# Association between erectile dysfunction and the severity of obstruction to airflow in patients with chronic obstructive pulmonary disease

## Asociación entre disfunción eréctil y la severidad de la obstrucción al flujo aéreo en pacientes con enfermedad pulmonar obstructiva crónica

María J. Pareja-Zabala[1,2], Carlos Aguirre[3], Abraham Alí-Munive[4], María C. Pareja-Zabala[5], Luis F. Guerrero[6], Sandra Huertas[6], Leidy P. Prada[6]*, and Luis F. Giraldo-Cadavid[7,8]

[1]Departamento de Investigación, Fundación Neumológica Colombiana, Bogotá; [2]Departamento de Epidemiología, Universidad de la Sabana, Chía; [3]Dirección de Educación, Fundación Neumológica Colombiana, Bogotá; [4]Dirección Médica, Fundación Neumológica Colombiana, Bogotá; [5]Facultad de Medicina, Fundación Universitaria Sanitas, Bogotá; [6]Consulta Externa y Programas Especiales, Fundación Neumológica Colombiana, Bogotá; [7]Servicio de Neumología Intervencionista, Fundación Neumológica Colombiana, Bogotá; [8]Departamento de Epidemiología y Medicina Interna, Universidad de la Sabana, Chía. Colombia

## Abstract

**Objectives:** The objective of this study was to explore a possible association between ED and the severity of airflow obstruction in patients with COPD. **Materials and methods:** A cross-sectional study was conducted using the International Index Erectile Function (IIEF), a scale validated and translated to Spanish. Bivariate analyses between subgroups were made for quantitative variables using a t-test for means and Mann–Whitney U for medians; qualitative variables were compared using the $\chi^2$ test or Fisher's test, depending on distribution. Confusion bias in the association between ED and airflow obstruction was controlled using a logistic regression model. **Results:** The Spanish version of the IIEF-15 scale was valid and applicable to the Colombian population. The prevalence of ED in COPD patients living at high altitudes was similar to that found at sea level. Such prevalence is higher than in general population. Beta-blockers increased 7 times the risk of ED, but we found no association between the degree of airflow obstruction and ED. **Conclusion:** Although the severity of COPD is not associated with ED, the prevalence of ED in COPD is higher than in general population. Therefore, ED screening in COPD patients using the IIEF could be justified. The strong association between beta-blockers and ED had not been previously described in patients with COPD but must be considered in their clinical management.

**Keywords:** Erectile dysfunction. COPD. International Index Erectile Function. Beta-blocker.

## Resumen

**Objetivos:** Explorar una posible asociación entre DE y severidad de la obstrucción al flujo aéreo en pacientes con EPOC. **Materiales y métodos:** Estudio de corte transversal aplicando el Índice Internacional de Función Eréctil (IIFE), validado y traducido al español. Se realizó análisis bivariado para variables cuantitativas usando prueba-t para medias y U de Mann Whitney para medianas; las variables cualitativas fueron comparadas usando prueba de Chi2 o test de Fisher, según distribución. Los sesgos de confusión en la asociación entre DE y obstrucción al flujo aéreo fueron controlados usando un modelo de regresión logística.

***Resultados:*** *La versión en español de la escala IIFE-15 fue aplicable en población colombiana. La prevalencia de DE en pacientes con EPOC viviendo a gran altura fue similar a lo encontrado a nivel del mar. Esta prevalencia es mayor que en población general. El uso de beta-bloqueadores aumentó hasta siete veces el riesgo de DE, pero no se encontró asociación entre el grado de obstrucción y la DE.* ***Conclusiones:*** *Aunque la severidad de la EPOC no está asociada con DE, la prevalencia de DE en EPOC es mayor que en población general. Está justificada la realización de tamizaje usando el IIFE. La asociación fuerte entre beta-bloqueadores y DE no se ha descrito previamente en pacientes con EPOC, pero debe considerarse en su manejo.*

***Palabras clave:*** *Disfunción eréctil. Enfermedad pulmonar obstructiva crónica. Índice internacional de función eréctil. Beta-bloqueador.*

## Introduction

Chronic obstructive pulmonary disease (COPD) is highly prevalent and heterogeneous in its clinical presentation and evolution[1]. It is characterized by chronic and usually progressive and persistent airflow obstruction. It is estimated that the prevalence worldwide is around 10%, 14% in Latin America[2], and 8.9% In Colombia[3]. In the last decades, the prevalence of COPD has grown exponentially[4].

