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Systematic Review/Meta-analysis

Prevalence of Cardiovascular Risk Factors in Women With Obstructive Coronary Disease Requiring Revascularization: A Meta-analysis

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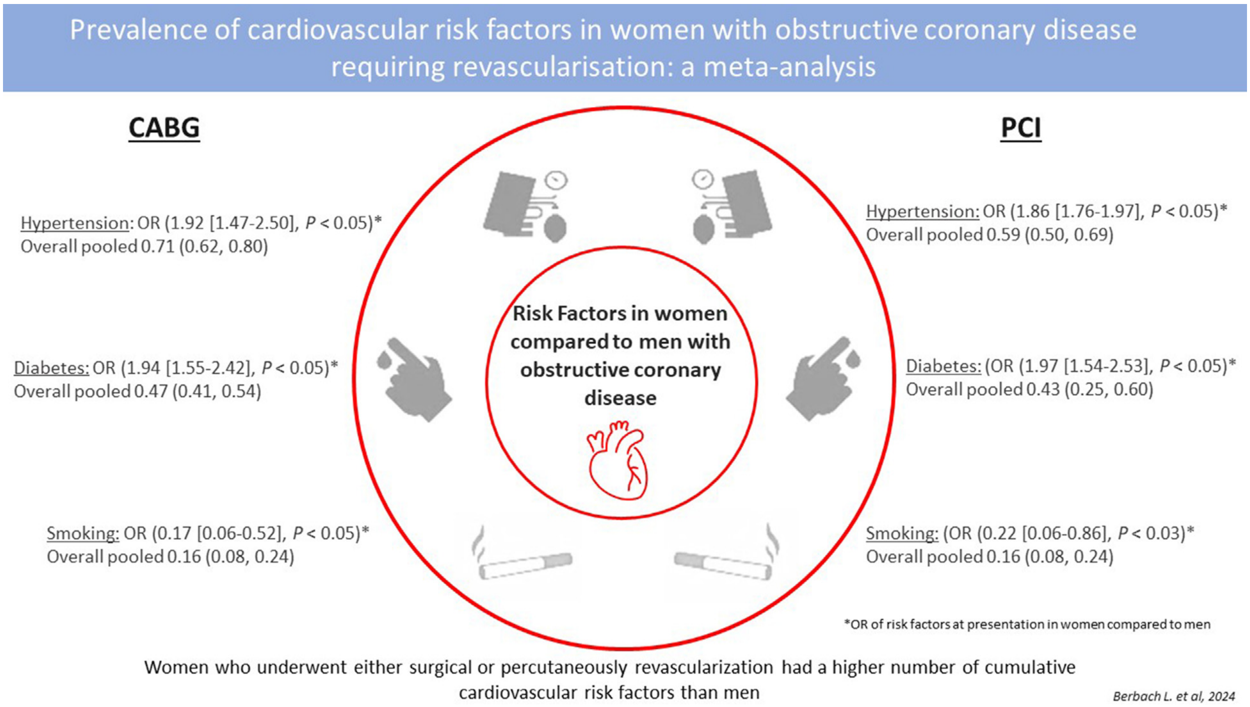

ABSTRACT

Background: Cardiovascular disease continues to be the primary cause of premature mortality in women, who previously have been overlooked in clinical trials. Several studies showed that women undergoing coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) present more cardiovascular risk factors at baseline, develop more postprocedural complications, and have a

RÉSUMÉ

Contexte : Les maladies cardiovasculaires demeurent la principale cause de décès prématurés chez les femmes, qui ont antérieurement été négligées dans les essais cliniques. Or, plusieurs études ont révélé que les femmes qui subissent un pontage aortocoronarien (PAC) ou une intervention coronarienne percutanée (ICP) présentent initialement plus de facteurs de risque cardiovasculaire, connaissent plus de

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higher mortality rate than men. The goal of this review is to analyze the difference between men and women in terms of the prevalence of individual cardiovascular risk factors.

