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State-of-the-Art on Gender Equality in Cardiovascular Research

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Abstract

Objectives: Research in cardiac pathologies has historically been affected by gender bias in clinical manifestations, risk factors, and clinical trials, evidencing the fundamental need to integrate gender equality. The aim of this study is to analyze research on cardiovascular disease (CVD) and gender equality, starting from 2015 when the sustainable development goals (SDGs) were established. The U.S. National Institutes of Health also urged the inclusion of sex as a biological variable in the research that underpins it.

Materials and Methods: International scientific production between 2015 and 2021 was evaluated using the Web of Science Citation Index-Expanded database, going deeper into the most prevalent pathophysiology and therapeutics that contribute to sex/gender-specific differences in cardiovascular (CV) research.

Results: A total of 288 out of the 848,178 original articles in cardiology dealt with gender equality (CV-SDG-5), with the USA being the main contributor. In the CV publications that integrate gender equality, the main thematic category was "public, environmental, and occupational health." The main pathologies highlighted were "hypertension," "diabetes mellitus," "stroke," and "myocardial infarction," and the predominant CV treatments were "hydroxymethylglutaryl-CoA reductase inhibitors" and "hypolipidemic agents."

Conclusions: Despite the efforts promoted by the 2030 Agenda and numerous public/private institutions promoting gender equality (SDG-5), only 0.03% of published CV research considers gender equality. This study highlights the importance of encouraging researchers to include sex and gender variables in their studies, and of increasing the commitment of public and/or private health research decision-makers to promote research that includes gender equality in its outcomes, in order to improve the diagnosis, treatment, and prognosis of CVD regardless of patient sex/gender.

Keywords: cardiovascular diseases; gender-related cardiovascular disease risk; SDG-5 gender equality; gender bias; women's hypertension; women's health care

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Introduction

Among the 17 sustainable development goals (SDGs) set by the United Nations (UN), the aim to improve global health by generating strategies, initiatives, and funding through global governance stands out.[1] Specifically, SDG-3, which focuses on health and well-being, has among its targets to reduce premature mortality from noncommunicable diseases (NCDs), such as cardiovascular diseases (CVD), cancer, diabetes, and chronic respiratory diseases, by one-third by 2030. CVD is the leading cause of death, and currently, no country is close to meeting the UN target or reducing risk factors such as hypertension, diabetes, and obesity.[2] According to the World Health Organization (WHO), 18 million people died from CVD in 2019, twice as many as from cancer, with stroke, diabetes, and obesity being the leading causes of death,[3] and ischemic heart disease being the cause of the highest overall age-standardized mortality from CVD.[4]

Several studies show that inequalities in age, sex, gender, country, and sociodemographic conditions affect CVD progression and mortality,[5] with sex referring to biological or physiological characteristics, and gender to socially constructed characteristics.[6] In 2022, the UN reported an insufficient reduction in mortality and the need for global cooperation and greater financial investment to overcome barriers to gender equality.[7] Despite a decline in CVD mortality among women in countries with high sociodemographic indices since 2012, there has been a reversal of the trend since 2017.[8] Conversely, in countries with low population growth, there has been an increase in CVD mortality among women, even outpacing that of men.[9] On the contrary, the reduction in CVD mortality is not equal between men and women for certain pathologies (coronary heart disease and stroke), with a greater reduction observed in men.[10,11] Some examples of inequalities in the perception and symptomatology of CVD between patients of different sex/gender have been described (acute coronary syndrome, coronary heart disease, and stroke,[12] atrial fibrillation,[13] torsades de pointes,[14] or carotid atherosclerosis disease[15]) along with biological differences, the prevalence of risk factors, and responses to treatment that contribute to differences in CVD mortality rates.[16] Therefore, CVD in women remain underresearched, underdiagnosed, and undertreated, and in 2019 these diseases amounted to 35% of total deaths in women and 45% of women over 20 years suffering from CVD.[17] This gender and sex disparity is evidence of gender bias in research, diagnosis, prevention, and access to cardiovascular (CV) care.[18] All this makes it necessary to further research on sex and gender equality in CVD, following the recommendations and guidelines of the UN Agenda 2030 on SDG-5, which focuses on achieving gender equality and women's empowerment.

Moreover, it is necessary to know the trends in research and clinical practice developed in cardiology from the perspective of gender equality, so it is of great interest to know the evolution of scientific production, collaboration, and impact in the field of CVD. To date, several bibliometric studies have been carried out in different CV areas, including ventricular arrhythmias,[19] coronary dysfunctions,[20] cardiothoracic surgery,[21] or heart transplantation.[22] However, no bibliometric studies have been carried out in relation to sex/gender variables in CV research in order to contribute to the design and implementation of policies on gender inequality in health.

