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Research Article

Seasonal and Weekly Variations in Acute Ischemic Stroke Admissions among COPD Patients

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Abstract

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading global cause of mortality, with incidence and prevalence on an upward trajectory. While firmly associated with cardiovascular disease, recent studies have shed light on a potential link between COPD and stroke. We aim to analyze the association between COPD and stroke while exploring seasonal and weekly variations in Acute Ischemic Stroke (AIS) admissions in our center.

Methods: Retrospectively identified patients with COPD from January 2004 to December 31st, 2018, who had AIS. Risk factors and seasonal, monthly, and weekly variations in admission patterns were recorded.

Results: A total of 329 cases of COPD with AIS admissions were identified, alongside 347 AIS patients without COPD matched by age and sex as a control group. The mean age at the time of AIS was 74.9 ± 10.7 years for the COPD group and 75.2 ± 11.5 years for the non-COPD group (p=NS). In the COPD group, 66% were males, compared to 58.8% in the control group (p=NS). Notably, the COPD cohort exhibited a higher prevalence of risk factors, including hypertension, hyperlipidemia, smoking, and ischemic heart disease. Seasonal variations were apparent, with winter showcasing the highest number of admissions in both groups, although no statistically significant difference was observed in the overall seasonal distribution. While no significant disparities were noted in the half-year distribution of AIS between groups, a higher incidence of strokes occurred during the cold half-year. Significant differences emerged in the distribution of AIS between weekdays and weekends. COPD patients demonstrated a higher frequency of AIS admissions on weekends compared to the control group (27.36% *vs.* 17%, p=0.0011).

Conclusion: This study highlights the influence of chronobiological factors on AIS in COPD patients. While no significant differences were identified in overall seasonal patterns, the distinct weekday and weekend admission rates suggest a potential role for weekly variations in stroke occurrence.

Key Words: Ischemic stroke; COPD; Seasonality; Weekends

Introduction

Chronic Obstructive Pulmonary Disease (COPD), ranked as the fourth leading global cause of death [1], and characterized by persistent respiratory symptoms and airflow limitation due to exposure to noxious particles or gases. Emerging evidence suggesting that COPD is not solely a pulmonary disease but may involve systemic inflammation, which could contribute to vascular changes and increase the risk of stroke. A few population-based studies [2] shows that colder temperatures have been shown to increase hospitalization and mortality rates in adults with COPD and cardiac disease [3]. Both COPD and stroke share common risk factors such as smoking, advanced age, and cardiovascular diseases. Each year, approximately 15,000 cases of stroke occur in Israel, of which about 85% are Acute Ischemic Stroke (AIS). Acute ischemic stroke is the third most common cause of chronic disability and the second cause of mortality in the Western world [4,5]. Mortality within 30 days of the stroke reaches up to 23%; about half of those who survive the event are likely to remain with a functional disability of varying degrees and about 40% with cognitive neurologic deficits.

The association between acute stroke and COPD has garnered increasing attention within the neurological field. Studies consistently indicated a notable prevalence of COPD among individuals who have experienced acute stroke. Recent data showed increased incidence of AIS in patients with COPD, [6-8] especially in the first two years after diagnosis. This interconnection is complex, involving shared risk factors such as smoking, advanced age, and cardiovascular conditions [9-13]. Moreover, the coexistence of COPD and acute stroke appears to be associated with adverse outcomes, potentially amplifying the challenges in the management of affected individuals [14]. One study found that 11.71% of adult patients hospitalized for stroke had COPD, with in-hospital mortality rates of 6.33%. The study revealed a modest but significant independent association between COPD and overall stroke mortality [14].

Understanding the intricate relationship between these two prevalent health issues is essential for optimizing patient care strategies and enhancing our comprehension of the broader impact that respiratory and cerebrovascular conditions can exert on one another. In this study, we investigated the seasonal variations and weekly distribution of patients with AIS and COPD in northern Israel, comparing them with a control group of AIS patients without COPD.

Methods

Cohort selection and geographic considerations

This study was approved by our medical center IRB committee. RHCC is a tertiary hospital, the largest in northern Israel, and serves a population of about 2 million, consisting mainly of two major ethnic groups - Jews and Arabs. The coast and northern Israel plateau are characterized by a Mediterranean climate with a warm, moist summer, and a mild winter with temperatures above 10° C. We included consecutive patients with COPD and AIS between 2004 and 2018. All patients were hospitalized at our center. AIS stroke was defined as patients who presented with acute neurological deficit to our emergency room in RMC. The diagnosis in each case was established clinically and by cerebral imaging (CT/CTP/CTA/MRI). COPD was defined classically by guidelines (Reference) and was reported when appeared in patients' medical history.

