Global trends in coronary artery disease and artificial intelligence relevant studies: a bibliometric analysis

X.-T. QI[1], H. WANG[1], D.-G. ZHU[2], L. ZHENG[1], X. CHENG[1], R.-J. ZHANG[3], H.-L. DONG[1]

[1]Department of Vascular Surgery, The Second Hospital of Shanxi Medical University, Taiyuan, China
[2]School of Nursing, Shanxi Medical University, Taiyuan, China
[3]Department of Nephrology, The Second Hospital of Shanxi Medical University, Taiyuan, China

X.-T. Qi, H. Wang, and D.-G. Zhu contributed equally to this work and share the first authorship

Abstract. – OBJECTIVE: Coronary artery disease (CAD) is a major global cause of death, greatly affecting life expectancy and quality of life for populations. With the advent of artificial intelligence (AI), there is new hope for accurately managing CAD. While recent studies have shown remarkable progress in AI and CAD research, there is a gap in comprehensive bibliometric analysis in this field. Therefore, this study aims to provide a thorough analysis of trends and hotspots in AI and CAD-related research utilizing bibliometrics.

MATERIALS AND METHODS: Publications on AI and CAD relevant research from 2009 to 2023 were searched through the WoS core database (WoSCC). CiteSpace, VOSviewer and Excel 365 were used to conduct the bibliometric analysis.

RESULTS: The bibliometric analysis included 1,248 publications, indicating a steady increase in AI and CAD-related publications annually. The United States of America (USA), China, and Germany were identified as the most influential countries in this field. Research institutions such as Cedars Sinai Med Ctr, Med Univ South Carolina, Harvard Med Sch and Capital Med Univ were the main contributors to research production. FRONT CARDIOVASC MED is the top-ranked journal, while J AM COLL CARDIOL emerged as the most cited journal. Schoepf, U. Joseph, Slomka, Piotr J., Berman, Daniel S. and Dey, Damini were the most prolific authors, while U. Rajendra Acharya was the most frequently co-cited author. Research related to the AI calculation of coronary flow reserve fraction and coronary artery calcification, based on coronary CT to identify CAD and cardiovascular risk, was a key research topic in this field. The potential link between cardiovascular risk stratification and radiomics is currently at the forefront of the field.

CONCLUSIONS: This study is the first to use a bibliometric approach to visualize and analyze AI and CAD-related research. The findings provide insights into recent research trends and hotspots in the field and can serve as a reference for scholars to identify critical issues in this field.

Key Words:
Coronary artery disease, Artificial intelligence, Bibliometrics, Radiomics, Diagnosis, Stratification.

Abbreviations

CAD: coronary artery disease; AI: artificial intelligence; WoSCC: WoS core database; USA: United States of America; FFR: fractional flow reserve; CT: computed tomography; XGBoost: the gradient boosting machine learning algorithm; ECG: electrocardiography; HRV: heart rate variability; MI: myocardial infarction; PCG: phonocardiogram; PPG: photoplethysmographic; OVG: orthogonal voltage gradient; MPI: myocardial perfusion imaging; PET: positron emission tomography; SPECT: single-photon emission computed tomography; CMR: cardiac magnetic resonance; WHMRA: whole-heart coronary magnetic resonance angiography; RF: random forest; CCN: convolutional neural network; CSAI: compressed sensing artificial intelligence; CCTA: coronary computed tomography angiography; ANN: artificial neural networks; MACE: major adverse cardiac events; TPD: total perfusion defects; CAC: coronary artery calcium; EAT: epicardial adipose tissue; PVAT: perivascular adipose tissue; FAI: fat attenuation index; ROI: regions of interest; LDCT: low-dose CT; CACS: coronary artery calcification score; PCAT: pericoronary adipose tissue; IVUS: intravascular ultrasound; VH: virtual histology.

Introduction

Coronary artery disease (CAD) is one of the most common cardiovascular diseases and has been identified as the leading cause of death in

Corresponding Author: H.-L. Dong, MD; e-mail: honglindong@sxmu.edu.cn

both developing and developed countries. The development of CAD is characterized by atherosclerosis, a chronic progressive inflammation that begins with the accumulation of lipids in the vessel wall and local inflammatory stimulation. This leads to hardening and thickening of the wall and plaque formation, which further results in the development of ischemic heart disease, stroke, and heart failure[1-3]. Current research on CAD encompasses a wide range of aspects, from exploring multiple molecular mechanisms[4] to in-depth mining of genetic metabolomics[5,6], and evaluating efficacy in clinical trials[7]. Furthermore, the emergence and application of artificial intelligence (AI) provide potential solutions for further interpretation and intervention in CAD.

Artificial Intelligence (AI) is a novel computer algorithm that simulates human thought and behavior patterns, allowing automatic processing and analysis of data. Machine learning, a popular subset of AI, is commonly categorized into two main groups: supervised and unsupervised learning. Supervised learning algorithms frequently include support vector machine, regularized regression, and decision tree[8], while unsupervised learning is embodied in deep learning, which produces automated predictions through artificial neural networks[9]. Recent research[10] has widely applied AI in various healthcare settings, including disease diagnosis, medical data management, drug development, health monitoring, and individualized treatment. The CAD research has garnered substantial attention due to the disease's high-profile status, and there has been a marked increase in studies predicting CAD diagnosis[11,12], accurate treatment[13,14], and prognosis[15,16] using machine learning approaches.

Bibliometrics is a valuable research tool utilized to analyze existing literature and identify trends within a specific research area. This method has received considerable attention in the fields of cardiac arrhythmias[17], prostate cancer[18], and more recently, COVID-19[19]. However, bibliometric studies in the fields of AI and CAD remain relatively scarce. Thus, based on the increasing number of studies within the field from 2009 to 2023, we will use bibliometric analysis to provide a detailed and comprehensive overview of the current status and future prospects of AI applied to CAD. We aim to conduct insightful discussions around potential research directions stemming from our analysis.

Materials and Methods

Data Source and Search Strategy

The study utilized data obtained from the WoSCC, which is highly regarded as one of the most authoritative literature databases for bibliometric visual analysis. Data retrieval was completed on 26 June 2023 to prevent any database updates that could pose a bias in the study's results. Three independent authors processed and downloaded the data and saved it in a "download_.txt" format. The search strategy used was as follows: TS=("Coronary Vessel*") OR TS=("Coronary Arteries") OR TS=("Coronary Artery") AND TS=("machine learning") OR TS=("artificial intelligence") OR TS=("Neural Network Model") OR TS=("Deep learning") AND LA=(English). The study literature selection criteria were: (I) Document type: articles; (II) Time span: up to 26 June 2023; (III) Document format: plain text files; (IV) Record content: complete records and cited references. A total of 1,248 documents were searched. The screening process is shown in Figure 1.

Data Analysis and Visualization

Citespace (Chaomei Chen, Drexel University, Philadelphia, PA, USA) and Vosviewer (Leiden University's Centre for Science and Technology Studies, Leiden, Netherlands) are powerful software for visualizing trends in subject areas, and it is widely used in bibliometrics[20,21]. CiteSpace 6.2.R4 and VoSviewer 1.6.19 were used to construct a visual bibliometric analysis based on collaborative network, co-occurrence analysis and co-citation analysis. Citespace is used in the co-occurrence analysis of country, institution and keyword, dual maps of journals, co-cited reference map, the bursts of keywords and co-cited references. Vosviewer is mainly used for co-citation and co-occurrence analysis of country, institution, journal, author and keyword[22]. The data used in this study were obtained from public databases and, therefore, did not require the approval of an Ethics Committee or Institutional Review Boards.

