



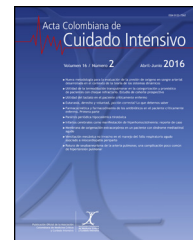
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Acta Colombiana de Cuidado Intensivo

www.elsevier.es/acci



CASE REPORT

Walking test as clinical assessment for unmasking occult hypoxemia in COVID-19: A case series



Nicolás Correa-Londoño^a, Juan Pablo Mesa-Murillo^b,
Jairo Giovanni Moncayo-Viveros^{a,*}, Juan Miguel Mejía-Sierra^a,
Ana María Sánchez-Moreno^a, Luisa Uribe-Londoño^a, Alejandro Agudelo-Escudero^a,
Erika Zumaqué-Valverde^a, Juan Nicolás Dallos-Ferreros^a, Pablo Arango-Guerra^a,
Andrés Ramírez-Vélez^b, Sara Moreno-Bedoya^a

^a CES Clinic, Medellín, Colombia

^b CES University, Medellín, Colombia

Received 18 May 2021; accepted 24 August 2021

Available online 23 December 2021

KEYWORDS

Coronavirus infection;
Hypoxia;
Oximetry;
Hospitalization;
Case report

Abstract SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) infection is a respiratory infection initially identified in Wuhan, China, in December 2019.

Some of the patients have been found to show no signs of respiratory distress; however, when oxygen saturation levels are measured, they are abnormally lower than expected in relation to their clinical condition.

This is why we collected a series of cases from patients diagnosed with COVID-19 (Coronavirus disease 2019) who underwent a 2-min walking test during the initial evaluation in the emergency department. A drop in oxygen saturation below 90% was considered a positive result. Eighty-five percent of patients with a positive walking test required in-hospital management and 70% required oxygen supplementation during hospitalization.

This clinical tool could help determine which of these patients might require in-hospital care due to occult hypoxemia, considering the current epidemiological situation and high bed occupancy rates.

© 2022 Asociación Colombiana de Medicina Crítica y Cuidado Intensivo. Published by Elsevier España, S.L.U. All rights reserved.

* Corresponding author.

E-mail address: jmonky76@gmail.com (J.G. Moncayo-Viveros).

PALABRAS CLAVE

Infección por
coronavirus;
Hipoxia;
Oximetría;
Hospitalización;
Reporte de caso

Test de la marcha como valoración clínica para desenmascarar hipoxemia oculta en COVID-19: serie de casos

Resumen La infección por SARS-CoV-2 – del inglés Severe Acute Respiratory Syndrome Coronavirus 2 – es una infección respiratoria identificada inicialmente en Wuhan, China, en diciembre de 2019.

Se ha encontrado que algunos de los pacientes no presentan signos de dificultad respiratoria; sin embargo, cuando se miden los niveles de saturación de oxígeno se encuentran anormalmente más bajos de lo esperado en relación con su condición clínica.

Esta es la razón por la que se han recopilado una serie de casos de pacientes con diagnóstico de COVID-19 – enfermedad por coronavirus 2019 – a quienes se les realizó una prueba de marcha de 2 minutos durante la evaluación inicial en el servicio de urgencias. Una caída en la saturación de oxígeno por debajo del 90% era considerada un resultado positivo. El 85% de los pacientes con una prueba de marcha positiva requirieron manejo intrahospitalario y el 70% precisaron suplementación de oxígeno durante la hospitalización.

Esta herramienta clínica puede ayudar a determinar cuáles de estos pacientes podrían requerir atención hospitalaria debido a hipoxemia oculta, considerando la situación epidemiológica actual y las altas tasas de ocupación de camas.

© 2022 Asociación Colombiana de Medicina Crítica y Cuidado Intensivo. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Introduction

The coronavirus 2019 disease is the name given to the pathology caused by the acute respiratory infection developed by SARS-CoV-2. Described initially in Wuhan (China) it spread rapidly causing around 1.85 million deaths worldwide and approximately 121 thousand in Colombia until August 2021.

Physiopathologically, the sensation of dyspnea occurs when there is an imbalance between the central neuronal stimulus of the respiratory center, located at the level of the medulla oblongata, and the pons at the level of the brainstem. The main stimuli to affect the respiratory drive are chemical changes captured by peripheral chemoreceptors, in addition to mechanoreceptors at the level of the lung parenchyma, which are activated and transformed into afferent signals in the presence of hypercapnia, hypoxemia, or parenchymal lung disease. These afferent signals are transmitted through the vagal nerve to the central nervous system, responsible for the process of generating dyspnea. It has been hypothesized that SARS-CoV-2 modifies the function of different neurological areas due to the virus's own neurotropism; being an example of this is the presentation of anosmia and ageusia as cardinal symptoms in the absence of important catarrhal symptoms.¹⁻³

It has been interesting to observe that patients with COVID-19 with pulmonary compromise rarely manifest with a feeling of breathlessness, even with low oxygen saturations; this is what has been called "silent hypoxemia" or "happy hypoxemia." This has made it somewhat challenging to identify patients who could potentially complicate and require inpatient management and even in a highly dependent unit.

