Bibliometric and Visualized Analysis of Hotspots in Biological Therapy for Chronic Obstructive Pulmonary Disease from 2000 to 2025

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a major global health challenge, characterized by persistent respiratory symptoms and airflow limitation. The global prevalence of COPD is approximately 10.3%, which has become the world's third leading cause of death. COPD not only greatly affects patients' quality of life but also brings a heavy economic burden to the world's healthcare systems. Biological therapy refers to the treatment of diseases with biological materials or biological response modifiers. Biologic therapies are gaining attention in managing COPD and are becoming a research hotspot.

Objective: The primary objective of this study is to conduct a bibliometric and visualized analysis of research hotspots and trends in biological therapies for Chronic Obstructive Pulmonary Disease (COPD) from 2000 to 2025. Using tools like CiteSpace, VOSviewer, R-Bibliometrix, and Origin, the study aims to:

Identify key contributing countries, institutions, authors, and journals.

Analyze collaboration networks and research impact.

Uncover emerging research themes and future directions through keyword co-occurrence, clustering, and burst detection.

Provide a comprehensive overview of the evolving landscape in COPD biological therapy to guide future research and clinical practice.

This objective is clearly stated in the Abstract and Introduction sections of the manuscript.

Methods: This study used the Web of Science Core Collection as the database. Then we used CiteSpace, VOSviewer, R-Bibliometrix, and Origin to visualize research on COPD and biologic therapies. These tools helped identify current research hotspots and predict future trends in the field.

Results: This study collected 474 publications related to the field from 205 countries and 2,010 institutions. The United States plays a central role in this research field. The University of Groningen has the highest number of publications. The most prolific authors are Cazzola, Mario, and Barnes, Peter J., who have the most citations. The most co-cited journal is the American Journal of Respiratory and Critical Care Medicine. The hot keywords include "therapy," "asthma," "airway inflammation," "risk," "cancer," "mepolizumab," and "expression," among others.

Conclusions: This study used visualization analysis to determine potential future research directions, which are as follows: (1) Exploring the pathophysiological roles of novel immune regulatory targets and developing intervention strategies; (2) Pushing for the fusion of interdisciplinary technologies. (3) Combine safety data from multiple centers with long-term follow-up and dynamic efficacy monitoring indicators. Through keyword analysis, current or future research hotspots may involve the link between monoclonal antibodies and COPD. At present, the research on biological therapy for COPD still needs further

development to offer patients safer and more cost-effective treatment options.

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Bibliometric and Visualized Analysis of Hotspots in Biological Therapy for Chronic Obstructive Pulmonary Disease from 2000 to 2025

Lei Xie, ‡[a] Yun He, ‡[a] Huiping Zhou,[b] Jiarui Lin,[b] Nuo Xu,[b] Mengyun Chen,[b] Jinglin Wu,[b] Zeli Liu,*[a] Wei Liu,*[a]

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Keywords: *Biological Therapy; Chronic Obstructive Pulmonary Disease; Citespace; Vosviewer; Bibliometrics; COPD*

Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a major global health challenge, characterized by persistent respiratory symptoms and airflow limitation. The global prevalence of COPD is approximately 10.3%, which has become the world's third leading cause of death. COPD not only greatly affects patients' quality of life but also brings a heavy economic burden to the world's healthcare systems. Biological therapy refers to the treatment of diseases with biological materials or biological response modifiers. Biologic therapies are gaining attention in managing COPD and are becoming a research hotspot.

Method: This study used the Web of Science Core Collection as the database. Then we used CiteSpace, VOSviewer, R-Bibliometrix, and Origin to visualize research on COPD and biologic therapies. These tools helped identify current research hotspots and predict future trends in the field.

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Conclusion: This study used visualization analysis to determine potential future research directions, which are as follows: (1) Exploring the pathophysiological roles of novel immune regulatory targets and developing intervention strategies; (2) Pushing for the fusion of interdisciplinary technologies. (3)

Combine safety data from multiple centers with long-term follow-up and dynamic efficacy monitoring indicators. Through keyword analysis, current or future research hotspots may involve the link between monoclonal antibodies and COPD. At present, the research on biological therapy for COPD still needs further development to offer patients safer and more cost-effective treatment options.

1.Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic and complex condition with significant heterogeneity. It is typically characterized by persistent respiratory symptoms and restricted airflow. The pathogenesis of this disease is complex and is related to long-term exposure to harmful particles or gases. At the same time, it also involves host genetic susceptibility, abnormal inflammatory response, and many other factors, which are intertwined with each other, resulting in greater heterogeneity in COPD patients[1].

According to the World Health Organization, the prevalence of COPD has reached a high of 10.3% worldwide, making it the third leading cause of death in the world, which seriously affects the quality of life of patients and adds a huge economic burden to the global health care system[2]. Symptoms such as difficulty breathing, cough, and expectoration often lead to a decline in physical function and increase the risk of hospitalization. In the advanced stages of the disease, COPD can also cause respiratory and heart failure problems[3], The current treatment of bronchiectasis mainly focuses on the use of long-acting $\beta_2$receptor agonists (LABAs) and long-acting anticholinergic drugs (LAMAs). In addition, inhaled glucocorticoids or ICS, also play an important role in the treatment of severe chronic obstructive pulmonary disease[4, 5]. These drugs can effectively relieve breathing difficulties, cough, and sputum-related symptoms, to a certain extent, and can reduce the frequency and severity of the disease[6]. It has to be pointed out that these treatments are not perfect, but there are some specific limitations, for example, although these drugs do have a certain range of symptoms that can be alleviated, in different patients, the treatment effect is different. Glucocorticoids are the main anti-inflammatory drugs used in the treatment of COPD, and long-term high doses, even when administered by inhalation, may cause serious adverse reactions, such as an increased risk of pneumonia in patients[7, 8].

Considering the limitations of the treatment of COPD, it is urgent and necessary to explore an alternative treatment strategy that can be both safe and effective. This treatment strategy should not only focus on alleviating symptoms but also have the effect of delaying disease progression. In recent years, with the continuous in-depth research on the inflammatory mechanism of COPD, biological therapy has gradually become a hot research direction. Biotherapy, which focuses on biologics that target specific cytokines and their receptors, can precisely regulate abnormal inflammatory responses in patients, with the potential to achieve more efficient disease management, reduce the frequency of acute exacerbations, and improve patient prognosis. However, at present, the application of biotherapy in the treatment of COPD is still in the exploratory stage, and relevant research results are scattered and lack systematic sorting. Bibliometrics, as a statistical method, enables quantitative analysis of research papers on specific topics using mathematical methods, as well as assessment of research quality, analysis of key research areas, and prediction of future research directions[9].

In this study, we relied on the Web of Science Core Collection (WOSCC) database and used statistical analysis software CiteSpace and VOSviewer to conduct a comprehensive bibliometric and visual analysis of the literature related to biotherapy for COPD from 2000 to 2025. After an in-depth analysis of the time distribution of literature publication, contributions from different countries and institutions, and co-occurrence of keywords, we identified research hotspots in this field and accurately predicted the development trend, which can provide a reliable reference for the treatment of chronic obstructive pulmonary disease.

2.Methods

2.1.Data sources and retrieval strategy

The Web of Science Core Collection, which includes records from high-quality academic journals, conference proceedings, and books globally, is recognized as a leading citation database worldwide. It is commonly used for bibliometric analysis. Data for our study were retrieved from the Science Citation Index Expanded (SCIE), part of the Web of Science Core Collection. Our search strategy is as follow: (TS=((Biological Therapy) OR (Biological Therapies) OR (Therapies, Biological) OR (Therapy, Biological) OR (Biologic Therapy) OR (Biologic Therapies) OR (Therapies, Biologic) OR (Therapy, Biologic) OR (Biotherapy) OR (Biotherapies))) AND TS=((Pulmonary Disease, Chronic Obstructive) OR (Chronic Obstructive Pulmonary Diseases) OR (COPD) OR (Chronic Obstructive Lung Disease) OR (Chronic Obstructive Pulmonary Disease) OR (COAD) OR (Chronic Obstructive Airway Disease) OR (Airflow Obstruction, Chronic) OR (Airflow Obstructions, Chronic) OR (Chronic Airflow Obstructions) OR (Chronic Airflow Obstruction)). Our search results were constrained as follows: document types: "article" and "review article". Language: English. Due to the daily updates of the database, which may affect our search results, the data in our study were downloaded on January 25, 2025. The search results were independently verified by two authors. A total of 474 publications were included. Figure 1B shows the workflow for the acquisition and processing of the 474 publications.

2.2.Data analysis

In order to further explore the research hotspots and development trends in the field of biotherapy for chronic obstructive pulmonary disease from 2000 to 2025, this study performeda visualized bibliometric analysis through the combined application of specialized software tools.