Synonym Replacement

Throughout the process of visualizing and analyzing our data, we identified some synonymous phrases that were expressed differently, such as "computed tomography angiography" and "CT angiography". To accurately describe the hotspots of AI research in CAD without affecting the overall analysis results, we optimized certain keyword

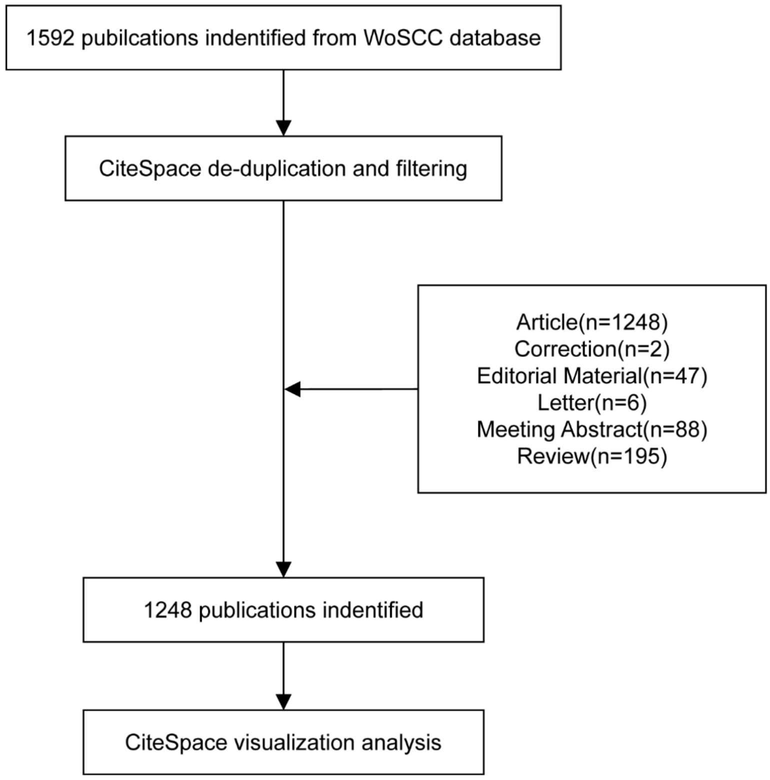

Figure 1. Flowchart of the screening process.

terms, such as converting computed tomography to CT.

Results

Publications Analysis

Figure 2 shows an overall trend of a steady increase in the number of articles published since 2009, which can be divided into two time periods. The first period, from 2009 to 2016, saw a preliminary stage of research on CAD through AI, despite extensive research on CAD during the same period. The second period, from 2017 to 2023, witnessed an exponential increase in the number of publications, reaching a peak of 356 publications in 2022. This remarkable growth showcases the dynamic and transformative capabilities of AI in CAD, indicating that a vast number of high-quality studies and articles can be produced in the future.

Visual Analysis of Countries/Regions and Institutions

As of 26 June 2023, a total of 1,592 papers have been searched through WoS. After importing CiteSpace 6.2.R4, 1,248 documents were extracted after data de-duplication and cleaning from 5,774 research institutions in 349 countries/regions, published in 399 journals.

Countries/Regions

Table I presents the top 10 countries in terms of the number of publications and their citation frequency. The United States (451) has the most publications and the highest number of citations, followed by China (340) and Germany (120). It is critical to underscore that although China ranked second in the number of publications, its citation frequency was considerably lower than the United States or even Germany. Centrality reveals the cooperation relationship between nodes, with higher centrality indicating closer cooperation between nodes. In the diagram, nodes with higher centrality are represented by the purple outer circle. Among the top ten publishing countries, Germany, England, and India exhibit high centrality, highlighting their crucial role in the collaborative network (Figure 3A). Figure 3B demonstrates the cooperation between countries and regions. The size of the nodes signifies the number of publica-

Table I. The Richmond Agitation-Sedation Scale (RASS).

Rank	Country/Region	Counts	Citations	Institution	Counts	Citations
1	Usa	451	9,594	Cedars Sinai Med Ctr	48	1,722
2	China	340	2,617	Med Univ South Carolina	40	942
3	Germany	120	3,022	Harvard Med Sch	36	519
4	South Korea	111	2,277	Capital Med Univ	34	444
5	Netherlands	104	2,831	Yonsei Univ	34	407
6	England	95	1,604	Shanghai Jiao Tong Univ	32	255
7	Italy	91	2,104	Stanford Univ	23	332
8	India	89	1,589	Univ Groningen	25	382
9	Canada	88	2,377	Univ Ulsan	25	529
10	Japan	75	1,613	Chinese Acad Med Sci & Peking Union Med Coll	24	227

tions, while the thickness of the connecting lines reflects the intensity of the cooperation. The United States showed the highest total link strength, demonstrating strong ties between the USA and other countries. This aligns with recent studies showing that globalized cooperation is becoming more prevalent, with developed countries such as the USA, Germany, and England playing a dominant role while developing countries such as China and India are also making significant contributions.

Institutions

Table I also presents the top 10 institutions in terms of publication frequency, along with their corresponding citation frequency. Among the institutional research collaboration networks, Cedars Sinai Med Ctr (48), Med Univ South Carolina (40), Harvard Med Sch (36), Capital Med Univ (34), and Yonsei Univ (34) constitute the research echelon with the highest contribution intensity. Notably, among the top ten institutions, four are located in the United States, three in China, two in Korea and one in the Netherlands, thereby highlighting the authority of the US in the field. In terms of centrality, 8 institutions, including Lundquist Institute (0.32), Harvard University (0.26), Cedars Sinai Medical Center (0.26), and German Heart Centre Munich (0.26), displayed high centrality values (Figure 3C), indicating a significant prominence in CAD and AI research.

According to VoSviewer analysis, Cedars Sinai Med Ctr (1,722) was cited most frequently, followed by Ngee Ann Polytechnic (1,108) and Med Univ South Carolina (842). All institutions were grouped into four closely related clusters (Figure 3D). With Cedars Sinai Med Ctr ranked highest in overall link strength, followed by Med Univ South Carolina and Stanford Univ. This indicates that institutions from

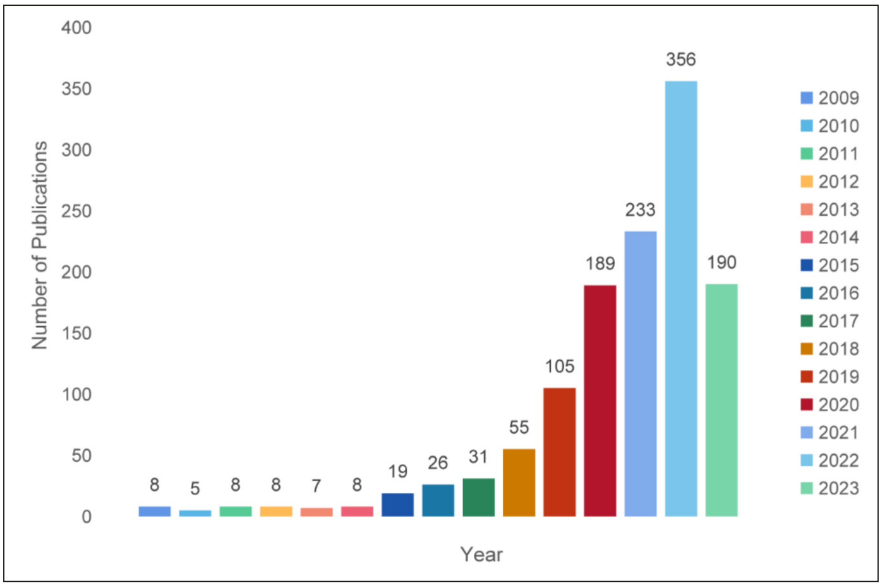

Figure 2. Trends in the number of publications.

Table II. The top 10 journals and co-cited journals related to CAD and AI.

Rank	Journal	Counts	IF (2022)	JCR (2022)	Co-cited journal (2022)	Citations	IF (2022)	JCR (2022)
1	Front Cardiovasc Med	45	3.6	Q2	J Am Coll Cardiol	2,262	24.0	Q1
2	Eur Radiol	39	5.9	Q1	Circulation	1,667	37.8	Q1
3	Comput Biol Med	31	7.7	Q1	Eur Heart J	1,273	39.3	Q1
4	Comput Meth Prog Bio	30	6.1	Q1	Jacc Cardiovasc Imag	980	14.0	Q1
5	Ieee Access	29	3.9	Q2	New Engl J Med	907	158.5	Q1
6	Sci. Rep	28	4.6	Q2	Ieee T Med Imaging	737	10.6	Q1
7	J Nucl Cardiol	24	2.4	Q1	Radiology	686	19.7	Q1
8	Appl Sci-Basel	22	2.7	Q2	J Cardiovasc Comput	662	5.4	Q1
9	Plos One	22	3.7	Q2	Comput Meth Prog Bio	588	6.1	Q1
10	Ieee T Med Imaging	20	10.6	Q1	Am J Cardiol	517	2.8	Q3

the US are more focused on enhancing communication and collaboration with each other.

Visual Analysis of Journals and Co-cited Journals

Publications on CAD and AI research are available in 399 journals. Table II highlights the top ten journals in terms of publication frequency and the top ten co-cited journals. Front Cardiovasc Med (45, IF=3.6) published the highest number of articles, followed by Eur Radiol (39, IF=5.9) and Comput Biol Med (31, IF=7.7). Among the top ten journals, five are in JCR Q1. We performed a network mapping of journals based on the number of journal publications. Figure 4A displays the citation links between Front Cardiovasc Med And Eur Radiol, Comput Biol Med, And Diagnostics.

