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ATHEROSCLEROSIS RESEARCH IN THE GENOMIC ERA: GLOBAL TRENDS FROM 1983 TO 2024

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ГЛОБАЛНИ ТЕНДЕНЦИИ В ИЗСЛЕДВАНИЯТА, СВЪРЗАНИ С АТЕРОСКЛЕРОЗАТА, ИЗПОЛЗВАЙКИ ПОДХОДИ, БАЗИРАНИ НА ГЕНОМА: 1983-2024 Г.

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Abstract. Atherosclerosis (AS) a chronic cardiovascular disease, poses a major threat to human health and remains one of the leading causes of mortality among the elderly. Genetic factors have long been recognized as contributors to the predisposition to heart and vascular diseases, with several studies suggesting that specific genetic variants may influence AS risk. This study employs a bibliometric analysis to explore scientific literature related to AS throughusing genomic approaches, base on Scopus data spanning 1983 to 2024. A total of 1,702 studies related to AS research employing genomic approaches were identified, comprising 1,137 research articles, 445 review articles, and 120 documents in other categories. The findings reveal a marked rise in interest in regarding genomic approaches to AS, particularly since 2017, with the United States, China, and the United Kingdom leading in research output. International collaborations are also prevalent, with the United States contributing the most publications. Although contributions from Indonesian authors remain limited, there is significant potential for future involvement. Notably, the most cited article, authored by Naghavi et al. in 2003, focusing on genomics in AS. Overall, the bibliometric analysis provides valuable insights into research trends and advancements in the study of atherosclerosis through genomic approaches.

Key words: atherosclerosis, genomics, bibliometrics, cardiology, health

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Резюме. Атеросклерозата (АС), хронично сърдечно-съдово заболяване, представлява сериозна заплаха за човешкото здраве и остава една от водещите причини за смъртност сред възрастните хора. Генетичните фактори отдавна са признати като фактори, допринасящи за предразположението към сърдечни и съдови заболявания, като няколко проучвания предполагат, че специфични генетични варианти могат да повлияят на риска от АС. В това проучване е използван библиометричен анализ за проучване на научната литература, свързана с АС, чрез използване на геномни подходи, въз основа на данни от Scopus, обхващащи периода 1983-2024 г. Идентифицирани са общо 1702 проучвания, свързани с изследвания на АС чрез използване на геномни подходи, които включват 1137 научни статии, 445 обзорни статии и 120 документа в други категории. Констатациите разкриват значително нарастване на интереса към геномните подходи към АС, особено от 2017 г. насам, като САЩ, Китай и Обединеното кралство са водещи по отношение на резултатите от изследванията. Преобладава и международното сътрудничество, като Съединените щати допринасят с най-много публикации. Въпреки че приносите на индонезийски автори остават ограничени, съществува значителен потенциал за бъдещо участие. Забележително е, че най-цитираната статия, чийто автор е Naghavi et al. през 2003 г., е посветена на геномиката при АС. Като цяло библиометричният анализ предоставя ценна информация за тенденциите в научните изследвания и напредъка в изучаването на атеросклерозата чрез геномни подходи.

Ключови думи: атеросклероза, геномика, библиометрия, кардиология, здраве

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Introduction

Atherosclerosis (AS) is a chronic cardiovascular disease with significant health risks [1, 2]. AS is one of the most common causes of death in elderly people [1]. The primary lesion of AS is characterized by lipid deposition in the arterial compartment, accompanied by the proliferation of smooth muscle cells and the fibrous matrix, which gradually progresses to the formation of AS plaques [3]. AS is usually considered a chronic inflammatory disease [4], because inflammation plays a vital role. Genetic factors have long been known to play a role in predisposition to cardiovascular disease.

In recent decades, the genomics revolution has opened up new opportunities to understand the relationship between genetic variants and cardiovascular disease [5]. Several studies have shown that certain genetic variants may influence the risk of AS [6, 7]. For example, the Arg389 genotype variant in the β1 adrenergic receptor is known to have higher activity compared to the Gly389 variant. This higher receptor activity may affect stress response and blood pressure regulation, which in turn may affect AS development. In addition, the study found that autophagy-related genes (*ARGs*) play a significant role in the pathophysiology of AS [8]. However, the role of genetic variants in AS remains a hot topic of research and results vary [9].

