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Visual Analysis of Stroke Complicated with Venous Thromboembolism Research Based on Web of Science Database

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Research Article

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ABSTRACT

Background: The incidence of venous thromboembolism within 2 weeks after stroke could be as high as 30%-80%, which seriously affected the health of patients. So far, the research on Stroke Complicated with Venous Thromboembolism (SCVT) has a history of several decades. In the era of big data, a large number of studies are published every year. It is a challenge to understand the important research in this field comprehensively and intuitively by manual reading.

Objective: The purpose of this study was to use a bibliometric approach to analyze the current research status, hotspots, and trends of SCVT, in order to help researchers comprehensively and intuitively understand this research field and further promote its development.

Design: A visual analysis was conducted.

Methods: Citespace (6.1.6) knowledge map software was used to visualize and analyze the related literatures of SCVT from January 1, 2012 to February 23, 2023 in web of science core collection database.

Results: A total of 14383 articles were included. In recent years, the number of articles published in the field of SCVT has generally shown an upward trend. The United States and Portugal were the countries with the highest publication and centrality. University Birmingham, Harvard Med Sch and Harvard University ranked the highest in terms of publication, centrality and burst. Lip, Gregory Y H, Lip, Gregory Y H, Kleinschnitz were the authors with the highest publication, centrality and burst respectively. Important keywords included atrial fibrillation, stroke, risk, diagnosis, apixaban, expert consensus, etc. There were 10 keyword clusters and 25 burst

Conclusion: In recent years, the study of SCVT has been widely concerned by the society. The research topics mainly focused on the efficacy and risk control of novel oral anticoagulants in the treatment of SCVT, the relationship between atrial fibrillation and SCVT, the impact of COVID-19 on SCVT, relationship between

SCVT and Percutaneous Coronary Intervention (PCI), and Cellular mechanism of SCVT. The frontiers of research included stroke prediction, novel oral anticoagulants, treatment modalities, mechanical thrombectomy, risk factors, and guidelines.

Keywords: Stroke; Venous thromboembolism; Atrial fibrillation; Bibliometric; Knowledge map

INTRODUCTION

Stroke is the main clinical type of cerebrovascular diseases. It is caused by the occlusion or rupture of cerebrovascular which affects the blood supply to the brain, leading to hypoxia and nutritional deficiency of brain tissue, resulting in severe neurological impairment and related functional damage in patients. Stroke is characterized by high morbidity, high disability and high mortality, and is currently the second leading cause of death in humans. In China, there are about 2 million new cases of stroke every year, 70%-80% of patients have limb movement disorder, and those with severe symptoms need to stay in bed for a long time and have limited activity [1]. Therefore, stroke patients are prone to develop Venous Thrombo Embolism (VTE), especially with old age, dehydration, obesity, past medical history, etc. VTE is one of the common and easily underestimated serious complications in stroke patients, and is one of the main causes of death after stroke. VTE includes Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE), which are two manifestations of the same disease at different sites. Deep vein thrombosis is a blood clot in a deep vein, usually in the legs. PE is a deep vein thrombosis in which an embolus breaks off from the vein wall and travels with venous blood to the lungs, partially or completely blocking the blood supply to the lungs, which can be fatal [2]. Several studies have shown that the incidence of VTE can be as high as 30% to 80% within 2 weeks after stroke without any intervention [3].

The occurrence of VTE in stroke patients has a serious impact on the prognosis of patients. First, the incidence of asymptomatic VTE is high, which is not conducive to early detection [4]. It has been reported that 34.78% to 74.5% of stroke patients complicated with DVT have no obvious clinical symptoms, that is, asymptomatic VTE usually occurs on the paralyzed limb, and the clinical manifestations of VTE are easily confused with the manifestations of the paralyzed limb and are difficult to distinguish [5]. Second, early VTE in stroke patients is an important independent risk factor for poor prognosis and death within 3 months, and significantly increases mortality. When the deep vein thrombus falls off, it migrates with the blood, which can block the pulmonary artery and its branches, causing PE, which is the most serious manifestation of VTE. Patients may experience dyspnea, chest pain, hemoptysis, syncope, and even death. PE developed in 50% to 60% of stroke patients with DVT and was one of the leading causes of death in stroke patients, accounting for 1/4 to 1/3 of acute deaths in stroke patients [6]. In addition, most stroke patients were elderly, inaccurate language expression, complicated with cardiopulmonary diseases, and symptoms were not easy to be found in time [7]. Moreover, when small thrombi block the pulmonary vascular bed with certain reserve capacity, the patient's symptoms were difficult to manifest or the symptoms were mild and not persistent, becoming occult PE, thus easily leading to misdiagnosis and delayed treatment, and the mortality rate of such patients could be as high as 30%.

Undoubtedly, more studies related to SCVT will remain the main way to solve this problem in the medical field [8]. Up to now, the study of SCVT has a history of several decades. In the era of big data, a large number of articles are published every year. It is a challenge to understand the important research in this field comprehensively and intuitively by manual reading. There are two main methods to obtain a comprehensive overview of a research field, namely narrative and systematic

literature reviews, both of which focus on research findings with the aim of drawing an overall conclusion [9]. Systematic literature reviews differ from narrative literature reviews in that they have clearly defined objectives and search methods, as well as clear inclusion and exclusion criteria [10]. However, such methods are difficult to analyze the whole discipline or a large field of research. In addition to the above two methods, we can also use the method of bibliometrics, a branch of information science, which is the science of quantitative analysis and research. Bibliometrics is a popular research method when studying the development of a certain discipline field [11]. It is based on statistics and big data. By statistically summarizing the research literature in a specific field, we can find the overall development status of the field. In addition, it is also widely used to evaluate the scientific research strength of universities or individuals, to understand the countries or departments with strong research strength in various disciplines, to find possible partners, to evaluate units and to find talents. Therefore, this study intended to use bibliometric methods to analyze the current situation, hot spots and trends of research related to SCVT, so as to help researchers comprehensively and intuitively understand this research field and further promote its development [12].

MATERIALS AND METHODS

Data collection

Bibliometric analysis relies on objective and comprehensive literature database. Currently, widely used databases include scopus, web of science, pubmed, embase, cochrane library, etc. Among them, the web of science database contains multi-disciplinary, high-impact, international and comprehensive large-scale academic journals. Therefore, it is reasonable and effective to choose the Web of Science database as our research data source [13].

Due to the high quality of Science Citation Index (SCI) literature and its great influence in the industry, Web of Science core database was used as the research platform. All collected articles were written in English and we used the following fields to retrieve data [14].