J Am Coll Cardiol (2,262, IF=24.0) topped the list of co-cited journals, with Circulation (1,667, IF=37.8) and Eur Heart J (1,273, IF=39.3) following closely. Among the top ten co-cited journals, nine are in JCR Q1. We constructed a co-citation network for the journals that met the criteria with a co-citation threshold of 70. Figure 4B displays a positive co-citation relationship between J Am Coll Cardiol and several other influential journals, including Circulation, Jacc Cardiovasc Imag, Eur Heart J, and New Engl J Med.

The dual-map overlay of journals reveals the citation relationship between citing and co-cited journals. The citing journals are marked on the left, while the cited journals are marked on the right, with the three main paths indicating the citation relationships (in green). As shown in Figure 4C, published articles related to CAD and AI are concentrated in the journals Medicine/Medical/Clinical, while most of the cited articles are published in the journals Heath/Nursing/Medicine, Molecular/Biology/Genetics and Systems/Computing/Computer.

Visual Analysis of Authors and Co-cited Authors

A total of 7,871 authors have participated in CAD and AI research. Table III displays the top ten authors in terms of publications and co-citations. Schoepf, U. Joseph (34) has the highest number of publications, followed by Slomka, Piotr J. (34), Berman, Daniel S (33) and Dey, Damini (33). Among these authors, four have a total citation count exceeding 1,000, with Slomka, Piotr J. leading at 1,400. The other three with more than 1,000 citations are Berman, Daniel S.

Table III. The top 10 authors and co-cited authors of CAD and AI research.

Rank	Authors	Counts	Citations	Total Link Strength	Co-cited author	Citations	Total Link Strength
1	Schoepf, U. Joseph	34	865	24,446	Acharya, U.Rajendra	305	2,685
2	Slomka, Piotr J.	34	1,400	35,258	Alizadehsani, Roohallah	215	1,862
3	Berman, Daniel S.	33	1,363	34,167	Budoff, Matthew J.	131	1,157
4	Dey, Damini	33	1,300	33,790	Ronneberger, Olaf	130	601
5	Acharya, U.Rajendra	22	1,108	2,413	Wolterink, Jelmer M.	130	1,201
6	Isgum, Ivana	21	877	9,912	Tesche,Christian	129	1,412
7	Kim, Young-hak	20	523	9,680	Coenen, Adriaan	115	1,486
8	Tesche, Christian	20	535	18,210	Breiman, Leo	99	307
9	Leiner, Tim	17	686	7,483	Dey, Damini	94	1,083

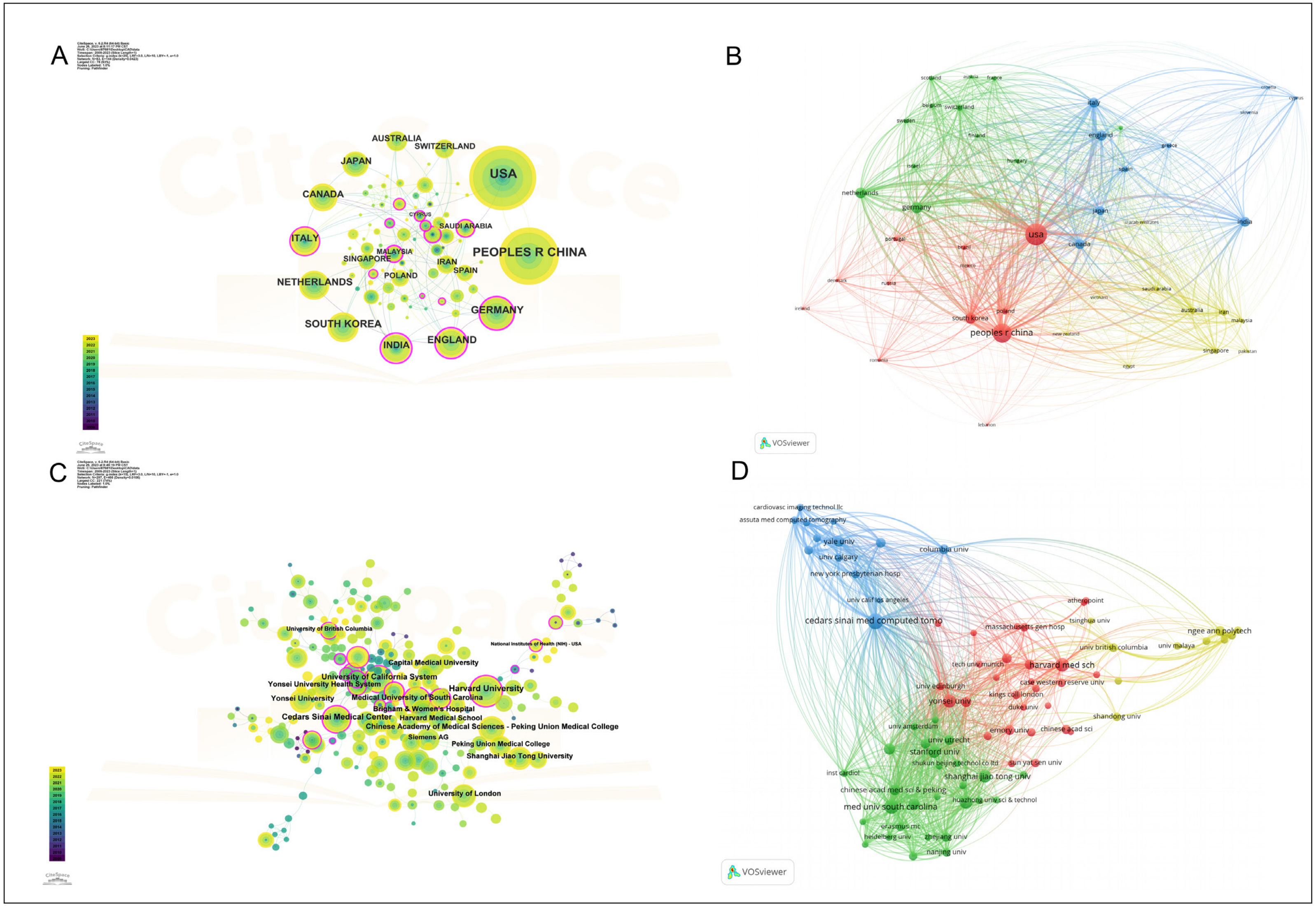

Figure 3. A network of national/regional and institutional cooperation in the field of CAD and AI (**A**) The collaboration network of countries/regions (Citesapce). **B**, Mapping of cooperation networks in countries/regions (VosViewer). **C**, The collaboration network of institutions (Citesapce). **D**, Collaborative network mapping of institutions (VosViewer).

(1,363), Dey, Damini (1,300) and Acharya, U. Rajendra (1,108), respectively. Co-citation data helps to identify influential researchers that attract interest among scholars. In this study, 7 scholars were co-cited more than 100 times, with Acharya, U. Rajendra (305), Alizadehsani, Roohallah (215), and Budoff, Matthew J. (131) being the top three. It is noteworthy that, although ranked only 5th in terms of the number of publications (22), Acharya, U. Rajendra still ranks first in terms of citations, highlighting the significance of this author in the CAD and AI field.

VoSviewer analysis revealed the collaborative networks among authors (Figure 5A). Slomka, Piotr J., Dey, Damini, Schoepf, U. Joseph, and Berman, Daniel S. were at the center of these networks. The co-cited author network (Figure 5B) indicated some active collaboration between authors, such as Acharya, U. Rajendra and Saba, Luca, Alizadehsani, Roohallah. However, we observed limited authorship overlap in neighboring clusters. Therefore, there may be a need for enhanced communication and collaboration in the future.

Visual Analysis of Articles and Co-cited References

We conducted a query for highly cited articles in CAD and AI research. The paper titled "Prediction of cardiovascular risk factors from retinal fundus photographs *via* deep learning"[23] has the highest total number of citations, but its link strength is not as great as desired, indicating poor relevance to research in CAD and AI.

A co-citation relationship in the literature refers to when two articles are cited by a third article at the same time. Table IV illustrates the top ten co-cited literature citations. The most cited study is a conference paper published in MACCAI 2015 by Olaf Ronneberger et al[24]. They trained an efficient medical image segmentation algorithm U-Net, which has been widely used in the identification of diseased coronary arteries. In addition, the study published in BIOMETRICS titled "Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach"[25] showed the highest centrality (0.85) and provided methodological support for the comparison of diagnostic performance of multiple models.

