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The relationship between polycystic ovary syndrome and coronary heart disease: a bibliometric analysis

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Background: Polycystic ovary syndrome (PCOS) is one of the most common gynecological endocrine diseases for women of puberty and reproductive age. PCOS can affect women's health for the rest of their lives since the incidence of coronary heart disease (CHD) may increase in the perimenopausal and senile periods among PCOS women compared with non-PCOS women.

Method: A literature retrieval based on the Science Citation Index Expanded (SCI-E) database. All obtained records results were downloaded in plain text format for subsequent analysis. VOSviewer v1.6.10, Citespace and Microsoft Excel 2010 software were utilized for analyzing the following terms: countries, institutions, authors, journals, references and keywords.

Results: There were 312 articles retrieved from January 1, 2000 to February 8, 2023, and the frequency of citations was 23,587. The United States, England, and Italy contributed the majority of the records. Harvard University, the University of Athens, and Monash University were the top 3 most productive institutions with publications on the relationship between PCOS and CHD. Journal of clinical endocrinology & metabolism ranked first with the highest publications (24 records), followed by Fertility and sterility (18 records). The keywords were divided into six clusters in the overlay keywords network: (1) the correlation between CHD risk factors and PCOS women; (2) the relationship between cardiovascular disease and female reproductive system hormone secretion; (3) the interaction between CHD and metabolic syndrome; (4) the relationship between c-reactive protein and endothelial function and oxidative stress in PCOS patients; (5) the potential positive effect of metformin on reducing CHD risk factors in PCOS patients; (6) the study of serum cholesterol and body-fat distribution in patients with CHD in PCOS. Oxidative stress, genome-wide association, obesity, primary prevention, and sex difference were main hotspots in this field in recent five years according to the keyword citation burst analysis.

Conclusion: The article obtained the hotspots and trends and provided a reference for subsequent research on the association between PCOS and CHD. Moreover, it is hypothesized that oxidative stress and genome-wide association were frontier hotspots in studies that explore the relationship between PCOS and CHD, and prevention research may be valued in the future.

KEYWORDS

polycystic ovary syndrome, coronary heart disease, bibliometric analysis, risk factor, VOSviewer, citespace

1 Introduction

Polycystic ovary syndrome (PCOS) is one of the most common gynecological endocrine diseases in adolescent and reproductive-age women, with an incidence of 6-10% (1, 2). Its clinical manifestations are varied and mainly characterized by irregular menstruation, anovulation or high androgen levels, infertility, and an increased risk of metabolic diseases (3). The risk of hypertension in PCOS women is twice that in non-PCOS women, which may be related to insulin resistance or hyperinsulinemia that damages vascular smooth muscle cells (VSMCs) and leads to the thickening and decreased elasticity of vascular walls (4). PCOS patients are prone to complications such as hypertension, abnormal lipid metabolism, type 2 diabetes mellitus (T2DM) and obesity, which are risk factors for coronary heart disease (CHD) (5). PCOS could enhance the overall cardiovascular risk, especially myocardial infarction, angina pectoris, and revascularization (6, 7). Increased serum triglyceride and low-density lipoprotein cholesterol (LDL-C) levels, decreased high-density lipoprotein cholesterol (HDL-C) cholesterol levels, and the altered ratio of apolipoprotein B to apolipoprotein A1 levels in PCOS patients are also associated with increased risk of CHD. In addition, high levels of C-reactive protein (CRP) and homocysteine in PCOS patients have been considered risk factors for the development of CHD (8, 9).

However, after searching various major databases, we found considerable literature on the relationship between the risk of CHD and PCOS. Although some scholars have done literature review studies (10–12), the studies' systematization and comprehensive visual analysis still need to be improved.

Bibliometric analysis is a method of analyzing, cleaning and mining the quantitative information of literature using mathematical and statistical functions, which explore structures, characteristics and laws of science and technology. The VOSviewer software developed by Van Eck of Netherlands University can intuitively display terms in different color clusters and clearly show the connections between clusters (13). CiteSpace software is a visual tool developed by Chen Chaomei that can realize keyword measurement and literature data analysis, which integrates cluster analysis and social network analysis. Also, both are important tools for mining research hotspots in a certain field and predicting development trends (14).

Science Citation Index Expanded (SCI-E) database, as one of the three major databases in the core collection of Web of Science (WOS) database, is an authoritative and high-impact citation index database of scientific journals. Therefore, this study intended to use VOSviewer and CiteSpace to visually analyze the literature related to the relationship between CHD and PCOS in the SCI-E database to explore the main research content and track the research hotspots. Based on the data analysis findings in the literature, we attempted to describe the significant impact of PCOS on the health integrity of patients in order to provide a reference for the further research direction of the relationship between PCOS and CHD and the preventive measures for PCOS patients with CHD.

2 Methods

2.1 Data source and search strategy

Our study referred to the general internationally accepted method of bibliometrics. The SCI-E database (<http://www.webofscience.com/>), the most common database for bibliometrics, was used to retrieve literature. The retrieval method was subject-term searching. Using keywords related to polycystic ovary syndrome, including “polycystic ovary syndrome”, “polycystic ovarian syndrome”, “PCOS”, and “Stein-Leventhal Syndrome”; and coronary heart disease-related keywords, including “coronary heart disease”, “CHD”, and “Coronary Diseases”, and operation method was “AND”. All obtained records results were downloaded in plain text format for subsequent analysis. We did all the searches and data exports on the same day (February 8, 2023) since metrics constantly changed over time.