VOSviewer (version 1.6.20) relies on co-present data to build quantitative maps of authors, journals, countries, or keywords. The software can generate network visualizations, overlay visualizations, and density visualizations to present the relationships between research elements in an intuitive graphical form. The different nodes in the visual map represent the author, journal, country, and other factors, and the node size reflects the number or frequency of the corresponding factors. Under normal circumstances, the larger the nodes, the higher the importance of the factors in the research. The thickness of the lines of each factor in the visualization diagram reflects the closeness of their correlation. The thicker the lines, the higher the degree of correlation between the factors. The color of the nodes is used to distinguish between different element clusters or times so that researchers can quickly identify the structure and development of the research field, which can more clearly present the core authors of the field, high-impact journals, major research countries, and hot research topics. CiteSpace This software, based on Java language development, is based on co-citation analysis. In this study, CiteSpace (version 6.4. R1) software was used to analyze the screened literature, including co-citation analysis for countries or regions and research institutions, citation double graph overlay analysis, co-citation reference analysis, and the strongest citation breakout reference analysis. Based on the above analysis methods, we can know the cooperation status of different countries/regions and institutions in the research field, accurately identify the core references, and intuitively show the dynamic change trend of research hotspots.

With the help of R software and R-Bibliometrix and R-GGploT2 tools, this study visually analyzes the number of publications in each Country, generates a Country Collaboration Map and a country collaboration string map, and further reveals the evolution law of research hotspots over time. In order to improve the clarity and accuracy of the existing visualizations, the professional web analysis tool Pajek was used to optimize the generated images.

This bibliometric analysis was reported in strict accordance with the PRISMA 2020 statement[10]to ensure scientific, transparent, and reproducible research processes.

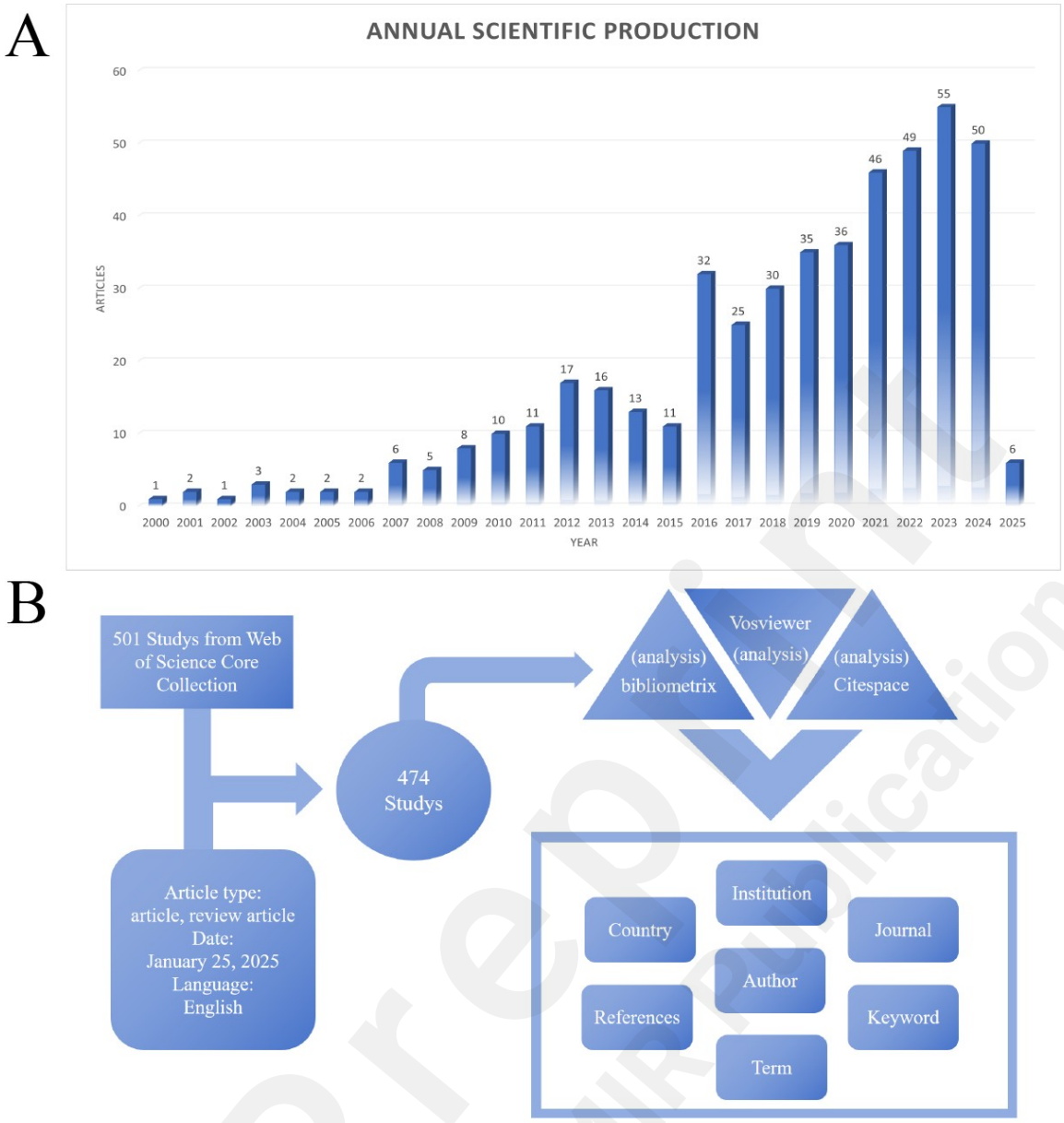

FIGURE 1 | (A) The trend in the annual publication volume of biological therapies for COPD. (B) A flowchart illustrating the process of article selection.

3. Result

3.1.Overall overview

This study includes 474 articles from the WOS database, published by 2,879 authors from 205 countries or regions, 2010 institutions, and 261 journals. Between 2000 and 2025, the annual number of publications (Figure 1A) showed a gradual increase from 2000 to 2012, slowed between 2012 and 2015 as well as between 2016 and 2017. It is worth noting that the number picked up again after 2017. 2023 had the highest number of publications, with 55 articles. Overall, the number of publications has generally increased over time. This shows that biological therapies are gaining attention in the field of COPD and have attracted the interest of many researchers.

3.2. Visual analysis of countries

According to the statistical results of the number of articles in Table 1, the United States ranked first

with 108 articles, indicating that the United States has absolute advantages in the research on the use of biological therapies to treat COPD. China followed closely behind the United States with 86 papers, which shows that China has invested a lot of energy and developed rapidly in the field of biomedical research in recent years. Looking further down, the number of articles published by the United Kingdom and Italy is 55, the two tied for third place. These European countries with a long-term accumulation of scientific research heritage and a relatively perfect scientific research system also have a high degree of activity in this field. The results of the study show that Australia's centrality value is 0.25, which is the highest in the world, indicating that it occupies a very key position in the international cooperation network, has close and extensive cooperation relations with other countries, and plays a key role in the connection of research cooperation. The centrality value of the United States is 0.17, which is at a relatively high level. Combined with the high number of published papers in the United States, it can be seen that the United States has a large number of scientific research outputs and occupies a relatively key position in international cooperation. The centrality values of the United Kingdom, Germany, and Sweden are 0.14, 0.13, and 0.19, respectively, indicating that these countries also have a strong influence in the international cooperation network. The centrality value of China is 0.02, which is relatively low compared with the above countries. Although it has published a large number of papers, it does not occupy a significant core position in the whole research network. The above centrality numerical data show that the number of published papers is not completely positively correlated with centrality, and its magnitude is affected by factors such as the research cooperation mode and the degree of correlation between countries.

The exported English literature data was imported into VOSviewer, and "Countries" under "Co-authorship" was selected for visual analysis of the country of the document. In the field of biotherapy for chronic obstructive pulmonary disease, a total of 60 countries have published articles in English journals, and we will perform a visual analysis of these countries. As shown in Figure 2B. The size of nodes in the figure shows that countries such as the USA, Germany, Italy, England, and the People's Republic of China have relatively large nodes, indicating that these countries have a relatively central position in the research of biotherapy for COPD. Combined with the results of centrality numerical analysis, it is further verified that the United States, relying on its own strong scientific research capabilities and rich scientific research resources, has made relatively large research achievements in this field and is in a leading position at the forefront of related research. Due to its increasing investment in the field of biomedicine in recent years, China's scientific research strength has been significantly improved, and its activity in this field has gradually increased, and it has become an increasingly key force in the international cooperation network.

The connections between the countries in Figure 2B represent the cooperation between them, and the thickness of these connections reflects the closeness of cooperation. Figure 2C shows a world map of countries, where the darker the color of the country, the greater the number of publications in that country. Figure 3A is a string of country collaborations, with numbers on the axis showing the number of national publications and arcs showing cooperation between countries. As can be seen from the above chart, the United States has a very close cooperative relationship with other countries. The United States has a relatively thick connection with many European countries such as Germany, Italy, and the United Kingdom, indicating that the above European and American countries have extensive and in-depth cooperation in this field, and this close cooperation may be due to similar scientific research concepts, perfect scientific research cooperation mechanisms and shared scientific research resources. China also has cooperation links with many countries, showing its active attitude towards international cooperation, but there is still room for improvement in the depth and breadth of cooperation with European and American countries. There are also some countries with small nodes and sparse connections, such as Slovakia and Iceland, suggesting that these countries started the research in this field late, invested relatively little in scientific research, or lacked effective international cooperation channels. To promote the balanced development of biotherapy research on COPD worldwide, the international community should strengthen scientific research support and cooperation guidance for these countries, build more international exchange platforms, and realize resource sharing and complementary advantages.

