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ABOUT

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Original Article

Hospitality Venues' Anti-tobacco Legislation Violation in 11 Different Cities in Türkiye

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Abstract

OBJECTIVE: In Türkiye, anti-tobacco legislation (Law No. 4207 on the Prevention and Control of Harms of Tobacco Products) aims to ensure a "tobacco-free" life for current and future generations. Thus, there are observations of violations in the hospitality sector. In this study, we aimed to observe the status of hospitality venues' violation of the law in 11 different cities in Türkiye.

MATERIAL AND METHODS: This descriptive study examined 772 hospitality venues in Ankara, Burdur, Diyarbakır, Giresun, Hatay, İstanbul, İzmir, Kars, Kayseri, Samsun, and Zonguldak between August 1 and October 10, 2023. The Google Forms survey, Microsoft Excel, and IBM SPSS Statistics (Version 23) programs were used for data collection, entry, and analysis. A logistic regression model was used to understand the associations between non-compliance and the characteristics of the venues.

RESULTS: During the observation of indoor spaces, tobacco products were used in 282 venues (37.1%). Non-compliance in bars, pubs, traditional coffee houses, and hookah cafes was statistically significantly higher than in the other venue types [odds ratio (OR)= 3.031, 95% confidence interval (CI): 1.699 to 5.408, $P < 0.001$]. The presence of a retractable roof and/or side wall (OR=5.362, 95% CI: 3.518 to 8.173, $p < 0.001$), later hour observations (OR= 2.120, 95% CI: 1.399 to 3.212, $p < 0.001$), and the existence of outdoor venues where smoking is permitted (OR= 3.165, 95% CI: 2.170 to 4.617, $p < 0.001$) also increased indoor violations.

CONCLUSION: The findings provided scientific evidence that violations of Turkish anti-tobacco legislation exist in hospitality venues. The public authorities are advised to play their vital role in preventing violations in indoor spaces.

KEYWORDS: Compliance, hospitality, tobacco-free

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INTRODUCTION

Tobacco control is a right to health that must be defended for the protection and promotion of individuals and communities. Türkiye is among the countries with the highest number of people aged 15+ years and older in millions in 2019.[1] In Türkiye, the prevalence of daily tobacco users has risen to 28.3% in 2022 according to the Turkish Statistical Institute data. The prevalence of male and female smokers is 41.3% and 15.5% respectively.[2]

Tobacco use also causes passive smoking, which is also a serious public health problem, increasing mortality and morbidity.[3] Since the 2000s, efforts of the World Health Organization (WHO) have achieved impacts in many parts of the world.[4] Framework Convention on Tobacco Control (FCTC)[5] has been a milestone in tobacco control, and Türkiye, as a partner country[6], modified its legislative acts compatible with the FCTC recommendations. In this regard, in Türkiye, the Law No. 4207 on the Prevention and Control of Harms of Tobacco Products, which was enacted in 1996 for tobacco control, was revised in 2008.[7] This revision constituted an important basis for strong tobacco control in the country, and with this revision, tobacco consumption in bars, cafes, and restaurants was banned.[8,9]

Legislative acts promoting tobacco control should seek reciprocity in practical life. Observations of hospitality venues open to the public provide an idea of whether anti-tobacco legislation is applied or not. There are research findings that define the compliance status of hospitality venues in different countries. In 2002, Basnet et al.[10] conducted a study to define the compliance status with smoke-free public places in Nepal and found only 26.3% compliance in entertainment, hospitality, and shopping venues, etc. Bangladesh data also defined a huge violation in hospitality venues, which Chowdhury et al.[11] showed in their research in 2023. Türkiye also has previous non-compliance data (49.0% for 2013 and 29.7% for 2014) in the hospitality sector.[12] Recent data are needed to define the actual situation in the country.

Based on the need to see the actual situation, we aimed to observe the hospitality venues open to the public in 11 different cities of Türkiye and to determine whether there are violations of anti-tobacco legislation.

Main Points

- There is a violation of tobacco-free legislation in almost all countries.
- The results of the study emphasized strong evidence about the existence of violations in different types of hospitality sectors in various cities in Türkiye. The use of other tobacco products in the venues has been confirmed with this study.
- The public authority can take the message of the study and play its role in preventing violations in the hospitality sector, as there is a strong legislative framework in the country.

MATERIAL AND METHODS

The Type of Research

The study is a descriptive epidemiological study.

Place and Sample of the Study

The study was conducted in Ankara, Burdur, Diyarbakır, Giresun, Hatay, İstanbul, İzmir, Kars, Kayseri, Samsun, Zonguldak cities of Türkiye (Figure 1).

İstanbul, Ankara and İzmir are the cities with the largest populations. The cities included in this study were selected based on their geographical regions. Finally, researchers living in these 11 cities collected the data.

Standardized observations of the hospitality venues located on popular streets were conducted.

A list of hospitality venues in the relevant cities was obtained from the website of the Confederation of Turkish Tradesmen and Craftsmen.[13] City center populations were determined according to the results of the Address-Based Population Registration System 2021 of the Turkish Statistical Institute.[2] The estimated number of venues was calculated from a linear regression model estimating the number of workplaces in the cities according to the population of the cities. Since the Confederation of Turkish Tradesmen and Craftsmen does not provide the number of venues such as hotels, restaurants, and cafes separately, the minimum number of observations to be made in the cities was obtained by dividing the estimated number of each city by one thousand and rounding up to the whole number. Finally, 772 observations were made in 11 different cities.

Data Collection Form, Pre-test, Data Entry, and Analysis

The data collection form was developed by the researchers in July-August 2023. The form was pre-tested by the researchers in each city. In the pretest phase, each researcher observed five venues. After the observations, the data collection form was finalized in "online meetings" attended by the researchers together. After finalizing the data collection form, a Google Forms survey was created.

Statistical Analysis

Data were collected between August 1 and October 10, 2023. The researchers entered the data they collected through Google Forms survey. The data were transferred from Google Forms survey to Microsoft-Excel and IBM SPSS Statistics (Version 23) programs. IBM SPSS Statistics (Version 23) was used for data entry and analysis.

The observed venue was recorded only once. The client characteristics observed were also recorded. Age categories were recorded based on the observation.

In addition to basic analysis, a binary logistic regression model was performed to analyze the associations between the violation status in the indoor places and selected variables like type of venue, time of observation, existence of a retractable

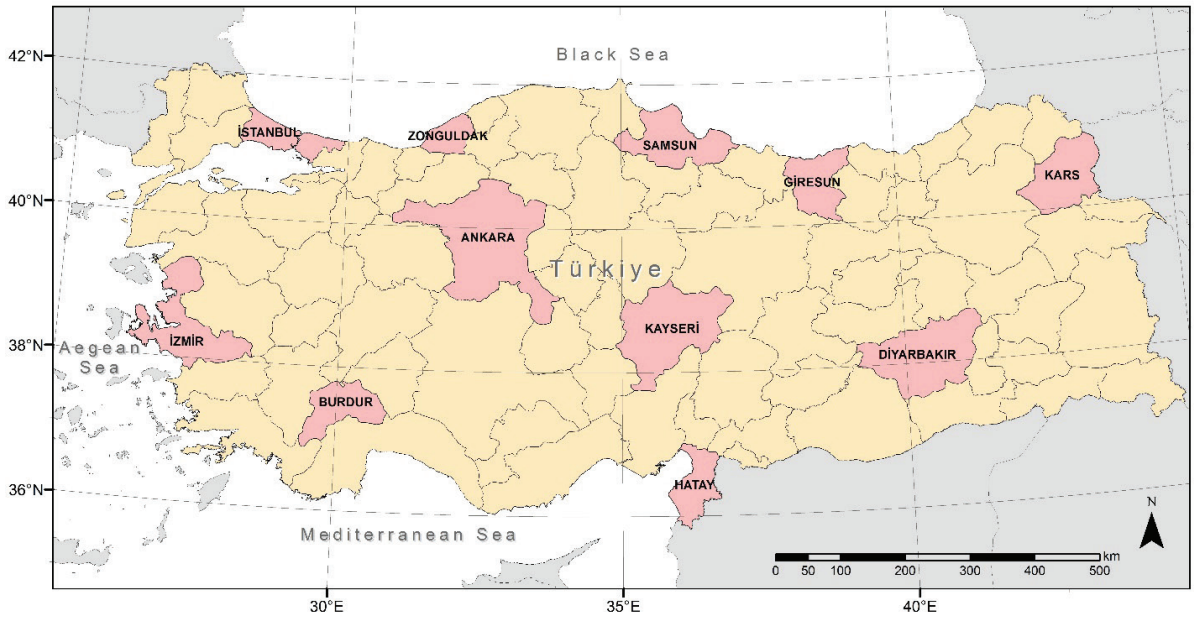

Figure 1. The 11 cities (out of 81) in which the study was conducted

roof and/or side wall in the venue, and existence of outdoor venues where smoking is permitted. Odds ratios (OR) [95% confidence interval (CI)] were estimated for each variable. A two-sided *P* value of less than 0.05 (two-sided) was set as statistically significant.

Ethical Issues

The written approval of the Hacettepe University Health Sciences Research Ethical Board was obtained to conduct the study (session dated: 23.05.2023, session numbered: 2023/09 and decision numbered: 2023/09-60). Official permission to participate in the study was also obtained from the institutions of the researchers. The researchers participated in the study as members of the Association of Public Health Specialists-Tobacco Control Working Group.

The preliminary findings of the study (in Turkish) were presented at the 25th National Public Health Congress in December 2023 12.[14] With the feedback obtained from the congress experience, another original work, the manuscript preparation phase, has been launched. This time, the authors planned the manuscript from a global tobacco control perspective and performed logistic regression modeling to understand the relationship between violations of the anti-tobacco legislation and selected variables. Because the authors came from 11 different cities, online communication tools were used. At each step, the content is approved. Finally, all authors have read and approved all the details.

RESULTS

In Table 1, selected characteristics of the venues were presented. The categories of 765 out of a total of 772 hospitality venues were evaluated. Of the 765 hospitality venues, 417 (54.5%) were café-pastry shops, 271 (35.4%) were restaurants, 62 (8.1%) were bar-pubs, 8 (1.0%) were coffee houses, and 7 (1.0%) were hookah cafes. Within the scope of the research, 485 (62.8%) of the 772 hospitality venues were observed on weekdays and 287 (37.2%) were observed on weekends. It was reported that it was raining during 38 (4.9%) observations. Most observations were made during and after noon. Of the 772 hospitality venues, 760 had indoor spaces (98.4%). Among the hospitality venues, 12 had completely open areas. In 579 of the venues, tobacco use was observed in open spaces (75.0%). Fifty venues (6.5%) had "designated non-smoking area" in their outdoor settings. During the observation, butts, packets, mouthpieces, paper, and similar waste related to tobacco products were thrown at 167 hospitality venues (22.3%).

Table 2 presents some of the indoor spaces (n = 760). In 282 (37.1%) venues, clients smoked in indoor spaces as a violation of Law No. 4207 on the Prevention and Control of Tobacco Products (PaCoTPs). Existence of obligatory legal warnings can be assessed in 733 hospitality venues. There were no legal warnings in 416 hospitality venues (56.8%). Of the 760 hospitality venues that were observed and assessed for the presence of ashtrays, 286 had ashtrays on the tables (38.0%). Of the 758 hospitality venues observed and assessed for the presence of tobacco smoke, 264 were reported to have tobacco smoke (34.8%). In addition, 391 hospitality venues were observed to have retractable roofs (51.7%), 441 venues to have retractable side walls (58.2%), and 414 venues to have air conditioning systems (67.6%).

Table 3 presents the selected characteristics of those who use tobacco products. There were violations in 282 venues (37.1%). In 194 venues (68.7%), women were smoking, and in 260 venues (92.2%), men were smoking where violations were detected against PaCoTPs. In 17 of 282 hospitality venues (where violations were detected), individuals under the age of 18 (6.0%), in 278 hospitality venues, individuals aged 18-64 (98.5%), and in 36 hospitality venues, individuals aged 65 and

Table 1. Characteristics of the hospitality venues (1 August-10 October 2023)

Characteristics	Number	Percentage
Category of hospitality venue (n = 765)*		
Café-pastry shops	417	54.5
Restaurant	271	35.4
Bar-pub	62	8.1
Coffee houses	8	1.0
Hookah cafes	7	1.0
Day of the observation (n = 772)		
Weekday	485	62.8
Weekend	287	37.2
Raining status during the observation (n = 772)		
Yes	38	4.9
No	734	95.1
Hour of the observation (n = 772)		
00.00-02.00	2	0.3
09.00-11.59	8	1.0
12.00-14.59	107	13.9
15.00-17.59	219	28.4
18.00-20.59	289	37.4
21.00-23.59	147	19.0
Indoor settings (n = 772)		
Yes	760	98.4
No	12	1.6
Existence of outdoor spaces where clients can smoke		
Yes	579	75.0
No	193	25.0
Existence of "designated as non-smoking area" in the outdoor setting of the venue (n = 772)		
Yes	50	6.5
No	722	93.5
Disposal of butts, packages, mouthpieces, paper, and similar waste related to tobacco products (n = 747)**		
Yes	167	22.3
No	580	77.7

*Category of 7 enterprises could not be distinguished.
**A total of 25 hospitality venues could not be assessed.

over (12.7%) were observed to use tobacco products. Cigarette smoking was observed in 267 of the venues (92.9%), hookah smoking was observed in 44 hospitality venues (15.6%), and e-cigarette smoking was observed in 31 hospitality venues (10.9%). Cigars, heated tobacco products, and pipes were also smoked in the hospitality venues.

Table 4 presents violations of the legislation according to the category of the venue and the observation hours. Violations were more prevalent in bar-pubs, traditional coffee houses, and hookah cafes than in café-pastry shops and restaurants. Violations were also more common at late hours than at earlier times of the day. Violations were more common in venues with retractable roofs and/or side walls. Indoor violations were more common in venues with outdoor spaces where smoking was not permitted.

Table 5 presents the existence of non-compliance according to selected characteristics of the hospitality venue. Non-compliance in bars, pubs, traditional coffee houses, and hookah cafes was statistically significantly higher than in the other venue types (OR=3.031, 95% CI: 1.699 to 5.408, $P < 0.001$). The presence of a retractable roof and/or side wall (OR=5.362, 95% CI: 3.518 to 8.173, $P < 0.001$), later hours observations (OR=2.120, 95% CI: 1.399 to 3.212, $P < 0.001$), and the existence of outdoor venues where smoking is permitted (OR=3.165, 95% CI: 2.170 to 4.617, $P < 0.001$) also increased indoor violations.

Table 2. Some features of the indoor spaces of hospitality venues (August 1-October 10, 2023)

Feature	Number	Percentage
Existence of clients who smoke in indoor spaces, which is a sign of violation of Law No. 4207 (n = 760)		
Yes	282	37.1
No	478	67.9
Existence of legal regulations and warnings about the penal consequences of non-compliance (n = 733*)		
Yes, it is not regulated according to the law	63	8.6
Yes, it exists and is regulated in accordance with the law (posted in a minimum size of ten centimeters and in publicly visible places)	254	34.6
No, there is not	416	56.8
Ashtrays on tables (n = 751)*		
Yes	286	38.0
No	465	62.0
Observation of tobacco smoke (n = 758)*		
Yes	264	34.8
No	494	65.2
Presence of retractable roof (n = 756)*		
Yes	391	51.7
No	365	48.3
Presence of a retractable side wall (transparent/matte pvc, glass/etc.) (n = 757)*		
Yes	441	58.2
No	316	41.8
Presence of air conditioning (n = 612)*		
Yes	414	67.6
No	198	32.4

*Number of observations for this category.

