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Global trends in restenosis research within acute coronary syndrome: a bibliometric analysis

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ABSTRACT. – OBJECTIVE: **According to the World Health Organization, 17.9 million individuals died from cardiovascular diseases (CVD) in 2019, constituting 32% of all global mortalities. In recent years, percutaneous coronary interventions such as stenting have become a common treatment approach for coronary artery disease (CAD). However, the problem of angina recurrence after stenting, associated with in-stent restenosis, persists. The aim of this study was to elucidate the intricate structure of relevant countries and regions, prominent research institutions, prolific authors, and recurring keywords shaping the landscape of this field.**

MATERIALS AND METHODS: **The search strategy involved Scopus and Web of Science Core Collection databases on December 13, 2023. Bibliometric analysis was performed using the Bibliometrix R-package.**

RESULTS: **An upward trend was found, characterized by an annual growth rate (AGR) of 6.82%. China leads with 17 publications, followed by Argentina with 14 and Italy with 9. Capital Medical University from China has published the largest number of articles in the field. The most significant number of publications were published in the American Journal of Cardiology. Among the top ten authors, Kim J. has published six articles and Yang C. has published four, making them the most productive in the field. "In-stent restenosis" and "percutaneous coronary intervention" were the most frequently used terms between 2002 and 2023.**

CONCLUSIONS: **It is important to note that the majority of studies examined were conducted in developed countries, which may influence the generalization of results. Nevertheless, there is also considerable attention to the topic from scientific groups in developing countries. This analysis helps identify gaps in the current research field and define directions for future studies.**

Key Words:
Acute coronary syndromes, Restenosis, Bibliometric analysis.

Introduction

According to the World Health Organization, 17.9 million individuals died from cardiovascular diseases (CVD) in 2019, constituting 32% of all global mortalities[1]. Among these fatalities, 85% were attributed to heart attacks and strokes[1], most frequently encountered in individuals over the age of 60[2]. There is a trend of decreasing age at onset[3,4]. The causes of myocardial infarction include coronary artery atherosclerosis and vasospasm[5,6].

In recent years, percutaneous coronary interventions such as stenting have become a common treatment approach for coronary artery disease (CAD). Coronary artery stenting is widely utilized for myocardial revascularization in CAD patients due to its low invasive nature, which enables rapid and effective patient recovery[7]. However, the problem of angina recurrence after stenting, associated with in-stent restenosis, persists[8,9]. The incidence of restenosis in coronary arteries varies from 2.7 to 33%[10]. In a study by Cassese et al[9], restenosis was identified in 25% (n = 2,643) of treated individuals. Over the observation period, 702 fatalities were recorded, with 218 occurring among patients with restenosis.

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Diabetes, dyslipidemia, female sex, renal failure, hypertension, and smoking were associated with an increased risk of restenosis, preceding coronary artery bypass grafting surgery, and congestive heart failure[10,11]. Additionally, younger age, longer stenting duration (≥ 48 months), chronic kidney disease, and the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers or ow-density lipoprotein (LDL) cholesterol levels above 70 mg/dL may also be contributing factors to arterial restenosis[12].

In recent years, several bibliometric analyses have been published focusing on drug-eluting stents (DES) and their role in the treatment of coronary artery disease (CAD) and prevention of restenosis[13]. Other studies[14] in this area have addressed trends in angioplasty research over the past two decades. These articles focused on specific treatment methods and strategies for preventing restenosis, as well as the use of angioplasty methods with and without restenosis. It is important to note that data retrieval for these analyses was limited to the Web of Science Core Collection database.

Recurrent coronary events pose a threat to patient health, lead to a decline in quality of life, and are associated with substantial economic burdens on healthcare systems. Additionally, there is a significant trend towards a reduction in Disability-Adjusted Life Years (DALY) and its components[15]. Moreover, the majority of deaths related to cardiovascular diseases (CVD) occur in low- and middle-income countries[1]. However, there is a notable discrepancy in the rate of this trend between wealthier and poorer regions of the world, which is a serious concern for healthcare policymakers[15]. Through meticulous bibliometric analysis, we aim to elucidate the intricate structure of relevant countries and regions, prominent research institutions, prolific authors, and recurring keywords shaping the landscape of this field. Furthermore, this analysis aims to highlight hotspots and cutting-edge areas of research, aiming to contribute to innovative perspectives on the future trajectory of restenosis in recurrent acute coronary syndromes.

Materials and Methods

Search Strategy

The search was conducted in the Scopus and Web of Science Core Collection databases on December 13, 2023 (Figure 1). We used a combination of keywords (**Supplementary File**) using Boolean operators (AND, OR, NOT). Research articles written in English were selected. The search results were exported in BibTeX format for Scopus and in plain text format for Web of Science Core Collection. Subsequently, the data were merged using code in R Studio (**Supplementary File**), resulting in a single Excel file.

Study Selection and Data Extraction

Two authors (Z.B and G.K.) rigorously analyzed the titles, abstracts, and full texts of the articles to ascertain their eligibility according to the aim of the study. In case of disagreements between authors, they referred to the third author to resolve any contentious issues.

