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Risk factors associated with phrenic nerve damage in patients post-COVID-19

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Abstract

Objective: *To identify risk factors for phrenic nerve injury, a condition impacting respiratory function, in post-COVID-19 patients, and to understand its role in neurological complications to inform clinical strategies.* **Methods:** *A cross-sectional study with retrospective data collection analyzed medical records and electrophysiological studies of 228 post-COVID-19 patients (114 with phrenic nerve damage confirmed by nerve conduction studies and 114 controls without it) from a public rehabilitation unit (Mexican Social Security Institute, Jan-Jul 2021). Analyzed variables included demographics, pre-existing comorbidities (e.g., obesity, asthma, and type 2 diabetes), COVID-19 clinical details, and electrophysiological parameters confirming phrenic nerve status.* **Results:** *Multivariable logistic regression identified obesity (odds ratio [OR] 10.36, $p < 0.001$), asthma (OR 7.93, $p = 0.02$), male sex (OR 2.2, $p = 0.01$), and advanced age (OR 1.07/year, $p < 0.001$) as significant independent risk factors for phrenic nerve damage. Type 2 diabetes mellitus approached statistical significance ($p = 0.05$) but was not an independent predictor in the final model. Descriptively, in patients with phrenic nerve damage, 49.12% received corticosteroids and 68.42% had other peripheral nerve involvement; however, these were not identified as significant independent risk factors in the adjusted analysis.* **Conclusions:** *Phrenic nerve injury is an important post-COVID-19 complication. The conditions of obesity, asthma, being of male sex, and presenting an advanced age emerged as significant independent risk factors, identified through multivariable analysis, adjusting for potential confounders. These findings highlight the need for vigilant monitoring and tailored management strategies in post-COVID-19 patients with these characteristics.*

Keywords: *Phrenic nerve damage. COVID-19. Risk factors. Long-term effects. Electrophysiological study.*

Factores de riesgo asociados con el daño al nervio frénico en pacientes Post-COVID-19

Resumen

Objetivo: *Identificar factores de riesgo para el daño al nervio frénico, una condición que afecta la función respiratoria, en pacientes post-COVID-19 y comprender su papel en complicaciones neurológicas para orientar estrategias clínicas.* **Métodos:** *Estudio transversal con recolección retrospectiva que analizó expedientes médicos y estudios electrofisiológicos de 228 pacientes post-COVID-19 (114 con daño confirmado al nervio frénico mediante estudios de conducción nerviosa y 114 controles sin daño) en una unidad pública de rehabilitación (IMSS, enero-julio 2021). Se evaluaron variables demográ-*

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ficas, comorbilidades preexistentes (obesidad, asma, diabetes tipo 2), detalles clínicos de COVID-19 y parámetros electrofisiológicos. **Resultados:** *La regresión logística multivariada identificó como factores de riesgo independientes significativos la obesidad (OR 10.36, p < 0.001), el asma (OR 7.93, p = 0.02), el sexo masculino (OR 2.2, p = 0.01) y la edad avanzada (OR 1.07 por año, p < 0.001). La diabetes tipo 2 estuvo cerca de la significancia estadística (p = 0.05) pero no fue predictor independiente en el modelo final. Descriptivamente, el 49.12% de pacientes con daño al nervio frénico recibió corticosteroides y el 68.42% presentó afectación de otros nervios periféricos; sin embargo, estos no fueron factores de riesgo independientes tras el análisis ajustado.* **Conclusiones:** *El daño al nervio frénico es una complicación relevante post-COVID-19. Obesidad, asma, sexo masculino y edad avanzada son factores de riesgo independientes. Estos resultados destacan la importancia de monitorear y manejar de forma personalizada a pacientes post-COVID-19 con estas características.*

Palabras clave: *Daño al nervio frénico. COVID-19. Factores de riesgo. Efectos a largo plazo. Estudio electrofisiológico.*

Introduction

COVID-19 was declared a global pandemic by the World Health Organization on March 11, 2020, a significant milestone in global health[1,2]. In addition to respiratory symptoms, individuals affected by COVID-19 have been reported to encounter a range of neurological consequences, including cognitive changes, headaches, and more severe illnesses, such as encephalitis and stroke[3]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) capacity to traverse the blood-brain barrier indicates a direct route for causing neurological harm[4]. Around 82% of COVID-19 patients who are admitted to the hospital show signs of neurological problems[5]. This highlights the urgent requirement for a thorough understanding of how the virus affects the nervous system, given the wide range of symptoms observed[6,7].