Methods: **A meta-analysis was conducted of original investigations with adult subjects who underwent surgical intervention or PCIs in which cardiovascular risk factors were evaluated, using the MEDLINE, Cochrane, Evidence-Based Medicine Reviews (EBMR), Ovid Embase, Google Scholar, and PubMed databases.**

Results: **Of the 4567 identified records found, 18 were retained for qualitative analysis. Prevalence of hypertension (CABG: 71% (95% confidence interval [CI] 64%, 78%]); PCI: (59% [95% CI 48%,70%]), and diabetes (CABG: 48% [95% CI 38%, 57%]); PCI 43% (95% CI 27%, 59%]) was high in women. Women who underwent either CABG or PCI had higher odds of having hypertension (CABG: odds ratio [OR] 1.92 [95% CI 1.47-2.50], $P < 0.05$); PCI: OR 1.86 [95% CI 1.76-1.97], $P < 0.05$]), and diabetes (CABG: OR 1.94 [95% CI 1.55-2.42], $P < 0.05$; PCI: OR 1.97 [95% CI 1.54-2.53], $P < 0.05$)). However, the prevalence of smoking among women, compared to men, was lower (CABG: 0.17 [95% CI 0.06-0.52], $P < 0.05$; PCI: 0.22 [95% CI 0.06-0.86], $P < 0.03$).**

Conclusion: **The review shows that women who underwent either surgical or percutaneous revascularization had higher odds of hypertension and diabetes, compared to men.**

complications postopératoires et affichent un taux de mortalité plus élevé que les hommes. Cette analyse visait à dégager les différences entre les hommes et les femmes quant à la prévalence de chacun des facteurs de risque cardiovasculaire.

Méthodologie : **Une méta-analyse a été menée sur des enquêtes originales auprès d'adultes ayant subi une intervention chirurgicale ou des ICP chez qui les facteurs de risque cardiovasculaire ont été évalués. Les bases de données interrogées étaient les suivantes : MEDLINE, Cochrane, Evidence-Based Medicine Reviews (EBMR), Ovid Embase, Google Scholar et PubMed.**

Résultats : **Parmi les 4567 dossiers recensés, 18 ont été retenus pour une analyse qualitative. La prévalence de l'hypertension (PAC : 71 % [intervalle de confiance {IC} à 95 % : 64 %; 78 %]); ICP : 59 % [IC à 95 % : 48 %; 70 %]) et du diabète (PAC : 48 % [IC à 95 % : 38 %; 57 %]); ICP : 43 % (IC à 95 % : 27 %; 59 %]) était élevée chez les femmes. Les femmes qui ont subi un PAC ou une ICP présentaient un risque accru d'hypertension (PAC : rapport de cotes [RC] de 1.92 [IC à 95 % : 1,47-2,50], $p < 0,05$); ICP : RC de 1,86 [IC à 95 % : 1,76-1,97], $p < 0,05$]) et de diabète (PAC : RC de 1,94 [IC à 95 % : 1,55-2,42], $p < 0,05$; ICP : RC de 1,97 [IC à 95 % : 1,54-2,53], $p < 0,05$). Cependant, le tabagisme était moins prévalent chez les femmes que chez les hommes (PAC : 0,17 [IC à 95 % : 0,06-0,52], $p < 0,05$; ICP : 0,22 [IC à 95 % : 0,06-0,86], $p < 0,03$).**

Conclusion : **L'analyse révèle que, par rapport aux hommes, les femmes qui ont subi une revascularisation chirurgicale ou percutanée présentaient plus de risque d'hypertension et de diabète.**

Lay Summary

Heart disease remains the leading cause of premature death in women. This review examined the frequency of risk factors in women and men with heart disease who underwent a procedure to unblock a heart artery. The results of the study demonstrated that the frequencies of 2 risk factors—high blood pressure and diabetes—were much higher in women than in men.