Figure 1A is a national map of biotherapeutics for the treatment of COPD, in which the colors of nodes are indicated by bands representing different times. The color of the ribbon starts from blue, gradually transitions to yellow, and finally to red, corresponding to a period such as 2017 to 2024, while the color of the nodes reflects the research activity of the corresponding country at different time nodes or the distribution of relevant research publication time. As can be seen from the figure, in recent years, the research of various countries in this field has continued to be active, and the scope of cooperation has been expanding. In the future, with the gradual deepening of the understanding of the pathogenesis of chronic obstructive pulmonary disease and the continuous progress of biomedical technology, it is expected that more countries will devote themselves to the research field of biotherapy for the treatment of chronic obstructive pulmonary disease. Cooperation between countries will also become closer and more diversified.

Table 1 The top 10 countries/regions in terms of the number of publications in the field of biological therapy for COPD from 2000 to 2025

Rank	Country/Region	Number	Centrality
1	USA	108	0.17
2	PEOPLES R CHINA	86	0.02
3	ENGLAND	55	0.14
4	ITALY	55	0.07
5	AUSTRALIA	27	0.25
6	GERMANY	27	0.13
7	SPAIN	26	0.06
8	FRANCE	18	0.01
9	CANADA	18	0.1
10	SWEDEN	17	0.19

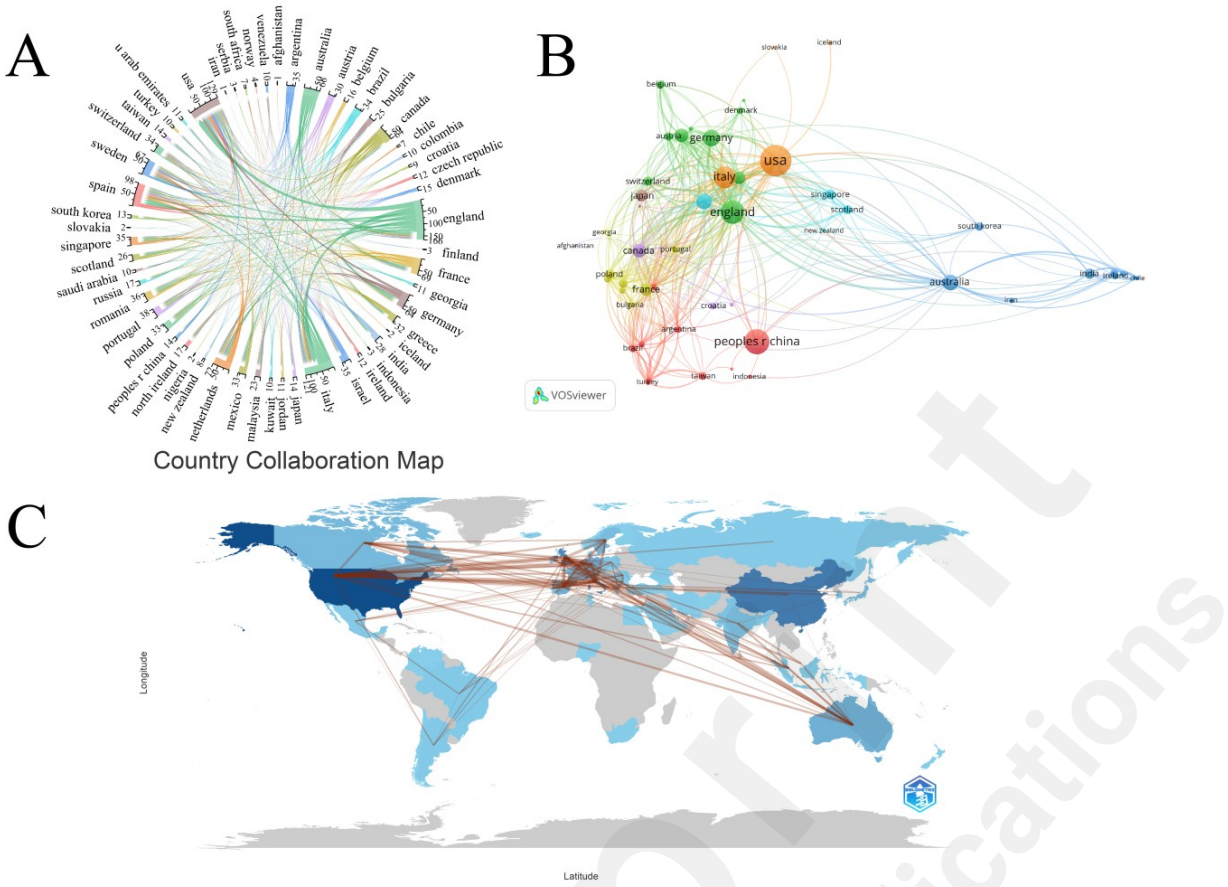

FIGURE 2 | (A) The Chord Diagram of International Cooperation. (B) Cooperation map of research countries/regions in the field of Biological therapy for chronic obstructive pulmonary disease from 2000 to 2025. (C) A World Map of International Cooperation.

3.3. Visual analysis of the institutions

The 474 articles came from 2,010 institutions. We used VOSviewer to conduct a co-occurrence network analysis of these institutions. Figure 3B shows a visualization network of institutions that published more than three articles. The size of each node is directly proportional to the number of publications from the institution, and the lines between nodes indicate collaborative relationships. The top 10 institutions contributed a total of 92 articles, which account for 5.86% of the total. These institutions received 3,672 citations representing 6.92% of the total citations. The total link strength of the top 10 institutions accounts for 5.41% of the total. The three institutions with the highest number of publications are: the University of Groningen (n = 12), the University of Ferrara (n = 11), and the University of Leicester (n = 10). The University of Leicester, which ranks third, has the highest number of citations. The top three institutions in terms of total link strength are as follows: the University of Groningen (87), the University of Ferrara (67), and the University of Technology Sydney (61). This shows that these institutions have close collaboration with other institutions that play an important role in the field of biological therapies for COPD.

3.4. Visual analysis of authors and co-cited authors

The relevant results of the top 10 authors in terms of publication volume are shown in Table 2. In terms of the number of publications, Cazzola, Mario, with the number of publications of 6, ranked first among the authors. Adcock, Ian M, Dua, Kamal, and Singh, Dave are tied for second place with five publications each. This was followed by Rogliani, Paola, Cosio, Borja G, Matera, Maria Gabriella, Brightling, Christopher E, and Calzetta, Luigino, who each published four papers. The data mentioned above clearly show that these authors have shown a high output in the field of biotherapy research for chronic obstructive pulmonary disease, and have become a key force in promoting the

development of research in this field.

According to Price's Law[11], the 474 articles included in this study involved 2746 authors. Among these authors, Cazzola and Mario have published the most articles, totaling 6. Calculated by Price's law formula, N=1.94. Therefore, it is determined that in this study, the number of published papers by the core authors should meet the standard of ≥2 papers. Through the calculation of VOSviewer software, the number of core authors is finally determined to be 148, and the core author density view result is shown in Figure 3. It can be inferred from the figure that foreign research in this field has formed a research team represented by Cazzola, Mario, Brightling, Christopher E, Adcock, Ian M, etc.

In Figure 3D, the density regions of different colors can intuitively show the distribution characteristics of the co-occurrence of authors. Starting from white, gradually changing to yellow, orange, and finally red, the color shows a trend of changing from light to dark, and this trend represents the gradual increase of the co-occurrence density of authors. The darker regions clearly show a higher co-occurrence frequency among authors within the region, which means that these authors are closely linked at the level of research collaboration. The dark area centered on "brightling, christopher e.," highlights the strong connections among the researchers surrounding the author. The formation of this close connection is either because they cooperate in similar research directions or have a strong correlation in research content to promote the development of research in a specific subfield. Looking at the lighter-colored areas, it can be found that in this area, the co-occurrence frequency between authors is relatively low. It is suggested that the research direction of these authors is relatively scattered, and there is less interaction with other authors in research cooperation and research associations. The size of the nodes in the figure also corresponds to the number of papers published by the author. The larger the node of the author, the greater the number of papers published by the author in this field, which directly reflects the author's activity and influence in this research field. It is worth noting that the top ten authors in the research field of biotherapy applied to COPD show a significant cross-over trend in the research direction, fully reflecting all the complex and comprehensive characteristics of the field itself, and many different research directions are intertwined, creating opportunities for the exchange and collision of academic ideas. Figure. 3B shows the network diagram of co-cited authors. Authors whose citation times are greater than 15 will be shown in the diagram, the lines indicate that there is a connection between them, and the node size is the authors' citation times. Table 2 shows that Barnes, Peter J (n=247), Pavord, Ian D (n=146), and Bafadhel, Mona (n=105) ranked the top three authors of the top five citation times, and the citation times were all greater than 100. The Total Link Strength (TSL) of the author can reflect the influence of the author. The TSL of Barnes, Peter J (n=4141) and Pavord, Ian D (4086), which are cited as the top two, still rank in the top two. Bafadhel, Mona (2784) ranked fourth in TSL, indicating that these three authors have a high influence in the field of biotherapy and COPD research, and their institutions should give more support.

