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Short Communication

Internal Medicine Section

Impact of COPD on Susceptibility and Severity of Viral Infections

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ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is linked to worse outcomes in respiratory viral infections, especially COVID-19. Understanding genetic and mechanistic connections may improve risk assessment and treatment strategies.

Aim: To investigate the genetic and biological links between COPD and respiratory viral infections.

Materials and Methods: Using three COVID-19 outcomes- SARS-CoV-2 infection, COVID-19 hospitalisation, and critical COVID-19 as representative cases. In parallel, we conducted literature-based functional pathway analysis to identify and map shared molecular, cellular, and tissue/organ-level mechanisms linking COPD to both COVID-19 and viral infections more broadly, enabling visualisation of biologically plausible pathways contributing to disease susceptibility and severity.

Results: Our Mendelian Randomisation (MR) analysis revealed a genetic predisposition in individuals with COPD to an increased risk of severe COVID-19 {Odds Ratio (OR)=1.16, 95% CI: 1.01–1.34, p=0.033}, while no reverse causal effect of COVID-19 on COPD was observed (p>0.37). Functional pathway analysis highlighted key overlapping molecular players- such as Transmembrane Serine Protease (TMPRSS2), Angiotensin-Converting Enzyme 2 (ACE2), Tumour Necrosis Factor (TNF), Interleukin (IL)-6, Interferons (IFNs), Dipeptidyl Peptidase-4 (DPP4) and Human Leukocyte Antigen (HLA) alleles- and dysregulated biological processes, including inflammation, oxidative stress, apoptosis, coagulation, angiogenesis, and immune responses. These findings support a model where SARS-CoV-2 infection exacerbates pre-existing pathological pathways in COPD, contributing to more severe disease outcomes.

Conclusion: This study provides genetic and mechanistic evidence supporting the heightened vulnerability of COPD patients to severe COVID-19 and general viral infections. The identified shared molecular pathways may inform future therapeutic targets and guide clinical risk stratification in chronic respiratory disease management.

Keywords: Chronic obstructive pulmonary disease, Functional pathway analysis, Mendelian randomisation, Respiratory viral infections, Risk stratification

INTRODUCTION

COVID-19, caused by the novel coronavirus SARS-CoV-2, with a mortality rate of 2.5%, primarily affects adults aged 30-50 years, with individuals over 65 years experiencing the highest fatality rate [1-3]. Various risk factors such as age, pre-existing medical conditions, compromised immune systems, and occupation significantly increase susceptibility, severity, and mortality risk in COVID-19 patients [3-5]. Additionally, biomarkers, genetic variants, and medical rehabilitation have been used to predict and improve prognosis, while treatment with antiviral medications, immunomodulatory drugs, and supportive care plays a crucial role in reducing symptoms and preventing complications [6-8].

COPD is a prevalent and debilitating lung disorder, primarily caused by smoking [9]. It affects approximately 10-15% of the global population and is responsible for about three million deaths annually, imposing a significant burden on public health [9].

Given the pulmonary tropism of SARS-CoV-2 and the chronic nature of COPD, there is growing interest in understanding how viral infections, especially COVID-19, may exacerbate chronic respiratory conditions [10,11]. COPD impairs lung function and weakens the immune response, making COPD patients more susceptible to COVID-19 [10,12].

Emerging evidence points toward shared inflammatory and immunological pathways, such as ACE2 upregulation, increased expression of TMPRSS2, and dysregulated cytokine signalling, which may collectively amplify disease severity in COPD patients infected with SARS-CoV-2 [11,12].

Despite strong clinical correlations, the presence of a causal genetic relationship between COPD and COVID-19 severity has not been firmly established. We hypothesise that COPD may predispose individuals to more severe outcomes from viral infections, including COVID-19, due to structural damage to the airways, impaired mucociliary clearance, and chronic immune dysregulation.