Moreover, the extended COVID syndrome encompasses neurological dysfunctions as a prevalent consequence of the disease, exhibiting symptoms that vary from weariness and difficulty breathing to severe neurological disorders[8,9]. Furthermore, neurological complications, specifically the impact on the phrenic nerve, are crucial for respiratory function and the possible vulnerability to COVID-19 infections. This is of utmost importance in this situation, as evidenced by its contribution to restoring respiratory function in patients recovering from COVID-19[10,11]. COVID-19 has been found to be associated with neuropathies, such as mononeuritis of the phrenic nerve[12]. This highlights the importance of further investigating these neurological symptoms.

This study specifically examines the occurrence of phrenic nerve injury in post-COVID-19 patients who received treatment at the North Physical Medicine and Rehabilitation Unit of the Mexican Social Security Institute (IMSS). It aims to explore risk variables associated with this condition, with an emphasis on demographic and clinical factors commonly observed in post-COVID-19 patients. By analyzing medical data and conducting electrophysiological investigations, our objective is to provide valuable insights into this problem that occurs after COVID-19. This will contribute to further clarifying an area that, despite emerging interest, still requires more targeted research regarding its pathophysiology and clinical implications.

Materials and methods

Study design

This study utilized a cross-sectional design with retrospective data collection. All information was obtained from existing medical records and previously conducted electrophysiological studies performed between January and July 2021. No prospective or contemporaneous data were collected during the study period.

Participants and sampling

This study included patients from the North Physical Medicine and Rehabilitation Unit of Traumatology, Orthopedics, and Rehabilitation, "Dr. Victorio de la Fuente Narváez" of the IMSS. A consecutive sampling method was used.

Inclusion criteria were: age 18 years or older, confirmed positive polymerase chain reaction (PCR) test for COVID-19, completion of an electrophysiological study for phrenic nerve conduction, and provision of informed consent. Exclusion criteria included: negative PCR result, history of cardiothoracic surgery, prior phrenic nerve damage, incomplete records, or absence of an electrophysiological study.

A total of 114 patients with phrenic nerve damage and 114 control individuals (without such damage), as confirmed through electrophysiological studies, were

included in the analysis. Their medical records were reviewed to identify potential associated risk factors.

A non-probabilistic cluster sampling approach was employed, with the sample including all eligible patients who met the inclusion criteria during the predefined period (January-July 2021) at the study site.

All patients with confirmed post-COVID-19 status who were referred for electrophysiological evaluation at the unit during the study period were considered for inclusion, regardless of the presence or absence of respiratory symptoms. However, referral patterns might have favored patients with clinical suspicion of neuromuscular or respiratory complications, which may introduce a degree of selection bias.

The timing between the onset of COVID-19 symptoms and the phrenic nerve conduction study did not exceed 3 months, as the retrospective analysis included data up to 6 months before the study period.

The following clinical and demographic variables were analyzed as covariates to assess their potential association with phrenic nerve damage in post-COVID-19 patients: corticosteroid administration, mechanical ventilation (MV), cerebrovascular accident (CVA), Guillain-Barré syndrome, type 2 diabetes mellitus (T2DM), systemic arterial hypertension (SAH), post-COVID-19 peripheral nerve injury, obesity, hypothyroidism, asthma, chronic obstructive pulmonary disease (COPD), prone positioning, age, sex, and weight. These variables were selected based on their known or suspected involvement in the pathophysiology of COVID-19-related neurological or respiratory complications.

Enhancing diagnostic precision in phrenic nerve analysis

Nerve conduction studies were performed using a Nicolet VikingQuest electromyography system. All studies were conducted by attending physicians and residents specialized in Physical Medicine and Rehabilitation.

Phrenic nerve conduction studies were performed using a bipolar surface electrode setup. The active electrode was placed on the eighth intercostal space along the midclavicular line, adjacent to the costochondral junction, on the same side as the electrical stimulus. The reference electrode was positioned 2 cm lateral to the active electrode, near the anterior axillary line, and the ground electrode was placed at the midsternal line. Electrical stimulation was delivered at Herb's point using intensities ranging from 70 to 100 mA, employing the method described by Flores et al.[13].

