

RESEARCH

Open Access



The DOSE index in chronic obstructive pulmonary disease: evaluating healthcare costs

Chin-Ling Li¹, Hui-Chuan Chang¹, Ching-Wan Tseng¹, Yuh-Chyn Tsai¹, Jui-Fang Liu^{3,4}, Chia-Chuan Chan², Meng-Lin Tsai⁵ and Shih-Feng Liu^{1,3,4,5,6,7*}

Abstract

Background and objectives The DOSE index, which incorporates Dyspnea, Obstruction, Smoking, and Exacerbations, is a widely used tool for assessing the severity and prognosis of Chronic Obstructive Pulmonary Disease (COPD). In addition to risk assessment, it has potential clinical utility in predicting healthcare costs, which are primarily driven by exacerbations. While several indices, such as the BODE (Body-mass index, Obstruction, Dyspnea, Exercise) and ADO (Age, Dyspnea, Obstruction) indices, exist for risk prediction, there is a lack of dedicated tools for forecasting healthcare costs. This study explores the potential of the DOSE index compared to other indices, including BODE, ADO, and the Charlson Comorbidity Index (CCI), for this purpose.

Materials and methods This cross-sectional retrospective study analyzed data from 396 COPD cases. We examined associations between the DOSE index, BODE index, ADO index, CCI, and healthcare costs, including hospitalizations and emergency room treatments. Healthcare costs were categorized as direct medical expenses.

Results Significant associations were observed between the DOSE index and various healthcare parameters. DOSE quartiles showed strong correlations with outpatient visits ($p=0.013$) and outpatient medical expenses ($p=0.011$). In addition, hospitalization frequency, duration, and associated costs were significantly correlated with higher DOSE quartiles ($p<0.001$). A significant difference was found when comparing DOSE quartiles between patients with high ($CCI \geq 3$) and low ($CCI < 3$) comorbidity scores ($p=0.018$). The DOSE index outperformed other indices, likely due to its inclusion of exacerbations, a key driver of healthcare costs.

Conclusion The DOSE index demonstrates potential in predicting healthcare costs, particularly due to its inclusion of exacerbation frequency. This study highlights the importance of considering exacerbations alongside traditional risk factors for more accurate cost forecasting in COPD management. Our findings suggest that the DOSE index may be a valuable tool in both clinical and economic assessments of COPD patients, though further research is warranted to validate these findings in larger datasets.

Keywords COPD, DOSE index, BODE index, ADO index, Medical cost

*Correspondence:

Shih-Feng Liu

liuphysico@yahoo.com.tw

Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive and debilitating respiratory condition characterized by persistent airflow limitation and respiratory symptoms [1–3]. Globally, it affects millions of individuals, imposing a significant burden on their physical, emotional, and socioeconomic well-being [4, 5]. COPD's severity is influenced by a complex interaction of factors, including shortness of breath, airflow obstruction, smoking history, and exacerbation frequency [6, 7]. Accurately assessing this multifaceted burden is essential for developing effective treatment plans that improve patients' quality of life [8, 9].

The DOSE (Dyspnea, Obstruction, Smoking, Exacerbation) index offers a multidimensional approach to evaluating COPD severity. This index incorporates four key components, each contributing to a comprehensive assessment [10, 11]. Dyspnea, the hallmark symptom of COPD, impacts patients' physical and emotional well-being, with its severity assessed using standardized questionnaires or scales [12]. Airflow obstruction, a central feature of COPD, is measured through spirometry, particularly by evaluating forced expiratory volume in one second (FEV1) and forced vital capacity (FVC). Smoking history, both current and past, plays a critical role in understanding disease progression, while the frequency of exacerbations—acute worsening episodes often leading to hospitalizations—provides further insight into disease burden [13–15].

By integrating these elements, the DOSE index delivers a comprehensive evaluation of COPD severity, allowing clinicians to capture a broader and more accurate picture of each patient's health status. This holistic perspective facilitates the development of personalized treatment plans that include pharmacological interventions, pulmonary rehabilitation, and lifestyle modifications to meet the individual needs of COPD patients. Additionally, the DOSE index has demonstrated potential as a prognostic tool for predicting disease progression, hospitalization risk, and overall mortality [16] [17].

While other indices, such as the BODE (Body-mass index, Obstruction, Dyspnea, Exercise) and ADO (Age, Dyspnea, Obstruction) indices, are widely used to assess COPD severity and prognosis, the DOSE index uniquely incorporates exacerbations—a key factor in healthcare cost escalation [18, 19]. Exacerbations, often resulting in hospital admissions, drive significant healthcare expenditures in COPD management [14, 20]. Therefore, understanding the relationship between the DOSE index and healthcare costs is essential for optimizing resource allocation in COPD care. This study aims to explore whether the DOSE index can serve as a valuable tool for

predicting healthcare costs in COPD, in addition to its established role in risk assessment.