2.2 Inclusion and exclusion criteria

The inclusion and exclusion of studies were based on the filters of the WOS database. The studies that met the following criteria were included (1): articles published in the period from January 1, 2000 to February 8, 2023 (2), articles about PCOS and CHD, (3) original articles or reviews, and (4) published in English. Exclusion criteria were (1) repeated publications, (2) proceeding paper, editorial material, meeting abstract, book chapters, letters, early access, correction, reprint, and other types. Two researchers strictly

screened the literature by detailed examining the abstract section according to the inclusion and exclusion criteria. The third researcher decided on the contents with differences and uncertainties.

2.3 Data collection and cleaning

The following basic information was collected for each article: countries, authors, institutions, journals, references and keywords. Keywords with the same meaning but in different styles were standardized: “syndrome pcos” was replaced by “polycystic ovary syndrome”, “coronary-artery disease” was replaced by “coronary heart disease”, “type 2 diabetes mellitus” was replaced by “type 2 diabetes”, “obese women” and “overweight” were replaced by “obesity”, “BMI” was replaced by “body mass index”.

2.4 Bibliometric software

The above plain text was imported into VOSviewer v.1.6.10 (13) and CiteSpace 5.5.R2 (14) software. VOSviewer (<http://www.vosviewer.com>) is software for mapping scientific knowledge, which can construct and visualize the relationship between network data. It shows the structure, evolution and cooperation of the knowledge domain with its outstanding feature of the ability of graphic display and large-scale data analysis. Compared with VOSviewer, CiteSpace software has its certain advantages in visualizing burst words and revealing the dynamic development and change of research hotspots and discipline.

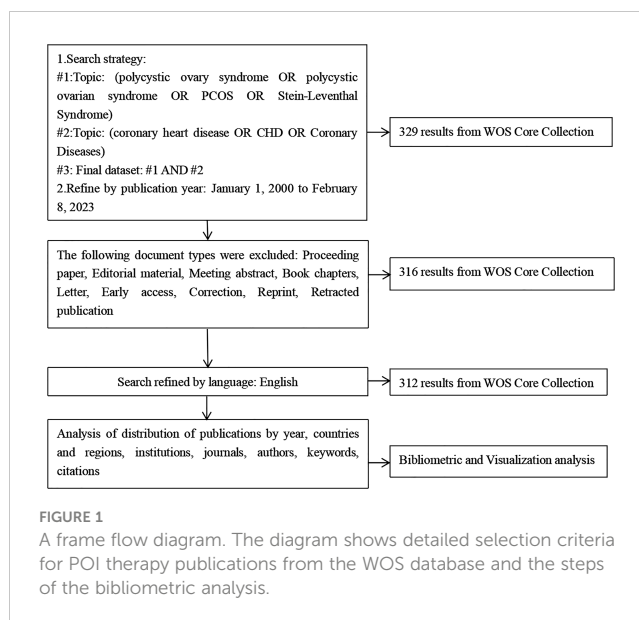
2.5 Data analysis

In the knowledge map generated by the VOSviewer, research projects were presented, including countries, institutions, authors, co-cited references and keywords, et al. The research projects can be demonstrated as nodes, and links between nodes represent collaboration, co-occurrence or co-citations among them. The bibliographic co-citation analysis and keyword co-occurrence analysis networks were used to construct a knowledge map of studies on the association between PCOS and CHD. Reference co-citation cluster analysis can summarize the main topics in the research field. Keyword co-occurrence analysis can illustrate the theme of the literature. The distribution trend of obtained research was generated by Microsoft Excel 2010 software. The burst words were analyzed by CiteSpace.

3 Results

3.1 Search results

There were a total of 312 records in the search results from January 1, 2000 to February 8, 2023 (Figure 1). More than half of the records were original articles (202/312, 64.7%), which greatly reflected the development trends and changes in the field of research on the association between CHD and PCOS. The



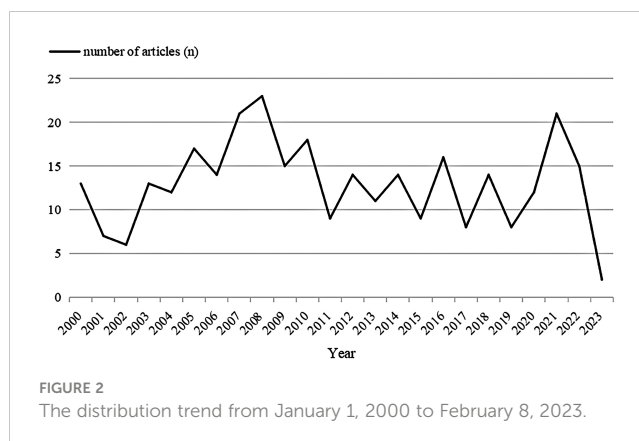
distribution of publications by year was shown in Figure 2, demonstrating a flat trend. As of February 8, 2023, there are only two articles, but this number will continue to increase.

3.2 Analysis of author's country of origin

According to the search results, 312 articles were from 46 countries, and the top 35 countries by the number of publications were presented in Figure 3. The top 10 countries engaged in studies on the association between PCOS and CHD were shown in Table 1. The United States of America (USA) had the largest number of publications (n=105), followed by England (n = 38) and Italy (n = 34). According to the citation analysis, there were 10,198 citations in the United States, followed by England (4,373 citations) and Australia (2,959 citations).

