Original Article

Revolutionizing vascular imaging: trends and future directions of 4D flow MRI based on a 20-year bibliometric analysis

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Background: Four-dimensional flow magnetic resonance imaging (4D flow MRI) is a promising new technology with potential clinical value in hemodynamic quantification. Although an increasing number of articles on 4D flow MRI have been published over the past decades, few studies have statistically analyzed these published articles. In this study, we aimed to perform a systematic and comprehensive bibliometric analysis of 4D flow MRI to explore the current hotspots and potential future directions.

Methods: The Web of Science Core Collection searched for literature on 4D flow MRI between 2003 and 2022. CiteSpace was utilized to analyze the literature data, including co-citation, cooperative network, cluster, and burst keyword analysis.

Results: A total of 1,069 articles were extracted for this study. The main research hotspots included the following: quantification and visualization of blood flow in different clinical settings, with keywords such as "cerebral aneurysm", "heart", "great vessel", "tetralogy of Fallot", "portal hypertension", and "stiffness"; optimization of image acquisition schemes, such as "resolution" and "reconstruction"; measurement and analysis of flow components and patterns, as indicated by keywords "pattern", "KE", "WSS", and "fluid dynamics". In addition, international consensus for metrics derived from 4D flow MRI and multimodality imaging may also be the future research direction.

Conclusions: The global domain of 4D flow MRI has grown over the last 2 decades. In the future, 4D flow MRI will evolve towards becoming a relatively short scan duration with adequate spatiotemporal resolution, expansion into the diagnosis and treatment of vascular disease in other related organs, and a shift in focus from vascular structure to function. In addition, artificial intelligence (AI) will assist in the clinical promotion and application of 4D flow MRI.

Keywords: Four-dimensional flow magnetic resonance imaging (4D flow MRI); bibliometric analysis; Web of Science; CiteSpace; visualization analysis

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Introduction

Quantitative flow imaging is clinically crucial in certain pathological conditions such as aneurysms, valvular heart disease, and portal hypertension. It provides visualization of vascular anatomy and valuable hemodynamic information (1-5). More recently, 4-dimensional (4D) flow magnetic resonance imaging (MRI), alternatively known as 4D phase contrast (PC) or 3-dimensional (3D) time-resolved PC with 3-directional velocity encoding (VENC), has been increasingly performed in both cardiac and multiple vascular regions of the body (6-8).

PC MRI was first described in the 1980s and measures blood flow velocity using bipolar magnetic field gradients along a single direction (9-11); on this basis, 4D flow MRI acquires 3D data by phase-encoding selected blood flow velocities in any 3 dimensions in a single scan and combining this with the temporal resolution to provide a comprehensive hemodynamic assessment, with full volumetric coverage of the cardiovascular territory throughout the cardiac cycle (6,12,13). Studies have shown that 4D flow MRI offers a reliable *in vivo* hemodynamic assessment for measuring 3D velocity in various vascular regions, with excellent correlation to the standard technique (2D PC) (14-16). Moreover, the derived fluid mechanics parameters, such as wall shear forces, pulse wave velocity (PWV), pressure gradients, and other metrics, have been suggested to predict the development of various cardiovascular pathologies (17-20).

Currently, the applications of 4D flow MRI have been extended to detect hemodynamic changes in large cerebral arteries and veins, carotid arteries, aorta, abdominal (hepatic and renal arteries), and peripheral vessels (21-24). Many articles have focused on improving the technique of 4D flow MRI and its clinical application, but few studies have statistically analyzed these publications. Bibliometrics, a widely used approach to analyze large scientific data, uses qualitative and quantitative analysis to assess research hotspots and trends (25-27). The CiteSpace software developed by Chen *et al.* is extensively used in the medical field and provides a robust bibliometric and visual analysis to examine the dynamics of disciplinary development over time (28,29).

In this study, we used CiteSpace (version 6.1. R6; https://citespace.podia.com/) to visualize and analyze the relevant literature on 4D flow MRI published in the Web of Science Core Collection (WoSCC) database between 2003 and 2022. We aimed to build a knowledge structure of 4D flow MRI and explore research hotspots, frontier areas, and growing trends in the field over time.

Methods

Data sources

The WoSCC database was used for a literature search on 4D flow MRI. The search terms included the following: Topic = ("4D flow MRI" OR "four-dimensional flow MRI" OR "four-dimensional flow" OR "4D flow" OR "4D PC MRI" OR "four-dimensional phase contrast MRI" OR "four-dimensional phase contrast" OR "four-dimensional PC" OR "4D PC" OR "3D time-resolved PC with three-directional velocity encoding") AND Language = English; literature type = article or review. All article searches and data extractions were performed on 20 January 2023 to avoid changes due to daily database updates.

Raw data were then acquired from WoSCC in plain-text format, including full records with references. All downloaded data were independently screened by reviewers (PS Ma and ZW Zhang) to exclude articles unrelated to 4D flow MRI. In case of disagreement between the 2 reviewers, a third independent reviewer (LS Zhu) was involved to assist in the decision-making process. *Figure 1* shows a flowchart of this study. As all data were obtained directly from the database, no ethical declaration is provided in this article.

Statistical analysis

Microsoft Excel 2016 (https://www.microsoft.com/en-au/microsoft-365/excel) and CiteSpace (version 6.1.R6) were utilized to analyze the collected data. Excel 2016 showed the annual publication trend in terms of the number of articles, whereas CiteSpace performed co-occurrence keyword analysis to explore research hotspots and emerging trends, keyword burst analysis to identify frontier areas, and the timeline view and cluster analysis of co-cited references to reveal the current hotspots and underlying knowledge structure of research on 4D flow MRI. The time parameters of the software were set to cover the period from 2003 to 2022, with a time interval of 1 year. The appropriate thresholds were determined based on distinct nodes, and the map clipping approaches were configured to "Pathfinder", "Pruning sliced networks", and "Pruning the merged network"; the visualization options were "Cluster View Static" and "Show Merged Network".