- **Retrieval strategy was TS (topic):** ((TS=(Stroke) OR TS=(Strokes) OR TS=(Cerebrovascular Accident) OR TS=(Cerebrovascular Accidents) OR TS=(CVA (Cerebrovascular Accident)) OR TS=(CVAs (Cerebrovascular Accident)) OR TS=(Cerebrovascular Apoplexy) OR TS=(Apoplexy, Cerebrovascular) OR TS=(Vascular Accident, Brain) OR TS=(Brain Vascular Accident) OR TS=(Brain Vascular Accidents) OR TS=(Vascular Accidents, Brain) OR TS=(Cerebrovascular Stroke) OR TS=(Cerebrovascular Strokes) OR TS=(Stroke, Cerebrovascular) OR TS=(Strokes, Cerebrovascular) OR TS=(Apoplexy) OR TS=(Cerebral Stroke) OR TS=(Cerebral Strokes) OR TS=(Stroke, Cerebral) OR TS=(Strokes, Cerebral) OR TS=(Stroke, Acute) OR TS=(Acute Stroke) OR TS=(Acute Strokes) OR TS=(Strokes, Acute) OR TS=(Cerebrovascular Accident, Acute) OR TS=(Acute Cerebrovascular Accident) OR TS=(Acute Cerebrovascular Accidents) OR TS=(Cerebrovascular Accidents, Acute))) and ((TS=(Venous thromboembolism) OR TS=(thrombosis) OR TS=(Embolism and Thrombosis) OR TS=(Thromboembolism) OR TS=(Venous Thromboembolism) OR TS=(Thromboses) OR TS=(Thrombus) OR TS=(Blood Clot) OR TS=(Blood Clots) OR TS=(Clot, Blood) OR TS=(Clots, Blood) OR TS=(Thromboembolism, Venous))).
- Since the purpose of this study was more inclined to find the research hotspots of SCVT in recent years, rather than exploring the development of its knowledge, we set the search time from January 1, 2012 to February 23, 2023.
- **Index:** (Science Citation Index Expanded (SCI-EXPANDE), Social Sciences Citation Index (SSCI), Conference Proceedings Citation Index–Science (CPCI-S), Conference Proceedings Citation Index-Social Science & Humanities (CPCI-SSH), Book Citation Index–Science (BKCI-S), Book Citation Index-Social Sciences and 85 Humanities (BKCI-

SSH)).

- **Document type:** Article or Review.
- **Inclusion criteria:** The topic of the literature was related to SCVT.
- **Exclusion criteria:** book chapters, book reviews, letters, conferences.
- **Quality control:** Two researchers screened the literatures respectively and cross-checked the results. They scanned the title and abstract of the article for screening. If they could not make it clear, they would consult the full text and decide.

Through the above search strategy, and after removing duplicate articles by Citespace software, we finally included 14383 articles as the data for analysis [15].

Instrument

Cite space (6.1.6) was used to analyze the resulting data. The settings for Citespace were as follows: The time span was from January 1, 2012 to February 23, 2023, the time slice was one year, and the threshold value of the time slice was set as 50. Network node types include country, author, institution, and keyword [16]. The selected content was pruned by the pathfinder method to obtain the corresponding knowledge map. Some other details could be seen in the upper left corner of the knowledge map. In the generated graph, N represented the number of network nodes, E represented the number of connections, Density represented the density of the network, Modularity was the evaluation index of network modularity, the greater the Modularity Q value, the better the clustering obtained by the network, and the Modularity Q value >0.3 means that the obtained network community structure was significant [17]. Silhouette value was used to measure the homogeneity of the network, the closer to 1 reflects the higher homogeneity of the network, above 0.5, indicated that the clustering results were reasonable. The node represented the citation ring, and the different colors and sizes of the ring represented the different years and the number of citations, which were used to represent the cited history of the document since its publication. For the knowledge map of the keyword distribution network, the distribution of the keyword frequency may reflect the cited frequency or the number of articles in a certain field, and the field with the highest number of articles or the most cited is often a research hotspot [18]. The higher the word frequency, the larger the nodes displayed in the knowledge map. At the same time, we can judge the co-occurrence times between nodes according to the thickness of the link keyword line, measure their affinity, and judge the time of word frequency by color. Cluster analysis referred to the analysis process of grouping a set of physical or abstract objects into a plurality of clusters composed of similar objects. In this study, in order to summarize the research hotspots of disciplines or fields, cluster analysis was used to show the relationship between high-frequency keywords. Burst indicated that the value of a variable changed greatly in a short period of time. The keywords with strong burst characteristics indicated that scholars have discovered new research fields and research perspectives in a certain period, thus showing the academic frontier in a certain period, which was shown in red in the graph [19].

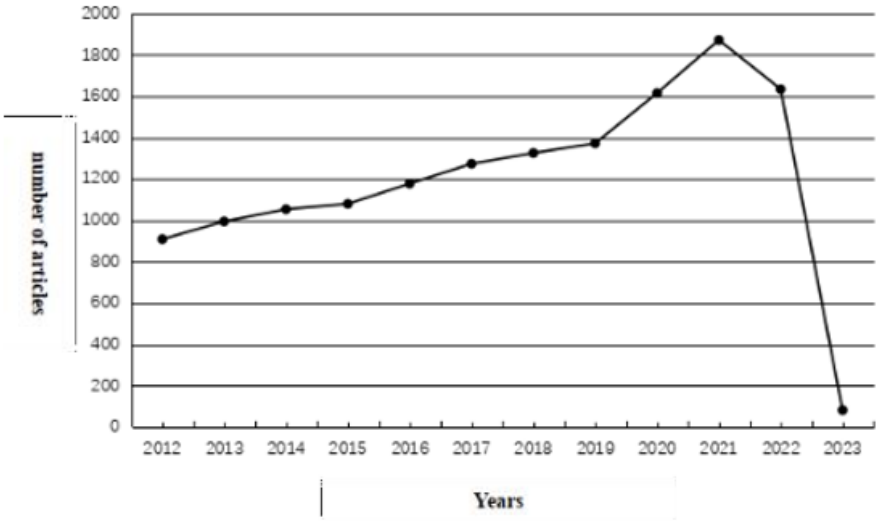
RESULTS

Analysis of annual publications

From 2012 to 2022, the number of articles published generally showed an upward trend, with the most obvious increase in 2020 and 2021, with 1615 and 1872 articles respectively. However, the number of articles published in 2022 decreased greatly compared with that in 2021, with 1634 articles [20]. As the statistical deadline was February 23, 2023, the statistics of the number of articles published in 2023 were incomplete, but more than 300 articles were published less than the same

period in 2022 [21]. Figure 1 showed the annual number of articles (Figure 1).

Figure 1. Analysis of annual publications.



Countries distribution

There were 58 nodes and 88 lines in the knowledge map of collaborating countries (Figure 2), and the density was only 0.0399. Table 1 listed the top 10 countries in terms of publication and centrality of studies on SCVT, which had a high degree of contribution in the field of SCVT. Among them, the United States had the largest publication, with publication of 5001, far higher than the second and later countries, indicating that the United States had a rich research foundation in this field and had made great contributions to the world's research in this field with far-reaching influence. The country with the highest centrality was Portugal, with a value of 0.93, indicating that it had the closest academic research cooperation with other countries and had also played an important role in research innovation in recent years. Other countries with high production included China, Germany, England, Italy, Canada, Japan, France, the Netherlands and Spain. Other countries with a high centrality include South Africa, Serbia, Mexico, Hungary, Argentina, Norway, Belgium, Thailand, and Colombia (Figure 2 and Table 1).

Figure 2. The knowledge map of collaborating countries.