The aim of this article is to analyze the current state of the scientific production that relates CVD to gender equality. We take 2015 as the starting point for our analysis because that is the year when the UN established the SDGs and the U.S. National Institutes of Health (NIH) initiated an expectation that sex as a biological variable should be factored into research designs, analyses, and reporting in vertebrate animal and human studies.[23,24]

Materials and Methods

Search strategy

The search of the literature relating to the CV field and gender equality was conducted using the Science Citation Index-Expanded (SCIE) database of the Web of Science (WoS) Core Collection. The search was limited to original articles excluding reviews, published between 2015 and 2021 and performed on October 19, 2022. The specific research profiles are described in Supplementary Appendix SA1. The search equation for CV articles ("CV" group) resulted from the combination of terms related to CV research (field: title-abstract-keywords) in addition to articles published in journals in the CV category of SCIE (field: Journal) (Supplementary Appendix SA1). A total of 848,178 records related exclusively to the "CV" group were obtained. Subsequently, to retrieve

articles on gender equality, specific terms that correspond to SDG-5 were selected and combined with the Scopus predefined terms for SDG-5. Finally, the previous CV search equation ("CV" group) merged with the SDG-5 query was conducted to obtain the sample of the study ("CV-SDG-5" group) (Supplementary Appendix SA1). A total of 403 documents were obtained, and they were included and organized in a relational database using the SQL software "Bibliometricos" (Supplementary Fig. S1).

Relevance analysis

Two researchers specializing in CVD and information science (C.R., J.C.V.Z.) screened the 403 retrieved documents and excluded 115 articles for lack of relevance to CVD and gender equality, which are listed in Supplementary Appendix SA2. A total of 288 articles finally formed the so-called "CV-SDG-5" group.

Database generation and information included

To compare the CV publications with the subset of publications dealing with SDG-5, the following information was extracted from the documents retrieved in both designed groups (CV and CV-SDG-5) and entered into a database generated in access: country, year, funding, access route, WoS subject category, and journal of publication. These variables were used to analyze the results. In the case of funding, it was assessed whether each published article was funded or unfunded. In addition, the journals with the most publications were analyzed according to the quartile (Q) in the 2021 edition of the Journal Citation Reports (JCR).

Subsequently, in the CV-SDG-5 group, the title of the article, the keywords, and the number of citations were also obtained. In order to find out the lines of research, the Major topics (the main subject of the document) and the Medical Subject Headings (MeSH) by which the documents were indexed in the PubMed/Medline database were extracted. The MeSH thesaurus provides a more exhaustive perception of knowledge by using a hierarchical and controlled language to index the documents compared with the systems used by other databases, such as the KeywordsPlus of SCIE of WoS.[25,26] The extraction of major topics and MeSH terms was done by searching the PubMed ID codes (PMIDs) of the 288 articles. A total of 282 documents (97.9%) were identified with PMIDs indexed in PubMed/Medline, of which 261 articles had MeSH terms assigned, that were downloaded to the access database generated for subsequent study.

Data analysis

A comparative analysis was made of the scientific production of the CV group with respect to CV-SDG-5, in terms of the number of articles, countries, funding, access route, WoS main collection categories, and journals. The impact analysis of the most productive journals was developed by selecting the JCR-SCIE category closest to the CV area and the Q that the journal occupies in that category. Regarding the study of open-access (OA) publishing models of the publications, it was carried out according to the current classification provided by the WoS Core Collection, which describes six different OA publishing models: Gold, Gold Hybrid, Free, Green Published, Green Accepted and Green Submitted.

The CV-SDG-5 group was then studied to assess the total number of citations received for the articles, the weighted citations (weighted citations = No. of citations received/years since publication), and the subject lines of the articles by analyzing keywords and descriptors.

Statistical analysis

In the CV and CV-SDG-5 groups, a descriptive analysis was performed to assess: country, year, funding, access route, WoS subject category, and journals. Explicit funding information was obtained for all articles retrieved in both groups and this field was normalized to funded or unfunded.

Funding and mode of publication were analyzed using Pearson's chi-square test, and statistically significant differences were considered to exist when $p < 0.05$.

In order to determine the main thematic lines, keywords were analyzed by developing a word cloud in the specific study of the CV-SDG-5, and an analysis of the frequency and occurrence of major topics and MeSH terms,[27] was also made.