Table 2 Ranking of Author Publication and co-cited author Citation in the field of Biological therapy for COPD

Rank	Author	Documents	Cited-Author	Citations	Total Link Strength
1	Cazzola, Mario	6	Barnes, Peter J	247	4141
2	Adcock, Ian M	5	Pavord, Ian D	146	4086
3	Dua, Kamal	5	Bafadhel, Mona	105	2784
4	Singh, Dave	5	Brightling, Christopher E	98	2923

Rank	Author	Documents	Cited-Author	Citations	Total Link Strength
5	Rogliani, Paola	4	Castro, Mario	88	2566
6	Cosio, Borja G	4	Singh, Dave	84	2162
7	Matera, Maria Gabriella	4	Cazzola, Mario	75	1701
8	Brightling, Christopher E	4	Rabe, Klaus F	74	1697
9	Calzetta, Luigino	4	Criner, Gerard J	74	1644
10	Miravitlles, Marc	3	Hanania, Nicola A	67	1860

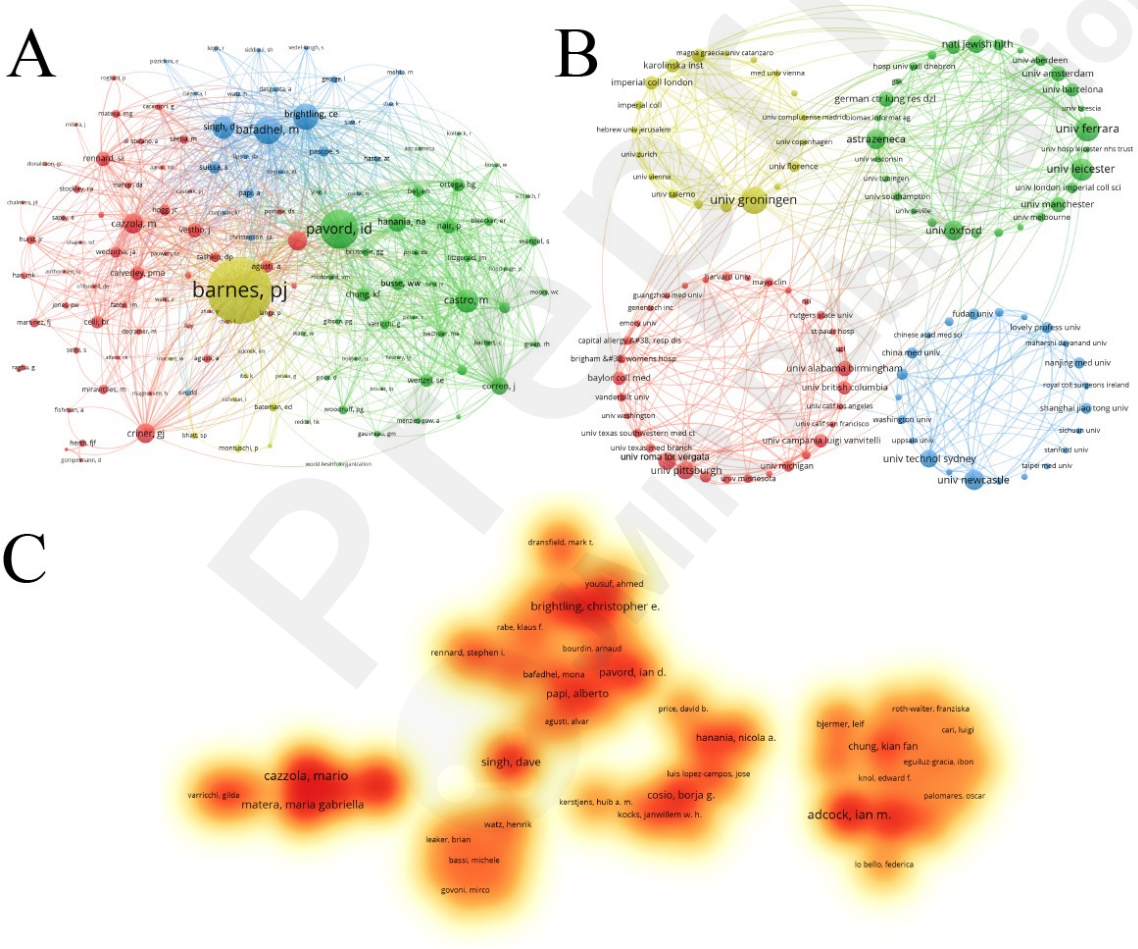

FIGURE 3 | (A) The Visualization Analysis of Co-citation Author Collaboration Networks. (B) The Visualization Analysis of Organizations Collaboration Networks. (C) Author Co-occurrence Density Map.

3.5. Visual analysis of co-cited journals

The co-citation network of journals is shown in Figure 4A. The size of each node is directly proportional to the number of citations from the co-cited journals, and the lines between nodes

indicate collaborative relationships. The purple outer rings indicate higher centrality. The top ten most cited journals are shown in Table 3, with the highest cited journal is the American Journal of Respiratory and Critical Care Medicine(n=352), followed by the European Respiratory Journal (334) and The New England Journal of Medicine (306). Among the top ten journals by citation count, the highest Impact Factor (IF) is Lancer(IF = 98.4), followed by The New England Journal of Medicine (IF = 96.2) and the American Journal of Respiratory and Critical Care Medicine (IF = 19.3). Figure 5 displays a dual-map overlay of journals, with cited journals on the right and citing journals on the left. Curved, colored paths between them indicate citation relationships, where journals on the right are primarily cited by those on the left. The number of publications for each journal is represented by the size of the ellipse, and journal topics are shown in white labels. Analysis of this figure reveals that journals in the fields of “MOLECULAR, BIOLOGY, GENETICS” and “HEALTH, NURSING, MEDICINE” are cited by those in the fields of “MEDICINE, MEDICAL, CLINICAL.” Additionally, journals in “MOLECULAR, BIOLOGY, IMMUNOLOGY” also cite those in “MOLECULAR, BIOLOGY, GENETICS.”

Table 3 Ranking of co-cited Journal Citation in the field of Biological therapy for COPD

Rank	Journal	Cited	Centrality	IF
1	American Journal of Respiratory and Critical Care Medicine	352	0.02	19.3
2	European Respiratory Journal	334	0.03	16.6
3	The New England Journal of Medicine	306	0.03	96.2
4	Chest	284	0.02	9.5
5	Lancet	271	0.01	98.4
6	Thorax	255	0.04	9
7	Journal of Allergy and Clinical Immunology	221	0.01	11.4
8	Plos One	198	0.02	2.9
9	Respiratory Research	185	0.02	4.7
10	Respiratory Medicine	179	0.01	3.5

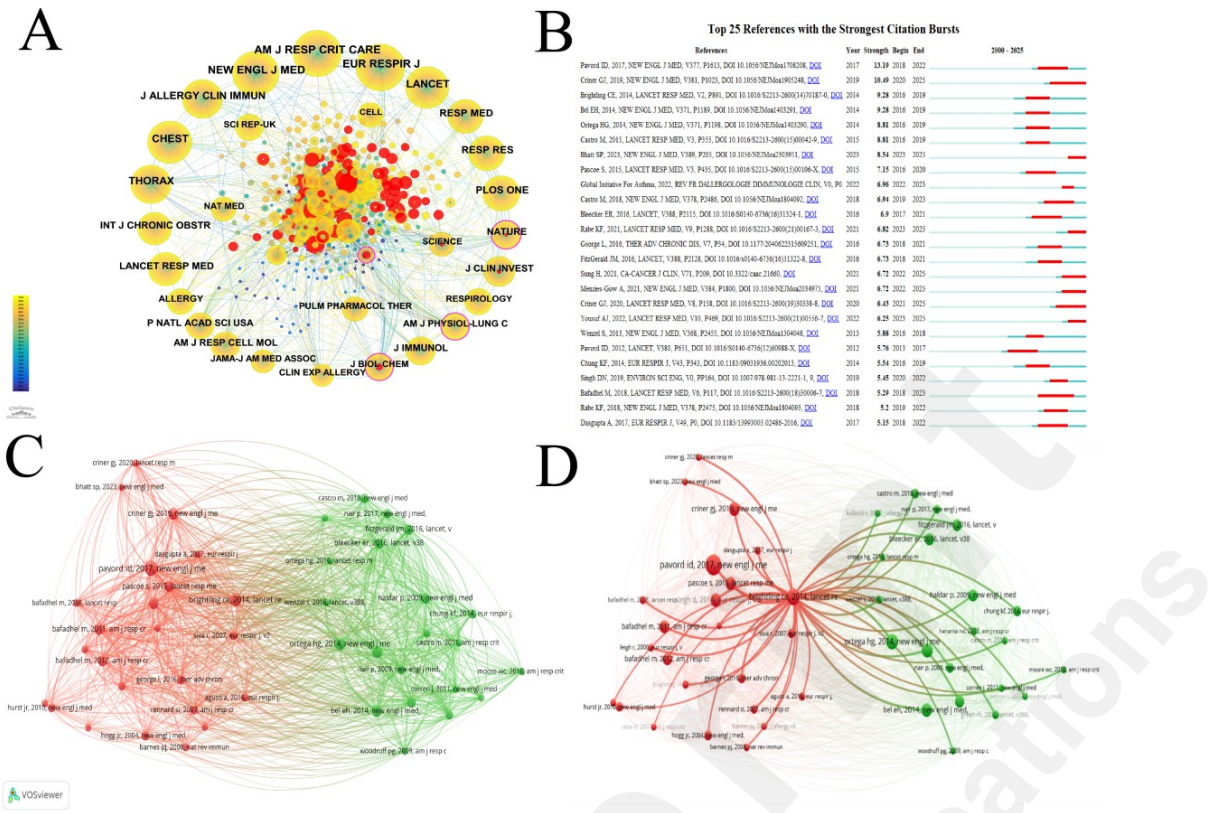

FIGURE 4 | (A) The Visualization Analysis of Co-citation Networks of Journals. (B) Top 25 References with the strongest citation bursts. (C) References co-citation network map. (D) Co-citation network centered on "Brightling CE, 2014, lancet re" in Chronic Respiratory Disease Research.