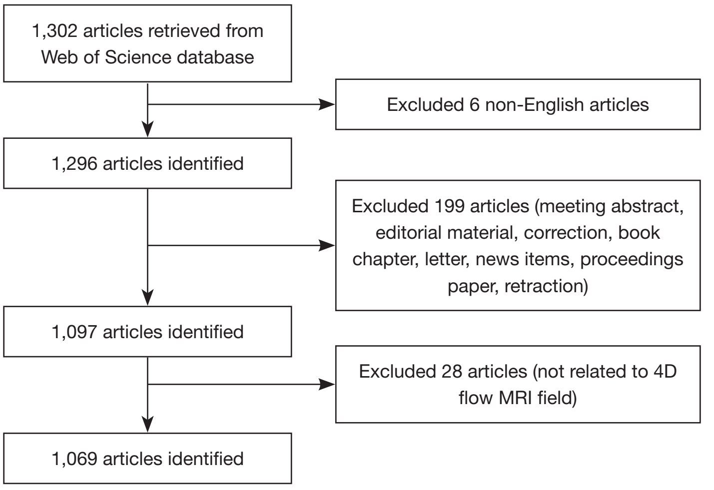

Figure 1 Flow diagram of literature selection. 4D flow MRI, 4-dimensional flow magnetic resonance imaging.

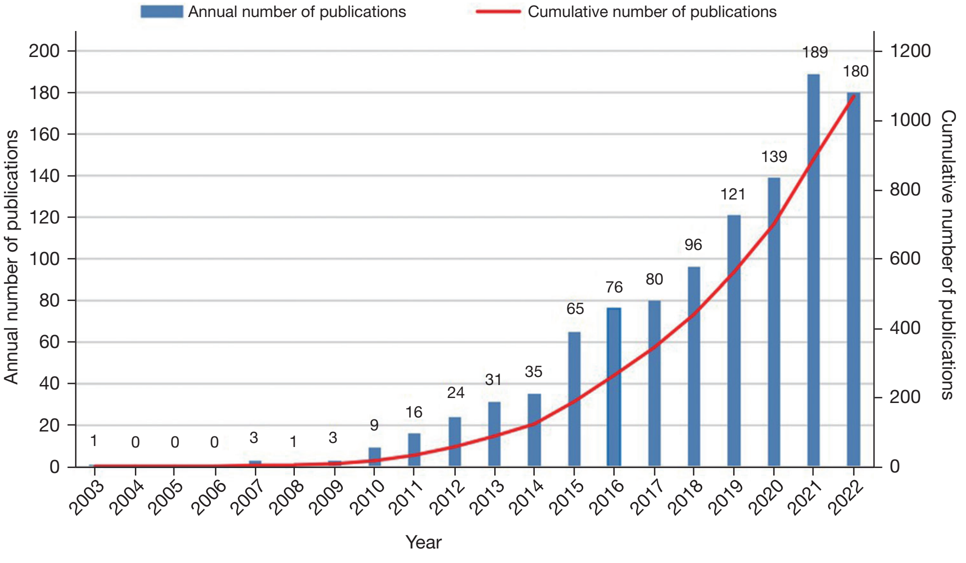

Figure 2 Annual and cumulative number of publications related to 4D flow MRI. 4D flow MRI, 4-dimensional flow magnetic resonance imaging.

Results

Annual publications

A total of 1,069 papers met the search criteria and were selected for further analysis. *Figure 2* shows the annual distribution of 4D flow MRI publications. The first period was between 2003 and 2009, when only a few 4D flow MRI studies were published each year. Since then, the number of publications has increased steadily and slowly from 2010 to 2014, remaining at 9–35 publications per year. Notably, there has been an increase in the number of published papers since 2015 (from 65 in 2015 to 180 in 2022), indicating that this field has consistently received growing attention from academics worldwide.

Analysis of journals

Articles on 4D flow MRI were published in 206 scholarly journals. The number of publications in the *Journal of Magnetic Resonance Imaging* was the highest [impact factor

Table 1 Top 10 most productive journals

Ranking	Journals	IF	No. of published papers
1	*Journal of Magnetic Resonance Imaging*	4.4	135
2	*Magnetic Resonance in Medicine*	3.3	80
3	*Journal of Cardiovascular Magnetic Resonance*	6.4	62
4	*European Radiology*	5.9	32
5	*Magnetic Resonance Imaging*	2.5	31
6	*International Journal of Cardiovascular Imaging*	2.1	29
7	*Frontiers in Cardiovascular Medicine*	3.6	24
8	*Magnetic Resonance in Medical Sciences*	3.0	23
9	*Scientific Reports*	4.6	23
10	*Annals of Biomedical Engineering*	3.8	21

IF, impact factor calculated in 2022.

(IF) 2022 =4.4; 135 publications], followed by *Magnetic Resonance in Medicine* (IF_{2022} =3.3; 80 publications), *Journal of Cardiovascular Magnetic Resonance* (IF_{2022} =6.4; 62 publications), and *European Radiology* (IF_{2022} =5.9; 32 publications). *Table 1* lists the top 10 journals with the most published 4D flow MRI studies, which may be a useful resource and inspiration for new investigators searching for further research.

Analysis of countries and institutes

A total of 1,069 research articles on 4D flow MRI were published in 48 countries/regions. *Figure 3A* shows the cooperative network involving over 10 countries or regions. The top 10 countries/regions are listed in *Table 2*. Betweenness centrality (BC) is a crucial metric that highlights the significance of a node within a network; nodes with higher BC play a more pivotal and influential