3.3 Universities and institutions

A total of 513 institutions were involved in these articles. Table 2 showed the top 15 institutions with more than five



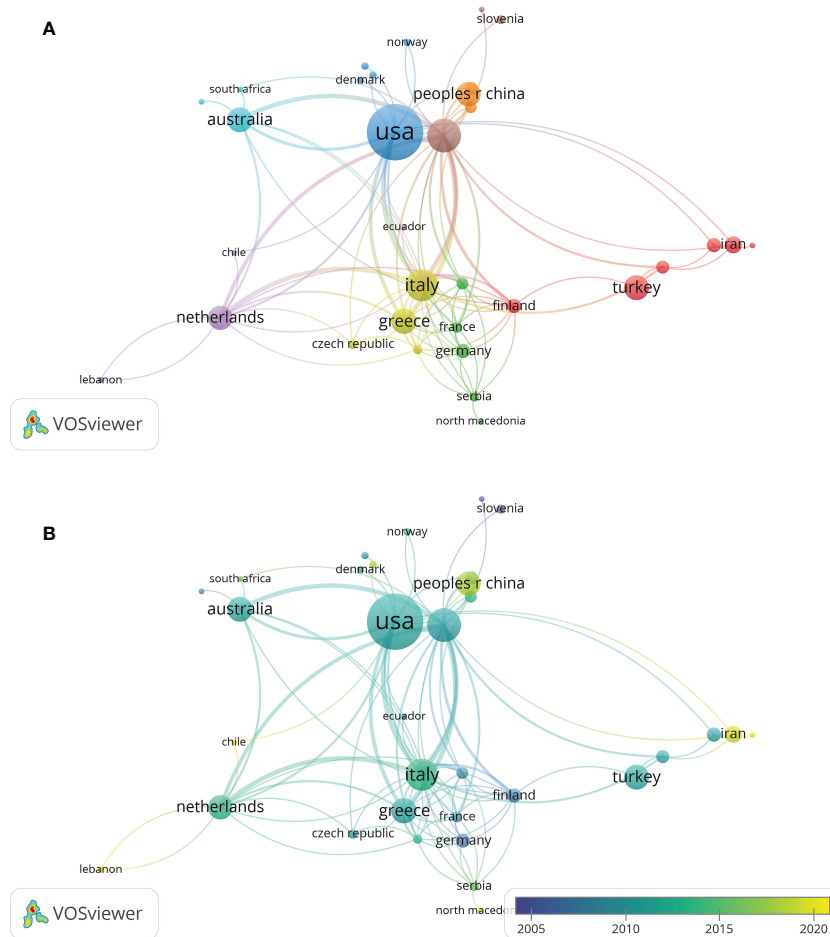


FIGURE 3
 A visualization map of countries. There are nodes (circles) in the figure, representing countries. The larger the circle, the more documents were produced by that country. A connection between 2 nodes means that 2 countries appear in a document simultaneously; that is, 2 countries have a cooperative relationship in this document. **(A)** Network diagram of the top 35 countries. **(B)** Dynamics and trends of the top 35.

TABLE 1 Top 10 most productive countries/regions with publications on the relationship of PCOS and CHD from 2000 to 2023.

Rank	Countries/regions	Documents (n)	Citations (n)	Average citations (n)	Total link strength
1	USA	105	10198	97.1238	23
2	England	38	4373	115.0789	25
3	Italy	34	1464	43.0588	15
4	Greece	22	1629	74.0455	9
5	Australia	21	2590	123.3333	8
6	Turkey	21	687	32.7143	2
7	Netherlands	20	1475	73.75	9
8	China	20	450	22.5	3
9	Iran	10	162	16.2	4
10	Spain	8	646	80.75	5

TABLE 2 Top 15 institutions with publications on the relationship of PCOS and CHD from 2000 to 2023.

Rank	Institution	Country/regions	Documents (n)	Citations (n)	Average citations (n)	Total link strength
1	Harvard University	USA	12	1387	116	47
2	University of Athens	Greece	10	1037	104	18
3	Monash University	Australia	9	1449	161	24
4	Aristotle University of Thessaloniki	Greece	8	464	58	7
5	Brigham & Womens Hospital	USA	8	781	98	23
6	Baylor College of Medicine	USA	6	1017	170	40
7	University of Glasgow	England	6	1937	323	7
8	University Medical Center Utrecht	Netherlands	6	481	80	15
9	Magna Graecia University Of Catanzaro	Greece	5	325	65	12
10	The Pennsylvania State University	USA	5	309	62	32
11	University College London	England	5	693	139	4
12	The University of Alabama at Birmingham	USA	5	431	86	22
13	University of California, San Francisco	USA	5	365	73	28
14	University of Pittsburgh	USA	5	483	97	15
15	Virginia Commonwealth University	USA	5	582	116	27

related publications. Among them, 8/15 were from the USA, 3/15 were from Greece, and 2/15 were from England. Harvard University was the top with the most publications, followed by the University of Athens, Monash University, Aristotle University of Thessaloniki, and Brigham & Women's Hospital. The top 15 institutions published 100 articles, accounting for 32.15% of the total. The University of Glasgow achieved the highest citations.

3.4 Analysis of author cooperation

A total of 1,518 authors were involved in related publications, authors with a frequency ≥ 2 times were incorporated in the collaboration network analysis, and 111 authors were obtained. Dr. Wang, Ping, Dr. Glueck, Charles J, Dr. Wild, Robert A, Dr. Lambrinouadaki, Irene, Dr. Azziz, and Dr. Ricardo had the highest number of publications. They were distributed in different clusters, showing close cooperative relationships with other authors (Figure 4). Although Dr. Wild, Robert A ranked non-first in the number of articles published, Dr. Wild, Robert A's group was at the center of the network, working tightly with other groups. In addition, Dr. Lambrinouadaki Irene was not associated with the center's collaboration network and had less collaboration with other authors.