Erectile dysfunction (ED) is a common disease among adult men defined as the inability to achieve and maintain an erection enough to allow satisfactory sexual performance[5]. It is a benign disorder that affects physical and psychosocial health affecting the quality of life of those who suffer from it and their families[6]. The prevalence in the general population of this disease varies in the different age groups, being more frequent in men > 60. The DENSA study, conducted to estimate the prevalence of ED in Latin American countries (Colombia, Ecuador, and Venezuela), found a prevalence of ED in Colombia of 52.8%[7] A global multivariate analysis estimates that the risk of ED increases by at least 10% for each year of age[8]. It is estimated that by 2025, 322 million men will suffer from this disease[9,10].

In COPD, a prevalence study carried out in 1982 found that approximately six out of 20 COPD patients were suffering from erectile dysfunction[11]. However, in more recent studies conducted in cities located at sea level, it was found that between 72% and 78% of patients with COPD suffer from some degree of ED[12-15]. Although a recent meta-analysis did not find a higher prevalence of ED in COPD patients when compared to patients without COPD, it documented an increased risk of moderate or severe ED in COPD patients[16].

Dyspnea, cough, muscle weakness, and decreased physical activity associated with low testosterone levels have been postulated as the leading causes of decreased sexual activity in patients suffering from COPD[13,15,17].

International Index Erectile Function (IIEF) was written in English and validated in 12 countries and ten languages, including Spanish. It was validated in Peru[18,19], a country with cultural and epidemiological characteristics like other Latin American countries. While evaluating these patients, physicians ignore the association with some comorbidities, such as ED[12,19]. Only one quality of life questionnaire for patients with asthma and/or COPD includes questions about sexuality Quality-of-life for Respiratory Illness Questionnaire (QOL-RIQ)[20]. A study showed that 87% of patients with COPD do not discuss their sexual problems with their doctor, and 78% do not share these problems with their partner[21].

The studies that evaluated the prevalence of ED in the COPD population were conducted at sea level, and the extrapolation of these criteria to high altitudes is questionable. Based on sea-level studies, it is impossible to ensure that the prevalence is the same, which is why the findings cannot be extrapolated[12,22] With these data, we could be underestimating the prevalence of ED negatively affecting the quality of life of patients with COPD, who are doomed to settle for low sexual satisfaction.

We aimed to assess if there is an association between ED and airflow obstruction in patients with COPD living at high altitudes and its prevalence and association with other medications or comorbidities. This study was conducted in a reference institution for pulmonary diseases in Bogota, Colombia, which is 2640 m above sea level, likely representative of populations living at high altitudes (≥ 2500 and < 3500 m).

## Materials and methods

This study was conducted as an observational cross-sectional survey in 150 male patients between 40 and 80 years of age with a confirmed diagnosis of COPD defined as the presence of a risk factor: smoking with ≥ 10 pack-year (PY) history and/or exposure to wood smoke ≥ 10 years in a closed room;

and persistent obstructive airflow limitation (forced expiratory volume in the first second [FEV1/forced vital capacity [FVC] < 70% after bronchodilator). The exclusion criteria were clinical instability during the past 8 weeks (defined by the need for hospitalizations or consultation for acute changes in symptoms or current medication), patients who refused to sign the informed consent, and patients who did not have or are not interested in having sexual activity. An Institutional Review Board approved the study protocol, and all subjects provided written informed consent.