Materials and methods

Study design

This cross-sectional retrospective study aims to investigate the correlation between the DOSE index and healthcare costs in COPD patients. While the efficacy of the DOSE index in assessing COPD risk is well-established [21–23], its role in predicting healthcare costs remains largely unexplored. By utilizing patient data from Kaohsiung Chang Gung Memorial Hospital [24], the study examines whether the DOSE index provides an added benefit over other indices such as BODE, ADO, and the Charlson Comorbidity Index (CCI) in forecasting healthcare expenditures, particularly through its incorporation of exacerbation frequency.

Study population

The study population consisted of COPD patients from the Kaohsiung Chang Gung Memorial Hospital electronic database. The study received approval from the Institutional Review Board (IRB: 201701293B0) of Chang Gung Medical Center. Retrospective data collection for the 6-min walk test (6MWT) spanned from January 31, 2015, to August 31, 2017, covering a period of 32 months. A total of 1063 patients were initially reviewed. Inclusion criteria for COPD patients included diagnosis codes ICD-9-CM: 490–496 and ICD-10-CM: J41–J44, with FEV1/FVC < 70% post-bronchodilator treatment, and complete clinical record data on the DOSE index, BODE index, ADO index, CCI, and healthcare costs. Exclusion criteria involved patients under the age of 40, as younger patients generally exhibit different disease progression than older populations, incomplete clinical data, or patients whose lung function did not meet COPD diagnostic criteria according to the GOLD guidelines [25, 26]. Figure 1 showed the flow chart of selected participants in this study.

Clinical variables

COPD patients were categorized into quartiles based on their DOSE index scores: Quartile 1 (Q1) included scores from 0 to 2, Quartile 2 (Q2) from 3 to 4, Quartile 3 (Q3) from 5 to 6, and Quartile 4 (Q4) from 7 to 8 [27, 28]. Additionally, the Charlson Comorbidity Index (CCI) was divided into high (CCI ≥ 3) and low (CCI < 3) categories [29, 30]. The following clinical variables were examined: age, gender, pack-years of smoking, lung function tests (FEV1, FVC, DLCO), 6-min walk distance (6MWD), body mass index (BMI), modified Medical Research Council (mMRC) dyspnea scale, frequency of outpatient visits, hospitalization frequency, hospitalization duration,

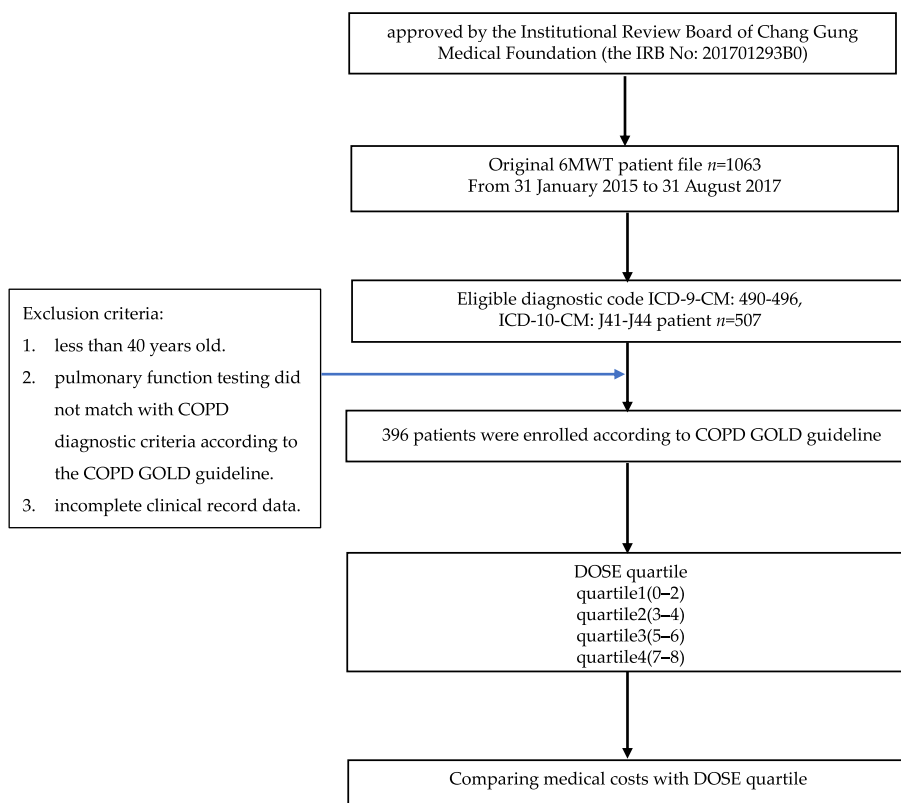


Fig. 1 Flow chart of selected participants in this study. Abbreviations: 6MWT, 6-min walk test; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; COPD, Chronic obstructive pulmonary disease; DOSE index, composite index of, dyspnea, airflow obstruction, smoking status, and exacerbation frequency

and healthcare costs, including hospitalizations and emergency room treatments. Both direct medical costs, such as outpatient and hospitalization expenses, were considered in this analysis.