Results

International scientific output on gender equality in CV research

Figure 1 shows the chronological evolution of international scientific production in the CV area. During the period analyzed (2015–2021), 848,178 articles were published on CV research (CV) which contrasts with 288 articles (0.03%) related to CV research and gender equality (CV-SDG-5), after excluding 115

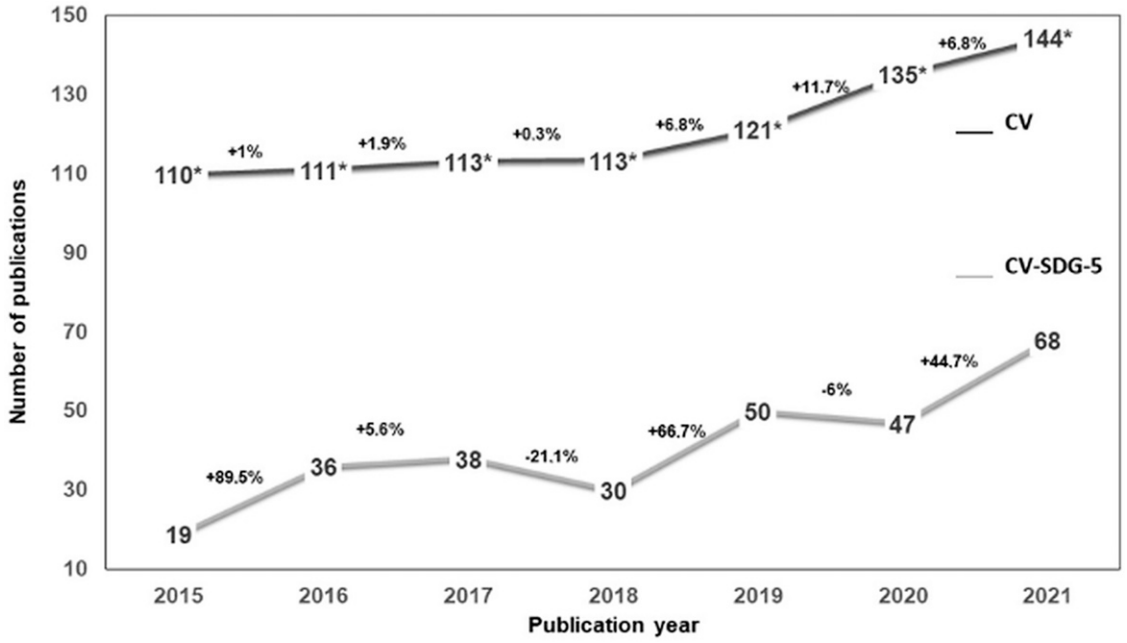

FIG. 1. Analysis of the chronological evolution of CV and CV-SDG-5 group publications. Representation of the number of publications and the annual percentage change, in the period 2015–2021. *The number of publications in the CV group has been divided by 1000 to adjust the scale of representation. CV, cardiovascular; CV-SDG, cardiovascular-sustainable development goals.

irrelevant articles. Both groups show an increasing trend in scientific production, but it is important to note that the percentage change obtained in 2021 compared with 2015 is 8 times higher in the CV-SDG-5 group (257.9%) compared with the CV group (31.4%). Interestingly, the percentage of funded articles in the CV-SDG-5 group (67.2%) was like that obtained for the CV group (60.8%).

Figure 2 shows the geographical distribution of the top-producing countries in CV and CV-SDG-5 research.

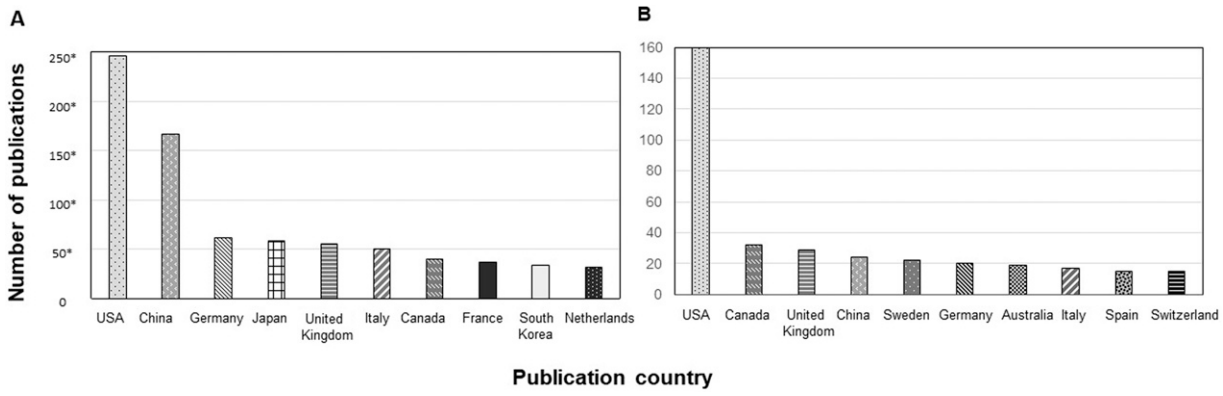

FIG. 2. Top 10 countries with the highest scientific production in the field of CV **(A)** and CV-SDG-5 **(B)**. *The number of publications in the CV group has been divided by 1000 to adjust the scale of representation.