Table 3. Some characteristics of those who were using tobacco products in the venues where violations of Law No. 4207 on PaCoTPs were detected (August 1-October 10, 2023)

Feature	Number	Percentage*
Sex		
Female smokers	194	68.7
Male smokers	260	92.2
Age group (year)		
Below 18	17	6.0
18-64	278	98.5
65 years	36	12.7
The type of tobacco used		
Cigarette	267	92.9
Waterpipe	44	15.6
E-cigarette	31	10.9
Cigar	3	1.0
Heated but not burned tobacco	2	0.7
Pipe	1	0.3

*Percentages for each variable were calculated over 282 venues where indoor space violations were observed.
PaCoTPs: Prevention and Control of Tobacco Products

Table 4. Violation of the legislation in indoor places by category of the venue and hour of observation (August 1-October 10, 2023)

Feature	Indoor tobacco use (violation of the legislation)			
	Yes		No	
	Number	Percentage	Number	Percentage
Category of the venue (n = 753*)**				
Café-pastry shops	163	39.7	248	60.3
Restaurant	64	23.9	204	76.1
Bar-pub	39	66.1	20	33.9
Traditional coffee houses in the city	6	75.0	2	25.0
Hookah cafes	6	85.7	1	14.3
Time of the observation (hour) (n = 760)**				
09.00-11.59	2	25.0	6	75.0
12.00-14.59	35	33.7	69	66.3
15.00-17.59	61	28.2	155	71.8
18.00-20.59	110	38.2	178	61.8
21.00-23.59	72	50.7	70	49.3
00.00-02.00	2	100.0	-	-
Having a retractable roof and/or side wall (n = 758*)****				
No	35	13.9	217	86.1
Yes	245	48.4	261	51.6
Existence of outdoor spaces where clients can smoke (n = 760)**				
No	111	58.7	78	41.3
Yes	171	29.9	400	70.1

*7 venues could not be categorized.
**$P < 0.01$.
***9 venues could not be categorized.

Table 5. Venue features associated with non-compliance (August 1-October 10, 2023)

Feature	OR	95% CI	*P*
Category of the venue			
Café-pastry shops and restaurants (reference)	1.00		
Bar-pub, traditional coffee houses, and hookah cafes	3.031	1.699-5.408	<0.001
Time of the observation (hour)			
09.00-20.59 (reference)	1.00		
21.00-02.00	2.120	1.399-3.212	<0.001
A retractable roof and/or sidewall			
No (reference)	1.00		
Yes	5.362	3.518-8.173	<0.001
Existence of outdoor spaces where clients can smoke n = 760*			
Yes (reference)	1.00		
No	3.165	2.170-4.617	<0.001

OR: odds ratio, CI: confidence interval

DISCUSSION

In this descriptive study, 772 hospitality venues were observed in 11 Turkish cities, where compliance with anti-tobacco legislation was evaluated through observation. The venues were located in different categories of the catering sector, such as café-pastry shops, restaurants, and bar-pubs. Less commonly, coffee houses and hookah cafes were also observed among the hospitality venues (Table 1). This diversity enabled the evaluation of tobacco control compliance in the hospitality sector with different target groups and purposes of use.

This study revealed significant deficiencies in compliance with the legislation. In 37.1% (n = 282) of the indoor spaces of 760 observed hospitality venues, tobacco products were consumed (Table 2). Studies have evaluated compliance with Türkiye's Law No. 4207. In a study conducted by Ay et al.[12] (2016) in the hospitality sector in 2013 and 2014, the frequency of violations was 49% and 29.7%, respectively. In Türkiye, compliance with legislation is also evaluated in taxis, which are among categories other than catering. In studies conducted by Öztürk et al.[15] (2018) and Erkoyun et al.[16] (2019) in taxis in different years and cities, it was found that there were violations (7.2%) of the Law among taxi drivers and taxi users. The level of compliance with legal regulations on tobacco control can be considered an important indicator of the effectiveness of tobacco control.

It was observed that there were deficiencies in warning messages for the public in the hospitality venues. For example, it was determined that there were no legal warnings (57.1%), there were ashtrays on the tables (38.0%), and there was tobacco smoke in the indoor areas (34.7%). The presence of retractable roofs and side walls was observed in 51.7% and 58.2% of the cases, respectively (Table 2), which are illegal and commonly used by opening them quickly when there is a control. These identified situations are examples of violations of the anti-tobacco legislation in Türkiye.[7]

Within the scope of the research, it was observed that butts, packages, mouthpieces, paper, and similar wastes related to tobacco products were thrown at 167 hospitality venues (22.3%) (Table 1). These results demonstrate that the implementation of anti-tobacco legislation is not sufficient. In addition, the results also emphasize the weak link between individuals' perceptions of maintaining indoor air quality. Therefore, there is a need to improve the awareness of tobacco users about the damage they cause to the environment while they smoke.

Cigarette smoking was observed in 267 venues (92.9%). Hookah use and e-cigarette smoking were the other frequent tobacco products observed in the indoor spaces of the venues (Table 3). This diversity is consistent with the tobacco products emphasized by WHO.[17] New generation tobacco products appear to be a growing risk, especially for young people.[18]

Table 5 shows that the existence of non-compliance was associated with a number of characteristics. Non-compliance in bars, pubs, traditional coffee houses, and hookah cafes was statistically significantly higher than in the other venue types. The presence of a retractable roof and/or side wall, later-hour observations, and the existence of outdoor areas where smoking is permitted also increased indoor violations. Fukuda et al.[19] (2023) found a higher frequency of siha ban violation in bars and nightclubs than in restaurants in Kenya. Inspections should be focused on these issues by the public authorities.

Our study has some strengths. First, we conducted the study in 11 different cities of Türkiye. Second, the research gave us the opportunity to evaluate the current situation in venues that the public frequently use. Third, the public authorities may use our results as a strong scientific rationale to prevent violations. The study has some limitations. First, the results are limited to observations, and in-person communication is not applied. Second, because only selected venues were observed in 11 cities, the results cannot be generalized.

CONCLUSION

In conclusion, this research, which was conducted in different cities of Türkiye in areas frequently used by the public, provides important data. To prevent the existing violations, it is recommended that the mechanisms through which Law No. 4207 is audited be revitalized by the public authority immediately and its continuity be ensured. The public should be informed about all aspects of tobacco control, and similar studies should be conducted regularly with a wider scope.

Ethics

Ethics Committee Approval: This study was approved by Hacettepe University Health Sciences Research Ethical Board study (session dated: 23.05.2023, session numbered: 2023/09 and decision numbered: 2023/09-60).

Informed Consent: As the study was conducted by the observations of the hospitality venues, there was no patient or individual participation.

Presented in: The basic findings of the study were presented at the 25th National Public Health Congress in December 2023.

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Footnotes

Authorship Contributions

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Original Article

Long-term Effects of COVID-19 on Sleep Patterns

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Abstract

OBJECTIVE: To examine the long-term impact of Coronavirus disease-2019 (COVID-19) on sleep patterns and the prevalence of sleep disorders and to increase public health awareness of long-term COVID-19.

MATERIAL AND METHODS: Using the Massachusetts General Brigham Research Patient Data Registry, Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) positive patients were surveyed about their sleep patterns before and after the viral infection. Information related to comorbid conditions and medications was obtained through chart review.

RESULTS: Two hundred and forty-six completed surveys were analyzed. Average age was 53.3±16.3 years, and they were predominantly non-hispanic white (84.1%) and female (74.3%). The mean body mass index (kg/m^2) was 29.9±6.9, and a greater proportion were non-smokers (63.2%). After COVID-19, there was an increase in the percentage of participants reporting difficulty initiating (39±49% vs. 31±46% prior to COVID-19 infection $P = 0.01$). Similarly, the participants reported difficulty in maintaining sleep after COVID infection (57% vs. 43% prior to infection $P < 0.001$). Additionally, there was an increase in the use of sleep aids (30% vs. 24% before the infection $P = 0.003$). The participants also reported a decrease in feeling rested and an increase in the need for napping (58% vs. 36%, $P < 0.0001$) and (27% vs. 40%, $P < 0.0001$) respectively. The sleep symptoms persisted beyond 12 months in 28% of the participants.

CONCLUSION: SARS-CoV-2 infection had negative effects on sleep, and a significant proportion of adults experienced insomnia and daytime sleepiness beyond 12 months after recovering from the initial infection.

KEYWORDS: Long Coronavirus disease-2019, insomnia, hypersomnia

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INTRODUCTION

The Coronavirus disease-2019 (COVID-19) pandemic has caused over 700 million cases and 7 million deaths globally.[1] However, a significant proportion of COVID-19 survivors experience a variety of ongoing symptoms characterized by persistence or recurrence of initial symptoms or emergence of new symptoms. Those so afflicted often refer to themselves as "long haulers" and the constellation of these symptoms is colloquially known as "long COVID-19". In October 2021, the World Health Organization proposed to define these symptoms as "post-COVID-19 condition", referring to any symptom(s) occurring in individuals with a probable or confirmed Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) infection within three months of infection and lasting for at least two months as long as there is no alternative diagnosis.[2] Similarly, in the United Kingdom, the National Institute for Health Excellence proposed a definition of "post-COVID-19 syndrome" for symptoms developing during or after infection with COVID-19 lasting for more than 12 weeks and after excluding alternative diagnoses.[3] The syndrome is now formally known as post-acute sequelae of SARS-CoV-2 (PASC). It has been estimated that approximately 100 million people suffer from PASC globally, and the total economic burden is estimated to be approximately 2.6-3.7 trillion dollars.[4] Estimates of the prevalence of PASC range from 7.5-41% in non-hospitalized adults depending on the criteria used to identify cases.[5]

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The most commonly reported symptoms of PASC are fatigue, brain fog, and sleep disturbance. Fatigue is a vague symptom that is difficult to separate from sleep disturbances. Although the prevalence of sleep disturbances in PASC is estimated to range from 18-40%,[6] most reports of sleep disturbances in PASC are non-specific; there are few reports of the exact symptoms, prevalence, evolution, and ultimate outcomes of sleep disturbances in PASC.[7-9] Nonetheless, a high prevalence of insomnia has been reported within the first six months after COVID-19 infection.[10] A large cohort study in the UK demonstrated an increased risk of fatigue and sleep problems[11]. Similarly, a recent study (the International COVID Sleep Study-II study)[12] demonstrated a high prevalence of insomnia (49.6%) and excessive daytime sleepiness (35.8%) among patients with PASC. Even if only 10% of those with PASC develop a sleep disorder, there would be an enormous social and economic impact. Therefore, documenting the time course of disturbed sleep related to COVID-19 may better prepare healthcare providers to manage and possibly mitigate the impact of PASC.

In this study, we report the incidence and prevalence rates of self-reported disturbed sleep symptoms and changes in sleep duration in a cohort of individuals with COVID-19 infection. In addition, we documented the persistence of these symptoms during the post-infection period. We hypothesized that symptoms of sleep disturbance related to COVID-19 will be heterogeneous and persist for an extended period after initial infection with SARS-CoV-2.

MATERIAL AND METHODS

The data used in this study were obtained from the Massachusetts General Brigham (MGB) Research Patient Data Registry (RPDR). This centralized clinical registry or data warehouse was established in 1991 and can be used to identify patients based on clinical and demographic information. Using this repository, we assembled a study cohort of patients who tested positive for SARS-CoV-2 at MGB hospitals between February 2020 and March 2021. After institutional review board approval, a RPDR query was run to identify patients aged above 18 years who were enrolled in the Research Opportunities Direct to You program. This outreach program allows patients to agree to be contacted directly by researchers without involvement from their clinicians.

The RPDR query included patients irrespective of gender and race who had a documented positive COVID-19 test. Patients with severe neurologic disease, those on chronic ventilatory support, pregnant women, or those in rehabilitation were excluded from this study. Using the Research Electronic Data Capture (REDCap) HIPAA-compliant web-based application, patients meeting the defined criteria were sent a survey (Appendix Survey 1). The survey was sent in two languages (English and Spanish). A total of 1,090 invitations were sent, and 290 responses were received. Participants who provided incomplete surveys were excluded, leaving a total of 246 for final analysis (22.6%). Comparisons of the mean age (53.3±16.3 vs. 51.0±16.5 years, $P = 0.09$) and sex distribution (74.3% vs. 68.8% female, $P = 0.35$) of respondents to non-respondents were not significantly different.

Main Points

- A significant proportion of Coronavirus disease-2019 (COVID-19) survivors suffer from ongoing symptoms, referred to as long-term COVID-19.
- Severe acute respiratory syndrome-Coronavirus-2 infection has negative effects on sleep.
- COVID-19 survivors may experience increased insomnia and daytime sleepiness beyond 12 months after the infection

In addition to demographic information, the survey included questions pertaining to the number of hours of sleep, difficulty initiating or maintaining sleep, daytime sleepiness, snoring, difficulty breathing while asleep, history of vivid dreams or hypnogogic hallucinations, and use of sleep aids before and after their diagnosis of COVID-19 (Appendix Survey 1). Information related to comorbid conditions and medications was obtained through chart review.

The study was approved by the Massachusetts General Brigham Institutional Review Board (protocol number: 2020P004011, date: 12.15.2020).

Statistical Analysis

Data are summarized as mean with standard deviation for continuous variables or frequency with proportions for categorical variables. Group comparisons before and after COVID-19 infection were examined using Student's paired sample t-test for continuous data or Pearson c^2 test for categorical data. As the response categories for self-reported sleep duration were ordinal, changes in the distribution of responses were determined using the Stuart-Maxwell marginal homogeneity test. To examine whether symptoms persisted beyond 12 months, the data were stratified into two categories ($\leq$12 months or >12 months) according to the duration of time after their COVID-19 diagnosis. Each respondent completed the survey. The effects of hypertension, heart disease, anxiety/depression, diabetes, and smoking on changes in sleep characteristics were assessed using McNemar's test. In all analyses, the statistical significance was set as $P < 0.05$. All statistical tests were performed using STATA v18 (MP-parallel Edition; STATA Corp, College Station TX) or IBM Statistical Package for the Social Sciences v28 (Armonk, NY).

RESULTS

Table 1 shows the baseline characteristics of the 246 participants who responded to the sleep survey. The average age was 53.3±16.3 years, and the respondents were predominantly non-hispanic white (84.1%) and female (74.3%). The mean BMI (kg/m^2) was 29.9±6.9, and a greater proportion were non-smokers (63.2%). College education and current employment were reported by 47.9% and 63.7% of respondents, respectively. Significant proportions of the cohort reported anxiety/depression (50.0%), hypertension (41.8%), heart disease (13.9%), and diabetes (13.7%). A previous sleep disorder diagnosis was noted in 37.0%. Hospital admission occurred in 11.3% of participants, and 7.9% of the patients had pneumonia as an admission diagnosis. Hospital admission, but not pneumonia, occurred more frequently in those with symptoms exceeding 12 months. Additionally, only one participant required mechanical ventilation.

Tables 2, 3 presents the effect of COVID-19 diagnosis on various sleep characteristics. Results for all participants are presented in Table 2. After the infection, a significantly greater number of participants reported difficulty initiating (31 vs. 39%, $P = 0.016$), and maintaining sleep (43 vs. 57%, $P < 0.001$), and increased use of sleep aids (24 vs. 30% $P = 0.006$) with incidence rates of 24%, 37%, and 12%, respectively. In addition, feeling unrested and the need for napping were greater (58 vs. 36%, $P < 0.001$) and (27 vs. 40% $P < 0.001$) with an incidence of 7.9% and 22.6%, respectively. Interestingly, a large number of participants reported having vivid dreams and hypnogogic hallucinations during the post-COVID-19 period. The incidence rate of vivid dreams was 31% after recovery from COVID-19. Although shortness of breath while sleeping increased slightly, the prevalence of snoring did not change. Figure 1 illustrates the distribution of self-reported sleep duration before and after COVID-19. There was a substantial shift in the distribution toward shorter sleep as well as a less perceptible change toward greater sleep ($P = 0.009$).

Table 3 shows the prevalence of sleep symptoms before and after COVID-19 after excluding individuals with pre-existing anxiety or depression. The patterns of change in the prevalence rates of COVID-19 were similar to those observed in the full cohort, although some symptoms were no longer statistically significant.