Ethical approval

This study followed ethical standards outlined in the Declaration of Helsinki and adhered to Good Clinical Practice guidelines. As a retrospective study, patient informed consent was not required for the review of medical records, and this waiver was approved by the Institutional Review Board (IRB: 201701293B0) at Kaohsiung Chang Gung Memorial Hospital.

Statistical analysis

Baseline characteristics were presented as mean ± standard deviation (SD), median (interquartile range, IQR), or percentages (N %). The distribution of the DOSE index and CCI was analyzed using descriptive statistics. Comparisons between the DOSE index quartiles and CCI groups were assessed using chi-square tests, Fisher’s exact test, and one-way analysis of variance (ANOVA). Post hoc comparisons were performed using the Scheffé

test. Linear trends were examined through one-way ANOVA and linear contrast. IBM SPSS Statistics for Windows, Version 26.0 (Armonk, NY, USA), was used to perform all statistical analyses to ensure rigor and reliability of the findings.

Results

This study investigated the relationships between various clinical indices (including Pulmonary Function Test (PFT) results, Body Mass Index (BMI), Charlson Comorbidity Index (CCI), Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage, DOSE index, ADO index, and BODE index) and healthcare costs in patients with Chronic Obstructive Pulmonary Disease (COPD). The goal was to determine how these indices, which reflect the clinical status of COPD patients, correlate with healthcare expenditures, particularly in relation to exacerbations, airflow limitation, comorbidities, and smoking history.

A total of 396 COPD patients were enrolled in the study. Among these patients, 87.6% were smokers, with an average smoking duration of 31.7 ± 18.5 years. The distribution of patients across the GOLD stages was

Table 1 Baseline characteristics of chronic obstructive pulmonary disease (COPD) patients

Factors	Mean ± Standard Deviation (SD) or n (%) n = 396
Age (years)	73.1 ± 9.5
Male (%)	382 (96.5)
Smoking	
Yes	347(87.6%)
No	49(12.4%)
Smoking history (pack-years)	31.7 ± 18.5
Body-mass index (BMI)	23.5 ± 4.1
FVC (% of predicted value)	79.7 ± 16.7
FEV1 (% of predicted value)	55.2 ± 18.2
FEV1/FVC (%)	52.7 ± 10.6
GOLD stage (%)	
Mild (I)	46 (11.6)
Moderate (II)	187 (47.2)
Severe (III)	140 (35.4)
Very severe (IV)	23 (5.8)
DLCO (%)	68.5 ± 21.0
6-MWD (m)	351.9 ± 111.6
mMRC	1.72 ± 0.9
mMRC dyspnea scale	
Scale 0/1/2/3/4	25/133/173/56/9
Exacerbations in previous year	
0–1	370(93.4%)
2–3	21(5.3%)
> 3	5(1.3%)
CCI	3.3 ± 2.8
DOSE INDEX	2.6 ± 1.1
BODE INDEX	3.0 ± 2.1
ADO INDEX	4.9 ± 1.8
DOSE quartile: Q1, Q2, Q3, Q4 (%)	
quartile 1	214 (54%)
quartile 2	164 (41.4%)
quartile 3	18 (4.5%)
quartile 4	0 (0%)
BODE quartile: Q1, Q2, Q3, Q4(%)	
quartile 1	188 (47.5)
quartile 2	109 (27.5)
quartile 3	71 (17.9)
quartile 4	28 (7.1)
ADO quartile: Q1, Q2, Q3, Q4 (%)	
quartile 1	40 (10.1)
quartile 2	124(31.3)
quartile 3	152 (38.4)
quartile 4	80 (20.2)

Abbreviations: FVC Forced vital capacity, FEV1 Forced expiratory volume in 1 s, 6 MWD 6-min walking distance, MRC score, Medical Research Council dyspnoea scale, GOLD Global Initiative for Chronic Obstructive Lung Disease, CCI Charlson comorbidity index, DOSE index Composite index of dyspnea, airflow obstruction, smoking status, and exacerbation frequency, BODE index Composite index of body mass index, airflow maximum expiratory pressure obstruction, dyspnoea, and exercise capacity, ADO index Composite index of age, dyspnoea, and airflow obstruction. Quartile 1 was defined by a score of 0–2, quartile 2 by a score of 3–4, quartile 3 by a score of 5–6, and quartile 4 by a score of 7–10

as follows: Stage I (11.6%), Stage II (47.2%), Stage III (35.4%), and Stage IV (5.8%). The mean age of the study population was 73.1 ± 9.5 years, and the majority were male (96.5%, or 382 individuals).

