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META-ANALYSIS

Zhao et al.: Galectin-3 and chronic obstructive pulmonary disease

Association between serum galectin-3 and chronic obstructive pulmonary disease: A

meta-analysis

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a significant public health issue characterized by progressive and irreversible airflow limitation. The aim of this metaanalysis was to determine the association between changes in serum galectin-3 levels and COPD and to assess the relationship between serum galectin-3 levels and acute exacerbations of COPD (AECOPD). Relevant observational studies were retrieved from electronic databases, including PubMed, Web of Science, Embase, Wanfang, and China National Knowledge Infrastructure (CNKI). A random-effects model was used to combine the data, incorporating the influence of between-study heterogeneity. Twelve case-control studies were included. The pooled results showed a significantly higher serum level of galectin-3 in patients with COPD compared to controls (standardized mean difference [SMD] 0.60; 95% confidence interval [CI] 0.40 - 0.80; P < 0.001; I = 68%). Further meta-analysis suggested higher levels of serum galectin-3 in patients with AECOPD compared to those with stable COPD (SMD 0.33; 95% CI 0.20 - 0.46; P < 0.001; $I^2 = 0\%$). Subgroup analyses according to the mean age of the participants, the proportion of males, and study quality scores did not significantly change the results (*P* for subgroup differences all > 0.05). In conclusion, patients with COPD were found to have higher serum levels of galectin-3, with levels further elevated in patients with AECOPD compared to those with stable COPD.

Keywords: Chronic obstructive pulmonary disease; galectin-3; acute exacerbation; biomarker.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a significant public health issue, often characterized by progressive and irreversible limitation of airflow [1-3]. The persistent airflow restriction is mainly due to bronchiolitis causing irreversible obstruction but could also be exacerbated by the destruction of lung tissue (emphysema) and excessive production of mucus (chronic bronchitis) [4]. Patients with COPD experience repeated episodes of greatly increased symptoms (acute exacerbations), which involve more pronounced local and systemic inflammation, leading to temporary deterioration in lung function, reduced quality of life, hospitalization, and increased risk for further disease progression [5, 6]. Due to the complex nature of COPD's pathophysiology, there is increasing interest in identifying potential biomarkers that can assist in both diagnosing and managing this condition [7, 8]. Galectin-3, a protein that binds to β -galactosides, has become a promising candidate due to its role in inflammation, fibrosis, tissue remodeling, and immune function [9-11]. An initial study involving patients with severe COPD indicated an elevated expression of galectin-3 and accumulation of neutrophils in the small airway epithelium [12]. This was found to be linked to epithelial proliferation and airway obstruction [12]. A subsequent preclinical investigation also suggested that exposure to cigarette smoke might trigger the release of galectin-3 in cultured airway epithelial cells, potentially contributing to the development of COPD [13]. However, previous studies examining changes in serum levels of galectin-3 among COPD patients have yielded conflicting findings [14-25]. While some studies reported higher serum levels of galectin-3 compared to healthy controls [18, 20, 23-25], others did not observe this difference [14, 17, 21, 22]. Given these uncertainties we aim to investigate the link between serum levels of galectn-3 and COPD through a meta-analysis.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (2020) [26, 27] was followed in this study. The Cochrane Handbook [28] for

systematic review and meta-analysis was referenced throughout the study. The study has been registered in Open Science Framework with the registration number of 10.17605/OSF.IO/WYCP7.

Search strategy

Five electronic databases including PubMed, Web of Science, Embase, Wanfang, and China National Knowledge Infrastructure (CNKI) were used for literature search with a predefined combined search term: (1) "chronic obstructive pulmonary disease" OR "COPD" OR "chronic obstructive lung disease" OR "chronic obstructive airway disease" OR "chronic obstructive airway disease" OR "emphysema" OR "chronic airflow limitation" OR "chronic airway obstruction" and (2) "galectin-3" OR "galectin 3". The search syntax used in the meta-analysis is shown in in Figure S1. Only studies with human subjects and published in English or Chinese peer-reviewed journals were included. A second-round check-up for the references of the relevant articles was also conducted. The final database search was achieved on January 25, 2024.

Inclusion and exclusion criteria

Inclusion criteria: (1) Observational studies in full-length articles; (2) Studies included adult patients with confirmed diagnosis of COPD without other concomitant cardiopulmonary diseases such as coronary artery disease, heart failure, or asthma etc., regardless of the disease status of COPD (AECOPD or stable COPD); (3) Serum galectin-3 was measured, and compared between patients with COPD and healthy controls, or between patients with AECOPD and stable COPD; (4) Difference of serum galectin-3 and its corresponding 95% confidence interval (CI) were reported or could be calculated from the original reports.

Reviews, meta-analysis, studies including patients with COPD and other concomitant cardiopulmonary diseases, studies measuring galectin-3 level in bronchoalveolar lavage fluid, or studies comparing serum galectin-3 between patients with COPD and patients with other cardiopulmonary diseases were excluded. For studies with potentially overlapped patient population, the one with the largest sample size was included in the meta-analysis.

Data collection and quality assessment

Two independent authors conducted literature search and analysis, data collection, and study quality assessing separately. If discrepancies were encountered, the corresponding author joined the discussion for final judgement. Data of study information, study design, diagnosis, demographic factors of the studied population, proportion of current smokers of the studied population, methods for measuring serum galectin-3 and variables that were adjusted or matched between cases and controls were extracted. Study quality assessment was achieved via the Newcastle–Ottawa Scale (NOS) [29] with scoring regarding the criteria for participant selection, comparability of the groups, and the validity of the outcomes. The scale ranged between 1-9 stars, with larger number of stars presenting higher study quality.

Ethical statement

Ethical approval was not required for this study in accordance with local/national guidelines. Written informed consent to participate in the study was not required in accordance with local/national guidelines.

Statistical analysis

The primary outcome of the meta-analysis was to investigate the difference between serum galectin-3 between patients with COPD and healthy controls, while the secondary outcome was to compare the serum galectin-3 between patients with AECOPD and stable COPD. The difference of serum galectin-3 between groups was summarized as standardized mean difference (SMD) and 95% CI because different methods were used for measuring galectin-3 [28]. Between study heterogeneity was estimated with the Cochrane Q test and the I² statistic [30, 31], with I² > 50% reflecting the significant statistical heterogeneity. A random-effect model was applied to combine the results by incorporating the influence of statistical heterogeneity [28]. Sensitivity analysis by excluding one study at a time was used to evaluate the robustness of the finding [28]. For the analysis with significant statistical heterogeneity, a univariate meta-regression analysis was performed to evaluate the potential impact of study

characteristics in continuous variables on the results, such as the mean age, percentile of males, and the NOS of the included studies. In addition, subgroup analysis was also performed to evaluate the study characteristics on the results, such as disease status, mean age, proportion of the males, and NOS, with the medians of the continuous variables as the cutoff values for defining subgroups. By construction of the funnel plots, the publication bias was estimated based on the visual judgement of the symmetry of the plots, supplemented with the Egger's regression asymmetry test [32]. A p < 0.05 reflects statistical significance. The RevMan (Version 5.1; Cochrane Collaboration, Oxford, UK) and Stata (version 17.0; Stata Corporation, College Station, TX) software packages were applied for these analyses.

RESULTS

Study inclusion

The process for identifying relevant studies for inclusion in the meta-analysis is presented in Figure 1. In brief, 342 potentially relevant records were obtained after comprehensive searches of the three databases, and 89 of them were excluded due to duplication. Subsequently, a screening via considering the titles and abstracts of the remaining records further led to the exclusion of 227 more studies, mostly because they were not related to the aim of the meta-analysis. Accordingly, the full texts of the 26 remaining records were read by two independent authors, and 14 of them were further removed for various reasons, as listed in Figure 1. Finally, 12 observational studies remained and were considered to be suitable for the subsequent quantitative analyses [14-25].

Overview of the study characteristics

Table 1 presents the summarized characteristics of the included studies. Overall, 12 casecontrol studies involving 1167 patients with COPD and 573 healthy controls were included in the meta-analysis (14-25). These studies were published between 2015 and 2024, and performed in Austria, the Netherlands, China, and Sweden. The mean ages of the included population were 47.7 to 69.2 years, with the percentiles of males of 37.9 to 77.5%. Serum galectin-3 was measured with the chemiluminescent microparticle immunoassay in one study (14), and with the enzyme-linked immunosorbent assay in the others (15-25). Potential variables such as age, sex, body mass index, and smoking status were matched or adjusted to a varying degree in ten studies (15-21, 23-25). The NOS of the included studies were six to nine stars, suggesting overall moderate to good study quality (Table 2).

Serum galectin-3 between patients with COPD and healthy controls

Nine studies compared serum level of galectin-3 between patients with COPD and healthy controls [14, 17, 18, 20-25]. Since four of them reported the difference of galectin-3 between cases and controls according to the disease status of COPD (AECOPD or stable COPD) [20, 21, 23, 25], these datasets were included independently, and the sample size of the control groups were equally split to avoid to overcome unit-of-analysis errors as detailed in Cochrane Handbook [28]. Overall, the pooled results showed a high serum level of galectin-3 in patients with COPD as compared to healthy controls (SMD: 0.60, 95% CI: 0.40 to 0.80, p < 0.001; I² = 68%; Figure 2).

Subsequent sensitivity analysis by excluding one dataset at a time showed consistent results (SMD: 0.55 to 0.65, p all < 0.05).

The meta-regression analysis suggested that study characteristics such as mean age, percentile of males, and NOS did nog significantly affect the results (Table 3). Results of the subgroup analysis showed according to disease status and mean age of the patients did not significantly affect the results (p for subgroup difference = 0.30 and 0.43, respectively; Figure 3A and 3B). A similar results were retrieved for studies with the proportions of the males \leq or > 60% (p for subgroup difference = 0.40; Figure 4A). In addition, the subgroup analysis according to the quality scores of the included studies did not significantly affect the results (p for subgroup difference = 0.55; Figure 4B).

Serum galectin-3 between patients with AECOPD and stable COPD

The meta-analysis with seven studies (15, 16, 19-21, 23, 25) further suggested a higher level of serum galectin-3 in patients with AECOPD as compared to stable COPD (SMD: 0.33, 95% CI: 0.20 to 0.46, p < 0.001; $I^2 = 0\%$; Figure 5A). Sensitivity analysis by omitting one study at a time did not significantly affect the results (SMD: 0.29 to 0.36, p all < 0.05). Further exploring meta-analysis suggested similar results in patients with mean ages < and ≥ 60 years, in studies with the proportions of the males \le or > 60%, and in studies with different quality scores (Figure 5B-5D, p for subgroup difference all > 0.05).

Publication bias evaluation

The funnel plots for the meta-analyses of the difference of serum galectin-3 between patients with COPD and health controls, and between patients with AECOPD and stable COPD are shown in Figure 6A and 6B. The symmetrical nature of the funnel plots suggested a low likelihood of publication biases. Results of the Egger's regression test also showed low risks of publication biases underlying the meta-analyses (p = 0.91 and 0.78, respectively).

DISCUSSION

This meta-analysis synthesized the findings from 12 case-control studies and found that individuals with COPD had higher levels of galectin-3 in their serum compared to healthy controls. Furthermore, it was noted that individuals experiencing acute exacerbations of COPD also had elevated levels of galectin-3 compared to those with stable COPD. Subsequent subgroup analyses according to age, sex, and study quality scores showed similar results. These findings indicate that increased serum galectin-3 levels could serve as a potential biomarker for both chronic and acute states of COPD.