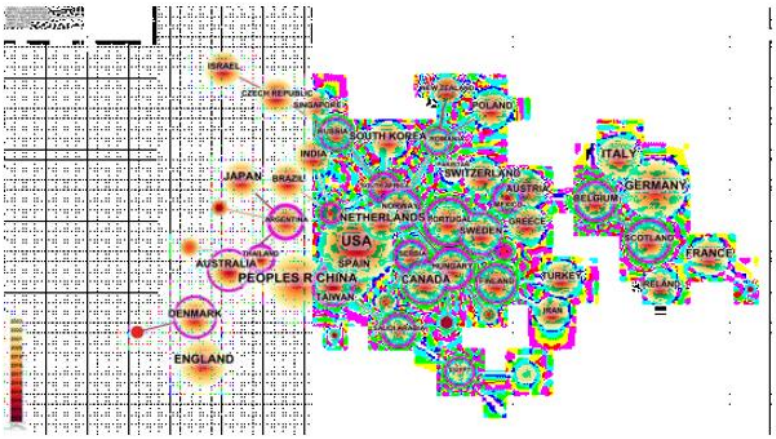


Table 1: Research distribution by countries.

Country	Count	Country	Centrality
USA	5001	Portugal	0.93
Peoples R China	1915	South Africa	0.61
Germany	1503	Serbia	0.52
England	1382	Mexico	0.51
Italy	1191	Hungary	0.48
Canada	987	Argentina	0.46
Japan	886	Norway	0.44
France	823	Belgium	0.39
Netherlands	671	Thailand	0.34
Spain	586	Colombia	0.33

Institutions distribution

There were 378 nodes and 960 links in the knowledge map of collaborating institutions (Figure 3), with a density of 0.0135. The Figure 3 indicated the institutional cooperation network was generally close. Table 2 listed the top 10 institutions in terms of publication, centrality, and burst to analyze the main institutions in the field of SCVT. University Birmingham, Harvard Med Sch and Mayo Clin were the top three institutions in terms of publication, with 339, 323 and 313 articles respectively. Harvard Med Sch, Stanford University and University Ulsan were the top three institutions in terms of centrality, with centrality of 0.3, 0.23 and 0.23 respectively. Harvard University, University Birmingham and University Liverpool were the top three institutions with burst of 50.92, 42.27 and 37.57 respectively. The literatures published by the above institutions have certain basic and key roles or turning points in the field of SCVT. More information was shown in Table 2.

Figure 3. The knowledge map of collaborating institutions.

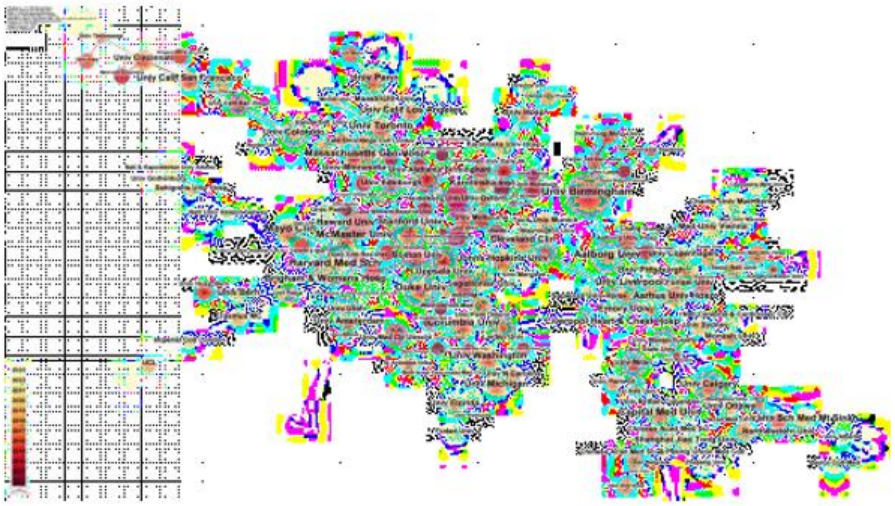


Table 2. Institutions distribution.

Institution	Count	Institution	Centrality	Institution	Burst
University Birmingham	339	Harvard Med Sch	0.3	Harvard University	50.92
Harvard Med Sch	323	Stanford University	0.23	University Birmingham	42.27
Mayo Clin	313	University Ulsan	0.23	University Liverpool	37.57
McMaster University	282	Emory University	0.2	Liverpool Heart and Chest Hosp	28.21
Aalborg University	276	University Utah	0.2	Heidelberg University	17.27
University Toronto	236	Massachusetts Gen Hosp	0.19	University Paris	16.55
Capital Med University	222	Washington University	0.18	Charite University Med Berlin	15.32
Duke University	219	University Glasgow	0.17	Fudan University	14.56
Columbia University	201	IRCCS Ist Clin Sci	0.17	Natl Cerebral and Cardiovasc Ctr	14.21
Stanford University	164	Maugeri Uppsala University	0.16	Aalborg University Hosp	14.17

In order to further explore the specific direction of cooperation between institutions, we conducted a keyword cluster analysis based on Figure 3. The clustering result was shown in Figure 4. The Modularity (Q value) of the knowledge map of was 0.8457, and the Mean Silhouette (S value) was 0.9636, which indicated that the clustering effect was very good, and could provide reliable evidence for exploring the specific cooperation direction among institutions. The results showed that there were 12 clusters, and the top of three cluster labels were thrombosis (cluster 0), atrial fibrillation (cluster 1), technique (cluster 2). In the first cluster, the representative institutions were McMaster University, Stanford University, Karolinska Inst, Uppsala University, Boston Univ. The specific information of the top 10 institutional cooperation keyword clusters was shown in Table 3.

Figure 4. Keyword cluster analysis of collaborating institutions.

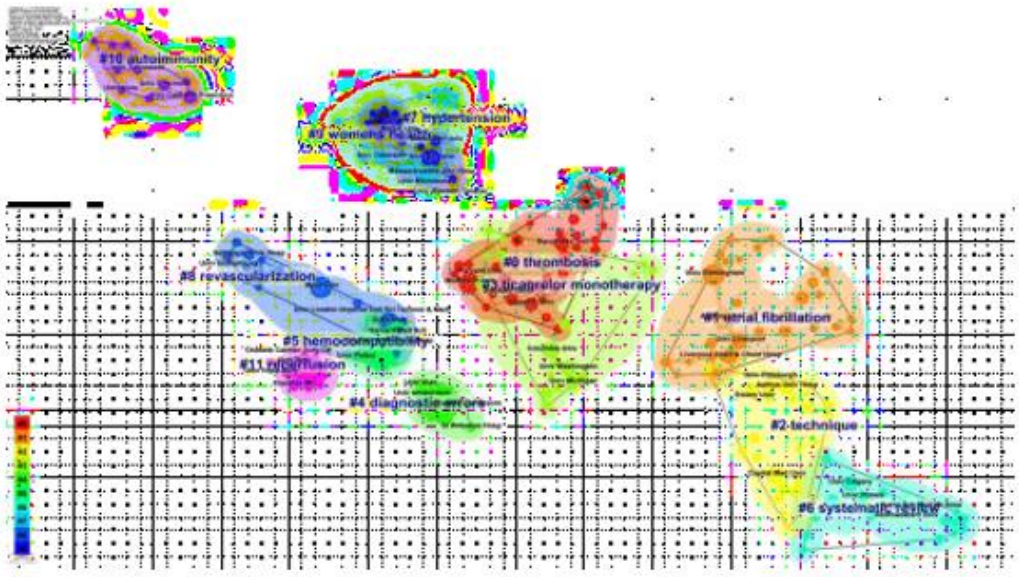


Table 3. Keyword cluster analysis of collaborating institutions.