The average BMI of the study population was 23.5 ± 4.1, and the mean forced expiratory volume in one second (FEV1) was 55.2 ± 18.2% of predicted values. The average diffusing capacity of the lungs for carbon monoxide (DLCO) was 68.5 ± 21.0%. The 6-min walk distance (6MWD) averaged 351.9 ± 111.6 m. The modified Medical Research Council (mMRC) dyspnea scale had an average score of 1.72 ± 0.9, indicating a mild to moderate impact of dyspnea on the patients' daily activities. In terms of exacerbations, most patients (93.4%) experienced 0–1 acute exacerbations in the past year, while the remaining 6.6% had 2 or more exacerbations.

The Charlson Comorbidity Index (CCI) for the COPD patients had an average score of 3.3 ± 2.8, reflecting a high prevalence of comorbidities in the cohort. The mean DOSE index was 2.6 ± 1.1, while the BODE index averaged 3.0 ± 2.1 and the ADO index averaged 4.9 ± 1.8. These indices, collectively, provide a multidimensional assessment of COPD severity and prognosis (Table 1).

To better understand the relationship between these indices and healthcare costs, patients were divided into quartiles based on their DOSE, BODE, and ADO index scores. For the DOSE index, Quartile 1 (scores 0–2) included 214 cases (54%), Quartile 2 (scores 3–4) included 164 cases (41.4%), and Quartile 3 (scores 5–6) included 18 cases (4.5%). Notably, there were no cases in Quartile 4 (scores 7–8), indicating that the highest severity category of the DOSE index was not represented in this cohort.

For the BODE index, Quartile 1 included 188 cases (47.5%), Quartile 2 included 109 cases (27.5%), Quartile 3 included 71 cases (17.9%), and Quartile 4 included 28 cases (7.1%). Regarding the ADO index, Quartile 1 comprised 40 patients (10.1%), Quartile 2 included 124 patients (31.3%), Quartile 3 had 152 patients (38.4%), and Quartile 4 included 80 patients (20.2%).

These results demonstrate the distribution of patients across different severity levels according to each index. The subsequent analysis will focus on how these quartiles correlate with healthcare costs, particularly in terms of outpatient visits, hospitalization frequency, and associated expenses.

Table 2 presents correlation between the DOSE index quartiles and healthcare costs. A statistically significant association was found between DOSE quartiles and the number of outpatient visits ($p = 0.013$), indicating that as the DOSE index score increases, the frequency of outpatient visits rises. Additionally, a significant correlation was observed between DOSE quartiles and outpatient

Table 2 Value of medical costs and Dose quartile

Classification	DOSE quartile	Frequency or Costs (Mean (95% CI))	p-value
number of outpatient visits	1	17.93 (15.22–20.63)	0.013
	2	21.05 (17.41–24.68)	
	3	23.22 (15.01–31.43)	
outpatient medical expenses	1	52321.91 (43595.06–61048.76)	0.011
	2	78380.31 (60366.38–96394.24)	
	3	72905.17(44177.86–101,632.48)	
number of hospitalizations	1	0.47 (0.36–0.58)	< 0.001
	2	1.2 (0.92–1.47)	
	3	5.06 (3.3–6.82)	
number of hospitalization days	1	4.21 (2.91–)5.52	< 0.001
	2	12.03 (9.08–14.98)	
	3	70.5 (42.5–98.5)	
hospitalization expenses	1	19262.11 (9833.22–28,691)	< 0.001
	2	39594.65 (26719.33–52469.96)	
	3	95011.72 (57306.43–132717.01)	
total hospitalization expenses	1	71584.02 (58192.97–84975.06)	< 0.001
	2	117974.97 (95856.49–140093.45)	
	3	167916.94 (119845.16–215988.73)	

medical expenses ($p=0.011$), suggesting higher medical costs are incurred by patients with more severe COPD as indicated by higher DOSE index scores.

For hospitalization parameters, including the number of hospitalizations, number of hospitalization days, hospitalization expenses, and total hospitalization expenses, a strong statistically significant correlation was found ($p<0.001$). These results indicate that patients in higher DOSE quartiles experienced more frequent and prolonged hospitalizations, leading to increased hospitalization costs. The data highlight a clear upward trend in healthcare costs associated with more severe COPD as reflected by higher DOSE index scores.