The MR is a method that leverages genetic variants as Instrumental Variables (IV) has emerged as a powerful tool for inferring causal associations while minimising confounding and reverse causation [13,14]. In this study, we apply bidirectional MR to evaluate the causal links between COPD and multiple COVID-19 outcomes, including SARS-CoV-2 infection, hospitalisation, and critical illness.

Additionally, we conduct extensive literature data mining to elucidate shared molecular and cellular pathways, aiming to uncover how viral infections may interact with chronic respiratory disease processes. This integrative approach seeks to provide novel insights into the biological mechanisms through which SARS-CoV-2 infection exacerbates COPD, and vice versa, offering a more comprehensive understanding of viral exacerbation in chronic lung disease.

MATERIALS AND METHODS

This study investigates the potential genetic and mechanistic interplay between COPD and respiratory viral infections, using COVID-19 as a representative case. We employed a two-pronged approach combining MR analysis to assess bidirectional genetic associations between COPD and COVID-19 outcomes, and literature-based functional pathway analysis to elucidate shared biological mechanisms across molecular, cellular, and tissue levels.

Genetic Links between COVID-19 and COPD using MR analysis

This study employed publicly available Genome-Wide Association Study (GWAS) summary data for both COVID-19 and COPD. The COVID-19 GWAS datasets were obtained from the COVID-19 Host Genetics Initiative (HGI) for the European population, accessed on April 8, 2022. These datasets included data on critical COVID-19 (13,769 cases and 1,072,442 controls), hospitalised COVID-19 (32,519 cases and 2,062,805 controls), and SARS-CoV-2 infection (122,616 cases and 2,475,240 controls) [15]. Additionally, the COPD dataset was sourced from FinnGen R9 (https://r9.risteys.finngen.fi/), consisting of 18,266 cases and 311,286 controls, all of European ancestry [16].

To infer potential causal associations, we conducted bidirectional MR using the Two-Sample MR R package [17]. We applied the Inverse-Variance Weighted (IVW) method as the primary estimator, complemented by Weighted Median (WM) and MR-Egger regression models to assess robustness. IVs were selected based on genome-wide significance ($p<5 \times 10^{-8}$) followed by Linkage Disequilibrium (LD) clumping using an r^2 threshold of <0.001 within a 10 Mb window to ensure independence. The strength of each IV was evaluated using F-statistics (with F > 10 considered sufficiently strong), and variants associated with known confounders were excluded where applicable. These validation steps were applied uniformly across all analyses to minimise potential bias from weak or pleiotropic instruments. The MR-Egger intercept was used to test for directional pleiotropy, while heterogeneity was assessed using Cochran's Q test and I^2 statistics, with $p<0.05$ and $I^2 > 0.25$ indicating significant heterogeneity [18].

Statistical Power Calculations

To evaluate the adequacy of the MR analyses, we conducted statistical power calculations using established formulas that relate the variance explained by genetic instruments (R^2), the sample size (N), and the detectable causal effect size. For each instrument set (IV_COPD_COVID7A/B/C), per-SNP R^2 values were calculated as $2 \times EAF \times (1 - EAF) \times \beta^2$ and summed to obtain total R^2. Power for a two-sided test ($\alpha=0.05$) was estimated from the non-centrality parameter (β/SE), where $SE \approx \sqrt{((1 - R^2)/(N \times R^2))}$. The approximate F-statistic was computed as $F = (R^2/(1-R^2)) \times ((N\_exposure-k-1) / k)$. Across all analyses, R^2 values ranged from 0.01 to 0.05, and outcome sample sizes were approximately one to two million participants, providing >80% power to detect moderate causal effects (OR ≈ 1.15-1.20). Detailed results are presented in [Supplementary data 1-3].