In both cases, the USA is the largest producer, however, Canada ranks second in CV-SDG-5 publications (Fig. 2B) and seventh in the world in CV publications (Fig. 2A). China also makes a big difference, ranking second in terms of total CV production, but falling to fourth in terms of CV-SDG-5 publications. U.K., Germany, and Italy remain in the top 10 in both groups. Australia, Spain, Sweden, and Switzerland are among the top 10 countries in terms of CV-SDG-5 production, although they do not appear as the most productive countries in CV research, ranking 11th, 12th, 16th, and 17th, respectively, in the world ranking.[28] France, the Netherlands, and South Korea have the opposite profile, with a significant number of publications in the CV overview but are nevertheless at the bottom of the ranking in terms of sex/gender parity studies in CV research (positions 12th, 15th, and 22nd, respectively).

Main thematic categories and journals

The analysis made on the thematic categories to which the retrieved publications belonged showed that 5 out of the 10 most frequent categories were common to both CV and CV-SDG-5 groups (Fig. 3). The category with the highest number of publications in the CV-SDG-5 group encompasses "Public, environmental, and occupational health." At the same time, the CV-SDG-5 group is also dominated by categories that do not strictly belong to the area of health sciences, such as "Environmental Sciences."

The retrieved articles were published in a total of 8357 journals in the CV group, compared with 171 journals in the CV-SDG-5 group, which means that only 2% of the journals in the CV group include studies on SDG-5 (according to the search strategy based on terms specifically related to SDG-5 or gender issues). In the ranking of the most productive journals that stand out for integrating SDG-5 in their publications on CV health, were found journals that cover broader areas of biomedical knowledge than just the CV field (Table 1). In both cases, but in different positions, eight journals stand out as being among the most productive in both the CV group and CV-SDG-5 (marked with an asterisk in Table 1).

Table 1 lists the journals with the highest number of articles in CV research, comparing their impact with those obtained for the CV-SDG-5 group according to the Q to which they belong by using the 2021 edition of the SCIE of the JCR.

Regarding the evaluation of the OA publishing models of the publications, statistically significant differences were obtained, showing that the CV-SDG-5 papers are more published under OA than those of the CV group ($p < 0.05$). In any case, both "Green published" (37.8% CV-SDG-5 and 37.1% CV group) and "Gold" (29.2% CV-SDG-5 and 27.9% CV group) are the preferred OA mode in both CV and CV-SDG-5 groups (Supplementary Fig. S2).

Further analysis of the impact of the CV-SDG-5 articles based on the quantification of citations received showed that there were no significant differences

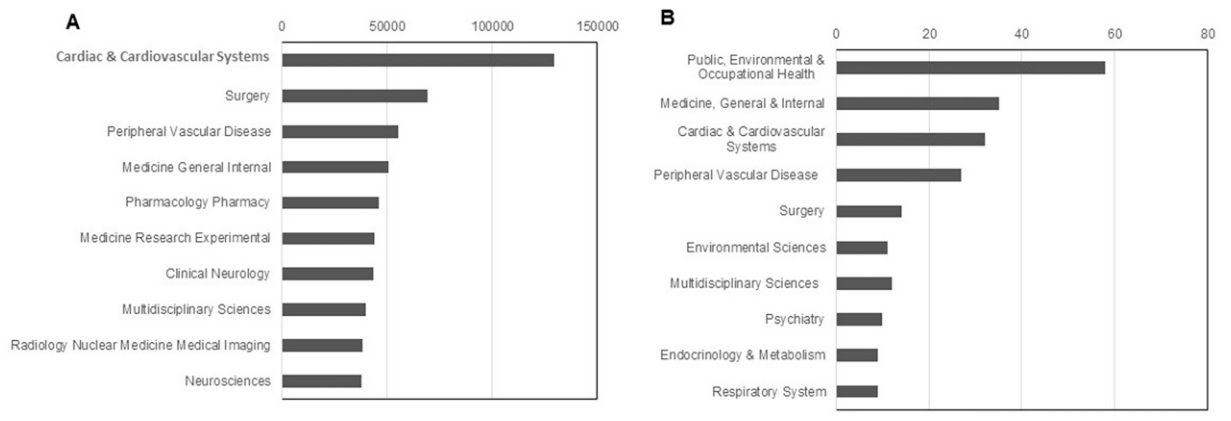

FIG. 3. The 10 most frequent WoS Categories in the scope of CV **(A)** and CV-SDG-5 **(B)**. WoS, web of science.