Atherosclerosis is not only a leading cause of cardiovascular disease but also presents a significant challenge for precision medicine due to its complex genetic underpinnings [10, 11]. Genomic studies have opened new pathways to unravel the intricate network of genetic variants influencing disease susceptibility, progression, and response to treatment [12]. By providing insights into the molecular mechanisms underlying AS, this research paves the way for novel diagnostic and therapeutic strategies. For instance, identifying specific genetic markers associated with plaque instability could enable early interventions and improve patient outcomes. This study's bibliometric analysis highlights these advancements and underscores the growing relevance of genomics in addressing this pressing global health issue [13].

Bibliometric analysis related to AS research was conducted to determine the relevance of the research and analyze global trends in AS research using genomic-based approaches over time [14, 15]. Information on AS disease research is presented in bibliographic data. This study will help map publication data through comprehensible visualizations to obtain useful information, such as keywords to determine research themes in certain disciplines, author affiliations with certain journals to determine the geographic scope of journals, and institutional collaborations. Bibliometric mapping is very important to help the scientific community and the general public [16]. The purpose of this study is to provide an overview of trends related to atherosclerosis disease using genomic-based approaches worldwide.

Methods

This study employs bibliometric analysis to explore various studies and scientific literature related to AS research using a genomic approach [17]. Several components were analyzed, including document type and language, publication trends, most frequent-

ly used keywords, citation analysis and the number of cited articles, and the most cited countries contributing to global trends in AS research using genomic-based approaches from 1983 to 2024 [18]. The analysis focused exclusively on English-language documents, with all non-English publications excluded to ensure consistency and clarity in the interpretation of data findings [19].

Database

This study investigates global trends in AS research using a genomics-based approach, utilizing Scopus data published between 1983 and 2024 (Scopus database). SciVerse Scopus, accessed on 05/24/2024, is one of the most reliable online databases for searching publications relevant to this study. Scopus was chosen for this analysis due to its numerous outstanding advantages over other online databases. First, Scopus offers comprehensive and detailed information, including features such as country affiliations, authors, journals, and institutions involved in the research [20]. Second, the database provides extensive citation data for each document group across scientific categories, serving as a valuable metric for assessing the reputation and impact of researchers globally [21].

Bibliometric Indicators

The criteria for the bibliometric analysis used in this study were as follows: 1) types of documents and languages, 2) publication trends, 3) keywords frequently used by researchers, 4) citation analysis and the number of cited articles, 5) the ten most cited countries, 6) the ten most active journals, and 7) international collaboration. Data on active, productive, and most cited publications were directly collected from the Scopus database by calculating the number of citations for each document. Additionally, data on the most cited publications were obtained from Scopus by analyzing the number of articles and citations from each country on a yearly basis. Two software tools were used to visualize the data: VOSviewer (version 1.6.16) and Biblioshiny [22].

Results

The findings of the global trend analysis in US research using a genomics-based research approach yielded 1702 documents from 1983 to 2024 sourced from the SCOPUS database.

Document Types and Languages

Our study analyzed articles on AS disease trends using a genomic-based approach, limited to English language publications available in the Scopus database from 1983 to 2024 (Table 1). A total of 1,702 studies were identified, comprising 1,137 research articles, 445 review articles, and 120 documents in other categories. The majority of the identified publications were research articles, highlighting the continued relevance and urgency of AS research using genomic-based approaches. This focus is particularly significant given that AS remains one of the leading causes of mortality worldwide. Furthermore, the availability of comprehensive resources and diverse reference types supports the growing interest in genomic approaches to AS research.