Today, heart disease is the leading cause of death worldwide.[1] In fact, cardiovascular disease (CVD) is the major cause of premature death in women and accounts for 35% of the total deaths in women worldwide that occurred in 2019.[2,3] Although CVD is more commonly known as a disease o "old age" or one of postmenopausal women in North America, more than 15,000 women under the age of 55 years die from heart disease every year.[1] These findings show that young women also are affected by heart disease and that they must be better investigated, diagnosed, cared for, and treated.

Several studies have shown that women undergoing surgery or percutaneous coronary intervention (PCI) for obstructive coronary artery disease (CAD) have more risk factors (RFs) than men do upon clinical presentation. Women affected by obstructive CAD have twice the mortality incidence of men.[4,5] After surgery for revascularization, women develop more complications, including major cardiovascular events (MACE), and mortality.[6,7] A commonly accepted finding is that traditional RFs, such as diabetes (DB), dyslipidemia (DLP), smoking, and hypertension (HTN), play an important role in the development of obstructive CAD, with progress having been made in the prevention and control of these RFs that, in turn, contributes to decreasing the incidence of obstructive CAD.[1] Although the importance of these RFs is well established, the RF profile of women with CAD requiring surgery or PCI remains unknown. A better understanding of the RF profile of these patients in contemporary practice may help in targeting primary prevention efforts and decreasing these major gaps in mortality and morbidity that have persisted over the years. In addition, sex differences in cardiac RFs, and nontraditional RFs (such as preeclampsia, gestational diabetes, hormonotherapy, etc.), are still not well studied.[8] We therefore sought to assess the prevalence and temporal trend of RFs in women with CAD who require medical, percutaneous, or surgical intervention.

The objectives of this literature review were to assess the prevalence of different cardiovascular RFs in women who underwent medical, surgical, or percutaneous coronary intervention, compared to those of men.

Material and Methods

This literature review was conducted through searches of the MEDLINE, Embase, Ovid, PubMed, Cochrane, Evidence-Based Medicine Reviews (EBMR), and Google Scholar databases (Supplemental Appendix S1). All articles published after January 1, 2000 were identified. The keywords used for the research were as follows: "risk factors" (smoking,

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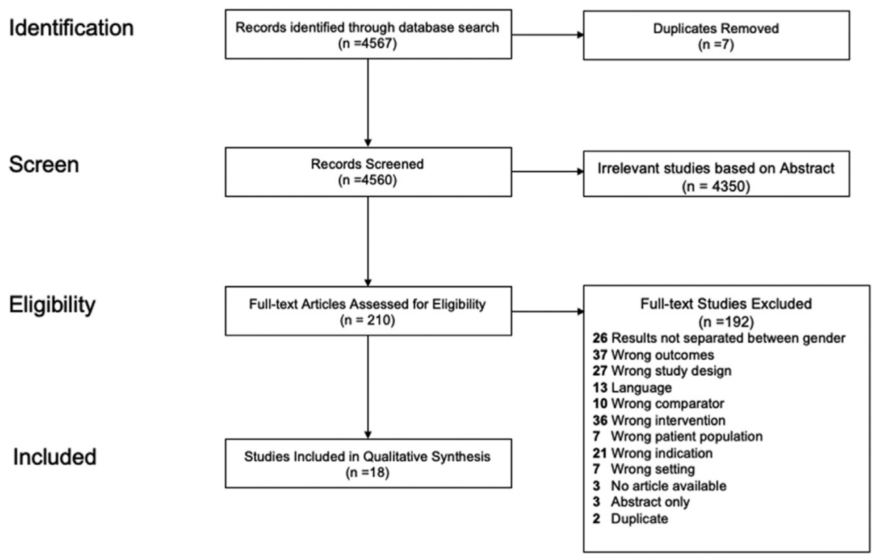

Figure 1. Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) flow diagram. CI, confidence interval; REML, restricted maximum likelihood.

diabetes, dyslipidemia, hyperlipidemia, obesity, hypertension) AND "Cardiovascular disease", "myocardial infarction" AND "coronary artery disease" AND "women" AND-OR "Cardiac intervention (cardiac surgery, coronary revascularization, PCI; Supplemental Appendix S1).