## Evaluation of psychometric characteristics of IIEF

Before the application of IIEF, the psychometric characteristics of the Spanish version translated and culturally adapted by the MAPI Research Institute of Lyon, France (one of the world's leading authorities on translation and cultural adaptation of quality-of-life questionnaires) were evaluated in two phases. In the first phase, through the constitution of a multidisciplinary bilingual (Spanish and English) committee of experts: A pulmonologist expert in COPD, a urologist expert in ED, a physiotherapist, and a qualified translator assessed the original version in English, and the translation into Spanish to ensure that the Spanish version was understandable and culturally equivalent to the Colombian culture. The second phase was a pilot study of 30 patients who evaluated the difficulty, time spent answering the questionnaire, and comprehension of each item.

## Other measurements

A demographic survey and Beck's depression inventory were applied; the perception of dyspnea was measured through the modified medical research council). The previous values of arterial gases, spirometry, and diffusion capacity of carbon monoxide were used to assess COPD and the symptoms.

## Statistical analysis

The Cronbach $\alpha$ statistic, test-retest reliability, and intraclass correlation coefficient evaluated the psychometric characteristics of the IIEF.

The descriptive analysis was made through means plus standard deviations or medians and interquartile range (IQR) according to the distribution of variables. For categorical variables, counts and percentages were used. The quantitative variables were compared using the t-test or Mann–Whitney U-test for non-parametric variables, while the frequencies of the qualitative variables were compared using the $\chi^2$ test. Bilateral hypotheses were formulated at two tails with a significance level of < 0.05.

A logistic regression model was used to evaluate possible covariates that could affect the association between the frequency of ED in the context of COPD. The multivariate model was constructed sequentially, initially through directed acyclic graphs (DAGS) with the variables that could be associated with the presence of ED. With these DAGS, we selected the potential confounding variables that were not in the causal path between the exposure and the effect. Variables with $p < 0.25$ in the bivariate analysis were included in the multivariate model (we used a p higher than the significance level to avoid missing any confounder). We eliminated those variables that, in the multivariate model, were not significantly associated with the effect (those with a two-tailed $p > 0.05$) and whose removal of the model did not significantly modify the regression coefficient of the leading independent variable to build the more parsimonious model. Finally, a Hosmer–Lemeshow test was used to determine the multivariate model goodness of fit.

The sample size was calculated, considering an average prevalence described in the literature of erectile dysfunction in patients with COPD of 75.5% with a confidence level of 95% and an accuracy of 7%; we calculated a sample of 150 patients for the prevalence study and of 160 patients for the multivariate logistic regression model. We used the statistical software Statistical Package for the Social Sciences version 22.

## Results

We included 169 men with a diagnosis of COPD confirmed by spirometry, with an average age of 69.9 years. The general characteristics are described in table 1. Most patients had moderate to severe airflow obstruction, and only 10.7% had a mild obstruction. We found decreased arterial oxygen pressure ($PaO_2$), oxygen saturation, and diffusing capacity for carbon monoxide (DLCO) percentage (Table 2). Regarding erectile function, the prevalence of ED was found in 78.8% of patients, with an average score of 15 in the IIEF (Table 3);

**Table 1.** General characteristics (n = 169)

| Characteristics | n (%) |
|---|---|
| Age | 69.9 (6) |
| BMI | 25.8 (4.6) |
| Marital status | |
|   Married | 114 (67.4) |
|   Free union | 9 (5.3) |
|   Divorced | 9 (5.3) |
|   Single | 8 (4.7) |
|   Widower | 6 (3.5) |
| Risk factor | |
|   Tobacco | 125 (74) |
|   Woodsmoke | 6 (3.6) |
|   Tobacco and woodsmoke | 38 (22.5) |
|   PY | 52.5 (32.5) |
|   Woodsmoke years | 22.25 (15) |
|   Active smoking | 9 (5.3) |
| Treatment | |
|   ARA-II | 60 (35.5) |
|   Statins | 58 (34.3) |
|   Beta-blockers | 35 (20.7) |
|   Calcium antagonists | 19 (11.2) |
|   ACE inhibitor | 16 (9.5) |
| Comorbidities | |
|   Coronary heart disease | 14 (8.3) |
|   Heart failure | 25 (14.8) |
|   Diabetes | 16 (9.5) |
|   Charlson comorbidity index (median; IQR) | 1 (IQR: 1-2) |

BMI: body mass index; ARA II: angiotensin receptor II antagonist; PY: pack-year; ACE: angiotensin-converting enzyme; IQR: interquartile range.