Table 1. Baseline characteristics

	All participants	**<12 months**	**≥12 months**	***P* value**
	246	**176**	**70**	
Age (yrs)	53.3±16.3	52.2±15.5	56.1±17.9	0.09
Sex (M/F %)	25.7/74.3	27.8/72.2	20.3/79.7	0.22
Hispanics (%)	6.9	6.3	8.6	0.52
Caucasians (%)	84.4	84.0	85.5	0.89
Employed (%)	63.7	65.5	60.0	0.42
Education (% college)	47.9	49.4	44.3	0.76
BMI (kg/m^2)	29.9±6.9	29.8±6.4	30.2±8.2	0.77
Smoking history (%):				
Never	63.2	64.1	60.4	
Current	6.2	5.5	8.3	0.70
Past	30.6	30.3	31.3	
Hypertension (%)	41.8	42.6	39.6	0.72
Anxiety/depression (%)	50.0	50.0	50.0	1.0
Diabetes (%)	13.7	12.0	19.0	0.25
Heart disease (%)	13.9	12.4	18.6	0.31
Duration between infection and survey (months)	7.4±3.9	5.4±1.9	13.3±0.8	**0.00**
Hospitalized (%)	11.3	8.5	19.1	**0.02**
Pneumonia (%)	7.9	6.8	11.1	**0.27**

BMI: body mass index, yrs: years, M: male, F: female

Table 2. Sleep symptoms before and after COVID-19 infection (n = 246)

	Pre-COVID-19 (%)	**Post-COVID-19 (%)**	***P* value**
Difficulty falling asleep	31	39	0.016
Difficulty staying asleep	43	57	<0.001
Use of sleep aids	24	30	0.006
Rested	58	36	<0.001
Napping	27	40	<0.001
Snoring	48	49	0.454
Difficulty breathing	10	14	0.049
Vivid dreams	44	56	<0.001
Hypnogogic hallucinations	3	10	<0.001

COVID-19: Coronavirus disease-2019

To evaluate the impact of COVID-19 infection severity, analyses were performed after stratification by hospital admission history and COVID-19 pneumonia. As shown in Appendix Tables 1, and 2, the number of participants who were hospitalized or who developed pneumonia was small. Nonetheless, the pattern of change in prevalence rates after COVID-19 infection were qualitatively similar in those with a history of hospital admission as well as those with a history of pneumonia. A previous diagnosis of a sleep disorder was noted in 37% of respondents (Appendix Table 3). Although some symptoms were not statistically significant, the pattern of change in these individuals was generally similar to that in individuals without a sleep disorder diagnosis. In particular, there was a marked increase in feeling unrested and a need to nap, both of which were noted in the overall cohort.

The long-term effects of COVID-19 on sleep are presented in Table 4. Overall, 64 participants (26%) experienced sleep symptoms after more than 12 months of COVID-19 treatment. The symptom pattern did not differ between those with a shorter vs. longer duration of past infection. As shown in Figure 2, sleep duration decreased similarly in those who were less than 12

Table 3. Sleep symptoms before and after COVID-19 infection, excluding pre-existing anxiety or depression (N = 92)

	Pre-COVID-19 (%)	Post-COVID-19 (%)	*P* value
Difficulty falling asleep	22	33	0.021
Difficulty staying asleep	39	53	0.011
Use of sleep aids	16	24	0.039
Rested	66	46	<0.001
Napping	23	28	0.508
Snoring	53	51	1.0
Difficulty breathing	8	13	0.063
Vivid dreams	41	54	0.019
Hypnogogic hallucinations	1	3	0.625

COVID-19: Coronavirus disease-2019

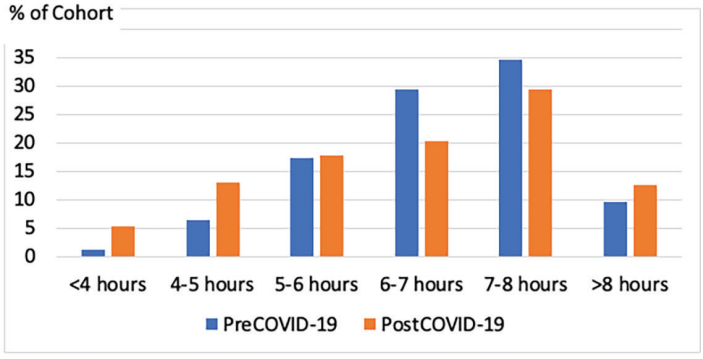

Figure 1. Distribution of self-reported sleep duration before and after COVID-19 infection. *P* = 0.009, pre-COVID-19 vs. post-COVID-19

COVID-19: Coronavirus disease-2019

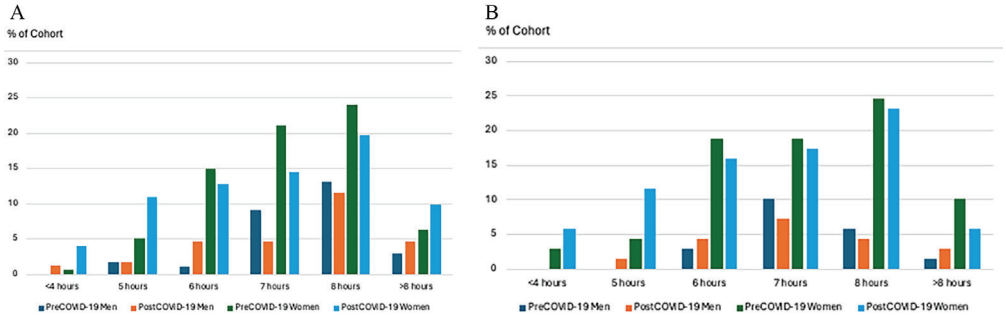

Figure 2. Distribution of self-reported sleep duration before and after COVID-19 infection stratified by sex for participants A) who were less than 12 months removed from infection (N = 183). *P* = 0.007, pre vs. post-COVID-19; *P* = 0.208, men pre vs. post-COVID-19; *P* = 0.017, women pre vs. post-COVID-19; B) for participants who were >12 months removed from infection (N = 64). *P* = 0.044, pre vs. post-COVID-19; *P* = 0.527 for men, pre vs. post-COVID-19; *P* = 0.056, women pre vs. post-COVID-19

COVID-19: Coronavirus disease-2019

Table 4. Sleep impairment associated with COVID-19 infection before and after 12 months

	<12 months		≥12 months	
	N = 183		N = 63	
	Pre-COVID-19	Post-COVID-19	Pre-COVID-19	Post-COVID-19
Difficulty falling asleep (%)	30±46	36±48	33±47	48±50
P	0.14		0.01	
Difficulty staying asleep (%)	43±49	55±49	43±49	61±49
P	0.001		0.009	
Use of sleep aids (%)	24±43	29±46	23±43	32±47
P	0.03		0.03	
Rested (%)	58±49	34±48	60±49	41±49
P	<0.001		0.002	
Napping (%)	29±45	41±49	23±42	38±49
P	<0.001		0.006	
Snoring (%)	50±50	50±50	43±49	47±50
P	0.74		0.26	
Difficulty breathing (%)	9±29	13±33	13±34	17±38
P	0.11		0.08	
Vivid dreams (%)	43±49	55±49	46±50	60±49
P	<0.001		0.006	
Hypnogogic hallucinations (%)	2±15	9±28	4±21	15±36
P	0.007		0.007	

COVID-19: Coronavirus disease-2019

months removed from the infection and those with 12 months or more removed from the infection. Furthermore, changes in sleep duration were primarily attributable to women.

Additional analyses (data not shown) demonstrated that changes in sleep characteristics after COVID-19 infection occurred irrespective of comorbid conditions, such as hypertension, heart disease, diabetes, and anxiety/depression.

DISCUSSION

In this study, we documented that after COVID-19 infection, there is a high incidence and prevalence of self-reported symptoms of sleep disturbance. In addition, these symptoms persist for over 12 months in many individuals. In addition, self-reported sleep duration changes were observed in many individuals, with most experiencing a decline but with an increase apparent in a few.

A bidirectional relationship exists between sleep and immunity, and sleep disturbances have been reported as consequences of infections, particularly viral infections.[13-15] Several sleep symptoms, including difficulties with sleep initiation and maintenance, reduced sleep time, prolonged sleep time, and daytime napping, have been reported. Prior studies on the neuropsychiatric consequences of COVID-19 showed that the most prevalent symptoms were sleep disturbances (27%) followed by fatigue (24%)[10] although another study found that fatigue (40%) was more common than sleep disturbances (29.4%).[16] However, reports of sleep disturbances in other studies were undifferentiated. Our findings demonstrate that symptoms of sleep disturbance associated with insomnia are common and increase after COVID-19 infection. In contrast, symptoms indicative of sleep-disordered breathing, such as snoring, did not increase. Our results are consistent with those of previous studies in confirming that disturbed sleep is highly prevalent after COVID-19 and but extend them by

demonstrating that it is a result of a high incidence of symptoms suggestive of insomnia.

Our cohort of COVID-19 survivors reported insomnia symptoms that persisted beyond 12 months following COVID-19 infection. Insomnia is a fairly well documented post-COVID-19 sequelae[17-20] and is one of the symptoms attributed to PASC. The average prevalence of post-COVID-19 insomnia is estimated at approximately 24%.[21] However, few studies document its time course. A previous study demonstrated persistence of insomnia for up to 30 days after COVID-19 infection.[22] A recent study of sailors on an aircraft carrier noted that over 50% of the participants reported at least one symptom of long-lived COVID-19 at 6, 9, and 12 months.[17] Our study extends the findings from previous studies by demonstrating that 28% of individuals with COVID-19 from a community can experience disturbed sleep for more than 12 months. Consistent with our findings, a high prevalence of sleep disturbances (67%) was reported among COVID-19 survivors in a recent uncontrolled prospective observational study.[23]

We observed that sleep duration decreased in many of our cohort and that it was present for 12 months or more after COVID-19 infection. However, in a small number of individuals, sleep duration has been shown to increase. These changes are similar to those observed in uninfected persons in the general population during the COVID-19 pandemic and have been associated with anxiety and depression.[24] It is possible that a similar relationship exists with individuals who have had COVID-19 infection, as there was a high prevalence of anxiety or depression in our cohort.

Fatigue is one of the most common persistent symptoms following COVID-19[16,25] and can last up to a year after infection.[26,20] It has been shown to occur concurrently with insomnia in some patients.[27] Post-infection fatigue syndrome has also been reported following infectious mononucleosis[28-30] suggesting that fatigue in these two conditions may share the same pathogenetic mechanism. Our analysis also revealed increased fatigue and the need for daytime napping among COVID-19 survivors, confirming previous reports. In a recent study using data from the German National Pandemic Cohort Network, the researchers found fatigue and cognitive deficits as the most prevalent long-term COVID-19 symptoms, and these symptoms improved over two years in more than half of the participants who recovered from post-COVID-19 syndrome.[31,25]

Vivid dreaming and hypnagogic hallucinations, which can be features of narcolepsy, occurred post-COVID-19 in our cohort, and these symptoms persisted for 12 months or more. Although COVID-19 has not been associated with an increased risk of narcolepsy[32], infection with SARS-CoV-22 may provide an opportunity to investigate the mechanisms related to the development of narcolepsy.[33] In a previous study examining the interaction between COVID-19 and multiple health behaviors (sleep, diet, and physical activity), the authors demonstrated increased vivid dreams and nightmares among 12% of participants, and the majority were linked to increased stress and anxiety (75%).[34] These symptoms were predominantly reported by women. To our knowledge, this is the first study to report vivid dreams and hypnagogic hallucinations as part of the neuropsychiatric consequences of COVID-19 infection and the persistence of these symptoms beyond 12 months.

Our study results indicated that women were more likely to experience a reduction in sleep duration after COVID-19. These findings are consistent with our previous research in a large general population, which demonstrated that sleep decline during the pandemic was more likely to occur in women.[24] In addition, studies from the Middle East and the West have demonstrated an increased risk of developing mental health problems among women during the COVID-19 pandemic;[35,36] mental health issues during the pandemic were major factors associated with changes in sleep duration.[24] In contrast, several studies from China have found no gender difference.[37,38] Further investigation is required.

Given the heterogeneity of PASC symptoms and, in particular, associated sleep disturbances, multispecialty collaboration is needed to treat afflicted individuals. However, due to the lack of specialists and long wait times, primary care providers are responsible for early recognition of sleep disorders in patients with PASC. Our study results emphasize that sleep disturbances are common and enduring in PASC and therefore require as much attention as other PASC-related symptoms. The World Health Organization, in its document "Support for rehabilitation self- management after COVID-19 related illness"[39] has published simple recommendations for improving sleep, which can be a useful tool for clinicians.

To our knowledge, this is the first study to examine the long-term effects of COVID-19 on disturbed sleep symptoms. However, we acknowledge some limitations. First, the response rate for our study was very low, which is concerning for non-response bias. However, we found no statistical difference between the age and sex distribution of respondents and non-respondents, suggesting that the two groups were not meaningfully different. Furthermore, some studies have explored the relationship between low response rates and non-response bias and found little relationship between the two.[40-42] Nevertheless, some degree of non-response bias cannot be excluded and should be considered when interpreting our results. Second, the study participants were contacted using the REDCap portal, and it is likely that patients without access to technology were not represented in this study, thereby causing sampling bias and skewing the interpretation. Third, the results of this study were based on self- reported sleep impairment, which may have caused reporting bias. Fourth, the majority of the study participants were women. Therefore, our findings related to sex differences should be interpreted with caution. Fifth, the cohort was comprised mainly of Caucasians and English-speaking participants despite our efforts to recruit Spanish speakers. Thus, our sample is not representative of the United States population, and the results may not be generalizable. Lastly, measures of sleep disturbance were self-reported; future studies using objective sleep measures are needed to better assess the long-term effects of COVID-19.

CONCLUSION

In this observational study, infection with SARS-CoV-2 had a negative effect on sleep, with a high proportion of adults experiencing difficulty initiating and maintaining sleep, feeling

unrested, and other symptoms of disturbed sleep lasting beyond 12 months after recovering from the initial infection. Future studies with a more diverse population and using objective sleep measures are needed to examine these relationships and to determine whether interventions can improve sleep health in individuals with PASC.

Ethics

Ethics Committee Approval: The study was approved by the Massachusetts General Brigham Institutional Review Board (protocol number: 2020P004011, date: 12.15.2020).

Informed Consent: Waived [patients who were enrolled in the Research Opportunities Direct to You (RODY) program were contacted]. This outreach program allows researchers to directly contact patients. Eligible patients were sent recruitment letters via secure email, and only after they agreed to participate, were the REDCAP sleep surveys sent.

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Footnotes

Authorship Contributions

Concept: S.B-A., O.S.F., S.F.Q., Design: S.B-A., O.S.F., S.F.Q., Data Collection or Processing: S.B-A., Analysis or Interpretation: S.B-A., S.F.Q., Literature Search: S.B-A., O.S.F., S.F.Q., Review and Editing: S.B-A., S.F.Q., Writing: S.B-A.

Conflict of Interest: SFQ has served as a consultant for Best Doctors, Bryte Foundation, Jazz Pharmaceuticals, and Whispersom. The remaining authors declare no conflict of interest.

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Click the link to access Appendix Tables 1, 2, 3, and the Appendix Survey: https://l24.im/vlHu

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Original Article

Psychometric Properties of the Turkish Version of the Breathlessness Catastrophizing Scale in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

OBJECTIVE: To examine the validity and reliability of the Turkish version of the Breathlessness Catastrophizing Scale (BCS) in patients with chronic obstructive pulmonary disease (COPD).

MATERIAL AND METHODS: Seventy patients with COPD (55 male/15 female, mean age: 68.7±7.3 years, FEV1%: 45.4±19.5) were included in this methodological study. Internal consistency was measured using Cronbach's α, and intra-rater reliability was assessed using the intraclass correlation coefficient (ICC). Correlations between the BCS and Modified Medical Research Council Dyspnea Scale (mMRCS), COPD Assessment Test (CAT), Hospital Anxiety and Depression Scale (HADS), Breathlessness Beliefs Questionnaire (BBQ), and St. the George Respiratory Questionnaire (SGRQ) scores were assessed for convergent validity. Known-group comparisons were performed according to COPD stage and dyspnea severity using the independent sample t-test.

RESULTS: Internal consistency was excellent (Cronbach's α=0.941), and the ICC for reliability was 0.955. The BCS score was correlated with the mMRCS (r=0.745), CAT (r=0.652), HADS anxiety (r=0.556) and depression (r=0.588), the BBQ (r=-0.567), and SGRQ (r=0.550-0.634) scores ($P < 0.05$). The BCS score was higher in patients with advanced COPD ($P = 0.003$) and those with severe dyspnea ($P < 0.001$).