Qualitative analysis

This literature review focused on articles discussing female patients who underwent a cardiac intervention (cardiac surgery and percutaneous revascularization) for obstructive CAD (myocardial infarction and CAD). Articles that dealt with mixed populations but had results that could be separated by sex were retained. To be included, articles had to be full text, had to be published after 2000, and had to report original data in English or French. Meta-analyses and other types of systematic and nonsystematic syntheses, as well as case reports and editorials, were excluded. Abstracts without complete peer-reviewed articles also were excluded. Articles that do not follow the inclusion criteria were excluded.

This review sought to assess the results that showed the prevalence of cardiovascular RFs in women with CVD requiring surgery or PCI, to potentially prevent cardiac interventions in women while intervening a priori on the different cardiovascular RFs found in this analysis. For each article that met inclusion criteria, we have summarized the RFs studied.

A primary screening of article titles and abstracts was conducted for relevance. Any references that were not excluded in the primary screening were subjected to a secondary screening, consisting of a detailed review of the entire article. Both primary and secondary screenings were independently performed by 2 of the authors (L.B. and C.N.A.N.). If any disagreements arose about the inclusion of an article, a third author (J.F.) also reviewed the references to determine whether the article was included. When the Articles were identified and retained for the qualitative analysis, the references of these articles were reviewed to ensure that all relevant references had indeed been identified by our database search (Fig. 1).

To assess the risk of bias, the authors examined the study methodology describing recruitment methods, inclusion and exclusion criteria, excluded patients and reasons for exclusion, loss to follow-up, and missing data. The authors required that these criteria be well defined in order to select articles. The statistical methodology used for evaluating the data was reviewed, and the assessment of bias was carried out using ROBINS-I checklists (**R**isk **o**f **B**ias **I**n **N**on-randomized **S**tudies of **I**nterventions) and Cochrane tools (Supplemental Appendix S2).

The primary endpoint of interest was the prevalence of cardiovascular RFs in women requiring surgical intervention or PCI. The odds of presenting cardiovascular RFs at the time of revascularization, in women compared to men, were also examined.

Effect measures

The pooled prevalences of cardiovascular RFs in women undergoing either PCI or surgical revascularization were generated using raw (untransformed) proportions, using them as an effect size in the meta-analysis, when the proportion is near 0.5, and in the binomial distribution when n is sufficiently large. A fixed-effects model was conducted initially, and if heterogeneity was present, then a random-effects model was used and presented, and heterogeneity was quantified using I^2. Results are presented in forest plots (Supplemental Figs. S1-S6).

To compare the proportions of women and men undergoing revascularization who were concomitantly affected by cardiovascular RFs of interest, odds ratios and confidence intervals (Cis) for each RF, according to sex, were calculated for each study; the pooled effect sizes are presented in forest plots. To account for the presence of heterogeneity, a random-effects model was used and presented, and heterogeneity was quantified using I^2. If the 95% CI for an odds ratio did not include 1.0, then the odds ratio was considered to be statistically significant at the 5% level. All statistical analyses were performed using STATA^T 18 (StataCorp, College Station, TX; Figs. 2-7).