This research may represent the first meta-analysis to compile data on the changes in serum galectin-3 levels among COPD patients. Before interpreting the results, it is important to acknowledge the rigorous methodology applied in this meta-analysis. A comprehensive search of five widely used electronic databases yielded 12 recent observational studies

relevant to this meta-analysis's objectives. Moreover, only studies involving COPD patients without other concurrent cardiopulmonary conditions were considered, aiming to minimize potential confounding effects from comorbidities on the meta-analysis results. Additionally, various sensitivity and subgroup analyses confirmed the robustness of the primary findings and indicated that neither individual datasets nor study characteristics such as mean ages, percentage of males or study quality scores significantly influenced the outcomes. Overall, these results highlight the potential utility of serum galectin-3 as a marker for identifying COPD and AECOPD patients, particularly among current smokers.

The potential reasons for the connection between elevated galectin-3 and COPD are complex. One study revealed increased galectin-3 expression in the small airway epithelium of COPD patients, along with an accumulation of neutrophils, which may contribute to epithelial growth and airway blockage in these individuals [12]. Another study found that exposure to cigarette smoke extract notably raised galectin-3 gene expression in airway epithelial cells from COPD patients but not those from healthy controls [13]. The induction of galectin-3 following cigarette smoke exposure was associated with neutrophilic airway inflammation [13]. Lastly, a recent study suggested that the build-up of galectin-3 in bronchial epithelial cells isolated from COPD patients could indicate insufficient autophagic breakdown and accelerated cellular aging—both known mechanisms underlying COPD progression [33]. Further research is necessary to uncover the main molecular pathways responsible for the link between increased galectin-3 levels and COPD.

Overall, the meta-analysis on serum galectin-3 levels in COPD reveals its potential as a diagnostic biomarker and prognostic indicator, with elevated levels associated with disease presence and exacerbations. Clinically, galectin-3 could aid in early COPD detection, stratification of patients based on exacerbation risk, and serve as a therapeutic target. Future research should focus on longitudinal studies to validate these associations, mechanistic investigations to understand its role in COPD pathophysiology, clinical trials to evaluate

targeted interventions, and subgroup analyses to identify responsive patient groups. Overall, galectin-3 shows promise in improving COPD management by providing insights into disease mechanisms and guiding personalized treatment strategies.

This study also has some limitations that should be noted. One significant issue is that this meta-analysis focused on comparing the different serum levels of galectin-3 between cases and controls, and it did not determine the optimal cutoff value of galectin-3 for discriminating COPD and AECOPD from the patient population. Additionally, all included studies were case-control studies with a cross-sectional design. Therefore, evaluating the dynamic changes of serum galectin-3 during COPD exacerbation and following treatments is necessary. Moreover, other potential confounding factors may affect the association between serum galectin-3 and COPD. For example, statins have been suggested to influence the level of serum galectin-3, which therefore may influence the association between galectin-3 and COPD (34). Lastly, our meta-analysis solely included observational studies, thus precluding the establishment of a causal relationship between galectin-3 in the development and acute exacerbation of COPD.

CONCLUSION

The results of the meta-analysis indicate that patients with COPD had higher serum galectin-3 levels. Moreover, individuals with AECOPD exhibited elevated galectin-3 compared to those with stable COPD. While further prospective studies are required to validate the connection between increased serum galectin-3 and the onset and acute exacerbation of COPD, this meta-analysis supports the potential utility of serum galectin-3 as a biomarker for identifying patients with COPD and AECOPD.

Data availability

All the data generated during the study are included within the manuscript.

REFERENCES

- Celli BR, Wedzicha JA. Update on Clinical Aspects of Chronic Obstructive Pulmonary Disease. N Engl J Med. 2019;381(13):1257-66.
- Christenson SA, Smith BM, Bafadhel M, Putcha N. Chronic obstructive pulmonary disease. Lancet. 2022;399(10342):2227-42.
- Mah J, Ritchie AI, Finney LJ. Selected updates on chronic obstructive pulmonary disease. Curr Opin Pulm Med. 2024;30(2):136-40.
- Agusti A, Hogg JC. Update on the Pathogenesis of Chronic Obstructive Pulmonary Disease. N Engl J Med. 2019;381(13):1248-56.
- Zhang J, Yi Q, Zhou C, Luo Y, Wei H, Ge H, et al. Characteristics, treatments, in-hospital and long-term outcomes among inpatients with acute exacerbation of chronic obstructive pulmonary disease in China: sex differences in a large cohort study. BMC Pulm Med. 2024;24(1):125.
- 6. Bhatt SP. Predicting Chronic Obstructive Pulmonary Disease Exacerbations: When the Past Does Not Inform the Future. Ann Am Thorac Soc. 2024;21(3):382-3.
- Hogea SP, Tudorache E, Fildan AP, Fira-Mladinescu O, Marc M, Oancea C. Risk factors of chronic obstructive pulmonary disease exacerbations. Clin Respir J. 2020;14(3):183-97.

- Mathioudakis AG, Janssens W, Sivapalan P, Singanayagam A, Dransfield MT, Jensen JS, et al. Acute exacerbations of chronic obstructive pulmonary disease: in search of diagnostic biomarkers and treatable traits. Thorax. 2020;75(6):520-7.
- Bouffette S, Botez I, De Ceuninck F. Targeting galectin-3 in inflammatory and fibrotic diseases. Trends Pharmacol Sci. 2023;44(8):519-31.
- 10. Stojanovic BS, Stojanovic B, Milovanovic J, Arsenijevic A, Dimitrijevic Stojanovic M, Arsenijevic N, et al. The Pivotal Role of Galectin-3 in Viral Infection: A Multifaceted Player in Host-Pathogen Interactions. Int J Mol Sci. 2023;24(11).
- Sharma JR, Dubey A, Yadav UCS. Cigarette smoke-induced galectin-3 as a diagnostic biomarker and therapeutic target in lung tissue remodeling. Life Sci. 2024;339:122433.
- Pilette C, Colinet B, Kiss R, Andre S, Kaltner H, Gabius HJ, et al. Increased galectin-3 expression and intra-epithelial neutrophils in small airways in severe COPD. Eur Respir J. 2007;29(5):914-22.
- 13. Pouwels SD, Hesse L, Faiz A, Lubbers J, Bodha PK, Ten Hacken NH, et al. Susceptibility for cigarette smoke-induced DAMP release and DAMP-induced inflammation in COPD. Am J Physiol Lung Cell Mol Physiol. 2016;311(5):L881-L92.
- 14. Mueller T, Leitner I, Egger M, Haltmayer M, Dieplinger B. Association of the biomarkers soluble ST2, galectin-3 and growth-differentiation factor-15 with heart failure and other non-cardiac diseases. Clin Chim Acta. 2015;445:155-60.

- 15. Pouwels SD, Nawijn MC, Bathoorn E, Riezebos-Brilman A, van Oosterhout AJ, Kerstjens HA, et al. Increased serum levels of LL37, HMGB1 and S100A9 during exacerbation in COPD patients. Eur Respir J. 2015;45(5):1482-5.
- 16. Feng W, Wu X, Li S, Zhai C, Wang J, Shi W, et al. Association of Serum Galectin-3 with the Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Med Sci Monit. 2017;23:4612-8.
- 17. Shen YH, Lu HY, Shen YQ, Chen R, Wu K, Gao XY. Clinical significance of serum galectin-3 and VAP-1 levels in patients with stable chronic obstructive pulmonary disease. Chin J Moder Med. 2018;28(32):107-11.
- Li HX, Zhang BJ, Ying F, Zhou LL. A study on the correlation between serum Gal-3 levels and cardiopulmonary function in stable COPD patients. Zhejiang J Clin Med. 2019;21(11):1467-9.
- Liu ZZ, Zhang J. Changes and clinical significance of serum Galectin-3 in patients with AECOPD. Clin Pulm J. 2019;24(3):450-3.
- 20. Du WH, Ji H, Li WS, Yan ZH, Zhu YL, Du ZP. Correlation Analysis of Serum Galectin 3, IL-38 Levels with Pulmonary Function in Patients with Chronic Obstructive
 Pulmonary Disease. J Clin Transfus Lab Med. 2020;22(2):152-6.
- 21. Mao JH, Wang HF, Yang LP. Changes and significance of Galectin 3 in patients with chronic obstructive pulmonary disease. Chin J Health Lab Tech. 2020;30(22):2768-73.

- 22. Sundqvist M, Andelid K, Ekberg-Jansson A, Bylund J, Karlsson-Bengtsson A, Linden A. Systemic Galectin-3 in Smokers with Chronic Obstructive Pulmonary Disease and Chronic Bronchitis: The Impact of Exacerbations. Int J Chron Obstruct Pulmon Dis. 2021;16:367-77.
- 23. Wang W, Wu W, Wang B, Zhang LC, Gao F. Diagnostic value of serum galectin-3 and interleukin-17 in acute exacerbation of chronic obstructive pulmonary disease. Chin Med. 2021;16(4):530-4.
- 24. Wang XL, Chen XF, Zhao XY, Huang H. The expression and correlation analysis of serum galectin-3 and miR-128-3p in patients with chronic obstructive pulmonary disease complicated pulmonary arterial hypertension. J Trop Med. 2023;23(1):30-4.
- 25. Zhang F, Ma GQ, He XL, La YN, Ma L, Chen XP. Diagnostic value of Tei index combined with serum Gal-3 and LCN-1 in COPD. Clin Pulm J. 2024;29(1):40-7.
- 26. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
- 27. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372:n160.

- 28. Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.2. The Cochrane Collaboration. 2021;<u>www.training.cochrane.org/handbook</u>.
- 29. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2010;http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
- 30. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539-58.
- 31. Patsopoulos NA, Evangelou E, Ioannidis JP. Sensitivity of between-study heterogeneity in meta-analysis: proposed metrics and empirical evaluation. Int J Epidemiol. 2008;37(5):1148-57.
- 32. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ: 1997;315(7109):629-34.
- 33. Araya J, Saito N, Hosaka Y, Ichikawa A, Kadota T, Fujita Y, et al. Impaired TRIM16-Mediated Lysophagy in Chronic Obstructive Pulmonary Disease Pathogenesis. J Immunol. 2021;207(1):65-76.
- 34. Kadoglou NP, Sfyroeras GS, Spathis A, Gkekas C, Gastounioti A, Mantas G, et al. Galectin-3, Carotid Plaque Vulnerability, and Potential Effects of Statin Therapy. Eur J Vasc Endovasc Surg. 2015;49(1):4-9.