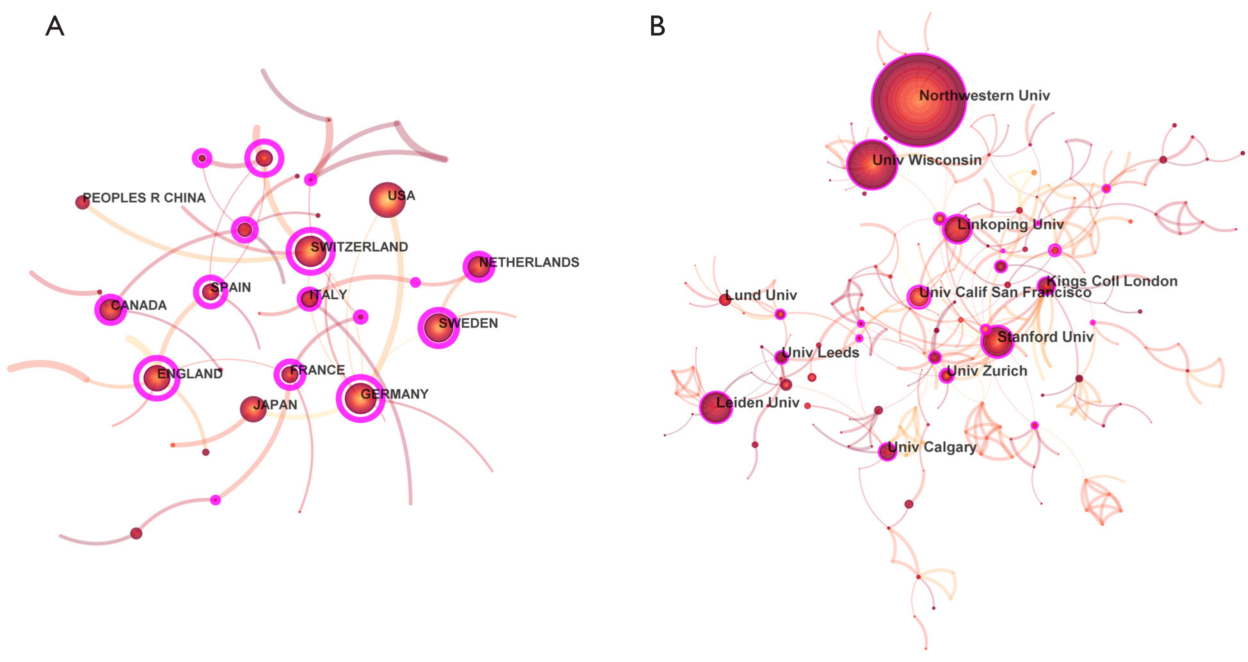

Figure 3 The visualization network map of cooperative between countries and institutions in the 4D flow MRI field from 2003 to 2022. (A) Cooperative network map of countries; (B) cooperative network map of institutions. Each node symbolizes a country or institution, while the connections between nodes represents the international cooperation. Each link represents a node-to-node connection, with the thickness of the links indicating the strength of the cooperative relationship. The presence of purple trimmings in those nodes indicates a stronger betweenness centrality. 4D flow MRI, 4-dimensional flow magnetic resonance imaging.

Table 2 Ranking of top 10 active countries/regions and institutions in search of the 4D flow MRI field from 2003 to 2022

Ranking	Country/region	Frequency	Centrality	Institution	Frequency	Centrality
1	USA	498	0	Northwestern Univ	171	0.17
2	Germany	221	0.9	Univ Wisconsin	92	0.17
3	Netherlands	119	0.31	Stanford Univ	64	0.38
4	England	108	1.01	Leiden Univ	60	0.11
5	Sweden	105	0.45	Linkoping Univ	53	0.34
6	Japan	89	0.08	Univ Calif San Francisco	40	0.44
7	Switzerland	80	0.94	Kings Coll London	36	0.11
8	China	60	0	Univ Calgary	32	0.15
9	Canada	52	0.24	Lund Univ	30	0.05
10	France	48	0.72	Univ Zurich	28	0.33

4D flow MRI, 4-dimensional flow magnetic resonance imaging.

role in the realm of 4D flow MRI. The United States of America (USA) produced the most articles [498], accounting for 46.6% of the total, followed by Germany (221 articles), the Netherlands (119 articles), the United Kingdom (UK) (108 articles), and Sweden (105 articles). Although the USA contributed the most articles, as can be seen in the diagram, its BC value was zero, suggesting that the USA is a world leader in this field but has limited international collaboration.

Nearly 263 institutes participated in 4D flow MRI research (*Figure 3B*). *Table 2* shows that Northwestern University published the highest number of papers [171], followed by Univ Wisconsin (92 articles), Stanford Univ (64 articles), Leiden Univ (60 articles), and Linkoping Univ (53 articles), each of which published 50 or more papers. In terms of BC, Univ Calif San Francisco (0.44), Stanford Univ (0.38), Linkoping Univ (0.34), Northwestern Univ (0.17), and Univ Wisconsin (0.17) collaborated closely with other institutions. In addition, 3 of the top 5 institutions with the most articles were from the USA, suggesting that Northwestern Univ, Univ Wisconsin, and Stanford Univ have conducted more in-depth research on 4D flow MRI.

Analysis of author co-authorship and co-citation

These 1,069 articles were written by 488 authors, with 255 co-authors. *Table 3* lists the top 10 prolific and highly co-cited authors. Markl was the leading author in the 4D Flow MRI field with 152 published studies, followed by Barker (79 articles) and Wieben (59 articles), who all focused on the study of hemodynamic quantification and visualization of vascular structure using 4D flow MRI data. The co-authorship network is shown in *Figure 4A*, where Markl, Johnson, Carr, Wieben, and Westenberg played an important role in the collaboration of researchers because of their greater centrality. A map of the relationships between all cited authors is shown in *Figure 4B*. Markl (588 co-citations) ranked first among the top 10 co-cited authors, followed by Dyverfeldt (400 co-citations), Hope (218 co-citations), and Stalder (208 co-citations).

Analysis of reference co-citation

A total of 19,431 references were obtained, with the top 15 co-cited references with their co-citation counts listed in *Table 4*. The paper by Dyverfeldt *et al.* titled "4D flow cardiovascular magnetic resonance consensus statement", published in the *Journal of Cardiovascular Magnetic Resonance* in 2015, is a key reference in the field of 4D flow MRI with a remarkable 187 co-citations. This paper is important because it provides a thorough analysis of 4D flow MRI in the context of cardiovascular applications, particularly in relation to the heart and large blood vessels such as the aorta and pulmonary arteries (30). The second most co-cited reference, "4D Flow MRI" by Markl *et al.* with 74 co-citations, plays a crucial role in summarizing acquisition strategies, including Cartesian and radial data acquisition, and analysis methods for 4D flow MRI, which has greatly shaped the research and clinical utilization of this imaging technique (13). Both papers serve as foundational resources

Table 3 Ranking of top 10 authors and co-cited authors in search of the 4D flow MRI field from 2003 to 2022

Ranking	Author's publication volume			Co-cited author		
	Author	Frequency	Centrality	Author	Frequency	Centrality
1	Markl, Michael	152	0.57	Markl M	588	0.01
2	Barker, Alex J	79	0.08	Dyverfeldt P	400	0.03
3	Wieben, Oliver	59	0.10	Hope MD	218	0.04
4	Ebbers, Tino	47	0.05	Stalder AF	208	0.00
5	Westenberg, Jos J M	41	0.10	Frydrychowicz A	203	0.00
6	Schnell, Susanne	38	0.08	Barker AJ	202	0.16
7	Johnson, Kevin M	31	0.40	Van Ooij P	199	0.05
8	Carr, James	30	0.14	Bock J	169	0.05
9	Roldan-alzate, Alejandro	27	0.02	Stankovic Z	161	0.00
10	Carlhall, Carl-Johan	27	0.01	Kilner PJ	156	0.00

4D flow MRI, 4-dimensional flow magnetic resonance imaging.