3.5 Distribution of publications by journals

A total of 170 journals were included in related research. The top 11 journals with more than five publications were shown in Table 3. Over the past 23 years, the Journal of clinical endocrinology

& metabolism (24 records) showed the highest number of publications, followed by Fertility and sterility (18 records) and Human reproduction (11 records). In addition, the 2021 impact factor (IF) ranged from 2.28 (Gynecological Endocrinology) to 17.18 (Human reproduction update). The 5-year IF ranged from 2.24 (Gynecological Endocrinology) to 19.42 (Human reproduction update). Moreover, the Journal of Clinical Endocrinology and Metabolism represented the highest H-index, indicating the higher quality of studies published in this journal.

3.6 Top 10 citation publications

Of the 312 records, the top 10 publications ranked by citation were listed in Table 4. The most cited article was published in Endocrine Reviews by Frank W Booth et al. in 2012 (15) with 1201 citations, which was higher than that of the second paper (955 citations) (16). The third (17) and fourth (18) cited papers were reviews, with 670 and 523 citations, respectively. The fifth article by Wild S, Pierpoint T et al. (19) conducted a long-term follow-up in women diagnosed with PCOS in the United Kingdom before 1979, which concluded that a history of non-fatal cerebrovascular disease and cardiovascular risk factors, including diabetes, were more common in PCOS women compared with non-PCOS women.

3.7 Co-citation distribution

Through the co-citation analysis of the cited documents of related research, the research foundation in this field can be

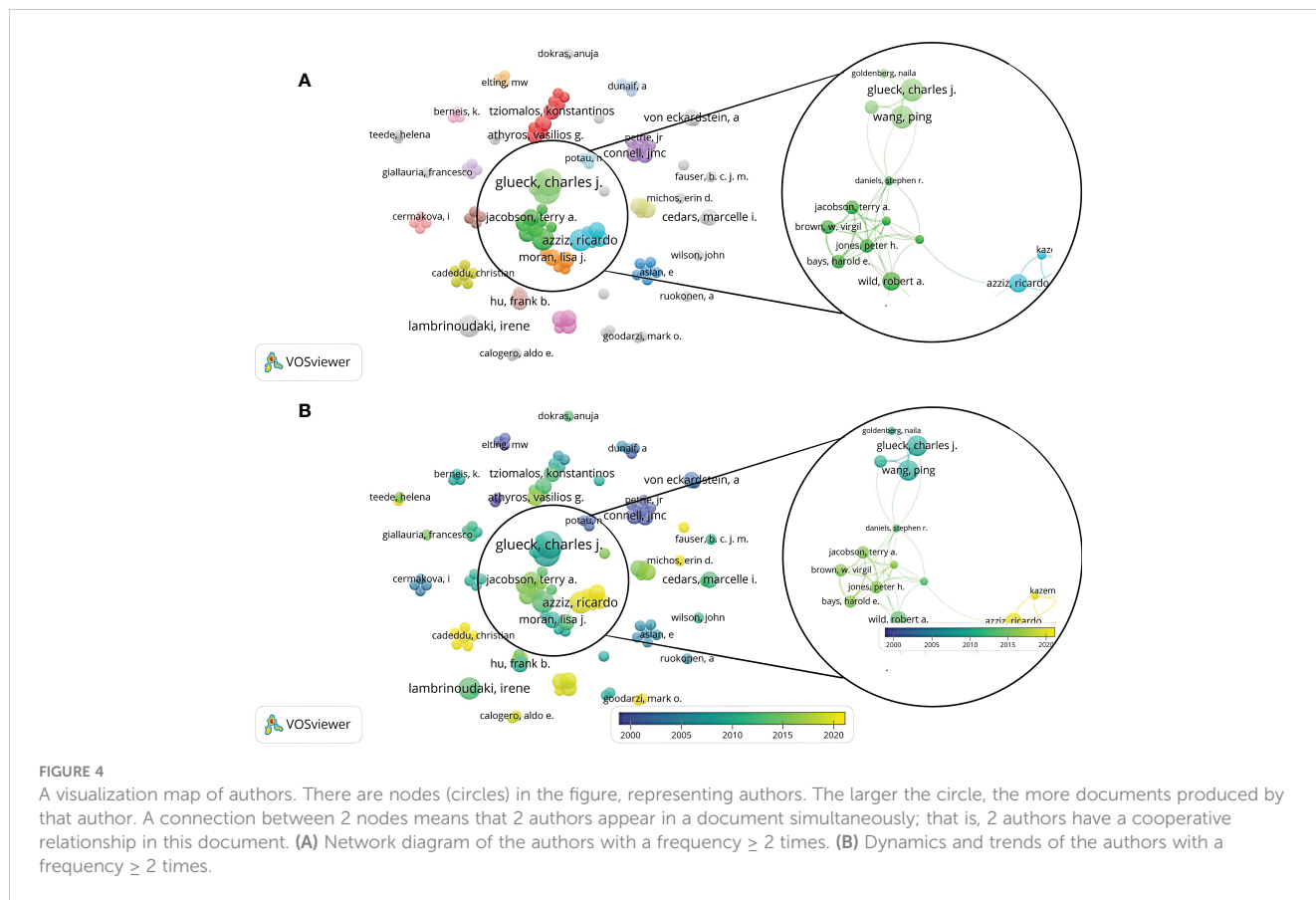


TABLE 3 Top 11 journals by the number of publications on the relationship of PCOS and CHD from 2000 to 2023.