Visualization and Statistical Tools

Bibliometrics and scientometrics research were conducted using the Bibliometrix R-package, which provides analytical tools. Data analysis was performed using R Studio v.4.3.2 software (Posit Software, PBC Boston, MA, USA) and the Biblioshiny package (https://www.bibliometrix.org/home/index.php). Countries, institutions, journals, and authors were analyzed. Additionally, Excel software was utilized for the visualization of certain figures.

Results

Summary of the Papers

The present bibliometric analysis includes 76 publications from 50 journals, with an average number of citations per document of 18.93. The average age of these publications is 9.29 years, covering the period from 2002 to 2023. Moreover, the analysis includes 670 authors with an international collaboration rate of 1.316% and an average of 9.64 co-authors per document. The number of references is 123, and 149 keywords were utilized.

Annual Analysis of Publication

Based on the data for the last two decades, annual scientific publications were analyzed (Figure 2). An upward trend was found, characterized by an annual growth rate (AGR) of 6.82%. Between 2002 and 2005, the number of annual publications remained stable at one article. In addition, one article per year was published in 2008, 2009, and 2017. Between 2006 and 2022, there was variability in the number of articles, which ranged from 2 to 6 in different years. Nevertheless, despite

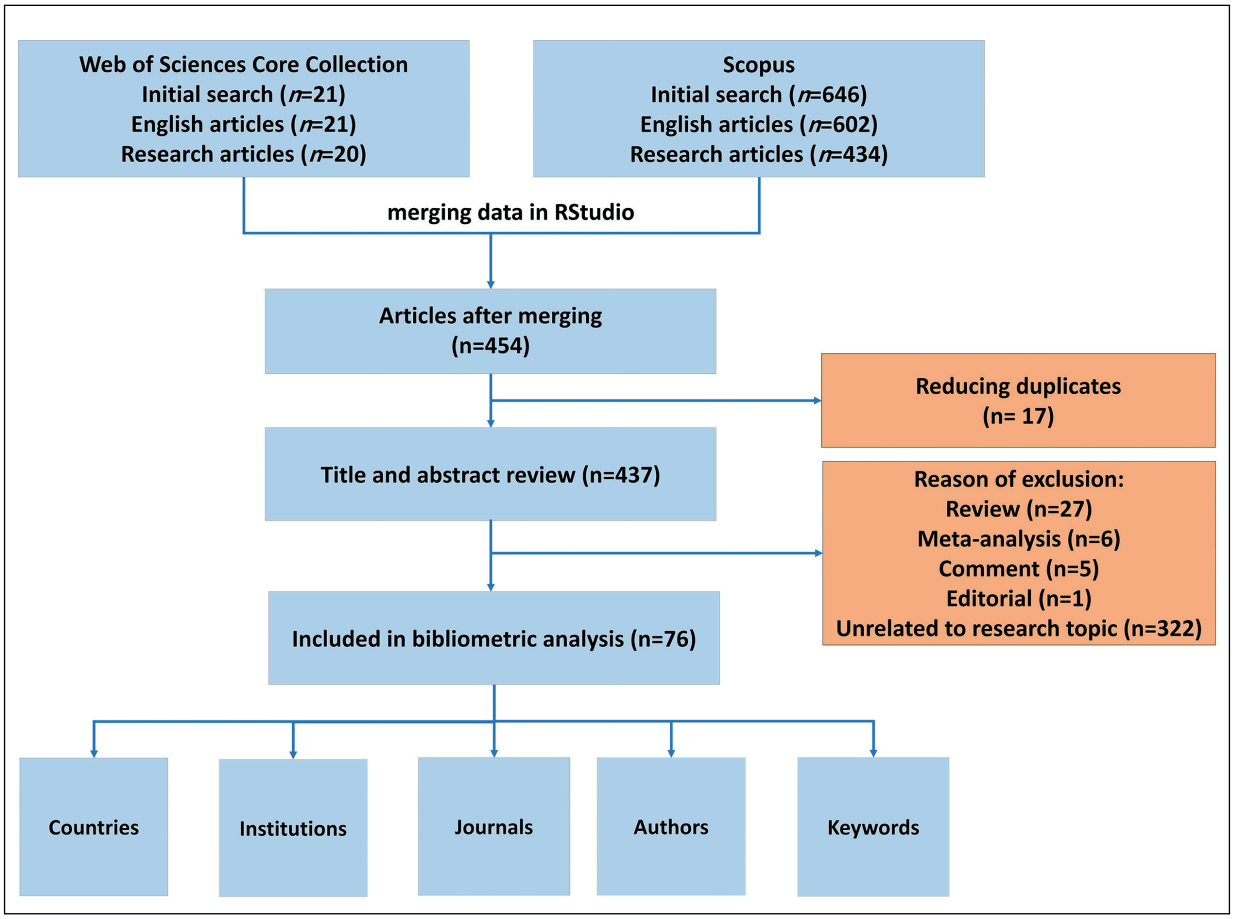

Figure 1. Flow chart for selection of articles for a bibliometric analysis of global trends in restenosis research within acute coronary syndrome.

fluctuations, there has been a steady increase in publications since 2006, reaching more than seven articles per year by 2022. The increase in the number of publications and the positive annual growth rate indicate an increasing interest of researchers in recurrent acute coronary syndrome after stent implantation.