Table 1. Ranking of Journals with the Highest Frequency of Publications in the CV and CV-SDG-5 Groups

CV						CV-SDG-5				
Ranking	Journal	Frequency (%)	Rank	Country	Category WoS	Journal	Frecuency (%)	Rank	Country	Category WoS
1	*PLoS One**	17,350 (2)	Q2	USA	Multidisciplinary sciences	*BMC Public Health*	10 (5.9)	Q2	England	Public, environmental, and occupational health
2	*Scientific Reports**	14,264 (1.6)	Q2	England	Multidisciplinary sciences	*American Journal of Cardiology**	9 (5.3)	Q3	USA	Cardiac and cardiovascular systems
3	*Medicine*	6519 (0.8)	Q3	USA	Medicine, general, and internal	*BMJ Open**	7 (4.1)	Q2	England	Medicine, general, and internal
4	*International Journal of Cardiology**	5461 (0.6)	Q2	Ireland	Cardiac and cardiovascular systems	*PLoS One**	7 (4.1)	Q2	USA	Multidisciplinary sciences
5	*Journal of the American Heart Association**	5033 (0.6)	Q2	USA	Cardiac and cardiovascular systems	*Journal of Vascular Surgery**	6 (3.5)	Q2	USA	Peripheral vascular disease
6	*American Journal of Cardiology**	4034 (0.5)	Q3	USA	Cardiac and cardiovascular systems	*International Journal of Cardiology**	5 (2.9)	Q2	Ireland	Cardiac and cardiovascular systems
7	*World Neurosurgery*	3791 (0.4)	Q3	USA	Surgery	*Social Science and Medicine*	5 (2.9)	Q2	England	Public, environmental, and occupational health
8	*International Journal of Molecular Sciences*	3790 (0.4)	Q1	Switzerland	Biochemistry and molecular biology	*Lancet*	5 (2.9)	Q1	England	Medicine, general, and internal
9	*BMJ Open**	3573 (0.4)	Q2	England	Medicine, general, and internal	*International Journal of Environmental Research and Public Health**	4 (2.4)	Q2	Switzerland	Public, environmental, and occupational health
10	*Annals of Thoracic Surgery*	3447 (0.4)	Q2	USA	Cardiac and cardiovascular systems	*Journal of Cardiothoracic and Vascular Anesthesia*	4 (2.4)	Q3	USA	Cardiac and cardiovascular systems
11	*International Journal of Clinical and Experimental Medicine*	3384 (0.4)	Q4	USA	Medicine, research, and experimental	*Journal of the American Heart Association**	4 (2.4)	Q2	USA	Cardiac and cardiovascular systems
12	*Journal of Clinical Medicine*	3256 (0.4)	Q2	Switzerland	Medicine, general, and internal	*Journal of Women's Health*	4 (2.4)	Q2	USA	Medicine, general and internal

(*continued*)

Table 1. (Continued)

CV						CV-SDG-5				
Ranking	Journal	Frequency (%)	Rank	Country	Category WoS	Journal	Frecuency (%)	Rank	Country	Category WoS
13	*Journal of Stroke Cerebrovascular Diseases*	3214 (0.4)	NOT INDEXED IN JCR			*BMC Health Services Research*	3 (1.8)	Q3	England	Healthcare sciences and services
14	*Annals of Vascular Surgery*	3211 (0.4)	Q2	USA	Peripheral vascular disease	*Circulation*	3 (1.8)	Q1	USA	Cardiac and cardiovascular systems
15	*Stroke*	3062 (0.4)	Q1	USA	Peripheral vascular disease	*Clinical Cardiology*	3 (1.8)	Q3	USA	Cardiac and cardiovascular systems
16	*Catheterization and Cardiovascular Interventions*	2971 (0.3)	Q3	USA	Cardiac and cardiovascular systems	*Diabetes Research and Clinical Practice*	3 (1.8)	Q1	Netherlands	Endocrinology and metabolism
17	*Frontiers in Physiology*	2906 (0.3)	Q1	Switzerland	Physiology	*Economics and Human Biology*	3 (1.8)	Q3	Netherlands	Public, environmental, and occupational health
18	*Journal of Vascular Surgery**	2876 (0.3)	Q1	USA	Surgery	*Journal of Psychosomatic Research*	3 (1.8)	Q2	England	Psychiatry
19	*Experimental and Therapeutic Medicine*	2610 (0.3)	Q4	Greece	Medicine, research, and experimental	*Journal of the American College of Cardiology*	3 (1.8)	Q1	USA	Cardiac and cardiovascular systems
20	*Molecular Medicine Reports*	2563 (0.3)	Q3	Greece	Medicine, research, and experimental	*Preventive Medicine*	3 (1.8)	Q2	USA	Medicine, general and internal
21	*Oncotarget*	2541 (0.3)	Q1	USA	Oncology	*Resuscitation*	3 (1.8)	Q1	Ireland	Emergency medicine
22	*International Journal of Environmental Research and Public Health**	2454 (0.3)	Q2	Switzerland	Public, environmental, and occupational health	*Scientific Reports**	3 (1.8)	Q2	England	Multidisciplinary sciences
23	*Biomed Research International*	2344 (0.3)	Q3	USA	Medicine, research, and experimental	*Vascular Medicine*	3 (1.8)	Q2	England	Peripheral vascular disease
24	*Nutrients*	2344 (0.3)	Q1	Switzerland	Nutrients and dietetics	*European Journal of Preventive Cardiology*	3 (1.8)	Q1	England	Cardiac and cardiovascular systems