Controls matching and variables

Controls were chronologically consecutive AIS patients, negative for COPD per diagnostic codes and symptoms; they were sex age matched to the COPD group. Data points extracted for any patient included demographics, date of hospitalization (weekday or weekend, month, season) as well as all vascular risk factors. AIS was defined as accepted in American heart association guidelines [15]. Vascular risk factors were defined as follows: hypertension (new diagnosis made in hospital, regular use of antihypertensive medications or diagnosis based on previous medical records); diabetes (new diagnosis in hospital, regular use of antidiabetic medications or previous diagnosis); hyperlipidemia: regular use of hyperlipidemia drugs or previous registries-based diagnosis; smoking (by patient's statement or by previous registries diagnosis); acute or chronic atrial fibrillation (new inpatient or previous registries diagnosis); ischemic heart disease (new diagnosis or known diagnosis from previous records). Seasons were defined as: Winter: December, January, and February; Spring: March, April, and May; Summer: June, July, and August; Fall: September, October and November. Friday and Saturday were defined as Weekend. A "warm" half-year was defined as the period from May to October.

Statistical Methods

All captured data was based on digitalized information collected from our computerized medical system capturing patients' data from birth including HMO based information. To examine potential differences in weekly, monthly, and seasonal variability in hospitalization, we hypothesized that a random chance would be as follows: A 2:5 ratio for weekends versus weekdays, 1/12 per month per year, 1/4 probability for each season and 1/2 probability for each half-year. The main statistical analysis included chi-square tests of ratio True vs. Expected Probability of Randomized Scattering. The number of cases between weekends/weekends, months, seasons, and half-year were examined. When significant differences between true and expected probabilities were detected, subtests were performed based on a reference point defined as the time with the smallest number of cases. To examine the effect of the time of hospitalization on hospital stay, we performed another statistical analysis using the Wilcoxon non-parametric test, which was the result of the non-normal dispersal of the data. USA).

Results

Demographics and risk factors

We identified 329 consecutive hospitalizations of patients with COPD due to AIS, parallel with 347 AIS patients without COPD as age sex matched controls. The mean age of at the time of AIS in COPD groups was 74.9 ± 10.7 years versus 75.2 ± 11.5 years in the non-COPD group. Two hundred and seventeen patients (66%) in the COPD group and 204 patients in (58.8%) in the control group were males, NS. Distribution of vascular disease and vascular risk factors in patients of both groups shown in Table 1. COPD group had significantly more risk factors including hypertension, hyperlipidemia, smoking, and ischemic heart disease.

Factor	AIS patients with COPD	AIS patients without COPD	P
Atrial Fibrillation	65 (19.76%)	76 (21.9%)	NS
Hypertension	277 (84.19%)	239 (68.88%)	<.0001
Diabetes	141 (42.86%)	154 (44.38%)	NS
Hyperlipidemia	226 (68.69%)	158 (45.53%)	<.0001
Smoking	263 (79.94%)	90 (25.94%)	<.0001
IHD*	128 (38.91%)	90 (25.94%)	0.0003

*IHD=Ischemic Heart Disease

Table 1: Distribution of vascular risk factors and vascular diseases in AIS patients with and without COPD.

Seasonal variables

Distribution of hospitalizations by months, seasons and half-years are shown in Tables 2, 3 and 4. February was the month with the highest number of AIS in the COPD group, when the maximum admissions in the control group were in February and March, NS. Winter was the season with the maximum number of admissions in both groups, without a statistical difference in the whole distribution by seasons between groups. In addition, no difference was found in the half-year distribution of strokes between groups, when more strokes occurred in a cold half-year in both groups. A statistically significant difference between the groups was found only in distribution of AIS by weekdays/weekends. In COPD patients, the number of AIS was higher on weekends as compared with the control group (90 (27.36%) AIS on weekends in the COPD group *vs* 59 (17%) AIS in the control group, p=0.0011, Table 5.