The Most Productive Country and Institutions

Figure 3 shows the distribution of country scientific production for the period under review. China had the highest number of publications with 17, followed by Argentina with 14 and Italy with 9. Table I shows the ten most productive

Table I. Key institutions contributing to publications of restenosis research within acute coronary syndrome.

Rank	Affiliation	Article	Country
1	Capital Medical University	5	China
2	Jordan University of Science and Technology	4	Jordan
3	Medical University of Lodz	4	Poland
4	Technische Universität München	4	Germany
5	Yonsei University College of Medicine	4	South Korea
6	Chinese Academy of Medical Sciences and Peking Union Medical College	3	China
7	Lokmanya Tilak Municipal Medical College	3	India
8	Osaka City University Graduate School of Medicine	3	Japan
9	Semmelweis University	3	Hungary
10	Universidade Federal de Minas Gerais	2	Brazil

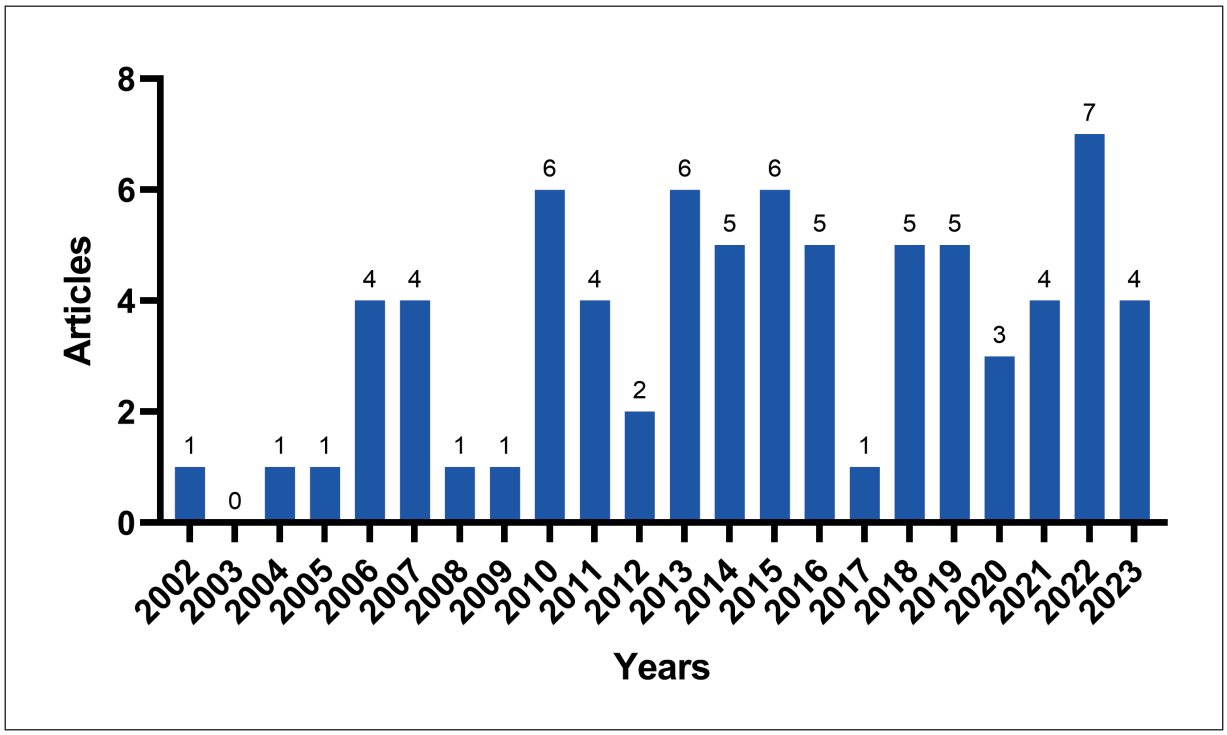

Figure 2. Annual publication of restenosis research within acute coronary syndrome trends over time (2002-2023).

institutions represented by different countries in Europe and Asia. Capital Medical University from China has published the largest number of articles (n = 5) in this field. Jordan University of Science and Technology, Medical University of Lodz, and Technische Universität München followed with four articles each. These universities are located in Jordan, Poland, and Germany, respectively. China stands out among the countries actively publishing articles in this field; moreover, the most productive university is also a university from China, which indicates a high interest in this subject in this country. Table II presents the countries with the most relevant contributions based on the affiliations of the corresponding authors, single-country publications (SCPs), multiple-country publications (MCPs), and MCP ratio (MCP/articles). Presented works are single-coun-

Table II. Top 10 most relevant countries by corresponding authors.