CONCLUSION: The Turkish version of the BCS is a valid and reliable tool for evaluating catastrophic dyspnea in patients with COPD.

KEYWORDS: Catastrophizing, chronic obstructive pulmonary disease, dyspnea, reliability, validity

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable condition characterized by a chronic inflammatory response in the airways and lung parenchyma to harmful particles and gases, resulting in progressive and persistent airway restriction.[1] The high morbidity and mortality rates associated with COPD, which is the third leading cause of death worldwide, make it a top public health concern.[2]

Shortness of breath, which significantly limits everyday activities, is the most common symptom of COPD and is a rather terrifying experience for many patients. This symptom is a significant indicator of exercise intolerance, poor quality of life, and even mortality.[3] According to previous studies, certain emotional and cognitive processes can influence how a person behaves, particularly regarding the sensation of shortness of breath. These processes can alter how a person perceives dyspnea, in addition to depression and anxiety.[4-7] These specific cognitive processes have been studied using different definitions, such as the formation of negative perceptions about shortness of breath, the fear of experiencing breathlessness, or catastrophizing shortness of breath.[4,5]

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Catastrophizing is characterized by an increase in people's threat values toward such situations and the impression that they are out of control. It is an exaggerated negative cognitive orientation toward destructive stimuli and experiences.[8] It encompasses negative emotional patterns such as magnification, despair, and an intense focus on damaging inputs. Patients who overreact to their shortness of breath are prone to developing an excessive sensitivity to fear of it, which may lead them to refrain from engaging in activities that might trigger it.[9,10] It is hypothesized that dyspnea-specific negative affectivity, such as breathlessness catastrophizing, contributes to increased dyspnea perception beyond the effects of general anxiety levels.[11]

There are limited options in the literature for determining the extent to which patients with COPD experience dyspnea. The Interpretation of Breathing Problems Questionnaire, which was created for patients with COPD, is hardly utilized because it is challenging to complete in a clinical environment.[12] The Breathlessness Beliefs Questionnaire (BBQ), which was developed later, evaluates patients' kinesiophobia rather than providing information about catastrophizing.[13] The Breathlessness Catastrophizing Scale (BCS), a version of the Pain Catastrophizing Scale (PCS)[8], is the standard for the evaluation of catastrophizing among patients with chronic pain, was created.[14] This newly constructed scale has been described as having additional benefits for therapeutic use and demonstrating the direct experiential aspects of catastrophization. The characterization of catastrophic thought in the scale is not limited to increased anxiety, morbidity, or death; each item requires a single quantitative rating. The BCS was found to have high convergent validity, reliability, and sensitivity to changes in the evaluation of dyspnea catastrophization in patients with COPD.[14] To the best of our knowledge, no study has examined the psychometric features of the Turkish version of the BCS in patients with COPD. Therefore, we aimed to investigate the reliability and construct validity of the Turkish version of the BCS in patients with COPD.

MATERIAL AND METHODS

Permission and Ethics

The scale was requested from its author for Turkish adaptation, and permission was obtained for its use. All participants provided written informed consent after receiving an explanation of the study's objectives and procedures. The study protocol was approved by the İzmir Katip Çelebi University Non-invasive Research Ethics Board (decision number: 0071, permission date: 23.02.2023). The study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki.

Main Points

- Multidimensional evaluation of dyspnea sensations in patients with chronic obstructive pulmonary disease (COPD) is critical.
- A catastrophizing breathlessness could affect patients' activity participation.
- The Breathlessness Catastrophizing Scale showed good psychometric properties in Turkish patients with COPD.

Participants and Procedures

This methodological study was conducted between May 2023 and November 2023. The study included patients with COPD who were followed up at the İzmir Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital.

The minimum sample size for validity and reliability studies is recommended to be between two and 20 people per item.[15] The BCS comprises 13 items; thus, the sample size was predicted to be between 26 and 260. Furthermore, it is proposed that a minimum of 21 participants were necessary to achieve an estimated intraclass correlation coefficient (ICC) value of ≥0.9.[16] The study was completed with 70 patients, who were reached in the time allocated for the study.

The inclusion criteria were: COPD diagnosis according to the diagnostic criteria established by the Global Initiative for Obstructive Lung Disease (GOLD)[1], age >18 years, no medication changes in the last three weeks, and ability to read and comprehend Turkish. The exclusion criteria were: having COPD exacerbation in the previous month, refusal to participate in the survey, failing to understand the questionnaire or other assessment methods, and not filling out the questionnaire properly.[17,18]

The translation of the BCS was performed in accordance with the guideline.[19] Face-to-face interviews were used by the same researcher to collect data. Additionally, the BBQ, the Hospital Anxiety Depression Scale (HADS), the St. George's Quality of Life Questionnaire (SGRQ), the COPD Assessment Test (CAT), and the Modified Medical Research Council Scale (mMRC) were administered to the patients on the same day for validity analysis. The second assessment identified 30 patients using a simple random sampling method with an envelope containing patient numbers,[20] and the measurements were performed seven days later for intra-rater reliability analysis.

Measurements

Sociodemographic characteristics (age, gender, education), physical measurements (body weight, height), and clinical data (disease duration, smoking habits, cigarette consumption, emergency admissions, and hospitalization in the last year) were recorded in the data form. Lung function was measured using a portable spirometer (Cosmed Pony FX, Rome, Italy) following the ATS guidelines.[21] The GOLD spirometric classification was employed to assess the disease's severity.[1]

Breathlessness Catastrophizing Scale

The BCS was developed from the PCS.[8] Participants are asked to score "the extent to which they have these thoughts and feelings when they experience breathlessness" on a 13-item scale.[14] Each item was rated on a scale of 0 to 4, with the options being "(0) not at all, (1) mild, (2) moderate, (3) a lot, and (4) always". The total score ranged from 0 to 52. A score of 0 indicates that shortness of breath is not perceived as catastrophic.

Breathlessness Beliefs Questionnaire

The BBQ includes 11 items that measure two dimensions of breathlessness beliefs: somatic focus and activity avoidance. Each item is scored 1-5 points. The total score ranged from 11 to 55. Low scores indicate no beliefs about dyspnea or dyspnea-related kinesiophobia. High BBQ-SF indicate the perception that the patient's illness is more dangerous. High BBQ-AA represent the patient's conviction that engaging in physical activity or exercising until one feels out of breath should be avoided since doing so may worsen their condition. Turkish validity and reliability of the scale were determined by Gurses et al.[18]

Hospital Anxiety and Depression Scale

The HADS is a four-point Likert scale, scored between 0 and 3, comprising a total of 14 questions, seven of which examine symptoms of depression and seven of which examine symptoms of anxiety. The lowest and highest possible scores on the two subscales are 0 and 21, respectively. Turkish validity and reliability study of this scale was performed by Aydemir et al.[22]

St. George's Respiratory Questionnaire

The SGRQ is a 50-item disease-specific quality of life questionnaire scored from 0 to 100. Lower scores indicate better quality of life regarding symptoms, activity, and the impact of COPD. Turkish validity and reliability of the scale were established by Polatlı et al.[23]

Modified Medical Research Council Scale

The mMRCS is a one-dimensional tool that rates breathlessness on five levels according to different physical activities. This scale consists of five items, rated from 0 to 4.[24] Participants were asked to indicate the level of activity that caused dyspnea.

Chronic Obstructive Pulmonary Disease Assessment Test

The CAT is an eight-question test that assesses the grade of the disease, symptom severity, and impact on the patient's quality of life. Each question was scored between 0 (no symptoms) and 5 (severe symptoms). The minimum and maximum evaluation scores were 0 and 40 for the perfect and worst health status. Turkish validity and reliability study of this test was performed by Yorgancıoğlu et al.[25]

Statistical Analysis

Statistical analysis was conducted using Statistical Package for the Social Sciences for Windows (version 21.0. Armonk, NY: IBM Corp., The normality of data distribution was assessed using the Shapiro-Wilk test and histogram graphics. Continuous variables were presented as mean (standard deviation) or median (25-75 interquartile range), whereas categorical variables were presented as numbers and percentages (%).

Construct validity was examined through factor analysis, convergent, and known-group validity. To identify the factor structure of the BCS, principal components explanatory factor analysis was applied, considering an explanatory rate of at least 60%.[26] The adequacy of sample size was determined using the Kaiser-Meyer-Olkin test (coefficient: 0.914), and Bartlett's test of sphericity revealed a *P* value of 0.001, indicating that the data distribution was suitable for factor analysis.

Reliability was assessed using Cronbach's α coefficient to measure internal consistency, with a value of at least 0.70 indicating adequate internal consistency.[27] The intra-rater reliability of the BCS was calculated at a 95% confidence interval (CI) using the ICC model (the two-way random effects and absolute agreement methods), where an ICC >0.90 indicated excellent reliability.[28]

Validity was analyzed using Pearson's correlation coefficients between the BCS and the other measures (BBQ, HADS, SGRQ, CAT, and mMRCS scores). The coefficients were reported as follows: (±0.10 to ±0.39), weak correlation; (±0.40 to ±0.69), moderate correlation; (±0.70 to ±0.89), strong correlation; and (±0.90 to ±1.00), very strong correlation.[29] Known-group validity was analyzed with COPD stage and dyspnea severity according to the mMRCS using the independent samples t-test. By determining the percentage of individuals who achieved the lowest or highest possible score on the BCS, floor and ceiling effects were investigated. Statistical significance was set at $P < 0.05$ for all analyses.

RESULTS

This study included a total of 70 patients with COPD. The characteristics of the patients are presented in Table 1, and the outcome measures are presented in Table 2. Principal component analysis indicated that the scale had a unifactorial structure, and the factor loadings varied between 0.638 and 0.848 (Table 3). The internal consistency of the BCS was excellent (Cronbach's α coefficient=0.941). The Cronbach's if item-deleted coefficients ranged from 0.934 to 0.941 (Table 3). The intra-rater reliability was excellent. The ICC was 0.955 at a 95% CI for the total score, ranging from 0.744 to 0.958 for each item (Table 3).

The BCS score was strongly correlated with the mMRCS (r=0.745) and moderately correlated with the CAT (r=0.652), the HADS anxiety (r=0.556) and depression (r=0.588), the SGRQ symptoms (r=0.550), activity (r=0.578), impact (r=0.558), and the total score (r=0.634), the BBQ activity avoidance (r=-0.468) somatic focus (r=-0.474) and the total (r=-0.567) scores ($P < 0.05$) (Table 4).

Known group analyses showed that the BCS score was higher in patients with advanced stage ($P = 0.003$) and severe dyspnea ($P < 0.001$) (Table 5). No floor or ceiling effects were observed for the BCS. One participant (1.4%) earned the lowest score of zero, while 2 people (2.9%) earned the highest score of 52.

DISCUSSION

In the present study, an exploration into the intra-rater reliability, internal consistency, construct validity (including convergent and known group analysis), as well as ceiling and floor effects, was conducted on the Turkish version of the BCS among patients with COPD. The findings indicated that the scale exhibited both validity and reliability. Minimal adaptation was deemed necessary, and all constituent items were in congruence with the Turkish demographics.

Table 1. Characteristics of patients

Variables (n = 70)	Mean (SD) or Median (25-75 IQR)	Minimum-maximum
Age (years)	68.1 (7.3)	52-80
Body mass index (kg/m^2)	26.2 (5.2)	17.2-39.8
Disease duration (years)	13.3 (9.3)	1-50
Consumption of cigarette (*P* *years)	47.3 (36.1)	0-180
Pulmonary function test		
FEV1 (%)	45.4 (19.5)	20-86
FVC (%)	61.5 (16.1)	29-85
FEV1/FVC	54.5 (13.7)	36-68
Emergency admission (n/last year)	1 (0-2)	0-12
Hospitalization (n/last year)	0 (0-1)	0-8
	n (%)	
Male gender	55 (78.6)	
Education		
Primary school	46 (65.7)	
Secondary school	10 (14.3)	
High school	9 (12.9)	
University	5 (7.1)	
Smoking habits		
Smoker	16 (22.9)	
Ex-smoker	50 (71.4)	
Never smoked	4 (5.7)	
COPD severity		
Stage 1	3 (4.3)	
Stage 2	22 (31.4)	
Stage 3	28 (40.0)	
Stage 4	17 (24.3)	

Data are expressed as mean (standard deviation), median (25-75 interquartile range), or n (percentage).
SD: standard deviation, IQR: interquartile range, FEV1: forced expiratory volume in the first second, FVC: forced vital capacity, COPD: chronic obstructive pulmonary disease

Originally developed by Solomon et al.[14] As a derivative of the PCS, the BCS has been demonstrated to be valid and reliable within COPD cohorts. Notably, no translations were performed into other languages. Consistent with the original study,[13] the Turkish version of the BCS exhibited a unifactorial structure and robust internal consistency. Factor loadings ranged from 0.638 to 0.848 across items, with the 12th item exhibiting the lowest loading. Furthermore, the deletion of this item yielded a Cronbach's α value of 0.941. Remarkably, patient interviews revealed notable challenges in comprehension of the 12th item, which were likely attributed to the advanced mean age and limited educational background of the participants. Therefore, practitioners are advised to exercise particular discretion when administering this medication in clinical settings.

Our investigation revealed some intra-rater reliability disparities compared with the original study.[14] Notably, while the ICC values in the original study ranged from 0.69 to 0.86, our analysis yielded values ranging from 0.744 to 0.958. We propose that this variance may stem from the different time intervals between the two measurements. Our measurements were separated by a seven-day interval, whereas in the original study, measurements were taken before and after pulmonary rehabilitation (PR). Furthermore, our observed breathlessness-catastrophizing scores exceeded those reported in the study that developed the BCS (26.64 vs. 18.25).[14] In the aforementioned study, item 5 garnered the lowest score, while item 8 received the highest. The heightened scores observed in our study may be ascribed to the comparatively older demographic with whom we collaborated. Additionally, supplemental oxygen therapy is known to mitigate hypoxia associated with COPD, thereby alleviating dyspnea symptoms by stimulating receptors in the upper airways.[30] Consequently, it is plausible that the patients in the original study, who were hospitalized and received oxygen support, exhibited lower symptomatology compared with our outpatient cohort.

To evaluate the validity of the Turkish version of the assessment tools, we integrated the CAT, which is frequently employed in everyday practice to evaluate and measure the effects of COPD symptoms on patients' health state.[31] It has been reported that an increased CAT score is associated with dyspnea.[32] In our

Table 2. Outcome measures of the patients

Variables (n = 70)	Mean (SD)	Minimum-maximum
Breathlessness Catastrophizing Scale (0-52)	26.6 (14.7)	0-52
Breathlessness Belief Questionnaire		
Activity avoidance (6-30)	17.5 (2.6)	12-24
Somatic focus (5-25)	14.2 (2.7)	10-20
Total (11-55)	31.7 (4.3)	22-43
COPD Assessment Test (0-40)	19.7 (9.8)	2-40
mMRC Dyspnea Scale (0-4)	2.2 (1.3)	0-4
Hospital Anxiety and Depression Scale		
Anxiety (0-21)	6.32 (4.7)	0-18
Depression (0-21)	6.45 (4.7)	0-18
St. George's Respiratory Questionnaire		
Symptom (0-100)	49.1 (23.6)	0-97.5
Activity (0-100)	67.7 (29.1)	0-100
Impact (0-100)	37.9 (23.6)	0-81.4
Total (0-100)	49.4 (23.5)	0.9-88.1

Data are expressed as mean (standard deviation).
SD: standard deviation, mMRC: Modified Medical Research Council, COPD: chronic obstructive pulmonary disease

Table 3. Intra-rater reliability, Cronbach's α values if item deleted, and factor loadings for each item in the Turkish version of the Breathlessness Catastrophizing Scale

Item	Mean (SD)	ICC (95% CI)	Internal consistency (Cronbach's α if item deleted)	Factor loadings
1	2.1 (1.4)	0.844 (0.676-0.925)	0.940	0.641
2	2.1 (1.3)	0.847 (0.679-0.927)	0.939	0.675
3	2.2 (1.5)	0.958 (0.912-0.980)	0.939	0.648
4	2.6 (1.3)	0.856 (0.699-0.931)	0.935	0.774
5	1.9 (1.4)	0.744 (0.456-0.878)	0.934	0.829
6	2.3 (1.5)	0.822 (0.628-0.915)	0.934	0.815
7	1.6 (1.6)	0.832 (0.650-0.919)	0.937	0.745
8	2.1 (1.5)	0.861 (0.706-0.934)	0.937	0.717
9	2.2 (1.6)	0.906 (0.797-0.956)	0.936	0.776
10	1.8 (1.6)	0.805 (0.595-0.907)	0.934	0.848
11	1.9 (1.5)	0.834 (0.654-0.920)	0.935	0.815
12	1.9 (1.6)	0.913 (0.815-0.959)	0.941	0.638
13	2.9 (1.4)	0.919 (0.831-0.962)	0.935	0.794
Total	26.6 (14.7)	0.955 (0.906-0.975)	-	-

Cronbach's α=0.941.
SD: standard deviation, CI: confidence interval, ICC: intraclass correlation coefficient

study, we predicted that the severity of breathlessness may be related to the severity of the disease perceived by patients, and our results confirmed this relationship.