Table 2. Distribution of admissions by month in AIS patients with and without COPD

Group/ month	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec	Total	P
COPD N	27	37	33	25	19	21	32	19	23	32	30	31	329	NS
%	8.21	11.25	10.03	7.60	5.78	6.38	9.73	5.78	6.99	9.73	9.12	9.42	48.67	
Non-COPD N	36	29	33	22	29	21	29	32	25	32	30	29	347	
%	10.37	8.36	9.51	6.34	8.36	6.05	8.36	9.22	7.20	9.22	8.65	8.36	51.33	
Total	63	66	66	47	48	42	61	51	48	64	60	60	676	
	9.32	9.76	9.76	6.95	7.10	6.21	9.02	7.54	7.10	9.47	8.88	8.88		

Group/season	Winter	Spring	Summer	Fall	Total	P
COPD (N)	95	77	72	85	329	NS
%	28.88	23.4	21.88	25.84	48.67	
Non-COPD (N)	94	84	82	87	347	
%	27.09	24.21	23.63	25.07	51.33	
Total (N)	189	161	154	172	676	
%	27.96	23.82	22.78	25.44	100	

Table 3: Distribution of admissions by season in AIS patients with and without COPD.

Group/season	Cold	Warm	Total	P
COPD (N)	190	139	329	NS
%	57.75	42.25	48.67	
Non-COPD (N)	189	158	347	
%	54.47	45.53	51.33	
Total (N)	379	297	676	
%	56.07	43.93	100	

Table 4: Distribution of admissions by half-year (cold-warm) in AIS patients with and without COPD.

Discussion

This study examines the seasonal, monthly, and weekly patterns of hospitalizations for ischemic stroke through a comparative analysis with an age- and sex-matched control group lacking COPD. Both groups exhibit congruent distributions, characterized by heightened hospitalizations during winter and a subsequent decline in summer. Notably, maximal hospitalization rates coincide in February and March for both cohorts. These findings align with existing literature on increased cardiovascular and cerebrovascular disease prevalence, including acute ischemic stroke, during winter months [16]. Results reveal a uniformity in seasonal, half-yearly, and monthly distributions for hospitalizations due to acute ischemic stroke in both cohorts.

In most studies, AIS rates were higher in winter compared to summer [17,18]. However, in some studies, there were no seasonal differences at all, [19,20] while an increased prevalence of AIS was found in spring in others [21]. There are several studies demonstrating the increased incidence of COPD exacerbations in the winter season compared to summer [3,22,23]. The reasons are attributed to a high rate of viral respiratory diseases, lower levels of vitamin D in winter compared to summer [24,25] systemic inflammation and oxidative stress. There are some data on the possible association between seasonality and various components of AIS in COPD patients. One study suggests that, despite the increased incidence of AIS among COPD patients, COPD is not an independent risk factor for ischemic stroke [7].

The only significant finding in our study was the higher number of admissions of AIS patients with COPD on weekends as compared with the control group, Table 5. The data about weekly AIS distribution may also be found in the literature, but to a smaller extent than about seasonal variations. Here, also, various studies brought contradictory findings, some of which showed an increased prevalence of hospitalizations due to AIS on the first day of the week upon return to work [12,26,27], while no significant weekly differences were found in others. To the best of our knowledge, there is no data in the literature comparing rates of admissions in AIS patients with and without COPD on weekdays and weekends. Fewer admissions on weekends in AIS patients without COPD as compared with AIS patients with COPD may point to COPD as an independent risk factor for AIS, which is not influenced by stress or other psychosocial factors changing on weekends and influencing AIS patients without COPD.

Group/season	Weekend	Weekday	Total	P
COPD (N)	90	239	329	0.001
%	27.36	72.64	48.67	
Non-COPD (N)	59	288	347	
%	17	83	51.33	
Total (N)	149	527	676	
%	22.04	77.96	100	

The current study is subject to several limitations. Firstly, it is a retrospective, hospital-based investigation, entailing inherent constraints associated with this study design. Secondly, cases exhibiting subacute ischemic strokes upon imaging were excluded from the study. Thirdly, the sample size of the COPD patient group with stroke is relatively modest.

In conclusion, the results of the study indicate some impact of the chronobiological factors on AIS in COPD patients. We were not able to show any seasonal or monthly differences in the distribution of admissions in stroke patients of both groups. However, we did find differences on weekend and weekday admission rates in stroke patients with and without COPD. Identifying the specific mechanisms responsible for this difference requires further research.

Statement of Ethics and Acknowledgments

This study protocol was reviewed and approved by Rambam medical center ethics committee. Written informed consent was not required, the study has been granted an exemption from requiring written informed consent by the same committee.

We have no acknowledgment to declare.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

H. E contributed to the design and implementation of the research, and to the writing of the manuscript.

H. M contributed to the writing of the manuscript.

S. E contributed to the writing of the manuscript.

H. R contributed to the writing of the manuscript.

T. G contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

S. S contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

Data Availability Statement

Data is available per reasonable request

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