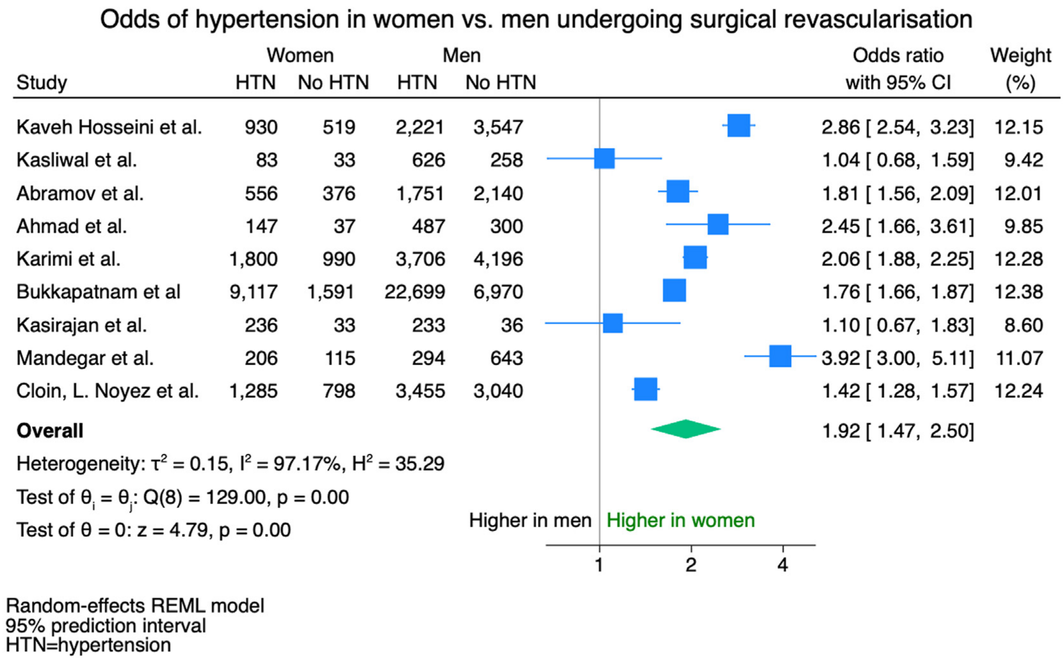

Figure 2. Odds of hypertension in women vs men undergoing surgical revascularization. CI, confidence interval, HTN, hypertension; REML, restricted maximum likelihood.

If collected data were insufficiently comparable for a meta-analysis, results were summarized using a narrative synthesis.

Results

Our database search found 4567 items on April 5, 2023. The primary screening excluded 7 duplicates. A comprehensive secondary screening excluded another 4350 irrelevant studies. Of the 210 remaining articles, 194 were excluded because of noneligibility. Finally, 18 studies that provided results for adult patients undergoing PCI or coronary artery bypass grafting (CABG) and presenting RFs were included (Fig. 1). Of these 18 studies, 6 addressed the RFs present in patients undergoing PCI, and 10 showed the RFs for patients undergoing CABG (Tables 1 and 2).