Previous studies have shown that the sensation of breathlessness is associated with anxiety and depression.[14,18,33] These typical symptoms are linked to a higher risk of death in COPD patients.[33] For this reason, we included psychological symptom assessment in our study due to its importance in COPD clinics using HADS, which are used more frequently in routine practice. Employing the HADS, we explored the interplay between breathlessness catastrophizing and anxiety/depression, given the frequent co-occurrence of psychological comorbidities in dyspneic patients, characterized by prevalent fear, anxiety, and depression.[34] Furthermore, we opted for the BBQ scale, which was tailored to assess patients' maladaptive cognitions regarding dyspnea and validated for use in patients with COPD.[18] Our study indicated that there was a moderate relationship between breathlessness catastrophizing and BBQ scores. Our results confirmed the hypothesis that patients who experience catastrophic shortness

Table 4. Validity analysis

Variables (n = 70)	The Breathlessness Catastrophizing Scale	
	r (95% CI)	*P**
Breathlessness Belief Questionnaire		
Activity avoidance	-0.468 (-0.688, -0.208)	0.001
Somatic focus	-0.482 (-0.676, -0.238)	0.001
Total	-0.567 (-0.751, -0.343)	<0.001
mMRC Dyspnea Scale	0.745 (0.538, 0.826)	<0.001
COPD Assessment Test	0.652 (0.479, 0.850)	<0.001
Hospital Anxiety and Depression Scale		
Anxiety	0.556 (0.382, 0.763)	<0.001
Depression	0.588 (0.381, 0.781)	<0.001
St. George's Respiratory Questionnaire		
Symptom	0.550 (0.331, 0.732)	<0.001
Activity	0.578 (0.317, 0.745)	<0.001
Impact	0.558 (0.386, 0.712)	<0.001
Total	0.634 (0.445, 0.780)	<0.001

*Pearson correlation analysis, r: correlation coefficient.
CI: confidence interval, mMRC: Modified Medical Research Council, COPD: chronic obstructive pulmonary disease

Table 5. Comparison of known-group validity

Variables (n = 70)	Known-group validity		*P**
Breathlessness Catastrophizing Scale (0-52)	COPD Stage 1-2 (n = 25)	COPD Stage 2-4 (n = 45)	0.003
	20.9 (12.7)	34.1 (10.3)	
	mMRC Score 0-1 (n = 28)	mMRC Score 2-4 (n = 42)	<0.001
	18.5 (11.5)	38.9 (9.6)	

Data are expressed as mean (standard deviation), *independent samples t-test.
mMRC: Modified Medical Research Council Dyspnea Scale, COPD: chronic obstructive pulmonary disease

of breath may have beliefs to avoid movement. Additionally, the SGRQ was utilized to investigate potential associations between dyspnea catastrophizing and quality of life, as fear of breathlessness significantly impacts quality of life.[35] Our findings revealed significant correlations between dyspnea and these measures, affirming the high convergent validity. Moreover, in addition to the original study, we conducted a known group validity analysis to identify elevated dyspnea in patients with severe dyspnea and advanced-stage COPD.

The sensation of breathlessness is multidimensional and has led to the development of various assessment tools. Although single-item rating scales are prevalent for emotional distress arising from recalled or immediate breathlessness episodes, multidimensional assessment tools offer a more comprehensive appraisal, encompassing affective distress.[36] The ATS recommends classifying instruments according to whether they address sensory-perceptual experience, affective distress, or impact on functional or emotional ability, thereby enabling a more sophisticated comprehension of the aspects of dyspnea.[3]

Based on the PCS, the BCS evaluates the emotional repercussions of breathlessness and presents a measure of catastrophic beliefs surrounding dyspnea. Accordingly, we posit that BCS enriches the multidimensional evaluation of dyspnea, providing clinicians diverse perspectives to inform therapeutic interventions.

Several limitations were identified in the present study. First, the lack of comparable literature on BCS in other languages limited our discussion of our results within existing research. Second, the absence of a rehabilitative intervention in our study precluded the assessment of BCS sensitivity to PR programs. Future investigations should consider evaluating the BCS's responsiveness to PR interventions. Third, not including an assessment of physical activity level or daily living activity, which are likely to be associated with breathlessness catastrophizing, can be considered another limitation.

Although dyspnea and its associated evaluations have been extensively examined in respiratory patient populations, further exploration across diverse disease groups is needed. Such initiatives would advance our understanding of dyspnea and its management in a variety of therapeutic settings.

CONCLUSION

In conclusion, our investigation underscores the robust psychometric properties of the Turkish version of the

Breathlessness Coping Scale (BCS) in assessing dyspnea in patients with COPD. Demonstrating a high level of internal consistency, reliability and construct validity, the BCS is a valuable tool for clinical and research domains within Turkish COPD cohorts.

Ethics

Ethics Committee Approval: The study protocol was approved by the İzmir Katip Çelebi University Non-invasive Research Ethics Board (decision number: 0071, permission date: 23.02.2023).

Informed Consent: All participants provided written informed consent after receiving an explanation of the study's objectives and procedures.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: H.Ş., Concept: Ş.D., İ.N., E.F., M.K., Design: Ş.D., İ.N., E.F., M.K., Data Collection or Processing: Ş.D., H.Ş., Analysis or Interpretation: İ.N., Literature Search: Ş.D., İ.N., Writing: Ş.D., İ.N., E.F., M.K.

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Original Article

Long-term Home Mechanical Ventilation of Children in İstanbul

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Abstract

OBJECTIVE: The aims of this multi-center study were to describe the characteristics of children receiving long-term home mechanical ventilation (HMV) in İstanbul and to compare the patients receiving non-invasive and invasive ventilation.

MATERIAL AND METHODS: This cross-sectional multicenter study included all children receiving long-term HMV followed by admission to six tertiary hospitals. The data were collected between May 2020 and May 2021. Demographic data and data regarding HMV were collected from the patient charts.

RESULTS: The study included 416 participants. The most common diagnoses were neuromuscular (35.1%) and neurological diseases (25.7%). Among the patients, 49.5% (n = 206) received non-invasive ventilation (NIV), whereas 50.5% (n = 210) received invasive ventilation. The median age at initiation was significantly younger in the invasive ventilation group than in the NIV group (10 vs. 41 months, $P < 0.001$). Most subjects in the NIV group (81.1%) received ventilation support only during sleep, whereas most subjects in the invasive ventilation group (55.7%) received continuous ventilator support ($P < 0.001$). In addition to ventilation support, 41.9% of the subjects in the invasive ventilation group and 28.6% in the NIV group received oxygen supplementation ($P = 0.002$). Within the last year, 59.1% (n = 246) of the subjects were hospitalized. The risk factors for hospitalization were invasive ventilation, continuous ventilatory support, oxygen supplementation, tube feeding, and swallowing dysfunction ($P = 0.002$, 0.009, <0.001, <0.001 and <0.001 respectively).

CONCLUSION: Despite the increasing use of NIV in most studies, half of the study population received invasive ventilation. Patients receiving invasive ventilation were more likely to require continuous ventilator support and oxygen supplementation and were at increased risk of hospitalization.

KEYWORDS: Non-invasive ventilation, neuromuscular disorders, long-term home mechanical ventilation, chronic respiratory failure

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INTRODUCTION

Advances in technology have increased the long-term survival rate of patients with chronic respiratory failure. Thus, the number of patients receiving long-term home mechanical ventilation (HMV) support is increasing worldwide. The number of children requiring HMV has consistently increased in high-income countries since the 1980s.[1-4] Currently, there is no national database for long-term HMV patients in Türkiye, and the prevalence of children requiring HMV is not well known. In recent decades, an increasing number of children have started long-term non-invasive ventilation (NIV) rather than invasive ventilation to improve survival rates and quality of life while avoiding complications related to tracheostomy. However, invasive ventilation via tracheostomy is still needed in selected cases.[5]

Successful care of this vulnerable population at home requires the presence of trained caregivers, access to medical equipment, and a care team. Full-time ventilatory support, supplemental oxygen requirement, and inadequate home nursing are frequent reasons for hospital re-admissions.[6]

The aims of this multi-center study were to describe the characteristics of children on long-term HMV in İstanbul, to compare patients receiving NIV and invasive ventilation, and to evaluate the frequency and risk factors of hospital admission in this population.

MATERIAL AND METHODS

Study Design and Participated Centers

We conducted a multicenter, cross-sectional study that included patients with long-term HMV followed by pediatric pulmonology divisions at six tertiary hospitals in İstanbul. The study was approved by the İstanbul Medipol University Ethics Committee (protocol number: 586, date: 06.08.2020). The ethics board waived the need for consent.

Data Collection

All children on long-term HMV follow-up at these six centers were included in the study. The data were collected between May 2020 and May 2021. Long-term HMV was defined as the requirement of mechanical support for breathing for all or part of the 24-hour day and living for at least three months outside the hospital or non-acute care settings.[7,8] Children on HMV for three months and those with tracheostomy but without ventilator support were excluded. Demographic characteristics, underlying diseases, comorbidities, characteristics of ventilation, duration between the decision to initiate and actual start of HMV, duration of HMV, and duration of ventilation use per day (during sleep versus continuous ventilatory support, ≥16 hours of HMV), feeding method, presence of swallowing dysfunction, and nutritional status at the time of the study were recorded. For patients receiving HMV for more than 12 months, data regarding hospitalizations during the last 12 months related to respiratory complications were obtained from medical records. Primary diagnoses for HMV were neuromuscular disorder (NMD), neurological disease (anoxic, hypoxic, or traumatic brain injury), congenital central hypoventilation syndrome, lung parenchymal disease, airway anomalies, congenital heart disease, genetic/syndromic/metabolic disease, and thoracic deformities. Indications for HMV were categorized as follows: acute exacerbation of underlying chronic disease, obstructive sleep apnea syndrome (OSAS), central or mixed apnea diagnosed by polysomnography (PSG); hypoxemia, hypoxemia and hypercapnia, persistent atelectasis, and increased work of breathing. The PSG criteria were as follows: moderate OSAS (obstructive apnea-hypopnea index >5 events/hr), central apnea with hypoventilation (central apnea index >5 events/hr), and isolated hypoxemia (SpO_2 <90% for >5 minutes).[9] Hypercapnia was defined as pCO_2 >45 mmHg in the venous blood gas analysis.[10] Education provided to caregivers of invasively ventilated subjects (bag-valve-mask ventilation, suctioning, tracheostomy care training, and as well as tracheostomy tube changing), equipment at home (suction, oxygen cylinder and concentrator, nebulizer, bag-valve-mask, pulse oximeter, power supply, humidifier, feeding pump), and availability of technical support for both groups were also recorded.

Main Points

- The use of invasive ventilation is higher in low-compared with high-resource countries.
- In this study, we revealed the challenges associated with initiating and sustaining a home mechanical ventilation program in a low-resource country.
- In addition, invasive ventilation, tube feeding, swallowing dysfunction, and malnutrition were risk factors for hospital re-admission.

Statistical Analysis

The IBM Statistical Package for the Social Sciences statistics (version 22.0 IBM Corp., Armonk, NY) software was used to analyze the data. Categorical variables are presented as numbers (n) and percentages (%). Continuous variables are reported as medians with interquartile range (IQR) because the data did not follow a normal distribution. Categorical variables were compared using Pearson's chi-square test and Fisher's exact test. Continuous variables for the two groups were compared using the Mann-Whitney U test. A P value <0.05 was considered significant.

RESULTS

Demographic Characteristics

A total of 416 patients from six pediatric pulmonology centers in İstanbul were included in the study. The median age of the children was 4.3 years (IQR: 2.0-10.3 years), and 54.1% were male. The demographic characteristics of the participants are presented in Table 1. According to weight and age z-scores, 132 (55%) subjects were malnourished. One hundred and sixty five (39.7%) children were fed orally, 96 (23.1%) were fed via nasogastric/nasoduodenal tube, 129 (31%) were fed via gastrostomy tube, and 8 (1.9%) were fed via more than one feeding route. Swallowing dysfunction was detected in 198 (47.6%) participants. While 30.8% (n = 60) of the NIV group had swallowing dysfunction, 72.3% (n = 138) of the invasive ventilation group had swallowing dysfunction (P < 0.001). In addition, a significantly greater proportion of subjects

receiving continuous ventilator support had swallowing dysfunction compared with subjects receiving ventilation support only during sleep (71.9% and 37.6% respectively, *P* < 0.001). Factors affecting malnutrition were identified. There were no statistically significant differences in the following variables: type of ventilation, age at initiation of HMV, duration between HMV decision and start of HMV, duration of HMV, oxygen supplement, presence of swallowing dysfunction, and presence of immobility. There was only a statistically significant difference in the presence of gastroesophageal reflux disease (49.3% vs. 34.4%, p = 0.008).

Characteristics of Ventilation Support

In the current study, 49.5% (n = 206) of children received NIV and 50.5% (n = 210) received invasive ventilation. The demographic data of the participants according to the type of ventilation are presented in Table 1. The median age at tracheostomy placement was 8.6 months (IQR: 4.5-30.7 months). In three centers, covering 56.3% (n = 234) of the study group, the NIV rate was 61.1% (n = 143). In the remaining three centers, the NIV rate was 34.6% (n = 63). In centers with a low NIV rate, both the number of children with NMD or neurological disease (70.3% vs. 53.4%, *P* < 0.001) and the number of children <2 years of age were significantly higher (30.2% vs. 20.9, p = 0.03). Among the children receiving NIV support, 61 (29.8%) received bilevel positive airway pressure-spontaneous (BPAP S) support and 137 (66.8%) received BPAP-spontaneous/timed (BPAP S/T) support. Nasal mask was used in 61.4% (n = 113), oro-nasal in 36.4% (n = 67), and full face masks in 2.2% (n = 4) of children. Thirty (15.2%) patients who received NIV and 117 (55.7%) patients who received invasive ventilation were on continuous ventilator support.

The Starting Location and Indications for Long-term HMV

HMV was initiated in the intensive care unit (ICU) following acute exacerbation of underlying chronic lung disease in 208 (50%) subjects and in the ward in 208 (50%) subjects. In cases where HMV was initiated in the ward, the decision to start was based on the PSG in 26.9% (n = 56) of the children and on blood gas and clinical status in 73.1% (n = 152). The starting location and indications for HMV, including NIV and invasive ventilation, are presented in Figure 1.

Primary Diagnosis for HMV

NMDs were the most common primary diagnosis, and 146 (35.1%) subjects had NMD. Most children with NMD (n = 102) had type 1 spinal muscular atrophy (SMA). Ninety-six percent of patients with SMA type 1 and type 2 were on nusinersen treatment, and none were on olgensis, which is not covered by health insurance in Türkiye. The distribution of underlying disorders in the NIV and invasive ventilation groups is presented in Table 2.

Hospital Re-admissions

Fifty-nine percent of the subjects were re-hospitalized within the last 12 months. Risk factors for hospitalization are presented in Table 3. Invasive ventilation, continuous ventilatory support, oxygen supplementation, tube feeding, the presence of swallowing dysfunction, and malnutrition according to weight for age z-scores were significantly higher in hospitalized patients (*P* values 0.002, 0.009, <0.001, <0.001, <0.001 and 0.03 respectively). In the multivariate logistic regression analysis, oxygen support [odds ratio (OR): 3,125; 95% confidence interval (CI): 1.8-5.3, *P* < 0.001] and tube/PEG feeding (OR: 3,928; 95% CI: 1.9-7.9, *P* < 0.001) were found to be significant risk factors for re-hospitalization.