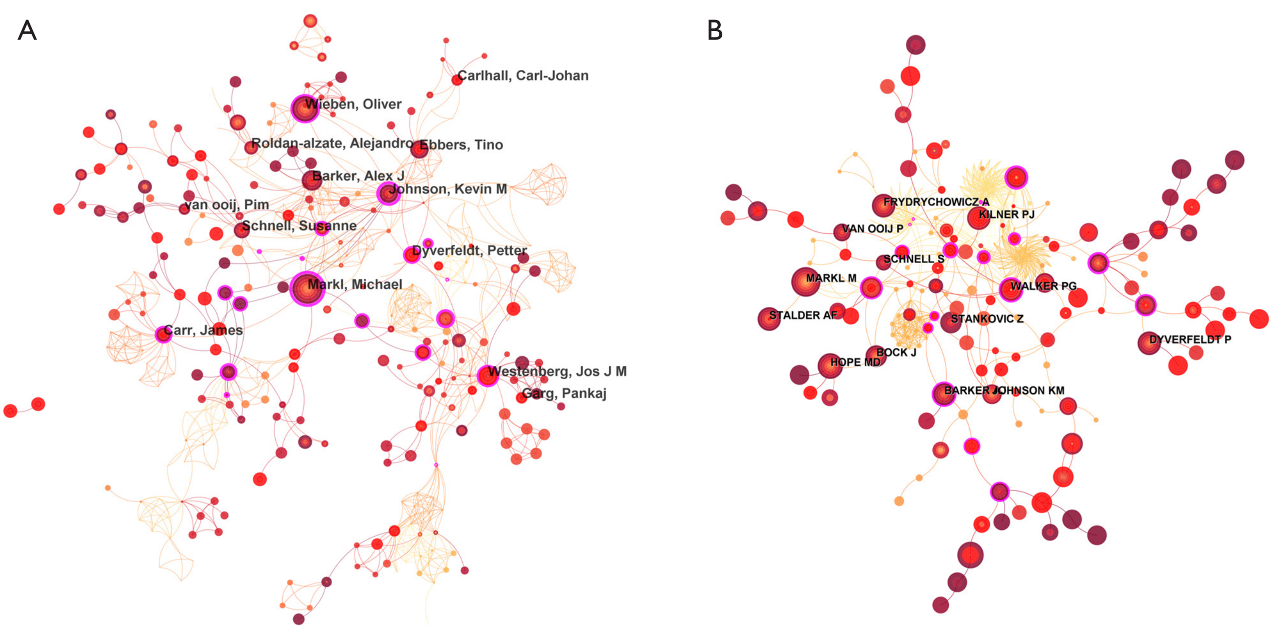

Figure 4 The visualization network map of cooperation and co-citation of authors in 4D flow MRI field from 2003 to 2022. (A) Cooperation network map of authors. The font size of each author's name represents the number of articles written by each author. The thickness of the curved connecting line shows the collaborative intensity between authors. (B) Co-citation network map of authors. The thickness of the curved connecting line shows the co-cited intensity between authors. 4D flow MRI, four-dimensional flow magnetic resonance imaging.

that continue to guide research and innovation in 4D flow MRI, influencing its growth and adoption.

The top 10 clusters, representing the main research hotspots, were generalized and ordered from the largest to smallest number of co-cited references (*Figure 5*). The modularity Q was 0.889 and the weighted average silhouette was 0.951, indicating a rational classification and uniformly distributed clusters internally. The first

Table 4 Top 15 references with the highest number of co-citations in 4D flow MRI from 2003 to 2022

References	Frequency	Centrality	Year
Dyverfeldt P, 2015 (30)	187	0	2015
Markl M, 2012 (13)	74	0	2012
Guzzardi DG, 2015 (31)	66	0.07	2015
Markl M, 2011 (32)	61	0	2011
Rodriguez-Palomares JF, 2018 (33)	57	0.12	2018
Potters WV, 2015 (34)	51	0.07	2015
Barker AJ, 2012 (35)	49	0.04	2012
Garcia J, 2019 (36)	45	0	2019
Mahadevia R, 2014 (37)	43	0	2014
Schnell S, 2017 (38)	42	0	2017
Bissell MM, 2013 (39)	42	0.1	2013
Ma LE, 2019 (40)	41	0	2019
Stankovic Z, 2014 (41)	41	0.01	2014
van Ooij P, 2016 (42)	37	0	2016
Hope MD, 2010 (21)	36	0.02	2010

4D flow MRI, 4-dimensional flow magnetic resonance imaging.

cluster was "#0 Fontan patient", followed by "#1 Valve-related hemodynamics", and "#2 Unruptured cerebral aneurysm". This suggests that hemodynamic analysis is currently focused on the heart and intracranial arteries, with less attention paid to abdominal vessels such as the portal vein. In addition, themes such as "Fontan patient", "aortic dilation", and "neurovascular application" have become important research hotspots, according to the timeline view (*Figure 6*).

Analysis of keywords and burst keywords

The keyword co-occurrence map is shown in *Figure 7A*. The term "Blood flow" was used the most (n=373 times), followed by "4D flow MRI" (n=315), "Quantification" (n=277), "Wall shear stress" (n=258), and "Phase contrast MRI" (n=185; *Table 5*). Among the top 10 most-cited keywords, the nodes representing "Wall shear stress" and "Pattern" are marked with purple circles and have a good BC of 0.13, indicating that these nodes may reflect developing trends in the field of 4D flow MRI.

In the keyword clustering map (*Figure 7B*), 18 clusters were identified. The values of modularity Q and silhouette S were 0.7276 and 0.8742, respectively. The clusters were classified into 2 categories: (I) 4D flow MRI technique ("computational fluid dynamics", "phase contrast", "wall shear stress", "resolution", "geometry", and "kinetic energy"); (II) Clinical applications related to 4D flow MRI, mainly involving quantification of hemodynamics in different parts of the body ["bicuspid aortic valve", "cerebrovascular hemodynamics", "human left ventricle", "thoracic aorta", "portal hypertension", "heart failure" and "abdominal aortic aneurysm" (*Table 6*)].