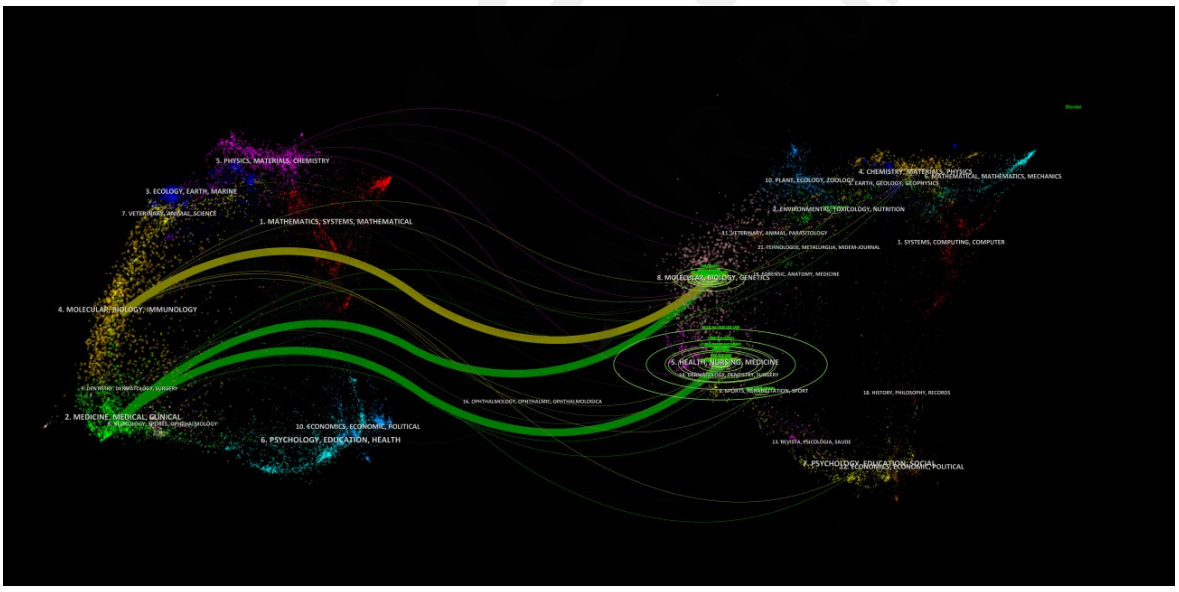

FIGURE 5 | The dual overlay of journals related to COPD for The Biological therapy

3.6. Visual analysis of the references

The main cited reference in Table 6 was published in top medical journals such as The New England Journal of Medicine and Lancet Respir Med. These journals are authoritative in the medical field, and their rigorous review process ensures the high quality of the literature. It can be seen from the side that the research results of biological therapy for COPD have been highly recognized in the academic

circle. The figure shows the top 25 references with the strongest cited bursts, suggesting that these references were frequently cited in a short period. The cited explosion intensity values of the literature in Figure 4B ranged from 5.15 (Dasgupta A, 2017)[12]to 13.19 (Pavord ID, 2017)[13], reflecting the great difference in the degree of attention received by different literatures in a specific period. The literature involves a variety of biologics, each of which has its unique mechanism of action, but all of which are closely related to the regulation of inflammatory response in COPD.

3.7. Visual analysis of the keywords

We used CiteSpace to generate a keyword co-occurrence network in Figure 6A. The size of each node is directly proportional to the frequency of the keywords, and the lines between nodes indicate collaborative relationships. The purple outer rings indicate higher centrality. The visualization shows only keywords whose frequency is more than 15 times. Table 4 indicates the top ten keywords by frequency. The top ten frequently appearing keywords with high centrality are as follows: “chronic obstructive pulmonary,” “obstructive pulmonary disease,” “therapy,” “asthma,” “airway inflammation,” and “risk.”A keyword clustering map was also generated using CiteSpace. Table 5 shows the top ten keyword clusters by size, and Figure 6D presents the visualization of these clusters, which are: “rheumatoid arthritis” (Cluster 0), “monoclonal antibodies” (Cluster 1), “colon adenocarcinoma” (Cluster 2), “phosphodiesterase 4 inhibitors” (Cluster 3), “phenotype” (Cluster 4), “precision medicine” (Cluster 5), “chronic obstructive pulmonary disease” (Cluster 6), “pulmonary delivery” (Cluster 7), “tobacco smoke” (Cluster 8), and “biologic therapy” (Cluster 9). Figure 6C shows the timeline of keywords. Nodes represent the frequency of keywords more than 10 times. “chronic obstructive pulmonary,” “therapy,” “obstructive pulmonary disease,” “quality of life,” “risk,” “cystic fibrosis,” and “oxidative stress,” are the early appearing keywords, These foundational keywords provide historical context for current research in biologic therapies for COPD. In the past five years, keywords like “lung cancer” and “colorectal cancer” have appeared more than 10 times. The top ten keywords by burst count are shown in Figure 7C. The keyword with the highest burst intensity is colon adenocarcinoma (n =6.21), followed by expression (6.09) and blood eosinophils (n=5.39), The keywords whose burst duration continues up to 2025 are as follows: colon adenocarcinoma(2022-2025),cancer(2022-2025), mepolizumab(2022-2025), expression(2021-2025). These keywords play an important role in the research of biological therapies for COPD.

Table 4 The top ten keywords by frequency.

Rank	Keyword	Number	Centrality
1	obstructive pulmonary disease	120	0.3
2	chronic obstructive pulmonary disease	112	0.43
3	double blind	61	0.08
4	therapy	44	0.16
5	expression	43	0.03
6	airway inflammation	40	0.13
7	asthma	37	0.14
8	exacerbations	33	0.07
9	inflammation	30	0.06
10	risk	28	0.1

Table 5 The ranking of the top ten keyword clusters by Size

Cluster	Label (LLR)	Size	Silhouette	mean(Year)
0	rheumatoid arthritis	51	0.739	2015

1	monoclonal antibodies	49	0.857	2013
2	colon adenocarcinoma	43	0.882	2016
3	phosphodiesterase 4 inhibitors	42	0.758	2011
4	phenotype	40	0.871	2015
5	precision medicine	34	0.786	2012
6	chronic obstructive pulmonary disease	33	0.814	2013
7	pulmonary delivery	32	0.858	2015
8	tobacco smoke	31	0.87	2011
9	biologic therapy	27	0.83	2010

Table 6 Top 10 cited literatures in the field of Biological therapy for COPD from 2000 to 2025

Rank	Citations	Year	Author	Journal	Title	Centrality
1	33	2017	Pavord ID	New England Journal of Medicine	Mepolizumab for Eosinophilic Chronic Obstructive Pulmonary Disease[14]	0.03
2	30	2019	Criner GJ	New England Journal of Medicine	Benralizumab for the Prevention of COPD Exacerbations[15]	0.07
3	20	2014	Brightling CE	Lancet Respiratory Medicine	Benralizumab for chronic obstructive pulmonary disease and sputum eosinophilia: a randomised, double-blind, placebo-controlled, phase 2a study[16]	0.01
4	20	2014	Bel EH	New England Journal of Medicine	Oral glucocorticoid-sparing effect of mepolizumab in eosinophilic asthma[17]	0.05
5	19	2015	Castro M	Lancet Respiratory Medicine	Reslizumab for inadequately controlled asthma with	0.01

Rank	Citations	Year	Author	Journal	Title	Centrality
					elevated blood eosinophil counts: results from two multicentre, parallel, double-blind, randomised, placebo-controlled, phase 3 trials[18]	
6	19	2014	Ortega HG	New England Journal of Medicine	Mepolizumab treatment in patients with severe eosinophilic asthma[19]	0.05
7	17	2015	Pascoe S	Lancet Respiratory Medicine	Blood eosinophil counts, exacerbations, and response to the addition of inhaled fluticasone furoate to vilanterol in patients with chronic obstructive pulmonary disease: a secondary analysis of data from two parallel randomised controlled trials[20]	0.02
8	17	2018	Castro M	New England Journal of Medicine	Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma[21]	0.05