Table 1. Document type of Global Trends for Atherosclerosis Using Genomic-based approach

Description	Results
Main information about data	
Timespan	1983:2024
Sources (Journals, Books, etc.)	813
Documents	1702
Annual Growth Rate %	6.59
Document Average Age	10.8
Average citations per document	45.17
References	97 299
Document contents	
Keywords Plus (ID)	12 493
Author's Keywords (DE)	3592
Authors	
Authors	9878
Authors of single-authored docs	88
Authors collaboration	
Single-authored docs	93
Co-Authors per Doc	7.81
International co-authorships %	22.8
Document types	
Article	1137
Book chapter	37
Book	5
Conference paper	36
Editorial	18
Erratum	1
Letter	5
Note	10
Reviews	445
Short survey	8

Author keywords

The keywords frequently used in AS disease research trends employing genomics-based approaches from 1983 to 2024 include atherosclerosis, genomics, cardiovascular disease, epidemiology, coronary artery disease, stroke, hypertension, and others. These author keywords are closely related to the term "atherosclerosis." The visualization of these keywords comprises nodes and interconnected lines. Each node

represents a keyword, while the lines indicate associations between them. The central and largest node, “atherosclerosis” signifies its role as the primary focus of the study. Surrounding nodes vary in size, reflecting their relative importance or frequency of association with “atherosclerosis”.

Colors are used to categorize related terms; for instance, terms like “coronary artery disease” and “myocardial infarction” are positioned close together and share similar colors, highlighting a thematic relationship (Fig. 1).

Publication Trends

The publication trend on AS can be observed from the number of articles published each year, as shown in Figure 2. In the early years, particularly around the 1980s, the number of publications on AS was relatively low, with only a few articles published annually. A noticeable increase began in the mid to late 1990s, reflecting the growing interest of researchers in this topic. The peak of publications occurred in 2022, with 125 articles, indicating that AS remains a highly relevant research topic that continues to capture the attention of many researchers. However, in 2023, the number of publications decreased to 89 articles, potentially due to various factors such as shifts in research priorities or global events. In 2024, the number of articles published so far is 41. It is important to note that the data for 2024 may be incomplete, as the year is ongoing. Despite fluctuations in publication numbers, AS continues to be a topic of significant interest to the scientific community.

The Most productive country in publications

Based on Figure 3, several countries stand out as the most productive in research publications on AS. The United States (USA) leads with the highest number of publications, totaling 4,366 articles. China follows in second place with 1,747 articles, and Italy ranks third with 607 articles. These countries have made sig-

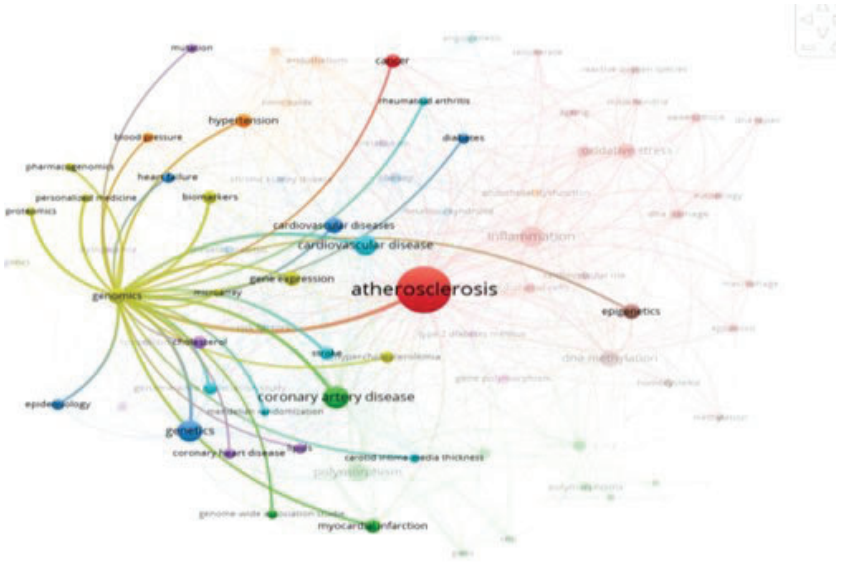

Fig. 1. Visualization of the most frequently occurring author keywords (minimum occurrence of 10 times) related to trends in atherosclerosis research using genomic approaches from 1983 to 2024, with a total of 74 keywords meeting this threshold