**Table 2.** COPD characteristics (n = 169)

| Characteristics | n (%) |
|---|---|
| Dyspnea (mMRC) | |
|   0 | 11 (6.5) |
|   1 | 87 (51.5) |
|   2 | 40 (23.7) |
|   3 | 23 (13.6) |
|   4 | 8 (4.7) |
| COPD severity (according to airflow obstruction) | |
|   Mild | 18 (10.7) |
|   Moderate | 92 (54.4) |
|   Severe | 42 (24.9) |
|   Very severe | 10 (5.9) |
| Spirometry | |
|   FVC POST, % | 90.8 (17.6) |
|   FEV1 post, % | 58.6 (18.6) |
|   FEV1/FVC | 0.51 (0.15) |
| Arterial blood gases | |
|   pH | 7.42 (0.03) |
|   $PCO_2$, mmHg | 36.69 (4.6) |
|   $HCO_3$, meq/L | 23.88 (3.2) |
|   $PaO_2$, mmHg | 55.07 (7.7) |
|   $SatO_2$, % | 87.75 (5.9) |
| DLCO | |
|   DLCO adjusted, % | 65.34 (25.5) |
|   AV, % | 82.65 (17.1) |
| 6MWD | |
|   Distance (meters) | 503.6 (90) |
|   $SatO_2$ start, % | 89.73 (7.3) |
|   $SatO_2$ end, % | 80.6 (6.3) |
| Treatment | |
|   SABA | 51 (30.2) |
|   LABA | 80 (47.3) |
|   ICS | 62 (36.7) |
|   LAMA | 123 (72.8) |
|   Oxygen | 55 (32.5) |

FEV1: forced expiratory volume in the first second; FVC: forced vital capacity; FEV1 post: forced expiratory volume in the first second; COPD: chronic obstructive pulmonary disease; 6MWD: 6-min walk distance; DLCO: diffusing capacity for carbon monoxide; AV: alveolar volume; SABA: short-acting beta-agonist; LABA: long-acting beta-agonist; ICS: inhaled corticosteroid; LAMA: long-acting anti-muscarinic; mMRC: modified medical research council.

however, in 27.2% of patients, erectile function was not evaluable (Table 3).

It was verified that the cross-cultural adaptation of the version in Spanish made in Peru is valid, following existing recommendations for scales that have already been translated and validated in the same language but in a different country than the subjects interviewed.

Regarding the transcultural adaptation and verification of the psychometric characteristics of the IIEF-15 scale, the interdisciplinary committee of experts evaluated each item of the scale in both the original version created by the author Raymond Rosen and the scale validated in Spanish in Peru by Zegarra et al., as well as the relevance of the application of the scale in the evaluation of the disease, the semantic, idiomatic and conceptual equivalence of the items, the applicability in the different regions of the country, and the daily routine of the situations raised in the questionnaire for the Colombian population, which determined that the scale validated in Peru is understandable and culturally equivalent to the Colombian population; however, minor changes in the syntactic order and the addition of

synonyms in parentheses to increase understanding were made. Regarding the feasibility of the survey, 99% of the patients filled out the questionnaire entirely in the test and the re-test, ≤ 1% of the answers were invalid or marked twice, and the average completion time was 6 (IQR: 5-10) min. Most of the patients had a high school or lower educational level. Finally, when assessing the psychometric characteristics of the IIEF-15 scale, Cronbach's α was 0.959, and the absolute intraclass correlation coefficient was 0.936 (95% CI: 0.873; 0.968) (p < 0.001).