Rank	Citations	Year	Author	Journal	Title	Centrality
9	17	2016	Bleecker ER	Lancet	Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists (SIROCCO): a randomised, multicentre, placebo-controlled phase 3 trial[22]	0.09
10	16	2018	Bafadhel M	Lancet Respiratory Medicine	Predictors of exacerbation risk and response to budesonide in patients with chronic obstructive pulmonary disease: a post-hoc analysis of three randomised trials[23]	0.11

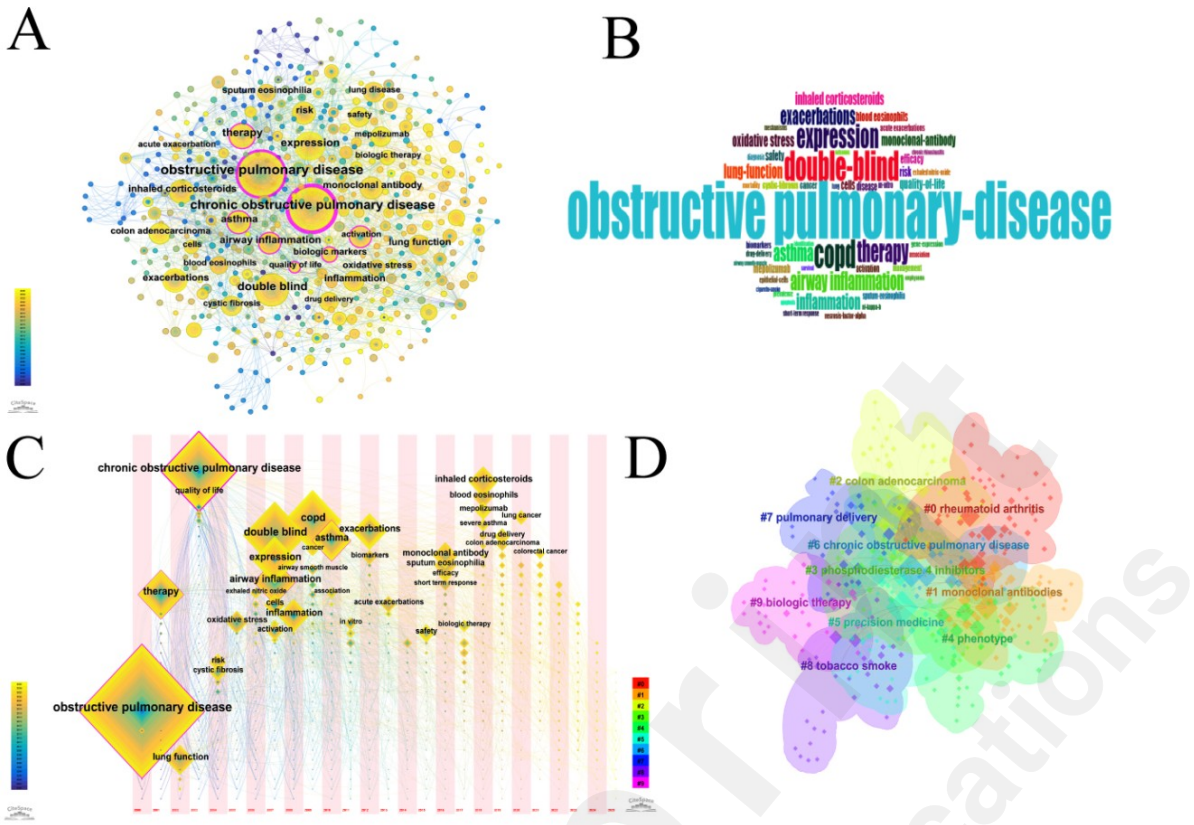

FIGURE 6 | (A) The co-occurrence network of keywords. (B) The Keyword Word Cloud: A Visual Representation of Key Concepts. (C) The Keyword Timeline Map. (D) Visualization Analysis of Keyword Clustering.

3.8. Visual analysis of the terms

We used VOSviewer to visualize the subject terms, generating a subject term co-occurrence map as shown in Figure 7A. The size of each node is directly proportional to the frequency of the terms, and the lines between nodes indicate collaborative relationships. Different colors on the map represent different clusters. A total of 13163 Meshes were extracted from 474 articles. 175 Mesh appeared more than 15 times. The link is 12535. The map shows that the subject terms are divided into three main categories: one centered on "chronic obstructive pulmonary disease" (Category 1), the second centered on "treatment" (Category 2), and the third centered on "cell" (Category 3). Cluster 1 mainly includes: “disease,” “asthma,” “review,” “inflammation,” and “role”; Cluster 2 includes: “patient,” “study,” and “effect”; and Cluster 3 includes: “mechanism,” “response,” “biomarker,” “pathway,” and “analysis.”Figure 7B presents the heatmap density of keywords, which shows that “chronic obstructive pulmonary disease” is the most prominent keyword, appearing 329 times, followed by “treatment” (292), “patient” (286), “study” (240), and “disease” (222)

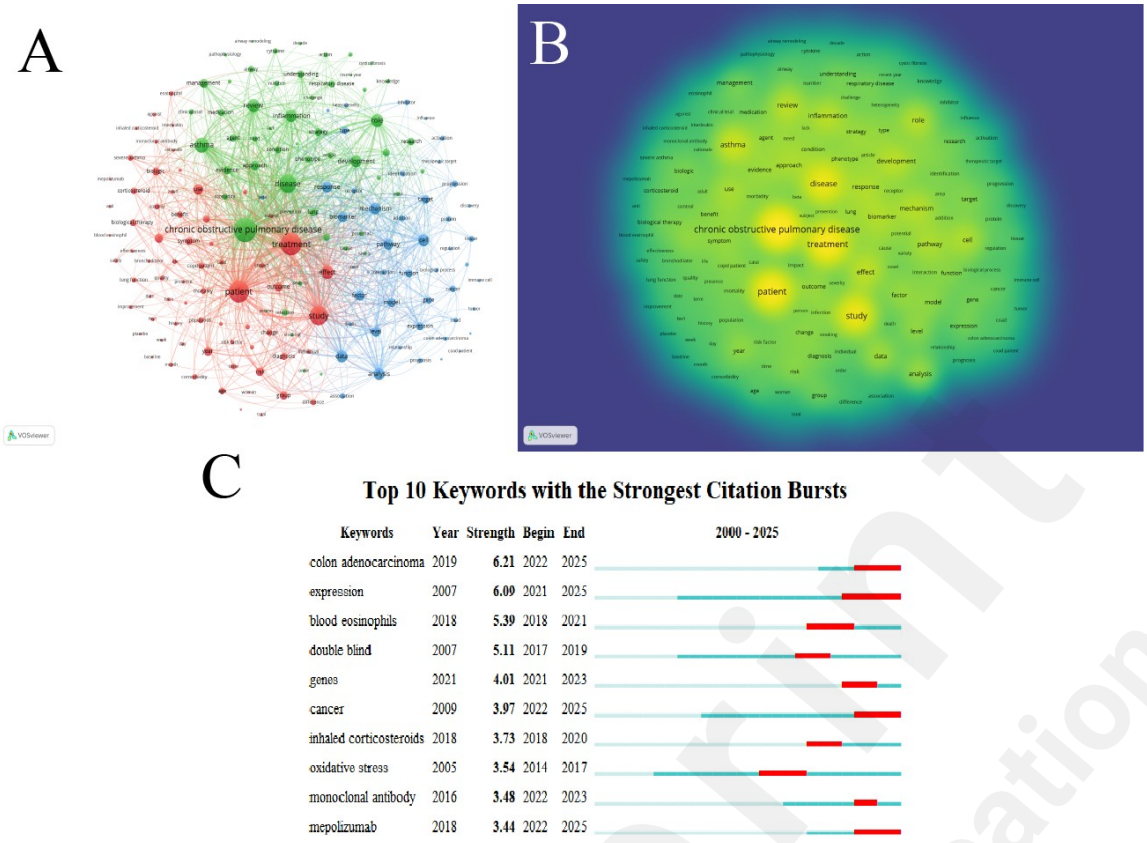

FIGURE 7 | (A) Visualization Analysis of Co-occurrence Networks of Terms. (B) Heatmap Density Visualization of Terms Co-occurrence. (C) Top 10 Keywords with the strongest citation bursts.

4. Discussion

Our study uses Citespace, Vosviewer, R-Bibliometrix, and Origin2024 for visualizing research on biological therapies for COPD. It identifies current research hotspots and predicts future trends in our study's field. Between 2000 and 2025, the number of publications on biological therapies for COPD has been increasing. Between 2000 and 2012, there was a slow increase in publications on biologic therapies for COPD. From 2012 to 2017, the growth was unstable. However, after 2012, there was a quick increase. Although there was a slight drop in 2024 compared to 2023, the number of publications in recent years has stayed above 40. All of the above indicate that the field has gained wide attention and remains a current research hotspot.