When the Charlson Comorbidity Index (CCI) was dichotomized into high ($CCI\geq 3$) and low ($CCI<3$) levels, a statistically significant difference was observed between the high and low CCI groups across DOSE quartiles ($p=0.018$). This finding underscores the importance of considering comorbidities when evaluating the impact of COPD severity on healthcare costs.

Further analysis of the relationship between DOSE quartiles and outpatient medical expenses revealed a positive and linear association with hospitalization expenses. As DOSE quartile levels increased, hospitalization expenses showed a corresponding rise ($p<0.001$). A similar linear trend was observed for the number of hospitalization days across the DOSE quartiles ($p<0.001$), as illustrated in Fig. 2. This trend demonstrates that patients with higher DOSE index scores not only incur higher medical expenses but also experience more extended hospital stays.

Table 2 consistently reflects a rise in total medical expenses as DOSE quartile levels increase, supporting the conclusion that the DOSE index is a useful tool for predicting healthcare costs associated with COPD.

Discussion

This study demonstrates the multifaceted utility of the DOSE index, revealing its dual role in assessing COPD severity and predicting healthcare costs. COPD is a complex, progressive disease that often presents with comorbidities, particularly cardiopulmonary complications, as patients age. The gradual decline in lung function further exacerbates respiratory difficulties. Our findings highlight a significant correlation between the DOSE index and healthcare costs, particularly when combined with the Charlson Comorbidity Index (CCI), underscoring the importance of integrating both indices for a more accurate estimation of healthcare expenses in COPD patients.

The healthcare burden of COPD is substantial, particularly during moderate to severe stages of the disease and in patients experiencing frequent exacerbations. The DOSE index, through its inclusion of the "Exacerbations" component, demonstrates a strong association with healthcare costs [13, 31], such as increased emergency room visits, hospitalizations, and ICU admissions. Exacerbations are a critical driver of costs in COPD management, as they are associated with heightened respiratory symptoms, including wheezing, coughing, and increased sputum production. These symptoms lead to worsening lung function and an accelerated decline in overall health

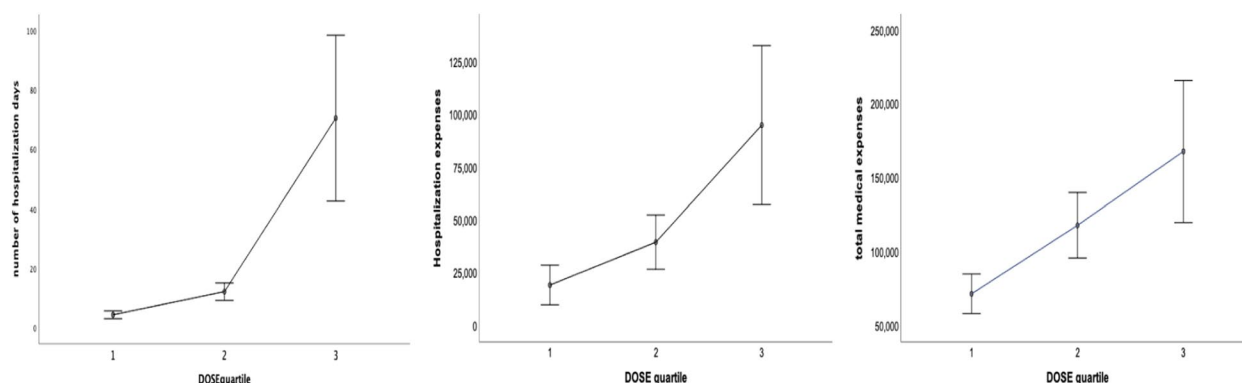


Fig. 2 Statistically significant differences the number of hospitalization days, number of hospitalizations and hospitalization expenses by DOSE quartile

[32, 33]. Forced expiratory volume in one second (FEV1) continues to serve as a key metric for clinicians to evaluate COPD severity, and its decline is strongly linked to an increased frequency of exacerbations [34, 35]. As disease severity escalates, patients require more extensive and costly medical interventions, further validating the importance of the "Exacerbations" component within the DOSE index in predicting healthcare costs for COPD patients.

While previous research has established the efficacy of other indices like BODE and ADO in predicting clinical outcomes and resource utilization in COPD patients [24, 36, 37], the DOSE index stands out due to its incorporation of exacerbation frequency, which is a critical determinant of healthcare costs [38]. This study extends the existing literature by confirming the correlation between the DOSE index and healthcare costs, providing strong evidence that the DOSE index is a valuable tool for predicting healthcare expenses in COPD management. Additionally, by comparing the DOSE index with other indices like BODE and ADO, we demonstrate that the inclusion of exacerbations offers a more comprehensive assessment of a patient's healthcare needs, which can guide clinical decision-making and resource allocation more effectively.

