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Effect of chronic obstructive pulmonary disease (COPD) on biventricular mechanics in patients without severe airflow obstruction

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ADMINISTRATIVE INFORMATION

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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 24 April 2025 and was last updated on 24 April 2025.

INTRODUCTION

Review question / Objective Over the last 15-year period only a few echocardiographic studies have accurately examined the biventricular mechanics by transthoracic echocardiography (TTE) implemented with speckle tracking echocardiography (STE) in patients affected by nonsevere chronic obstructive pulmonary disease (COPD). These studies aimed at identifying an early STE marker of subclinical myocardial dysfunction, in the presence of preserved left ventricular ejection fraction (LVEF) on TTE, in COPD patients without severe airflow obstruction. The present systematic review and meta-analysis has been designed to summarize the principal findings of these studies and to quantify the effect of COPD on biventricular mechanics in patients without advanced lung disease. The pathophysiological mechanisms underpinning subclinical myocardial dysfunction in COPD patients will be discussed as well.

Condition being studied Chronic obstructive pulmonary disease (COPD) is a heterogeneous group of lung diseases (including chronic bronchitis and emphysema), characterized by chronic respiratory symptoms due to persistent and progressive airway obstruction, caused by significant exposure to noxious particles or gases [1]. Its prevalence is rapidly increased during the last decades, affecting to over 400 million people globally [2].

COPD is frequently associated with several cardiovascular comorbidities, especially pulmonary hypertension (PH), cardiac arrhythmias and coronary artery disease (CAD) [3-5]. The increased cardiovascular disease burden of COPD patients represents a leading cause of morbidity and mortality in these patients [6].

In clinical practice, most COPD patients are referred to the outpatient cardiology clinics by pulmonologists or internal medicine physicians, to perform conventional transthoracic echocardiography (TTE) for assessing pulmonary

hemodynamics. It is noteworthy that severe PH and right ventricular (RV) systolic dysfunction are detectable by TTE only in patients with advanced COPD [7]. However, cardiovascular risk factors and comorbidities may affect cardiac function even in mild-to-moderate COPD, without affecting global cardiac contractility assessed by left ventricular ejection fraction (LVEF). For this reason, in recent years, researchers have focused their attention on the identification of early markers of myocardial systolic function, that could be more sensitive than LVEF in detecting subclinical myocardial organ damage.

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METHODS

Search strategy Two reviewers (A.S. and M.B.) will independently access PubMed, Embase and Scopus databases to research all echocardiographic studies that, regardless of timeframe, performed conventional TTE implemented with STE analysis of biventricular mechanics in COPD patients without severe airflow limitation. The search strategy will include the following terms: “chronic obstructive pulmonary disease” OR “COPD” AND “echocardiography” OR “speckle tracking echocardiography” AND “cardiac function” AND “biventricular mechanics” OR “left ventricular mechanics” OR “left ventricular global longitudinal strain” OR “LV-GLS” AND “right ventricular mechanics” OR right ventricular global longitudinal strain” OR “RV-GLS”. No language restrictions will be imposed.

Participant or population All case-control studies assessing cardiac function by traditional TTE implemented with STE analysis of biventricular mechanics in hemodynamically stable COPD patients without advanced lung disease vs. healthy individuals without COPD, will be included in this systematic review and meta-analysis.
Criteria of exclusion will be: echocardiographic studies focused on COPD patients in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage IV [defined by forced expiratory volume in the first second (FEV1) <30% of predicted values and FEV1/forced vital capacity (FVC) ratio <70%], with severe PH, hemodinamic instability, acute respiratory failure and/or congestive right heart failure (RHF); imaging studies who performed TTE in COPD patients without concomitant assessment of myocardial strain parameters by STE, echocardiographic studies who analyzed COPD individuals without controls, nonechocardiographic studies, and finally nonclinical studies.

Intervention All case-control studies assessing cardiac function by traditional TTE implemented with STE analysis of biventricular mechanics in hemodynamically stable COPD patients without advanced lung disease vs. healthy individuals without COPD.

Comparator Healthy individuals without COPD.

Study designs to be included Case-control studies.

Eligibility criteria All case-control studies assessing cardiac function by traditional TTE implemented with STE analysis of biventricular

mechanics in hemodynamically stable COPD patients without advanced lung disease vs. healthy individuals without COPD, will be included in this systematic review and meta-analysis.
Criteria of exclusion will be: echocardiographic studies focused on COPD patients in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage IV [defined by forced expiratory volume in the first second (FEV1) <30% of predicted values and FEV1/forced vital capacity (FVC) ratio <70%], with severe PH, hemodinamic instability, acute respiratory failure and/or congestive right heart failure (RHF); imaging studies who performed TTE in COPD patients without concomitant assessment of myocardial strain parameters by STE, echocardiographic studies who analyzed COPD individuals without controls, nonechocardiographic studies, and finally nonclinical studies.

Information sources Two reviewers (A.S. and M.B.) will independently access PubMed, Embase and Scopus databases to research all echocardiographic studies that, regardless of timeframe, performed conventional TTE implemented with STE analysis of biventricular mechanics in COPD patients without severe airflow limitation.

Main outcome(s) The primary endpoint will be to quantify the effect of COPD on LV-GLS and RV-GLS in individuals without advanced lung disease.

Additional outcome(s) To quantify the effect of COPD on LVEF and TAPSE in individuals without advanced lung disease.

Quality assessment / Risk of bias analysis The risk of bias (RoB) will be assessed by using the National Institutes of Health (NIH) Quality Assessment of Case-Control Studies. Two authors (A.S. and G.L.N.) will independently estimate the quality rating of each study as “good”, “fair”, or “poor”. The Cohen’s Kappa coefficient will be employed to quantify the level of agreement between the two raters.

Strategy of data synthesis Continuous data (LV-GLS, RV-GLS, LVEF and TAPSE) will be pooled as the standardized mean difference (SMD) comparing COPD cohorts with healthy controls. The overall SMDs of LV-GLS, RV-GLS and LVEF will be calculated using the random-effect model, due to the increased between-study heterogeneity. The I-squared statistic (I2) will be used to quantify the percentage of variation across studies. Publication bias will be assessed by using Begg’s funnel plots and Egger’s test. Meta-regression analysis will be performed to determine whether the effect of COPD on biventricular mechanics might be influenced by potential confounders, such as age, BMI and SBP for LV-GLS, and the ultrasound machine employed for STE analysis and systolic pulmonary artery pressure (sPAP) for RV-GLS. The statistical analysis will be performed with the software Comprehensive Meta-Analysis version 3.0 (Biostat, Englewood, NJ, USA) and two-tailed p values below 0.05 will be considered statistically significant.

Subgroup analysis N/A.

Sensitivity analysis Sensitivity analyses will be performed to explore the impact of removing each of the studies on the overall SMDs of LV-GLS, RV-GLS and TAPSE.

Country(ies) involved Italy.

Keywords chronic obstructive pulmonary disease; COPD; subclinical myocardial dysfunction; LV-GLS; RV-GLS.

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