Molecular, Cellular, and Tissue-Level Interactions via Knowledge-Based Analysis

Recognising that genetic associations alone may not fully capture the complex interplay between COPD, COVID-19, and broader viral infections, we conducted an in-depth exploration of shared mechanisms using a knowledge-based, literature-driven mining approach. This analysis was performed using an AI-powered semantic search engine developed by AIC LLC (https://www.gousinfo.com/en/advancedsearch.html), which integrates multiple biomedical databases, including PubMed, GenBank, PDB, Ensembl, and others, as described in the official user guide (https://www.gousinfo.com/en/userguide.html, FAQ section). The platform performs real-time searches that capture the latest available data and employs AI-based quality control processes to automatically exclude non-qualified results using the adjusted binomial method [19]. Search queries combined disease and gene terms relevant to this study, and retrieved results were filtered based on biological plausibility, publication quality, and citation frequency. Only validated gene-disease or mechanistic associations were retained for downstream analysis.

Our investigation focused on systematically identifying and connecting molecular, cellular, and tissue/organ-level components and pathways implicated in the three conditions. Specifically, we mapped interactions spanning molecular signaling (e.g., apoptosis, cytokine release, oxidative stress), immune and inflammatory processes, and tissue-level effects (e.g., damage or modulation of the lungs, cardiovascular system, immune system, and central nervous system). These findings lead to pathway constructions that illustrate the functional network architecture linking COPD to both COVID-19 and viral infection across multiple biological layers.

To ensure rigour, we applied strict filtering criteria to exclude coincidental or unsupported associations and emphasised biologically plausible, literature-supported connections based on reference count, polarity, and statistical significance (e.g., q-values). The resulting multi-scale knowledge graph reveals how pre-existing COPD may amplify vulnerability to viral infections and highlights shared pathological pathways that could drive disease severity and progression.

RESULTS

MR analysis results: COVID-19 on COPD

The analyses encompass three factors: SARS-CoV-2 infection, hospitalisation due to COVID-19, and critical COVID-19, with COPD serving as the resultant outcome.

Three MR methods, namely Inverse Variance Weighted (IVW), WM, and MR-Egger, are employed for each combination of exposure and outcome. The findings are consolidated based on the estimated effect size (b), Standard Error (SE), OR along with its 95% Confidence Interval (CI), and p-value.

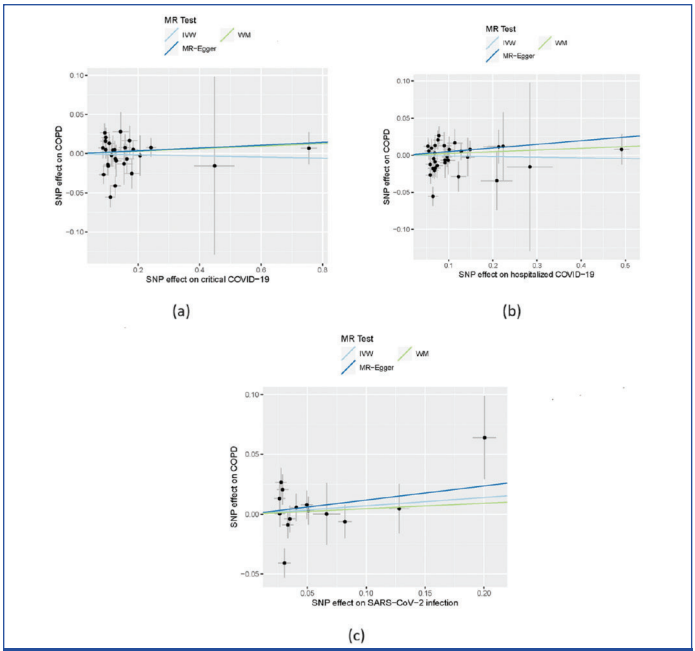
Overall, the MR analyses reveal no apparent causal effects of SARS-CoV-2 infection, hospitalised COVID-19, or critical COVID-19 on COPD. Across all methods and exposure-outcome pairs, the estimated effect sizes hover around null, with wide CIs overlapping 1.00, and p-values indicating no statistical significance. Therefore, according to these MR analyses, there is no evidence to suggest a causal effect of COVID-19 on COPD at the genetic level [Table/Fig-1,2].