Criteria for electrophysiological abnormalities

Defining prolonged motor responses in the electrophysiological studies was anchored in scientifically established criteria. Latencies classified as prolonged were set between 6 and 8 ms, and reduced amplitudes were defined within a range of 500-800 mV. These criteria, reflecting the parameters found in Ricoy et al.'s research on diaphragmatic dysfunction, facilitated a consistent and accurate identification of electrophysiological abnormalities across the patient cohort[14].

Data analysis

Descriptive statistics were used to summarize patient characteristics. Continuous variables were reported as mean ± standard deviation or median and interquartile range, depending on their distribution. Categorical variables were summarized as frequencies and percentages.

Phrenic nerve injury was analyzed as a binary dependent variable (present = 1, absent = 0). A multivariable binary logistic regression model was used to assess associations between phrenic nerve injury and selected covariates. Each covariate was coded as binary (1 = present, 0 = absent). Results are reported as odds ratios with 95% confidence intervals and corresponding p-values.

The χ^2 test was used separately to compare baseline characteristics between patients with and without phrenic nerve damage. This was not part of the regression model but served to identify initial group differences.

$p < 0.05$ was considered statistically significant. All statistical analyses were performed using R Statistical Software (version 4.2.0).

Results

Baseline characteristics

A total of 114 post-COVID-19 patients with phrenic nerve damage were included. The mean age was 49 ± 10.7 years, with a range of 27-71 years, and 74.5% (n = 85) were male.

The most frequent comorbidities observed were obesity (37.71%), T2DM (32.45%), and SAH (28.94%). Other less prevalent conditions included asthma (5.26%), hypothyroidism (5.26%), CVA (4.38%), Guillain-Barré syndrome (1.75%), and COPD (0.78%).

Regarding treatment modalities, 56 patients (49.12%) received corticosteroids during hospitalization, and 20 patients (17.54%) required MV. This aligns with the

Table 1. This table provides a detailed breakdown of the most frequent neuropathic conditions identified in patients post-COVID-19. Each condition represents a specific type of peripheral nerve involvement, with frequencies and percentages reflecting their incidence within the patient cohort. The category "other types of neuropathies" includes less common neuropathies

Condition	Frequency	%
Right phrenic nerve neuropathy	36	11.84
Bilateral phrenic nerve neuropathy	35	11.51
Bilateral tibial nerve neuropathy	31	10.20
Left peroneal nerve neuropathy	24	7.89
Left phrenic nerve neuropathy	21	6.91
Right peroneal nerve neuropathy	20	6.58
Right median nerve neuropathy	19	6.25
Bilateral peroneal nerve neuropathy	17	5.59
Left median nerve neuropathy	15	4.93
Right tibial nerve neuropathy	14	4.61
Left tibial nerve neuropathy	11	3.62
Left superficial peroneal nerve neuropathy	10	3.29
Right sensory median nerve neuropathy	6	1.97
Bilateral superficial peroneal nerve neuropathy	6	1.97
Other types of neuropathies	39	12.83

Table 2. Comorbidities in patients with phrenic nerve damage. Detailed breakdown of the percentage of patients with each comorbidity. Include the prevalence of obesity, type 2 diabetes mellitus, and systemic arterial hypertension, and consider adding other relevant comorbidities

Comorbidity	%
Obesity	37.71
Type 2 diabetes mellitus	32.45
Systemic arterial hypertension	28.94
Cerebral vascular accident	4.38
Asthma	5.26
Hypothyroidism	5.26
Guillain-Barré syndrome	1.75
COPD	0.78

COPD: chronic obstructive pulmonary disease.

recommendations from the treatment guidelines for COVID-19 in Mexico, which advise the use of corticosteroids in patients with severe disease to improve clinical outcomes, particularly among those requiring supplemental oxygen[15].

While the primary focus of this study was phrenic nerve damage, other peripheral nerve involvements were identified and are detailed in table 1.

Phrenic nerve conduction studies measured latency and amplitude of compound muscle action potentials (CMAP). Normal latency ranges from 6 to 8 m in healthy adults, with typical CMAP amplitudes between 500 and 800 μV. Prolonged latency or reduced amplitude indicates phrenic nerve dysfunction, consistent with demyelination or axonal injury.

The logistic regression model's fit was assessed using the Hosmer-Lemeshow goodness-of-fit test, which yielded a borderline p-value ($p \approx 0.05$). This result suggests a marginally acceptable fit but also indicates that the model may not perfectly capture the data structure.

Risk factors

Table 2 provides a detailed analysis of potential risk factors for phrenic nerve damage. It compares the prevalence of specific variables in patients with and without phrenic nerve damage and includes results from the binary logistic regression analysis.