TABLES AND FIGURES WITH LEGENDS

TABLE 1. Characteristics of the included studies

| Study | Country | Design | No. of patients with AECOPD | No. of patients with stable COPD | No. of healthy controls | Mean age (years) | Males (%) | Current smoking (%) | Methods for measuring serum Gal-3 | Variables matched or adjusted |
|-----------------|--------------------|--------|--------------------------------------|---|-------------------------------|---------------------|-----------|---------------------------|---|-------------------------------------|
| Mueller 2015 | Austria | CC | 15 | 0 | 22 | 48.1 | 70.3 | 32.4 | CMIA | None |
| Pouwels 2015 | The Netherlands | СС | 40 | 40 | | 63.6 | 77.5 | 45 | ELISA | Age, sex, smoking, and BMI |
| Feng 2017 | China | СС | 44 | 44 | 0 | 69.2 | 77.3 | 20.5 | ELISA | Age, sex, smoking, and BMI |
| Shen 2018 | China | CC | 0 | 100 | 100 | 55.2 | 79 | NR | ELISA | Age, sex, and smoking |
| Liu 2019 | China | СС | 60 | 60 | 0 | 68.7 | 76.7 | 63.3 | ELISA | Age, sex, BMI, and smoking |
| Li 2019 | China | CC | 0 | 42 | 30 | 47.7 | 50 | NR | ELISA | Age and sex |

| Du 2020 | China | СС | 151 | 107 | 129 | 68.9 | 57.9 | NR | ELISA | Age and sex |
|-------------------|--------|----|-----|-----|-----|------|------|------|-------|----------------------|
| Mao 2020 | China | СС | 40 | 40 | 40 | 56.7 | 60 | NR | ELISA | Age and sex |
| Sundqvist 2021 | Sweden | СС | 0 | 56 | 20 | 61.4 | 37.9 | 82.1 | ELISA | None |
| Wang 2021 | China | СС | 71 | 79 | 74 | 58 | 59.5 | NR | ELISA | Age and sex |
| Wang 2023 | China | СС | 0 | 64 | 60 | 64.2 | 66.9 | NR | ELISA | Age, sex, and BMI |
| Zhang 2024 | China | CC | 60 | 54 | 98 | 56.2 | 61.3 | NR | ELISA | Age, sex, and BMI |

COPD: Chronic obstructive pulmonary disease; AECOPD: Acute exacerbated COPD; Gal-3: Galectin-3; CMIA: Chemiluminescent microparticle immunoassay;

ELISA: Enzyme-linked immunosorbent assay; CC: Case-control; BMI: Body mass index; NR: Not reported.

| Study | Adequate definition of the cases | Representativeness of the cases | Selection of controls | Definition of controls | Controlled for age and sex | Controlled for other confoundings | Ascertainment of the exposure | Same method of ascertainment of exposure for cases and controls | Non- response rate | Overall |
|----------------|---|------------------------------------|--------------------------|---------------------------|----------------------------------|---|----------------------------------|--|--------------------------|---------|
| Mueller 2015 | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 1 | 6 |
| Pouwels 2015 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Feng 2017 | 1 | 0 | 1 | 1 | | 1 | 1 | 1 | 1 | 8 |
| Shen 2018 | 0 | 0 | 1 | 1 | Ì, | 1 | 1 | 1 | 1 | 7 |
| Liu 2019 | 1 | 1 | 1 | | 1 | 1 | 1 | 1 | 1 | 9 |
| Li 2019 | 1 | 0 | | | 1 | 0 | 1 | 1 | 1 | 7 |
| Du 2020 | 0 | 1 | 1 | | 1 | 0 | 1 | 1 | 1 | 7 |
| Mao 2020 | 1 | 1 | | 1 | 1 | 0 | 1 | 1 | 1 | 8 |
| Sundqvist 2021 | 1 | 0 | | 1 | 0 | 0 | 1 | 1 | 1 | 6 |
| Wang 2021 | 1 | 0 | y ₁ | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Wang 2023 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Zhang 2024 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 9 |

TABLE 2. Study quality evaluation via the Newcastle-Ottawa Scale

 TABLE 3. Univariate meta-regression analysis for the SMD of serum Gal-3 between

 patients with COPD and healthy controls

| Variables | SMD of serum Gal-3 | | | | | | | | | |
|------------------|--------------------|-------------------|----------|--|--|--|--|--|--|--|
| | Coefficient | 95% CI | P values | | | | | | | |
| Mean age (years) | 0.013 | -0.025 to 0.050 | 0.48 | | | | | | | |
| Males (%) | -0.0088 | -0.0343 to 0.0168 | 0.47 | | | | | | | |
| NOS | 0.062 | -0.204 to 0.327 | 0.62 | | | | | | | |

COPD: Chronic obstructive pulmonary disease; SMD: Standardized mean difference; Gal-3:

Galectin 3; CI: Confidence interval; NOS: Newcastle-Ottawa Scale.

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| | c | OPD | | С | ontrol | | \$ | Std. Mean Difference | Std. Mean Difference |
|---|----------------------|---------|---------|----------|--------|----------|--------|----------------------|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% Cl |
| Mueller 2015 | 14 | 10.4 | 15 | 13 | 10.4 | 22 | 5.2% | 0.09 [-0.56, 0.75] | |
| Shen 2018 | 11.5 | 16.7 | 100 | 8.5 | 18.4 | 100 | 9.6% | 0.17 [-0.11, 0.45] | |
| Li 2019 | 26.2 | 12.7 | 42 | 12.2 | 19.5 | 30 | 6.9% | 0.87 [0.38, 1.36] | |
| Du 2020 AECOPD | 33.3 | 20.5 | 151 | 17.74 | 10.2 | 65 | 9.3% | 0.86 [0.56, 1.16] | |
| Du 2020 stable COPD | 28.5 | 17.3 | 107 | 17.74 | 10.2 | 64 | 9.1% | 0.71 [0.39, 1.03] | |
| Mao 2020 AECOPD | 11.4 | 13.6 | 40 | 7.6 | 19.9 | 20 | 6.4% | 0.24 [-0.30, 0.77] | |
| Mao 2020 stable COPD | 8.5 | 10.4 | 40 | 7.6 | 19.9 | 20 | 6.4% | 0.06 [-0.47, 0.60] | |
| Sundqvist 2021 | 12.8 | 10.2 | 56 | 10.1 | 18.8 | 20 | 6.7% | 0.21 [-0.31, 0.72] | |
| Wang 2021 AECOPD | 35.1 | 18.9 | 71 | 14.1 | 11.2 | 37 | 7.6% | 1.25 [0.82, 1.68] | |
| Wang 2021 stable COPD | 27.2 | 16.5 | 79 | 14.1 | 11.2 | 37 | 8.0% | 0.87 [0.46, 1.27] | |
| Wang 2023 | 27.4 | 22.1 | 64 | 15.02 | 19.1 | 60 | 8.6% | 0.59 [0.23, 0.95] | |
| Zhang 2024 AECOPD | 33.87 | 19.4 | 60 | 16 | 16.6 | 49 | 8.0% | 0.98 [0.58, 1.37] | |
| Zhang 2024 stable COPD | 25.87 | 18.4 | 54 | 16 | 16.6 | 49 | 8.1% | 0.56 [0.16, 0.95] | |
| Total (95% CI) | | | 879 | | | 573 | 100.0% | 0.60 [0.40, 0.80] | • |
| Heterogeneity: Tau ² = 0.09; | Chi ² = 3 | 7.58, 0 | df = 12 | (P = 0.0 |)002); | l² = 689 | % | | |
| Test for overall effect: Z = 5 | .84 (P < | 0.000 | 01) | - | ,. | | | | -2 -1 U 1 2 Lower Gal-3 in COPD Higher Gal-3 in COPD |
| | | | | | | | | | Lower Gallo III GOLD Thigher Gallo III GOLD |

FIGURE 2. Forest plots for the meta-analysis comparing the serum galectin-3 level between patients with COPD and healthy controls.