Country	Articles	SCP[a]	MCP[b]	Frequency	MCP_Ratio[c]
China	12	12	0	0.158	0.000
Italy	9	9	0	0.118	0.000
Usa	9	9	0	0.118	0.000
Japan	5	5	0	0.066	0.000
Korea	5	5	0	0.066	0.000
Germany	4	4	0	0.053	0.000
Poland	3	3	0	0.039	0.000
Turkey	3	3	0	0.039	0.000
India	2	2	0	0.026	0.000
Switzerland	2	2	0	0.026	0.000
Argentina	1	0	1	0.013	1.000

[a]Single-country publication (SCP), indicating that the authors of the publication are from the same country. [b]Multiple-country publications (MCPs), indicating that the authors of the publication are from multiple countries, which means the cooperation between countries. [c]MCP/articles, indicating the ratio of co-authored articles in the country's published articles.

Table III. Most relevant journals, the impact factor (IF), and Journal Citation Reports (JCR) categories related to restenosis research within the acute coronary syndrome.

Rank	Journal	Article	IF	JCR category, SCIE*
1	American Journal of Cardiology	7	2.8	Cardiac & Cardiovascular systems – SCIE (Q3)
2	American Heart Journal	4	4.8	Cardiac & Cardiovascular systems – SCIE (Q1)
3	Eurointervention	4	6.2	Cardiac & Cardiovascular systems – SCIE (Q1)
4	European Heart Journal	3	39.3	Cardiac & Cardiovascular systems – SCIE (Q1)
5	International Journal of Cardiology	3	3.5	Cardiac & Cardiovascular systems – SCIE (Q2)
6	Anatolian Journal of Cardiology	2	1.3	Cardiac & Cardiovascular systems – SCIE (Q4)
7	Angiology	2	2.8	Peripheral vascular disease – SCIE (Q3)
8	Biomarkers in Medicine	2	2.2	Medicine, Research & Experimental – SCIE (Q4)
9	BMC Cardiovascular Disorders	2	2.1	Cardiac & Cardiovascular systems – SCIE (Q3)
10	Cardiovascular Diabetology	2	9.3	Cardiac & Cardiovascular systems – SCIE (Q1)

*SCIE: Science Citation Index Expanded.

try publications. Only Argentina has the highest MCP ratio, and 1,000 other countries are the countries with the lowest ratio (0.000) in the top 11 list.

Journals

Bradford's Law describes the distribution of scientific articles across journals[16,17]. Figure 4 shows the top eight journals that researchers consider to be the primary for publication. The largest number of publications (n = 5) were published in the "American Journal of Cardiology". "American Heart Journal and Eurointervention" followed with four articles each. In the list of most cited sources, the "European Heart Journal" had the highest impact factor with IF = 39.3, followed by "Cardiovascular Diabetology" with an impact factor of 9.3. In addition, the majority of journals (40%) are categorized as quartile first (Q1) in Science Citation Index Expanded (SCIE) by Journal Citation Report (Table III).

Contributions of Authors

Among the top ten authors, Kim J., with six articles, and Yang C., with four articles, are the most productive and have published the most papers in the field of restenosis (Figure 5A). Additionally, Figure 5B presents the dynamics of the produc-

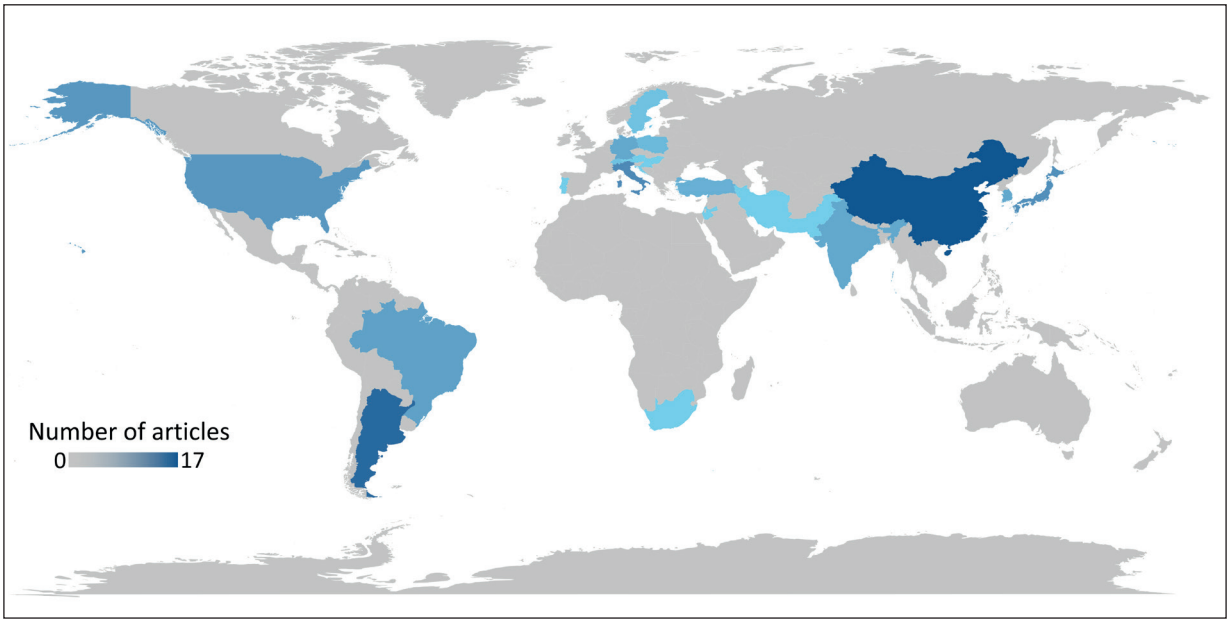

Figure 3. The annual number of publications of restenosis research within acute coronary syndrome in the top ten prolific countries from 2002-2023.