Our findings, however, come with several limitations. First, as this is a retrospective study, further prospective research is needed to validate these results in a broader clinical setting. Previous studies on the DOSE, BODE, and ADO indices have primarily focused on predicting mortality and disease prognosis, with limited exploration of their relationship with medical costs. Additionally, this study predominantly included male patients who underwent the 6-min walk test (6MWT), which may impact the generalizability of our findings due to gender-related factors, particularly in Taiwan [39], where the majority of

smokers are male. Lastly, as the study relies on data from a single medical center, the results may not be fully representative of the broader COPD population. Our analysis focused on direct medical costs, as governed by the National Health Insurance Administration [40–42], and did not explore indirect costs such as loss of productivity or quality of life.

Conclusion

This study confirms that the DOSE index is strongly associated with various healthcare parameters, including the number of outpatient visits, outpatient medical expenses, hospitalization frequency, hospitalization days, hospitalization expenses, and total healthcare costs. The DOSE index emerges as a valuable tool for predicting healthcare costs in COPD patients and offers clinicians a comprehensive framework for effective disease management and resource allocation. By integrating both clinical severity and exacerbation frequency, the DOSE index provides actionable insights for optimizing the care of COPD patients.

Authors' contributions

S.-F.L. had a role in the study conceptualization, formal analysis, methodology, software, supervision, writing—original draft, writing, review and editing. C.-L.L. had a role in the study conceptualization, data curation, formal analysis, methodology, software, and writing. H.-C.C., C.-W.T., Y.-C.T., C.-C.C. and M.-L.T. had a role in data curation and formal analysis. J.-F.L. had a role in the study formal analysis and editing. All authors have read and agreed to the published version of the manuscript.

Institutional review board

The study was approved by the Chang Gung Medical Foundation Institutional Review Board Committee (IRB: 201701293B0) on 6 September 2017

Funding

This research received no external funding.

Data availability

The data supporting this research are available from C.-L.L.

Declarations

Ethics approval and consent to participate

A waiver of informed consent was obtained from participants, which was approved by the Chang Gung Medical Foundation Institutional Review Board Committee.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Respiratory Therapy, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung 833, Taiwan. ²Kaohsiung Municipal Feng Shan Hospital under the management of Chang Gung Medical Foundation, Kaohsiung, Taiwan. ³Department of Respiratory Care, Chang Gung University of Science and Technology, Chiayi 600, Taiwan. ⁴Chronic Diseases and Health Promotion Research Center, Chang Gung University of Science and Technology, Chiayi, 600, Taiwan. ⁵Department of Internal Medicine, Division of Pulmonary and Critical Care Medicine, Kaohsiung Chang Gung Memorial Hospital, Ta-Pei Road, Niasong District, Kaohsiung 123, Taiwan. ⁶College of Medicine, Chang Gung University, Taoyuan 333, Taiwan. ⁷School of Medicine, College of Medicine, National SunYat-Sen University, Kaohsiung, Taiwan.

