

Female Infertility: Cardiovascular Disease Risk Factor or Marker of a Population at Cardiovascular Risk?

Maria Alayde Mendonça Rivera,^{1,2} Ivan Romero Rivera,^{1,2} Glauca Maria Moraes de Oliveira³

Universidade Federal de Alagoas,¹ Maceió, AL – Brazil

Santa Casa de Misericórdia de Maceió,² AL – Brazil

Universidade Federal do Rio de Janeiro,³ Rio de Janeiro, RJ – Brazil

According to the World Health Organization, approximately 17.5% of the adult population (1 in every 6 people in the world) suffers from infertility, defined as the inability to conceive after 12 months of regular unprotected sexual intercourse.¹ The prevalence varies little between regions, with similar rates in high-, middle-, and low-income countries, constituting a global public health problem.¹

Approximately 85% of infertile couples have an identifiable cause for infertility, whereas the remaining 15% have unexplained infertility. As shown in the Figure 1, infertility can be attributed to numerous causes and risk factors, the treatment of which can eventually contribute to the couple's fertility.¹

Cardiovascular disease (CVD) accounts for, on average, 30% of global mortality in men and women and encompasses a broad spectrum of diseases, with different forms and degrees of presentation, including ischemic heart disease (sudden cardiac death, acute myocardial infarction, unstable angina, stable angina); cerebrovascular disease (ischemic and hemorrhagic stroke, transient ischemic attack, subarachnoid hemorrhage); peripheral vascular disease; heart failure (with preserved, intermediate, and reduced ejection fraction); and atrial fibrillation.²

This group of diseases shares numerous risk factors common to men and women (aging, family history, hypertension, diabetes, hypercholesterolemia, smoking), in addition to others that are exclusive (early menarche, menstrual disorders, premature ovarian failure, polycystic ovary syndrome, endometriosis) or have a greater impact on women (depression, anxiety).²

In women, it is observed that numerous risk factors for infertility (smoking, obesity, polycystic ovary syndrome, premature ovarian failure, menstrual disorders, autoimmune diseases, endometriosis) are also related to the development of CVD, making it necessary to

expand and deepen research in this field, considering the multiplicity of causes of infertility, as well as the multiplicity of causes and clinical expression of CVD.¹⁻⁴

Based on observational studies, infertility has been considered a marker for the development of immunological diseases, cancer, and CVD and for a shorter life expectancy in men and women, although it is unclear whether this propensity occurs for reasons related to lifestyle (for example, greater alcohol consumption, smoking, or unhealthy eating habits), biological mechanisms, or an interaction of both.⁵

In men, infertility is associated with a higher incidence of testicular, prostate, bladder, and thyroid cancer; melanoma; lymphoma; ischemic heart disease; diabetes; and hypertension.⁶

In women, infertility increases the incidence of breast, ovarian, and endometrial cancer. When associated with polycystic ovary syndrome, infertility appears to increase the incidence of hypertension (after 45 years of age), hypercholesterolemia, and diabetes mellitus (before 45 years). Other hormonal changes related to infertility (menstrual irregularities, premature ovarian failure, spontaneous abortions) may be associated with the future occurrence of CVD, in the form of ischemic heart disease, stroke, and heart failure.⁷⁻⁹

There are no clinical trials on infertility and the future risk of CVD. Cross-sectional observational studies have shown that women diagnosed with infertility have worse cardiovascular health, with higher body mass index; higher levels of total cholesterol, LDL-cholesterol, triglycerides, blood glucose, and C-reactive protein; and lower levels of HDL-cholesterol,⁷⁻⁹ as well as a higher prevalence of metabolic syndrome⁹ and mental health conditions such as anxiety and depression.¹ This profile contributes independently to the future risk of CVD.³

Regarding the future development of CVD in women diagnosed with infertility, there are still inconsistent results. Based on longitudinal observational studies, with follow-ups ranging from 7 to 28 years, there are reports that infertility is associated with a higher prevalence of dyslipidemia and diabetes, as well as a higher future risk of ischemic heart disease, stroke, and heart failure with preserved ejection fraction. Other studies have shown no association between infertility and the future occurrence of obesity, hypertension, metabolic syndrome, heart failure, and stroke.⁷⁻⁹

Considering the high prevalence of female infertility in the world population,¹ the frequent association of this condition with other cardiovascular risk factors,²⁻⁵ and the lack of data on the long-term impact of hormonal infertility treatment on the future maternal risk of CVD,¹⁰ there is a need for clinical

Keywords

Infertility; Risk Factor; Cardiovascular Disease; Female Sex.