In terms of the overall network structure obtained from the analysis of countries, even though the current international cooperation network has a certain complexity, there is still room for optimization. At present, in the field of biotherapy of COPD, the relevant research cooperation is mainly concentrated in a few core countries, such as the United States, Germany, Italy, the United Kingdom, and other countries, and there is room for further strengthening of cooperation between different regions. According to the existing data analysis, there is still a lot of room for the development of scientific research cooperation between Asia and Europe, and the two sides may cooperate more extensively and deeply in frontier areas such as the integration of traditional medicine and biological therapies, to integrate the differentiated advantages of various countries in theory, technology and resources, and form a synergistic innovation effect. From the visual analysis of institutions, we can see that the University of Groningen, the University of Ferrara, and the University of Leicester rank in the top three in terms of the number of documents. The countries of these institutions are the Netherlands, Italy, Britain, etc. All of them are from European countries, and the University of Leicester has the highest number of citations, indicating that these institutions have a relatively significant influence in the research field. The University of Groningen, the University of Ferrara, and the University of Technology Sydney have the top three TSL rankings, demonstrating the

close partnership between them and other institutions at the heart of the research network. Future international cooperation needs to be more actively promoted, especially with these core institutions, to integrate resources, share data, and promote the rapid development of research in this field. The focus on emerging research directions and the optimization of collaborative networks will also help to enhance the academic impact of institutions and promote continued progress in academic research in this field.

In the analysis of the authors, the research directions of Adcock, Ian M, and Rogliani, Paola showed a large crossover in the two aspects of the inflammatory mechanism of COPD and the effects of biological therapies on inflammatory targets. Adcock, Ian M. focused on the intracellular signaling pathways in the pathogenesis of COPD and the regulatory mechanisms of inflammation-related transcription factors. His research focuses on the activation of NF-κB[14], MAPK[15], and other signaling pathways in COPD inflammation, and how biologics regulate these pathways to reduce inflammation. Rogliani, Paola also focused on studying the inflammatory mechanism of COPD, but more emphasis was placed on the role of inflammatory cells (such as eosinophils[16], neutrophils[17], etc.) and cytokines (such as IL-6[18], TNF-α[19], etc.) in the pathological process of COPD. A better understanding of how biologics target precisely those inflammatory cells and cytokines could lead to more effective ways to block the inflammatory cascade and thus achieve the goal of treating COPD. Through their respective studies, they may jointly verify the changes in some key inflammatory targets under the action of biological therapies, giving a more comprehensive theoretical basis for the development and optimization of biological agents.

The research of Cazzola, Mario, and Calzetta, Luigino intersects with drug treatment strategies for COPD, especially biotherapy combined with traditional medicine. Cazzola, Mario delves into the pharmacological properties of biologics, such as pharmacokinetics, pharmacodynamics, and interactions with receptors[19]. Attention is also paid to how to combine these biologics with traditional COPD drugs [20] (such as inhaled glucocorticoids, long-actingβ_2 receptor agonists, long-acting anticholinergics, etc.) to achieve better therapeutic effects. Calzetta and Luigino's research also focused on drug combination therapy strategies[21]. He carried out research from the perspective of clinical practice, mainly analyzing the efficacy and safety of different drug combinations in the real world. Large-scale clinical observations and data analysis work were used to assess the impact of biologics combined with conventional drugs on acute exacerbations, improved lung function, and quality of life in patients with COPD[22]. By combining basic pharmacological research and clinical practice observations, the two may work together to explore personalized combination treatment options that are more appropriate for COPD patients.

Matera, Maria Gabriella, Brightling, and Christopher E's respective research directions intersect in the field of evaluating the clinical efficacy of biologic therapies for COPD. The former may be more focused on developing and validating more accurate and comprehensive measures and methods for assessing efficacy. In this study, we found that her research focused on a combination of pulmonary function indicators (FEV1, FVC, etc.), inflammatory markers, and patient-reported outcome indicators (dyspnea score, quality of life questionnaire score, etc.) to evaluate the efficacy of biologic therapies[23]. The latter systematically evaluates the clinical efficacy of different biologics by designing and participating in multiple clinical trials[24-26]. His research focuses on differences in the efficacy of biological agents in different patient populations, including patients with varying degrees of disease and inflammatory phenotypes, and on how these differences can be used to implement precision treatment. By learning from each other's research methods and achievements, they may improve the efficacy evaluation system and provide corresponding evidence for the application of biological agents.

The most cited author is Barnes, Peter J[27], whose research shows that inhaling a combination of long-acting beta-agonists (LABA) and corticosteroids can be beneficial for COPD recovery. This mechanism may relate to enhanced glucocorticoid receptor nuclear translocation in COPD sputum macrophages. The second-ranked named Pavord, Ian D[28], mainly focuses on the relationship between eosinophils and COPD, as he has revealed that sputum IL-1 beta, serum CXCL10, and peripheral eosinophils may be linked to COPD exacerbations by studying COPD biomarkers. Simultaneously, this article was also published in the top-ranked journal for co-citation counts,

"American Journal of Respiratory and Critical Care Medicine." Pavord, Ian D's research indicates[29] that COPD patients who frequently receive triple therapy may experience exacerbations associated with ongoing eosinophilic inflammation. The mechanism of the result may be that eosinophils use up the targets of biological therapies. It is worth noting that the additional Mabolizumab has higher efficacy in patients with the eosinophilic phenotype of COPD[30].

The top three journals by citation count in the co-citation analysis are as follows: American Journal of Respiratory and Critical Care Medicine, European Respiratory Journal, and The New England Journal of Medicine. These three journals have IF greater than 10, and they are ranked in the Q1 category by the Journal Citation Reports (JCR). Notably, the fifth-ranked journal, "Lancet," has the highest IF among the top ten cited journals, reaching 98.4. The above shows that these journals are highly influential in biological therapies for COPD. Staying updated on the latest developments in these journals may help you stay informed on cutting-edge research.

Further analysis and summary of the cited literature with the highest number of co-citations were made, and the following monoclonal antibodies were discussed: (1) Mepolizumab: its core mechanism of action is to specifically bind interleukin-5 (IL-5) and inactivate it, thereby inhibiting eosinophile-mediated inflammation[31]. Relevant studies have been conducted on patients with severe eosinophilic asthma[32], and it has been found that IL-5 plays an indispensable role in the production, differentiation, activation, and life process of eosinophils. The high binding of mepolizumab to IL-5 effectively blocked the interaction between IL-5 and its receptor and inhibited the related biological functions of eosinophils. This effect significantly reduces the number of eosinophils in the patient's blood and sputum, and thus reduces the frequency of acute exacerbations of asthma. Lung function indicators such as forced expiratory volume in the first second (FEV1) improved, as did SGRQ scores and ACQ scores, indicating that patients had reduced respiratory symptoms and improved quality of life. Another study found that the mechanism of action of mepolizumab in reducing oral glucocorticoid consumption was also based on the inhibition of IL-5[33]. Mepolizumab achieves a glucocorticoid-saving effect by reducing eosinophilic inflammatory response while maintaining asthma control and reducing patients' dependence on oral glucocorticoids, offering clinical treatment possibilities to reduce glucocorticoid-related side effects. Studies have also focused on patients with COPD, further verifying the mechanism of action of mepolizumab in this disease[13]. Eosinophil-mediated inflammation is involved in the pathological process of COPD. By inhibiting IL-5, mepolizumab regulates the function of eosinophils and relieves airway inflammation, thereby positively affecting the condition of COPD patients. Although COPD and bronchial asthma have significant heterogeneity in clinical manifestations, they show a high degree of similarity in the key pathophysiological link - eosinophil-mediated airway inflammation. As a targeted biologic agent, the mechanism of action of mepolizumab is mainly based on the precise regulation of eosinophilic signaling pathways, and it has also shown certain therapeutic effects in the clinical treatment practice of COPD. (2) Raylizumab: As a humanized monoclonal antibody, Raylizumab works primarily by interfering with the maturation process of eosinophils and promoting their programmed death [34].In patients with COPD, abnormal maturation and survival of eosinophils can cause airway inflammation to persist, leading to adverse events such as acute exacerbations of asthma[35].Relizumab binds to IL-5, blocking its support signal for eosinophils' maturation and survival, thereby reducing the number of eosinophils [36].One study confirmed through two large phase 3 trials that patients treated with Raylizumab experienced a significant reduction in the frequency of acute exacerbations of clinical asthma, improvements in lung function, and improvements in FEV1 indicators. This suggests that relizumab can effectively relieve airway obstruction and improve respiratory function in patients, and its efficacy is consistent in patients with different baseline characteristics (OCS-dependent, LABA use), suggesting a broad applicability for patients with moderate to severe asthma. After clinical evaluation, the patient's ACQ score was significantly reduced, and the ASUI score was significantly improved. The improvement of this series of quantitative indicators directly reflected that the patient's airway inflammation was effectively controlled, and the asthma symptoms were significantly relieved. These results indicate that ralizumab can play a positive role in COPD by interfering with the maturation of eosinophils and inducing apoptosis. (3) Benalizumab: Benalizumab primarily targets IL-5 receptor alpha and achieves effective clearance of eosinophils from blood and sputum by enhancing antibody-dependent cell-

