MEANDROS MEDICAL AND DENTAL JOURNAL
June 2024 25(2):182-193

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1490284

Research Article

PULMONARY EMBOLISM AND SYSTEMIC THROMBOLYTIC THERAPY: AN IN-DEPTH BIBLIOMETRIC ANALYSIS OF GLOBAL RESEARCH TRENDS

Tuğba ÇİÇEK[1]*

[1] Clinic of Pulmonology, Konya Numune Hospital, Konya, TURKEY

*Correspondence: dr.tugbacicek@hotmail.com

ABSTRACT

Objective: Pulmonary embolism is a life-threatening condition often resulting from deep vein thrombosis, with significant morbidity and mortality. Thrombolytic therapy is a common treatment, particularly in high-risk cases. Despite numerous studies on pulmonary embolism, a comprehensive bibliometric analysis of research trends and impacts, especially regarding thrombolytic therapy, is lacking.

Materials and Methods: This bibliometric analysis utilized the Web of Science database to collect and evaluate literature published between January 1, 2004, and December 31, 2023. A total of 282 articles were selected based on specific inclusion criteria. Data were analyzed using VOSviewer and Bibliometrix R, focusing on publication trends, citation counts, and collaborative networks.

Results: The analysis identified a progressive increase in pulmonary embolism-related publications, peaking in 2020 and 2022. The United States led in publication volume, followed by Turkey and China. Despite high publication numbers, Turkey's citation count was relatively low, highlighting potential gaps in research impact and quality. The study also revealed that European countries exhibit stronger international collaborations compared to the United States. Key research trends shifted post-2018 towards topics such as mortality, bleeding, COVID-19, and extracorporeal membrane oxygenation.

Conclusion: This bibliometric analysis provides a detailed overview of the research landscape on pulmonary embolism and thrombolytic therapy, highlighting evolving research priorities, the significance of funding opportunities, and the importance of international collaborations. The study's insights can guide future research directions and inform clinical practices, ultimately aiming to improve patient outcomes.

Keywords: Bibliometrics, citations, collaborations, pulmonary embolism, thrombolytic therapy

Received: 26 May 2024
Revised: 10 June 2024
Accepted: 11 June 2024
Published: 31 August 2024

MEANDROS MEDICAL AND DENTAL JOURNAL
June 2024 25(2):182-194

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1490284

INTRODUCTION

Pulmonary embolism (PE), which usually occurs as a complication of deep vein thrombosis, is a life-threatening condition and a leading cause of cardiovascular mortality (1). The annual incidence of PE ranges from 39 to 115 per 100,000 people (1,2). PE symptoms vary widely, from asymptomatic cases to severe shock. Clinically, acute PE is classified based on the patient's hemodynamic status. It is crucial to quickly identify high-risk, intermediate-risk, and low-risk patients upon diagnosis due to the differing treatment approaches. Acute right ventricular failure is typically present in high-risk PE patients. The presence of hypotension and cardiogenic shock due to acute right ventricular failure in patients is associated with early mortality, with an exceptionally high mortality rate, particularly within the first 2 hours (3). Prompt diagnosis and rapid initiation of reperfusion therapy are crucial in this patient group with high early mortality. Among reperfusion therapies, systemic thrombolytic therapy is one of the most commonly used treatments. In patients where systemic thrombolytic therapy is contraindicated or does not improve clinical outcomes, surgical embolectomy or catheter-directed thrombolytic therapy is recommended (1,4). Post-thrombolytic therapy, 98% of patients have shown improved right ventricular function as assessed by transthoracic echocardiography (1). Rapid improvement in patients reduces early mortality rates as a result of thrombolytic therapy. A meta-analysis of studies utilizing thrombolytic therapy in PE patients has also demonstrated a significant reduction in mortality (5). Bibliometric analysis is the statistical analysis of scientific publications. Bibliometric studies reveal the publications with the highest impact on a given topic, collaborations between countries, authors, and institutions, and identify active journals with a specific methodology (6). Additionally, it examines the frequency and trends of citations of published studies in the literature. These analyses help researchers save time in literature reviews and quickly access summaries of thousands of scientific findings. These analyses can also help determine which research projects should receive funding support. Due to the increasing number of publications in the literature, the value of bibliometric analysis is also rising. While numerous bibliometric analyses of PE exist, there appears to be a gap in the literature that specifically addresses the intersection of PE and thrombolytic therapy. This study embarks on a detailed bibliometric and statistical analysis of two decades of publications on PE and thrombolytic therapy, aiming to identify trending topics, highlight the most impactful studies, and map out international research collaborations.