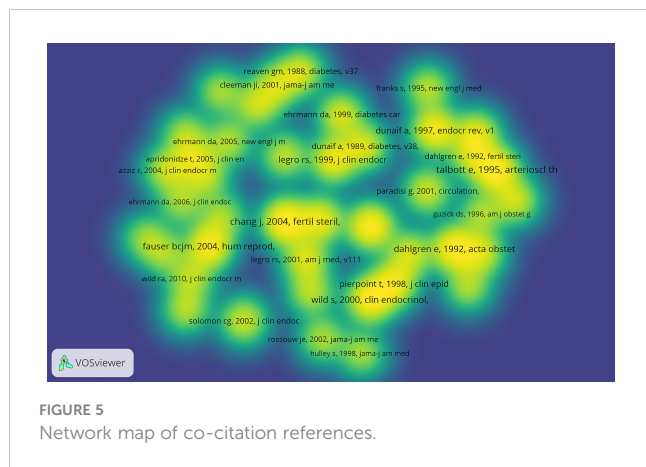
Rank	Journals	Documents (n)	Citations (n)	Average citations (n)	Total link strength	2021 IF	5-year IF	H-index
1	Journal of clinical endocrinology & metabolism	24	2880	120	92	6.13	6.83	363
2	Fertility and sterility	18	996	55	36	7.49	8.11	217
3	Human reproduction	11	758	67	27	6.35	7.74	236
4	Clinical endocrinology	7	629	90	39	3.52	3.82	153
5	Current pharmaceutical design	6	100	17	6	3.31	3.55	166
6	European journal of endocrinology	6	293	49	13	6.56	6.81	155
7	Gynecological endocrinology	6	219	37	5	2.28	2.24	65
8	Human reproduction update	6	1307	218	32	17.18	19.42	190
9	Metabolism-clinical and experimental	6	286	48	19	13.93	10.86	145
10	Journal of endocrinological investigation	5	176	35	15	5.47	4.63	87
11	Maturitas	5	138	28	10	5.11	5.52	105

effectively constructed. Of the 23,587 cited references, the minimum number of citations for a single document was set at 20. By analyzing the citation frequency of 23,587 documents, 42 documents reached the threshold (Figure 5). The size of the node corresponds to the frequency of references. Analysis of the top 10

citation publications was represented in Table 5. Of the 3227 journals of cited references, the minimum number of citations for a single journal was set at 100. By analyzing the citation number of the journals, 51 journals reached the threshold (Figure 6). The size of the node corresponds to the number of cited references.

TABLE 4 Top 10 citation publications.

Rank	Authors	Number of citations (n)	Titles	Journals
1	Booth (2012)	1201	Lack of exercise is a major cause of chronic diseases	Comprehensive physiology
2	Pedersen (2015)	955	Exercise as medicine - evidence for prescribing exercise as therapy in 26 different chronic diseases	Scandinavian journal of medicine & science in sports
3	Moran (2010)	670	Impaired glucose tolerance, type 2 diabetes and metabolic syndrome in polycystic ovary syndrome: a systematic review and meta-analysis	Human reproduction update
4	Liu (2003)	523	Androgens and cardiovascular disease	Endocrine reviews
5	Wild (2000)	469	Cardiovascular disease in women with polycystic ovary syndrome at long-term follow-up: a retrospective cohort study	Clinical endocrinology
6	Wu (2003)	440	Androgens and coronary artery disease	Endocrine reviews
7	Garvey (2016)	393	American association of clinical endocrinologists and american college of endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity	Endocrine practice
8	Talbott (2000)	382	Evidence for association between polycystic ovary syndrome and premature carotid atherosclerosis in middle-aged women	Arteriosclerosis thrombosis and vascular biology
9	Samson (2014)	338	Metabolic syndrome	Endocrinology and metabolism clinics of north america
10	Solomon (2002)	338	Menstrual cycle irregularity and risk for future cardiovascular disease	Journal of clinical endocrinology & metabolism



estrogen plus progestin, insulin sensitivity, genome-wide association, metabolism, and dyslipidemia, et al.

The keywords were divided into six categories in different colors: (1) the interaction between CHD risk factors and PCOS women; (2) the relationship between cardiovascular disease and female reproductive system hormone secretion; (3) the interaction between CHD and metabolic syndrome; (4) the relationship between c-reactive protein and endothelial function and oxidative stress in PCOS patients; (5) the potential positive effect of metformin on reducing CHD risk factors in PCOS patients; (6) the study of serum cholesterol and body-fat distribution in patients with CHD in PCOS.

Burst words detection results revealed that popular keywords had undergone obvious annual changes (Figure 8). In recent five years, the most popular keywords included “oxidative stress”, “genome-wide association”, “obesity”, “primary prevention”, and “sex difference”.