It has been difficult to predict the need for admission to inpatient care due to the exponential rise of the COVID-19

cases and the lack of tools during the first evaluation of those patients without a significant respiratory compromise. Given the socio-economic conditions of our country, the high demand and little relative availability of hospital beds, it is necessary to design a method to identify patients who have a potential risk of complications, oxygen requirements, and need for a high dependency unit and who it can be applicable from triage, attention in emergency services of any level of complexity, ambulatory programs, and outpatient monitoring for the administration of the health resource.

Previous studies have described the walking or exercise test (6 min walk) as an easy measure for decision-making at emergency rooms and ambulatory care.⁴ The following article describes a case series of patients, observed in a tertiary-level hospital in the city of Medellín, Colombia, who were admitted with a diagnosis of COVID-19 without clinical signs of respiratory distress, neither requirement of oxygen supplementation to achieve a SatO_2 more than 92%, given the reference value for the altitude of the city.

Hereby, this case series presents the data of the patients that followed the walking test during medical attention exposing the plausibility of the utilization (in all areas, starting with triage up to high dependency services) for early establishing which patients could benefit from inpatient care.

Case series

We obtained the data of 27 patients with COVID-19, diagnosed by reverse transcription polymerase chain reaction (RT-PCR) through nasopharyngeal aspirate. They were admitted to the emergency department in a tertiary-level hospital in Medellín (Colombia), without oxygen requirement ($\text{Sat} > 92\%$) and with hemodynamic stability (no requirement for vasoactive support to achieve mean arterial

Table 1 Demographic and clinical characteristics.

Variable	Walking test			
	Positive (n = 20)		Negative (n = 7)	
<i>Gender</i>				
Female	5	25%	2	40%
Male	15	75%	3	60%
Age (years)	51	±13	38	±15
<i>Comorbidities</i>				
Arterial hypertension	6	30%	0	0%
Diabetes mellitus	4	20%	0	0%
COPD/Asthma	3	15%	2	40%
PaO ₂ /FiO ₂	292	±39	304	±66
Required hospitalization	17	85%	2	40%
Lenght of stay (days)	6	±4	4	±4
Required high dependency unit	2	10%	0	0%
Required supplemental oxygen during hospitalization	14	70%	2	40%

pressure >90 mmHg and adequate peripheral perfusion). The demographic data, rest vital signs and posttest vital signs were collected from electronic medical history.

During the medical evaluation, a walking test was performed. The test consisted of asking the patient to walk around the room for 2 min long. A positive result was considered as a drop in the oximetry below 90% after the walking test.

The categorical variables were expressed with absolute frequency and percentual distribution. The continuous variable reported with median and standard deviation (SD), according to the data distribution using the Shapiro-Wilk test.

This report was made following the CARE guidelines (Consensus-based Clinical Case Reporting Guideline Development).

Most of the patients were masculine (74%), with a ratio of 2:1 man to woman and a mean age of 48 years (±14). The main comorbidities of the patients were arterial hypertension (25.9%), followed by diabetes and COPD/asthma with 14% and 18.5%, respectively. Along with the patients that had positive walking test results, 30% had arterial hypertension, 20% diabetes mellitus, and 15% COPD/Asthma.

The mean of the oxygenation index (PaO₂/FiO₂) was 291 mmHg ± 43.

Of the patients with a positive walking test, 85% required inpatient care, 70% required oxygen supplementation, and 10% were admitted to a high dependency unit during the hospital care. The mean length of stay was six days, and most of the patients had a minimum stay of 48 h.

Table 1 shows patients characteristics according to the walking test results.

Discussion

The infection from SARS-CoV-2 has a broad spectrum of clinical presentations in terms of severity. It has been possible to characterize approximately that 81% of cases have been mild, 14% severe, and critical in a 5%.⁵ In the study of Guan

et al., they report that only 18.7% of 1099 hospitalized patients from COVID-19 manifested dyspnea despite being hypoxemic, having significant radiographic compromise, and requiring supplemental oxygen.⁶ Considering the preceding and given that the number of cases of SARS-CoV-2 infection is on the rise, it is considered necessary and pertinent to propose a clinical tool that helps to identify patients who may potentially require in-hospital treatment, to allow the establishment of early therapeutic measures from ambulatory or emergency services in order to improve the prognosis and ensure better clinical follow-up.

In the literature, there are tests such as the 2-min walking test as a reference, which has been used in different pulmonary pathologies with interstitial involvement (ILD, P. Jirovecii pneumonia, among others), with positive results that have helped clinical decision making, so we think it can be extrapolated to SARS-CoV-2 infection.⁷ Several publications recommend or suggest the use of a walking test or exercise in patients with SARS-CoV-2 infection. Mantha et al. argue that using a 6-min walk test in patients under 70 years of age on day 4 or 5 of the disease helps to stratify their risk and whether they will potentially require inpatient management.⁸ This was also proposed by Abolhasani et al., who propose that the deterioration in oxygenation during the 6-min walk can be used to identify those patients who should be referred for inpatient management.⁹ In the case of Pandit et al., they recommend that the use of the same test can be used for outpatient or hospital supervision, carried out even by the same patient under the supervision of a family member or health professional, to identify patients who require other therapeutic measures early.^{4,10}

In the collected cases, it was observed that from the second minute of the walking test, the patients already had a drop in SatO₂%, which we suppose led to the suspension of the maneuver. It is reasonable, understanding the context of low functional capacity of the COVID19 patient, not to extend the test until 6 min.