A logistic regression model was constructed sequentially with the presence of ED (yes/no) as the dependent variable and using DAGS; in the bivariate

**Table 3.** Erectile dysfunction characteristics (n = 169)

| Characteristics | n (%) |
|---|---|
| ED prevalence | 97 (78.8) |
| IIEF | |
| IIEF1 | 15 (9.1) |
| IIEF2 | 15.75 (10.2) |
| ED severity | |
| Non-evaluable | 46 (27.2) |
| No dysfunction | 26 (15.4) |
| Mild | 21 (12.4) |
| Mild to moderate | 25 (14.8) |
| Moderate | 38 (22.5) |
| Severe | 13 (7.7) |

IIEF: international index of erectile function; IIEF2: applied 7-15 days after the first test (IIEF1); ED: erectile dysfunction.

**Table 4.** Bivariate analyses

| Variable | p |
|---|---|
| Age | 0.030 |
| PY | 0.088 |
| Woodsmoke years | 0.046 |
| Dyspnea | 0.132 |
| Beck depression inventory | < 0.001 |
| FEV1 post | 0.603 |
| FEV1/FVC | 0.228 |
| 6MWD | 0.194 |
| Marital status | 0.243 |
| Heart failure | 0.080 |
| Beta-blocker use | 0.039 |
| ACE-inhibitor | 0.173 |
| Statin use | 0.196 |

PY: pack-year index; FEV1: forced expiratory volume in the first second; FVC: forced vital capacity; ACE: angiotensin-converting enzyme; 6MWD: 6-min walk distance.

analysis, the variables associated with ED with $p < 0.25$ were: age, number of PY smoked, years of exposition to wood smoke, dyspnea, Beck's depression score, FEV1/FVC, meters in the 6-min walk test, marital status, heart failure, use of beta-blocker, angiotensin converting enzyme inhibitors, and statins (Table 4); such variables were included in the multivariate model. The most parsimonious multivariate model included beta-blocker and statin use; the variable FEV1 was also included in the analysis because it was part of the main objective. However, no statistical association was found in the bivariate analysis ($p = 0.603$) or the multivariate model. In the final model, the use of a beta-blocker had an odds ratio of 7 ($p = 0.016$), statins 0.35 ($p = 0.032$), and FEV1 0.004 ($p = 0.730$) (Table 5). Finally, the model's goodness of fit was demonstrated by the Hosmer–Lemeshow test ($p = 0.199$).

## Discussion

The results of this study showed that the prevalence of ED patients with COPD living at a high altitude is high (78.8%). The findings align with the previous studies in cities located at sea level, where they found a prevalence between 72% and 78%[12-14]. According to our study, there is no association between FEV1 and the presence or severity of ED in patients with COPD. However, such an association cannot be completely rule-out, considering the limitations of our study design. Our results also support that $PaO_2$ is not associated with the degree of ED.

The high prevalence of ED in patients with COPD compared with the general population, supported by the findings of our study and by the literature, leads us to believe that even if airflow obstruction seems not to be a contributing factor to ED, other factors present in COPD, like the inflammatory cascade perhaps related to the history of heavy smoking, could be contributing to the pathophysiology of ED[23], and should be explored in future studies.

It should also be considered that this high prevalence of ED may be because the diagnosis of COPD is usually made after several years of the onset of symptoms when the patient reaches an advanced age. Therefore, in our cohort, as in similar studies, most patients were > 60 years, and it has been widely described that age is strongly associated with ED[24], probably due to the progressive decrease in age of sex hormones, as well as an androgenic deficiency that causes adipocyte proliferation in the corpora cavernosa and causes tissue damage in the smooth muscle, which interferes with the veno-occlusive mechanism of the erection, and initiates the cycle of ischemia, tissue damage, and fibrosis[25].