MATERIALS AND METHODS

We used the Web of Science (WoS) database for collecting literature data. To remove discrepancies brought up by daily database changes, all papers published between January 1, 2004, and December 31, 2023 were extracted from the WoS database and downloaded on May 15, 2024. Articles that were not written in English were not considered. Original research, case reports, reviews, and meta-analyses on pulmonary embolism and thrombolytic therapy were included in this study. Excluded from the analyses were the following: duplicate papers, irrelevant articles, letters to the editors, book chapters, conference proceedings, and communications. The full record and cited references, including title, keywords,

MEANDROS MEDICAL AND DENTAL JOURNAL
June 2024 25(2):182-194
Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1490284

authors, journals, country, and institution of each article were gathered and saved as a BibTeX format and tab-delimited text file. Publications were systematically searched in the WoS database using the following query: TI = ((pulmonary embolism OR pulmonary thromboembolism OR venous thromboembolism) AND (thrombolytic OR fibrinolytic OR thrombolysis)). Research on mechanical, pharmacomechanical, and catheter-based endovascular thrombectomy was not included in the study. The final bibliometric analysis included a total of 282 articles. The citation indexes utilized were the Science Citation Index Expanded, Emerging Sources Citation Index, and Social Sciences Citation Index.

This study focuses on an analysis of publicly available scientific literature and does not encompass patients, medical research, or any sort of personal data. Since ethical approval is not necessary for bibliometric research due to the absence of human or animal participants, ethical approval was not obtained for this study.

Data analyses and visualization

Data access was achieved through the online library of the Nation's Library of the Presidency (Ankara, Turkey). The WoS intrinsic instruments were used to examine essential features of the chosen literature. For analysis and graph drawing, the collected data was entered into an MS Excel spreadsheet. The VOSviewer (Version 1.6.20, Leiden University, Leiden, the Netherlands) was used for bibliometric visualizations. The retrieved data were processed using the Bibliometrix R software package (RStudio for Windows Version: 2024.04.1+748) (http://www.bibliometrix.org) (7).

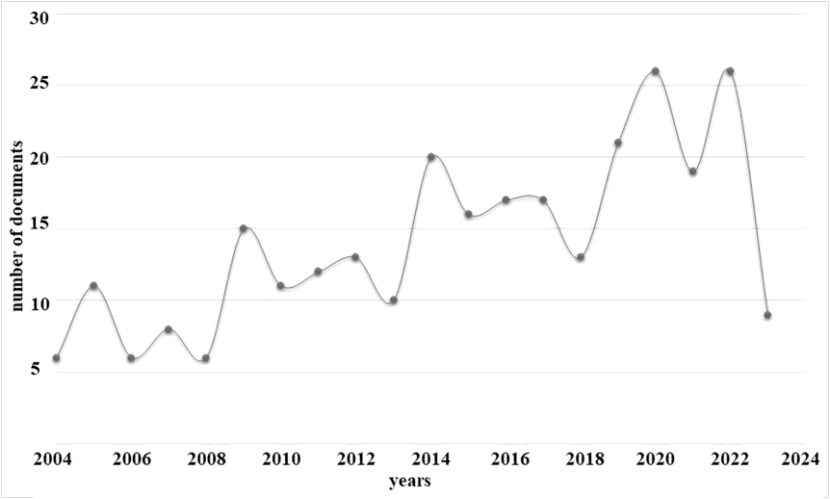

Figure 1. The numerical distribution of pulmonary embolism and thrombolytic therapy research articles published within the last two decades.

MEANDROS MEDICAL AND DENTAL JOURNAL
June 2024 25(2):182-194

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1490284

RESULTS

Using the specified search strategy, an initial search in the WoS database yielded 1086 records. Limiting the date range to 2004-2023 reduced the results to 736. After excluding non-English documents, 695 records remained. Further exclusions of book chapters, conference abstracts, letters, and irrelevant articles narrowed it down to 332. Each article was then individually reviewed, and those primarily related to catheter-directed or pharmacomechanical thrombolysis were removed, resulting in a final set of 282 articles. The bibliometric analysis was conducted on these remaining 282 articles.