MR analysis results: COPD on COVID-19

In general, these analyses reveal no evident causal links between COPD and SARS-CoV-2 infection or hospitalised COVID-19. For the influence of COPD on critical COVID-19, only the WM method showed significance (OR=1.16; p=0.033) [Table/Fig-3,4].

Exposure	Outcome	Method	N_IV	b (se)	OR (95%CI)	P
SARS-CoV-2 infection	COPD	IVW	14	0.070 (0.095)	1.07 (0.89-1.29)	0.46
SARS-CoV-2 infection	COPD	WM	14	0.046 (0.097)	1.05 (0.87-1.27)	0.64
SARS-CoV-2 infection	COPD	MR-Egger	14	0.118 (0.188)	1.13 (0.78-1.63)	0.54
Hospitalised COVID-19	COPD	IVW	32	-0.009 (0.030)	0.99 (0.93-1.05)	0.77
Hospitalised COVID-19	COPD	WM	32	0.023 (0.036)	1.02 (0.95-1.10)	0.51
Hospitalised COVID-19	COPD	MR-Egger	32	0.049 (0.054)	1.05 (0.94-1.17)	0.37
Critical COVID-19	COPD	IVW	27	-0.007 (0.024)	0.99 (0.95-1.04)	0.77
Critical COVID-19	COPD	WM	27	0.016 (0.025)	1.02 (0.97-1.07)	0.52
Critical COVID-19	COPD	MR-Egger	27	0.018 (0.043)	1.02 (0.94-1.11)	0.680

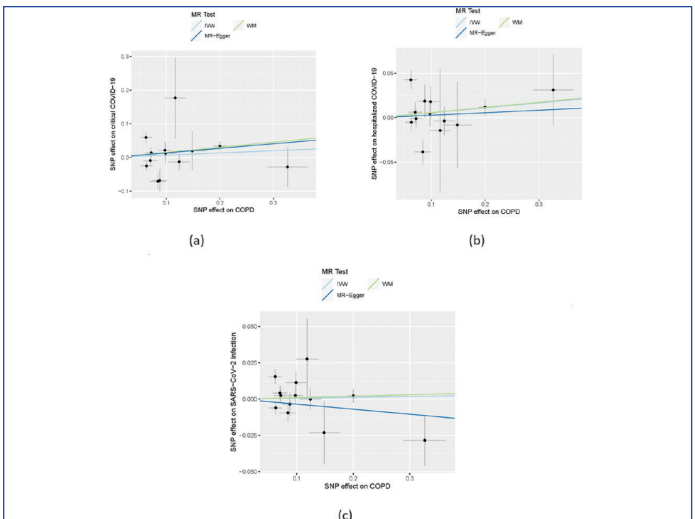
[Table/Fig-1]: The causal effect of COVID-19 on COPD.
IVW: Inverse variance weighted; WM: Weighted median; OR: Odds ratio; CI: Confidence interval; N_IV: Number of instrumental variables



[Table/Fig-2]: Causal effects of COVID-19 on COPD: a) Critical COVID-19 on COPD; b) Hospitalised COVID-19 on COPD; (c) SARS-CoV-2 infections on COPD. The lines depict the effect sizes (b) of the MR analysis.
IVW: Inverse variance weighted; WM: Weighted median.

Exposure	Outcome	Method	N_IV	b (se)	OR (95%CI)	P
COPD	SARS-CoV-2 infection	IVW	13	0.006 (0.022)	1.01 (0.96-1.05)	0.78
COPD	SARS-CoV-2 infection	WM	13	0.010 (0.021)	1.01 (0.97-1.05)	0.63
COPD	SARS-CoV-2 infection	MR-Egger	13	-0.035 (0.048)	0.97 (0.88-1.06)	0.49
COPD	Hospitalised COVID-19	IVW	13	0.056 (0.051)	1.06 (0.96-1.17)	0.28
COPD	Hospitalised COVID-19	WM	13	0.058 (0.045)	1.06 (0.97-1.16)	0.20
COPD	Hospitalised COVID-19	MR-Egger	13	0.028 (0.115)	1.03 (0.82-1.29)	0.81
COPD	Critical COVID-19	IVW	13	0.067 (0.093)	1.07 (0.89-1.28)	0.47
COPD	Critical COVID-19	WM	13	0.151 (0.071)	1.16 (1.01-1.34)	0.033
COPD	Critical COVID-19	MR-Egger	13	0.135 (0.205)	1.14 (0.77-1.71)	0.52

[Table/Fig-3]: The causal effect of COPD on COVID-19.