Table 1. Demographic data of patients according to ventilation type

	NIV (n = 206) Median (interquartile range)	Invasive ventilation (n = 210) Median (interquartile range)	Total (n = 416) Median (interquartile range)	*P*
Age, years,	6.5 (2.3-13)	3.9 (2-7.4)	4.3 (2-10.3)	**<0.001**
Sex n (%)				
Male	112 (54.4)	113 (53.8)	225 (54.1)	0.90
Female	94 (45.6)	97 (46.2)	191 (45.9)	
Nutritional status				
WAZ	-1.3 [-2.9-(-0.1)]	-0.9 (-2.0-0.4)	-1.2 (-2.7-0.1)	0.06
HAZ	-1.5 [-3.1-(-0.6)]	-1.4 [-2.5-(-0.2)]	-1.5 [-2.9-(-0.3)]	0.23
BMI z-score	-0.5 (-2.3-0.8)	0.2 (-1.8-1.5)	-0.3 (-2.0-1.1)	0.17
Ventilation data				
Age at HMV initiation (months)	41 (11-123)	10 (5-43)	18 (7-83)	**<0.001**
Duration between HMV decision and HMV start	8 (2-16)	30 (15-45)	15 (5-30)	**<0.001**
Duration of HMV, months	14 (6-32)	17 (6-37)	16 (6-36)	0.21
HMV during sleep n (%)	167 (81.1)	71 (33.8)	238 (57.2)	**<0.001**
Continuous ventilator support n (%)	30 (14.6)	117 (55.7)	147 (35.3)	**<0.001**
Number of patients receiving oxygen n (%)	59 (28.6)	88 (41.9)	147 (35.3)	**0.002**

NIV: non-invasive ventilation, WAZ: weight for age z-score, HAZ: height for age z-score, BMI: body mass index, HMV: home mechanical ventilation

Characteristics of Home Care and Education

The primary caregivers of the subjects were mothers in 93.9% (n = 371), fathers in 1.8% (n = 7), other family members in 1% (n = 4), nurses in 0.8% (n = 3), and more than one person in 2.5% (n = 10). Only 1.9% of the NIV group and 6.2% of the invasive ventilation group used a back-up ventilator.

According to parental reports, 86.6% of the caregivers received suction training, 80.5% received tracheostomy care training, 87.1% received bag-valve-mask ventilation training, and 65.7% received tracheostomy tube change training in the invasive ventilation group. However, only 37.1% of the patients changed the tracheostomy tube before discharge. A spare tracheostomy tube was available in 80.5% of children, while a smaller tube was available in only 59.5% of children. Thirty-eight percent (n = 80) of families used the sterile technique, 28.1% (n = 59) used the clean technique, and 23.3% (n = 49) used the modified sterile technique for tracheostomy tube change. While 60.9%

Table 2. Distribution of underlying disorders in the NIV and invasive ventilation groups

	Non-invasive (n, %)	Invasiveness (n, %)
NMD (n = 146)	71 (34.5)	75 (35.7)
Neurological diseases (n = 107)	36 (17.5)	71 (33.8)
Lung parenchymal diseases (n = 60)	48 (23.3)	12 (5.7)
Airway anomalies, sleep apnea (n = 13)	10 (4.9)	3 (1.4)
Congenital heart diseases (n = 13)	6 (2.9)	7 (3.3)
Genetic, syndromic, and metabolic diseases (n = 67)	29 (14.1)	38 (18.1)
Congenital central hypoventilation syndrome (n = 7)	4 (1.9)	3 (1.4)
Thorax deformities (n = 3)	2 (1.0)	1 (0.5)

NMD: neuromuscular disorder, NIV: non-invasive ventilation

Table 3. Comparison of children who required hospitalization within the last year with children who did not require hospitalization

		Hospitalization		
		No (n = 132) n (%)	Yes (n = 246) n (%)	*P* value
Ventilation mode	NIV	82 (42.5)	111 (57.5)	**0.002**
	Invasive ventilation	50 (27)	135 (73)	
Need for ventilation	On sleep	93 (40.3)	138 (59.7)	**0.009**
	Continuous	36 (26.7)	99 (73.3)	
Presence of oxygen supplementation		29 (20.0)	116 (80.0)	**<0.001**
Feeding method	Oral	85 (52.8)	76 (47.2)	**<0.001**
	Tube feeding/ gastrectomy	47 (21.7)	170 (78.3)	
Presence of swallowing dysfunction		46 (24.3)	143 (75.7)	**<0.001**
Malnutrition according to the WAZ		44 (33.3)	88 (66.7)	**0.03**

NIV: non-invasive ventilator, WAZ: weight for age z-score

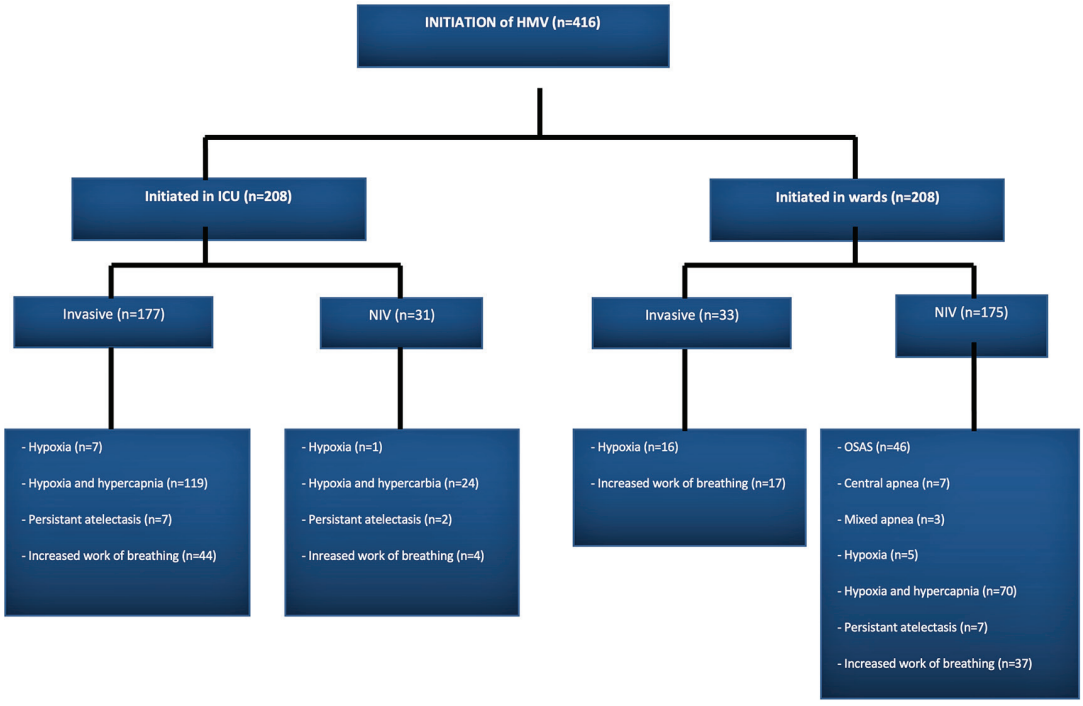

Figure 1. The starting location and indications for long-term HMV

HMV: home mechanical ventilation, ICU: intensive care unit, NIV: non-invasive ventilator, OSAS: obstructive sleep apnea syndrome

(n = 128) of the subjects were suctioned at a depth of 0.5-1 cm past the cannula tip, 13.3% (n = 28) of the caregivers advanced the suction catheter until the carina, where resistance was met.

DISCUSSION

The current study showed that the number of children receiving invasive ventilation was higher than that receiving NIV, and invasive ventilation, tube feeding, swallowing dysfunction, malnutrition were the risk factors for hospital re-admissions. In contrast to other studies reporting invasive HMV rates of 13-49%, these rates remained high in İstanbul.[1-4,7] Advances in pediatric critical care and the availability of improved technology have resulted in prolonged life expectancy among patients on HMV.[5] HMV minimizes disruptions to family life, prevents nosocomial infections, decreases hospitalization, and lowers healthcare costs.[11] Tibballs et al.[12] reported that healthcare costs are seven times lower at home and 25 times lower in the ICU. Several studies have shown that well-organized referral hospitals from low- and middle-income countries can also implement adequate HMV programs.[5,13] NIV is a simpler method for assisted ventilation, which prevents tracheostomy-related complications, including acute airway blockage by secretions, accidental decannulation, tracheal injury, and respiratory infections, whereas invasive ventilation is a life-support ventilation method, requiring more skills and 24-hour caregiving at a higher cost.[14,15] Significant differences in the proportion of children receiving long-term invasive ventilation versus NIV at home have been reported between countries. The reported rates of invasive ventilation vary globally between 14% and 49%.[1,4] Another interesting finding was detected in the United Kingdom's report on the 10-year progress. The proportion of children who underwent 24-h tracheostomy ventilation decreased from 23.4% to 9.5%, and they attribute this to their increasing experience with NIV.[1] Our invasive ventilation rate might decrease in the future as a result of the knowledge this study has provided.

In this study, half of the subjects were placed on invasive ventilation. The median age of children who received invasive ventilation was significantly lower than that of children who received NIV (3.9 vs. 6.5 years). Invasive ventilation/NIV rates vary between the study centers due to differences in clinical management and the patients' underlying etiologies and ages. The NIV rate was 66% in the three centers that participated in the current study, including the 60% study group. The NIV rate was 34% at the other three centers. In centers with a low NIV rate, the number of children with NMD and neurological disease was significantly higher (70.3% and 53.4%, respectively), and the number of children <2 years of age was higher. Invasive ventilation is usually considered an effective first-line supportive care option for children with SMA type 1 and/or younger children, especially when continuous ventilator support is needed. The availability of PSG may be another contributing factor to decision-making. Centers with sleep laboratories may be more likely to initiate NIV in infants or young children, and surveillance PSGs can facilitate elective NIV initiation by detecting nocturnal hypoventilation and sleep problems. In our study, HMV was initiated after PSG in only 13.5% of the participants because pediatric sleep laboratories are not widely available in Türkiye. The proportion of patients who underwent sleep study before starting HMV differs between countries and centers. Although Kim et al.[17] reported that PSG was possible only in a limited number of patients (3.3%) in South Korea, Leske et al.[16] reported that 70% of patients had sleep studies before ventilation initiation in Argentina.

Although the percentage of primary indications for HMV use in children varies among countries, NMDs are frequently the most prevalent diagnosis, followed by encephalopathy and hypoxic brain damage. These variabilities may be influenced by many factors, such as cultural characteristics, healthcare systems, the extent of reimbursement programs, and access to HMV.[17] In our study, 55% of patients with long-term HMV had NMD or neurological disease. This result was consistent with other studies in the literature.[1-3]

Several studies have reported that malnutrition is associated with a poorer quality of life, worse pulmonary function, a higher risk of mortality, a higher risk of infections, and decreased physical conditioning in adults with chronic respiratory failure requiring HMV.[18-20] However, to our knowledge, only one study has evaluated the relationship between nutritional status and respiratory outcomes in children.[21] Although the assessment of feeding and nutrition is vital, there are no clinical practice guidelines for HMV in children that outline optimal nutritional management. A scoping review protocol on feeding and swallowing outcomes of children receiving long-term ventilation has just been published, and the findings of this research will fill in many of the knowledge gaps on this topic.[22] In this study, malnutrition was detected in 32% of subjects, and hospitalization rates were higher in subjects with malnutrition. Forty-seven percent of our subjects also had clinical findings suggestive of swallowing disorders, and the frequency of re-hospitalization in these children was also significantly higher. Feeding and swallowing difficulties may be caused by any medical condition, injury, developmental delay, decreased oral stimulation, medical instability at the beginning of long-term ventilation, and length of invasive ventilation.[23-25] In the analyses of factors affecting malnutrition in our study, only the presence of gastroesophageal reflux disease was detected significantly more frequently in children with malnutrition (49.3% vs. 34.4%), but we cannot claim that this is a reason for malnutrition. Timely evaluation of feeding and swallowing by a speech and language therapist is vital for these children, and necessary precautions should be taken to prevent complications such as aspiration pneumonia and atelectasis.

Children on HMV are vulnerable and frequently require re-admission.[6] Re-admissions often occur shortly after discharge due to inadequate training of families and community health providers. Patients and/or caregivers should be appropriately trained to know how to operate the equipment, identify problems, and seek assistance when needed. Although educational materials are widely available, a lack of educational programs was reported by 27% of respondents in an ERS survey.[26] Our study revealed that 80-90% of the caregivers received education on tracheostomy care and suctioning, basic life support, home ventilator, and equipment. However, only 37.1% of the patients stated that they had changed the tracheostomy tube before discharge. There is a need to implement standardized training programs for caregivers of children requiring invasive ventilation.

Based on these results, we started standard education programs for healthcare providers and caregivers of invasively ventilated children in centers participating in this study. The education program consisted of theoretical and practical sessions using a simulation model.[27,28] Pediatric pulmonologists who completed the program trained the caregivers.

This study has several limitations. The current study included patients who were seen for a pulmonology clinic follow-up visit within 1 year at the six study centers, and data were collected retrospectively. We assumed that all long-term HMV patients in İstanbul are followed at one of the study centers, although it is probable that a small number of patients are not followed by a pediatric pulmonologist and are not included in the study. Additionally, the rate of hospital re-admissions may have been low as a result of the isolation due to the coronavirus pandemic. Despite these limitations, our study is the first multicenter study to include a large number of patients with HMV in Türkiye.

CONCLUSION

Children on long-term HMV are a diverse group of patients with complex medical problems, including respiratory, nutritional, and swallowing difficulties, and multidisciplinary follow-up is important to improve quality of life and decrease morbidity and mortality. In our study, invasive ventilation was higher than that in other studies, and invasive ventilation, tube feeding, swallowing dysfunction, and malnutrition were found to be higher in hospitalized patients, and gastroesophageal reflux disease was detected more frequently in children with malnutrition. Although this study characterized several previously unknown trends regarding HMV use in our region, a national registry is necessary to reveal the status of HMV use in the country. A national registry of pediatric patients with long-term HMV was recently approved as a research project by the Turkish Thoracic Society. Data from the current study will aid in planning the national registry and ultimately the optimal healthcare system for patients with long-term HMV.

Ethics

Ethics Committee Approval: The study was approved by the İstanbul Medipol University Ethics Committee (protocol number: 586, date: 06.08.2020).

Informed Consent: The ethics board waived the need for consent. So the informed consent was not obtained.

Footnotes

Authorship Contributions

Concept: M.Y., A.P.E., E.A., N.B.I., A.A.K., E.E.E., Y.G., S.O., E.C., S.G., Z.S.U., H.C., B.K., F.K., Design: M.Y., A.P.E., E.A., N.B.I., A.A.K., E.E.E., Y.G., S.O., E.C., S.G., Z.S.U., H.C., B.K., F.K., Data Collection or Processing: M.Y., F.U., E.H., H.Y., S.C.O., E.K., C.Y.Y., A.K.B., Z.R.O., A.G., A.S., M.K., H.B.K., Y.A., S.U., Analysis or Interpretation: M.Y., P.A., E.E.E., Y.G., S.O., E.C., S.G., Z.S.U., H.C., R.E., B.K., F.K., Literature Search: M.Y., A.P.E., E.A., N.B.I., Writing: M.Y., F.U., E.H., F.K.