We used Citespace to construct a map of the co-cited literature and its clusters (Figure 6A, B). The top 7 clusters, according to the LLR algorithm, are quantitative coronary angiography (Cluster #0), fractional flow reserve (Cluster #1), feature selection (Cluster #2), ivus (Cluster #3), x-ray computed (Cluster #4), invasive coronary angiography (Cluster #5), deep learning (Cluster #6). Additionally, to reveal the association with time, we performed a timeline view of the co-cited literature after clustering (Figure 6C). Cluster

Table IV. The top 10 co-cited references of CAD and AI research.

Rank	Year	First Author	Title	Local citations
1	2015	Olaf Ronneberger	U-Net: Convolutional Networks for Biomedical Image Segmentation	110
2	1990	A S Agatston	Quantification of coronary artery calcium using ultrafast computed tomography	93
3	1988	E R DeLong	Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach	84
4	2020	Juhani Knuuti	2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes	77
5	2017	Manish Motwani	Machine learning for prediction of all-cause mortality in patients with suspected coronary artery disease: a 5-year multicentre prospective registry analysis	77
6	2018	Adriaan Coenen	Diagnostic Accuracy of a Machine-Learning Approach to Coronary Computed Tomographic Angiography-Based Fractional Flow Reserve: Result From the MACHINE Consortium	64
7	2014	Bjarne L Nørgaard	Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps)	64
8	2009	Pim A L Tonino	Fractional flow reserve versus angiography for guiding percutaneous coronary intervention	57
9	2016	Lucian Itu	A machine-learning approach for computation of fractional flow reserve from coronary computed tomography	56
10	2014	Jonathon Leipsic	SCCT guidelines for the interpretation and reporting of coronary CT angiography: a report of the Society of Cardiovascular Computed Tomography Guidelines Committee	55

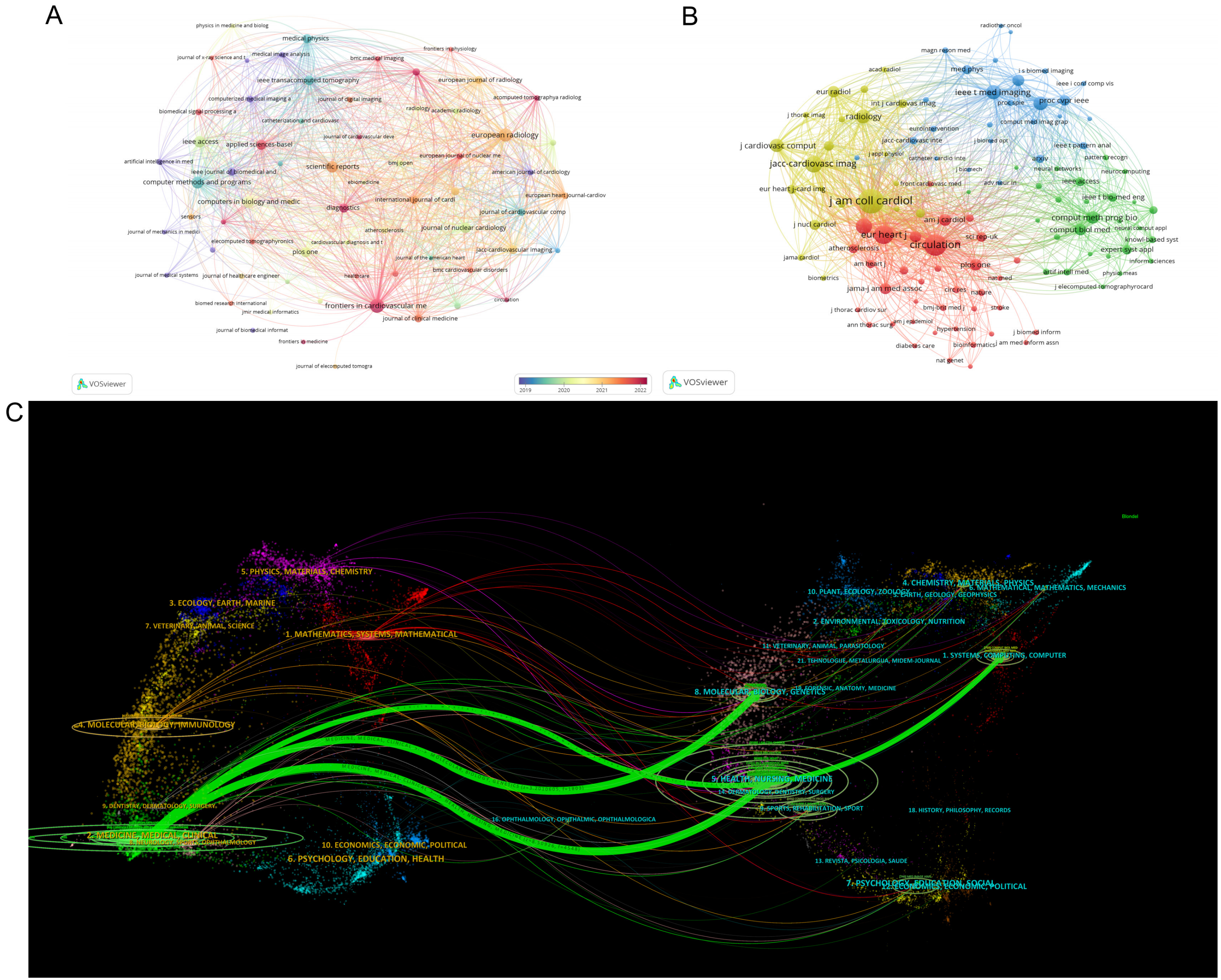

Figure 4. Visual analysis of journals. **A**, The network of article sources journals. **B**, The network of co-cited journals. **C**, The dual-map overlay of journals.

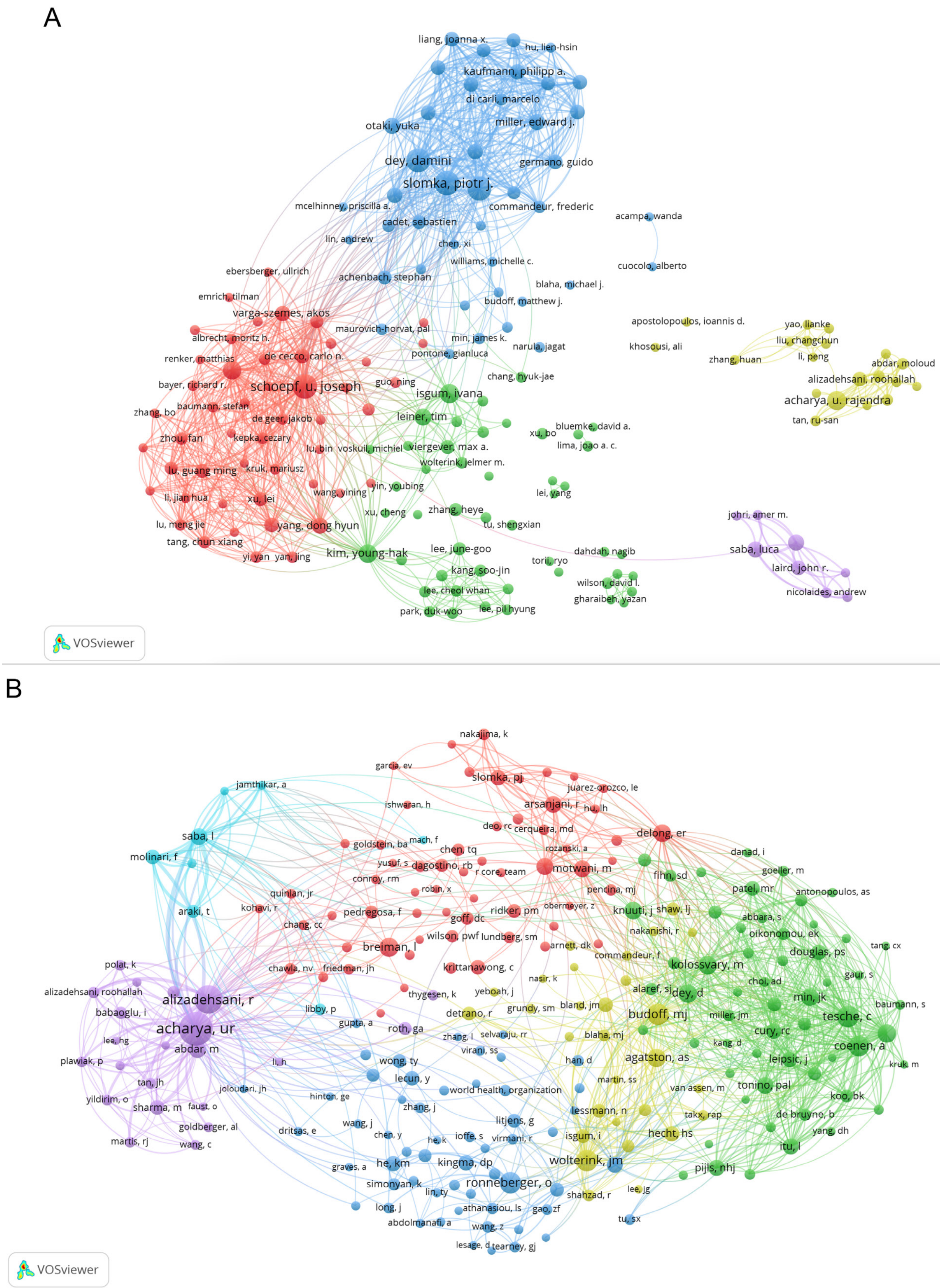

Figure 5. Visual analysis of authors. **A**, The collaboration network of scholars. **B**, The network of co-cited authors.