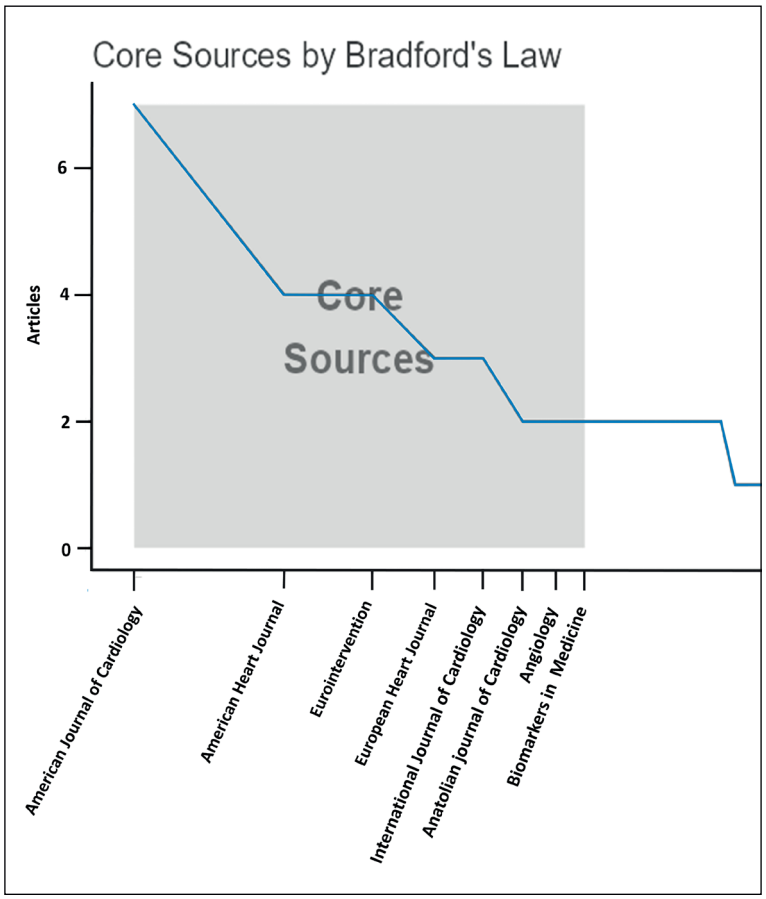

Figure 4. Core journal distribution according to Bradford's law (2002-2023) related to restenosis research within acute coronary syndrome.

tion of the works of the mentioned authors over time. Kim J. showed activity in 2007 and 2008, publishing two articles in each of these years, with total citations per year of 3.72 and 1.18, respectively. Yang C. and Chen M. also started their publication activity in 2007 and have remained active until now. Their most recent publications date back to 2022, indicating their long-term interest in this area of research. We should also note Chen M. and Liu Y. achieved the highest citation rate, reaching 10.5 for their papers published in 2021.

Authors Keywords

"In-stent restenosis" and "percutaneous coronary intervention" were the most frequently used terms between 2002 and 2023 (Figure 6A). The use of the term "In-stent restenosis" peaked in 2020, while "drug-eluting stent" started to be actively used from 2019 to 2020. "Restenosis" and "percutaneous coronary intervention" were the most popular in 2018. Among the earliest terms in use are "angioplasty" and "stent", which were popular in 2009 and 2010, respectively (Figure 6B).

The primary themes encompass the study of restenosis and in-stent restenosis, reflecting efforts to elucidate the mechanisms and risks associated with recurrent arterial narrowing post-intervention. Additionally, there is a focus on enhancing percutaneous coronary intervention (PCI) techniques for the treatment of coronary artery disease and acute coronary syndrome. Significant attention is directed towards the development and assessment of stent efficacy, particularly drug-eluting stents, and the prevention of stent thrombosis. Emerging areas of interest include advanced imaging techniques, biodegradable stents, and genetic research. Potential gaps in the field involve a lack of long-term data, the investigation of patient-specific risk factors, and the need for comparative studies of various treatment modalities and stent types.