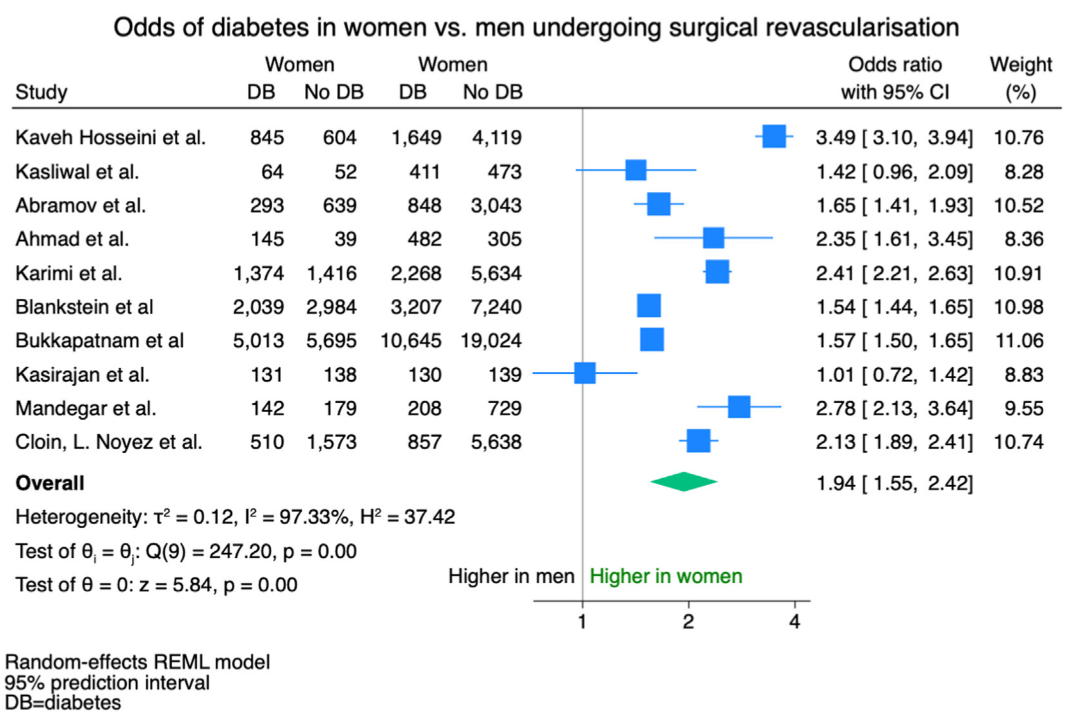

Figure 3. Odds of diabetes in women vs men undergoing surgical revascularization. CI, confidence interval; DB, diabetes; REML, restricted maximum likelihood.

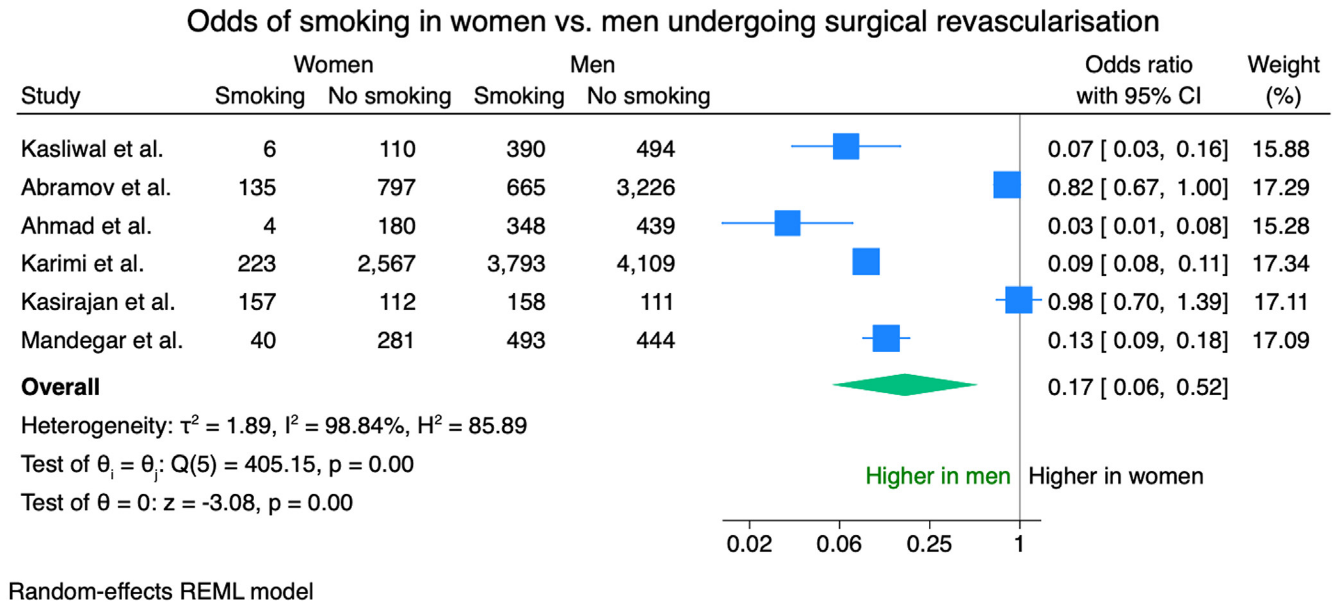

Figure 4. Odds of smoking in women vs men undergoing surgical revascularization. REML, restricted maximum likelihood.