The rank represents the quartile of the journal obtained from the JCR (SCIE) 2021 database. Q1–Q4 represent the journals from highest to lowest impact factor in their category.
CV, cardiovascular; CV-SDG, cardiovascular-sustainable development goals; JCR, journal citation reports; SCIE, Science Citation Index-Expanded; WoS, web of science.

between the evaluated years, suggesting a very similar trend throughout the period between 2015 and 2021. The weighted mean number of citations per year was set at an average of 22.4 citations per year (7.9 standard deviations) (Supplementary Fig. S3).

Thematic analysis of publications on CV research and gender equality

Thematic analysis across the 3733 keywords retrieved from the 116 articles on CV-SDG-5 (75% of the articles contained author keywords) shows an important trend in the use of certain terms from the social domain and not so specific to CV medicine, such as "social determinants of health", "depression", and "gender gap," which are among the most frequently used keywords (Supplementary Fig. S4).

In order to characterize the main thematic lines of CV research and gender equality, as well as the emerging trends worldwide, an evaluation of Major topics and MeSH terms was carried out. Regarding major topics, 378 different major topics were obtained from the 282 articles. The analysis showed a hybrid character of the publications of the CV-SDG-5 group since half of the major topics were from the CV field among the top 10 ("CVD" $n = 24$, "Hypertension" $n = 13$, "Stroke" $n = 12$, "Cardiology" $n = 11$, and "Myocardial infarction" $n = 10$), together with terms related to gender differences, such as "Healthcare disparities" ($n = 27$) and "Health status disparities" ($n = 13$), followed by "Sex factors" and "Sexism" (11 and 9 articles, respectively) (Fig. 4A).

Concerning MeSH, a total of 364 different terms were identified and the most prominent MeSH terms were: "Humans" ($n = 259$), "Female" ($n = 245$), "Male" ($n = 214$), "Middle-aged" ($n = 136$), "Aged" ($n = 125$), and "Sex factors" ($n = 99$) (Fig. 4B).

To describe the content of the CV-SDG-5 publications more accurately, the 95 MeSH terms that were descriptors of CV pathologies, treatments, or CV risk factors (CVRFs) were selected and their frequency of occurrence in the articles was quantified. The most prominent MeSH terms were "Hypertension" (7%), "Diabetes Mellitus" (5%), "Stroke" (5%), "Smoking" (4%), and "Myocardial Infarction" (4%) (Fig. 4C). When looking more specifically at CV therapy treatments, the most common terms were "Hydroxymethylglutaryl-CoA Reductase Inhibitors" (HMG-CoA reductase inhibitors) and "Hypolipidemic Agents" (present in 4% and 1.4% of articles, respectively).

Discussion

The aim of this study is to analyze the presence of SDG-5, which focuses on the empowerment of women and girls, to characterize the state of gender equality research in the field of cardiology during the 5-year period 2015–2021. In this regard, 848,178 papers on cardiology, in general, have been found and have allowed putting into context the 288 articles related to gender equality in aspects such as scientific production by years, funded/unfunded, geographical location, open publications, and their impact. Subsequently, the subject matter was analyzed using the major topics and MeSH terms to discover where the current focal points of interest are.

The first thing that can be observed is that research has increased both in the overall area of cardiology and in publications that include SDG-5. There is a strong difference in the increase in publications in the case of work that includes gender equality, which is much higher than the increase in CV publications. This growth may be related to the launch of the 2030 Agenda for Sustainable Development and the SDGs in 2015, which, in addition to a short period of adaptation and knowledge of the SDGs, has had an impact on society, policies, and strategic lines, such as the current Council of Europe Gender Equality Strategy 2018–2023.[29] No differences were observed in terms of funding, but the CV-SDG-5 group contains a higher number of scientific articles that are OA. This is in line with the United Nations Educational, Scientific and Cultural Organization-UNESCO's assertion that open science can be a powerful tool for reducing inequalities, especially when it comes to providing access to knowledge for the most vulnerable populations.[30]

In the last 5 years, 5 out of the 10 most productive countries in cardiology have included gender equality in their research, mostly those from the Americas and Europe, with only two representatives from other continents (Australia and China). This is in line with the ranking on SDG compliance reported by the University of Cambridge.[31]