Table 1. Country of origin of the authors with the highest number of publications.

Country	Number of articles	Percentage
USA	72	25.53
Turkey	34	12.05
Peoples R China	31	10.99
Germany	23	8.15
Italy	18	6.38
France	17	6.02
Greece	15	5.31
England	12	4.25
Japan	11	3.90
Canada	9	3.19
India	9	3.19
Australia	8	2.83
South Korea	7	2.48
Netherlands	6	2.12

The first publication in the WoS database on pulmonary embolism and thrombolytic therapy dates back to 1980. However, our study specifically evaluated articles from the last two decades. The distribution of published articles over the years is illustrated in Figure 1. Accordingly, the number of published articles has progressively increased over the years, peaking in 2020 and 2022 with the highest counts of 26 articles each, accounting for 9.22% of the total.

The majority of the publications obtained were from the research area of cardiovascular system cardiology (n=97; 34.40%), followed by general internal medicine (n=89; 31.56%), emergency medicine (n=38; 13.47%), hematology (n=38; 13.47%), and respiratory system (n=29; 10.28%), among other areas.

The United States had the highest number of published articles (n=72; 25.53%), followed by Turkey (n=34; 12.05%), China (n=31; 10.99%), Germany (n=23; 8.15%), and Italy (n=18; 6.38%) (Table 1). The retrieved articles totally received 4848 citations, resulting in an average of 17.19 citations per article. The H-index for these articles was determined to be 30. Figure 2 displays the ten most cited countries according to citation count and average citations per article. The USA emerged as the country with the most citations (n=1757), with an average of 28.8 citations per article, ranking sixth in average article citations. On the other hand, Switzerland, which is ranked fifth in terms of overall citations, is in first place for average citations per article. Another noteworthy point is that while Turkey ranks second in the

MEANDROS MEDICAL AND DENTAL JOURNAL
June 2024 25(2):182-194

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1490284

total number of articles, it falls to ninth place in citation count and does not feature in the top ten for average article citations.

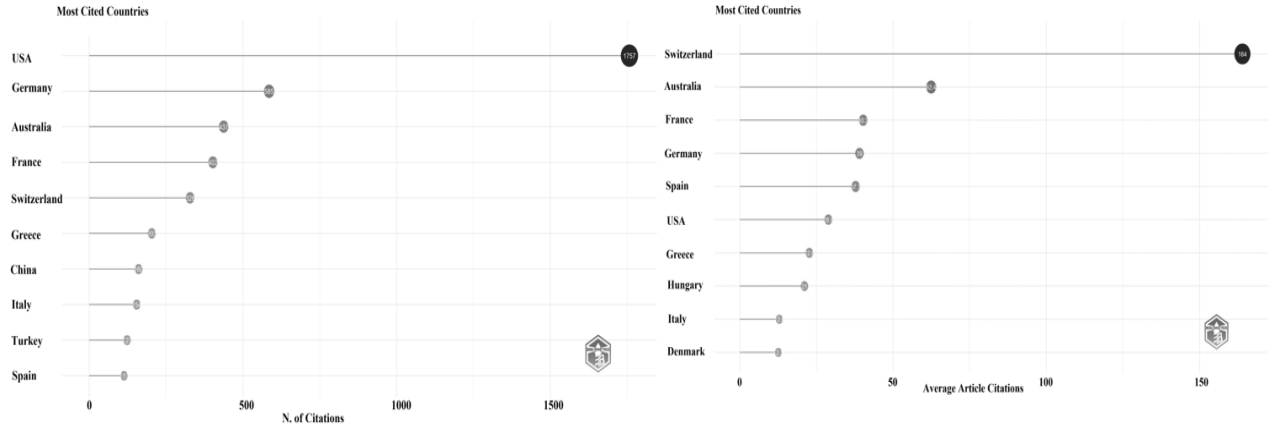

Figure 2. Top 10 most cited countries based on the number of citations (left) and average citations per article (right).

Among the studies funded by various agencies, 43 were identified. The top three supporting organizations were Boehringer Ingelheim, the Federal Ministry of Education and Research (BMBF) in Germany, and the National Natural Science Foundation of China (NSFC). The countries with the highest number of funded articles were China (n=13, 30.23%), the USA (n=13, 30.23%), and Germany (n=9, 20.93%). Turkey was at the bottom of the list, with support for only one article (n=1, 2.33%).