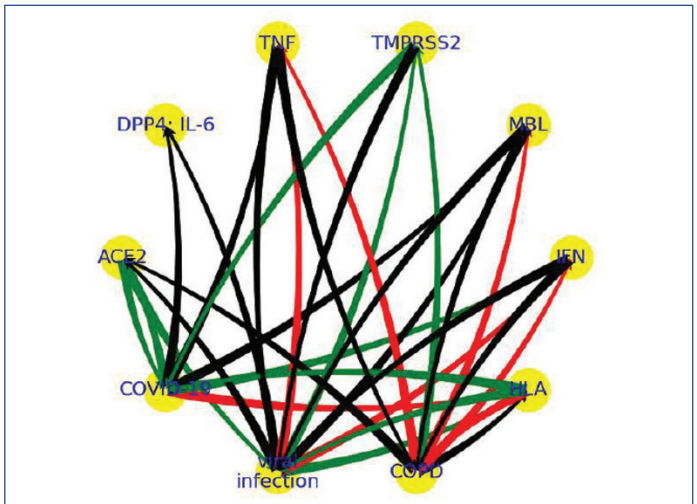
[Table/Fig-4]: Causal effects of COPD on COVID-19: a) COPD on Critical COVID-19; b) COPD on hospitalised COVID-19; c) COPD on SARS-CoV-2 infections. The lines depict the effect sizes (b) of the MR analysis.

Although no directional pleiotropy was detected in the MR analyses (MR-Egger intercept P > 0.05), significant heterogeneity was observed across several models (Cochran's Q p<0.05; [Supplementary data S4], indicating variability in the estimated causal effects of COPD on COVID-19 outcomes across instruments. Such heterogeneity may reduce the reliability of both the IVW and MR-Egger estimates and could partly explain the inconsistent significance across methods. Therefore, the modest association observed using the WM approach for critical COVID-19 (OR=1.16, P=0.033) should be interpreted with caution. Further studies with larger and more homogeneous datasets are warranted to validate this potential relationship.

To assess the robustness of the MR estimates, we performed sensitivity analyses including MR-Egger intercept tests for directional pleiotropy and heterogeneity assessments using Cochran's Q and I^2 statistics. No evidence of directional pleiotropy was observed across outcomes (MR-Egger intercept P > 0.05). Some heterogeneity was detected for certain outcomes, for example, IVW models for SARS-CoV-2 infection (Q=22.48, P=0.033, I^2=46.6%), hospitalised COVID-19 (Q=26.34, P=9.60 × 10^{-3}, I^2=54.4%), and critical COVID-19 (Q=38.73, P=1.17×10^{-4}, I^2=69%), indicating that the MR estimates should be interpreted with caution. WM results were largely consistent, and MR-Egger estimates showed similar directionality but wider CIs, supporting the overall robustness of the findings.

Molecular-level connection of COVID-19 and COPD

The molecular functional network connecting COPD to both COVID-19 and general viral infections reveals a complex interplay of molecular and immune pathways, highlighting several key mediators [Table/Fig-5]. COPD appears to upregulate TMPRSS2 and ACE2, two known viral entry receptors, potentially increasing susceptibility to infections like COVID-19. It also negatively regulates immune components such as TNF, IFN, and MBL, suggesting a dampened antiviral response. ACE2, TMPRSS2, HLA, and MBL are shared nodes linking COPD to both COVID-19 and broader viral infections, underscoring convergent mechanisms of viral vulnerability. The network also shows that viral infections and COVID-19 may modulate immune responses via IFN, TNF, and DPP4: IL-6, further influencing COPD pathology. Overall, this integrative network highlights how COPD may both facilitate viral entry and impair immune defense, thereby increasing risk and severity of current and future respiratory viral infections.