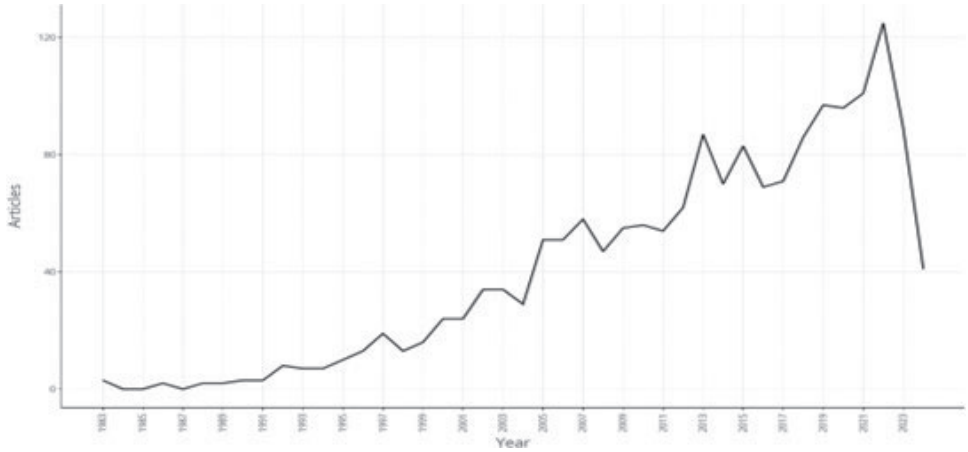

Fig. 2. Trends in scientific publications on atherosclerosis research utilizing genomic approaches from 1983 to 2024

nificant contributions to AS research and play a crucial role in advancing the understanding of this disease.

Source of documents

Figure 4 illustrates the number of research documents published by various scientific journals related to AS. The journal Arteriosclerosis, Thrombosis, and Vascular Biology (ATVB) has the highest number of publications, indicating its prominence in AS research. Additionally, several other journals play a significant role in this field, including the International Journal of Molecular Sciences, PLOS ONE, Circulation Research, and Frontiers in Genetics. This information can help researchers identify the primary outlets for AS research and recognize leading journals in the field. However, it is important to note that this figure provides only a general overview and does not assess the quality or impact of the research published. For a deeper understanding, researchers should refer to the individual articles published in these journals.

The Most relevant affiliation

Figure 5 displays the number of articles published by various institutions in AS research. Harvard Medical School is the leading affiliate, with 188 articles published, making it the most prominent institution in this field. Following in second place is the University of Washington, with 160 articles published in AS research. In third place is the University of California, which has published 94 articles in this area.

Collaboration among authors from multiple continents

In the field of science, international cooperation is crucial. Scientists from different countries can collaborate to exchange information related to specific research areas. According to, such collaboration helps disseminate knowledge and provides access to funding for countries or organizations that cannot afford advanced technology. A One Country Publication