The burst keyword mapping (*Figure 8*) shows the top 25 keywords with the highest burst strength. The first keyword burst, "visualization", had the highest burst strength (14.79) and lasted from 2003 to 2016. The second keyword burst, "velocity mapping", began in 2003 and lasted until 2013. The above data show that researchers have been focusing on visualizing vasculature and quantifying hemodynamics from 4D flow MRI for many years. The keywords "stiffness" and "tetralogy of Fallot" have attracted considerable attention in the past 4 years.

Discussion

To our knowledge, this is the first bibliometric analysis to be carried out for 4D flow MRI. Since its introduction, the technique has grown in popularity among researchers because it offers comprehensive volumetric assessment of blood flow and allows retrospective analysis at any angle (43,44), features that are not possible with conventional 2D PC-MRI. The number of articles published on 4D flow MRI has witnessed a remarkable surge over the last 2 decades, from one in 2003 to 180 in 2022.

General information

Among many countries, the USA has made the largest contribution. Three of the top 5 most productive institutions (Northwestern Univ, Univ Wisconsin, and Stanford Univ) and 7 of the top 10 prolific authors are from the USA. However, the low BC value suggests that increased collaboration and scholarly communication with other countries or institutions is needed to facilitate growth and advancement in this field. The remaining 4 of the top 5 active countries (Germany, Netherlands, England, and Sweden) are key collaborators with other countries in terms of their high BC values, despite publishing fewer articles than the USA.

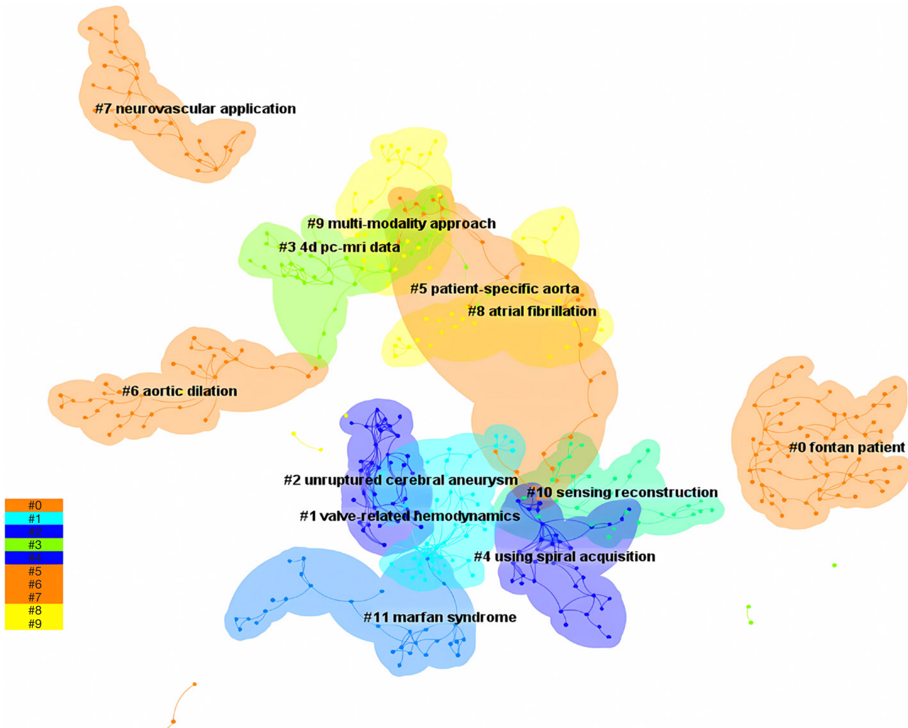

Figure 5 Cluster visualization of the reference co-citation network in 4D flow MRI from 2003 to 2022. The different-colored shapes represent different cluster; the brighter the shape is, the more recently it appears. The number of nodes covered by each shape is proportional to the number of co-cited references of each cluster. 4D flow MRI, 4-dimensional flow magnetic resonance imaging.

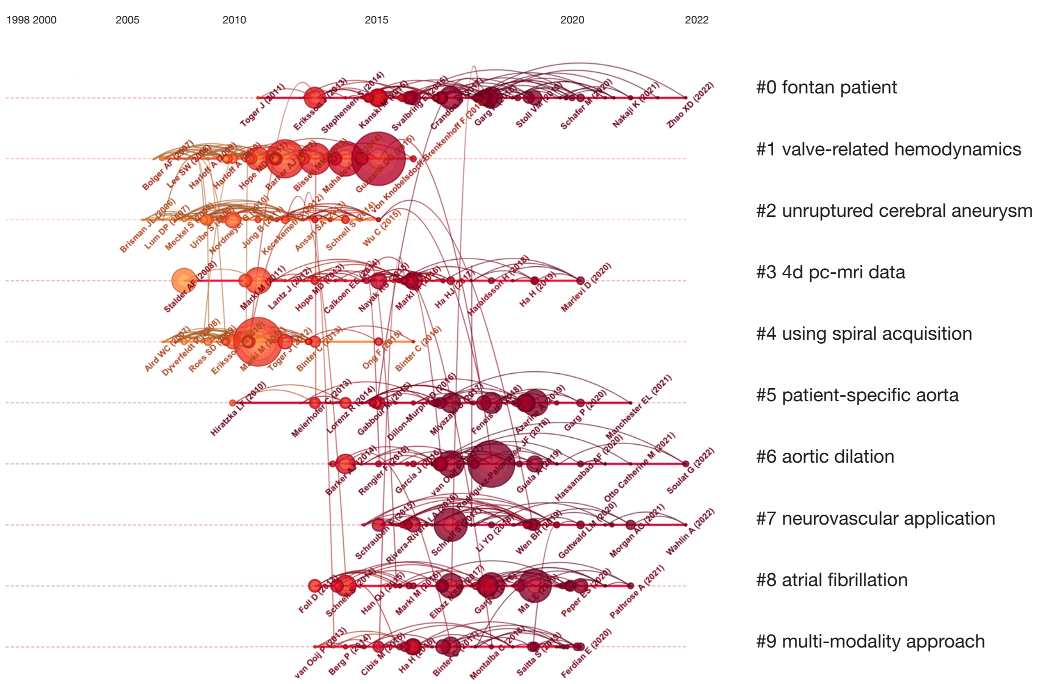

Figure 6 The timeline view of the knowledge map from the RCA of the 4D flow MRI field from 2003 to 2022. RCA, reference co-citation analysis; 4D flow MRI, 4-dimensional flow magnetic resonance imaging; PC MRI, phase-contrast magnetic resonance imaging.