Mailing Address: Maria Alayde Mendonça Rivera •

Universidade Federal de Alagoas Faculdade de Medicina – BR 104. Postal Code 57072-900, Campus A. C. Simões Maceió, AL – Brazil

E-mail: malayde1@uol.com.br, malayde@cardiol.br

Manuscript received April 14, 2026, revised manuscript April 16, 2026, accepted April 16, 2026

Editor responsible for the review: Carlos Rochitte

DOI: <https://doi.org/10.36660/abc.20250250i>

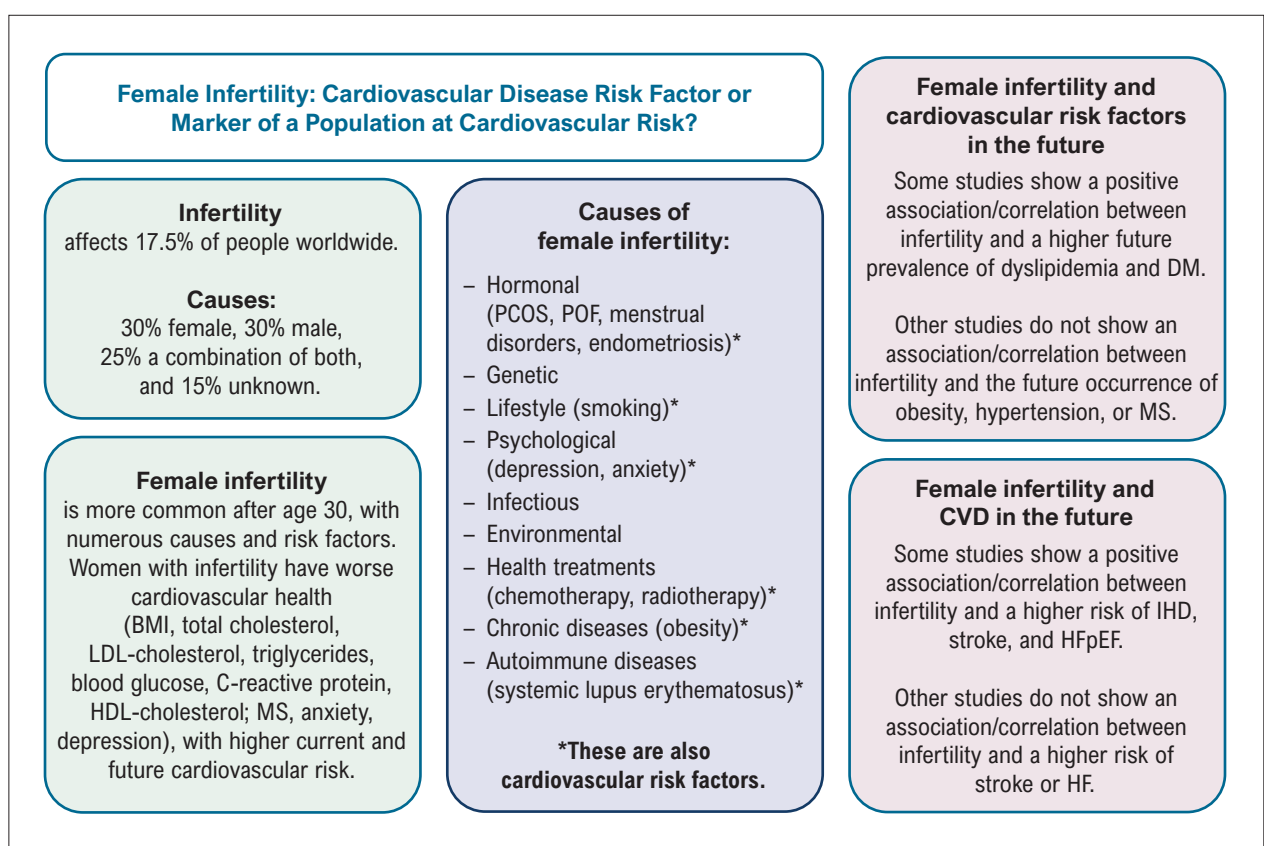


Figure 1 – Female infertility and cardiovascular risk. BMI: body mass index; DM: diabetes mellitus; HDL: high-density lipoprotein; HF: heart failure; HFpEF: heart failure with preserved ejection fraction; IHD: ischemic heart disease; LDL: low-density lipoprotein; MS: metabolic syndrome; PCOS: polycystic ovary syndrome; POF: premature ovarian failure.

trials designed to address these questions, in order to expand women's cardiovascular care.

Author Contributions

Conception and design of the research, Acquisition of data, Analysis and interpretation of the data and Writing of the manuscript: Rivera MAM, Rivera IR, Oliveira GMM; Critical revision of the manuscript for intellectual content: Rivera MAM, Rivera IR.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

Use of Artificial Intelligence

The authors did not use any artificial intelligence tools in the development of this work.

Data Availability Statement

The underlying content of the research text is contained within the manuscript.

References

1. World Health Organization. Infertility Prevalence Estimates, 1990–2021. Geneva: World Health Organization; 2023.
2. Oliveira GMM, Almeida MCC, Marques-Santos C, Costa MENC, Carvalho RCM, Freire CMV, et al. Position Statement on Women's Cardiovascular Health - 2022. *Arq Bras Cardiol.* 2022;119(5):815-82. doi: 10.36660/abc.20220734.