On the contrary, the works of the CV-SDG-5 group belong to multidisciplinary WoS thematic areas close to the social sciences, highlighting the category "Public, Environmental, and Occupational Health", which underlines the importance of the gender perspective in sociocultural, economic, and environmental factors related to CV health.[32] An analysis of the scientific

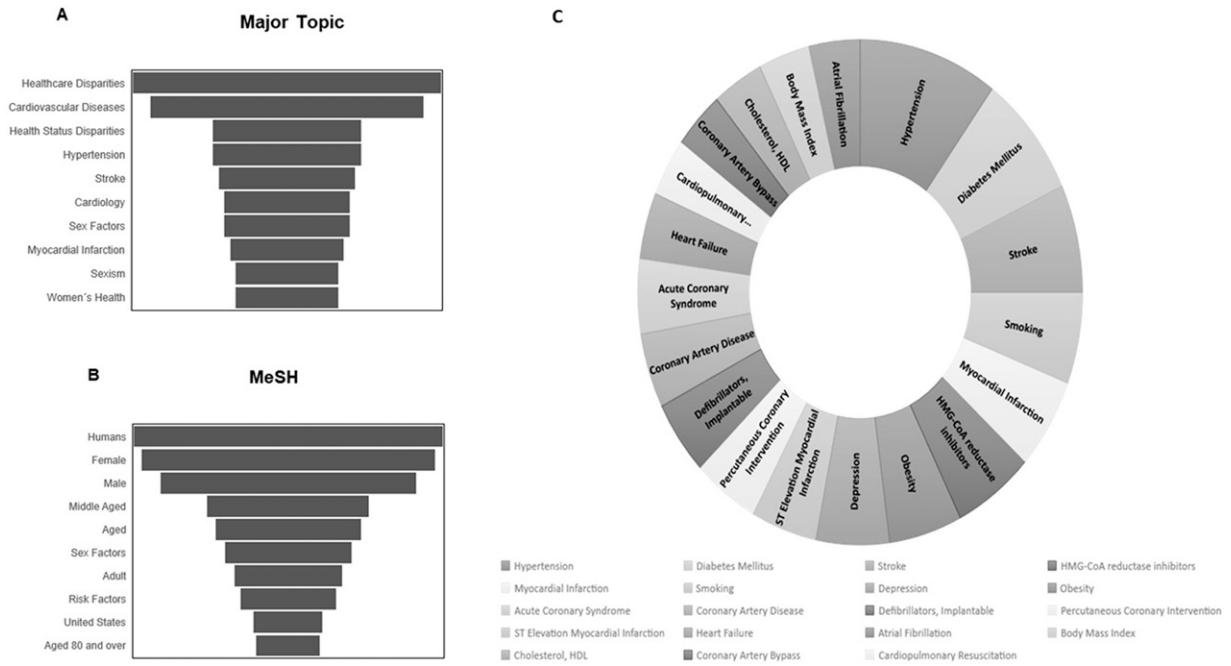

FIG. 4. Analysis of the principal lines of the cardiovascular research linked with gender equality (CV-SDG-5). Frequency of Major topic **(A)**. Frequency of MeSH terminology **(B)**. MeSH terminology related to gender equality on cardiovascular risk factors, treatments, and pathologies (MeSH terms with a frequency higher than 7 are represented) **(C)**. MeSH, medical subject headings.

impact of the most productive journals reveals that articles addressing gender equality in cardiology are published in those journals with the highest scientific impact, indicating their relevance and their influence on scientific policymakers. In addition, there are three highly cited articles on CV-SDG-5 in 2018 (53.5, 42.8 and 101.8 citations, respectively) and another article in the Lancet in 2017 with 521.8 citations analyzing gender differences in global health standing out, showing an increasing interest in the scientific community related to the research in the CV area taking into account gender equality. In the same vein, our study shows the commitment of certain CV journals to also contribute to the dissemination of studies that take into account SDG-5 and CV health, thereby increasing the awareness of researchers and clinicians about the importance of integrating sex and gender variables at all stages of biomedical research,[33] and to CV clinical practice.[24,34]