The risk factor analysis in table 3 suggests that obesity, asthma, male sex, and increasing age are significant risk factors for phrenic nerve damage. Type 2 diabetes approaches significance, but the possibility of a type 1 error cannot be ruled out. The Hosmer-Lemeshow test yielded a $p = 0.05$, indicating that the model fits well and can predict data within the observed range.

Discussion

Our study identified age as a primary risk factor for phrenic nerve damage in post-COVID-19 patients. This aligns with findings by Wu et al., who suggest an increased likelihood of neurological complications with advancing age[16]. Pietrobon et al. define immunosenescence as a decline in innate and adaptive immunity leading to increased pro-inflammatory cytokines,

Table 3. Risk factors associated with phrenic nerve damage

Risk factor	W/L phrenic nerve	WO/L phrenic nerve	B	χ^2	p	OR	IC 95%	
Age	$\bar{x}$ = 49 ± 10.7	$\bar{x}$ = 44 ± 9.7	0.07	14.66	< 0.001	1.07	1.03	1.1
Sex	M (85) F (29)	M (63) F (51)	1.08	2.46	0.01	2.2	1.19	4.4
Asthma	6	2	2.07	2.195	0.02	7.93	1.39	65.12
Obesity	43	7	2.33	16.28	< 0.001	10.36	4.49	27.34
T2DM	37	19	1.15	4.24	0.05	-	-	-
PN injury	78	50	–0.83	2.2	0.14	-	-	-
CVA	5	5	–1.54	1.31	0.25	-	-	-
SAH	33	18	–0.08	0.02	0.88	-	-	-
GBS	2	0	20.41	0	1	-	-	-
MV	20	0	30.08	0	1	-	-	-
Prone	5	0	16.49	0	1	-	-	-
COPD	1	0	–9.35	0	1	-	-	-
Hypothyroidism	6	1	–12.26	0	1	-	-	-
Corticosteroids	56	0	29.85	0	1	-	-	-

W/L: with lesion (non-control group); WO/L: without lesion (control group); PN injury: periferic nerves injury; CVA: cerebrovascular event; SAH: systemic arterial hypertension; GBS: Guillian-Barre syndrome; T2DM: type 2 diabetes mellitus; MV: mechanical ventilation; Prone: prone position; COPD: chronic obstructive pulmonary disease; OR: odds ratio.
By analyzing only the statistically significant variables, age, sex, asthma, and obesity, the regression model achieves a similar result compared to a model that includes all variables (in R Studio).

which could contribute to this damage, as observed in SARS-CoV-2 patients[17].

Previous research has identified an association between COVID-19 and cerebrovascular disease, including ischemic and hemorrhagic strokes, attributed to hyperinflammatory and hypercoagulable states induced by the infection[18]. These align with our observations, suggesting that similar inflammatory mechanisms may contribute to peripheral nerve damage, such as the phrenic nerve.

In addition, a systematic review with meta-analysis showed a significant relationship between age and the development of neurological complications in COVID-19 patients, including cerebrovascular diseases, peripheral neuropathies, and encephalopathies[19]. This suggests that observing aging-associated chronic inflammatory processes may predispose older individuals to a higher risk of neurological damage.

A retrospective study highlights a relationship between COVID-19 and abnormalities in electroneuromyographic studies, such as an increase in non-evoked motor and sensory nerves, as well as impairments in motor nerve latency, amplitude, and conduction velocity[20]. This suggests that the interaction between comorbidities and the severity of the disease may exacerbate neuromuscular damage, highlighting the need for detailed neurophysiological evaluations in this population.

Advanced age, alongside diabetes mellitus and other factors, significantly increases the risk of developing severe neurological complications in COVID-19 patients, which in turn raises the risk of death by 7.6 times, highlighting the importance of considering age in the management of post-COVID-19 patients[21].

In addition, risk factors for severe COVID-19 in hospitalized adults of different ages can influence the severity and outcomes of COVID-19[22]. This is relevant for a better understanding of how age influences the risk and severity of phrenic nerve damage in post-COVID-19 patients. Collectively, these findings highlight the importance of a detailed neurological assessment in elderly post-COVID-19 patients, especially those with comorbidities that may exacerbate neurological damage.