3.8 Analysis of keywords

A total of 1,491 keywords were extracted from the retrieved records. The minimum number of keyword occurrences threshold is set to 5, and 115 reached the threshold. The network map of the 115 keywords was shown in Figure 7A. Table 6 listed the top 10 keywords for each cluster. Table 7 listed the ranking of the top 10 keywords according to their frequency. 4 of the top 10 keywords were clustered in the red cluster. The top 3 keywords were “coronary heart disease (n=1641)”, “polycystic ovary syndrome (n=1614)”, and “insulin-resistance (n=1090)”. Figure 7B shows that the hot research directions of CHD and PCOS in recent ten years were oxidative stress, fatty liver-disease, primary prevention,

4 Discussion

This study conducted a statistical analysis of the literature on the WOS database to retrieve studies on the association between PCOS and CHD and obtained a total of 312 pieces of literature, generally reflecting the trend and hot spot of related research. Its research fields mainly focused on endocrinology metabolism, obstetrics and gynecology, cardiovascular diseases, and reproductive medicine, et al., indicating that the research field was relatively popular. The distribution trend result showed that the literature was on the rise from 2002 to 2008. However, it appeared to be a steady trend in recent years, which reflected that

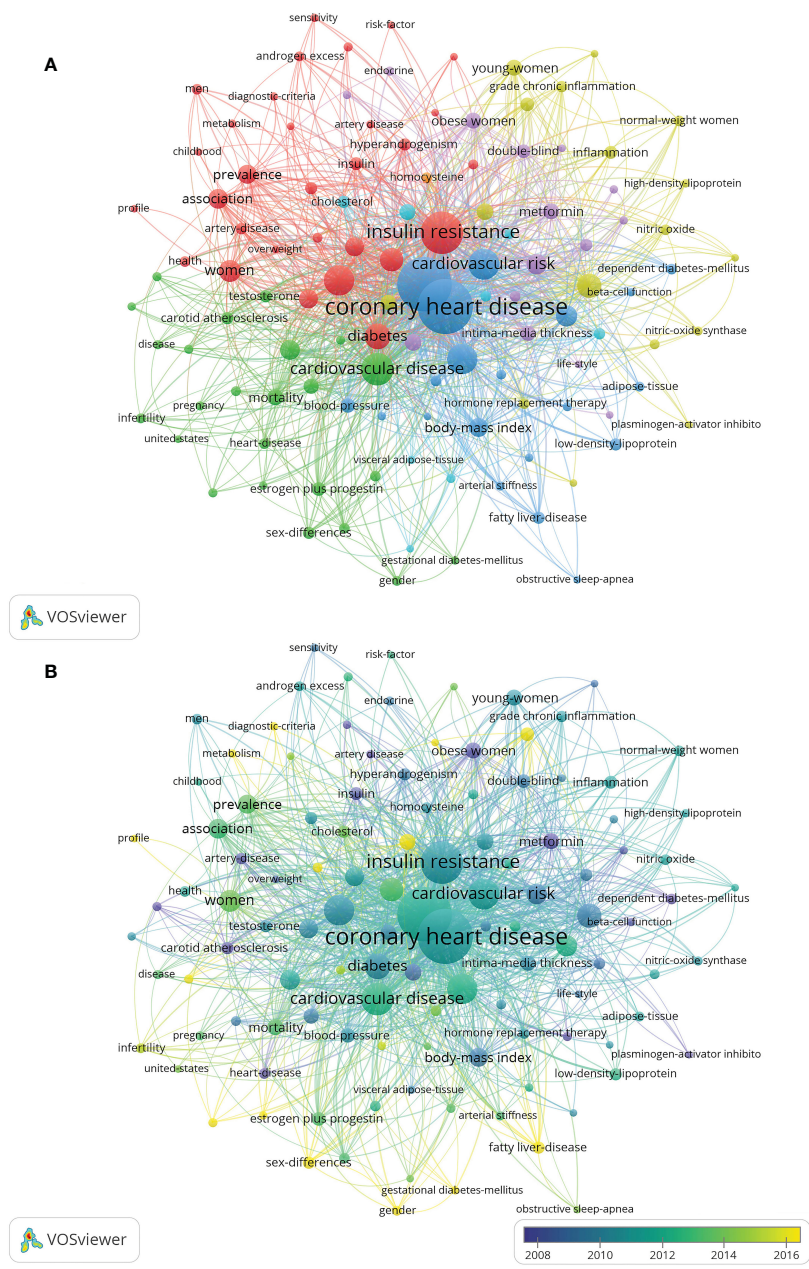


FIGURE 7 Visualization map of keywords. The minimum number of keyword occurrences threshold is set to 5. Of the 1,491 keywords involved in CHD in PCOS, 115 reached the threshold. **(A)** Network diagram of the keywords. **(B)** Dynamics and trends of the keywords.

comprehensive analysis of co-citation frequency showed that Wild, Talbott and other representatives had higher citation frequency on the whole. Journals with high co-citation frequency were mainly in the field of reproduction and endocrine metabolism.

A keyword is a high summary and refinement of the literature content, which reflects the core substance and value of the full article and responds to hot spots and research frontiers. Six categories were obtained by cluster analysis of keywords. The first cluster emphasized the association between CHD risk factors and PCOS. CHD risk factors include insulin resistance, diabetes and obesity et al. The incidence of cardiovascular disease (including hypertension and dyslipidemia) was higher in PCOS women than in

non-PCOS women (27). Young women with PCOS were at increased risk of myocardial infarction, angina and revascularization, but weight and T2DM were modifiable potential risk factors that warranted intervention (6). A study conducted on Chinese women with PCOS showed that serum lipids, glucose, insulin and homeostasis model assessment of insulin resistance (HOMA-IR) levels were higher in the hypertensives group than in the normotensive group after matching for BMI, which indicated that elevated blood pressure was a marker of metabolic risk and should be measured and monitored in PCOS women (28). In particular, a considerable number of young women with a long course of PCOS disease had

TABLE 6 Co-occurrence analysis of keywords and top 10 keywords in the 6 clusters.