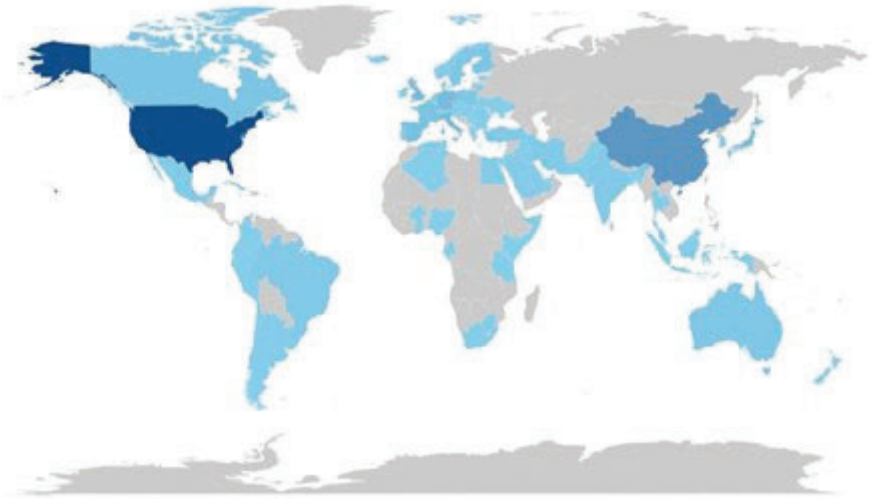

Fig. 3. The most productive countries in publications on atherosclerosis research utilizing genomic approaches from 1983 to 2024

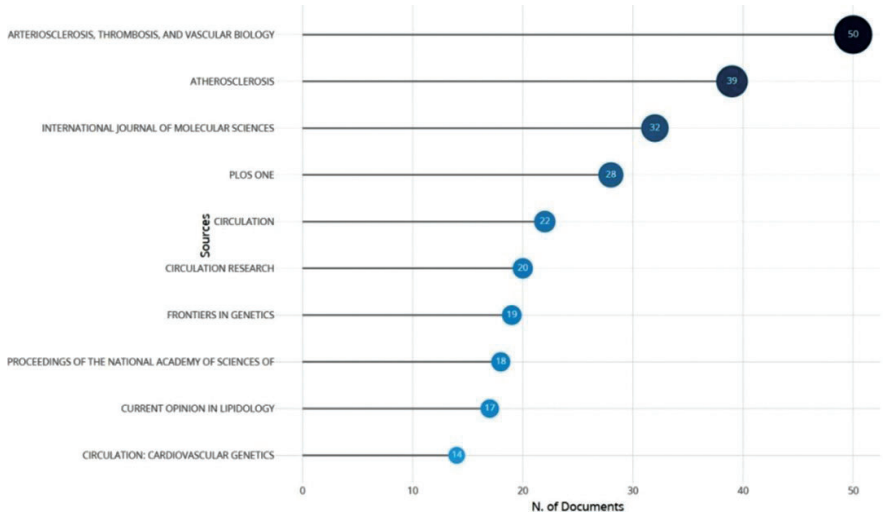

Fig. 4. Sources of documents related to atherosclerosis research using genomic information

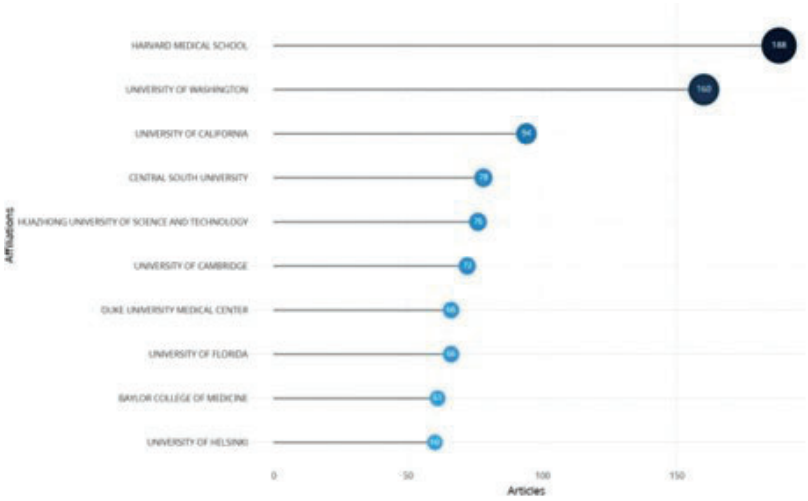

Fig. 5. The most relevant affiliations in publications on atherosclerosis research utilizing genomic approaches from 1983 to 2024

(SCP) refers to articles written by authors from the same country, showcasing national collaboration. In contrast, a Multi-Country Publication (MCP) involves authors from multiple countries and represents international collaboration. MCPs are particularly valuable, as they tend to be cited more frequently than SCPs. The largest collaboration in AS research using genomics-based approaches is seen in the USA, with a total of 443 articles – 329 SCPs and 114 MCPs. China follows with 201 articles – 164 SCPs and 45 MCPs. Finland has the fewest publications. While the USA, China, and Italy lead in MCPs, it is noteworthy that Israel has no researchers involved in MCP collaborations (Figure 6).

