoxaemia; adoption of a more rapid and shallow breathing pattern; and higher levels of respiratory neural drive during cardiopulmonary exercise testing (CPET) compared to their non-dyspnoea counterparts, as shown in other restrictive lung diseases (Faisal et al., 2016). Employing CPET to assess mechanisms underpinning dyspnoea in other chronic lung diseases has provided important insights and may be valuable in characterizing patients recovering from COVID-19.

This study has some limitations. For example, we did not quantify the severity of persistent dyspnoea since patients were only asked to report the presence or absence of dyspnoea, nor did we have any information on symptoms, pulmonary function, and 6MWT prior to diagnosis with COVID-19. Additional studies are also needed to extrapolate these findings from a single centre to other ethnicities.

5. Conclusions

We have shown that dyspnoea is a common persistent symptom across varying degrees of initial COVID-19 severity. Patients with persistent dyspnoea had a number of abnormalities compared to well-matched patients without dyspnoea, including greater restriction on spirometry, lower D_{LCO}, reduced functional capacity, and increased desaturation and exertional symptoms during a 6MWT. This suggests that there is a true physiological mechanism that may explain persistent dyspnoea after COVID-19. Futures studies are needed to determine if the aforementioned abnormalities in resting pulmonary function translate into abnormal cardiorespiratory and sensory responses during exercise as well as the degree to which underlying physiologic abnormalities may be modified by therapeutic interventions such as rehabilitation programs.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Arturo Cortés-Telles: Conceptualization, Project administration, Supervision, Data curation, Formal analysis, Writing - review & editing. **Stephanie López-Romero:** Data curation, Formal analysis, Writing - review & editing. **Esperanza Figueroa-Hurtado:** Data curation, Formal analysis, Writing - review & editing. **Yuri Noemi Pou-Aguilar:** Data curation, Formal analysis, Writing - review & editing. **Alyson W. Wong:** Writing - review & editing. **Kathryn M. Milne:** Writing - review & editing. **Christopher J. Ryerson:** Writing - review & editing. **Jordan A. Guenette:** Conceptualization, Data curation, Formal analysis, Writing - original draft, Writing - review & editing.

References

Carfì, A., Bernabei, R., Landi, F., Gemelli Against COVID-19 Post-Acute Care Study Group, 2020. Persistent symptoms in patients after acute COVID-19. JAMA 324, 603–605.

Enright, P.L., Sherrill, D.L., 1998. Reference equations for the six-minute walk in healthy adults. Am. J. Respir. Crit. Care Med. 158, 1384–1387.

Faisal, A., Alghamdi, B.J., Ciavaglia, C.E., Elbehairy, A.F., Webb, K.A., Ora, J., Neder, J. A., O'Donnell, D.E., 2016. Common mechanisms of dyspnea in chronic interstitial and obstructive lung disorders. Am. J. Respir. Crit. Care Med. 193, 299–309.

Garrigues, E., Janvier, P., Kherabi, Y., Le Bot, A., Hamon, A., Gouze, H., Doucet, L., Berkani, S., Oliosi, E., Mallart, E., Corre, F., Zarrouk, V., Moyer, J.D., Galy, A., Honsel, V., Fantin, B., Nguyen, Y., 2020. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. J. Infect. 81 e4-e6.

Giannouchos, T.V., Sussman, R.A., Mier, J.M., Poulas, K., Farsalinos, K., 2020. Characteristics and risk factors for COVID-19 diagnosis and adverse outcomes in Mexico: an analysis of 89,756 laboratory-confirmed COVID-19 cases. Eur. Respir. J. Online Ahead of Print.

Hankinson, J.L., Odencrantz, J.R., Fedan, K.B., 1999. Spirometric reference values from a sample of the general U.S. Population. Am. J. Respir. Crit. Care Med. 159, 179–187.

Holland, A.E., Spruit, M.A., Troosters, T., Puhan, M.A., Pepin, V., Saey, D., McCormack, M.C., Carlin, B.W., Sciurba, F.C., Pitta, F., Wanger, J., MacIntyre, N., Kaminsky, D.A., Culver, B.H., Revill, S.M., Hernandes, N.A., Andrianopoulos, V., Camillo, C.A., Mitchell, K.E., Lee, A.L., Hill, C.J., Singh, S.J., 2014. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. Eur. Respir. J. 44, 1428–1446.

Laviolette, L., Laveneziana, P., ERS Research Seminar Faculty, 2014. Dyspnoea: a multidimensional and multidisciplinary approach. Eur. Respir. J. 43, 1750–1762.

MacIntyre, N., Crapo, R.O., Viegi, G., Johnson, D.C., van der Grinten, C.P., Brusasco, V., Burgos, F., Casaburi, R., Coates, A., Enright, P., Gustafsson, P., Hankinson, J., Jensen, R., McKay, R., Miller, M.R., Navajas, D., Pedersen, O.F., Pellegrino, R., Wanger, J., 2005. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. Eur. Respir. J. 26, 720–735.

Mackey, K., Ayers, C.K., Kondo, K.K., Saha, S., Advani, S.M., Young, S., Spencer, H., Rusek, M., Anderson, J., Veazie, S., Smith, M., Kansagara, D., 2020. Racial and ethnic disparities in COVID-19-related infections, hospitalizations, and deaths : a systematic review. Ann. Intern. Med. https://doi.org/10.7326/M20-6306 online ahead of print M20-6306.

Miller, M.R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., Coates, A., Crapo, R., Enright, P., van der Grinten, C.P., Gustafsson, P., Jensen, R., Johnson, D.C., MacIntyre, N., McKay, R., Navajas, D., Pedersen, O.F., Pellegrino, R., Viegi, G., Wanger, J., 2005. Standardisation of spirometry. Eur. Respir. J. 26, 319–338.

Moxham, J., Jolley, C., 2009. Breathlessness, fatigue and the respiratory muscles. Clin. Med. Lond. (Lond) 9, 448–452.

Ogedegbe, G., Ravenell, J., Adhikari, S., Butler, M., Cook, T., Francois, F., Iturrate, E., Jean-Louis, G., Jones, S.A., Onakomaiya, D., Petrilli, C.M., Pulgarin, C., Regan, S., Reynolds, H., Seixas, A., Volpicelli, F.M., Horwitz, L.I., 2020. Assessment of racial/ethnic disparities in hospitalization and mortality in patients with COVID-19 in New York City. JAMA Netw Open 3, e2026881.

Parra-Rodriguez, L., Gonzalez-Meljem, J.M., Gomez-Dantes, H., Gutierrez-Robledo, L.M., Lopez-Ortega, M., Garcia-Pena, C., Medina-Campos, R.H., 2020. The burden of disease in Mexican older adults: premature mortality challenging a limited-resource health system. J. Aging Health 32, 543–553.

Stanojevic, S., Graham, B.L., Cooper, B.G., Thompson, B.R., Carter, K.W., Francis, R.W., Hall, G.L., on behalf of the Global Lung Function Initiative TLCO working group, 2017. Official ERS technical standards: global Lung Function Initiative reference values for the carbon monoxide transfer factor for Caucasians. Eur. Respir. J. 50, 1700010.

Wong, A.W., Shah, A.S., Johnston, J.C., Carlsten, C., Ryerson, C.J., 2020. Patient-reported outcome measures after COVID-19: a prospective cohort study. Eur. Respir. J. 56, 2003276.