Discussion

This bibliometric analysis was performed to analyze the worldwide sources of restenosis in

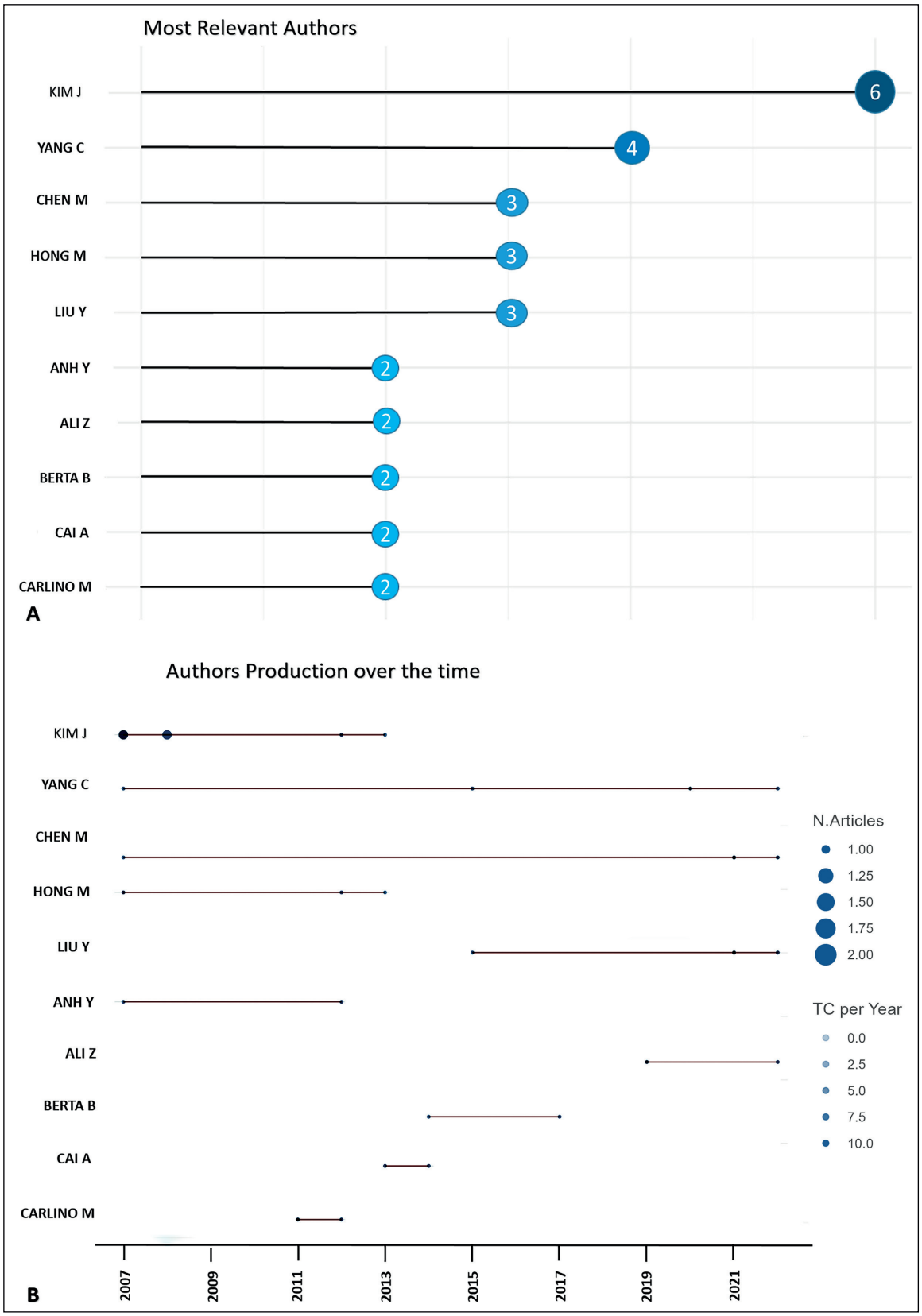

Figure 5. Most relevant authors. **A**, Authors' production over time. **B**, Related to restenosis research within acute coronary syndrome.