Cluster	Color	Keywords (occurrences)
Cluster 1	red	insulin resistance (146) risk factors(74) diabetes(53) obesity(45) women(39) association(31) postmenopausal women(30) prevalence(30) term-follow-up(30) insulin(14)
Cluster 2	green	cardiovascular disease(88) myocardial-infarction(31) mortality(22) hypertension(19) estrogen plus progestin(15) sex-differences(13) carotid atherosclerosis(13) testosterone(13) menopause(10) heart-disease(10)
Cluster 3	blue	coronary heart disease(248) polycystic ovary syndrome(241) cardiovascular risk(80) metabolic syndrome(74) type 2 diabetes(36) body-mass index (30) blood-pressure(18) fatty liver-disease(13) low-density-lipoprotein(12) dependent diabetes-mellitus(9)
Cluster 4	yellow	c-reactive protein(48) endothelial function(24) young-women(21) atherosclerosis(20) oxidative stress(15) inflammation(14) grade chronic inflammation(11) hormone replacement therapy(10) nitric oxide(10) normal-weight women(9)
Cluster 5	purple	impaired glucose-tolerance(34) hormone-binding globulin(23) metformin(22) obese women(21) intima-media thickness(19) double-blind(15) plasminogen-activator inhibitor-1(13) weight-loss (9)endocrin (7) estradiol-cyproterone acetate(6)
Cluster 6	indigo	dyslipidemia(22) cholesterol(13) 3rd national-health(11) body-fat distribution(10) density-lipoprotein cholesterol(8) nutrition examination survey (7) visceral adipose-tissue(6) gender differences(5)

TABLE 7 Ranking of keywords usage frequency.

Rank	Keyword	Cluster	Total link strength	Frequency
1	coronary heart disease	3	248	1641
2	polycystic ovary syndrome	3	241	1614
3	insulin resistance	1	146	1090
4	cardiovascular disease	2	88	698
5	cardiovascular risk	3	80	573
6	risk factors	1	74	535
7	metabolic syndrome	3	74	580
8	diabetes	1	53	421
9	c-reactive protein	4	48	360
10	obesity	1	45	361

a significantly increased risk of CHD and should have a long-term health management plan. Even if treatment measures have been taken for the occurrence of cardiovascular disease, continuous or even lifelong follow-up should be conducted. Although there was a strong association between CHD risk factors and PCOS, no evidence suggested that women with PCOS might be affected by an increased risk of cardiovascular death (29).

The second cluster focused on the relationship between cardiovascular disease and female reproductive system hormone secretion. Testosterone promoted visceral fat accumulation and insulin resistance by inhibiting lipolysis and promoting adipogenesis (30). Furthermore, increased visceral fat was directly related to insulin resistance and carotid intima-media thickness (31, 32). According to existing studies, androgen excess and insulin resistance may be responsible for developing all features of metabolic syndrome in PCOS (29). Future studies should investigate in detail the potential role of androgen excess in determining insulin resistance status, particularly in relation to the high risk of developing T2DM.

The third and sixth clusters demonstrated the interaction between CHD and metabolic syndromes such as diabetes-mellitus and dyslipidemia et al. in PCOS patients. Both obese and non-obese PCOS patients had greater visceral fat than non-PCOS controls (33). Also, visceral fat index (VAI) levels were higher in the PCOS group than non-PCOS control after matching for age and BMI (34). PCOS women were more likely to be obese than in non-PCOS controls and prone to have more visceral fat and a higher visceral fat index, which was strongly associated with insulin resistance (34). Furthermore, studies have shown that lipid accumulation (LAP) measurement can help identify a high cardiometabolic risk subgroup in PCOS patients (35). In summary, PCOS was associated with several endocrine and metabolic diseases, including obesity, insulin resistance and diabetes, hypertension, and dyslipidemia, which increased the risk of subclinical cardiovascular disease (1). Although the presence of lipid abnormalities, fibrinolysis abnormalities, and insulin resistance predictably placed PCOS patients at high risk for cardiovascular disease (36), further and more prospective studies should be conducted to evaluate their correlation.

Top 25 Keywords with the Strongest Citation Bursts

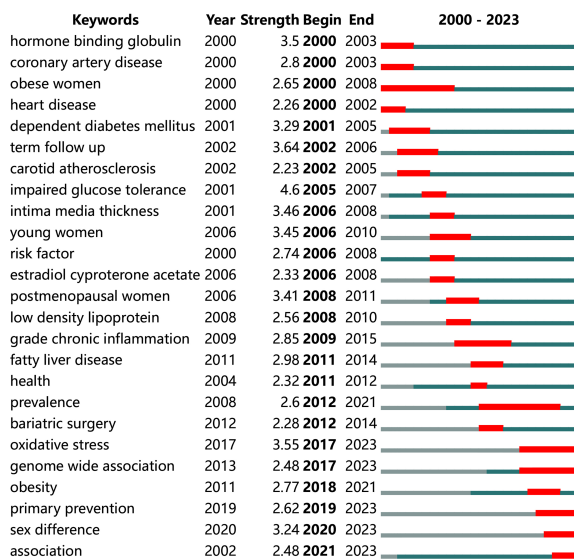


FIGURE 8
Top 25 keywords with the strongest citation bursts.