| | 0 | OPD | | C | ontrol | | | Std Mean Difference | Std Mean Difference |
|---|---|--|---|--|---|---|---|--|---|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV Random 95% Cl | IV Random 95% Cl |
| 1.2.1 AECOPD versus con | ntrol | 00 | Total | mean | 00 | Total | Weight | | |
| Mueller 2015 | 14 | 10.4 | 15 | 13 | 10.4 | 22 | 5.2% | 0.09[-0.56, 0.75] | _ |
| Du 2020 AECOPD | 33.3 | 20.5 | 151 | 17.74 | 10.2 | 65 | 9.3% | 0.86 [0.56, 1.16] | |
| Mao 2020 AECOPD | 11.4 | 13.6 | 40 | 76 | 10.2 | 20 | 6.4% | 0.24 [-0.30, 0.77] | |
| Wang 2021 AECOPD | 35.1 | 18.9 | 71 | 14.1 | 11.2 | 37 | 7.6% | 1 25 [0 82 1 68] | |
| Zhang 2024 AECOPD | 33.87 | 10.0 | 60 | 16 | 16.6 | 10 | 8.0% | 0.98 [0.58, 1.37] | |
| Subtotal (95% CI) | 55.07 | 13.4 | 337 | 10 | 10.0 | 193 | 36.6% | 0.74 [0.37, 1.10] | • |
| Heterogeneity: $Tau^2 = 0.12$ | $Chi^2 = 1$ | 3 66 (| df = 4 (1) | P = 0.00 | 18)∙ I² : | = 71% | | | |
| Test for overall effect: $Z = 3$ | 8.95 (P < | 0.000 | 1) | 0.00 | 50), 1 | / 1/0 | | | |
| 1.2.2 Stable COPD versus | control | | | | | | | | |
| Shen 2018 | 11.5 | 16.7 | 100 | 8.5 | 18.4 | 100 | 9.6% | 0.17 [-0.11, 0.45] | + |
| Li 2019 | 26.2 | 12.7 | 42 | 12.2 | 19.5 | 30 | 6.9% | 0.87 [0.38, 1.36] | — |
| Du 2020 stable COPD | 28.5 | 17.3 | 107 | 17.74 | 10.2 | 64 | 9.1% | 0.71 [0.39, 1.03] | - |
| Mao 2020 stable COPD | 8.5 | 10.4 | 40 | 7.6 | 19.9 | 20 | 6.4% | 0.06 [-0.47, 0.60] | _ |
| Sundavist 2021 | 12.8 | 10.2 | 56 | 10.1 | 18.8 | 20 | 6.7% | 0.21 [-0.31, 0.72] | - - |
| Wang 2021 stable COPD | 27.2 | 16.5 | 79 | 14.1 | 11.2 | 37 | 8.0% | 0.87 [0.46, 1.27] | —— |
| Wang 2023 | 27.4 | 22.1 | 64 | 15.02 | 19.1 | 60 | 8.6% | 0.59 [0.23, 0.95] | - |
| Zhang 2024 stable COPD | 25.87 | 18.4 | 54 | 16 | 16.6 | 49 | 8.1% | 0.56 [0.16, 0.95] | — - |
| Subtotal (95% CI) | 20101 | | 542 | | | 380 | 63.4% | 0.51 [0.30, 0.73] | • |
| Heterogeneity: $Tau^2 = 0.05$: | : Chi² = 1 | 6.60. (| df = 7 (| P = 0.02 | 2): ² = | 58% | | • • • | |
| Test for overall effect: Z = 4 | .66 (P < | 0.000 | 01) | | -,, - | | | | |
| | | | | | | | | | |
| Total (95% CI) | | | 879 | | | 573 | 100.0% | 0.60 [0.40, 0.80] | |
| Total (95% CI) Heterogeneity: Tau ² = 0.09 | : Chi² = 3 | 37.58 | 879 df = 12 | (P = 0.0) | 002): | 573 1 ² = 68 ⁰ | 100.0% % | 0.60 [0.40, 0.80] | i |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 | ; Chi² = 3 5.84 (P < | 87.58, o | 879 df = 12 01) | (P = 0.0 | 0002); | 573 ² = 689 | 100.0% % | 0.60 [0.40, 0.80] | -2 -1 0 1 2 |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subgroup difference | ; Chi² = 3 5.84 (P < es: Chi² : | 87.58, 0 0.0000 = 1.08. | 879 df = 12 01) df = 1 | (P = 0.0 | 0002); 30), I² = | 573 I² = 689 = 7.8% | 100.0% % | 0.60 [0.40, 0.80] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference | ; Chi² = 3 5.84 (P < es: Chi² : | 87.58, 0 0.0000 = 1.08. | 879 df = 12 01) . df = 1 | (P = 0.0 (P = 0.3 | 0002); 30). I² = | 573 ² = 689 = 7.8% | 100.0% % | 0.60 [0.40, 0.80] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference | ; Chi² = 3 5.84 (P < es: Chi² : 0 | 87.58, 0 0.0000 = 1.08. COPD | 879 df = 12 01) . df = 1 | (P = 0.0 (P = 0.3 C | 0002); 30). I² = | 573 ² = 689 = 7.8% | 100.0% % | 0.60 [0.40, 0.80] Std. Mean Difference | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup | ; Chi² = 3 5.84 (P < es: Chi² : C Mean | 87.58, 0 0.0000 = 1.08. COPD SD | 879 df = 12 01) . df = 1 <u>Total</u> | (P = 0.0 (P = 0.3 C <u>Mean</u> | 0002); 30). I ² = ontrol SD | 573 ² = 689 = 7.8% <u>Total</u> | 100.0% % Weight | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% CI | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years | ; Chi² = 3 5.84 (P < es: Chi² : C Mean | 37.58, 0 0.0000 = 1.08. COPD SD | 879 df = 12 01) . df = 1 <u>Total</u> | (P = 0.0 (P = 0.3 C <u>Mean</u> | 0002); 30). I ² : ontrol SD | 573 I ² = 689 = 7.8% <u>Total</u> | 100.0% % Weight | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% CI | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 | ; Chi ² = 3 5.84 (P < es: Chi ² = 0 <u>Mean</u> ; 14 | 87.58, 0 0.0000 = 1.08. COPD SD 10.4 | 879 df = 12 01) . df = 1 <u>Total</u> | (P = 0.((P = 0.3 C <u>Mean</u> 13 | 0002); 30). I ² = ontrol <u>SD</u> 10.4 | 573 ² = 689 = 7.8% <u>Total</u> 22 | 100.0% % Weight 5.2% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 | ; Chi ² = 3 5.84 (P < es: Chi ² : 0 <u>Mean</u> ; 14 11.5 | 07.58, 0 0.0000 = 1.08. COPD SD 10.4 16.7 | 879 df = 12 01) . df = 1 <u>Total</u> 15 100 | (P = 0.0 (P = 0.3 C <u>Mean</u> 13 8.5 | 0002); 30). I ² = ontrol SD 10.4 18.4 | 573 I ² = 689 = 7.8% <u>Total</u> 22 100 | 100.0% % Weight 5.2% 9.6% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% Cl 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 | ; Chi ² = 3 5.84 (P < es: Chi ² = (<u>Mean</u> ; 14 11.5 26.2 | 07.58, 0 0.0000 = 1.08. COPD SD 10.4 16.7 12.7 | 879 df = 12 01) . df = 1 <u>Total</u> 15 100 42 | (P = 0.0 (P = 0.3 C <u>Mean</u> 13 8.5 12.2 | 0002); 30). I ² = ontrol SD 10.4 18.4 19.5 | 573 I ² = 689 = 7.8% <u>Total</u> 22 100 30 | 100.0% % Weight 5.2% 9.6% 6.9% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD | ; Chi ² = 3 i.84 (P < es: Chi ² : | 37.58, 0 0.0000 = 1.08. COPD SD 10.4 16.7 12.7 13.6 | 879 df = 12 01) . df = 1 Total 15 100 42 40 | (P = 0.0 (P = 0.3 C Mean 13 8.5 12.2 7.6 | 0002); 30). I ² = ontrol SD 10.4 18.4 19.5 19.9 | 573 I ² = 689 = 7.8% <u>Total</u> 22 100 30 20 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 stable COPD | ; Chi ² = 3 i.84 (P < es: Chi ² : | 37.58, 0 0.0000 = 1.08. COPD SD 10.4 16.7 12.7 13.6 10.4 | 879 df = 12 01) df = 1 Total 15 100 42 40 40 | (P = 0.0 (P = 0.3 C Mean 13 8.5 12.2 7.6 7.6 | 0002); 30). I ² = ontrol SD 10.4 18.4 19.5 19.9 19.9 | 573 ² = 68 ⁹ = 7.8% <u>Total</u> 22 100 30 20 20 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 6.4% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 stable COPD Wang 2021 AECOPD | ; Chi ² = 3 5.84 (P < es: Chi ² = 0 <u>Mean</u> 5 114 11.5 26.2 11.4 8.5 35.1 | 37.58, c 0.0000 = 1.08. COPD SD 10.4 16.7 12.7 13.6 10.4 18.9 | 879 df = 12 01) df = 1 Total 15 100 42 40 40 71 | (P = 0.0 (P = 0.3 C Mean 13 8.5 12.2 7.6 7.6 14.1 | 0002); 30). ² = 000000000000000000000000000000000000 | 573 ² = 689 = 7.8% <u>Total</u> 22 100 30 20 20 37 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 6.4% 7.6% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 AECOPD Wang 2021 AECOPD Wang 2021 stable COPD | ; Chi ² = 3 5.84 (P < es: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 11.4 8.5 35.1 27.2 | 0.0000 1.08. 0.0000 1.08. 0.00000 0.00000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 0.0000 | 879 df = 12 01) df = 1 Total 15 100 42 40 40 71 79 | (P = 0.0 (P = 0.3 C Mean 13 8.5 12.2 7.6 7.6 14.1 14.1 | 0002); 30). ² = 000000000000000000000000000000000000 | 573 ² = 68 ⁹ = 7.8% Total 22 100 30 20 20 37 37 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 6.4% 7.6% 8.0% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random. 95% Cl 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 stable COPD Wang 2021 AECOPD Wang 2021 stable COPD Subtotal (95% CI) | ; Chi ² = 3 5.84 (P < es: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 11.4 8.5 35.1 27.2 | 07.58, 0 0.0000 = 1.08. COPD SD 10.4 16.7 12.7 13.6 10.4 18.9 16.5 | 879 df = 12 01) df = 1 <u>Total</u> 15 100 42 40 40 71 79 387 | (P = 0.0 (P = 0.3 C Mean 13 8.5 12.2 7.6 7.6 7.6 14.1 14.1 | 0002); 30). I ² = ontrol SD 10.4 18.4 19.5 19.9 19.9 11.2 11.2 | 573 ² = 68 ⁹ = 7.8% Total 22 100 30 20 20 37 37 266 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 7.6% 8.0% 50.2% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 AECOPD Wang 2021 AECOPD Wang 2021 stable COPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; | ; Chi ² = 3 5.84 (P < es: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 11.4 8.5 35.1 27.2 ; Chi ² = 2 | 27.58, 0 0.0000 = 1.08. COPD SD 10.4 16.7 12.7 13.6 10.4 18.9 16.5 27.24, 0 | 879 df = 12 01) df = 1 15 100 42 40 40 71 79 387 df = 6 (1 | (P = 0.0 (P = 0.3 (P = 0.3 (P = 0.3 (P = 0.3 (P = 0.3 (P = 0.0 (P = 0.0) | 0002); 30). ² = ontrol 5D 10.4 18.4 19.5 19.9 19.9 11.2 11.2 001); ² | 573 ² = 68° = 7.8% Total 22 100 30 20 20 37 37 266 = 78% | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 7.6% 8.0% 50.2% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] | Std. Mean Difference IV. Random. 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 Stable COPD Wang 2021 AECOPD Wang 2021 AECOPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: Z = 2 | ; Chi ² = 3 5.84 (P < es: Chi ² = 0 0 0 0 0 0 0 0 0 0 0 0 0 | 57.58, 6 0.0000 = 1.08. COPD SD 10.4 16.7 12.7 13.6 10.4 18.9 16.5 (7.24, 0.005) | 879 df = 12 01) df = 1 15 100 42 40 40 71 79 387 df = 6 (l | (P = 0.0 (P = 0.3 C 13 8.5 12.2 7.6 7.6 7.6 14.1 14.1 P = 0.00 | 0002); 30). ² = ontrol <u>SD</u> 10.4 18.4 19.5 19.9 19.9 11.2 11.2 001); ² | 573 ² = 68° = 7.8% <u>Total</u> 22 100 30 20 20 37 37 266 = 78% | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 7.6% 8.0% 50.2% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% Cl 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] | Std. Mean Difference IV. Random, 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 stable COPD Wang 2021 AECOPD Wang 2021 stable COPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: Z = 2 1.3.2 Mean age ≥ 60 year | ; Chi ² = 3 5.84 (P < es: Chi ² = Mean 14 11.5 26.2 11.4 8.5 35.1 27.2 ; Chi ² = 2 2.81 (P = | 57.58, (0.0000 = 1.08. COPD 5D 10.4 16.7 12.7 13.6 10.4 18.9 16.5 27.24, (0.005) | 879 df = 12 201) df = 1 15 100 42 40 40 71 79 387 df = 6 (l | (P = 0.0 (P = 0.3 C 13 8.5 12.2 7.6 7.6 14.1 14.1 14.1 P = 0.00 | 0002); 30). ² = 00000 50 10.4 18.4 19.5 19.9 19.9 11.2 11.2 11.2 2001); ² | 573 ² = 68% = 7.8% <u>Total</u> 22 100 20 20 37 266 = 78% | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 6.4% 6.4% 5.0% 50.2% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] | Std. Mean Difference IV. Random. 