In this case, the goal was to adopt these recommendations and observe the behavior of the patients who had

a positive walk test with confirmed SARS-CoV-2 infection. When analyzing the data, it was observed that the patients who had a positive test required hospitalization in 85% and a hospital stay greater than 48 h. It draws attention and justifies that the patients who had a positive test needed closer monitoring since 70% required oxygen supplementation during hospitalization. Another important characteristic of this study is, compared with the recommendations that have emerged in the literature, the data analysis showed this test could be applied to patients under 60 or 70 years of age in the context of COVID-19.^{8–10} It was observed that this strategy was applied in patients with an average age of 51 years. These patients were observed to have more comorbidities, consistent with a higher risk of deterioration and complications.⁶ It is clarified that although there are recommendations regarding the application of the walking or exercise test in the context of COVID-19, they are extrapolations of its use in other pulmonary pathologies, and there is no study to date that validates the use of this strategy.

Concerning the above, this study intends to propose a cost-effective and easy-to-use resource to all kinds of institutions in outpatient and inpatient care settings that help health care professionals make decisions related to the management of those patients, like hospitalization or oxygen supplementation. Thanks to the concluded results of the case series, the emergency department from which the data were taken included the walking test in its standard-of-care as part of its initial medical evaluation for COVID-19 patients.

Given that there has been an overflow of patients with this pathology, saturating health services, this strategy could help reduce the costs and take better advantage of the health care staff.

Hypoxia is an independent factor associated with higher mortality in the context of SARS-CoV-2 infection; therefore, its recognition is necessary. Multiple models and classification scales have been developed, which try to stratify and predict the possible adverse outcome and mortality in this group of patients and validated for their use in this context. Between them, the NEWS 2, MEWS, REMS, Carr final, qSOFA, CURB65, among others.

In the study by Gupta et al., 22 prognostic models were applied in 411 patients with SARS-CoV-2 infection, reviewing the validity of the different prognostic scores. However, the univariable predictors that achieved to predict the most accurate clinical outcome and mortality were the oxygen desaturation by pulse oximetry and age, demonstrating that any other prognostic model could offer a greater benefit than these two predictors.

There is still no study with adequate methodological rigor to determine how the walking test manages to discriminate the possibility or risk of clinical deterioration in patients with SARS-CoV-2 infection. Therefore, this study intends to consider the walking test for the creation of prognostic models and to validate it as a possible independent factor of paraclinical parameters in patients with COVID-19.

Conclusion

Given the infection rates by SARS-CoV-2, associated with the high occupation percentages and the increase in health resources consumption, it is necessary to create clinical tools that allow the detection of patients who require in-hospital treatment. A simple-to-perform walking test is presented, which could help to identify patients with occult hypoxemia. Studies with greater methodological rigor are required to validate its performance.

Funding

This research corresponds to an unpublished work that has not been published previously. The authors declare that the work did not receive funding from public, commercial, or non-profit entities.

Conflict of interest

The authors declare that there is no potential conflict of interest related to the execution of the research work or the publication of the article.

References

1. Verma URAK. Happy hypoxemia in COVID-19-A neural hypothesis. *ACS Chem Neurosci*. 2020;11:1865–7.
2. Li Y-C, Bai W-Z, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J Med Virol*. 2020;92:552–5.
3. Nouri-Vaskeh M, Sharifi A, Khalili N, Zand R, Sharifi A. Dyspneic and non-dyspneic (silent) hypoxemia in COVID-19: possible neurological mechanism. *Clin Neurol Neurosurg*. 2020;198:106217.
4. Kalin A, Javid B, Knight M, Inada-Kim M, Greenhalgh T. What is the efficacy and safety of rapid exercise tests for exertional desaturation in COVID-19: a rapid review protocol. *Resp Med*. 2020.
5. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis*. 2020;20:669–77.
6. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020. [NEJMoa2002032](#).
7. Sauleda J, Gea J, Aran X, Aguar MC, Orozco-Levi M, Broquetas JM. Simplified exercise test for the initial differential diagnosis of *Pneumocystis carinii* pneumonia in HIV antibody positive patients. *Thorax*. 1994;49:112–4.
8. 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.
9. Noormohammadpour P, Abolhasani M. Besides other signs can a 6-min walk test be applied as a criterion for going to the hospital with a diagnosis of COVID-19? *Adv J Emerg Med*. 2020;4(2s):e42.
10. Pandit R, Vaity C, Mulakavalupil B, Matthew A, Sabnis K, Joshi S. Unmasking hypoxia in COVID 19 – six minute walk test. *J Assoc Phys India*. 2020;68:50–1.