Citation analysis and number of articles cited

Identified the top 10 most-cited articles on AS research Using Genomics-based Approaches from 1983 to 2024 (Table 2). One article published in Circulation by Morteza Naghavi [23], titled “From Vulnerable Plaque to Vulnerable Patient: A Call for New Definitions and Risk Assessment Strategies: Part I” received the highest number of citations, with 1,983 citations and an average of 90.14 citations per year. Following this, another article by Morteza Naghavi [24] also published in Circulation, titled “From Vulnerable Plaque to Vulnerable Patient: A Call for New Definitions and Risk Assessment Strategies Part II” garnered significant attention, with 1,383 citations and an average of

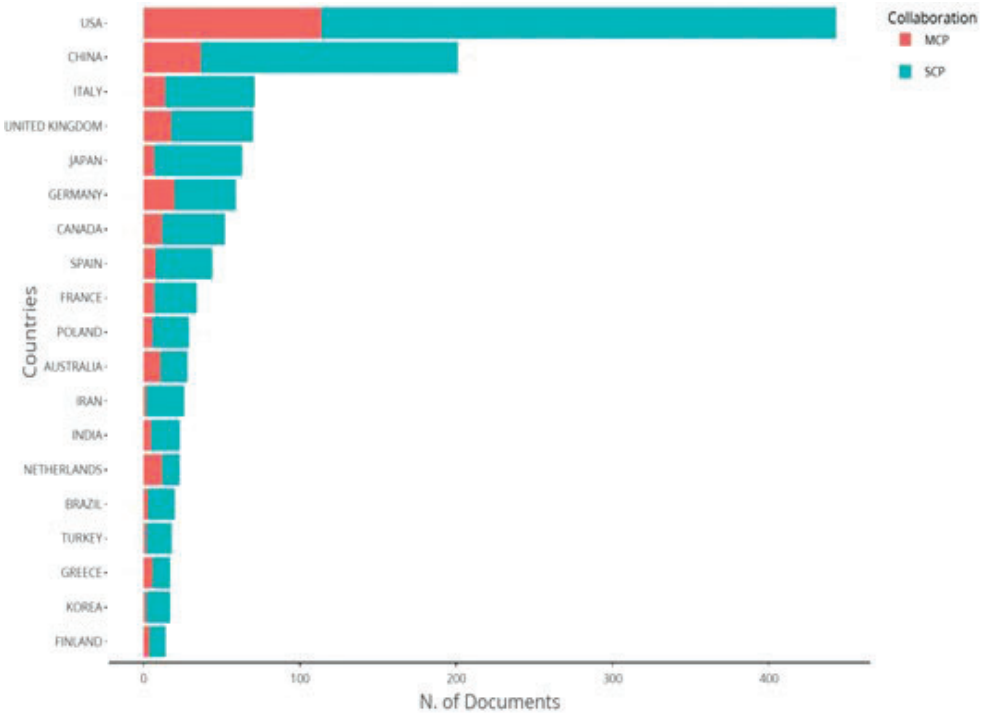

Fig. 6. Collaboration among authors from multiple continents in publications on atherosclerosis research utilizing genomic approaches from 1983 to 2024. MCP; Multi-Country Publication; SCP: Singlle-Country Publication

Table 2. Top 10 Most Cited Global Documents in Publications on Atherosclerosis Research Utilizing Genomic Approaches from 1983 to 2024