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Wang 2021 AECOPD Wang 2021 AECOPD Wang 2021 AECOPD Wang 2021 AECOPD Wang 2021 AECOPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: Z = 2 1.3.2 Mean age \geq 60 year Du 2020 AECOPD | ; Chi ² = 3 i.84 (P < es: Chi ² = | 57.58, (0.0000 = 1.08. COPD 5D 10.4 16.7 12.7 13.6 10.4 18.9 16.5 7.24, (0.005) 20.5 | 879 df = 12 01) df = 1 Total 15 100 42 40 40 71 79 387 74 df = 6 (l | (P = 0.0 (P = 0.3 C Mean 13 8.5 12.2 7.6 7.6 14.1 14.1 P = 0.00 17.74 | 0002); 30). I ² = ontrol <u>SD</u> 10.4 18.4 19.9 19.9 11.2 11.2 001); I ² 10.2 | 573 1 ² = 68 ² = 7.8% <u>Total</u> 22 100 30 20 30 20 37 37 266 65 | 100.0% % Weight 5.2% 9.6% 6.4% 6.4% 6.4% 7.6% 8.0% 50.2% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% Cl 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] 0.86 [0.56, 1.16] | Std. Mean Difference IV. Random, 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Wang 2021 AECOPD Wang 2021 AECOPD Wang 2021 stable COPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: Z = 2 1.3.2 Mean age \geq 60 year Du 2020 stable COPD Du 2020 stable COPD | ; Chi ² = 3 5,84 (P < es: Chi ² = 0 0 14 11.5 26.2 11.4 8.5 35.1 27.2 2.81 (P = 2.81 (P = 33.3 28.5 | 67.58, (0.0000 = 1.08. COPD 5D 10.4 16.7 12.7 13.6 10.4 16.5 16.5 27.24, (0.005) 20.5 17.3 | 879 df = 12 01) df = 1 Total 15 100 42 40 40 71 79 387 7df = 6 (l) | (P = 0.((P = 0.3) (P = 0.3) (P = 0.3) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.1) (P = 0.2) (P = 0.2) (P = 0.2) (P = 0.3) (P = 0. | 0002); 30). ² = ontrol <u>SD</u> 10.4 19.9 19.9 19.9 11.2 11.2 2001); ² 10.2 10.2 | 573 1 ² = 68 ^c 7.8% Total 22 100 30 20 30 20 30 20 37 266 = 7.8% 65 64 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 7.6% 8.0% 50.2% 9.3% 9.3% 9.1% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] | Std. Mean Difference IV. Random, 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Wang 2021 AECOPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: Z = 2 1.3.2 Mean age \geq 60 year Du 2020 stable COPD Sundqvist 2021 | ; Chi ² = 3 5.84 (P < es: Chi ² = Mean 14 11.5 26.2 11.4 8.5 35.1 27.2 ; Chi ² = 2 2.81 (P = * 33.3 28.5 12.8 | 57.58, (0.0000 = 1.08. COPD 5D 10.4 16.7 12.7 13.6 10.4 18.9 16.5 7.24, (0.005) 20.5 17.3 10.2 | 879 df = 12 01) df = 1 15 100 42 40 40 40 71 79 387 79 387 101 107 56 | (P = 0.0 (P = 0.3) (P = 0.3) (P = 0.3) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.1) (P = 0.1) (P = 0.1) (P = 0.3) (P = 0. | 0002); 30). ² = ontrol <u>SD</u> 10.4 18.4 19.5 19.9 19.9 11.2 11.2 11.2 001); ² 10.2 10.2 10.2 10.2 10.2 | 573 1 ² = 68 ^c 7.8% Total 22 100 30 20 30 20 37 36 65 64 20 26 26 26 26 26 26 26 26 20 20 20 20 20 20 20 20 20 20 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 6.4% 50.2% 9.3% 9.1% 6.7% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] | Std. Mean Difference IV. Random, 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Wang 2021 stable COPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: Z = 2 1.3.2 Mean age ≥ 60 year Du 2020 stable COPD Sundqvist 2021 Wang 2023 | ; Chi ² = 3 5.84 (P < es: Chi ² = Mean 14 11.5 26.2 11.4 8.5 35.1 27.2 ; Chi ² = 2 2.81 (P = 33.3 28.5 12.8 27.4 | 7.58, (0.0000 = 1.08. SD 10.4 16.7 12.7 13.6 10.4 18.9 16.5 77.24, (0.005) 20.55 17.3 10.2 22.1 | 879 df = 12 101) df = 1 15 100 42 40 40 40 71 79 387 71 79 387 151 107 56 64 | (P = 0.0 (P = 0.3) (P = 0.3) (P = 0.3) (P = 0.3) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.1) (P = 0.2) (P = 0.3) (P = 0. | 0002); 30). ² = ontrol <u>SD</u> 10.4 18.4 19.5 19.9 19.9 11.2 10.2 10.2 10.2 10.2 10.2 10.2 10.2 10.2 10.4 | 573 573 573 573 573 573 573 573 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 6.4% 6.4% 50.2% 9.3% 9.3% 9.1% 6.7% 8.6% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 0.59 [0.23, 0.951] | Std. Mean Difference IV. Random. 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 stable COPD Wang 2021 AECOPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: Z = 2 1.3.2 Mean age \geq 60 year Du 2020 stable COPD Du 2020 stable COPD Sundqvist 2021 Wang 2023 Zhang 2024 AECOPD | ; Chi ² = 3 i.84 (P < es: Chi ² = (Mean 14 11.5 26.2 11.4 8.5 35.1 27.2 : Chi ² = 2 .81 (P = 33.3 28.5 12.8 27.4 33.87 | 7.58, (0.0000 = 1.08. COPD SD 10.4 16.7 12.7 13.6 10.4 18.9 16.5 7.24, (0.005) 20.5 17.3 10.2 22.1 19.4 | 879 df = 12 01) df = 1 15 100 42 40 40 40 40 79 387 79 387 107 56 64 60 | (P = 0.0 (P = 0.3 (P | 0002); 30). ² = ontrol <u>SD</u> 10.4 18.4 19.5 19.9 11.2 11.2 10.2 10.2 18.8 19.1 16.6 | 573 573 12 = 68' 7 - 22 100 20 20 20 20 20 20 37 266 65 64 20 65 64 20 60 49 | 100.0% % Weight 5.2% 9.6% 6.4% 6.4% 6.4% 7.6% 8.0% 50.2% 9.3% 9.1% 6.7% 8.6% 8.0% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 0.59 [0.23, 0.95] 0.98 [0.58, 1.37] | Std. Mean Difference IV. Random. 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: $Z = 5$ Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 stable COPD Wang 2021 stable COPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: $Z = 2$ 1.3.2 Mean age ≥ 60 year Du 2020 stable COPD Sundqvist 2021 Wang 2023 Zhang 2024 Stable COPD | ; Chi ² = 3 5.84 (P < es: Chi ² = (Mean 14 11.5 26.2 11.4 8.5 35.1 27.2 ; Chi ² = 2 2.81 (P = 33.3 28.5 12.8 27.4 33.87 25.87 | 7.58, (0.0000 = 1.08. COPD SD 10.4 16.7 12.7 13.6 10.4 18.9 16.5 7.24, (0.005) 7.73, 10.2 22.5 17.3 10.2 22.1 19.4 18.4 | 879 677 677 677 677 677 677 677 6 | (P = 0.0 (P = 0.3 (P = 0.3 (P = 0.3 13 8.5 12.2 7.6 7.6 7.6 7.6 7.6 7.6 7.6 14.1 14.1 17.74 10.1 15.02 16 16 | 20002); 30). ² : ontrol <u>SD</u> 10.4 18.4 19.5 19.9 11.2 11.2 11.2 11.2 10.2 10.2 18.8 19.1 16.6 16.6 | 573 573 12 = 68' Total 22 100 30 20 30 20 37 266 5 64 20 60 49 49 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 7.6% 8.0% 50.2% 9.3% 9.1% 6.7% 8.6% 8.6% 8.1% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 0.59 [0.23, 0.95] 0.98 [0.28, 1.37] 0.56 [0.16, 0.951] | Std. Mean Difference IV. Random. 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 AECOPD Wang 2021 AELOPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: Z = 2 1.3.2 Mean age ≥ 60 year Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 Wang 2023 Zhang 2024 AECOPD Zhang 2024 AECOPD Zhang 2024 Stable COPD Subtotal (95% CI) | ; Chi ² = 3 5.84 (P < es: Chi ² = Mean 14 11.5 26.2 11.4 8.5 35.1 27.2 ; Chi ² = 2 2.81 (P = 33.3 28.5 12.8 27.4 33.87 25.87 | 17.58, (0.0000 = 1.08. COPD 10.4 16.7 12.7 13.6 10.4 16.7 20.5 17.3 10.2 22.5 17.3 10.2 22.1 19.4 18.4 | 879 df = 12 10) df = 1 15 100 42 40 40 71 79 387 df = 6 (l)) 151 107 56 64 60 42 492 | (P = 0.0 (P = 0.3) (P = 0.3) (P = 0.3) (P = 0.3) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.1) (P = 0.1) (P = 0.2) (P = 0.3) (P = 0. | 20002); 30). ² = ontrol <u>SD</u> 10.4 18.4 19.9 11.2 11.2 10.2 10.2 10.2 10.2 10.2 10.2 10.2 10.2 10.2 10.4 10.4 10.4 10.4 19.9 11.2 10.4 10.4 10.4 19.9 10.4 10.4 10.5 10.4 10.4 10.4 10.4 10.5 10.4 10.4 10.5 10.4 10.5 10.4 10.5 10.4 10.5 10.4 10.5 | 573 573 12 = 68' Total 22 100 30 20 20 30 20 37 37 266 = 78% 655 64 20 60 49 9 307 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 6.4% 6.4% 50.2% 9.3% 9.1% 6.7% 8.6% 8.0% 8.0% 8.1% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 0.59 [0.23, 0.95] 0.98 [0.58, 1.37] 0.56 [0.16, 0.95] 0.69 [0.50, 0.871] | Std. Mean Difference IV. Random. 95% Cl |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5 Test for subaroup difference Study or Subgroup 1.3.1 Mean age < 60 years Mueller 2015 Shen 2018 Li 2019 Mao 2020 AECOPD Mao 2020 stable COPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.18; Test for overall effect: Z = 2 1.3.2 Mean age ≥ 60 year Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 Wang 2023 Zhang 2024 AECOPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.02 Hang 2024 AECOPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.02 Heterogeneity: Tau ² = 0.02 Heteroge | ; Chi ² = 3 5.84 (P < es: Chi ² = (Mean 14 11.5 26.2 11.4 8.5 35.1 27.2 ; Chi ² = 2 2.81 (P = 33.3 28.5 12.8 27.4 33.87 25.87 ; Chi ² = 7 ; Chi | 7.58, (0.0000 = 1.08. COPD SD 10.4 16.7 12.7 13.6 10.4 18.9 16.5 20.55 17.3 10.2 22.1 19.4 18.4 .30, df | 879 9 df = 12 10) df = 1 15 100 42 40 40 40 40 71 79 387 71 107 56 64 64 60 64 492 f = 5 (P | (P = 0.0) (P = 0.3) (P = 0.3) (P = 0.3) (P = 0.3) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.3) (P | 0002); 30). ² = ontrol <u>SD</u> 10.4 18.4 19.5 19.9 19.9 19.9 11.2 11.2 10.2 10.2 10.2 18.8 19.1 16.6 16.6 19.5 19.1 19.5 10.2 1 | 573 573 1 ² = 68' Total 22 100 30 20 20 20 20 20 20 20 20 20 2 | 100.0% % Weight 5.2% 9.6% 6.9% 6.4% 6.4% 6.4% 50.2% 9.3% 9.3% 9.3% 9.3% 8.0% 8.6% 8.0% 8.1% 49.8% | 0.60 [0.40, 0.80] Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.52 [0.16, 0.89] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 0.59 [0.23, 0.95] 0.98 [0.58, 1.37] 0.56 [0.16, 0.95] 0.69 [0.50, 0.87] | Std. Mean Difference IV. Random, 95% Cl |