Finally, we can emphasize that regardless of the severity of COPD, the prevalence of ED is very high; therefore, COPD patients should be screened for this condition. In our population, we found a strong association between the use of beta-blockers and the presence of ED, previously described in patients with

**Table 5.** Final multivariate model

| Variable | b | EE b | Exp B (OR) | IC 95% | | p | r² | p |
|---|---|---|---|---|---|---|---|---|
| | | | | Low | High | | | |
| Beta-blocker | 1.947 | 0.812 | 7.01 | 1.4 | 34.4 | 0.016 | 0.117 | 0.023 |
| Statins | −1.056 | 0.492 | 0.35 | 0.1 | 0.9 | 0.032 | | |
| FEV1 post | 0.004 | 0.012 | 1.00 | 0.98 | 1.03 | 0.730 | | |

FEV1: forced expiratory volume in the first second; OR: odds ratio; IC: confidence interval.

cardiovascular disease[26-28], especially if they consume this group of medications[28]. Although the association of ED with beta-blockers had not been previously described in patients with COPD, it is biologically plausible, especially in patients with additional risk factors for ED. The use of nebivolol, a third-generation beta-blocker, does not seem to negatively influence the sexual function of patients who consume it[26,29], and may have favorable effects in users of traditional beta-blockers when switching to this drug[27]. In this group of patients, statins could be a protective factor for ED. Therefore, we recommend that evaluating erectile function in patients with COPD should be a routine procedure in the usual consultation. This screening should be done with the instrument that we have validated in this study in the Colombian population since it is easy and rapid completion (6 min) to make comprehensive assessments and timely interventions, such as addressing urology specialists, which impact the quality of life of patients with COPD.

## Conclusion

Erectile dysfunction is an under-questioned topic by doctors caring for COPD patients, and patients rarely comment on sexual problems with their doctors. Furthermore, there is only one COPD quality of life questionnaire, including items about sexuality (QOL-RIQ)[20].

Although the severity of COPD is not associated with ED, the prevalence of ED in COPD is higher than in the general population. We recommend screening for ED in patients with COPD using the IIEF questionnaire. Beta-blockers have a strong association with ED in COPD patients that had not been previously described in COPD.

## Funding

This research received no specific grant from any funding agency.

## Conflicts of interest

The authors declare no conflicts of interest.

## Ethical disclosures

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

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

## References

1. Montes de Oca M, López Varela MV, Acuña A, Schiavi E, Rey MA, Jardim J, et al. ALAT-2014 chronic obstructive pulmonary disease (COPD) clinical practice guidelines: questions and answers. Arch Bronconeumol. 2015;51:403-16.
2. Menezes AM, Perez-Padilla R, Jardim JR, Muiño A, Lopez MV, Valdivia G, et al. Chronic obstructive pulmonary disease in five Latin American cities (the PLATINO study): a prevalence study. Lancet. 2005;366:1875-81.
3. Caballero A, Torres-Duque CA, Jaramillo C, Bolívar F, Sanabria F, Osorio P, et al. Prevalence of COPD in five Colombian cities situated at low, medium, and high altitude (PREPOCOL study). Chest. 2008;133:343-9.
4. Pauwels RA, Rabe KF. Burden and clinical features of chronic obstructive pulmonary disease (COPD). Lancet. 2004;364:613-20.
5. NIH consensus conference. Impotence. NIH consensus development panel on impotence. JAMA. 1993;270:83-90.
6. Hatzimouratidis K, Amar E, Eardley I, Giuliano F, Hatzichristou D, Montorsi F, et al. Guidelines on male sexual dysfunction: erectile dysfunction and premature ejaculation. Eur Urol. 2010;57:804-14.
7. Morillo LE, Díaz J, Estevez E, Costa A, Méndez H, Dávila H, et al. Prevalence of erectile dysfunction in Colombia, Ecuador, and Venezuela: a population-based study (DENSA). Int J Impot Res. 2002;14 Suppl 2:S10-8.
8. Nicolosi A, Moreira ED Jr., Shirai M, Bin Mohd Tambi MI, Glasser DB. Epidemiology of erectile dysfunction in four countries: cross-national study of the prevalence and correlates of erectile dysfunction. Urology. 2003;61:201-6.
9. Eleazu C, Obianuju N, Eleazu K, Kalu W. The role of dietary polyphenols in the management of erectile dysfunction-Mechanisms of action. Biomed Pharmacother. 2017;88:644-52.
10. Ayta IA, McKinlay JB, Krane RJ. The likely worldwide increase in erectile dysfunction between 1995 and 2025 and some possible policy consequences. BJU Int. 1999;84:50-6.
11. Fletcher EC, Martin RJ. Sexual dysfunction and erectile impotence in chronic obstructive pulmonary disease. Chest. 1982;81:413-21.