The mean age in our study was 49 years, consistent with data from the Secretary of Prevention and Promotion of Health[23]. Likewise, to relate male gender as a significant risk factor for phrenic nerve damage in post-COVID-19 patients, one can include a study by Jin et al., where it was found that there were more severe

COVID-19 cases in men than in women, according to the clinical classification of severity. This study suggests that there are differences in morbidity and mortality between men and women with COVID-19[24]. These findings highlight the need to consider gender in the evaluation and treatment of patients with COVID-19, especially in those who present neurological manifestations such as phrenic nerve damage.

Most patients with post-COVID-19 phrenic nerve damage in our study were male, a trend also noted by Vahidy et al., and others about severe COVID-19 outcomes[25].

In our post-COVID-19 study, obesity, SAH, and T2DM emerged as predominant comorbidities associated with phrenic nerve damage. Nalbandian et al. have reported a range of post-COVID-19 clinical manifestations, including persistent dyspnea and exercise intolerance, which are not always explainable through conventional clinical assessments[26].

In addition, the predominant presence of obesity, SAH, and T2DM in our study reflects findings reported in the literature, where these comorbidities are associated with an increase in the severity of COVID-19[27].

An extensive analysis indicates that these patients have a higher risk of severe clinical outcomes, including intensive care unit (ICU) admission and higher mortality rates. This pattern of comorbidities could influence the development of neurological complications, such as damage to the phrenic nerve. The relationship between these chronic conditions and post-COVID-19 phrenic nerve dysfunction underscores the importance of a comprehensive assessment that includes metabolic and vascular risk factors in the recovery of post-COVID-19 patients[28].

Clinical manifestations such as persistent dyspnea and exercise intolerance, reported by Nalbandian et al.[26], may be more frequent in patients with these comorbidities, as these symptoms, often not fully explainable through conventional clinical assessments, could be related to phrenic nerve dysfunction. This reinforces the need to improve systematic evaluations of phrenic nerve function in post-COVID-19 patients, especially in those with obesity, hypertension, and diabetes. Implementing detailed evaluation protocols for phrenic nerve function could help better identify and manage these neurological complications, contributing to a more effective and personalized recovery[29].

Our study addressed this gap by implementing an electrophysiological survey on phrenic nerve conduction. This survey revealed a significant association between these comorbidities and phrenic nerve damage, which has important implications for treating and predicting outcomes in post-COVID-19 patients.

We also identified asthma as a risk factor, though its relationship with COVID-19 severity remains a subject of ongoing debate[30].

Diaphragmatic dysfunction can occur in COVID-19 patients, potentially exacerbated using thoracic support devices, as suggested by Ramani et al. Our study found a lower proportion of patients requiring MV, yet we consider direct neuromuscular involvement by SARS-CoV-2 a plausible contributor to diaphragmatic dysfunction. Autopsy studies have revealed ACE2 expression in the human diaphragm and SARS-CoV-2 ribonucleic acid in some COVID-19 patients[31].

The relationship between asthma and phrenic nerve damage in COVID-19 patients could be mediated through various pathways. Studies have suggested that alterations in lung function and inflammatory responses in asthmatic patients may influence the severity of respiratory infections, including COVID-19[32]. On the other hand, an analysis by Sunjaya et al. indicates that asthmatic patients did not show a significant increase in the severity of COVID-19, suggesting a complex interaction between asthma, an anti-inflammatory medication used, and the body's response to the virus[33].

Therefore, our findings suggest that asthma in post-COVID-19 patients warrants particular attention in neurological evaluation, particularly those showing phrenic nerve damage. Given that respiratory function can be compromised in asthmatic patients, it is crucial to consider how asthma might affect the recovery from phrenic nerve damage. Understanding the interplay between asthma, COVID-19, and phrenic nerve damage can offer valuable insights for improving neurological and respiratory outcomes in this population[34].

Notably, in our study, obesity was the most significant comorbidity. Obese patients faced a higher risk of hospitalization and severe disease, including an increased likelihood of ICU admission. Men with obesity, type 2 diabetes, or SAH were particularly susceptible to complications[35].

In this context, obesity emerges as a critical risk factor in the exacerbation of phrenic nerve damage. Obesity, characterized by a chronic inflammatory state, has been shown to increase the severity of COVID-19, leading to a greater need for hospitalization and MV, as evidenced in studies reporting a higher prevalence of obesity in critical COVID-19 patients[36]. Given that the majority of our post-COVID-19 phrenic nerve damage patients were male, it is crucial to consider how the

intersection of gender and obesity may influence the severity of neurological damage.