The fourth cluster illustrated the relationship between CRP, endothelial function, and oxidative stress in PCOS. As previously mentioned, PCOS patients had more visceral fat, its adipocyte hypertrophy triggered an inflammatory response, and hyperandrogenemia exacerbated the inflammatory response (37). Moreover, mononuclear cells in adipose tissue were initiated to secrete pro-inflammatory cytokines in response to glucose and saturated fat uptake (38). Jena et al. studied 58 women newly diagnosed with PCOS and found that inflammatory markers were higher in patients with PCOS than in non-PCOS control after matching for age and BMI (33). In addition, insulin resistance, oxidative stress, elevated plasma homocysteine levels, and changes in lipid profiles (a risk factor for cardiovascular disease) were more frequent in PCOS compared with healthy subjects (39). Serum high-sensitive CRP (HS-CRP) levels in patients with PCOS were positively correlated with BMI, LDL, total cholesterol (TC) and triglyceride and negatively correlated with HDL (40). Previous studies had shown a strong correlation between homocysteine and CRP expression in VSMCs, and elevated homocysteine levels induced CRP expression at the transcriptional and translational levels by controlling the n-methyl-D-aspartate receptor (NMDAR) signaling pathway in VSMCs (41, 42). Elevated homocysteine enhanced platelet adhesion to endothelial cells while promoting the production of pre-thrombotic factors such as tissue plasminogen activators and beta-thromboglobulin (43, 44). Therefore, endothelial dysfunction may be one of the multiple mechanisms that may increase the risk of CHD in PCOS, especially by resulting in arterial hypertension, which was strongly associated with disordered levels of reactive oxygen species (ROS) generated in oxidative stress progress (45).

As for the fifth cluster, we concluded the potential positive effect of metformin on reducing CHD risk factors in PCOS patients. A

study by Velazquez et al. (46) included 16 non-diabetic PCOS patients who took metformin (1.5 g/d) for eight weeks. The results found that metformin reduced PCOS patients' levels of the anti-proto plasminogen activator inhibitor type 1 with a 1.3% decrease in BMI. Metformin may be preferred over combined oral contraceptives (COCs) in patients with PCOS since COCs were associated with an increased risk of thrombosis compared to metformin. What's more, Burchall et al. (47) studied 60 overweight women with PCOS (mean BMI 37 kg/m²) who were randomly assigned to the metformin group, high-dose oral COC group, or low-dose COC plus spironolactone group. The results showed that abnormal coagulation events were observed in two COC groups but not in the metformin group. In addition, studies have shown that metformin had an advantage in reducing diastolic blood pressure and triglyceride, thereby predicting favorable metabolic and cardiovascular outcomes in women with PCOS. Moreover, metformin was more effective in reducing hyperandrogenemia indicators (48). However, there were different opinions. A previous study had shown that metformin could promote menstrual recovery in PCOS patients to a certain extent but has no regulating effect on fasting insulin, HOMA-IR, blood lipid, androstenedione and other secretory indicators (49). Carotid intima-media thickness (IMT), ambulatory blood pressure monitoring (ABPM) and other cardiovascular risk factors were not significantly affected (50). More studies are needed to explore the role of metformin in reducing the risk of CHD in PCOS patients.

This study detected 25 burst words that appeared from 2000 to 2023. The burst words reflected the emerging trends and abrupt changes in current research hotspots. According to Figure 8, the research hotspots in the recent five years were oxidative stress, genome-wide association, obesity, primary prevention, and sex difference. Since 2017, oxidative stress and genome-wide association have been maintained a high level of attention. Previous literature indicated a significant increase in oxidative stress in PCOS, leading to metabolic dysfunction and cardiovascular disorder features (51, 52). Therefore, the development of prevention and treatment strategies for CHD risk in these patients should involve further research on reducing oxidative stress. With the coming era of big data, genome-wide association study (GWAS) was an effective research strategy for the identification of disease susceptibility genes/loci, which pointed out the direction of PCOS research and laid a solid foundation for personalized diagnosis, prognosis and treatment of PCOS (53–55). Although GWAS provided important clues to the genetic basis of CHD in PCOS, further research is required, such as fine-mapping of susceptibility sites and functional studies of risk genes. Since 2018, burst words gradually turned to obesity and primary prevention, suggesting that the majority of scholars realize the importance of prevention. Also, previous studies suggested that after PCOS was diagnosed in obese women, they should be given primary prevention of CHD during the early stage (56, 57). Moreover, it is worth noting that sex different in the recent three years with a high strength score, and its research duration was shorter than other burst words, indicating the research results were still insufficient and there was less breakthrough research.

Similar to other bibliometrics studies, our research had some shortcomings that must be addressed. Our study's limitations were as follows: This study only retrieved the most commonly used WOS database, lacking studies on other databases, resulting in some relevant articles may not have been covered. Also, we retrieved articles written in English; thus non-English studies with high quality were not included in our study. Moreover, part of the meta-analysis was recognized as the original article in the WOS database, which may cause discrepancies in the number of reviews and original articles.

5 Conclusion

This study explored the relationship between PCOS and CHD and displayed a deep insight into the status and trends of the research field with the bibliometric analysis method. In recent five years, the hotspots of the association between PCOS and CHD were oxidative stress, genome-wide association, obesity, primary prevention, and sex difference. Our study had a certain reference value for further research on the relationship between PCOS and CHD and future relevant research topics hunting.

Data availability statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

Author contributions

XL and HH contributed equally to the research. XL, YW and HH retrieved articles. XL and HH wrote the first draft of the

manuscript. HZ and LW performed the data collection. JY provided figures. JF and SF critically revised the paper. SF designed research. JF provided funding support. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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