Paper	Year	Journal	PMID	Total Citations	TC per Year	Normalized TC
Naghav IM	2003	Circulation-a	14530185	1983	90.14	13.89
Naghav IM	2003	Circulation	14557340	1348	61.27	9.44
Lasda E	2014	RNA	25404635	965	87.73	20.51
Koren O	2011	Proc Natl Acad Sci USA	20937873	861	61.50	15.40
Piedrahita JA	1992	Proc Natl Acad Sci USA	1584779	796	24.12	4.65
Zafra-Stone S	2007	Mol Nutr Food Res	17533652	763	42.39	15.28
Denny JC	2013	Nat Biotechnol	24270849	645	53.75	11.92
YJ Gang	1995	Am J Pathol	35970037	639	21.30	3.69
Eldin C	2017	Clin Microbiol Rev	27856520	600	75.00	12.97
Kalman S	1999	Nat Genet	10192388	594	22.85	4.20

PMID: PubMed Unique Identifier

61.27 citations per year. Based on this information, we anticipate that this journal will continue to be a highly cited source for AS Research Using Genomics-based Approaches in the future. Additionally, this data will provide researchers with valuable insights into journal selection, helping them choose the most relevant journals for their research.

Discussion

The findings of this bibliometric analysis underscore the critical role of genomic research in advancing our understanding of AS [25]. The identification of key genetic variants and pathways involved in atherosclerotic plaque formation provides valuable insights into disease etiology and progression [26, 27]. These insights have significant implications for clinical practice, particularly in the development of personalized medicine approaches [28]. For example, targeting genes associated with inflammation or lipid metabolism could lead to more effective therapies with fewer side effects, individual variability in genetics and health conditions must be considered [29, 30]. However, it is important to note that identifying these variants does not automatically imply effective therapies, extensive validation and clinical trials are necessary to establish causation. In addition, the increasing trend of International collaboration highlights the potential for shared knowledge and technology transfer. This exchange is essential for accelerating progress in the field of cardiovascular diseases globally [31].

Modern genomic technologies have advanced previous methodologies in terms of data coverage and analytical resolution, yet challenges remain regarding data interpretation and ethical considerations [32]. For example, Genome-Wide Association Studies (GWAS) enable the identification of genome-wide genetic variants associated with AS risk [33, 34]. However, it is essential to acknowledge that many relevant genes may still be undiscovered [35]. GWAS have identified variants in genes involved in inflammation, lipid metabolism, and plaque stability, which are important targets for therapeutic development. Single-cell RNA sequencing (scRNA-seq) offers high resolution by enabling analysis of gene expression at the single-cell level [36]. This technology helps reveal cellular heterogeneity within atherosclerotic plaques, such as the specific roles of macrophages and smooth muscle cells in plaque formation [37, 38]. This information not only enhances the understanding of molecular mechanisms but can also be used to identify novel biomarkers for early diagnosis. In addition, CRISPR-Cas9 technology enables high precision genetic manipulation to validate genes identified as potential drivers of AS [39]. This approach provides functional validation that was not possible with previous genetic techniques, such as PCR or microarrays, which were limited primarily to genetic correlation analysis [40, 41].

By integrating data from these genomic technologies, genetic diagnosis in AS patients becomes more precise. However, translating research findings into clinical practice is a lengthy process that requires careful consideration [42]. This study is a bibliometric analysis focusing on global trends in genomics-based AS research. Therefore, an in-depth analysis of the types of genetic techniques used, method development, and details of data availability in the analyzed publications are beyond the scope of this study. This study aims to provide macro insights into publication trends, collaboration patterns, and geographic contributions while emphasizing the need for future research focusing on specific genetic methods and techniques to complement these insights.

Concluion

The trend in the publication of articles related to AS studies using genomic-based approaches has shown

a consistent increase from 1983 to 2024. This study demonstrates that research on AS using genomic-based approaches is gaining populariy and has become a significant area of focus. SCOPUS data indicates a rapid rise in publications since 2017, with the USA, China and the United Kingdom emerging as the most productive countries in the research field. On going international collaboration is evident, with the USA leading in publication output. The most cited article identified in this analysis is by Naghavi et al. (2003), which discusses genomic-based approaches to studying AS. Overall, this bibliometric analysis provides valuable insights into the evolving research trends related to AS studies using genomic methodologies.

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