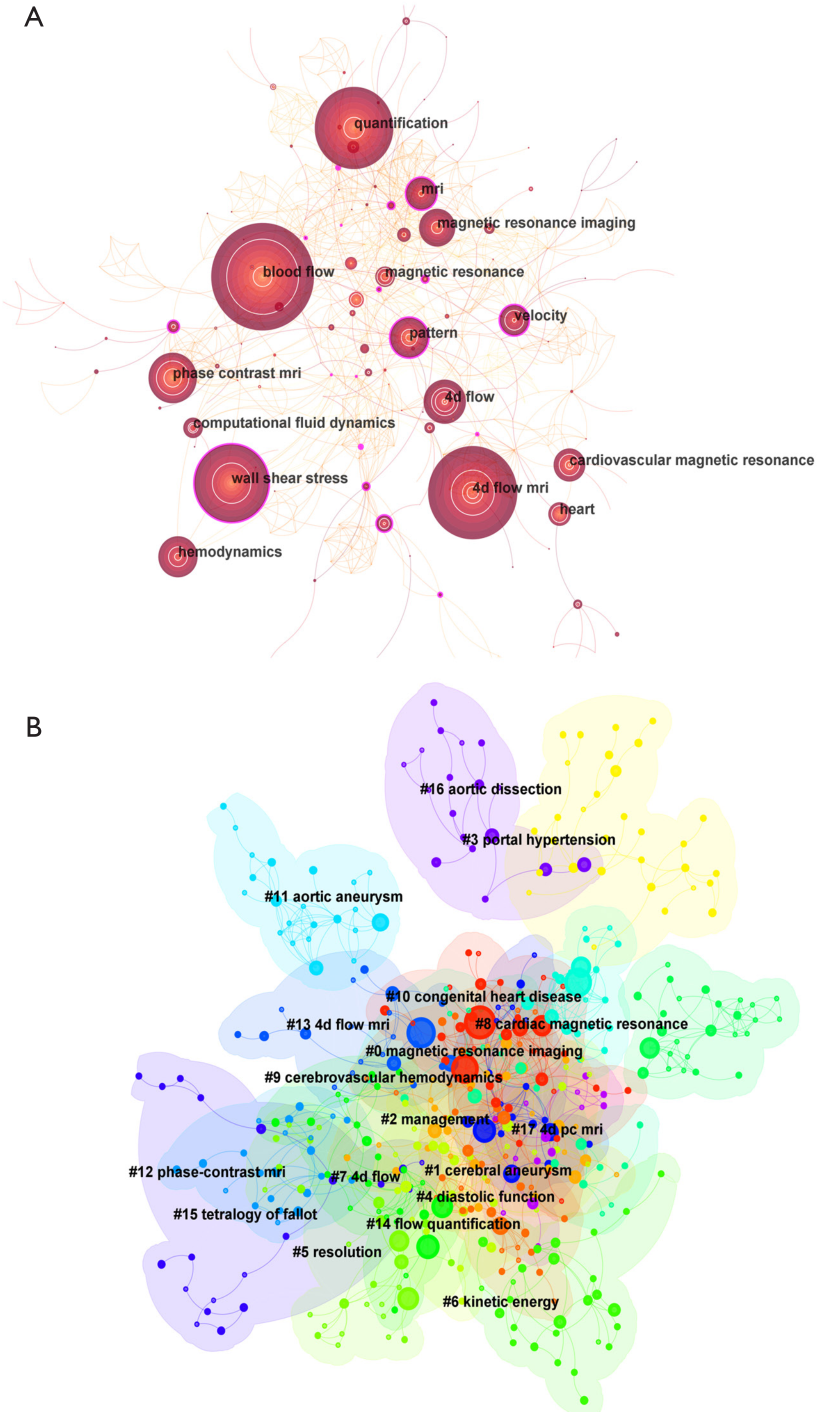

Figure 7 The visualization network map of keywords. (A) Network map of keyword co-occurrence; (B) network map of keyword clusters. 4D flow MRI, 4-dimensional flow magnetic resonance imaging; PC MRI, phase-contrast magnetic resonance imaging.

Table 5 Top 20 high-frequency keywords related to 4D flow MRI from 2003 to 2022

Ranking	Count	Centrality	Keywords	Ranking	Count	Centrality	Keywords
1	373	0.04	Blood flow	11	126	0.09	MRI
2	315	0.01	4D flow MRI	12	122	0.01	Velocity
3	277	0.01	Quantification	13	90	0.00	Heart
4	258	0.13	Wall shear stress	14	87	0.05	Magnetic resonance
5	185	0.06	Phase contrast MRI	15	84	0.06	Computational fluid dynamics
6	175	0.00	4D flow	16	83	0.06	Visualization
7	161	0.01	Hemodynamics	17	75	0.02	Bicuspid aortic value
8	156	0.13	Pattern	18	65	0.11	Disease
9	137	0.02	Magnetic resonance imaging	19	60	0.00	Valve
10	133	0.05	Cardiovascular magnetic resonance	20	57	0.13	Congenital heart disease

4D flow MRI, 4-dimensional flow magnetic resonance imaging.

