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Association of gastroesophageal reflux disease with risk of pulmonary diseases

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ADMINISTRATIVE INFORMATION

Support - None.

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Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 3 September 2024 and was last updated on 3 September 2024.

INTRODUCTION

Review question / Objective This meta-analysis aimed to further clarify the impact of GERD on the subsequent development of pulmonary diseases based on available evidence.

Condition being studied Concurrent pulmonary diseases are common in patients with gastroesophageal reflux disease (GERD). However, whether GERD promotes the development of pulmonary diseases still lacks quantitative evidence and remains uncertain. We conducted a meta-analysis to determine the risk of subsequent development of pulmonary diseases in GERD patients.

METHODS

Search strategy The PubMed, EMbase, Web of Science and Cochrane Library databases were searched from database inception up to July 12, 2024 with following terms: gastroesophageal reflux, gastro-oesophageal reflux, chronic obstructive pulmonary disease, COPD, asthma, pulmonary tuberculosis, pneumonia, pulmonary fibrosis, pulmonary embolism, lung cancer, bronchitis, bronchiectasis, pulmonary disease, respiratory disease, risk, incidence and morbidity. During the search, MeSH terms and free texts were applied and references in included studies were also reviewed.

Participant or population GERD patiens and non-GERD population.

Intervention GERD was diagnosed according to the symptoms such as the acid reflux and heartburn, gastroscope, PPI test or 24-hour esophageal pH monitoring before the incidence of pulmonary diseases.

Comparator The incidence rates of pulmonary diseases were compared between the GERD and non-GERD groups.

Study designs to be included Cohort studies.

Eligibility criteria Studies met following criteria were included: 1) GERD was diagnosed according

to the symptoms such as the acid reflux and heartburn, gastroscope, PPI test or 24-hour esophageal pH monitoring before the incidence of pulmonary diseases; 2) pulmonary diseases were diagnosed according to the symptoms, blood, etiological, imageological, pathological examinations and (or) bronchoscopy; 3) the incidence rates of pulmonary diseases were compared between the GERD and non-GERD groups, representing as odds ratios (ORs) with 95% confidence intervals (CIs) or providing enough data to calculate them; 4) full texts were available; 5) if the data were severely overlapped or duplicated, only the latest or most comprehensive studies were included.

Information sources The following data were extracted from each included studies: name of first author, publication year, data source, age, sample size, number of GERD cases, treatment history of GERD (treated vs untreated), source of OR (multivariate vs univariate), endpoint, OR and 95% CI for corresponding endpoint.

Main outcome(s) Asthma and pneumonia.

Additional outcome(s) The pulmonary fibrosis (PF), chronic obstructive pulmonary disease (COPD), lung cancer, interstitial lung disease (ILD), bronchiectasis, bronchitis, acute lung injury (ALI), pulmonary embolism, pulmonary tuberculosis (PTB) and non-tuberculous mycobacteria pulmonary disease (NTMPD).

Quality assessment / Risk of bias analysis All included studies in our meta-analysis were cohort studies. Therefore, the Newcastle–Ottawa scale (NOS) was used for quality evaluation including the cohort selection, comparability and outcome measurement, and studies with a NOS score＞5 were regarded as high-quality studies.

Strategy of data synthesis All statistical analyses were conducted by STATA (version 15.0, StataCorp LLC, College Station, Texas, USA) software. The heterogeneity among included studies was assessed by the I2 statistic and Q test. When significant heterogeneity was observed, presented as I2>50% and/or P<0.1, the random-effects model was used; or the fixed-effects model was applied [8]. The ORs with 95% CIs were combined to evaluate the association between presence of GERD and subsequent development of pulmonary diseases. If ORs and 95% CIs were both reported in the multivariate and univariate analyses, data from multivariate analysis were extracted and applied preferentially. Besides, Begg's funnel plot and Egger's test were performed to identify publication bias for the asthma and pneumonia [9, 10]. Significant publication bias was defined as the noticeably asymmetric Begg's funnel plot and P value<0.05 of Egger's test, and then the trim-and-fill method was applied to evaluate the impact of potentially unpublished studies on the stability of overall pooled results, with an inspection level of α=0.05 [11].

Subgroup analysis Furthermore, subgroup analyses stratified by the treatment of GERD (treated vs untreated), age (adult vs child) and source of OR (multivariate vs univariate) were also conducted to identify the impact of these factors on the association of GERD with development of pulmonary diseases.All statistical analyses were conducted by STATA (version 15.0, StataCorp LLC, College Station, Texas, USA) software. The heterogeneity among included studies was assessed by the I2 statistic and Q test. When significant heterogeneity was observed, presented as I2>50% and/or P<0.1, the random-effects model was used; or the fixed-effects model was applied [8]. The ORs with 95% CIs were combined to evaluate the association between presence of GERD and subsequent development of pulmonary diseases. If ORs and 95% CIs were both reported in the multivariate and univariate analyses, data from multivariate analysis were extracted and applied preferentially. Besides, Begg's funnel plot and Egger's test were performed to identify publication bias for the asthma and pneumonia [9, 10]. Significant publication bias was defined as the noticeably asymmetric Begg's funnel plot and P value<0.05 of Egger's test, and then the trim-and-fill method was applied to evaluate the impact of potentially unpublished studies on the stability of overall pooled results, with an inspection level of α=0.05 [11].

Sensitivity analysis A sensitivity analysis was conducted to clarify the source of heterogeneity and evaluate the stability of the pooled results.

Language restriction No.

Country(ies) involved China - West China Hospital, Sichuan University.

Keywords Gastroesophageal reflux disease; pulmonary disease; risk; meta-analysis.

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