Figures 3a and 3b illustrate the top countries by publication count and a world map showcasing scientific production and collaborations. The USA leads with the highest number of articles (n=61) and single-country publications (SCP) (n=56). Turkey follows with 34 articles and 32 SCP, and China ranks third with 32 articles and 30 SCP. However, in multiple-country publications (MCP), Germany and Greece share the top position with 6 MCP each, while the USA is second with 5 MCP. Although the USA ranks first in article count, inter-country collaborations are notably more prevalent among European countries.

The top three journals with the highest number of publications are the American Journal of Emergency Medicine, the Journal of Thrombosis and Thrombolysis, and Clinical and Applied Thrombosis Hemostasis. The journals with the highest total citations are the American Journal of Cardiology, Chest, and the American Journal of Medicine. In terms of citations per article, the leading journals are the American Journal of Cardiology, Chest, and the Archives of Internal Medicine (Table 2).

MEANDROS MEDICAL AND DENTAL JOURNAL
June 2024 25(2):182-194

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1490284

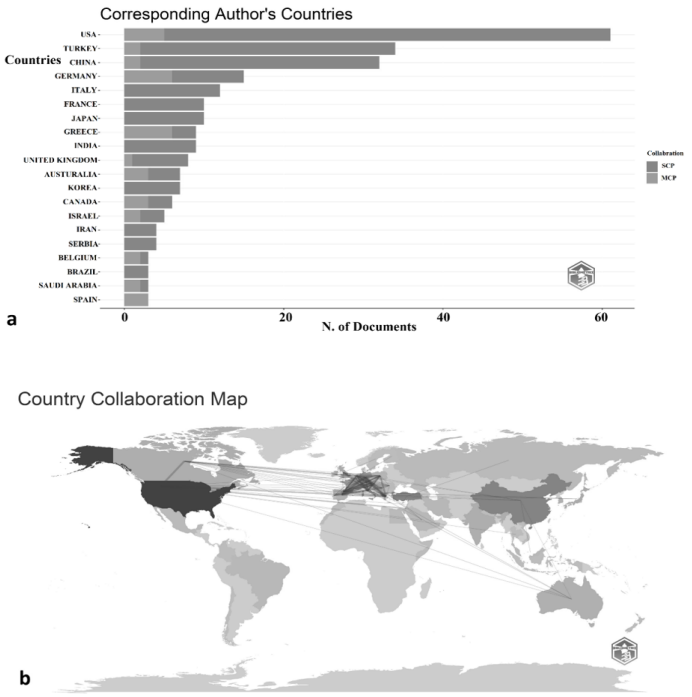

Figure 3. a. Most relevant countries based on the number of publications about the pulmonary embolism and thrombolytic therapy and international collaboration (SCP: Single country publications MCP: Multiple country publications). **b.** World map illustrating the scientific output and collaborations of countries.

Table 2. Journals with the highest number of articles, total citations and citations per article.

Journal name	Number of articles n, (%)	Total citation	Citation per article
American Journal of Emergency Medicine	14 (4.96)	116	8.29
Journal of Thrombosis and Thrombolysis	12 (4.25)	177	14.75
Clinical and Applied Thrombosis Hemostasis	7 (2.48)	21	3
Chest	6 (2.12)	381	63.50
Journal of Emergency Medicine	6 (2.12)	31	5.16
Cureus Journal of Medical Science	5 (1.77)	1	0.20
Thrombosis and Haemostasis	5 (1.77)	118	23.60
American Journal of Cardiology	4 (1.41)	407	101.75
American Journal of Medicine	4 (1.41)	260	65
Archives of Internal Medicine	4 (1.41)	122	30.50
International Journal of Cardiology	4 (1.41)	43	10.75
Resuscitation	4 (1.41)	38	9.50
Thrombosis Research	4 (1.41)	64	16

Table 3 summarized the 10 most cited papers on the pulmonary embolism and thrombolytic therapy according to the WoS database (2, 5, 8-15). The most cited article, authored by Chatterjee et al. (8), was published in JAMA - Journal of the American Medical Association in 2014 and has been cited 522 times in the WoS database.