Moreover, obesity not only increases the risk of severe COVID-19 complications but also complicates its management and diagnosis. The accumulation of visceral fat, particularly in young patients with obesity, can be a predictor of COVID-19 severity, contributing to respiratory failure and, potentially, phrenic nerve damage, as obesity has been shown to negatively impact the efficacy of MV, which is particularly relevant for our study, where most patients with phrenic nerve damage required ventilatory support[37].

Collectively, these findings highlight the importance of a detailed neurological evaluation of post-COVID-19 patients, especially those with comorbidities such as obesity, which can exacerbate neurological damage.

Corticosteroid treatment in the ICU has been linked to muscle weakness, as noted by McClafferty et al., but was less common in our study[38].

In contrast to our findings of a significant prevalence of demyelinating neuropathies in post-COVID-19 patients, the study by Law et al.[39] reports a lower rate of phrenic nerve neuropathy in a similar cohort. In addition, this higher prevalence counters studies such as that of Lotan et al. and others, which suggest that although demyelinating events of the central nervous system associated with SARS-CoV-2 infection have been reported, the rate of these events is relatively low compared to the prevalence of SARS-CoV-2 infection[40]. This indicates that, although there is a relationship between COVID-19 and demyelinating diseases, their incidence may be lower than what our results suggest.

The variability in the presentation of these neurological symptoms reflects the complexity of COVID-19's impact on the nervous system and could contribute to the differences observed in studies on demyelinating neuropathies[41].

Critical illness polyneuropathy (CIP), described by Ramani et al.[31] and others, is a concern in patients with extended hospital stays. Interestingly, in our post-COVID-19 patients with phrenic nerve damage, we found that demyelinating pathology was more prevalent. Therefore, the prevalence of demyelinating pathology in our study highlights the need for a personalized diagnostic and therapeutic approach for post-COVID-19 patients with phrenic nerve damage. The findings suggest that CIP and other demyelinating neuropathies may be a significant concern in these patients, especially those with prolonged hospital stays. Thus, continued research is crucial to understanding these pathological mechanisms better and developing more effective treatment strategies[42].

Finally, it is crucial to recognize the importance of assessment tools in COVID-19. A study conducted by Alvarado-Martínez et al. evaluated the accuracy of prognostic scales for predicting mortality in COVID-19 patients. They found that certain scales, such as the COVID-GRAM critical illness risk score, were particularly effective. This underscores the need for precise and reliable evaluation methods in the clinical management of COVID-19. The underlying risk factors and complications associated with COVID-19, such as phrenic nerve damage, require meticulous attention and detailed evaluations to improve patient outcomes and quality of life[43].

Limitations of the study

This study has limitations that should be acknowledged. First, the sample was derived from a single rehabilitation center using non-probabilistic cluster sampling, which may introduce selection bias, particularly as patients referred for electrophysiological studies likely had neuromuscular or respiratory symptoms. In addition, data on some potentially relevant clinical variables, such as the severity of COVID-19 infection or duration of MV, were limited or unavailable, which may confound the associations observed. Finally, electrophysiological measurements were based on specific latency and amplitude thresholds that, while grounded in literature, may not capture the full spectrum of phrenic nerve dysfunction.

Implications for future research

Future studies should aim to address the limitations identified in this research by adopting prospective longitudinal designs that allow for causal inference and temporal assessment of phrenic nerve injury progression in post-COVID-19 patients.

Conclusion

Obesity, SAH, asthma, advanced age, and male gender are identified as significant risk factors for phrenic nerve damage in post-COVID-19 patients. Despite tending significance, type 2 diabetes failed to establish itself as an unequivocal risk factor. These observations underscore the importance of conducting thorough demographic analysis and assessing comorbidities when attempting to comprehend the neurological consequences of COVID-19. They also emphasize the need

for diligent clinical monitoring and care among a wide range of patients. Identifying these particular risk factors enhances our understanding of the neurological consequences of COVID-19 and facilitates the development of more customized and effective treatment strategies. Acquiring such knowledge is crucial for the clinical management of those affected, supporting an integrated approach that combines risk factor investigation with clinical evaluation to improve recovery and quality of life for individuals who have recovered from COVID-19.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The authors have obtained approval from the Ethics Committee for the analysis of routinely collected and anonymized clinical data; therefore, individual informed consent was not required. Relevant ethical recommendations have been followed.

Declaration on the use of artificial intelligence (AI). The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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