Cluster ID	Size	Silho uette	Mean (Year)	Label (LLR)	Representative institutions (count)
0	36	0.894	2014	Thrombosis; traumatic brain injury;	McMaster Univ (282)

				smoking; son thrombolysis; operator-independent device atrial fibrillation;	Stanford Univ (164) Karolinska Inst (109) Uppsala Univ (91) Boston Univ (77)
1	31	0.972	2017	Thromboembolism; integrated car; cha (2) ds (2)-VASC score; oral anticoagulants technique;	Univ Birmingham (339) Aalborg Univ (276) Univ Liverpool (158) Liverpool Heart & Chest Hosp (122) Med Univ Vienna (83)
2	26	0.985	2017	Hemorrhagic transformation; angioplasty; cerebral ischemiaticagrelor monotherapy;	Capital Med Univ (222 Aarhus Univ Hosp (145) Emory Univ (125) Univ Pittsburgh (109) Shanghai Jiao Tong Univ (81)
3	23	0.938	2015	Factor viii; quality improvement; p2y (12) inhibitors; menopausal hormone therapy	Columbia Univ (201) Univ Washington (144) Harvard Univ (140) Univ Michigan (131) Univ Florida (72)
4	22	0.999	2020	Diagnostic error; adverse effects; randomized controlled trials as topic; sinus thrombosis; atrial fibrillation hemocompatibility; hypertensive disorders of pregnancy pharma coepidemiology;	Univ Amsterdam (110) Univ Utah (55) Univ Med Ctr Utrecht (35) St Antonius Hosp (20) Univ Athens (10) Harvard Med Sch (323) Brigham & Womens Hosp (155)
5	20	0.975	2021	Vascular surgical procedures; thrombectomy	Univ Padua (14) Univ London Imperial Coll Sci Technol & Med (10) Univ Calgary (136) Icahn Sch Med Mt Sinai (125)
6	18	0.96	2017	Systematic review; compression stockings; 4d flow mri; orthostasis; syncope hypertension;	Univ Ottawa (92) Northwestern Univ (57) Univ British Columbia (50) Massachusetts Gen Hosp (153) Univ Penn (151)
7	17	0.935	2018	Sleep apnea; pediatric stroke; blunt cerebrovascular injury; integrins revascularization;	Univ Colorado (101) Univ Minnesota (87) Vanderbilt Univ (42)
8	16	0.984	2017	Technology; watchman; Left Ventricular Assist Device (LVAD); ventricular assist devices	Duke Clin Res Inst (28) Mayo Clin (313) Duke Univ (219) Sahlgrens Univ Hosp (39) Univ Gothenburg (31)
9	14	0.977	2020	Women's health; optical coherence tomography; stem; medical outcomes; hyperacute stroke care	Univ Toronto (236) Maastricht Univ (61) McGill Univ (20) Univ Western Ontario (7) Univ Montreal (2)

Author's distribution

The knowledge map of collaborating authors had a total of 805 nodes and 1898 links (Figure 5), with a density of only 0.0059. The Figure 5 showed that there were many high-contribution authors in the field of SCVT, but the cooperation among authors was relatively weak. Table 3 listed the top 10 authors in terms of publication, centrality, and burst to analyze the lead authors in the area of SCVT. Lip, Gregory Y H, Mehran, Roxana, Torp-pedersen, Christian were the top three authors in terms of publication, with publication of 408, 61 and 52 articles respectively. The number of articles published by the first

author accounts for 49.94% of the total number of articles published by the top ten authors. Lip, Gregory Y H, Mehran, Roxana, Torp-pedersen, Christian were the top three authors in centrality, with centrality of 0.29, 0.21 and 0.19 respectively. Kleinschnitz, Christoph, Lane, Deirdre A, Liu, Yang were the top three authors in terms of burst, with burst of 11.45, 10.07 and 8.6 respectively. The literatures published by the above authors have certain basic and key role or turning point in the field of SCVT. The more information was shown in Table 4.

Figure 5. The knowledge map of collaborating authors.

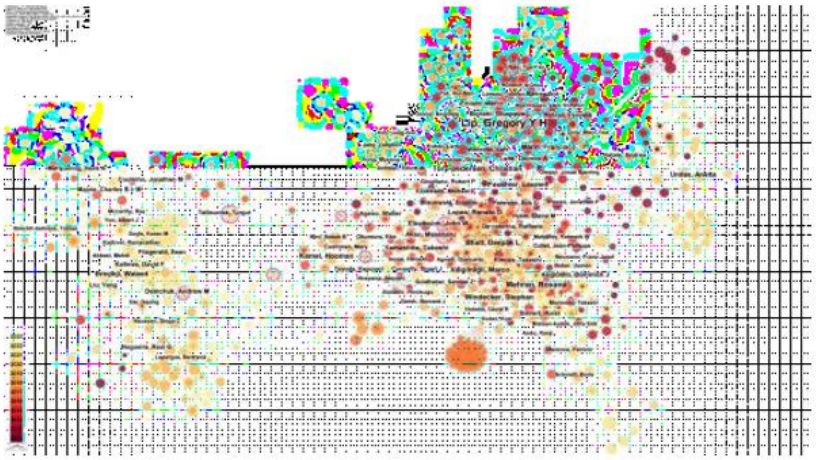


Table 4. Authors distribution.

Author	Count	Author	Centrality	Author	Burst
Lip, Gregory YH	408	Lip, Gregory YH	0.29	Kleinschnitz, Christoph	11.45
Mehran, Roxana	61	Akao, Masaharu	0.21	Lane, Deirdre A	10.07
Torp-pedersen, Christian	52	Demchuk, Andrew M	0.19	Liu, Yang	8.6
Bhatt, Deepak L	47	Tatlisumak, Turgut	0.16	Larsen, Torben	8.06
Valgimigli, Marco	45	Toyoda, Kazunori	0.16	Brinjikji, Waleed	7.99
Kamel, Hooman	43	Koga, Masatoshi	0.16	Fitzgerald, Sean	7.89
Fauchier, Laurent	41	Eikelboom, John W	0.14	Majoie, Charles B L M	7.6
Windecker, Stephan	41	Berkowitz, Scott D	0.12	Kraft, Peter	7.39
Undas, Anetta	40	Kimura, Takeshi	0.1	Lee, Michael S	7.37
Marin, Francisco	39	Valgimigli, Marco	0.09	Navi, Babak B	7.24

In order to further explore the specific direction of cooperation among authors, we conducted a cluster analysis of keywords on the basis of Figure 5. The result was shown in Figure 6. The modularity (Q value) of this knowledge map was 0.8632, and the Mean Silhouette (S value) was 0.9529, which had a good clustering effect and could provide reliable evidence for exploring the specific cooperation direction among authors. Through analysis, 12 clusters were obtained. The top three cluster labels were percutaneous coronary intervention (cluster 0), atrial fibrillation (cluster 1) and cardioversion (cluster 2). In the first cluster, representative authors were Mehran, Roxana, Bhatt, Deepak L, Valgimigli, Marco, Windecker, Stephan, Angiolillo, Dominick J. The specific information of the top 10 authors' collaborative keyword clustering was shown in Table 5.