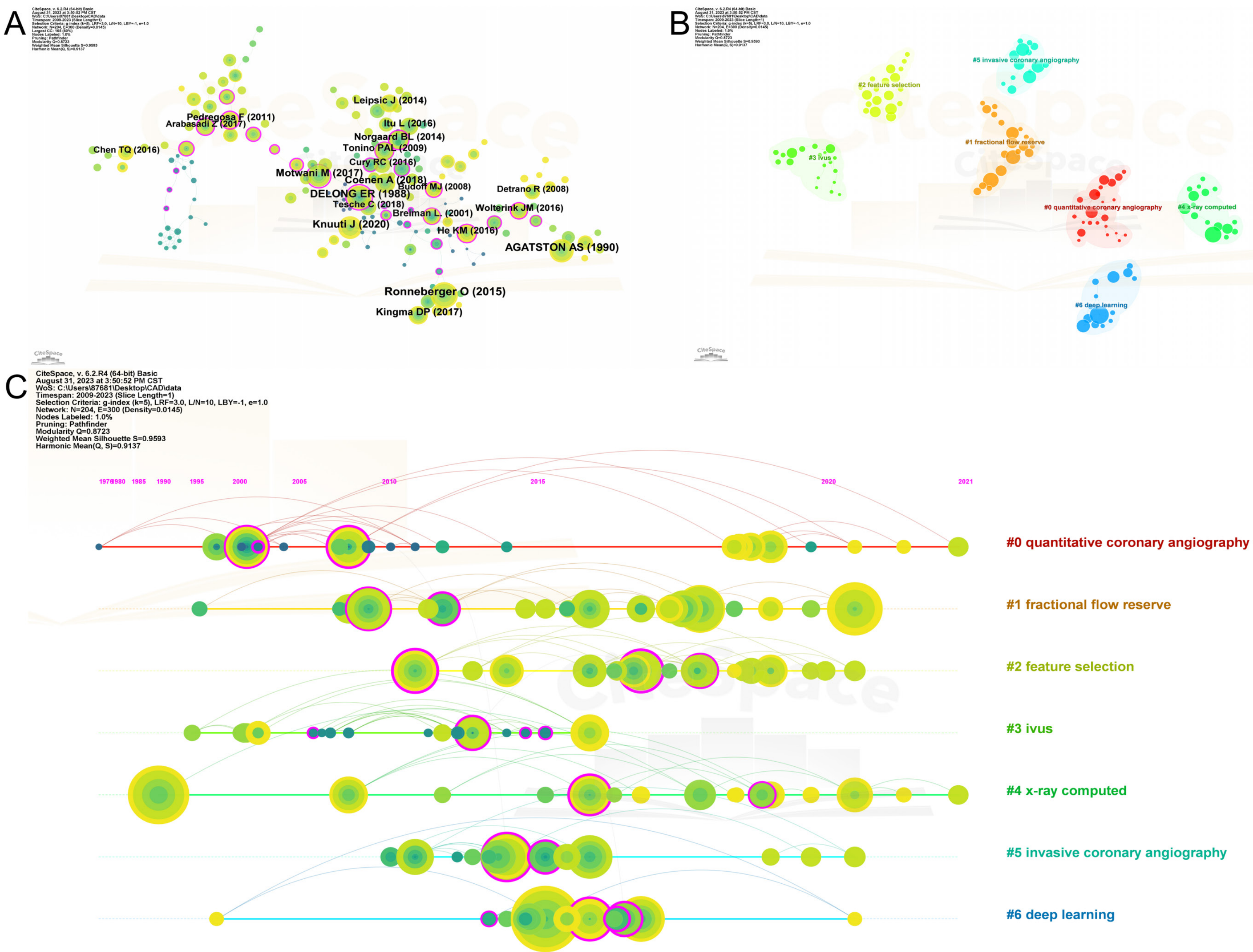

Figure 6. Visual analysis of co-cited references. **A-B**, Cluster analysis of co-cited references. **C**, The clustering timeline map of co-cited references.

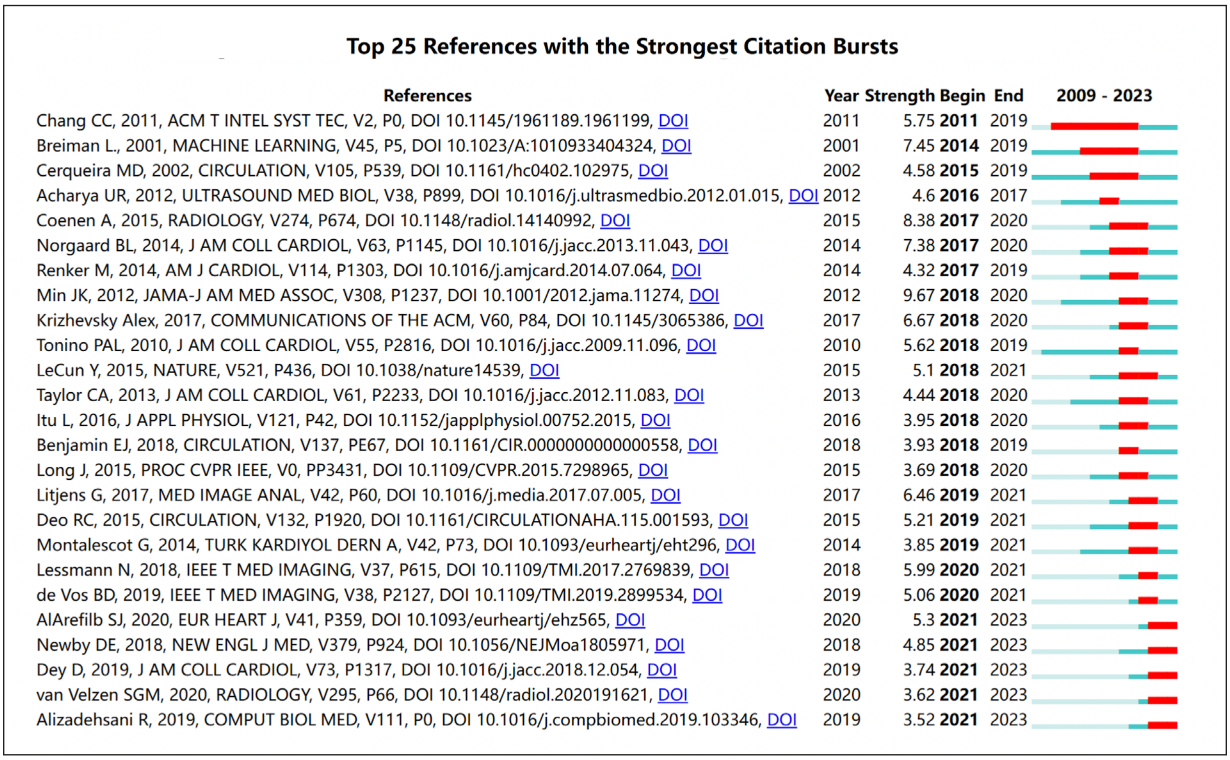

Figure 7. Citation burst mapping of references.

#0 is currently the most studied class, and Cluster #0 and Cluster #4 are currently the most popular classes. Future research is probably more focused on quantitative coronary angiography and computed X-rays.