Table 6 Top 10 clusters of keywords in 4D flow MRI from 2003 to 2022

Cluster ID	Size	Silhouette value	Mean year	Cluster label	Label (LLR)
0	38	0.845	2012	Magnetic resonance imaging	Magnetic resonance imaging; wall shear stress; phase contrast; bicuspid aortic valve; geometry
1	38	0.901	2014	Cerebral aneurysm	Cerebral aneurysm; computational fluid dynamics; intracranial aneurysm; intracranial aneurysms; relative residence time
2	34	0.682	2014	Management	Management; thoracic aorta; fetal; patient-specific heat map; automatic labeling
3	31	0.858	2018	Portal hypertension	Portal hypertension; cirrhosis; aortic disease; relative pressure; portal vein
4	30	0.802	2017	Diastolic function	Diastolic function; heart failure; flow components; 3d cine; human left ventricle
5	29	0.926	2014	Resolution	Resolution; aneurysm; abdominal aortic aneurysm; volunteer; reconstruction
6	27	0.866	2017	Kinetic energy	Kinetic energy; atrial fibrillation; cardiac MRI; stasis; left ventricle
7	27	0.941	2014	4D flow	4D flow; Alzheimer's disease; middle cerebral artery; pulsatility index; 4D flow CMR
8	26	0.913	2012	Cardiac magnetic resonance	Cardiac magnetic resonance; cerebrospinal fluid; syringomyelia; Chiari malformation; Marfan syndrome
9	22	0.873	2017	Cerebrovascular hemodynamics	Cerebrovascular hemodynamics; aortic hemodynamics; patient-specific simulation; computational fluid dynamics; image-based modeling

4D flow MRI, 4-dimensional flow magnetic resonance imaging; LLR, log-likelihood ratio; CMR, cardiovascular magnetic resonance.

Figure 8 Top 25 burst keywords related to 4D flow MRI from 2003 to 2022. The green line indicates time period from 2003–2022, while the red line reflects the durations of each burst keyword. 4D flow MRI, 4-dimensional flow magnetic resonance imaging.

The most influential author was found to be Markl from the USA, who ranked first in both cited papers [588] and published papers [152]. Most of Markl's articles were published in top radiology or cardiovascular journals, such as the *Journal of Cardiovascular Magnetic Resonance*, *Journal of Magnetic Resonance Imaging*, *Circulation: Cardiovascular Imaging and Radiology*. Among Markl's publications, the article "4D flow cardiovascular magnetic resonance consensus statement", issued in the *Journal of Cardiovascular Magnetic Resonance* in 2015, was the most representative. The article is well known for its contribution to the development of consensus recommendations for the entire process of clinical implementation of 4D flow MRI, including patient preparation, data acquisition, handling, and analysis, as well as for providing an overview of potential clinical applications in various vascular regions, which is critical in guiding the direction of 4D flow MRI research. Dyverfeldt (30) from Sweden and Hope (45) from the USA have also made substantial contributions to the field, all focused on investigating the value of 4D flow MRI in visualizing and quantifying blood flow characteristics related to the cardiovascular system (33,35,46).

Research hotspots

Based on the above analysis, the hotspots and frontiers were separated into 2 major categories: technologies and clinical applications. The former contributes to the advancement of medical imaging and the quantification of complex hemodynamic parameters, whereas the latter is essential for diagnosis, ongoing monitoring, and treatment strategy optimization across a range of disease states.

4D flow technique

Early research on 4D flow MRI focused on advancing acquisition techniques and data analysis strategies, with keywords mainly including "wall shear stress", "phase-contrast MRI", "4D flow", "hemodynamics", "pattern", "velocity mapping", "visualization", "resolution", "reconstruction", and "kinetic energy". Non-Cartesian sampling, such as radial samplings [vastly undersampled isotropic projection reconstruction (PC-VIPR)] and spiral sampling, is a promising approach for accelerated PC-MRI acquisition compared to Cartesian sampling (47-49). In addition, approaches such as parallel imaging and compressed sensing are often used in tandem to further reduce acquisition time (50-52). On account of the complexity of 4D flow MRI data (3 spatial dimensions, 3 velocity directions, and time within cardiac cycles), researchers are actively seeking ways to optimize sequences to achieve higher image quality while scanning in a reasonable amount of time. Currently, the main tools used to process 4D flow MRI data include the commercial software cvi42 (https://www.circlecvi.com/), known for its user-friendly interface and automated quantification of blood flow parameters, and the in-house tool (e.g., Python, MATLAB), which allows customization through scripting. Notably, there is still significant variability in indicators obtained from 4D flow MRI across different post-processing software packages (53). Future work should focus on developing more intelligent automated algorithms, improving the quality of open-source tools, and further evaluating the consistency of various software to accelerate the use of post-processing tools in clinical settings.

VENC, crucial for estimating blood flow, emerged as an early research hotspot that persisted for almost a decade, as shown by keyword burst analysis. When it comes to 4D flow MRI, VENC is an essential component that makes it possible to precisely quantify blood flow. Researchers have investigated the appropriate range of VENC in detail in latest years, namely, 30–60 cm/s for the normal portal system and 80–120 cm/s for cerebrovascular applications (6,8). However, due to the disease's complexity and diversity, there is no uniform standard for VENC, and it should be determined based on the clinical setting.

Furthermore, the emergence of advanced hemodynamic indices such as kinetic energy (KE) and wall shear stress (WSS) has intrigued the public interest (46,54). The KE of intracardiac blood flow reflects the myocardial work expended in accelerating the blood, and its value lies in its ability to provide detailed insights into the dynamic motion and energetic properties of fluids, particularly within the cardiovascular system studied by 4D flow MRI (55,56). WSS is a critical parameter in the study of fluid dynamics within blood vessels, representing the frictional force exerted tangentially by blood flow on the arterial endothelial layer. It directly influences the onset and progression of atherosclerosis, regulates endothelial function, and provides crucial information for risk assessment and treatment strategies (37,39,57,58). However, accurate determination of WSS faces numerous challenges, such as complex data processing, resolution and image quality concerns, motion artefacts, signal-to-noise ratio (SNR) issues, limitations in hemodynamics modelling, and translation of findings into clinical practice (59-61). Further advances are needed in data processing techniques, motion correction algorithms, mathematical modelling, improvement of SNR, and interdisciplinary collaboration between researchers and clinicians.

Surprisingly, artificial intelligence (AI) has not yet been identified in our hotspot analysis, despite reports of its use in the reconstruction of 4D flow MRI data (62,63) and the vessel segmentation of morphological images (64). This may be due to the fact that AI research in this area is still in its infancy, with few papers published. It is reasonable to expect that the progression of AI will play a pivotal role in expediting the clinical adoption and advancement of 4D flow MRI.