Figure 6. Keyword cluster analysis of collaborating authors

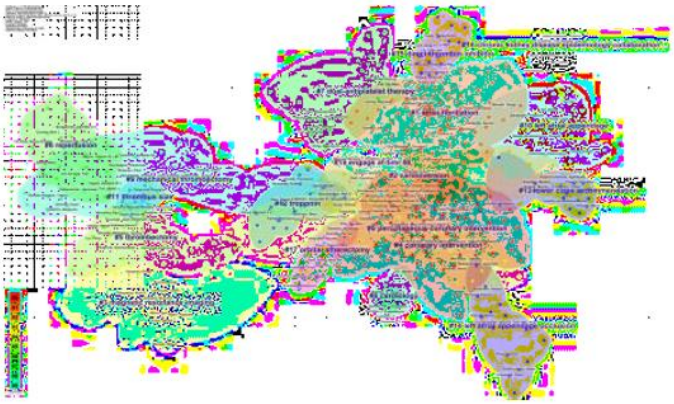


Table 5. Keyword cluster analysis of collaborating authors.

Cluster ID	Size	Silho uette	Mean (Year)	Label (LLR)	Representative authors (count)
0	95	0.853	2016	Percutaneous coronary intervention; dual antiplatelet therapy; atrial fibrillation; ticagrelor; antiplatelet therapy	Mehran, Roxana (61) Bhatt, Deepak L (47) Valgimigli, Marco (45) Windecker, Stephan (41) Angiolillo, Dominick J (30)
1	71	0.977	2014	Atrial fibrillation; thrombectomy; epidemiology; integrated care; oral anticoagulation	Lip, Gregory Y H (408) Torp-pedersen, Christian (52) Fauchier, Laurent (41) Marin, Francisco (39) Boriani, Giuseppe (33)
2	61	0.927	2013	Cardioversion; daumab; focused update; anticoagulation agents bigatran; idaruciz	Lopes, Renato D (36) Eikelboom, John W (30) De caterina, Raffaele (26) Ezekowitz, Michael D (22) Peterson, Eric D (22) Nogueira, Raul G (25)
3	43	0.947	2018	Magnetic resonance imaging; thrombectomy; atrial fibrillation; fibrinolysis; ischemic stroke coronary intervention;	Haussen, Diogo C (18) Lapergue, Bertrand (15) Mazighi, Mikael (14) Piotin, Michel (13)
4	37	0.984	2017	Warfarin control; anticoagulation; elderly; thromboembolism thrombectomy; atrial fibrillation;	Yamashita, Takeshi (35) Akao, Masaharu (28) Kimura, Takeshi (27) Inoue, Hiroshi (22) Okumura, Ken (21) Brinjikji, Waleed (35)
5	33	0.937	2019	Embolic; middle cerebral artery; intervention reperfusion; thrombus density;	Demchuk, Andrew M (30) Liu, Yang (26) Fitzgerald, Sean (24) Kallmes, David F (23) Marquering, Henk A (25) Majoie, Charles B L M (23)
6	29	0.984	2019	Segmentation; ct angiography; permeability dual-antiplatelet therapy;	Yoo, Albert J (15) Dippel, Diederik W J (13) van der lugt, Aad (8) Joung, Boyoung (18) Kim, Jung-Sun (17)
7	27	0.997	2017	Drug-eluting stent(s); meta-analysis; percutaneous coronary intervention;	Hong, Myeong-Ki (16) Pak, Hui-Nam (15)

				coronary artery bypass cardiology; cardiology;	Jang, Yangsoo (15)
8	25	0.998	2017	Intracranial hemorrhage; pulmonary embolism; intracranial hemorrhage; cardiovascular diseases mechanical thrombectomy; mechanical thrombectomy;	Chi, Gerald (10) Vertes, A (4) Barbarash, O (4) Yagensky, A (4) Karpenko, O (4)
9	25	0.975	2018	Histology; atrial fibrillation; cerebral venous thrombosis; acute stroke	Coutinho, Jonathan M (26) Tatlisumak, Turgut (21) Boeckh-behrens, Tobias (16) Kaesmacher, Johannes (14) Zimmer, Claus (14)

Research Trends of stroke complicated with venous thromboembolism

Analysis of important keywords: Figure 7 showed the knowledge map of keyword distribution network, which included 128 nodes, 206 lines and a density of 0.0253. Table 6 listed the top 10 keywords in frequency and centrality, with frequency of 2928, 2385 and 2086 respectively. The three keywords with the highest frequency were atrial fibrillation, stroke and risk. The top three keywords of centrality were diagnosis, apixaban, and expert consensus, with centrality of 0.88, 0.41, and 0.39, respectively. The more information was shown in Table 6.

Figure 7. The knowledge map of keyword distribution.

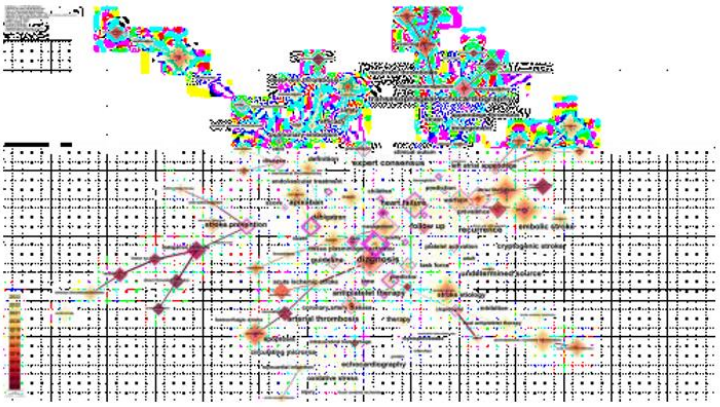


Table 6. Keywords distribution

Keyword	Count	Keyword	Centrality
Atrial fibrillation	2928	Diagnosis	0.88
Stroke	2385	Apixaban	0.41
Risk	2086	Expert consensus	0.39
Ischemic stroke	1907	Heart failure	0.38
Management	1627	Stroke prevention	0.32
Warfarin	1396	Recurrent thrombosis	0.32
Risk factor	1386	Antiplatelet therapy	0.28
Venous thromboembolism	1264	Echocardiography	0.28
Acute ischemic stroke	1164	Clinical outcm	0.26
Therapy	1072	Children	0.25

Analysis of research topic

In order to further understand the research topics of SCVT in recent years, the keywords were clustered based on the knowledge map of keyword distribution network to obtain the knowledge map of keyword clustering. Figure 8 showed that the Modularity (Q value) of the knowledge map of keyword clustering was 0.7656 and the Mean Silhouette (S value) was 0.9298, which indicated that the clustering effect was good and provided a reliable reference for research in this field. The specific clustering information was shown in Table 7.

Figure 8. The knowledge map of keyword clustering.