3. Skåra KH, Hernáez Á, Næss Ø, Fraser A, Lawlor DA, Burgess S, et al. Cardiovascular Disease Risk Factors and Infertility: Multivariable Analyses and One-Sample Mendelian Randomization Analyses in the Trøndelag Health Study. *Hum Reprod Open.* 2024;2024(3):hoae033. doi: 10.1093/hropen/hoae033.
4. Luo M, Li J, Xiao X, Wu P, Zhang Y. Associations between Cardiovascular Health and Female Infertility: A National Population-Based Study. *PLoS One.* 2024;19(7):e0306476. doi: 10.1371/journal.pone.0306476.
5. Tang H, Yang X, Li Z, Zhang Y, Chen H, Dai M, et al. Association between Female Infertility and Stroke Mortality: Evidence from the PLCO Cancer Screening Trial. *Front Endocrinol.* 2024;15:1433930. doi: 10.3389/fendo.2024.1433930.
6. Farland LV, Wang YX, Gaskins AJ, Rich-Edwards JW, Wang S, Magnus MC, et al. Infertility and Risk of Cardiovascular Disease: A Prospective Cohort Study. *J Am Heart Assoc.* 2023;12(5):e027755. doi: 10.1161/JAHA.122.027755.
7. Murugappan G, Leonard SA, Farland LV, Lau ES, Shadyab AH, Wild RA, et al. Association of Infertility with Atherosclerotic Cardiovascular Disease among Postmenopausal Participants in the Women's Health Initiative. *Fertil Steril.* 2022;117(5):1038-46. doi: 10.1016/j.fertnstert.2022.02.005.
8. Zhu F, Qi H, Bos M, Boersma E, Kavousi M. Female Reproductive Factors and Risk of New-Onset Heart Failure: Findings from UK Biobank. *JACC Heart Fail.* 2023;11(9):1203-12. doi: 10.1016/j.jchf.2023.02.019.
9. Cairncross ZF, Ahmed SB, Dumanski SM, Nerenberg KA, Metcalfe A. Infertility and the Risk of Cardiovascular Disease: Findings from the Study of Women's Health Across the Nation (SWAN). *CJC Open.* 2020;3(4):400-8. doi: 10.1016/j.cjco.2020.11.011.
10. Farland LV, Grodstein F, Srouji SS, Forman JP, Rich-Edwards J, Chavarro JE, et al. Infertility, Fertility Treatment, and Risk of Hypertension. *Fertil Steril.* 2015;104(2):391-7. doi: 10.1016/j.fertnstert.2015.04.043.



This is an open-access article distributed under the terms of the Creative Commons Attribution License