Received: 26 February 2024 Accepted: 25 October 2024

Published online: 08 November 2024

References

- Dutta S, Goel N, Kumar R. Assessment of frailty and its predictors in chronic obstructive pulmonary disease. *Lung India*. 2024;41(1):17–24.
- Venkatesan P. GOLD COPD report: 2023 update. *Lancet Respir Med*. 2023;11(1):18.
- Ritchie AI, Wedzicha JA. Definition, causes, pathogenesis, and consequences of chronic obstructive pulmonary disease exacerbations. *Clin Chest Med*. 2020;41(3):421–38.
- Adeloye D, Song P, Zhu Y, Campbell H, Sheikh A, Rudan I. Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. *Lancet Respir Med*. 2022;10(5):447–58.
- Chen S, Kuhn M, Prettnr K, Yu F, Yang T, Bärnighausen T, Bloom DE, Wang C. The global economic burden of chronic obstructive pulmonary disease for 204 countries and territories in 2020–50: a health-augmented macro-economic modelling study. *Lancet Glob Health*. 2023;11(8):e1183–93.
- Vogelmeier CF, Roman-Rodriguez M, Singh D, Han MK, Rodriguez-Roisin R, Ferguson GT. Goals of COPD treatment: Focus on symptoms and exacerbations. *Respir Med*. 2020;166: 105938.
- Sandelowsky H, Weinreich UM, Aarli BB, Sundh J, Høines K, Stratelis G, Løkke A, Janson C, Jensen C, Larsson K. COPD—do the right thing. *BMC Fam Pract*. 2021;22(1):244.
- Rehman A, Ahmad Hassali MA, Muhammad SA, Shah S, Abbas S, Hyder Ali IAB, Salman A. The economic burden of chronic obstructive pulmonary disease (COPD) in the USA, Europe, and Asia: results from a systematic review of the literature. *Expert Rev Pharmacoecon Outcomes Res*. 2020;20(6):661–72.
- Gutiérrez Villegas C, Paz-Zulueta M, Herrero-Montes M, Parás-Bravo P, Madrazo Pérez M. Cost analysis of chronic obstructive pulmonary disease (COPD): a systematic review. *Heal Econ Rev*. 2021;11(1):1–12.
- Sundh J, Montgomery S, Ställberg B, Lisspers K. Assessment of COPD in primary care: new evidence supports use of the DOSE index. *Prim Care Respir J*. 2013;22(2):142–3.
- Rolink M, van Dijk W, van den Haak-Rongen S, Pieters W, Schermer T, van den Bemt L. Using the DOSE index to predict changes in health status of patients with COPD: a prospective cohort study. *Prim Care Respir J*. 2013;22(2):169–74.
- Oishi K, Matsunaga K, Harada M, Suizu J, Murakawa K, Chikumoto A, Ohteru Y, Matsuda K, Uehara S, Hamada K. A new dyspnea evaluation system focusing on patients' perceptions of dyspnea and their living disabilities: the linkage between COPD and frailty. *J Clin Med*. 2020;9(11):3580.
- Iheanacho I, Zhang S, King D, Rizzo M, Ismaila AS. Economic burden of chronic obstructive pulmonary disease (COPD): a systematic literature review. *Int J Chron Obstruct Pulmon Dis*. 2020;15:439–60.
- Sethi S, Make BJ, Robinson SB, Kumar S, Pollack M, Moretz C, Dreyfus J, Xi A, Powell D, Feigler N. Relationship of COPD exacerbation severity and frequency on risks for future events and economic burden in the medicare fee-for-service population. *Int J Chron Obstruct Pulmon Dis*. 2022;17:593–608.
- Hurst JR, Skolnik N, Hansen GJ, Anzueto A, Donaldson GC, Dransfield MT, Varghese P. Understanding the impact of chronic obstructive pulmonary disease exacerbations on patient health and quality of life. *Eur J Intern Med*. 2020;73:1–6.
- Bloom C, Ricciardi F, Smeeth L, Stone P, Quint J. Predicting COPD 1-year mortality using prognostic predictors routinely measured in primary care. *BMC Med*. 2019;17:1–10.
- Athlin Å, Giezeman M, Hasselgren M, Montgomery S, Lisspers K, Ställberg B, Janson C, Sundh J. Prediction of Mortality Using Different COPD Risk Assessments—A 12-Year Follow-Up. *Int J Chron Obstruct Pulmon Dis*. 2021;16:665–75.
- Singh D, Criner GJ, Naya I, Jones PW, Tombs L, Lipson DA, Han MK. Measuring disease activity in COPD: is clinically important deterioration the answer? *Respir Res*. 2020;21:1–13.
- Jones RC, Donaldson GC, Chavannes NH, Kida K, Dickson-Spillmann M, Harding S, Wedzicha JA, Price D, Hyland ME. Derivation and validation of a composite index of severity in chronic obstructive pulmonary disease: the DOSE Index. *Am J Respir Crit Care Med*. 2009;180(12):1189–95.
- Stanford RH, Engel-Nitz NM, Bancroft T, Essoi B. The identification and cost of acute chronic obstructive pulmonary disease exacerbations in a United States population healthcare claims database. *COPD*. 2020;17(5):499–508.
- Jones RC, Price D, Chavannes NH, Lee AJ, Hyland ME, Ställberg B, Lisspers K, Sundh J, Van Der Molen T, Tsiligianni I. Multi-component assessment of chronic obstructive pulmonary disease: an evaluation of the ADO and DOSE indices and the global obstructive lung disease categories in international primary care data sets. *NPJ primary care respiratory medicine*. 2016;26(1):1–7.
- Chavannes NH, Jones R, Postma DS, Rennard S. Using COPD multidimensional indices in routine clinical practice: DOSE meets all criteria. *Prim Care Respir J*. 2012;21(3):245–6.
- Motegi T, Jones RC, Ishii T, Hattori K, Kusunoki Y, Furutate R, Yamada K, Gemma A, Kida K. A comparison of three multidimensional indices of COPD severity as predictors of future exacerbations. *Int J Chron Obstruct Pulmon Dis*. 2013;8:259–71.
- Li C-L, Chang H-C, Tseng C-W, Tsai Y-C, Liu J-F, Tsai M-L, Lin M-C, Liu S-F. Comparison of BODE and ADO Indices in Predicting COPD-Related Medical Costs. *Medicina*. 2023;59(3):577.
- Fazleen A, Wilkinson T. Early COPD: current evidence for diagnosis and management. *Ther Adv Respir Dis*. 2020;14:1753466620942128.
- Venkatesan P. GOLD COPD report: 2024 update. *Lancet Respir Med*. 2024;12(1):15–6.
- Ong K-C, Earnest A, Lu S-J. A multidimensional grading system (BODE index) as predictor of hospitalization for COPD. *Chest*. 2005;128(6):3810–6.
- Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, Pinto Plata V, Cabral HJ. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med*. 2004;350(10):1005–12.
- Shao W, Zhang Z, Zhang J, Feng H, Liang C, Liu D. Charlson comorbidity index as a predictor of short-term outcomes after pulmonary resection. *J Thorac Dis*. 2020;12(11):6670.
- Yıldız A, Yiğit A, Benli AR. The prognostic role of Charlson comorbidity index for critically ill elderly patients. *Eur Res J*. 2020;6(1):67–72.
- Rehman AU, Hassali MAA, Muhammad SA, Harun SN, Shah S, Abbas S. The economic burden of chronic obstructive pulmonary disease (COPD) in Europe: results from a systematic review of the literature. *Eur J Health Econ*. 2020;21:181–94.
- Thomas M, Radwan A, Stonham C, Marshall S. COPD exacerbation frequency, pharmacotherapy and resource use: an observational study in UK primary care. *COPD*. 2014;11(3):300–9.
- Kerkhof M, Voorham J, Dorinsky P, Cabrera C, Darken P, Kocks JW, Sadatsafavi M, Sin DD, Carter V, Price DB. The long-term burden of COPD exacerbations during maintenance therapy and lung function decline. *Int J Chron Obstruct Pulmon Dis*. 2020;15:1909–18.