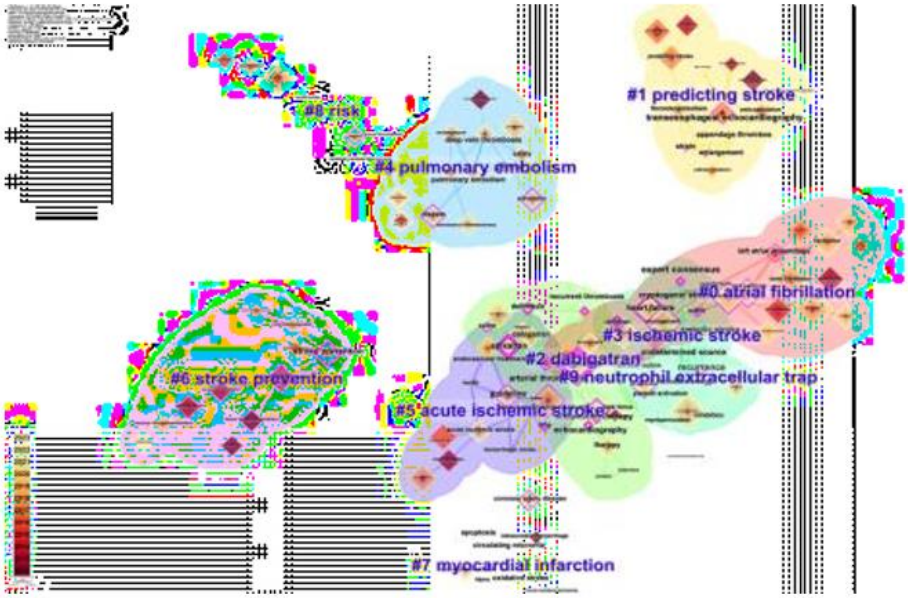


Table 7. Keyword cluster Information.

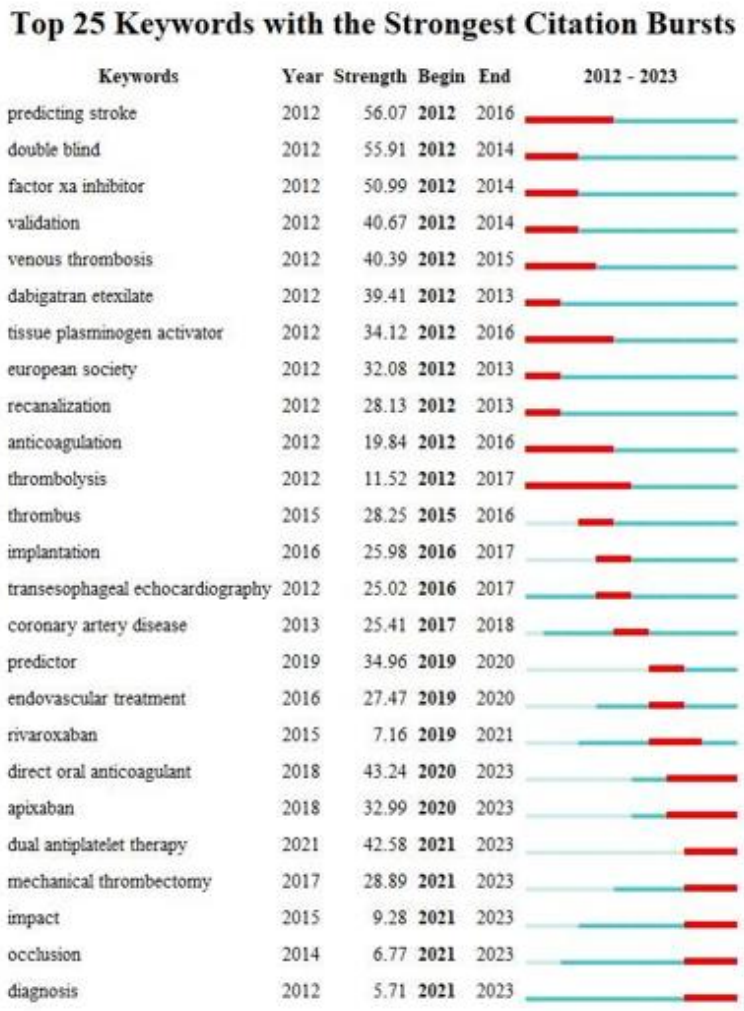
Cluster ID	Size	Silho uette	Mean (Year)	Label (LLR)
0	19	0.972	2014	Atrial fibrillation; left atrial appendage; left atrial appendage closure; acute ischemic stroke; ischemic stroke
1	14	0.984	2016	Predicting stroke; risk stratification; transesophageal echocardiography; venous thromboembolism; thromboembolism
2	14	0.894	2017	Dabigatran; rivaroxaban; apixaban; warfarin; direct oral anticoagulants
3	13	0.866	2018	Ischemic stroke; heart failure; mortality; warfarin; rivaroxaban
4	13	1	2013	Pulmonary embolism; deep vein thrombosis; efficacy; atrial fibrillation; safetacute ischemic stroke;
5	12	0.748	2016	Thrombolysis; tissue plasminogen activator; atrial fibrillation; thrombecto my stroke prevention;
6	12	0.956	2014	Venous thromboembolism; dabigatran etexilate; oral anticoagulant; antithrombotic therapy myocardial infarction;
7	9	0.929	2018	Cardiovascular disease; coronary artery disease; atrial fibrillation; cardiovascular diseases
8	8	0.986	2017	Risk; association; event; venous thrombosis; end arterectomy
9	7	0.911	2023	Neutrophil extracellular trap; causal association; neutrophil

				extracellular trap; neuroprotectant; ath erosclerotic plaques

Analysis of research frontier

In this study, 25 burst keywords were obtained through citespace's burst word analysis function, and the specific results were shown in Figure 9. The outburst keywords had their own year attributes and clearly presented the academic research frontier hot spots in corresponding years.

Figure 9. Keywords with the strongest citation bursts.



DISCUSSION

The research on SCVT has been on the rise in general, especially since 2019, and the literature volume in 2021 was the largest. The reason may be that the novel coronavirus pandemic at the end of 2019 prompted scholars to discover more research directions related to novel coronavirus and thus achieve more research results. However, since 2022, the annual number of published papers has declined, and the number of published papers in 2023 was less than the same period last year, which may be due to the relatively saturated research on novel corona-related stroke complicated with venous

thromboembolism. The annual number of published papers in 2023 is expected to be less than that in 2022, but the overall number of studies on stroke complicated with venous thromboembolism is still very high, which has a certain research heat. The countries with the highest number of publications and centrality were developed countries, among which the United States accounts for the highest proportion. Although the number of articles published in Portugal was lower than that in the United States, it had a good centrality in the national cooperative network, which indicated that Portugal had a high influence in the field of research on stroke complicated with venous thromboembolism. Surprisingly, the top 10 countries with the highest number of publications are completely different from the top 10 countries with the highest number of centrality. The reason may be that the latter, due to lack of sufficient research foundation, were more willing to promote the development of research through cooperation, so as to improve social influence. From the map of national cooperation network, the links between countries were loose, which indicated that the cooperation between countries was weak. In the future, countries with a rich research base, such as the United States, can be relied upon to strengthen cooperation between countries to support the discovery of new research directions.