Table 3. The top cited 10 articles on the pulmonary embolism and thrombolytic therapy according to the Web of Science database.

	Manuscript title	First Author	Year	Citations
1	Thrombolysis for Pulmonary Embolism and Risk of All-Cause Mortality, Major Bleeding, and Intracranial Hemorrhage A Meta-analysis	Chatterjee, S (8)	2014	522
2	Thrombolysis compared with heparin for the initial treatment of pulmonary embolism - A meta-analysis of the randomized controlled trials	Wan, S (9)	2004	424
3	Moderate Pulmonary Embolism Treated With Thrombolysis (from the MOPETT Trial)	Sharifi, M (10)	2013	383
4	Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis	Marti, C (5)	2015	326
5	Management of unsuccessful thrombolysis in acute massive pulmonary embolism	Meneveau, N (11)	2006	221
6	Impact of Thrombolytic Therapy on the Long-Term Outcome of Intermediate-Risk Pulmonary Embolism	Konstantinides, SV (12)	2017	217
7	Thrombolytic Therapy in Unstable Patients with Acute Pulmonary Embolism: Saves Lives but Underused	Stein, PD (13)	2012	205
8	Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germany	Keller, K (2)	2020	167
9	Six-Month Echocardiographic Study in Patients With Submassive Pulmonary Embolism and Right Ventricle Dysfunction: Comparison of Thrombolysis With Heparin	Fasullo, S (14)	2011	102
10	Mobile thrombi of the right heart in pulmonary embolism - Delayed disappearance after thrombolytic treatment	Ferrari, E (15)	2005	77

VOSviewer identified a complete set of 116 keywords. Setting the minimum occurrence threshold to 1 included all these keywords in the analysis. However, four were excluded due to lack of connections. The tool calculated the total co-occurrence strength for each keyword, ultimately clustering 112 keywords into 19 distinct groups. These clusters were interconnected by 358 links, resulting in a total link strength of 394 (Figure 4).

Figure 5 shows a trend analysis of papers about pulmonary embolism and thrombolytic therapy. This was made using Biblioshiny, which lets you see how research topics change over time. This analysis is highly useful for finding new areas, understanding how dynamics are changing, learning from the past, and planning future research directions. Figure 5 reveals that early research primarily focused on topics such as deep venous thrombosis, heparin, echocardiography, thrombolysis, thrombolytic treatment, anticoagulants, and fibrinolysis. Notably, after 2018, there was a discernible shift in research emphasis

MEANDROS MEDICAL AND DENTAL JOURNAL
June 2024 25(2):182-194
Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1490284

towards mortality, bleeding, Coronavirus Disease 2019 (COVID-19), and extracorporeal membrane oxygenation (ECMO).

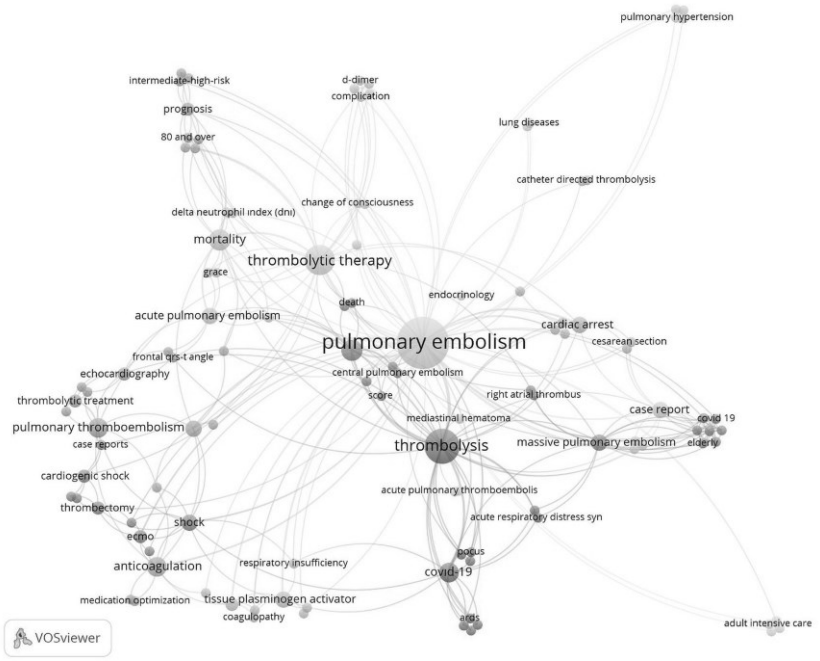

Figure 4. The network visualization of keyword co-occurrence analysis.