Figure 7 depicts the top 25 references with the strongest citation bursts. Citation burst refers to a reference that has been frequently cited over a period. James K Min's article "Diagnostic accuracy of fractional flow reserve from anatomic CT angiography", published in 2012, demonstrated the highest explosive intensity and highlighted the excellent performance of noninvasive fractional flow reserve (FFR) computed from CT plus CT in the diagnosis of coronary artery lesions[26]. The longest bursts were published by Chang and Lin[27], running from 2011 to 2019, and somewhat normalizing the application of support vector machine algorithm in cardiovascular diseases. The article published by Al'Aref et al[28] still displays burst up to now. They scored the coronary artery calcification score (CACS) of coronary computed tomography angiography (CCTA) following the Agatston method and showed high accuracy in predicting obstructive CAD using the gradient boosting machine learning algorithm (XGBoost) combined with clinical features.

Visual Analysis of Keywords

Analyzing the co-occurrence of keywords can assist researchers in understanding the current state of AI in the CAD field. Table V presents the top 20 keywords in terms of frequency, with "coronary artery disease" being the most commonly occurring one (403), followed by "machine learning" (331), "deep learning" (216) and "artificial intelligence" (159). The keywords were categorized into four groups using VoSviewer's co-occurrence analysis prompts (Figure 8A). The green cluster represents research centered around developing CAD diagnostic models. The red clusters focus on CAD prognostic models characterized by CCTA and coronary artery calcium. The yellow cluster investigates radiomics based on deep learning and image segmentation. Lastly, the blue cluster explores the application of different machine-learning classification algorithms in CAD.

Figures 8B and 8C illustrate the timeline view of keyword clustering constructed by Citespace. Cluster #0 (ct angiography) is the largest currently researched topic, with the earliest studies artery disease and angiographic severity dating back to 2010. Ischemic heart disease is currently at the forefront of this area's research. The latest clusters being studied belong to two categories: #6

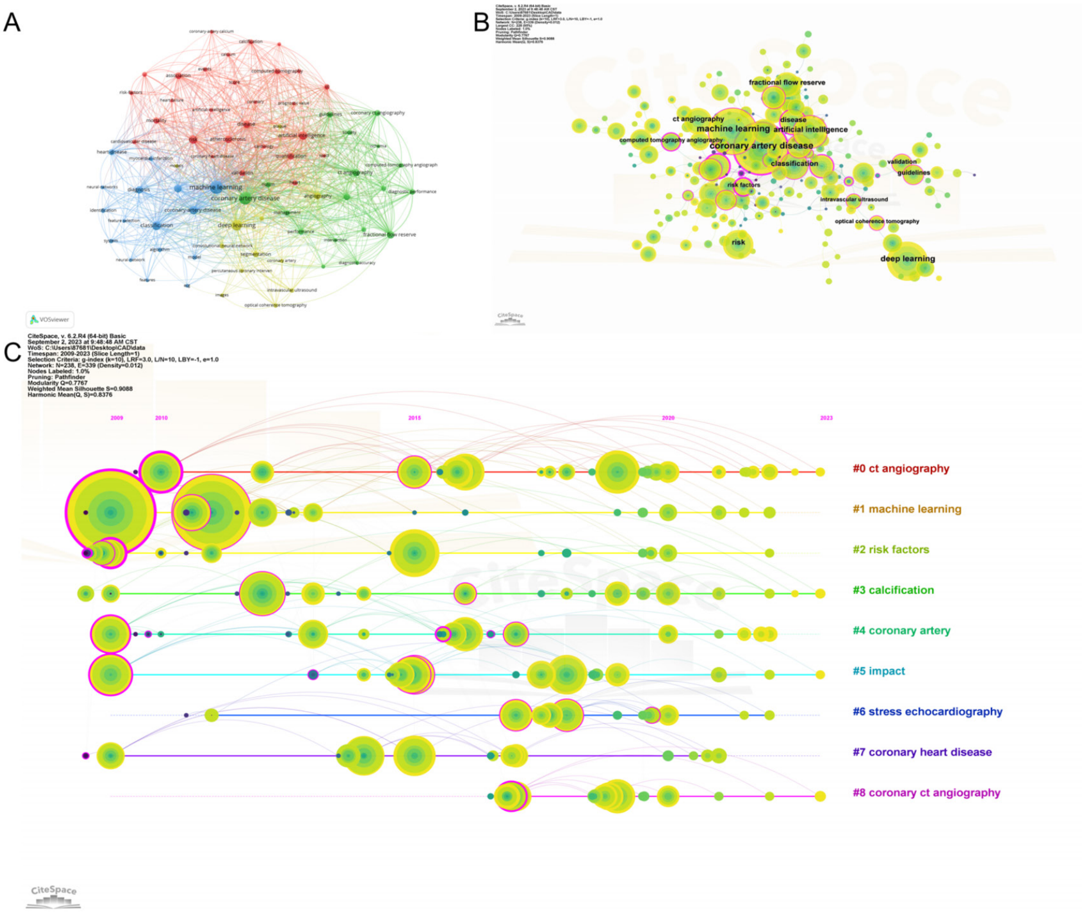

Figure 8. Visual analysis of keywords. **A-B**, Cluster analysis of keywords. **C**, The clustering timeline map of keywords.

Table V. The top 20 keywords of CAD and AI research.

Rank	Keywords	Centrality	Counts	Year
1	coronary artery disease	0.46	403	2009
2	machine learning	0.13	331	2011
3	deep learning	0.06	216	2018
4	artificial intelligence	0.15	159	2009
5	risk	0	126	2015
6	classification	0.14	118	2012
7	disease	0.22	104	2009
8	fractional flow reserve	0.05	103	2015
9	computed tomography angiography	0	102	2019
10	diagnosis	0.09	89	2014
11	artery disease	0.52	88	2010
12	prediction	0.03	88	2018
13	association	0.15	86	2015
14	angiography	0.38	79	2009
15	cardiovascular disease	0.09	76	2016
16	quantification	0.11	76	2015
17	heart disease	0.13	71	2011
18	computed tomography	0	66	2016
19	coronary computed tomography angiography	0.08	64	2019
20	guidelines	0.13	62	2018

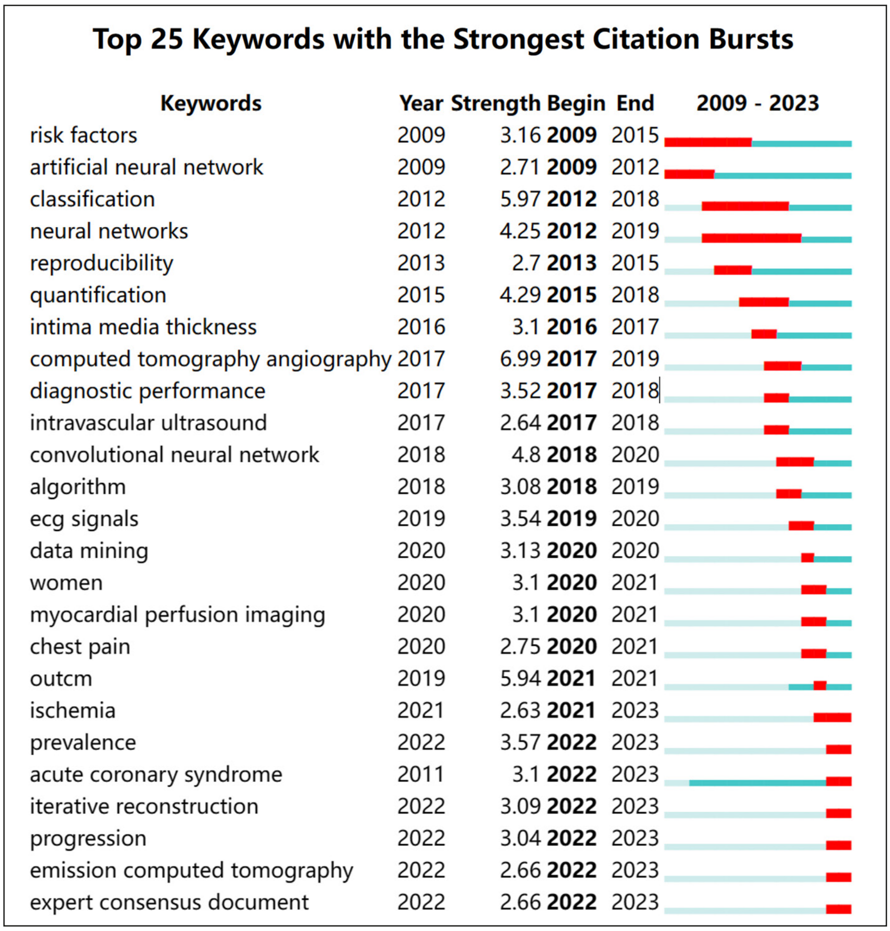

Figure 9. Citation burst mapping of keywords.

(stress echocardiography), with research focusing on myocardial perfusion SPECT and deep neural network, and #8 (coronary CT angiography), with research centered around vessel segmentation.