Clinical application

Clinical research on 4D flow MRI is mainly focused on the quantitative analysis of blood flow in the neurovascular, portal, and cardiovascular systems. 4D flow MRI research hotspots in the brain are "cerebral aneurysm", "intracranial aneurysm", and "middle cerebral artery", categorized as Cluster 1 and 9. When used in the intracranial setting, 4D flow MRI is a useful tool for evaluating aneurysm wall instability and describing blood flow patterns in patients with intracranial aneurysms and determining how they correlate with aneurysm growth and risk of rupture

(65-67). Zhang *et al.* found that WSS and low mean vorticity were significantly associated with the aneurysmal wall enhancement (AWE) pattern (an indicator of the inflammatory process) in a study of 48 patients with 49 unruptured intracranial aneurysms, highlighting the potential of flow dynamics to predict aneurysm formation and rupture (68). Another survey by Futami *et al.* showed that the minimum WSS points were associated with wall instability in unruptured cerebral aneurysms (69). However, a study combining computational fluid dynamics (CFD) and *in vitro* particle velocimetry found that minor variations in the flow field and spatial resolution between modalities strongly influenced normalized WSS distributions (70), suggesting that further multimodality analysis to validate the clinical feasibility of hemodynamic parameters may be a future research trend.

The quantification of hemodynamics and the analysis of flow components in multiple pathophysiological states are the main research hotspots in the cardiac field. Representative keywords are "bicuspid aortic valve", "diastolic function", "heart failure", and "atrial fibrillation". Previous studies have shown that bicuspid aortic valve (BAV) is associated with complex, disturbed blood flow dynamics compared to participants with normal tricuspid aortic valves, even in the absence of aortic valve disease or aortic dilatation (21). Notably, the concept of "patient-specific heat maps" has been extensively applied to the aorta and is gradually extending to BAV patients (33,71), for whom WSS heat maps are generated, showing areas of increased or decreased WSS according to keyword clustering analysis (*Table 6*). A prospective study involving 20 BAV patients showed the consistency between a heat map increase in WSS (>95% of normal values) and histological wall damage (greater medial elastin degradation) (31). The creation of a WSS map is essential because it allows for the identification of abnormalities linked to different pathological conditions by comparing an individual's WSS distribution with a healthy baseline. Furthermore, this approach contributes to the advancement of clinical research by establishing benchmarks for the study of blood flow dynamics, ultimately improving our understanding of the clinical significance of WSS in relation to various illnesses. However, 4D flow MRI-derived flow parameters are still in an exploratory stage, and there is no agreement on their normal values. This is an essential topic that will be addressed in future research.

The research hotspots for the portal system are categorized as Cluster 3, with representative keywords such as "portal hypertension", "cirrhosis", and "portal vein". Over the past decade, 4D flow MRI techniques have shown great promise in visualizing vascular morphology and defining hemodynamic features in the cirrhotic population. A growing body of evidence supports the feasibility and robust internal consistency of 4D flow MRI in measuring hemodynamics in patients with cirrhosis (22,72,73). In addition, the flow parameters determined by 4D flow have been reported to be predictive of the prevalence and severity of liver cirrhosis and portal hypertension (50). In a study recruiting participants who were scheduled for both 4D flow MRI and gastroesophageal endoscopy, Motosugi *et al.* proposed the fractional flow change (FFC) index to quantify shunting from the portal vein and splenic vein to the varices, and a value of less than 0 is associated with endoscopic evaluation of high-risk esophageal varices (74). These findings suggest that parameters-derived 4D flow MRI could be useful in assessing the likelihood of ruptured esophageal varices and risk stratification. More basic research is needed to establish the specific mechanism of altered hemodynamic parameters associated with cirrhosis from a pathophysiological standpoint.

Emerging trends and frontiers

The burst analysis of keywords reveals the emerging trends related to 4D flow MRI. As illustrated in *Figure 8*, the research focus of 4D flow MRI has advanced from flow visualization ("visualization", "velocity mapping", "healthy volunteer", "reproducibility", and "angiography") to preliminary clinical application in various vascular regions of the body ("cerebral aneurysm", "heart", "aorta", "great vessel" and "tetralogy of Fallot"). However, many aspects of 4D flow MRI have yet to be explored.

Firstly, there is still much room in speeding up data acquisition of 4D flow MRI. Although several accelerated imaging approaches, such as non-Cartesian sampling, have been adopted for 4D flow MRI, imaging is still relatively time-consuming, and additional acceleration is expected as sequences evolve. Second, as indicated by the keywords "pattern", "parameter", and "fluid dynamics", the analysis of blood flow patterns and components in diverse clinical contexts remains a popular research area. The concept of creating a WSS heat mapping across individuals and patient cohorts has recently been validated and is mostly limited to the aorta (71). There is still a lack of uniform standards for baseline values in different organs, and multicenter studies across countries are required to establish confidence intervals and the robustness of relevant parameters. Thirdly, "stiffness" has been a focus of attention over the past 4 years. Aortic stiffness assessment utilizing PWV derived from 4D flow MRI can reflect the severity of arterial dysfunction, and its feasibility has been demonstrated through *in vivo* models (75-79). More basic studies are required to understand the underlying mechanisms by which these imaging indicators reflect microscopic vascular alterations. Furthermore, multimodal imaging is predicted to emerge as a new trend in the field's development (80,81). For instance, integrating 4D flow MRI and the liver stiffness assessed by magnetic resonance elastography to elucidate the inherent link between the hemodynamic properties of the portal vein and the liver stiffness in patients with chronic liver disease.

Limitations

There were several limitations to this study. Firstly, due to database variation in the CiteSpace software's bibliometric analysis, only the WoSCC database was examined, while other important databases from PubMed or Google were ignored. As a result, the articles found may not be completely representative of all 4D flow MRI research. Second, CiteSpace was used to perform a general assessment of the present state of 4D flow imaging. Since full texts were not reviewed, some details might have been missed. Third, the retrieved articles were exclusively published in English, resulting in some linguistic bias.

Conclusions

We identified the overall scientific output of 4D flow MRI research from 2003 to 2022. The main directions for 4D flow MRI research are as follows: (I) the research hotspots remain in optimizing the 4D data acquisition scheme and exploring its applicability in different clinical settings, with keywords primarily including "visualization", "resolution", "brain", "tetralogy of Fallot", and "portal hypertension"; (II) multicenter collaborations are required to establish consensus or guidelines for determining the normal range of parameters derived from 4D flow MRI and to verify their robustness; (III) it was also noted that the research focus is gradually shifting from flow quantification to the analysis of microscopic vascular changes, such as "WSS" and "PWV"; (IV) the use of multimodality imaging will be crucial in the clinical evaluation and risk stratification in some certain diseases.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-1227/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Institutional Review Board approval was not required because our study was a bibliometric analysis that used only publicly available data.

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