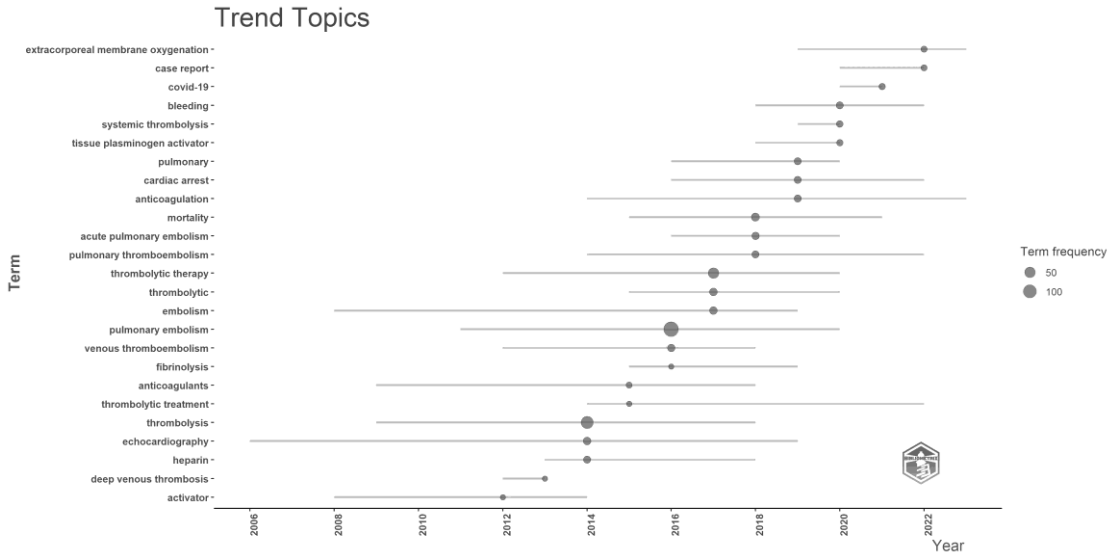

Figure 5. Examination of popular topics in articles about pulmonary embolism and thrombolytic therapy.

MEANDROS MEDICAL AND DENTAL JOURNAL
June 2024 25(2):182-194

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1490284

DISCUSSION

The incidence of PE, characterized by high morbidity and mortality, has shown an increasing trend in recent decades due to rising risk factors such as malignancy and obesity (16). Thrombolytic therapy is particularly effective in high-risk PE patients presenting with hypotensive shock. However, due to the significant risk of bleeding associated with this treatment, it must be administered with great caution. There are numerous studies indicating that COVID-19 may increase the risk of PE (17). The disease burden of PE is expected to become increasingly significant, thereby enhancing the importance of thrombolytic therapy.

Given the growing body of literature on PE and thrombolytic therapy, it is imperative to elucidate the knowledge structure and research trends. This will enable researchers and clinicians to gain a comprehensive understanding of the disease and its essential treatments. This bibliometric analysis provides a comprehensive overview of the research landscape on PE and thrombolytic therapy over the past two decades. To our knowledge, this is the first study to systematically analyze the research characteristics and focal points of PE and thrombolytic therapy using a bibliometric approach, with the goal of identifying future research directions in this field.

This bibliometric study analyzed a total of 282 publications. Although the focus was on the last 20 years, the earliest related publication dates back to 1980 (18). Despite some fluctuations, the number of publications has generally increased over the years, peaking in 2020 and 2022. This surge suggests heightened research activity, possibly driven by advancements in medical technology, increased awareness of PE, and emerging global health challenges such as COVID-19.

Our findings reveal that the majority of the scientific papers on this topic originated from the United States, aligning with previous studies that utilized similar methodologies in other fields. The US was followed by Turkey and China in terms of the number of publications. This dominance can be attributed to several factors, including substantial financial support for scientific activities, enhanced research infrastructure, and a high number of researchers.