Currently, there is less clinical trial data available on women due to the over-representation of men and the historical exclusion of women from these trials, with only 38% of clinical trial participants being women by 2020.[35] This has led to gender bias in drug development and has created a need for new studies with re-adjust therapeutic strategies in women for certain heart diseases, antihypertensive treatments digoxin or aspirin and statins.[36,37] The thematic analysis of our study (keywords, Major topics, and MeSH terms) reveals the most frequent drug and pathologies in CV-SDG-5 publications "HMG-CoA reductase inhibitors," "Hypertension," "Stroke," and "Myocardial infarction," which is consistent with previous research on the differences between men and women in the onset, development, and evolution of these pathologies. For example, hypertensive women have a higher risk of mortality than men,[38,39] as well as there are differences in the risk of stroke and myocardial infarction, pathologies in which multiple differences between men and women have been clearly evidenced.[38–41] On the contrary, our study highlights high density lipoproteins (HDL) cholesterol and statins, which makes sense since the regulation of lipid profile by these treatments applied in CVD represents

one of the major gender differences in treatment and response.[42] Furthermore, it has also been observed that the most prominent risk factors are diabetes mellitus, smoking, depression, obesity/body mass index, and HDL cholesterol. This is in line with the classification of Vogel et al.,[18] which includes 5 of these CVRFs in the category of those that "affect both sexes," but depression is classified among "those CVRFs that indirectly affect women's CV health" and that are related to their socioeconomic and psychological environment.[18] Diabetes mellitus is also prominent in our study, which is logical as women with diabetes mellitus are at higher risk of CVD than men respectively.[43]

In the USA, strategies for the inclusion of sex and gender perspectives in health research have been developed. In this context, the NIH[23] and the U.S. Food and Drug Administration (FDA) are committed to supporting science and clinical trials that incorporate sex and gender perspectives.[44] In June 2015, the NIH published notice number NOT-OD-15-102 entitled "Consideration of sex as a biological variable in NIH-funded research", which was followed by formal guidance on the new policy for the inclusion of the sex variable,[23] in health research, including CV medicine. Additional guidance, which was developed by the NIH Office of Research on Women's Health in partnership with the FDA Office of Women's Health in 2020, is titled "Bench-to-Bedside: Integrating Sex and Gender to Improve Human Health."[23] In 2017, WHO introduced a policy on gender parity in staffing participating in the UN system-wide action plan on gender equality and the empowerment of women (UN-SWAP)[45] and evaluating the integration of issues related to gender, equality, and human rights.[46,47] This recommendation to mainstream gender in research is reflected in both the 2030 Agenda and the SDGs.[46] Furthermore gender affects all SDG targets as it interacts with and influences other determinants in health system risks and responses.[48]

Our study reveals a worrying lack of gender equality in international CV research, with only 0.03% of publications assessing the presence of SDG-5. The U.S. is a leader in scientific production in both cardiology research and CV research related to gender equality. In CV-SDG-5 research, diabetes mellitus, smoking, depression, and obesity are among the most common risk factors in the publications analyzed. It is advisable to strengthen policies that lead to studies on therapeutic and preventive strategies for women in these areas.

Conclusion

In conclusion, our study detected a significant increase in studies incorporating gender equality in CV research since 2015. However, a recent study analyzing clinical practice guidelines in cardiology showed gaps in management and specific recommendations for female CV patients.[49] This has led to the need for updates that reflect the importance of sex/gender inclusion in this field. Therefore, although there have been important socioeconomic efforts to promote knowledge of sex/gender differences in CVD for more than 20 years, it is still necessary to develop actions aimed at integrating the gender perspective in research, clinical practice, medical care, and the perception of patients themselves.

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Authors' Contributions

C.R.: Conceptualization, methodology, data collection, formal analysis, and writing—original draft, review, and editing. A.S.C.: Conceptualization, data collection, methodology, formal analysis, and writing—original draft. R.L.D.: Conceptualization, methodology, formal analysis, writing—original draft, review and editing, supervision, and funding acquisition. J.C.V.Z.: Conceptualization, methodology, formal analysis, writing—original draft, review and editing, supervision, and funding acquisition.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are available in the Zenodo repository. Available from: https://zenodo.org/record/7648814

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The authors declare that they have no competing interests.

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Supplementary Material

Supplementary Figure S1
Supplementary Figure S3
Supplementary Figure S4
Supplementary Appendix SA1
Supplementary Appendix SA2

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Abbreviations Used

CV = Cardiovascular
CVD = Cardiovascular disease
CVRFs = Cardiovascular Risk Factors
FDA = Food and Drug Administration
HDL = High Density Lipoproteins
HMG-CoA = reductase inhibitors Hydroxymethylglutaryl-CoA reductase inhibitors
JCR = Journal Citation Reports
MeSH = Medical Subject Headings
NCDs = Noncommunicable-diseases
NIH = U.S. National Institutes of Health
OA = Open-Access
PMIDs = PubMed ID codes
Q = Quartile
SCIE = Science Citation Index-Expanded
SDG-3 = Sustainable Development Goal Number 3
SDG-5 = Sustainable Development Goal Number 5
SDGs = Sustainable Development Goals
UN = United Nations
UNESCO = United Nations Educational, Scientific and Cultural Organization
UN-SWAP = UN System wide action plan on gender equality and the empowerment of women
WHO = World Health Organization
WoS = Web of Science