 Total (95% CI)
 879
 573
 100.0%
 0.60 [0.40, 0.80]

 Heterogeneity: Tau² = 0.09; Chi² = 37.58, df = 12 (P = 0.0002); l² = 68%
 -2 -1 0 1 2

 Test for overall effect: Z = 5.84 (P < 0.00001)</td>
 Test for suboroup differences: Chi² = 0.63. df = 1 (P = 0.43). l² = 0%
 0.60 0.40, 0.80 0.60 0.40, 0.80

FIGURE 3. Forest plots for the subgroup analyses comparing the serum galectin-3 level between patients with COPD and healthy controls. (A) forest plots for the subgroup analyses according to the disease status; (B) forest plots for the subgroup analyses according to the mean age of the population.

Α

| Study or Subgroup | | COPD | | C | ontrol | | | Std. Mean Difference | Std. Mean Difference |
|--|---|---|---|---|--|--|--|---|---|
| STRAT OF SUNMISHING | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV. Random. 95% CI |
| 1.4.1 Males ≤ 60% | | | | | | | | | |
| Li 2019 | 26.2 | 12.7 | 42 | 12.2 | 19.5 | 30 | 6.9% | 0.87 [0.38, 1.36] | · · · · · · |
| Du 2020 AECOPD | 33.3 | 20.5 | 151 | 17.74 | 10.2 | 65 | 9.3% | 0.86 [0.56, 1.16] | · · · · |
| Du 2020 stable COPD | 28.5 | 17.3 | 107 | 17.74 | 10.2 | 64 | 9.1% | 0.71 [0.39, 1.03] | - |
| Mao 2020 AECOPD | 11.4 | 13.6 | 40 | 7.6 | 19.9 | 20 | 6.4% | 0.24 [-0.30, 0.77] | |
| Mao 2020 stable COPD | 8.5 | 10.4 | 40 | 7.6 | 19.9 | 20 | 6.4% | 0.06 [-0.47, 0.60] | _ _ |
| Sundavist 2021 | 12.8 | 10.2 | 56 | 10.1 | 18.8 | 20 | 6.7% | 0.21 [-0.31, 0.72] | |
| Wang 2021 AECOPD | 35.1 | 18.9 | 71 | 14.1 | 11.2 | 37 | 7.6% | 1.25 [0.82, 1.68] | |
| Wang 2021 stable COPD Subtotal (95% CI) | 27.2 | 16.5 | 79 586 | 14.1 | 11.2 | 37 293 | 8.0% 60.4% | 0.87 [0.46, 1.27] | $\overline{\bullet}$ |
| Heterogeneity: $Tau^2 = 0.09$ | Chi² = 2 | 0.20 | df = 7 (1) | P = 0.00 | (5): l ² = | = 65% | | | |
| Test for overall effect: $Z = 5$. | 11 (P < | 0.0000 | D1) | 0.00 | 0), 1 | 0070 | | | |
| 1.4.2 Males > 60% | | | | | | | | | |
| Mueller 2015 | 14 | 10.4 | 15 | 13 | 10.4 | 22 | 5.2% | 0.09 [-0.56, 0.75] | |
| Shen 2018 | 11.5 | 16.7 | 100 | 8.5 | 18.4 | 100 | 9.6% | 0.17 [-0.11, 0.45] | + - - |
| Wang 2023 | 27.4 | 22.1 | 64 | 15.02 | 19.1 | 60 | 8.6% | 0.59 [0.23, 0.95] | - |
| Zhang 2024 AECOPD | 33.87 | 19.4 | 60 | 16 | 16.6 | 49 | 8.0% | 0.98 [0.58, 1.37] | |
| Zhang 2024 stable COPD | 25.87 | 18.4 | 54 | 16 | 16.6 | 49 | 8.1% | 0.56 [0.16, 0.95] | |
| Subtotal (95% CI) | | | 293 | | | 280 | 39.6% | 0.50 [0.18, 0.81] | |
| Heterogeneity: Tau ² = 0.08; | Chi² = 1 | 2.52, 0 | df = 4 (F | P = 0.01 |); 2 = | 68% | | | |
| Test for overall effect: Z = 3. | 12 (P = | 0.002) |) | | | | | | |
| | | | 970 | | | 573 | 100 0% | 0 60 10 40 0 801 | • |
| Total (95% CI) | | | 0/9 | | | 5/5 | 100.0 % | 0.00 [0.40, 0.00] | |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; | Chi² = 3 | 7.58, 0 | df = 12 | (P = 0.0 | 002); | l ² = 689 | % | 0.00 [0.40, 0.00] | -2 -1 0 1 2 |
| Total (95% CI) Heterogeneity: $Tau^2 = 0.09$; Test for overall effect: $Z = 5.8$ | Chi² = 3 84 (P < | 7.58, d | df = 12 01) | (P = 0.0 | 0002); | l ² = 689 | % | 0.00 [0.40, 0.00] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5.0 Test for subaroup differences | Chi² = 3 84 (P < s: Chi² = | 7.58, 0 0.0000 = 0.70. | df = 12 01) df = 1 | (P = 0.0 (P = 0.4 | 0002); 0). I² = | 1² = 68% | % | 0.00 [0.40, 0.00] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for subaroup difference: | Chi² = 3 84 (P < s: Chi² = | 7.58, 0 0.0000 = 0.70. | df = 12 01) . df = 1 | (P = 0.0 (P = 0.4 | 0002); .0). I² = | ² = 689 = 0% | % | 0.00 [0.40, 0.00] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CC |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5.1 Test for subaroup difference: | Chi² = 3 84 (P < s: Chi² = | 7.58, 0 0.0000 = 0.70. | df = 12 01) df = 1 | (P = 0.0 (P = 0.4 C | 0002); .0). I ² = ontrol | 1 ² = 689 | % | Std. Mean Difference | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5.1 Test for subaroup difference: Study or Subgroup | Chi ² = 3 84 (P < s: Chi ² = (Mean | 7.58, 0 0.0000 = 0.70. = 0.70 SD | df = 12 01) df = 1 <u>Total</u> | (P = 0.0 (P = 0.4 C <u>Mean</u> | 0002); 0). I ² = ontrol SD | ² = 689 = 0% Total | Weight | Std. Mean Difference | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for subaroup difference: Study or Subgroup 1.5.1 NOS 6-7 | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> | 7.58, (0.000(= 0.70. COPD SD | df = 12 01) df = 1 <u>Total</u> | (P = 0.0 (P = 0.4 C <u>Mean</u> | 0002); .0). ² = ontrol SD | 2 = 689 = 0% Total | Weight | Std. Mean Difference | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for subaroup difference: Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 | 7.58, 0 0.0000 = 0.70. COPD SD | df = 12 01) df = 1 <u>Total</u> | (P = 0.0 (P = 0.4 C <u>Mean</u> 13 | 0002); 0). ² = ontrol SD | 1 ² = 689 = 0% <u>Total</u> 22 | Weight 5.2% | Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for suboroup difference: <u>Study or Subgroup</u> 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 | 7.58, 0 0.0000 = 0.70. COPD SD 10.4 16.7 | df = 12 01) df = 1 <u>Total</u> 15 100 | (P = 0.0 (P = 0.4 (P = 0.4 C Mean 13 8.5 | 0002); .0). ² = ontrol SD 10.4 18.4 | 1 ² = 689 = 0% <u>Total</u> 22 100 | Weight 5.2% 9.6% | Std. Mean Difference <u>IV. Random. 95% CI</u> 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for subaroup difference: Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 | 7.58, 0 0.0000 = 0.70. COPD SD 10.4 16.7 12.7 | df = 12 01) df = 1 <u>Total</u> 15 100 42 | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 | 0002); 0). I ² = 000000000000000000000000000000000000 | 1 ² = 689 = 0% <u>Total</u> 22 100 30 | Weight 5.2% 9.6% 6.9% | Std. Mean Difference <u>IV. Random. 95% Cl</u> 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; · Test for overall effect: Z = 5.: Test for subaroup difference: Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 33.3 | 7.58, 0 0.0000 = 0.70. COPD SD 10.4 16.7 12.7 20.5 | df = 12 01) df = 1 Total 15 100 42 151 | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 | 0002); 0). ² = 000000000000000000000000000000000000 | 22 100 30 65 | Weight 5.2% 9.6% 6.9% 9.3% | Std. Mean Difference <u>IV. Random, 95% CI</u> 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for subaroup difference: Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 stable COPD | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 33.3 28.5 | 7.58, 0 0.0000 = 0.70. COPD SD 10.4 16.7 12.7 20.5 17.3 | df = 12 01) df = 1 Total 15 100 42 151 107 | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 17.74 | 0002); 0). ² = 000000000000000000000000000000000000 | 1 ² = 689 = 0% Total 22 100 30 65 64 | Weight 5.2% 9.6% 6.9% 9.3% 9.1% | Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for subaroub difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 33.3 28.5 12.8 | 7.58, 0 0.0000 = 0.70. COPD SD 10.4 16.7 12.7 20.5 17.3 10.2 | df = 12 01) df = 1 Total 15 100 42 151 107 56 | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 17.74 10.1 | 0002); 0). ² = 0ntrol SD 10.4 18.4 19.5 10.2 10.2 18.8 | 22 100 30 65 64 20 | Weight 5.2% 9.6% 6.9% 9.3% 9.1% 6.7% | Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for suboroup difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 Wang 2021 AECOPD | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 33.3 28.5 12.8 35.1 | 7.58, 0 0.0000 = 0.70. COPD SD 10.4 16.7 12.7 20.5 17.3 10.2 18.9 | df = 12 01) df = 1 Total 15 100 42 151 107 56 71 | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 17.74 10.1 14.1 | 0002); 0). ² = 0ntrol SD 10.4 18.4 19.5 10.2 10.2 18.8 11.2 | 22 100 30 65 64 20 37 | Weight 5.2% 9.6% 6.9% 9.3% 9.3% 6.7% 7.6% | Std. Mean Difference <u>IV. Random. 