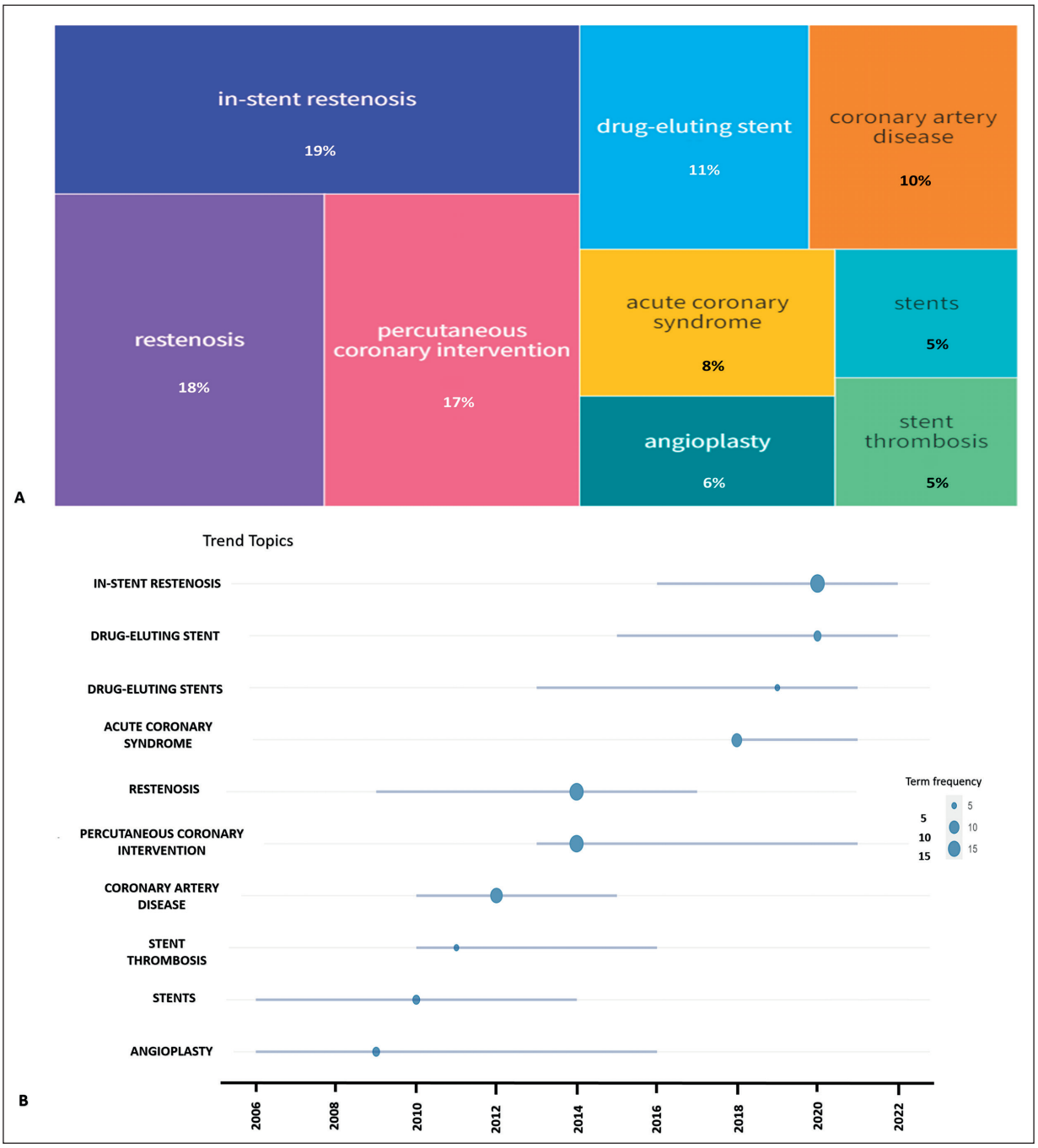

Figure 6. **A**, Most relevant authors' key words. **B**, Authors' keywords trends topic between 2006-2022.

patients with recurrent coronary syndrome from 2002 to 2023. Several significant findings are noteworthy: (1) identifying the most productive countries and institutions, (2) identifying important journals with high impact factors and Journal Citation Reports (JCR) rankings, (3) assessing influential authors and authors' most common keywords, and (4) investigating the potential impact of these key findings on legislators and health care providers. The results of the analysis showed a significant growth of scientific articles devoted to restenosis problems over the last 20 years.

This analysis helps identify gaps in the current research field and define directions for future stud-

ies. The observed trends in publication highlight significant advancements driven by technological innovations, increased funding, and international collaborations, leading to improved clinical outcomes and optimized treatments for cardiovascular diseases. However, the predominance of studies from developed countries highlights the need for more research in low- and middle-income regions to ensure global applicability and equity in healthcare advancements. Future research should focus on long-term outcomes, cost-effectiveness, personalized medicine, and implementation science to further enhance the clinical and public health impact of cardiovascular interventions.

This upward trend indicates an increasing recognition of the importance of understanding restenosis in patients with recurrent acute coronary syndrome. Moreover, it also emphasizes the importance of exploring innovative approaches to address these challenges effectively.

In a broader perspective, there has been a noticeable increase in the number of published studies addressing the issue of restenosis in patients with recurrent acute coronary syndrome. This trend is directly related to the global phenomenon of increasing numbers of patients with cardiovascular disease[1,18] and undergoing percutaneous coronary interventions[19]. A significant portion of publications are mainly represented by research aimed at improving the treatment of restenosis as acute coronary syndrome outcomes using new treatment therapy and technologies. For example, Latib et al[20] found that a group of patients with drug-eluting stent in-stent restenosis (DES-ISR) is identified as a high-risk group that is at increased risk of events, particularly repeat revascularization during long-term follow-up. However, Gori et al[21] found that implantation of coronary bioresorbable scaffolds (BVS) after twelve months, according to clinical, intracoronary imaging, and vasomotor function data, shows good results with a low mortality rate. The top 10 documents, in terms of average annual citations, covered a range of studies. These include investigating the neointimal characteristics of drug-eluting stents (DESs) and comparing them with bare metal stents (BMSs)[22], as well as the benefits of routine follow-up angiography after coronary stenting[9]. Additionally, the evaluation of the interval between the previous intervention and the occurrence of clinical in-stent restenosis in patients with myocardial infarction revealed a shorter duration compared to patients without myocardial infarction[23]. Furthermore, comparisons of the clinical presentation of in-stent restenosis with restenosis without stenting were conducted[24]. High levels of plasma oxidized LDL after acute myocardial infarction were found to predict stent restenosis[25]. These findings indicate that researchers worldwide are increasingly engaged in studying the outcomes of restenosis in patients with cardiovascular diseases and seeking methods for their prevention.