12. Köseo lu N, Köseo lu H, Ceylan E, Cimrin HA, Ozalevli S, Esen A. Erectile dysfunction prevalence and sexual function status in patients with chronic obstructive pulmonary disease. J Urol. 2005;174:249-52.

13. Collins EG, Halabi S, Langston M, Schnell T, Tobin MJ, Laghi F. Sexual dysfunction in men with COPD: impact on quality of life and survival. Lung. 2012;190:545-56.

14. Kahraman H, Sen B, Koksal N, Kilinç M, Resim S. Erectile dysfunction and sex hormone changes in chronic obstructive pulmonary disease patients. Multidiscip Respir Med. 2013;8:66.

15. Karadag F, Ozcan H, Karul AB, Ceylan E, Cildag O. Correlates of erectile dysfunction in moderate-to-severe chronic obstructive pulmonary disease patients. Respirology. 2007;12:248-53.

16. Luo L, Zhao S, Wang J, Liu Y, Zhu Z, Xiang Q, et al. Association between chronic obstructive pulmonary disease and risk of erectile dysfunction: a systematic review and meta-analysis. Int J Impot Res. 2020;32:159-66.

17. Schönhofer B. Sexuality in patients with restricted breathing. Med Klin (Munich). 2002;97:344-9.

18. Zegarra L, Loza C, Pérez V. Psychometric validation of the International Index of Erectile Function in patients with erectile dysfunction in Perú. Rev Peru Med Exp Salud Publica. 2011;28:477-83.

19. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology. 1997;49:822-30.

20. Maillé AR, Koning CJ, Zwinderman AH, Willems LN, Dijkman JH, Kaptein AA. The development of the "Quality-of-life for Respiratory Illness Questionnaire (QOL-RIQ)": a disease-specific quality-of-life questionnaire for patients with mild to moderate chronic non-specific lung disease. Respir Med. 1997;91:297-309.

21. Kaptein AA, van Klink RC, de Kok F, Scharloo M, Snoei L, Broadbent E, et al. Sexuality in patients with asthma and COPD. Respir Med. 2008;102:198-204.

22. Shen TC, Chen WC, Lin CL, Chen CH, Tu CY, Hsia TC, et al. The risk of erectile dysfunction in chronic obstructive pulmonary disease: a population-based cohort study in Taiwan. Medicine (Baltimore). 2015;94:e448.

23. Chung RY, Chan D, Woo J, Kwok T, Leung JC, Lai FT, et al. Erectile dysfunction is associated with subsequent cardiovascular and respiratory mortality in cohort of 1,436 Chinese elderly men. J Sex Med. 2015;12:1568-76.

24. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts male aging study. J Urol. 1994;151:54-61.

25. Echeverri Tirado LC, Ferrer JE, Herrera AM. Aging and erectile dysfunction. Sex Med Rev. 2016;4:63-73.

26. Cordero A, Bertomeu-Martínez V, Mazón P, Fácila L, Bertomeu-González V, Conthe P, et al. Erectile dysfunction in high-risk hypertensive patients treated with beta-blockade agents. Cardiovasc Ther. 2010;28:15-22.

27. Doumas M, Tsakiris A, Douma S, Grigorakis A, Papadopoulos A, Hounta A, et al. Beneficial effects of switching from beta-blockers to nebivolol on the erectile function of hypertensive patients. Asian J Androl. 2006;8:177-82.

28. Francis ME, Kusek JW, Nyberg LM, Eggers PW. The contribution of common medical conditions and drug exposures to erectile dysfunction in adult males. J Urol. 2007;178:591-6.

29. Baumhäkel M, Schlimmer N, Kratz M, Hackett G, Jackson G, Böhm M. Cardiovascular risk, drugs and erectile function--a systematic analysis. Int J Clin Pract. 2011;65:289-98.