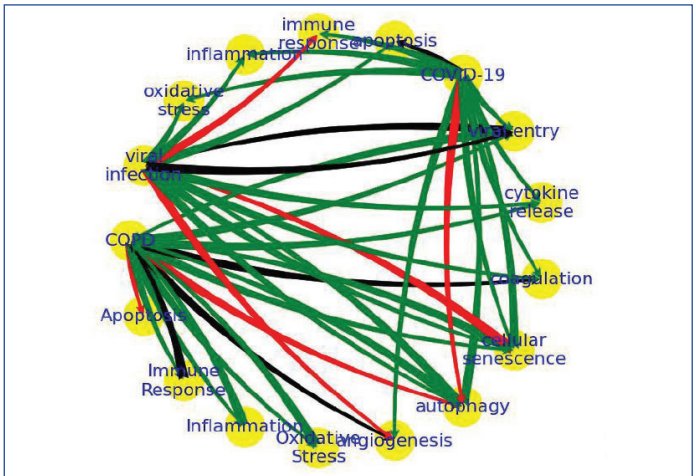


[Table/Fig-5]: Molecular pathways connecting COPD and COVID-19.

Cell process level connection of COVID-19 and COPD

The cell process functional pathway network connecting COPD to both COVID-19 and general viral infections highlights several shared and COPD-influenced biological processes, as illustrated in [Table/Fig-4]. COPD shows significant positive associations with inflammation (q=1.18×10^{-4}), oxidative stress (q=0.0026), cytokine

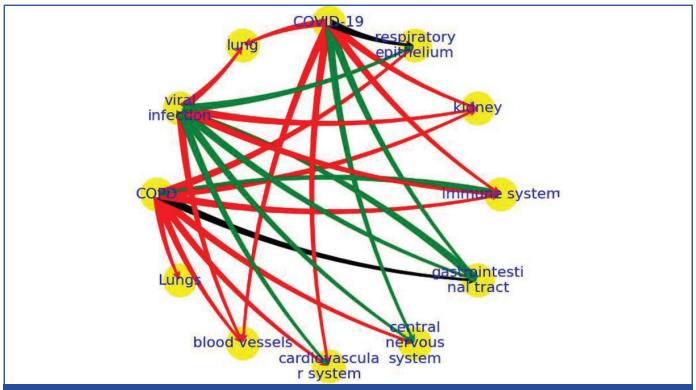
release ($q=1.18\times10^{-4}$), and cellular senescence ($q=2.94\times10^{-6}$), while negatively regulating apoptosis ($q=1.18\times10^{-4}$) and autophagy. COVID-19 similarly promotes cytokine release ($q=1.22\times10^{-8}$), oxidative stress ($q=5.49\times10^{-8}$), coagulation, inflammation, and immune responses, overlapping extensively with COPD pathways. Viral infection pathways also align with those of COPD and COVID-19, showing enhanced inflammation, oxidative stress, cytokine release, and cellular senescence, but with a negative effect on angiogenesis ($q=0.0105$) and immune response ($q=0.0693$). Shared biological mechanisms such as autophagy, viral entry, coagulation, and apoptosis appear central to disease interactions. Altogether, the network underscores how COPD predisposes individuals to amplified host responses that are also commonly activated during viral infections, contributing to greater disease severity and complications [Table/Fig-6].



[Table/Fig-6]: Cell process pathways connecting COPD and COVID-19.