Prominent journals covering a wide range of topics, including cardiology, angiology, biomarkers, dialectology, and journals related to medical interventions, were represented in the field of studying restenosis. Moreover, the majority of journals in the core sources were highly influential. The selection of high-impact peer-reviewed journals is crucial to ensure the credibility of scientific results, thereby guaranteeing the quality of evidence[26]. This is important because many policymakers and healthcare providers rely on high-quality evidence when making decisions[27]. Authors take various factors into account when deciding which journals to submit their work to. Among these factors are the journal's impact factor, JCR category, open access availability, indexing in databases, and publication costs[28].

Publications on the studied topic were represented not only by high-income countries such as China and the USA but also by those with middle income, including Argentina and Turkey, which corresponds to the findings of the study by Aminde et al[29]. It must be noted that the development of outcomes in cardiovascular diseases may also depend on the income level of patients, even in countries with universal health insurance and reliable social protection systems. Landon et al[30], found that patients with a low income had higher adjusted 30-day and 1-year mortality rates compared to those with high income, while the frequency of cardiac catheterization and percutaneous coronary interventions was lower. Additionally, patients with high income had shorter lengths of hospitalization and lower rates of readmission[30]. Furthermore, we identified a lack of representation of authors from low-income countries. This may indicate that these regions face severe challenges due to inadequate support services[31]. Factors contributing to this imbalance include limited research funding, insufficient institutional support, and restricted educational opportunities in low-income settings. Furthermore, limited access to technological resources and language barriers further negatively impact participation in research.

The bibliometric analysis conducted on the global literature related to restenosis in patients with recurrent coronary syndrome identified key terms used by the authors. Among these terms are "in-stent restenosis", "restenosis", "percutaneous coronary intervention", "coronary artery disease", "acute coronary syndrome", "angioplasty", "drug-eluting stenting", "stents", and "stent thrombosis". These terms demonstrate a significant interest among authors in the main outcomes of acute coronary syndrome, such as thrombosis and restenosis, and also indicate the researchers' interest in cardiovascular interventions[9]. Nowadays, researchers and healthcare professionals in the field actively study factors contributing to restenosis and seek treatment to reduce mortality from outcomes[22,23].

Limitations of the Study

Our bibliometric analysis has several limitations, including the influence of database coverage, language bias, and regional differences in research practices. Using only Web of Science and Scopus databases means that the findings are limited to the journals indexed by these databases, potentially overlooking significant research published elsewhere. Language bias is another concern, as focusing exclusively on English-language articles may exclude important studies published in other languages, skewing the representation of global research. Additionally, variations in research practices and publication standards across different regions can affect the visibility and impact of research, leading to an imbalanced view of the field. However, unlike other bibliometric studies, we combined data from both databases, thereby increasing the number of articles covering this topic.

Conclusions

In this bibliometric analysis, we have attempted to systematize and evaluate the available worldwide literature on the topic. Analyzing publications allowed us to identify the main trends and directions of research in the development of restenosis in patients with recurrent acute coronary syndrome. We found significant interest from the scientific community in this topic, indicating its relevance and importance. It is important to note that the majority of studies examined were conducted in developed countries, which may influence the generalization of results. Nevertheless, there is also considerable attention to the topic from scientific groups in developing countries. This analysis helps identify gaps in the current research field and define directions for future studies. Based on the identified trends, it can be concluded that further research on restenosis prevention is necessary to develop methodology and practical applications. We hope that the results of this analysis will serve as a basis for the development of new treatment strategies and methods in the field of restenosis, promoting scientific progress and improving practice.

Based on the findings of this bibliometric analysis on restenosis in patients with recurrent acute coronary syndrome from 2002 to 2023, several recommendations for future research directions, collaborations, and strategies can be outlined. Firstly, there is a clear need to foster international collaborations that transcend geographic boundaries to ensure a comprehensive understanding of restenosis mechanisms and management practices across diverse populations. Collaborative efforts can help mitigate the influence of regional disparities in research practices identified in this study, thereby enriching the global perspective on restenosis. Secondly, future research should prioritize investigating innovative treatment therapies and technologies, as evidenced by studies on drug-eluting stents (DES) for in-stent restenosis and coronary bioresorbable scaffolds (BVS), which have shown promising outcomes. Thirdly, efforts should be made to enhance the representation of low-income countries in research publications and collaborations, addressing disparities in research funding, institutional support, and access to technological resources. Lastly, focusing on the dissemination of research findings in high-impact journals with robust peer-review processes will ensure that evidence-based practices in restenosis management inform policymaking and healthcare decisions globally.

Conflict of Interest

The authors declare that they have no conflict of interest.

Authors' Contributions

Conceptualization, A.K., N.M. and G.K; data curation, G.K., Z.B., and P.A.; formal analysis, G.K., Z.B., and P.A; investigation, A.K., N.M., G.K. Z.B., and P.A.; methodology, A.K., N.M., N.T., and G.K; software, Z.B., and P.A.; supervision, A.K., N.M., and G.K.; writing–original draft, Z.B.; writing–review and editing, A.K., N.M., G.K., Z.B., N.T., and P.A.

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Not applicable.

Ethics Approval
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Availability of Data and Materials
Data is available on request from the corresponding author.

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