Most of the top ten institutions were from developed countries such as the United States and the United Kingdom, which further indicated the core research strength of corresponding countries, and pointed out the direction for subsequent scholars to find appropriate cooperation or learning institutions in various countries. Harvard University has a great influence in the research field of SCVT in recent years, due to its high number of publications and the best centrality and emergence. In addition, Univ Birmingham, which has the highest number of publications, is in second place for prominence, but it does not appear in the top 10 for centrality, indicating that its contribution to publication is very high, but its global social impact still needs to be improved. From the keyword clustering map of institutional cooperation, we can see that the cooperation between institutions is not only close, but also more concentrated, and each cooperative group has its own independent direction of cooperation. The main directions of cooperation for McMaster University, Stanford University Karolinska Inst and other institutions include thrombosis; traumatic brain injury; smoking, etc. The main directions of cooperation between institutions such as University Birmingham, Aalborg University and University Liverpool include atrial fibrillation; thromboembolism, etc. The main cooperation directions of Capital Med University, Aarhus University Hospital, Emory University and other institutions include technique; hemorrhagic transformation; angioplasty; cerebral ischemia, etc. The specific directions of inter-institutional cooperation have been listed in detail in our research. In the future, researchers can preliminarily select their own research directions and cooperation intention institutions based on this.

The prolific author in the field of study on SCVT is Lip, Gregory Y H from the University of Liverpool. With 408 published papers, he is far higher than the second author and ranks first in the ranking of author centrality, which further indicates that he has an extremely important influence in this field. Most of his published research topics in this field are related to atrial fibrillation, stroke and anticoagulation therapy, and his specific research directions mainly involve the occurrence mechanism, risk management, prevention and anticoagulation therapy of stroke combined with atrial fibrillation. Kleinschnitz, Christop from University Hospital Essen ranks the first in the emergent, which indicates that his published papers in this field are increasing rapidly in recent years. Through literature review, it is found that his research in this field is mainly focused on the basic research on ischemic brain death complicated with thrombus. In particular, studies on the relationship between platelets and stroke. As can be seen from the keyword clustering map of author cooperation, the cooperation between authors is close, and the relationship between author cooperation groups is close. The directions of cooperation by Mehran, Roxana, Bhatt, Deepak L, Valgimigli, Marco and other authors included percutaneous coronary intervention; dual antiplatelet therapy; atrial fibrillation; ticagrelor; antiplatelet therapy; The directions of cooperation by Lip, Gregory Y H, Torp-pedersen, Christian, Fauchier, Laurent and others include atrial fibrillation;

thrombectomy; epidemiology; integrated care; oral anticoagulation; Lopes, Renato D, Eikelboom, John W, de caterina, Raffaele and others collaborated in cardioversion; dabigatran; idarucizumab; focused update; anticoagulation agents. In the future, researchers can use this as a basis to initially screen out their own research direction and choose appropriate partners.

From the distribution network of keywords, it can be seen that the distribution network of keywords is generally centralized, but there are also many branches of the network, indicating that the research of stroke complicated with venous thromboembolism in recent years extends many research sub-directions based on the general direction. Based on the results of keyword cluster analysis and literature review, we concluded that five major research topics included the efficacy and risk control of novel oral anticoagulants in the treatment of SCVT, the relationship between atrial fibrillation and SCVT, the impact of COVID-19 on SCVT, relationship between SCVT and Percutaneous Coronary Intervention (PCI), and cellular mechanism of SCVT.

Efficacy and risk control of novel oral anticoagulants in the treatment of SCVT

The treatment of stroke complicated with venous thromboembolism is mainly anticoagulant, which is necessary to prevent clot obstruction and obtain recirculation. In recent years, several new oral anticoagulant drugs have become one of the research hotspots in this field, including dabigatran. rivaroxaban; apixaban; warfarin; direct oral anticoagulants. Despite the high cost of these oral anticoagulants, they are popular among patients and providers due to their efficacy, ease of use, and good safety profile, and are also favored by researchers, with research focusing on the therapeutic effect and risk control of these drugs in specific diseases.

Relationship between atrial fibrillation and SCVT

Atrial fibrillation is one of the most common arrhythmias, and the incidence of atrial fibrillation increases with age. Atrial fibrillation not only affects cardiac function, but also causes cerebral embolism caused by thrombus shedding. In recent years, with the increasing incidence of atrial fibrillation and the gradual refinement of studies on the etiology of stroke, studies on cerebral infarction associated with atrial fibrillation have attracted extensive attention in the academic community. Atrial fibrillation increases the risk of stroke (including ischemic stroke, hemorrhagic stroke, and cerebral hemorrhage) by a factor of 5. If the risk of cerebral infarction in patients with atrial fibrillation can be accurately predicted before stroke onset, it will help patients and their families to better choose prevention and treatment programs, and doctors can make more reasonable medical decisions. The results show that the study of risk factors for stroke in patients with atrial fibrillation is one of the research hotspots in this field. At present, the standard used to assess the risk of stroke is CHADS2 score or CHA2DS2-VASc score. Many atrial fibrillation guidelines have repeatedly recommended the use of CHA2DS2-VASc score to predict the risk rate of stroke in patients with atrial fibrillation, but there are still many other factors believed to be related to stroke in patients with atrial fibrillation. For example, age, hypertension, vascular disease, prolonged PR interval, Left Ventricular End-Diastolic Diameter (LVEDD), previous ICH, myocardial infarction, vascular disease, and renal failure.

Impact of COVID-19 on SCVT

The global public health crisis caused by COVID-19 has lasted longer than many of us hoped and expected, and we will be negatively affected by the COVID-19 pandemic, whether in the form of destruction of social living environments or direct physical damage after infection with SARS-CoV-2. In recent years, due to the COVID-19 pandemic, the relationship between cerebral apoplexy combined with venous thromboembolism and novel coronavirus has gradually become one of the

research hotspots in this field. Studies have shown that COVID-19 may be susceptible to venous and arterial thromboembolic disease due to excessive inflammation, hypoxia, fixation, and Diffuse Intravascular Coagulation (DIC). All patients reported by Kananeh et al. had moderate to severe COVID-19 symptoms, required ICU admission, and had significantly elevated D-dimer levels. This is also consistent with Malentacchi et al. and Roushdy et al., who reported impaired coagulation and elevated D-dimer levels in patients with moderate to severe SARS-CoV-2 infection and concurrent arterial and cerebral vein thrombosis. Klok FA et al. evaluated all COVID-19 patients admitted to the ICU of 19 Dutch university hospitals and 2 Dutch teaching hospitals, and found that the incidence of thrombotic complications in ICU patients infected with COVID-19 was very high (19%). It is recommended that all COVID-19 patients admitted to the ICU should be strictly prescribed prophylactic drugs for thrombosis to reduce the risk of stroke or thrombosis. Undoubtedly, as the COVID-19 pandemic continues, more studies are needed in the future to further clarify the relationship between COVID-19 and stroke complicated with venous thromboembolism.