Tissue/organ level connection of COVID-19 and COPD

The tissue/organ-level pathway network connecting COPD with COVID-19 and viral infections highlights widespread systemic effects, particularly on the respiratory and immune systems. COPD shows strong negative associations with the lungs ($q=3.48\times10^{-8}$), blood vessels and cardiovascular system (both $q=4.99\times10^{-5}$), immune system and respiratory epithelium ($q=6.41\times10^{-6}$), and kidney ($q=0.0064$), indicating broad tissue-level impairment. COVID-19 mirrors this pattern, significantly affecting the immune system and kidney (both $q \approx 1.55\times10^{-6}$), as well as the cardiovascular system, blood vessels, and lungs, while also showing positive associations with the central nervous system and gastrointestinal tract. Similarly, viral infections influence many of the same tissues, including negative effects on the lung ($q=0.0067$), blood vessels, immune system, and kidney, while positively affecting the central nervous system, gastrointestinal tract, and respiratory epithelium. These overlapping impacts suggest that COPD-induced vulnerabilities in key organs-especially the lungs, immune system, and vasculature underlie heightened susceptibility and severity to both COVID-19 and broader viral infections [Table/Fig-7].



[Table/Fig-7]: Tissue/organ pathways connecting COPD and COVID-19.

DISCUSSION

At the genetic level, our MR analysis suggests that genetic predisposition to COPD may elevate the risk of critical COVID-19, but not the less severe forms of the disease. Additionally, genetic susceptibility to COVID-19 does not appear to be associated with the risk of COPD at the genetic level. However, the absence of direct causality does not imply a lack of association; rather, these conditions exhibit intricate interactions across molecular, cellular, and tissue levels.

To explore these interactions beyond genetic associations, we integrated knowledge-based literature mining, which revealed converging mechanisms linking COPD, COVID-19, and broader viral infections. This multi-scale approach provided deeper insight into how chronic respiratory pathology may exacerbate viral disease outcomes and vice versa.

At the molecular level, TMPRSS2 emerges as a significant factor in the interplay between COVID-19 and COPD. TMPRSS2 overexpression exacerbates mucus production and airway remodeling in COPD, potentially heightening susceptibility to severe COVID-19 infections [20]. Conversely, elevated TMPRSS2 expression is associated with increased vulnerability to COVID-19, particularly among lung cancer patients [21]. The rs12329760 polymorphism in TMPRSS2 is linked to reduced severity of COVID-19 [22], and TMPRSS2 inhibitors may represent a potential therapeutic avenue, but further experimental and clinical studies are needed to assess their efficacy and safety in COPD patients [23]. Moreover, Lower TMPRSS2 expression in COPD could contribute to severe lung injury during COVID-19 infection, highlighting a possible mechanism that warrants additional investigation before informing clinical management [24].

Additional molecular mechanisms shared between COPD and viral infections- including COVID-19- include reduced interferon [25], upregulated ACE2 expression [26], and altered cytokine profiles such as increased IL-6 and TNF levels [27,28], and disruption of innate immune defenses such as altered MBL and DPP4 activity [29,30]. These immune and inflammatory imbalances can facilitate viral entry and persistence, contributing to the severity of respiratory infections in COPD patients.

At the cellular level, viral infections, including COVID-19, can exacerbate chronic inflammation in COPD by triggering excessive immune activation. SARS-CoV-2-induced cytokine storms, oxidative stress, and immune cell dysregulation further impair pulmonary function and heighten the risk of complications such as multi-organ failure [31]. Additionally, the disruption of cellular senescence and apoptosis pathways by viral pathogens may synergise with age-related deterioration in COPD, accelerating disease progression [32]. Importantly, COPD itself alters susceptibility to viral infections through a range of cellular mechanisms. Chronic inflammation and impaired epithelial barrier function reduce mucociliary clearance and innate immune responses, promoting viral replication and persistence [33]. COPD-induced oxidative stress and coagulation abnormalities may also compound the vascular and thrombotic complications commonly observed in COVID-19 [34,35]. Dysregulated apoptosis and senescence may enhance tissue damage during acute viral infections [36,37]. These cellular mechanisms suggest pathways by which COPD may increase susceptibility to viral infections, though their direct impact on patient outcomes requires further validation in clinical studies.