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Review

Non-invasive Mechanical Ventilation in Lung Cancer: Physiological Principles and Clinical Utilization in Surgical and Non-surgical Settings

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Abstract

Non-invasive mechanical ventilation (NIMV) has emerged as a pivotal intervention for the care of individuals with lung cancer. NIMV offers substantial advantages in enhancing oxygenation, optimizing respiratory function, elevating pulmonary capacities, and facilitating patient comfort. NIMV's utility extends to enhancing clinical conditions that range from chronic obstructive pulmonary disease and emphysematous lung ailments to aiding patients with lung cancer facing acute respiratory failure. Furthermore, NIVM includes perioperative pulmonary rehabilitation. This approach is particularly relevant for individuals with limited lung capacity. Since both non-invasive positive pressure ventilation modes, including BiLevel positive airway pressure and continuous positive airway pressure, address the underlying pathophysiological mechanisms that contribute to postoperative respiratory failure, the proactive and early integration of NIMV has the potential to significantly enhance gas exchange and overall respiratory performance in meticulously chosen patients within the perioperative phase. Although non-intubated video-assisted thoracic surgery represents an interesting field of application for NIMV strategies, further studies are needed to optimize operative modalities. Lastly, NIMV has a pivotal role in the settings of intensive care and palliative care units, thereby cementing its versatile utility across various medical contexts.

KEYWORDS: Non-invasive mechanical ventilation, lung cancer, acute respiratory failure, chronic obstructive pulmonary disease, palliative use of non-invasive ventilation, non-invasive positive pressure ventilation, BiLevel positive airway pressure, continuous positive airway pressure

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INTRODUCTION

Lung cancer is the third most common malignancy. It is the primary driver of cancer-related fatalities on a global scale, affecting individuals regardless of gender.[1] The occurrence of acute respiratory failure (ARF), which leads to hypoxia with or without hypercapnia, becomes intricately woven with oncological factors, potential coexisting conditions like exacerbation of chronic obstructive pulmonary disease (COPD), and treatment-related complications. This interplay can significantly influence the clinical trajectory of patients undergoing surgical resection and those exploring non-surgical therapeutic options.[2] Moreover, ARF is a life-threatening condition that may manifest early in the course of the disease or become a prominent feature as the disease progresses to its advanced stages.[3]

In lung cancer patients, invasive mechanical ventilation (IMV) remains a widespread strategy for managing respiratory insufficiency issues. Despite improvements, this approach is burdened by a significant mortality rate, which can affect up to 50% of patients requiring postoperative care or other motivations.[4] Moreover, the emergence of complications like ventilator-associated pneumonia, barotrauma, and tracheal damage in this setting raises important concerns.[5]

Non-invasive mechanical ventilation (NIMV) has emerged as a critical intervention for the management of lung cancer, offering significant benefits in improving oxygenation, optimizing respiratory physiology, and enhancing pulmonary functions.[6] It is a powerful strategy for increasing patient comfort. This comprehensive approach involves

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the application of different techniques, which contribute to alleviating respiratory distress and enhancing the overall quality of life for individuals facing the challenges of lung cancer. NIVM can be useful in optimizing clinical conditions ranging from COPD and emphysematous lung disease to the management of lung cancer patients facing ARF. Furthermore, it extends to perioperative pulmonary rehabilitation (PPR), providing respiratory support during the perioperative phase for patients undergoing procedures such as intraoperative lateral decubitus position and one-lung ventilation, with a particular focus on those with limited lung capacity. Additionally, NIVM can be used to determine significance in non-intubated lung resections. Lastly, a notable role of NIVM is its utilization in intensive care and palliative care units.[7]

The purpose of this review is to explore the physiological foundations of the applications of NIVM techniques and their diverse fields of use.

1. Physiological Principles

Some evidence suggests that NIMV can effectively counteract a range of physiological and mechanical abnormalities linked to respiratory failure in individuals with lung cancer.[8,9]

A cascade of physiological changes can disrupt the delicate balance of oxygenation within the respiratory system in patients with lung cancer. These changes encompass different factors, prominently including ventilation-perfusion ratio (V/Q) mismatch and lung tissue alterations. Understanding these alterations is crucial for appreciating the role of NIVM in rectifying these challenges and sustaining optimal oxygen saturation (Table 1).

Addressing V/Q mismatch is a key aspect of NIMV. Lung malignancy can cause imbalances between alveolar ventilation and the corresponding vascular perfusion required for efficient gas exchange. Factors such as tumors, inflammatory processes, and obstructions in the airways can perturb the airflow, directing it away from regions that are adequately perfused. This diversion contributes to the uneven distribution of oxygen uptake. Consequently, the resultant V/Q mismatch engenders suboptimal oxygenation levels, leading to hypoxemia and respiratory distress. Enhancing ventilation in alveoli that were previously underutilized due to V/Q alterations, NIMV, and especially non-invasive positive pressure ventilation (NIPPV) modes, such as BiLevel positive airway pressure (BiPap) and continuous positive airway pressure (CPAP), can assist in rebalancing the V/Q. This leads to more efficient oxygen uptake and carbon dioxide elimination since alveolar recruitment and augmentation of alveolar ventilation increase FiO_2 and reverse hypercapnia and acidosis.[10]

Main Points

- Non-invasive mechanical ventilation (NIMV) is effective in managing acute respiratory failure in patients with lung cancer, particularly those with specific conditions like chronic obstructive pulmonary disease.
- Key factors such as early initiation of NIMV, underlying cause of respiratory failure, and patient's functional status are critical indicators for the success of NIMV therapy.
- NIMV is a potential bridge therapy that can stabilize patients, allowing them to proceed to further cancer treatments that might have otherwise been delayed because of respiratory complications.
- Proper patient selection and continuous monitoring are essential for optimizing outcomes with NIMV, reducing the risk of treatment failure, and improving overall survival rates.
- Further high-quality research is needed to confirm the role of NIVM and to better understand the surgical strategies and long-term outcomes of this therapy in patients with lung cancer.

The V/Q mismatch is caused by complex lung tissue alterations. The presence of lung cancer can cause structural changes. Tumors can compress or invade the parenchyma of the lung, leading to reduced lung compliance and decreased functional lung volume. Additionally, inflammation and scarring induced by cancer can compromise lung tissue elasticity, further hampering efficient oxygen exchange.[11] Through carefully calibrated positive-pressure delivery, NIMV has the potential to exert a positive impact by improving pulmonary compliance. It can also prevent lung collapse by ensuring optimal lung inflation.

In the context of cancer, muscle fatigue, often called cancer-related fatigue, is a complex and multifaceted phenomenon that can affect various muscle groups throughout the body. It is a common and distressing symptom experienced by many individuals undergoing cancer treatment and those with advanced cancer. The exact mechanisms underlying muscle fatigue are not fully understood, but several factors, such as anticancer treatments, cancer-related Inflammation, metabolic changes, pain, and psychological factors, contribute to its development.[12] Despite this intricate context, NIMV can help avoid fatigue in respiratory muscles through a combination of physiological mechanisms that reduce the work of breathing and enhance overall respiratory efficiency. The key mechanism is reduced workload. The positive pressure reduces the effort required by the respiratory muscles, especially the diaphragm, to generate the necessary negative pressure for inhalation. By lightening the workload on these muscles, NIMV helps prevent muscle fatigue. Moreover, NIMV optimizes gas exchange and reduces the need for rapid, deep breathing, which can lead to muscle fatigue over time. It also helps maintain optimal lung volumes and compliance, making it easier for the respiratory muscles to function effectively and preventing lung collapse with atelectasis. The application of positive end-expiratory pressure reduces the workload required by the inspiratory muscles to initiate the next breath. In addition, NIMV provides intermittent periods of rest for the respiratory muscles. In other words, by assisting with breathing during moments of increased demand, NIMV allows the muscles to recover and regain their strength, thereby preventing sustained fatigue. Finally, NIMV can enhance patient comfort and reduce anxiety related to breathing difficulties.[13] This relaxation indirectly reduces the overall stress on respiratory muscles.[14] The combination of improved oxygenation and reduced work of breathing alleviates the respiratory distress often experienced by patients with lung cancer. This, in turn, enhances their comfort and quality of life.

Table 1. Physiopathological foundation of non-invasive mechanical ventilation in lung cancer

Process	Mechanism(s)	NIVM effects
V/Q ratio mismatch	Due to cancer itself, inflammation, and airway obstruction.	- Improved alveolar ventilation. - Improvement in V/Q.
Alterations in lung tissue	Reduced lung compliance and decreased functional lung volume.	- Improved compliance. - Increased FRC. - Enhanced recruitment. - Prevention of lung collapse.
Muscle fatigue	Anticancer treatments, cancer-related Inflammation, metabolic changes, pain, and Psychological factors.	- Reduced workload. - Improved lung mechanics. - Enhanced gas exchange. - Promotion of rest and recovery. - Increased patient comfort. - Reduced anxiety related to breathing difficulties.
Heart failure or fluid overload	Due to cancer itself and anticancer treatments.	- Reduced venous return. - Improved heart function.

NIMV: non-invasive mechanical ventilation, V/Q: ventilation-perfusion ratio, FRC: functional residual capacity

The effects on cardiac function have been extensively investigated for the treatment of cardiogenic pulmonary edema.[15] The effects manifest in a comprehensive array of outcomes. For instance, NIMV is a valuable intervention for patients with heart failure or fluid overload, particularly given that increased mean intrathoracic pressure leads to reduced venous return. On the other hand, a reduction in cardiac output/pulmonary perfusion induces a compensatory increase in right ventricular afterload.[13] In the postoperative setting, physiological investigations have demonstrated the effectiveness of BiPap and CPAP in enhancing lung aeration and arterial oxygenation. These interventions also reduce atelectasis without inducing adverse hemodynamic effects during the period following extubation.[16]

2. Management of Acute Respiratory Failure

In the context of lung cancer, ARF can stem from a range of factors. These determinants encompass the impact of the primary disease on lung function and the chest wall, pulmonary emboli, radiation-induced pneumonitis, aspiration events, treatment-related immunosuppression leading to sepsis or pneumonia, drug-associated toxicity, presence of concurrent conditions like heart failure, and exacerbation of COPD. Among these factors, COPD exacerbation is the most prevalent and observed cause of ARF[17] and is a leading cause of hospital admissions.[18]

When not contraindicated, for example in conditions of respiratory arrest or unstable cardiorespiratory status, in uncooperative patients, or for inability to protect the airway, NIMV can be a less invasive alternative for effectively managing respiratory distress and enhancing comfort in patients with cancer and ARF. The judicious selection of NIMV is guided by specific indications, ensuring its appropriate utilization in the context of lung cancer care.

Patients with lung cancer and pre-existing chronic respiratory conditions, such as COPD or interstitial lung disease, may experience acute exacerbations. NIMV can help stabilize respiratory function, alleviate distress, and prevent the need for IMV. This approach can serve as a bridge to recovery in cases of reversible respiratory distress, such as infections. It supports patients until their condition stabilizes and their lung function improves. Moreover, NIVM modes can be employed to prevent intubation in patients at risk of respiratory failure. Early initiation of NIMV may obviate the need for IMV, thereby reducing the incidence of complications associated with intubation. NIMV can also be employed to manage ARF while allowing bronchoscopy without endotracheal intubation (Figure 1).

Furthermore, according to the European Respiratory Society guidelines, prompt implementation of NIPPV is recommended for immunocompromised patients experiencing ARF.[19]

NIVM can be used to treat hypoxemic or hypercapnic respiratory failure. In the former condition, augmenting oxygenation and preventing the progression of respiratory failure are indicated, particularly in cases in which IMV is considered excessive. Impaired gas exchange can manifest as hypercapnic respiratory failure, which is characterized by elevated carbon dioxide levels. In this condition, calibrated NIMV interventions can help remove excess carbon dioxide, improve ventilation, and enhancing acid-base balance. Therefore, the significant benefit of NIVM is its ability to circumvent the need for intubation. It can be applied preemptively to prevent intubation in patients with respiratory failure. The timely introduction of NIMV might mitigate the requirement for IMV, thereby diminishing the complications associated with this approach. Considering the elevated mortality rate observed in the intensive care unit (ICU) among patients with cancer, adopting NIMV as an initial approach can be a favorable strategy for patients with lung cancer in the hospital ward. This approach is also useful for mitigating the potential complications associated with IMV.[9]

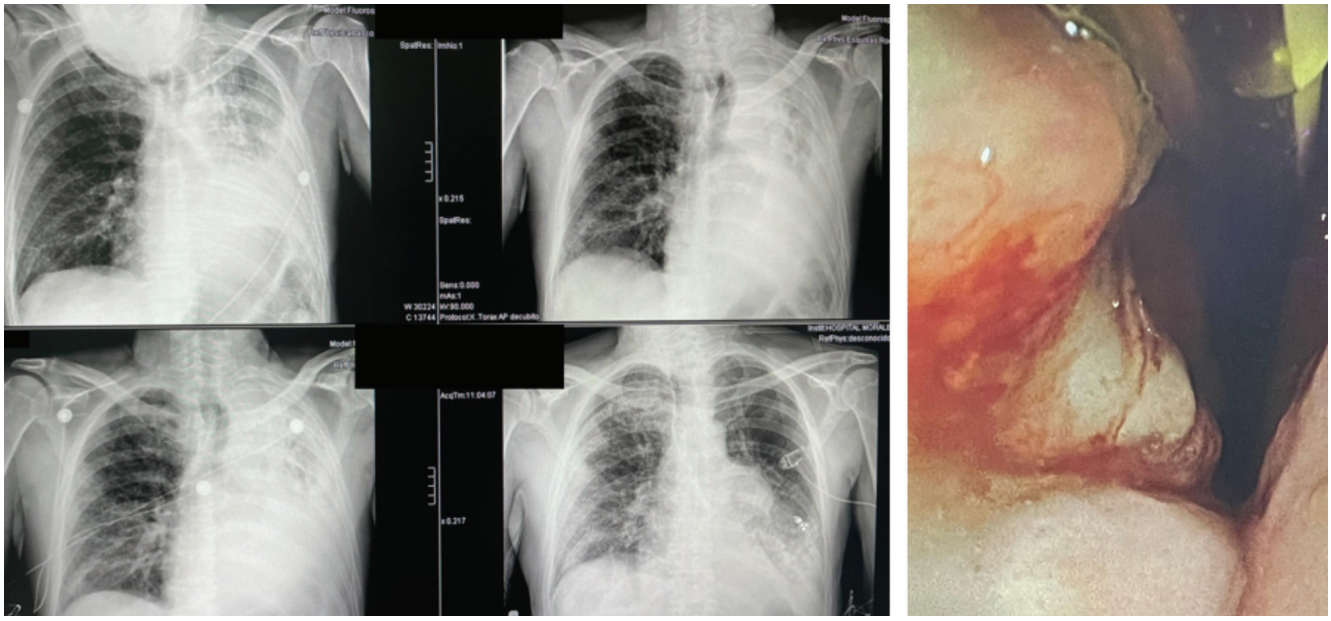

Figure 1. A 63-year-old male patient (left lung) with acute respiratory failure. BiLevel ventilation (IPAP: 25 cmH_2O; EPAP: 8 cmH_2O) during bronchoscopy. Chest X-rays at the start of the treatment (top images, the left with facial mask application), during (bottom left), and after the bronchoscopy (bottom right), with no endotracheal intubation

IPAP: inspiratory positive airway pressure

3. Perioperative Management

3.1. Preoperative Pulmonary Rehabilitation

The presence of COPD substantially increases the risk of perioperative pulmonary complications, and significant lung function impairment can contraindicate surgical treatment.[20] Preoperative implementation of NIMV strategies can enhance exercise tolerance, symptomatic well-being, and overall quality of life for patients with COPD undergoing lung volume reduction surgery.[21] This approach is particularly relevant for individuals with limited lung capacity. However, the precise impact of PPR on the clinical progression of patients with COPD or those with frailty stemming from various causes, characterized by impaired pulmonary function, and those undergoing lung cancer resection remains to be fully understood. This aspect is of paramount importance because the reduction in lung tissue can severely impede postoperative ventilatory function or diffusion capacity, increasing their vulnerability to post-surgical issues. As a result, clinical factors combined with findings from the preoperative assessment, such as forced expiratory volume in one second and single-breath predicted diffusing capacity of the lung for carbon monoxide, play a crucial role in determining operability.[22]

The role of PPR in lung cancer surgery is gaining recognition and constitutes an integral component of the enhanced recovery pathway.[23] Although evidence indicates that PPR can enhance preoperative pulmonary function and functional status, reduce perioperative pulmonary complications, and expedite postoperative recovery, study outcomes have not been consistently aligned.[24,25] The lack of standardized preoperative rehabilitation protocols regarding the NIMV approach and outcome assessment across different clinical settings further hinders the implementation of PPR. For example, Mujovic et al.[26] evaluated pulmonary function using spirometry, the 6-min walking distance test, and the Borg scale at three time points: upon admission, post-PPR, and after surgery. Recently, multimodal rehabilitative protocols have been implemented, including cardiorespiratory muscle training and breathing exercises, education, and pharmacological interventions. Surprisingly, approximately 40% of high-risk patients underwent surgery, achieving outcomes comparable to those of patients categorized as having a low risk of adverse events or mortality.[21] Consequently, many medical centers do not routinely employ PPR in these situations, owing to concerns regarding surgery delays and the absence of concrete evidence demonstrating the advantages of PPR for such patients.