95% Cl</u> 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for subaroup difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 Wang 2021 AECOPD Wang 2021 stable COPD Subtotal (95% CI) | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 33.3 28.5 12.8 35.1 27.2 | 7.58, 0 0.0000 = 0.70. SD 10.4 16.7 12.7 20.5 17.3 10.2 18.9 16.5 | df = 12 01) df = 1 Total 15 100 42 151 107 56 71 79 621 | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 17.74 10.1 14.1 14.1 | 0002); 0). ² = 00002); 00002); 00002 10.4 10.4 10.2 10.2 10.2 10.2 10.2 10.2 10.2 10.2 | 22 100 22 100 30 65 64 20 37 37 375 | Weight 5.2% 9.6% 6.9% 9.3% 9.1% 6.7% 7.6% 8.0% 62.5% | Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.65 [0.36, 0.93] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for suboroup difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 Wang 2021 AECOPD Wang 2021 AECOPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.12; | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 33.3 28.5 12.8 35.1 27.2 Chi ² = 2 | 7.58, 0 0.0000 = 0.70. COPD SD 10.4 16.7 12.7 20.5 17.3 10.2 18.9 16.5 | df = 12 01) df = 1 Total 15 100 42 151 107 56 71 79 621 df = 7 (1 | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 10.1 14.1 14.1 14.1 P = 0.00 | 0002); 0). ² = 000000000000000000000000000000000000 | 575 12 = 68% = 0% Total 22 100 30 65 64 20 37 37 375 = 75% | Weight 5.2% 9.6% 9.3% 9.1% 6.7% 7.6% 8.0% 6.2.5% | Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.65 [0.36, 0.93] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CC Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5.: Test for suboroup difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 Wang 2021 AECOPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.12; Test for overall effect: Z = 4. | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 33.3 28.5 12.8 35.1 27.2 Chi ² = 2 49 (P < | 7.58, (0.0000 sD 10.4 16.7 12.7 20.5 17.3 10.2 18.9 16.5 88.31, (0.0000 | df = 12 01) df = 1 Total 15 100 42 151 107 56 71 79 621 df = 7 (0 01) | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 17.74 10.1 14.1 14.1 P = 0.00 | 0002); 0). I ² = ontrol <u>SD</u> 10.4 18.4 19.5 10.2 10.2 18.8 11.2 11.2 002); I ² | 22 100 22 100 30 65 64 20 37 375 5 = 75% | Weight 5.2% 9.6% 6.9% 9.3% 9.1% 6.7% 7.6% 8.0% 62.5% | Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.65 [0.36, 0.93] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CC Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5.: Test for subaroup difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 Wang 2021 AECOPD Wang 2021 AECOPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.12; Test for overall effect: Z = 4. 1.5.2 NOS 8-9 | Chi ² = 3 84 (P < s: Chi ² = 0 <u>Mean</u> 14 11.5 26.2 33.3 28.5 12.8 35.1 27.2 Chi ² = 2 49 (P < | 7.58, (0.0000 e 0.70. COPD 5D 10.4 16.7 12.7 20.5 17.3 10.2 18.9 16.5 8.31, (0.0000 | df = 12 01) df = 1 15 100 42 151 107 56 71 79 621 df = 7 (1 01) | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 17.74 10.1 14.1 14.1 14.1 P = 0.00 | 0002); 0). ² = 000000000000000000000000000000000000 | Total 22 100 30 65 64 20 37 375 = 75% | Weight 5.2% 9.6% 6.9% 9.3% 9.1% 6.7% 8.0% 62.5% | Std. Mean Difference IV. Random. 95% Cl 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.65 [0.36, 0.93] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5.: Test for subaroup difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 Wang 2021 AECOPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.12; Test for overall effect: Z = 4. 1.5.2 NOS 8-9 Mao 2020 AECOPD | Chi ² = 3 84 (P < s: Chi ² = 0 14 11.5 26.2 33.3 28.5 12.8 35.1 27.2 Chi ² = 2 49 (P < | 7.58, c 0.0000 = 0.70. COPD SD 10.4 16.7 12.7 20.5 17.3 10.2 18.9 16.5 88.31, (0.0000 | df = 12 101) df = 1 15 100 42 151 107 56 71 79 621 df = 7 ((001) 40 | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 17.74 10.1 14.1 14.1 P = 0.00 7.6 | 0002); 0). ² = ontrol <u>SD</u> 10.4 18.4 19.5 10.2 18.8 11.2 11.2 002); ² 19.9 | 22 100 20 30 65 65 65 65 65 65 65 65 65 65 85 20 | Weight 5.2% 9.6% 6.9% 9.1% 6.7% 7.6% 8.0% 62.5% | Std. Mean Difference IV. Random. 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.65 [0.36, 0.93] 0.24 [-0.30, 0.77] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for subaroup difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 AECOPD Wang 2021 AECOPD Wang 2021 AECOPD Wang 2021 AECOPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.12; Test for overall effect: Z = 4. 1.5.2 NOS 8-9 Mao 2020 AECOPD Mao 2020 stable COPD | Chi ² = 3 84 (P < s: Chi ² = 0 14 11.5 26.2 33.3 28.5 12.8 35.1 27.2 Chi ² = 2 49 (P < 11.4 8.5 | 7.58, c 0.0000 = 0.70. COPD SD 10.4 16.7 12.7 20.5 17.3 10.2 18.9 16.5 88.31, 0 0.0000 13.6 10.4 | 107 107 107 107 107 107 107 107 | (P = 0.0 (P = 0.4 C Mean 13 8.5 12.2 17.74 10.1 14.1 14.1 14.1 P = 0.00 7.6 7.6 7.6 | 0002); 0). I ² = ontrol SD 10.4 18.4 19.5 10.2 10.2 18.8 11.2 11.2 1022); I ² 19.9 19.9 | 22 100 30 65 64 20 37 375 375 20 20 20 | Weight 5.2% 9.6% 9.3% 9.1% 6.7% 7.6% 8.0% 62.5% | Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.65 [0.36, 0.93] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; Test for overall effect: Z = 5. Test for suboroup difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 AECOPD Wang 2021 AECOPD Wang 2021 AECOPD Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.12; Test for overall effect: Z = 4. 1.5.2 NOS 8-9 Mao 2020 AECOPD Mao 2020 stable COPD Wang 2021 | Chi ² = 3 84 (P < s: Chi ² = 0 14 11.5 26.2 33.3 28.5 12.8 35.1 27.2 Chi ² = 2 .49 (P < 11.4 8.5 27.4 | 7.58, c 0.0000 = 0.70. COPD SD 10.4 16.7 12.7 20.5 17.3 10.2 18.9 16.5 88.31, i 0.0000 13.66 10.4 22.1 | df = 12 15 100 15 100 10 100 100 100 1 | (P = 0.0 (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.4) (P = 0 | 0002); ² = ontrol <u>SD</u> 10.4 18.4 19.5 10.2 10.2 10.2 10.2 10.2 10.2 11.2 10.2 11.2 11.2 19.9 19.9 19.9 19.9 | 22 100 22 100 30 30 65 64 20 37 375 2' = 75% 20 20 60 | Weight 5.2% 9.6% 6.9% 9.3% 9.3% 9.1% 6.7% 7.6% 8.0% 62.5% 9.6.4% 6.4% 8.6% | Std. Mean Difference IV. Random, 95% CI 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.65 [0.36, 0.93] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 0.59 [0.23, 0.95] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random, 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; · Test for overall effect: Z = 5.: Test for subaroun difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 stable COPD Sundqvist 2021 Wang 2021 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.12; Test for overall effect: Z = 4. 1.5.2 NOS 8-9 Mao 2020 AECOPD Mao 2020 stable COPD Mao 2020 Stable COPD | Chi ² = 3 84 (P < s: Chi ² = 0 Mean 14 11.5 26.2 33.3 28.5 12.8 35.1 27.2 Chi ² = 2 49 (P < 11.4 8.5 27.4 33.87 | 7.58, 6 0.0000 = 0.70. SD 10.4 16.7 20.5 17.3 10.2 18.9 16.5 88.31, 0.0000 13.66 10.4 22.1 19.4 | (1) (1) (1) (1) (1) (1) (1) (1) (1) (1) | (P = 0.0 (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.0) (P = 0.4 (P = 0.4 (P = 0.4 (P = 0.4) (P = 0.4 (P = 0.4) (P = 0. | 0002); 0). I ² = 0 ontrol SD 10.4 18.4 19.5 10.2 10.2 10.2 10.2 10.2 11.2 10.2 11.2 10.2 11.2 11.2 10.2); I ² | Total 22 68° 100 30 65 64 00 37 375 75% 20 20 200 60 49 49 | Weight 5.2% 9.6% 6.9% 9.3% 9.3% 9.1% 6.7% 8.0% 62.5% | Std. Mean Difference IV. Random. 95% Cl 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.65 [0.36, 0.93] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 0.59 [0.23, 0.95] 0.98 [0.58, 1.37] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |
| Total (95% CI) Heterogeneity: Tau ² = 0.09; · Test for overall effect: Z = 5.: Test for subaroup difference Study or Subgroup 1.5.1 NOS 6-7 Mueller 2015 Shen 2018 Li 2019 Du 2020 AECOPD Du 2020 stable COPD Subtotal (95% CI) Heterogeneity: Tau ² = 0.12; Test for overall effect: Z = 4. 1.5.2 NOS 8-9 Mao 2020 AECOPD Mao 2020 stable COPD Wang 2023 Zhang 2024 AECOPD Zhang 2024 AECOPD Zhang 2024 AECOPD | Chi ² = 3 84 (P < s: Chi ² = 0 14 11.5 26.2 33.3 28.5 12.8 35.1 27.2 Chi ² = 2 49 (P < 11.4 8.5 27.4 33.87 25.87 | 7.58, c 0.0000 = 0.70. SD 10.4 16.7 20.5 17.3 10.2 18.9 16.5 88.31, 1 0.0000 13.6 10.4 22.1 19.4 19.4 | Total 15 10 15 100 42 151 107 56 711 79 621 40 40 60 54 | (P = 0.0 (P = 0.4 (P = 0.4) (P = 0.4 (P = 0.4) (P = 0.4 (P = 0.4) (P = 0.4 (P = 0.4) (P = 0. | 0002); 0). ² = ontrol <u>SD</u> 10.4 18.4 19.5 10.2 18.8 11.2 11.2 10.2); i ² 19.9 19.9 19.9 19.9 19.1 16.6 16.6 | 222 100 30 65 64 20 37 375 375 20 20 60 49 49 | Weight 5.2% 9.6% 6.9% 9.3% 9.1% 6.7% 7.6% 8.0% 62.5% 9 6.4% 8.6% 8.0% 8.1% | Std. Mean Difference IV. Random. 95% Cl 0.09 [-0.56, 0.75] 0.17 [-0.11, 0.45] 0.87 [0.38, 1.36] 0.86 [0.56, 1.16] 0.71 [0.39, 1.03] 0.21 [-0.31, 0.72] 1.25 [0.82, 1.68] 0.87 [0.46, 1.27] 0.65 [0.36, 0.93] 0.24 [-0.30, 0.77] 0.06 [-0.47, 0.60] 0.59 [0.23, 0.95] 0.98 [0.58, 1.37] 0.56 [0.16, 0.95] | -2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in CO Std. Mean Difference IV. Random. 95% CI |