34. Larsson K, Janson C, Lisspers K, Ställberg B, Johansson G, Gutzwiller FS, Mezzi K, Bjerregaard BK, Jorgensen L. The impact of exacerbation frequency on clinical and economic outcomes in Swedish COPD patients: the ARCTIC study. *Int J Chron Obstruct Pulmon Dis.* 2021;16:701–13.
35. Guo J, Chen Y, Zhang W, Tong S, Dong J. Moderate and severe exacerbations have a significant impact on health-related quality of life, utility, and lung function in patients with chronic obstructive pulmonary disease: a meta-analysis. *Int J Surg.* 2020;78:28–35.
36. Li C-L, Lin M-H, Tsai Y-C, Tseng C-W, Chang C-L, Shen L-S, Kuo H-C, Liu S-F. The Impact of the Age, Dyspnoea, and Airflow Obstruction (ADO) Index on the Medical Burden of Chronic Obstructive Pulmonary Disease (COPD). *J Clin Med.* 2022;11(7):1893.
37. Li C-L, Lin M-H, Chen P-S, Tsai Y-C, Shen L-S, Kuo H-C, Liu S-F. Using the BODE index and comorbidities to predict health utilization resources in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis.* 2020;15:389–95.
38. Shah CH, Onukwugha E, Zafari Z, Villalonga-Olives E, Park J-e, Slejko JF. Economic burden of comorbidities among COPD Patients hospitalized for acute exacerbations: an analysis of a commercially insured population. *Expert Rev Pharmacoecon Outcomes Res.* 2022;22(4):683–90.
39. Wen C, Tsai S, Chen C, Cheng T, Tsai M, Levy D. Smoking attributable mortality for Taiwan and its projection to 2020 under different smoking scenarios. *Tob Control.* 2005;14(suppl 1):i76–80.
40. Wu T-Y, Majeed A, Kuo KN. An overview of the healthcare system in Taiwan. *London journal of primary care.* 2010;3(2):115–9.
41. Cheng S-L, Lin C-H, Chu K-A, Chiu K-L, Lin S-H, Lin H-C, Ko H-K, Chen Y-C, Chen C-H, Sheu C-C. Update on guidelines for the treatment of COPD in Taiwan using evidence and GRADE system-based recommendations. *J Formos Med Assoc.* 2021;120(10):1821–44.
42. Cheng S-L, Li Y-R, Huang N, Yu C-J, Wang H-C, Lin M-C, Chiu K-C, Hsu W-H, Chen C-Z, Sheu C-C. Effectiveness of Nationwide COPD pay-for-performance program on COPD exacerbations in Taiwan. *Int J Chron Obstruct Pulmon Dis.* 2021;16:2869–81.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.