Relationship between SCVT and Percutaneous Coronary Intervention (PCI)

Millions of patients worldwide undergo coronary stenting each year to treat ischemic heart disease. Stent placement is associated with the treatment of ischemic events unrelated to coronary artery disease, such as stroke or death from cardiovascular causes. In addition, approximately 5% to 8% of patients undergoing Percutaneous Coronary Intervention (PCI) have atrial fibrillation, and the treatment strategy for stent-receiving atrial fibrillation patients must balance the risk of stent thrombosis with the risk of stroke and bleeding. The common practice supported by the guidelines is triple therapy, which, however, can lead to excessive bleeding, with an incidence of 2.2% within the first month of treatment and 4% to 12% in the first year of treatment. This prompts researchers to carry out more targeted studies on this aspect, thus forming one of the research hotspots of stroke complicated with venous thromboembolism. A randomized controlled study by Mauri L, et al., showed that dual antiplatelet therapy more than 1 year after placement of a drug-eluting stent significantly reduced the risk of stent thrombosis and major unintentional cerebrovascular events, but was associated with an increased risk of bleeding, compared with aspirin therapy alone. Among patients receiving PCI, clopidogrel monotherapy resulted in a significantly lower rate of cardiovascular and bleeding events after 12 months of DAPT compared with one month of dual antiplatelet therapy DAPT combined with aspirin and clopidogrel. Jolly SS 'study showed that routine manual thrombectomy was associated with an increased incidence of stroke within 30 days in STEMI patients undergoing primary PCI compared to PCI alone.

Cellular mechanism of SCVT

Neutrophil extracellular trap Nets consist of strands of DNA extruded from activated or dying neutrophils, decorated with various protein mediators such as neutrophil elastase or nitrogen urea. The latter has the function of promoting monocyte adhesion and migration, as well as influencing the pro-inflammatory tendency of macrophages. NET release is thought to be the host innate immune response to capture and kill pathogens entering the bloodstream. Locally, activating hemostatic mechanisms may help prevent systemic transmission. However, these same protective processes can increase thrombosis if these mechanisms are abnormal or over-activated. Interest in NET has been increasing since Fucks et al predicted the production of NET, one of the mechanisms of action of neutrophils. Mereweather LJ et al. 's study showed that platelet-neutrophil interaction leads to neutrophil activation, which leads to the release of Neutrophil Extracellular Trap (NET), catechin (LL-22), Myeloperoxidase (MPO), production of Reactive Oxygen Species (ROS), and ultimately thrombosis. How to reasonably inhibit NET activation may be the key to prevent thrombosis caused by NET. Wu ML et al have demonstrated that CD21, a novel phthalein neuroprotector, may regulate the platelet-net-thrombin axis and partly prevent ischemic brain injury

by inducing Adenosine Monophosphorate-Activated Protein Kinase (AMPK) inhibitor activation. In addition, it has been shown that leukocyte/neutrophilic recruitment can be significantly reduced by inhibiting platelet releases such as HMBG1, thus reducing NET formation. In recent years, similar studies on the cellular mechanism of stroke complicated with venous thromboembolism have emerged endlessly, which is also an urgent direction to explore and clarify in the field of stroke complicated with venous thromboembolism in the future.

CONCLUSION

Through bibliometric analysis, this study objectively understood the core research strength in the field of SCVT, and provided a basis for seeking better author cooperation in the future. In addition, this study also captured the research trends and hot spots in this field in recent years, indicating the direction for subsequent relevant research. Future research can be carried out in combination with the 5 hot spots and emergent keywords analyzed in this study to carry out more meaningful research directions, such as the mechanism and treatment of venous thromboembolism complicated by atrial fibrillation and stroke.

LIMITATIONS

We used data from web of science for bibliometric analysis, there are other publicly and commercially available bibliometric databases such as Scopus, Medline, and PubMed. However, this database was chosen for a number of reasons, for example, PubMed records do not include information on cited literature, so it is not possible to use PubMed for citation analysis. In addition, this study only uses one econometric analysis tool, and future studies can use different analysis tools to analyze more data.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

DECLARATION OF COMPETING INTEREST

None.

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REFERENCES

1. Saini V, et al. Global Epidemiology of Stroke and Access to Acute Ischemic Stroke Interventions. Neurology. 2021;97:S6-S16.
2. Caprio FZ, et al. Cerebrovascular Disease: Primary and Secondary Stroke Prevention. Med Clin North Am. 2019;103:295-308.
3. Wu S, et al. Stroke in China: advances and challenges in epidemiology, prevention, and management. Lancet Neurol. 2019;18:394-405.
4. Heit JA, et al. Epidemiology of venous thromboembolism. Nat Rev Cardiol. 2015;12:464-74.
5. Wolberg AS, et al. Venous thrombosis. Nat Rev Dis Primers. 2015;1:15006.
6. Collaboration CT, et al. Effectiveness of intermittent pneumatic compression in reduction of risk of deep vein thrombosis in patients who have had a stroke (CLOTS 3): a multicentre randomised controlled trial. Lancet. 2013;382:516-524.
7. Bembenek JP, et al. Deep venous thrombosis in acute stroke patients. Clin Appl Thromb Hemost. 2012;18:258-64.
8. Wang Y, et al. Clinical Risk Factors of Asymptomatic Deep Venous Thrombosis in Patients with Acute Stroke. Clin Appl Thromb Hemost. 2019;25.
9. Cai Q, et al. Patients with venous thromboembolism after spontaneous intracerebral hemorrhage: a review. Thromb J. 2021;19:93.
10. Li J, et al. In-hospital venous thromboembolism is associated with poor outcome in patients with spontaneous intracerebral hemorrhage: A multicenter, prospective study. J Stroke Cerebrovasc Dis. 2020;29:104958.
11. Freund Y, et al. Acute Pulmonary Embolism: A Review. JAMA. 2022;328:1336-45.
12. Pongmoragot J, et al. Pulmonary embolism in ischemic stroke: clinical presentation, risk factors, and outcome. J Am Heart Assoc. 2013;2:e000372.
13. East AT, et al. What is the optimal duration of treatment for DVT? An update on evidence-based medicine of treatment for DVT. Semin Vasc Surg. 2010;23:182-91.
14. Ahmad N, et al. Looking for asymptomatic pulmonary embolism in patients with deep vein thrombosis: is it the right practice? Am J Med. 2011;124:e15.
15. Gasparyan AY, et al. Writing a narrative biomedical review: considerations for authors, peer reviewers, and editors. Rheumatol Int. 2011;31:1409-17.
16. Akobeng AK. Understanding systematic reviews and meta-analysis. Arch Dis Child. 2005;90:845-8.
17. Jones T, et al. Finding a way through the scientific literature: indexes and measures. World Neurosurg. 2011;76:36-8.
18. Silva BBI, et al. Pigeon Circovirus over Three Decades of Research: Bibliometrics, Scoping Review, and Perspectives. Viruses. 2022;14.
19. Peng C, et al. Bibliometric and visualized analysis of ocular drug delivery from 2001 to 2020. J Control Release. 2022;345:625-45.
20. Liu J, et al. Bibliometric Analysis of Nursing Informatics Research. Stud Health Technol Inform. 2021;284:47-9.
21. Koo M. Systemic Lupus Erythematosus Research: A Bibliometric Analysis over a 50-Year Period. Int J Environ Res Public Health. 2021;18.