Interestingly, while Turkey ranks second in the total number of articles, it falls to nineth place in citation count and does not appear in the top ten for average citations per article. This discrepancy suggests that while Turkish researchers are prolific in publishing, their work may not be as widely cited, indicating a potential area for improvement in research quality or dissemination. Funding plays a crucial role in supporting research activities. Our analysis identified Boehringer Ingelheim, the Federal Ministry of Education and Research (BMBF) in Germany, and the National Natural Science Foundation of China (NSFC) as the top funding organizations. The countries receiving the most funding were China, the USA, and Germany, while Turkey received minimal financial support, with only one funded article. Insufficient financial support for research, prioritizing academic promotion over producing high-quality scientific work, and failing to anticipate or engage with emerging scientific trends may account for Turkey's low citation count, despite its high number of publications.

MEANDROS MEDICAL AND DENTAL JOURNAL
June 2024 25(2):182-194

Meandros Medical and Dental Journal
doi: 10.69601/meandrosmdj.1490284

The analysis of journals revealed that the American Journal of Emergency Medicine, the Journal of Thrombosis and Thrombolysis, and Clinical and Applied Thrombosis Hemostasis are the top sources of publications in this field. In terms of citation impact, the American Journal of Cardiology, Chest, and the American Journal of Medicine lead the way, highlighting their influence and the high quality of research they publish.

European countries demonstrate stronger international collaborations, as indicated by the significant number of MCPs. This trend highlights the crucial role of collaborative research efforts in advancing the fields of PE and thrombolytic therapy. While the USA leads in total article count and SCPs, inter-country collaborations are markedly more prevalent among European, emphasizing the importance of international research partnerships in this domain.

The keyword analysis identified 112 keywords, which were organized into 19 clusters, indicating a diverse range of research themes and focal areas within the field. This clustering provides valuable insights into the interconnectedness of various research topics and underscores the multidisciplinary nature of PE and thrombolytic therapy research. Trend analysis using Biblioshiny revealed that early research primarily focused on deep venous thrombosis, heparin, echocardiography, thrombolysis, thrombolytic treatment, anticoagulants, and fibrinolysis. However, post-2018, there was a notable shift towards topics such as mortality, bleeding, COVID-19, and ECMO. This shift reflects evolving research priorities, emerging challenges in PE treatment, advancements in technology, and the impact of the global pandemic.

Citation analyses offer a compelling overview of the most significant accomplishments within a field, illustrating how research has progressed over the past few decades. An analysis of the 10 most cited papers on PE and thrombolytic therapy, according to the WoS database, revealed that the most cited article is by Chatterjee et al. titled "Thrombolysis for Pulmonary Embolism and Risk of All-Cause Mortality, Major Bleeding, and Intracranial Hemorrhage: A Meta-Analysis" this seminal work was published in JAMA - Journal of the American Medical Association in 2014 and has garnered 522 citations in the WoS database (8). This meta-analysis aimed to evaluate the mortality benefits and bleeding risks associated with thrombolytic therapy compared to anticoagulation in patients with acute pulmonary embolism, including those with intermediate-risk PE. The critical evaluation of thrombolysis in PE treatment in this publication has had a significant impact on the field. It has become the most cited work in this field as a result of the substantial attention it has attracted from the research community due to its influential findings.

Limitations

This study has several limitations that should be acknowledged. First, the analysis was based solely on publications indexed in the WoS database, which may not capture the entire body of relevant literature, potentially leading to a selection bias. Second, the exclusion of non-English articles may have omitted significant research contributions from non-English speaking countries. Third, the bibliometric approach, while useful for identifying trends and patterns, is inadequate for evaluating the quality of the studies. Lastly, the study's reliance on citation metrics as indicators of research impact may overlook the nuanced

and multifaceted nature of scientific influence. Future research should consider incorporating multiple databases and qualitative assessments to provide a more comprehensive evaluation of the field.

CONCLUSION

In conclusion, this bibliometric analysis offers a comprehensive overview of the research landscape on PE and thrombolytic therapy over the past two decades. The study identifies key research trends, highlights influential studies, the impact of funding on research productivity, and underscores the importance of international collaborations. The findings reveal that while the US leads in the number of publications, European countries demonstrate stronger collaborative efforts. The analysis also shows a notable shift in research focus post-2018 towards emerging challenges such as COVID-19 and ECMO. This evolving research landscape underscores the increasing significance of thrombolytic therapy in the context of rising PE incidence. Our study provides valuable insights that can guide future research directions and inform clinical practices, ultimately contributing to improved patient outcomes.