At the tissue and organ levels, knowledge-based literature mining highlighted convergent pathophysiological effects of COPD and viral infections on multiple organ systems. COVID-19-induced hyperinflammation and vascular damage can exacerbate pre-existing COPD complications, such as pulmonary hypertension and endothelial dysfunction [38]. Moreover, SARS-CoV-2's nephrotoxic effects may be more pronounced in COPD patients who are already vulnerable to organ injury [39].

COPD also impacts the systemic trajectory of viral diseases. The structural damage, chronic inflammation, and immune exhaustion characteristic of COPD can increase viral load, prolong infection, and heighten complications across respiratory and extrapulmonary systems. These findings indicate potential mechanisms through which COPD may exacerbate viral disease outcomes. However, the clinical significance of these interactions remains to be confirmed in prospective patient cohorts.

Beyond COVID-19, COPD is a well-established risk factor for a wide spectrum of respiratory viral infections, such as influenza, RSV, and rhinovirus, as well as bacterial pneumonias [40]. This broad infectious susceptibility is driven by impaired mucociliary clearance [41], epithelial dysfunction [42], and chronic airway inflammation [43]. Further, COPD-related immune impairments- including reduced macrophage and neutrophil function [44,45] and diminished antiviral responses [46]- compromise host defense mechanisms. Persistent colonisation with pathogens such as Haemophilus influenzae and Streptococcus pneumoniae also contributes to secondary infections and chronic inflammation [43].

These shared biological features, now visualised through our knowledge-based literature mining, underscore COPD as a general amplifier of vulnerability to respiratory viral infections, not limited to COVID-19. While our MR findings focused on causal links specific to SARS-CoV-2 outcomes, the broader network-based insights reveal how COPD may influence the severity of diverse respiratory infections through converging molecular and cellular pathways.

Although our findings reveal important molecular and systemic overlaps between COPD and viral infections, several unknowns remain. While the MR analysis in this study focused on the genetic connection between COPD and COVID-19 as a representative case of respiratory viral infections, future research should broaden this scope to include other infectious diseases beyond COVID-19. Investigating the genetic predisposition and shared pathological mechanisms between COPD and additional viral or bacterial infections will further clarify COPD's role as a general risk factor for infectious disease severity and progression. Moreover, future studies should aim to validate these pathways in patient cohorts, integrate real-world clinical data, and explore therapeutic strategies that target these shared mechanisms.

Limitation(s)

Several limitations should be considered when interpreting our findings. First, the MR analyses provide suggestive evidence of a potential causal effect of COPD on critical COVID-19, but only the weighted median method reached statistical significance, whereas the IVW and MR-Egger methods did not. Significant heterogeneity was observed across several models (Cochran's Q $p<0.05$; I^2 up to 69%), which may reduce the reliability of effect estimates and warrants cautious interpretation. Second, multiple testing across three COVID-19 outcomes and three MR methods was performed without formal correction, raising the possibility of false-positive findings. Third, while our literature-based pathway analysis provides a comprehensive mechanistic overview, it relies on an AI-powered mining platform and is not a formal systematic review. This approach may introduce selection bias and does not fully account for unpublished or contradictory evidence. Fourth, the study populations were restricted to individuals of European ancestry, which may limit generalisability to other populations. Finally, while our integrative analysis highlights biologically plausible pathways linking COPD and viral infections, the functional and clinical implications remain hypothetical and require experimental validation.

CONCLUSION(S)

Our study provides genetic evidence that COPD may increase the risk of developing critical COVID-19, while genetic susceptibility to COVID-19 does not appear to influence the risk of COPD causally. In addition to this unidirectional genetic link, the systemic immune dysfunction and structural airway abnormalities associated with COPD highlight its role as a general risk factor for respiratory infections beyond COVID-19. These findings emphasise the importance of targeted prevention and management strategies for individuals with COPD, particularly in the context of emerging respiratory pathogens.

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