Heterogeneity: Tau² = 0.09; Chi² = 37.58, df = 12 (P = 0.0002); l² = 68% Test for overall effect: Z = 5.84 (P < 0.00001) Test for subaroup differences: Chi² = 0.35. df = 1 (P = 0.55). l² = 0%

879

Total (95% CI)

-2 -1 0 1 2 Lower Gal-3 in COPD Higher Gal-3 in COPD

FIGURE 4. Forest plots for the subgroup analyses comparing the serum galectin-3 level between patients with COPD and healthy controls. (A) forest plots for the subgroup analyses according to the proportion of the males; (B) forest plots for the subgroup analyses according to the study quality scores.

573 100.0%

0.60 [0.40, 0.80]

| - | AECO | PD | Stab | le COF | D | s | Std. Mean Difference | Std. Mean Difference |
|--|--|---|-----------------------|-----------------|-----------------------------------|----------|------------------------|--|
| Study or Subgroup | Mean S | D Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV. Random, 95% CI |
| Pouwels 2015 | 1.07 5.1 | 2 40 | 1.1 | 4.74 | 40 | 9.2% | -0.01 [-0.44, 0.43] | |
| Feng 2017 | 31.1 12. | 5 44 | 27.3 | 13.1 | 44 | 10.0% | 0.29 [-0.13, 0.71] | - |
| Liu 2019 | 33.6 8. | 7 60 | 28.5 | 8.5 | 60 | 13.2% | 0.59 [0.22, 0.95] | |
| Du 2020 | 33.3 20. | 5 151 | 28.5 | 17.3 | 107 | 28.7% | 0.25 [0.00, 0.50] | |
| Mao 2020 | 11.4 13. | 6 40 | 8.5 | 10.4 | 40 | 9.2% | 0.24 [-0.20, 0.68] | |
| Wang 2021 | 35.1 18. | 9 71 | 27.2 | 16.5 | 79 | 16.8% | 0.44 [0.12, 0.77] | |
| Zhang 2024 | 33.87 19. | 4 60 | 25.87 | 18.4 | 54 | 12.8% | 0.42 [0.05, 0.79] | |
| • | | | | | | | | |
| Total (95% CI) | | 466 | | | 424 | 100.0% | 0.33 [0.20, 0.46] | • |
| Heterogeneity: Tau ² = | = 0.00: Chi ² = | 5.50 df = | = 6 (P = | 0.48): 1 | $^{2} = 0\%$ | | | |
| Test for overall effect | : 7 = 4.84 (P | < 0.00001 | 0 | ,, . | 0,0 | | | -1 -0.5 0 0.5 1 |
| | . 2 - 4.04 (1 | - 0.0000 | , | | | | l | Lower Gal-3 in AECOPD Higher Gal-3 in AECO |
| | COL | РП | | Contro | ы | | Std Mean Difference | Std. Mean Difference |
| Study or Subgroup | Mean | SD Tota | d Moar | n SC |) Tota | Weight | t IV Random 95% C | IV Random 95% Cl |
| | | | u wear | | 1012 | a weigh | 1 IV, Kaliuolii, 95% C | |
| 1.7.1 Mean age < 60 |) years | | | | | | | |
| Mao 2020 | 11.4 13 | 3.6 40 | 0 8.5 | 5 10.4 | 4 | 0 9.2% | 0.24 [-0.20, 0.68] | |
| Wang 2021 | 35.1 18 | 3.9 7 [°] | 1 27.2 | 2 16.5 | 5 7 | 9 16.8% | 6 0.44 [0.12, 0.77] | |
| Zhang 2024 | 33.87 19 | 9.4 6 | 0 25.87 | 7 18.4 | ا 5 | 4 12.8% | 6 0.42 [0.05, 0.79] | |
| Subtotal (95% CI) | | 17 | 1 | | 17: | 3 38.8% | 6 0.39 [0.17, 0.60] | |
| Heterogeneity: Tau ² | = 0.00. Chi ² | = 0.60 dt | E = 2 (P | = 0.74 |)· I ² = 0 | 10/_ | | |
| Test for overall effec | t: Z = 3.55 (P | e = 0.000, di | 4) | - 0.74 |), I – C | //0 | | |
| 1.7.2 Mean age ≥ 6 | 60 years | | | | | | | |
| Pouwels 2015 | 1.07 5 | 12 4 | 0 1 | 1 4 74 | L 4 | 0 92% | -0.01 [-0 44 0 43] | |
| Feng 2017 | 21 1 1 | 25 4 | 4 27 | 3 12 1 | 1 | 4 10.0% | 0.20[_0.12,0.74] | · |
| | 01.1 12 | | - 21.5 | 5 13.1 E 0 - | . 4 | + 10.0% | | |
| LIU 2019 | 33.6 8 | 5.7 6 | J 28. | ວ 8.5 | 6 | U 13.2% | 0.59 [0.22, 0.95] | |
| Du 2020 | 33.3 20 | 0.5 15 | 1 28.5 | 5 17.3 | 3 10 | 7 28.7% | 0.25 [0.00, 0.50] | |
| Subtotal (95% CI) | | 29 | 5 | | 25 | 1 61.2% | 6 0.29 [0.08, 0.51] | |
| Heterogeneity: Tau ² | = 0.02: Chi ² : | = 4.43. di | f = 3 (P | = 0.22 |); ² = 3 | 2% | | |
| Test for overall effec | t: Z = 2.66 (P | = 0.008 |) - (. | | | | | |
| - | | | | | | | | |
| i otal (95% CI) | - 0.00: 01: 2 | 460 | | - 0.40 | 424 | 4 100.0% | 0.33 [0.20, 0.46] | |
| neterogeneity: Tau ² | = 0.00; Chi ² : | = 5.50, di | і=ю(Р | = 0.48 |); I^ = (| 170 | | -1 -0.5 0 0.5 1 |
| Test for overall effec | t: Z = 4.84 (P | < 0.000 | 01) | | | | | Lower Gal-3 in COPD Higher Gal-3 in CO |
| Test for subaroup di | fferences: Ch | i ² = 0.38. | df = 1 (| (P = 0. | 54). I² : | = 0% | | |
| | | | | | | | | |
| | AECO | PD | Stab | le COF | סי | s | Std. Mean Difference | Std. Mean Difference |
| Study or Subgroup | Mean S | D Total | Mean | SD | Total | Weight | IV. Random. 95% CI | IV. Random, 95% CI |
| 1.8.1 Males ≤ 60% | | | | | | - | | |
| Du 2020 | 33.3 20 | 5 151 | 28.5 | 17.3 | 107 | 28 7% | 0.25 (0.00, 0.50) | _ |
| Du 2020 | 11 4 12 | 6 40 | 20.5 | 10.4 | 40 | 20.7 /0 | 0.23 [0.00, 0.30] | |
| Mao 2020 | 11.4 13. | 6 40 | 8.5 | 10.4 | 40 | 9.2% | 0.24 [-0.20, 0.68] | |
| Wang 2021 | 35.1 18. | 9 /1 | 27.2 | 16.5 | 79 | 16.8% | 0.44 [0.12, 0.77] | |
| Subtotal (95% CI) | | 262 | | | 226 | 54.7% | 0.31 [0.13, 0.49] | |
| Heterogeneity: Tau ² = | = 0.00; Chi² = | 1.00, df = | = 2 (P = | 0.61); I | $ ^{2} = 0\%$ | | | |
| Test for overall effect | : Z = 3.34 (P = | = 0.0008) | | | | | | |
| | | | | | | | | |
| 1.8.2 Males > 60% | | | | | | | | |
| Pouwels 2015 | 1.07 5.1 | 2 40 | 1.1 | 4.74 | 40 | 9.2% | -0.01 [-0.44, 0.43] | |
| Feng 2017 | 31.1 12. | 5 44 | 27.3 | 13.1 | 44 | 10.0% | 0.29 [-0.13, 0.71] | |
| Liu 2019 | 33.6 8. | 7 60 | 28.5 | 8.5 | 60 | 13.2% | 0.59 [0.22, 0.95] | _ |
| Zhang 2024 | 33.87 19 | 4 60 | 25.87 | 18.4 | 54 | 12.8% | 0.42 [0.05, 0.79] | |
| Subtotal (95% CI) | 55.67 15. | 204 | 20.07 | 10.4 | 108 | 12.0% | 0.35 [0.11 0.59] | |
| Unterestation Tax2 | - 0.00. 01:2 - | 4 20 -46 - | - 2 (D - | 0.001 | 2 - 040 | 40.070 | 0.00 [0.11, 0.00] | |
| Heterogeneity: Tau ² = | = 0.02; Chi ² = | 4.38, df = | = 3 (P = | 0.22); I | ~ = 31% | 0 | | |
| l est for overall effect | : Z = 2.82 (P = | = 0.005) | | | | | | |
| Total (95% CI) | | 466 | | | 424 | 100.0% | 0.33 [0.20. 0 46] | • |
| Heterogeneity: Tau ² | = 0.00° Chi2 - | 5 50 df - | 6 (P - | 0 48\- 1 | 2 = 00/ | | | -++ - ++ |
| Toot for overall offer the | - 3.00, CHF = | < 0.00, ui = | - u (r ² = | u.+0), I | - 0% | | | -1 -0.5 0 0.5 1 |
| Test for subgroup diff | . 2 - 4.04 (P · | < 0.00001 ! = 0.06 m | ') if = 1 (P | = 0.80 |), ² = 0 | 0% | l | Lower Gal-3 in AECOPD Higher Gal-3 in AECO |
| | aronooa. On | 5.00. L | | 0.00 | t | | | |
| | COPE | 0 | Co | ontrol | | \$ | Std. Mean Difference | Std. Mean Difference |
| Study or Subgroup | Mean SE |) Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| 1.9.1 NOS 6-7 | | | | | | | | |
| Du 2020 | 33.3 20 4 | 5 151 | 28 5 | 17 3 | 107 | 28 7% | 0.25 [0.00_0.50] | ⊢_ ∎ |
| Wang 2021 | 25 4 49 4 | 2 101 | 20.0 | 16.5 | 70 | 16 00/ | 0.44 [0.40, 0.30] | |
| wally 2021 | 33.1 18.9 | , /1 | 21.2 | 10.5 | 19 | 10.0% | 0.44 [0.12, 0.77] | |
| Subtotal (95% CI) | | 222 | | | 186 | 45.5% | 0.32 [0.12, 0.52] | |
| Heterogeneity: Tau ² = | 0.00; Chi ² = 0 | 0.88, df = | 1 (P = | 0.35); | l² = 0% |) | | |
| Test for overall effect: | Z = 3.19 (P = | 0.001) | | | | | | |
| 1.9.2 NOS 8-9 | | | | | | | | |
| Pouwels 2015 | 107 544 | A0 | 4 4 | 1 74 | 40 | 0.20/ | [24 0 44 0 1 10 0- | |
| Pouweis 2015 | 1.07 5.12 | 2 40 | 1.1 | 4.74 | 40 | 9.2% | -0.01 [-0.44, 0.43] | |
| Feng 2017 | 31.1 12.5 | o 44 | 27.3 | 13.1 | 44 | 10.0% | 0.29 [-0.13, 0.71] | |
| Liu 2019 | 33.6 8.7 | 7 60 | 28.5 | 8.5 | 60 | 13.2% | 0.59 [0.22, 0.95] | |
| Mao 2020 | 11.4 13.6 | 6 40 | 8.5 | 10.4 | 40 | 9.2% | 0.24 [-0.20, 0.68] | -+ |
| Zhang 2024 | 33.87 10 | 1 60 | 25.87 | 18.4 | 54 | 12.8% | 0 42 10 05 0 701 | |
| Subtotal (95% CI) | 55.57 13.5 | 2/1/ | 20.07 | 10.4 | 238 | 54 5% | 0.33 [0.14 0.53] | |
| Sastotal (35 /0 01) | | 4.04 | | 0.001 | 2.00 | J-7.J/0 | 0.00 [0.14, 0.00] | - |
| Latorog | 0.01/ 01/2 | | 4 (12 = | 0.33); | r = 13' | 70 | | |
| Heterogeneity: Tau ² = | 0.01; Chi ² = 4 | 4.01, ui - | . (. | | | | | I |
| Heterogeneity: Tau ² = Test for overall effect: | 0.01; Chi² = 4 Z = 3.35 (P = | +.61, di = • 0.0008) | . (. | | | | | |
| Heterogeneity: Tau ² = Test for overall effect: | 0.01; Chi² = 4 Z = 3.35 (P = | 4.01, d1 - 4.00008) | . (. | | 424 | 100.0% | 0 33 [0 20 0 46] | |
| Heterogeneity: Tau ² = Test for overall effect: Total (95% CI) | 0.01; Chi ² = 4 Z = 3.35 (P = | 4.61, d1 - 0.0008) 466 | 6 (D - | 0.49% | 424 | 100.0% | 0.33 [0.20, 0.46] | • |
| Heterogeneity: Tau ² = Test for overall effect: Total (95% CI) Heterogeneity: Tau ² = | 0.01; Chi ² = 4 Z = 3.35 (P = 0.00; Chi ² = 5 | 4.61, d1 = 0.0008) 466 5.50, df = | 6 (P = | 0.48); | 424 ² = 0% | 100.0% | 0.33 [0.20, 0.46] | -1 -0.5 0 0.5 1 |
| Heterogeneity: Tau ² = Test for overall effect: Total (95% CI) Heterogeneity: Tau ² = Test for overall effect: | 0.01; Chi ² = 4 Z = 3.35 (P = 0.00; Chi ² = 4 Z = 4.84 (P < | 4.61, d1 = 0.0008) 466 5.50, df = 0.00001 | 6 (P = | 0.48); | 424 ² = 0% | 100.0% | 0.33 [0.20, 0.46] | -1 -0.5 0 0.5 1 Lower Gal-3 in COPD Higher Gal-3 in COF |

FIGURE 5. Forest plots for the meta-analysis comparing the serum galectin-3 level between patients with AECOPD and stable COPD. (A) forest plots for the overall meta-analysis; (B) forest plots for the subgroup analyses according to the mean ages of the participants; (C) forest plots for the subgroup analyses according to the proportions of the males; (D) forest plots for the subgroup analyses according to the study quality scores;.





FIGURE 6. Funnel plots for the publication biases underlying the meta-analyses. (A) funnel plots for the meta-analysis comparing the serum galectin-3 level between patients with COPD and healthy controls; (B) funnel plots for the meta-analysis comparing the serum galectin-3 level between patients with AECOPD and stable COPD.

SUPPLEMENTAL DATA

("galectin-3" OR "galectin 3") AND ("chronic obstructive pulmonary disease" OR "COPD" OR "chronic obstructive lung disease" OR "chronic obstructive airway disease" OR "emphysema" OR "chronic airflow limitation" OR "chronic airway obstruction")

FIGURE S1. The search syntax used in the meta-analysis.