We conducted a burst test on the keywords, and Figure 9 lists the top 25 burst-intensity keywords. The highest burst was experienced by "computed tomography angiography". The longest-lasting bursts were observed in "neural networks", spanning up to eight years. "acute coronary syndrome", "iterative reconstruction" and "emission computed tomography" are currently undergoing bursts, with a greater focus on radiomics.

Discussion

Global Research Distribution

The study retrieved 1,248 articles on AI in CAD from the WoSCC database from 1 January 2009 to 26 June 2023, from 5,774 research institutions in 349 countries/regions, published in 399 journals, while a total of 7,871 authors participated in the study. Our analysis reveals that the number of relevant articles published has increased significantly year by year over the last 15 years and that the interest of researchers in the field continues to rise. The explosive growth of publications from 2017 to date is closely linked to the rapid development of AI, and the continuous optimization of several algorithmic models in the field of artificial intelligence has facilitated further CAD research under the AI label.

Analysis of countries/regions enables visualization of global collaboration trends in a particular area. As we can observe from the above results, the authoritative position of the United States is evident, with China and Germany also occupying important positions. The higher centrality of Germany, England, and India has recently shown a central bridging role in this field. Although the USA and China have the highest number of publications, their centrality does not match the volume of publications. As shown in Table I, four of the top ten institutions in terms of number of publications are from the USA, with Lundquist Institute being more prominently central. Overall, the USA is the absolute dominant player in AI and CAD research and collaborates extensively with countries/regions such as China, South Korea and Italy.

The analysis of journals provides an accurate picture of the core key journals in a particular field. As shown in Table II, the top ten journals and co-cited journals are all high-quality journals, with FRONT CARDIOVASC MED having the highest number of publications, which has contributed significantly to the development of the field. J AM COLL CARDIOL is not only the most co-cited but also leads in the number of articles published, and it has profoundly influenced the course of the field.

Current Status of AI Research in CAD

CAD, as a traditional risk factor for death in the population, has been favored by many scholars, and AI-oriented CAD research has shown great vigor in the modern era, along with the new iteration of AI technology. Firstly, in the era of precision medicine, the high incidence of CAD in the population provides a prerequisite for the application of artificial intelligence. For patients under different physiological conditions, multi-dimensional analysis based on big data is carried out to explore new ideas for CAD personalized treatment and drug development. Secondly, the diagnosis and treatment of CAD are inseparable from cardiovascular multimodal images. The results of electrocardiogram, echocardiography, and CTTA are closely related to images. The iterative reconstruction and image segmentation brought by artificial intelligence undoubtedly simplify the workload of cardiologists. Moreover, natural language processing (NLP) in the analysis of electronic health records and phone recordings also highlighted the characteristics associated with CAD[29]. Finally, due to different regional populations, large-scale epidemiological data can determine the key factors influencing CAD and guide CAD prevention in different areas.

The continuous improvement of AI technology and the innovation of CAD researchers have led to the diversification of research directions, and the current frontiers are more focused on three major directions: the construction and validation of models for early diagnosis of coronary artery disease, the study of prognostic models of coronary artery disease characterized by plaque, and the study of imaging histological features in CAD risk stratification. The second is the study of prognostic models for coronary artery disease characterized by plaque, and the third is the study of imaging radiomics features in CAD risk stratification.

Learning large amounts of data to automatically diagnose diseases is a major direction for AI applications in medicine. Diagnosis of CAD by coronary angiography is necessary, but due to its invasiveness, a non-invasive, economical and reliable way to identify CAD early is more respected by researchers. On the other hand, there is still some variation between diagnostic models due to differences in the content and sample size of the analyzed data sets. Currently, multiple types of dimensional data are being used for CAD diagnosis, with a more prominent trend toward non-invasive imaging as a key target, in addition to traditional demographic characteristics, social life factors, and clinical laboratory indicators. Electrocardiography (ECG) is widely promoted as a screening test for cardiac function in admitted patients and can accurately and rapidly predict obstructive vessels by learning 12-lead ECG alone[30-32], in addition, ECG-based heart rate variability (HRV) has been shown[33] to predict CAD and myocardial infarction (MI). Previous studies in the literature have shown the presence of abnormal heart sounds in patients with coronary stenosis, and Pathak et al[34] explored the use of phonocardiogram (PCG) in the diagnosis of CAD disease through multinuclear learning. In particular, the dual dimensional analysis of ECG and PCG showed superior performance for the detection of CAD[35]. Patients with CAD are often accompanied by hemodynamic alterations, and the elastic network model construction of photoplethysmographic (PPG) with a three-dimensional orthogonal voltage gradient (OVG) can accurately identify CAD[36]. Stress echocardiography shows localized regions of abnormal ventricular wall motion in patients with CAD, and artificial intelligence helps clinicians diagnose CAD effectively and quickly by identifying abnormal regions before and after motion[37]. The deep learning model of coronary artery calcification identified by echocardiography also realizes the risk stratification of coronary artery disease[38]. Nuclear imaging (SPECT, PET/CT) myocardial perfusion imaging (MPI) has become the gold standard for non-invasive detection of CAD, single-photon emission computed tomography (SPECT) MPI is dominant in the diagnosis of

CAD, and deep learning-based MPI models can classify CAD patients in a short time[39]. The latest research[40] proposes that the polar map-free 3D deep learning algorithm eliminates the previous steps of axis and manual correction, simplifies the process of data processing, and demonstrates an efficient ability to predict CAD. In addition, the inclusion of low-risk populations has increased the sensitivity of MPI models to more accurately guide clinical CAD patient stratification[41]. Positron emission tomography/computed tomography (PET/CT) MPI has shown[42] advantages for the detection of myocardial ischemia due to its higher image resolution. The CT attenuation correction scan during PET reduces the radiation dose to the patient, and the automatic coronary artery calcification (CAC) score trained by the CNN model reduces the time required for visual evaluation, which is more suitable for clinical application[43]. Cardiac magnetic resonance (CMR) allows accurate assessment of cardiac structure and function, myocardial perfusion and ischemic infarct areas, and analysis of CMR 2D images based on random forest (RF)-convolutional neural network (CNN)-F accurately assesses CAD[44]. For patients with renal failure suspected of MI, a deep learning framework based on non-contrast-enhanced cardiac cine MRI also outlines the location and area of MI satisfactorily[45]. Whole-heart coronary magnetic resonance angiography (WHCMRA) often cannot be applied on a large scale because of image quality, and the CNN model proposed by Prof. Kobayashi et al[46] improves this situation, and a compressed sensing artificial intelligence (CSAI) framework was introduced to bring a better future for MRA diagnostic CAD[47]. Notably, the deep CNN model based on retrospective analysis of chest radiographs of patients who suspected angina pectoris shows a good prior probability of CAD prediction, but it still needs further external validation[48]. In addition to the imaging examinations mentioned above, CCTA[49], a hot topic of interest in the last decade, has seen vigorous progress in cross-integration with artificial intelligence. Deep CNN, as the most prominent focus, has played a crucial role in coronary image segmentation and CAD-RADS classification[50-55]. A novel CCTA image segmentation algorithm, CAS-Net, brings new ideas for the determination of coronary artery lesions[56]. Moreover, Yoneyama et al[57] used a hybrid image of SPECT MPI and CCTA CAD models constructed based on artificial neural networks (ANN) also showed excellent performance. The FFR reflects the hemodynamic status of the coronary artery branches to the supplied myocardial region, and the CT-FFR obtained based on CCTA calculations achieved a judgment power consistent with CCTA for CAD classification[58,59], and the combined application of CT-FFR and CCTA further enhanced the performance of the CCTA-based models alone[60,61]. Surprisingly, in patients with moderate coronary stenosis (50-90%), the combined application of CT-FFR and CCTA even outperformed the diagnostic potential of invasive coronary angiography (ICA)[62].

Due to the unique nature of CAD, not only does it require early diagnosis, long-term detection, and timely treatment, but it also requires accurate prediction of adverse cardiovascular events to better guide clinical intervention. Previous studies[63] have shown that several blood biochemical parameters can predict the occurrence of major adverse cardiac events (MACE), but the rapid development of clinical imaging and the continuous improvement of imaging technology has greatly contributed to the interest of investigators in image analysis, so it has become a recent research hotspot to determine the occurrence of MACE in CAD patients by mining the parameters of medical imaging, such as plaque characteristics, hemodynamics, etc. Two-dimensional echocardiography can provide many variables that reflect cardiac structure and ventricular function.