mediated cytotoxicity (ADCC)[37].Results of a study in patients with COPD and sputum eosinophilia showed[38]that Benalizumab can rapidly and significantly reduce eosinophilia counts in blood and sputum, thanks to its unique de-fibrillated structure, which enhances its affinity with natural killer cell (NK cell) surface receptors, so it can mediate ADCC more efficiently. It should not be ignored that the results of this study did not meet expectations in reducing the rate of acute exacerbations of COPD, possibly due to the complexity of COPD conditions and the influence of the study sample size and other factors. Another study in patients with severe asthma showed that Benalizumab could significantly reduce the rate of acute exacerbation of asthma and improve lung function[39], which further confirmed the mechanism by which Benalizumab plays a therapeutic role in the treatment of asthma by clearing eosinophils. (4) Benalizumab: A study further evaluated the role of Benalizumab in preventing acute exacerbations of COPD. Although no significant effect has been achieved in reducing the annual rate of acute exacerbations, studies have reconfirmed its inhibitory effect on eosinophils in blood and sputum[40], suggesting that the mechanism of action of Benalizumab in the treatment of COPD may be complex and may involve some immunomodulatory mechanisms that have not been fully clarified. □5□Dupilumab: dupilumab is a fully humanized monoclonal antibody that specifically acts on interleukin-4 receptor α (IL-4Rα) to inhibit type 2 inflammation by blocking IL-4 and IL-13 signaling[41]. In patients with asthma and some COPD, type 2 inflammatory response plays a key role in the occurrence and development of the disease, and its level is directly related to clinical efficacy[42].As key cytokines in type 2 inflammatory response, IL-4 and IL-13 are involved in the recruitment and activation of various inflammatory cells, as well as pathologic processes such as airway remodeling. By blocking the signaling pathway of IL-4 and IL-13, dupilumab can inhibit the release of a variety of inflammatory cytokines, such as eosinophilic chemokines, thymus, and activation regulatory chemokines (TARC), to alleviate airway inflammation and allergic reactions[41]. Studies have shown that patients treated with Pliuzumab have significantly reduced the rate of acute exacerbation of asthma, significantly improved lung function, and increased asthma control questionnaire scores[43]. Although this study was mainly aimed at patients with asthma, given that COPD and asthma have certain similarities in some pathological mechanisms, this mechanism of dupilumab provides an important reference direction for the study of COPD treatment.

In order to see the interrelationships among the literature, we built a literature citation network, as shown in Figures 4C and 4D. In the co-citation analysis diagram of literature, some earlier published literature provided theoretical and methodological foundations for subsequent research, and based on quoting earlier literature, subsequent research was further expanded and deepened. The preliminary findings of the early exploratory study[38] on the application of Benalizumab in patients with COPD provided an important basis for the subsequent phase 3 clinical trial[40]. Such citation relationships represent the inheritance and accumulation of knowledge in the field of biotherapy for COPD. We also found that the citation network presented a clustering feature, literature around the same biologics or similar research topics was more frequently cited, and closely related research clusters were formed, which mapped the development trajectories of different research directions in this field.

The analysis of cited literature outbreak found that the literature published by Pavord ID in NEW ENGL J MED in 2017 became the most influential study with the highest cited outbreak intensity (13.19), and its cited outbreak period lasted from 2018 to 2022. The study involved groundbreaking evidence of biologic agents (such as anti-IL-5 /IL-5R monoclonal antibody) in the treatment of COPD[13], prompting subsequent clinical trials and guideline updates. Among them, the studies of Criner GJ in 2019 and Bhatt SP in 2023 occupy the high impact status in recent years with the cited outbreak intensity of 10.49 and 8.54, respectively, and the outbreak period of both will last until 2025. It is suggested that the current research focus is novel biological targets (such as IL-4/IL-13, TSLP)[44] and drug efficacy verification[40].

As can be seen from Figure 4B, the publication years of this literature covered 2012-2023 and showed a relatively concentrated publication trend during 2014-2016: 4 literature were published in 2014 and 2016, and 3 literature were published in 2015. This distribution characteristic suggests that important progress has been made in multiple dimensions related to COPD during this period. The

cited outbreak intensity of literature published from 2014 to 2015 was moderate (8.81-9.28), and the outbreak period was concentrated from 2016 to 2019, mainly involving the exploration of anti-inflammatory mechanisms and early efficacy data[33, 34, 38], indicating the transition of biotherapy during this period from proof-of-concept to clinical transformation stage. The literature explosion period published after 2020 mostly lasted until 2025, suggesting that research focuses on the development of precision medicine (such as biomarker-guided therapy) and long-acting drugs (such as bispecific antibodies)[45, 46]. However, the latest literature (such as Bhatt SP) published in 2023 has an outbreak period starting from the year of publication, suggesting that targeting small-molecule pathways (such as JAK-STAT inhibitors) and novel delivery techniques (such as inhalation mab) may become an emerging research hotspot[44]. The outbreak literature (e.g., Rabe KF 2021), with an outbreak period lasting until 2025, focuses on real-world efficacy validation and patient-stratified care, emphasizing the need to transition from clinical trials to personalized medicine[46].

We are concerned that the outbreak starting years of highly cited literature are widely distributed in the period 2012-2022. This distribution feature is reflected in the research process of this field, and there are research results that have aroused wide attention in different periods, indicating that this field has always maintained an active research trend. The duration of the literature outbreak is also diversified. In some works of literature, such as that published by Criner GJ in 2019, the cited outbreak lasts from 2019 to 2025, and the longer period indicates that the research results have a relatively lasting influence[40]. Some literature, such as the Global Initiative for Asthma (2022), have a relatively short outbreak period, lasting from 2022 to 2023, but their intensity is significant (6.96), reflecting the immediate guidance role of international consensus on clinical practice and research direction[8].

Based on the time-dimensional information, we found that the research progress of biotherapy for chronic obstructive pulmonary disease (COPD) presents a phased evolution. From 2014 to 2019, the research paradigm in this field focuses on exploring the molecular mechanism of disease (such as the regulation of inflammatory pathways [47-49]) and the preliminary clinical validation of biologics (such as the randomized controlled trial against IL-5/IL-5Rα monoclonal antibody[13, 50]。The research focus in this field has gradually shifted to phenotyping systems driven by precision medicine, the development of long-acting targeted biologics (such as bi-specific antibody technology[44]。, and evidence-based evaluation of efficacy and safety based on real-world data (RWD) [51, 52]. Future studies may focus on the following directions: First, the pathophysiological effects and intervention strategies of novel immune regulatory targets (such as thymic stromal lymphopoietin TSLP, interleukin-33 /IL-33 and their receptor complexes) may be further explored[53]. Second, clinical practice guidelines may be optimized based on evidence-based medical evidence, transforming from "monotherapy" to a "precision and dynamic" treatment paradigm.

The result of keyword analysis reveals the most frequent keywords include: “therapy,” “asthma,” “airway inflammation,” and “risk.” The keywords whose burst duration continues up to now are as follows: “cancer”, “mepolizumab”, and “expression”. These results show that these fields may be current or future research hotspots and deserve more attention. Combining keyword analysis with clustering, we found that the research hotspot may involve the link between monoclonal antibodies in biological therapies and COPD. For COPD patients with the eosinophilic phenotype, adding monoclonal antibodies to corticosteroid therapy can enhance efficacy. This result indicates that IL-5 may be a key regulator of eosinophil production, so developing IL-5 antibodies can offer additional options for patients who are ineffective with corticosteroids[54]. The article published in "The New England Journal of Medicine" by Pavord, Ian D[13] indicates that mepolizumab as an add-on therapy for eosinophilic phenotype COPD patients can help reduce COPD exacerbations, and it also shows that eosinophilic inflammation may be linked to the disease's exacerbations. A recent meta-analysis[55] indicates that Dupilumab, which targets IL-4 and IL-13[44] may be more effective than mepolizumab in reducing exacerbations for eosinophilic phenotype COPD patients[55]. This also requires attention.

5. Conclusion

This study analyzed 474 articles on biological therapies for COPD and created various network maps. The articles are from 205 countries or regions and 2,010 institutions. The most prolific author

is Cazzola, Mario. The most cited author is Barnes, Peter J. The most cited journal is the "American Journal of Respiratory and Critical Care Medicine." The most cited reference is "Mepolizumab for Eosinophilic Chronic Obstructive Pulmonary Disease." Analyzing highly cited references with strong burst counts points to future research directions: (1) Exploring the pathophysiological roles of novel immune regulatory targets and developing intervention strategies; (2) Pushing for the fusion of interdisciplinary technologies. (3) Combine safety data from multiple centers with long-term follow-up and dynamic efficacy monitoring indicators. Through keyword analysis, current or future research hotspots may involve the link between monoclonal antibodies and COPD. Biologic therapies, used as add-on treatments, can offer new options for COPD patients who are responding badly to conventional therapy. So the research on biological therapies for COPD still needs to develop, to give patients safer and cost-effective therapy options.

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Supplementary Files