3.2. Indications After Pulmonary Resection

Postoperative pulmonary complications are the primary causes of mortality and morbidity following lung resection. These complications include acute lung injury, acute respiratory distress syndrome (ARDS), and pneumonia. Additionally, within the domain of thoracic surgery, alongside postoperative pain, ARF is associated with compromised functionality of respiratory muscles. Changes in respiratory function manifest early after surgery, and diaphragm dysfunction may extend up to seven days, contributing to a notable decline in arterial oxygenation.[27] Moreover, minimally invasive thoracoscopic surgery necessitates the implementation of a one-lung ventilation technique, which has the potential to result in suboptimal lung expansion and persistent microatelectasis in the postoperative phase.[28] In this complex scenario, the proactive use of NIMV was proposed to effectively reduce the incidence of respiratory challenges during the crucial postoperative phase.[29] Postoperative NIPPV may effectively mitigate or prevent microatelectasis following pulmonary resection.

Overall, NIMV techniques can address a spectrum of challenges and potential complications during the recovery

phase, providing targeted support to optimize patient outcomes (Table 2).

Following lung resection, for example, patients might encounter situations where gas exchange is compromised, leading to carbon dioxide retention. NIMV becomes a crucial intervention in such cases, as it helps maintain proper gas exchange dynamics by enhancing ventilation and oxygenation. In particular, NIMV helps overcome V/Q mismatch and facilitates the elimination of excess carbon dioxide. Moreover, it is useful for preventing postoperative complications. It helps maintain lung volume, prevent atelectasis, and promote alveolar recruitment. By ensuring optimal functioning of the remaining lung tissue, NIMV reduces the risk of respiratory complications such as pneumonia and ARDS. Moreover, in the aftermath of lung resection, patients might experience challenges related to secretion retention and excessive mucus production; thus, NIMV may help address secretion retention and mucus hypersecretion by facilitating effective airway clearance. Moreover, this approach can reduce the likelihood of postoperative respiratory infections and related complications.

Among the different strategies, NIPPV plays a key role in postoperative NIMV. This NIVM modality delivers pressurized gas to the airway, increasing transpulmonary pressure, and expanding the lungs through a mask or interface, all while avoiding invasive routes, such as endotracheal tubes, oronasal tubes, or Tracheostomy. This technique enhances functional residual capacity (FRC) and reopens collapsed airways, resulting in improved oxygenation, reduced carbon dioxide buildup, and decreased respiratory effort. In particular, NIPPV encompasses two main types: CPAP, which employs a single pressure level during exhalation, and Bi-PAP, which utilizes two distinct pressure levels for both inhalation and exhalation, inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP), respectively. The key difference is that BiLevel variation can amplify tidal volume and potentially assist during the inhalation phase. Surprisingly, despite these potential advantages, a Cochrane analysis has revealed that the use of NIPPV in the postoperative phase following pulmonary resection does not appear to confer any additional benefits across various assessed outcomes. These outcomes included pulmonary complications, intubation rates, mortality, postoperative antibiotic usage, length of stay in the ICU, duration of hospitalization, and adverse effects linked to NIPPV. Nevertheless, it is important to highlight that the authors of the analysis acknowledged a certain degree of limitation in the quality of evidence presented. This assessment ranged from very low to low and moderate due to the relatively small number of studies available for analysis, as well as their limited sample sizes and infrequent occurrence of observed outcomes. Consequently, their conclusions remain subject to these inherent limitations,[30] and further studies are needed to confirm the findings of the analysis. The patient population that would benefit most from postsurgical NIVM is still being identified. In individuals who underwent pulmonary lobectomy, Okada et al.[31] initiated NIVM immediately after surgery until the morning of the postoperative day. They implemented Bi-PAP using the spontaneous/timed mode with an IPAP ranging from 6 to 12 cmH_2O and EPAP ranging from 4 to 6 cmH_2O. This intervention resulted in enhanced oxygenation, particularly noticeable among patients with a PaO_2/FiO_2 ratio of 300 or lower, those aged 70 years or older, individuals with a body mass index of 25 kg/m^2 or higher, and those undergoing one-lung ventilation for a duration exceeding 180 minutes. The results are highly significant, and they underline that patients with COPD could be good candidates for postoperative NIMV. Moreover, the age-related strength decline and reduced chest wall compliance impact respiratory muscle performance. Additionally, obesity can lead to impaired respiratory function due to restricted diaphragmatic movement, resulting in decreased FRC and elevated atelectasis risk.[32] Lastly, one-lung ventilation causes collapse of the surgical lung and may induce gravity-driven microatelectasis on the non-surgical side.[33]

During the postoperative phase, the utilization of NIVM extends to other areas of application. For patients transitioning from IMV, NIMV can facilitate weaning by gradually reducing ventilator support. This approach helps restore independent breathing while minimizing the risk of extubation failure.

Extended research should focus on the application of NIMV techniques in the context of non-intubated video-assisted thoracic surgery (NI-VATS). This surgical approach combines the advantages of non-intubated surgery with the benefits of minimally invasive techniques. Initially, NI-VATS was used for delicate patients in whom general anesthesia and/or orotracheal intubation was considered impractical. However, NI-VATS indications have progressively broadened to encompass various patient scenarios, as the procedure's safety and feasibility have been increasingly validated.[34] Progressive increase in pCO_2 levels during surgical procedures is a significant concern in anesthesiology. Consequently, an excessive elevation of pCO_2 (above 80 mmHg) is a prevalent factor leading to the decision for intubation.[35] These aspects can stimulate the utilization of NIMV techniques, although

Table 2. Potential advantages of non-invasive mechanical ventilation after lung resection

Process	Mechanism(s)
Improving gas exchange and CO_2 retention	NIMV can effectively ameliorate ventilation-perfusion imbalances, promoting efficient oxygenation and CO_2 elimination processes.
Prevention of complications	NIMV promotes alveolar recruitment and lung volume
Support in secretion retention and mucus hypersecretion	Improving airway clearance by mobilizing and expelling secretions
Weaning from mechanical ventilation	Gradual reduction in ventilator support

For example, pneumonia and acute respiratory distress syndrome.
NIMV: non-invasive mechanical ventilation

spontaneous breathing is mostly supported by high-flow nasal cannula (HFNC) oxygen therapy.[36] Conversely, certain physiopathological data associated with the procedure should be carefully assessed. For example, during NI-VATS, spontaneous ventilation and effective diaphragm contractions are sustained. This position ensures ideal V/Q matching in the dependent lung. Nevertheless, lateral decubitus positioning and iatrogenic pneumothorax resulting from pleural cavity opening can induce notable alterations in the V/Q, occasionally provoking respiratory disturbances that are often transient but potentially perilous. Additionally, in non-intubated procedures, distinctions in ventilation dynamics arise compared with mechanical ventilation pendulum due to spontaneous breathing and the absence of one-lung ventilation mechanisms. First, carbon dioxide rebreathing. In the dependent lung, a portion of the inhaled air volume is exhaled into the non-dependent lung during expiration, and is then re-inhaled by the dependent lung during the subsequent inspiration phase. This pendulum-like motion has the potential to trigger hypoxia and hypercapnia. This phenomenon can cause conversion to orotracheal intubation.[37] Furthermore, while hypercapnia can pose a concern during non-intubated surgery, there exists a significant degree of tolerance for this condition. In fact, the concept of permissive hypercapnia is anticipated to enhance V/Q through hypoxic pulmonary vasoconstriction, which in turn augments parenchymal compliance and facilitates direct dilation of small airways.[38] Given these considerations, additional research is required to refine the procedural aspects of HFNC and NIVM implementation.

A special concern is the potential for intrabronchial pressure induced by NIPPV to increase pulmonary air leaks. Prolonged air leakage is a primary complication of lung surgery. This factor significantly influences the duration of postoperative hospitalization, the rate of ICU readmission, and in-hospital mortality.[39] Clinical investigations have shown that this complication could occur in up to 10% of patients who undergo NIPPV.[31] Therefore, this condition should be carefully treated before starting NIMV therapy.

4. Non-invasive Mechanical Ventilation Support in Palliative Care Units

In the context of cancer care, promoting the integration of NIMV as a crucial element within palliative approaches has emerged as a prominent and compelling suggestion. This directive gains particular significance in its targeted focus on ameliorating dyspnea, a distressing symptom that is widely encountered by individuals grappling with cancer-related challenges.[40] The strategic integration of NIMV into the broader framework of palliative care endeavors not only to elevate the overall quality of life for these patients but also to offer tangible relief from the burdensome effects of compromised respiratory function. On these premises, the guidelines recommend the use of NIMV for dyspneic patients with terminal cancer for palliation.[19]

In addition to addressing dyspnea, there are additional advantages that prove especially beneficial in managing patients within the context of palliative care. NIMV offers a viable strategy to potentially improve outcomes and decrease the necessity for ICU admission. In a previous study, Gristina et al.[41] found that among patients with hematological malignancies who were admitted to the ICU due to respiratory failure, NIMV was associated with lower mortality rates than IMV. In another retrospective study conducted on patients with cancer, including those with solid tumors and admitted to medical ICUs for immediate or delayed NIMV for ARF, 57.5% were discharged from the ICU, and 42.5% were discharged from the hospital. On the contrary, among those who required IMV, only 1 was discharged from the hospital.[42] Therefore, during the terminal stages of lung cancer, NIMV can offer comfort care by alleviating dyspnea and respiratory distress, enhancing patient comfort, and allowing peaceful end-of-life care. Skillfully employing NIVM in advanced lung cancer cases, Kızılgöz et al.[9] achieved a remarkable decrease in ICU admissions and a notable extension of survival. Particularly significant is the study's impressive hospital discharge rate of 71%, encompassing the entire study cohort (n = 42). Results are applicable regardless of the disease stage, particular cellular subtype involved, or underlying factors contributing to the respiratory condition.

CONCLUSION

In the management of patients with lung neoplasms, NIVM has various potential applications. By addressing pre-existing lung conditions, facilitating surgical maneuvers, and promoting postoperative recovery, NIMV contributes to a holistic approach that optimizes surgical outcomes and patient well-being. For those ineligible for surgical resection, this approach can enhance respiratory performance, demonstrating utility across diverse clinical contexts, including palliative care. Therefore, as the understanding of NIMV's potential continues to evolve, its role in perioperative lung cancer care remains a dynamic area of exploration and innovation. High-quality clinical studies are required to evaluate the roles of different NIVM strategies and to determine the best timing to initiate therapy.

Footnotes

Authorship Contributions

Concept: M.C., A.M.E., Design: M.C., A.M.E., Data Collection or Processing: M.C., Analysis or Interpretation: A.M.E., Literature Search: M.C., Writing: M.C.

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Letter to the Editor

Can E-cigarettes Be the Source of Lead Toxicity?

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DEAR EDITOR,

To date, many health effects of e-cigarettes have been published such as acute lung injury and cancer.[1,2] In this letter, we would like to report a case of lead toxicity, which is most likely caused by e-cigarettes.

A 31-year-old man was referred to our hospital because of high blood lead levels (18.8 µg/dL) detected during a job application examination. Laboratory confirmation was made in the hospital. An increase in the blood lead levels of the patient was observed at two-week intervals (50.8 µg/dL and 97.3 µg/dL, respectively). During this period, he was unemployed for the last 1.5 months. He had previously worked as a waiter in various cafeterias for 1.5 years. Before that, he worked in the manufacture of accumulators for two months, over 1.5 years ago. He did not identify any hobbies or side jobs that could expose him to lead. He had never had any surgery or accidents other than appendicitis 27 years ago. He had no chronic diseases and was not taking any medications. He had two children and was divorced. He lived alone in a reinforced concrete building in the city center. The plumbing of the building was new. In terms of oral intake sources, the use of cookware containing lead was questioned.

It was learned that he had vaped e-cigarettes for two months, hoping that it would help him quit smoking. He purchased it from an online shopping website. He used to charge the battery daily and often found himself reflexively playing with it in his hand. No other new source of exposure has been identified since the last occupational lead exposure in accumulator production occurred 1.5 years ago. He was hospitalized, and chelation therapy with 40 mg/kg/day of ethylenediaminetetraacetic acid (EDTA) was administered. After treatment, the blood lead level decreased to 19.3 µg/dL. He was discharged with advice to avoid e-cigarettes.

Today, lead is identified as one of the 10 chemicals that pose a significant public health problem, and political steps are being taken to reduce exposure. Legal regulations on lead-based gasoline and leaded paint are examples of this.[3] However, it is a well-known fact that several consumer products may still contain lead.[3]

Electronic cigarettes are rapidly becoming an alternative to traditional cigarette smoking. According to chromatographic and spectroscopic measurements in the literature, similar contents such as formaldehyde, acetaldehyde, nitrosamine, toluene, lead, nickel, and cadmium were detected in the vapors of different brands.[4,5] Lead or other metal contents are mainly caused by the battery coil,[5] but can also occur through liquid contamination under poor production conditions.

Exposure to lead can occur via inhalation, ingestion, and dermal absorption routes.[3] If electronic cigarettes were defined as the source of exposure in our case, it can be said that lead could have been ingested into the body in all three ways.

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First, inhalation of liquid that may be contaminated with lead; second, transdermal absorption by holding the battery in the palm for a long time; and last, oral ingestion through contact with the contaminated hand to mouth.

Of course, in this evaluation, possible exposure to accumulator manufacturing over 1.5 years ago was not neglected in this patient. Because accumulator manufacturing is a well-known industry associated with lead exposure. However, the newly increasing trend in patient blood lead levels necessitated a search for a new source of exposure.

In this report, arguments are presented that e-cigarettes, which are marketed as alternatives to traditional cigarettes, may cause lead poisoning in addition to their known health effects. Comprehensive research on this topic is required.

Ethics

Informed Consent: It was obtained from the patient to report the case in the medical literature.

Footnotes

Authorship Contributions

Concept: M.D.A., S.Y., O.K., Design: M.D.A., S.Y., O.K., Data Collection or Processing: M.D.A., Literature Search: M.D.A., S.Y., O.K., Writing: M.D.A.

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Erratum

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The mistake has been made inadvertently by the author.

i. The name information of the 4th author is incorrect on page 197.

Cemre Hilal Kesen Yurtcanli, Murat Tuğberk Bakar, Şükran Peker, **Nadide Pinar Ay**

The name information of the 4th author has been corrected on page 197.

Cemre Hilal Kesen Yurtcanli, Murat Tuğberk Bakar, Şükran Peker, **Pinar Ay**

ii. The name information of the 4th author is incorrect in the "Cite this article as" section on page 197.

Cite this article as: Yurtcanli CHK, Bakar MT, Peker Ş, **Ay NP.** Factors related to tobacco cessation attempts among turkish adolescents: A structural equation model analysis. Thorac Res Pract. 2024;25(6):197-202.

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iii. The name information of the 4th author is incorrect in the Author Contributions section on page 201.

Author Contributions: Concept – Ş.P., **N.P.A.**; Design – M.T.B., C.H.K.Y., Ş.P., **N.P.A.**; Supervision – **N.P.A.**; Materials – M.T.B., C.H.K.Y., Ş.P., **N.P.A.**; Data Collection and/or Processing – M.T.B., C.H.K.Y.; Analysis and/ or Interpretation – M.T.B., C.H.K.Y., Ş.P.; Literature Review – M.T.B., C.H.K.Y., Ş.P.; Writing – C.H.K.Y., **N.P.A.**; Critical Review – M.T.B., C.H.K.Y., Ş.P., **N.P.A.**

The name information of the 4th author has been corrected in the Author Contributions section on page 201.

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