Composite Variables

The derivation of the transthoracic echocardiographic heart failure index (HFI) constructed by left ventricular mass index (LVMI), left atrial volume index (LAVI), mitral regurgitation (MR), and left ventricular outflow tract velocity-time integral (VTILVOT) and diastolic dysfunction (DD) performs well in the prediction of heart failure in CAD patients[64]. The advantages of SPECT MPI in CAD prognosis have been extensively studied[65], and the prediction of per-vessel revascularization within 90 days in patients with suspected CAD by machine learning of SPECT MPI imaging radiomics features is even better than clinical nuclear cardiologists. The model, after simplifying several imaging radiomics variables, had mildly reduced accuracy for MACE, but its predictive interpretation and clinical utility were more prominent[66], and the deep learning model showed better accuracy and calibration than traditional logistic regression models in predicting death and MI[67]. The semi-quantitative assessment of myocardial perfusion defects after SPECT has been proven to predict MACE. IPTD as the difference between stress-total perfusion defects (TPD) and rest-TPD is different in men and women, and women with moderate to severe myocardial ischemia (IPTD > 5%) show a worse prognosis[68]. The prediction of CAD prognosis by CMR has been accepted by the general public, and Pezel et al[69] showed high predictive value in predicting 10-year mortality in CAD patients based on a machine learning model of 5 parameters of stress CMR and 11 clinical data. The newly proposed fully automated MRI parameter analysis software did not differ from manual segmentation in predicting MACE within 1 year due to the time-bound nature of MRI image segmentation and simplifies the workflow[70]. Non-invasive FFR obtained by CCTA is considered to have more excellent diagnostic performance compared to CCTA and ICA, and several studies by Qiao et al[14,71] showed that machine learning-based FFRCT has better predictive potential for adverse events compared to CCTA. Machine learning CT-FFR has also shown[72] a certain prognostic value in the occurrence of MACE and in-stent restenosis after coronary stent implantation. Previous studies[73,74] have shown that CAC score and epicardial adipose tissue (EAT) have some predictive value in cardiovascular risk stratification, and EAT quantification based on deep learning models integrating fully automated analysis of non-enhanced cardiac CT data can adequately predict MACE. Perivascular adipose tissue (PVAT) is closely associated with its perivascular structural alterations, and coronary PVAT radiomic features outperform the conventional CCTA model in predicting MACE within 5 years of CAD[15]. It is worth mentioning that another indicator associated with adipose tissue, fat attenuation index (FAI), reflects coronary inflammation, and the results obtained from unsupervised cluster analysis suggest that high FAI is associated with high-risk plaques and represents a higher risk of MACE[75].

Over the past decade, there has been a significant shift in risk stratification and therapeutic management of coronary artery stenosis, where the focus is no longer limited to the severity of intraluminal stenosis, but where the intrinsic characteristics of plaque morphology are also of concern. Although clinical indicators and blood biochemical markers have performed well in CAD stratification[76,77], decisions about the risk of adverse coronary events still have some shortcomings. Therefore, how to accurately identify plaque has become the frontier of research to explore the prognosis of patients with CAD. With the rapid development of accurate quantitative medical imaging technology, image recognition technology, and data algorithm updates, the mining and analysis of big medical image data can be realized. The combination of plaque identification and image radiomics is critical. Traditional image radiomics analysis is reflected in the extraction and modeling of high-throughput features of regions of interest (ROI) in CT, PET and MRI. Automatic Cardiac CT CAC score based on the convolutional neural network shows the height of the artificial measurement consistency and significantly reduces the analysis time[78]. Low-dose CT (LDCT) for lung cancer screening can identify arterial calcification. Homayounieh et al[79] completed cardiac image segmentation and radiomic feature extraction using existing models and found that whole-heart imaging radiomics of LDCT can diagnose coronary stenosis and predict cardiovascular disease risk. Similarly, semi-quantitative coronary artery calcium volume (CACV) based on LDCT artificial intelligence CNN prototype also showed similar results[80]. Recently, the fully automatic CAC score comparison between ECG-gated cardiac CT and non-ECG-gated LDCT has shown[81] good reliability, but the results in different institutions show evident heterogeneity, so it may need further verification. Assessment of the coronary artery calcification degree is usually measured using the coronary artery calcification score (CACS), and the XGBoost model combining CACS with clinical features accurately reflects CAD risk stratification[28].

The application of imaging radiomics in CAD is mostly focused on CCTA images. Several previous studies[82-84] have shown that the use of radiomic features of CCTA plaque regions can accurately and rapidly identify unstable plaques in coronary arteries. At the same time, the radiomics features associated with unstable plaques are associated with the occurrence of adverse cardiovascular events[85]. In addition to coronary plaque studies, the radiomic features of pericoronary adipose tissue (PCAT) have also been extensively studied[86,87] in the last two years, whether it is of certain significance in the evaluation of coronary artery stenosis or acute coronary syndromes such as myocardial ischemia and myocardial infarction[88-91]. In addition, PCAT is more advantageous in predicting the occurrence of MACE within 3 years compared with EAT[92]. In recent years, new imaging techniques have been gradually applied in radiomics, such as intravascular ultrasound (IVUS) and virtual histology (VH), which can also diagnose unstable plaques and thus prevent MACE occurrence[93]. IVPA, as a new type of intravascular imaging, has been confirmed to detect atherosclerotic plaque, but the cardiac motion artifact limits the use of CAD. Motion and Artifact Correction (MAC) - Net, as a new type of deep learning algorithm, has been used to correct coronary IVPA artifacts. It provides a prerequisite for the application of IVPA in the diagnosis of CAD[94].

The Future Vision of AI in CAD

In the nearly 100 years in which clinical researchers have been studying coronary artery disease, our understanding of coronary artery disease has become clearer. With the advent of the era of artificial intelligence, we are acutely aware that the next research boom in coronary artery disease is about to take off. In recent years, researchers have moved away from focusing solely on the diagnosis of CAD and instead have focused more on the issue of cardiovascular risk stratification after CAD. In terms of research methods, the rise of radiomics has placed higher demands on the quality of medical images while also promoting the use of medical images for the comprehensive management of CAD. With the rapid development of radiomics, the orientation of clinical medical images to predict the occurrence of cardiovascular risk will be at the forefront of research on artificial intelligence in CAD in the next decade.

Limitations

This study is the first visual review and analysis of AI applications in coronary artery disease through bibliometrics in the last 15 years, but there are still some limitations. First, we tried to refine the search strategy as much as possible, so it is inevitable that there are certain articles with low relevance. Second, we only selected the WOSCC to complete the literature search and collection; Pubmed, Google Scholar, and other databases were not included in our study, so there may be some articles missing. Finally, there may be some bias in the results of this study due to problems such as changes in institutional names or unidentifiable author ranking.

Conclusions

In this study, we searched for AI and CAD-related research over the last 15 years through bibliometric analysis. FRONT CARDIOVASC MED, EUR RADIOL and J AM COLL CARDIOL are the influential journals in this field. Schoepf, U. Joseph and Acharya, U. Rajendra are the leading authors in this field. Future research may be more towards the potential link between cardiovascular risk stratification and radiomics. Our study illustrates the full range of applications of AI in CAD and the relationship between them, providing important clues to current trends and future directions of their research. The visualization study based on Citespace and VoSviewer software will hopefully provide researchers with a comprehensive view of the current general trends in the field.

Conflict of Interest

The authors declare that they have no conflict of interests.

Data Availability

The original contribution presented in this study is included in the article. Further inquiries can be directed to the corresponding author.

Authors' Contribution

H.-L. Dong: Presentation of the study concept. X.-T. Qi, H. Wang, and R.-J. Zhang: Study design. X.-T. Qi: Data analysis. X.-T. Qi, H. Wang, and D.-G. Zhu: completed the downloading and saving of all data and was responsible for the integrity of the data as well as the accuracy of the data analysis, data interpretation, and manuscript drafting. X.-T. Qi, H. Wang, R.-J. Zhang, D.-G. Zhu, L. Zheng, X. Cheng, and H.-L. Dong critically revised the manuscript. All authors contributed to the article and approved the submitted version.

Informed Consent

Not applicable.

Ethics Approval

Not applicable.

Funding

None.

Acknowledgements

We thank Dr. X.-Y. Yue and Dr. Z.-C. Lu for their assistance in data analysis and acquisition.

ORCID ID

X.-T. Qi: 0000-0002-2486-8045
H. Wang: 0000-0001-7408-0398
D.-G. Zhu: 0000-0003-2459-8222
L. Zheng: 0000-0002-5755-7470
X. Cheng:0009-0002-9539-899X
R.-J. Zhang: 0000-0003-0697-2217
H.-L. Dong: 0000-0002-5924-7003

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