Acknowledgments

None.

Authorship contributions

T.C.**:** Concept, design, data collection, analyses, and writing.

Data availability statement

Data are available upon reasonable request.

Declaration of competing interest

The author declared no conflict of interest.

Ethics

Ethical approval was not required for this study as it involves bibliometric research, which does not include human or animal participants.

Funding

The author declared that this study received no financial support.

REFERENCES

1. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2020; 41: 543-603.

2. Keller K, Hobohm L, Ebner M, Kresoja KP, Münzel T, Konstantinides SV, et al. Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germany. Eur Heart J 2020; 41: 522-9.

3. Carroll BJ, Larnard EA, Pinto DS, Giri J, Secemsky EA. Percutaneous Management of High-Risk Pulmonary Embolism. Circ Cardiovasc Interv 2023; 16: e012166.

4. Stevens SM, Woller SC, Baumann Kreuziger L, Bounameaux H, Doerschug K, Geersing GJ, et al. Executive Summary: Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. Chest 2021; 160: 2247-59.

5. Marti C, John G, Konstantinides S, Combescure C, Sanchez O, Lankeit M, et al. Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis. Eur Heart J 2015; 36: 605-14.

6. De Bellis N. Bibliometrics and citation analysis: from the science citation index to cybermetrics. The Scarecrow Press; 2009.

7. Aria M, Cuccurullo C. bibliometrix: An R-tool for comprehensive science mapping analysis. J Informetr 2017; 11: 959-75.

8. Chatterjee S, Chakraborty A, Weinberg I, Kadakia M, Wilensky RL, Sardar P, et al. Thrombolysis for pulmonary embolism and risk of all-cause mortality, major bleeding, and intracranial hemorrhage: a meta-analysis. JAMA 2014; 311: 2414-21.

9. Wan S, Quinlan DJ, Agnelli G, Eikelboom JW. Thrombolysis compared with heparin for the initial treatment of pulmonary embolism - A meta-analysis of the randomized controlled trials. Circulation 2004; 110: 744-9.

10. Sharifi M, Bay C, Skrocki L, Rahimi F, Mehdipour M, Investigators M. Moderate Pulmonary Embolism Treated With Thrombolysis (from the "MOPETT" Trial). Am J Cardiol 2013; 111: 273-7.

11. Meneveau N, Séronde MF, Blonde MC, Legalery P, Didier-Petit K, Briand F, et al. Management of unsuccessful thrombolysis in acute massive pulmonary embolism. Chest 2006; 129: 1043-50.

12. Konstantinides SV, Vicaut E, Danays T, Becattini C, Bertoletti L, Beyer-Westendorf J, et al. Impact of Thrombolytic Therapy on the Long-Term Outcome of Intermediate-Risk Pulmonary Embolism. J Am Coll Cardiol 2017; 69: 1536-44.

13. Stein PD, Matta F. Thrombolytic Therapy in Unstable Patients with Acute Pulmonary Embolism: Saves Lives but Underused. Am J Med 2012; 125: 465-70.

14. Fasullo S, Scalzo S, Maringhini G, Ganci F, Cannizzaro S, Basile I, et al. Six-Month Echocardiographic Study in Patients With Submassive Pulmonary Embolism and Right Ventricle Dysfunction: Comparison of Thrombolysis With Heparin. Am J Med Sci 2011; 341: 33-9.

15. Ferrari E, Benhamou M, Berthier F, Baudouy M. Mobile thrombi of the right heart in pulmonary embolism - Delayed disappearance after thrombolytic treatment. Chest 2005; 127: 1051-3.

16. Di Nisio M, van Es N, Büller HR. Deep vein thrombosis and pulmonary embolism. The Lancet 2016; 388: 3060-73.

17. Poissy J, Goutay J, Caplan M, Parmentier E, Duburcq T, Lassalle F, et al. Pulmonary Embolism in Patients With COVID-19: Awareness of an Increased Prevalence. Circulation 2020; 142: 184-6.

18. Parisi AF. Should fibrinolytic drugs be used to treat acute pulmonary-embolism. J Cardiovasc Med 1980; 5: 793.