Results are presented according to the different interventions studied in the articles. For clarity, the results were separated as being either for CABG or PCI. Table 3 summarizes the overall pooled prevalence of smoking, hypertension, and diabetes in women who underwent PCI or CABG. Figures 2-7 show the pooled odds ratio of RFs in women vs men (CABG and PCI); the pooled prevalence of cardiovascular risks in women for each RF (CABG and PCI) are presented in forest plots (Supplemental Figs. S1-S6).

CABG

Nine articles compared hypertension in women vs men undergoing surgical intervention. The overall pooled prevalence of hypertension in women undergoing CABG was 71% (95% CI, 64%, 78%). The pooled odds ratio (OR) of hypertension suggested that the odds of having hypertension were higher in women, compared to men (OR 1.92 [95% CI, 1.47-2.50], $P < 0.05$; Fig. 2).[5,15-18,20-23]

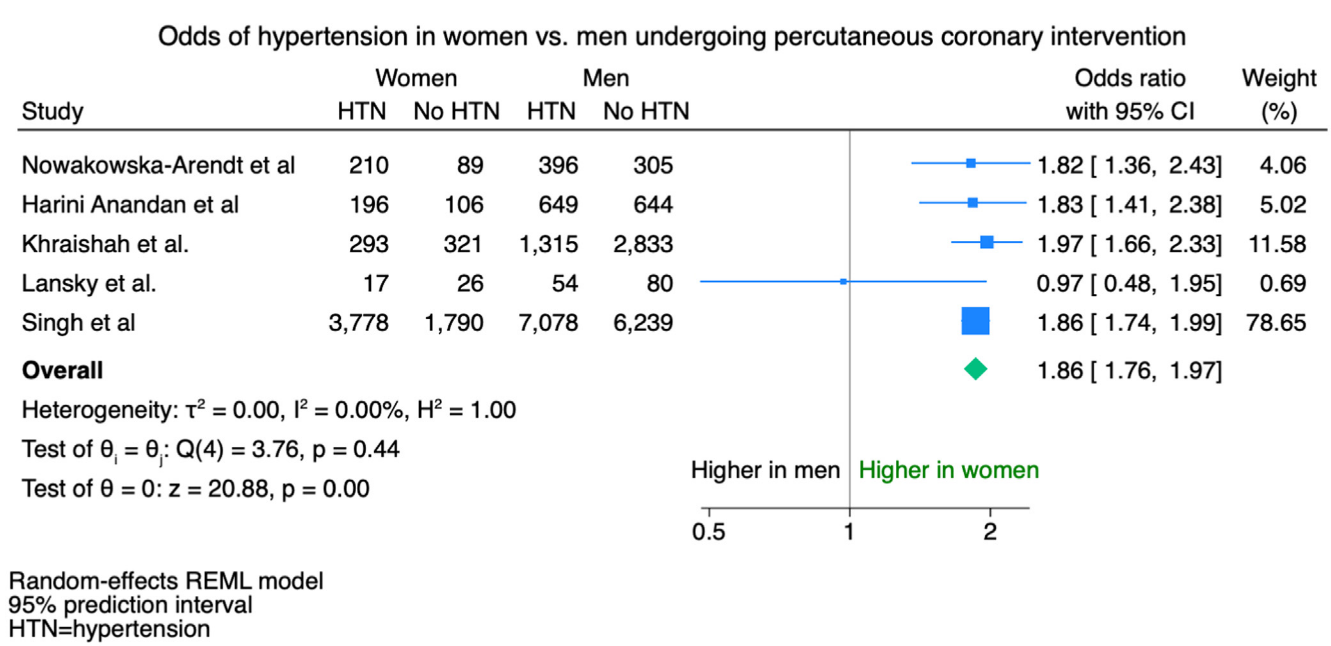

Figure 5. Odds of hypertension in women vs men undergoing percutaneous coronary intervention. REML, restricted maximum likelihood.

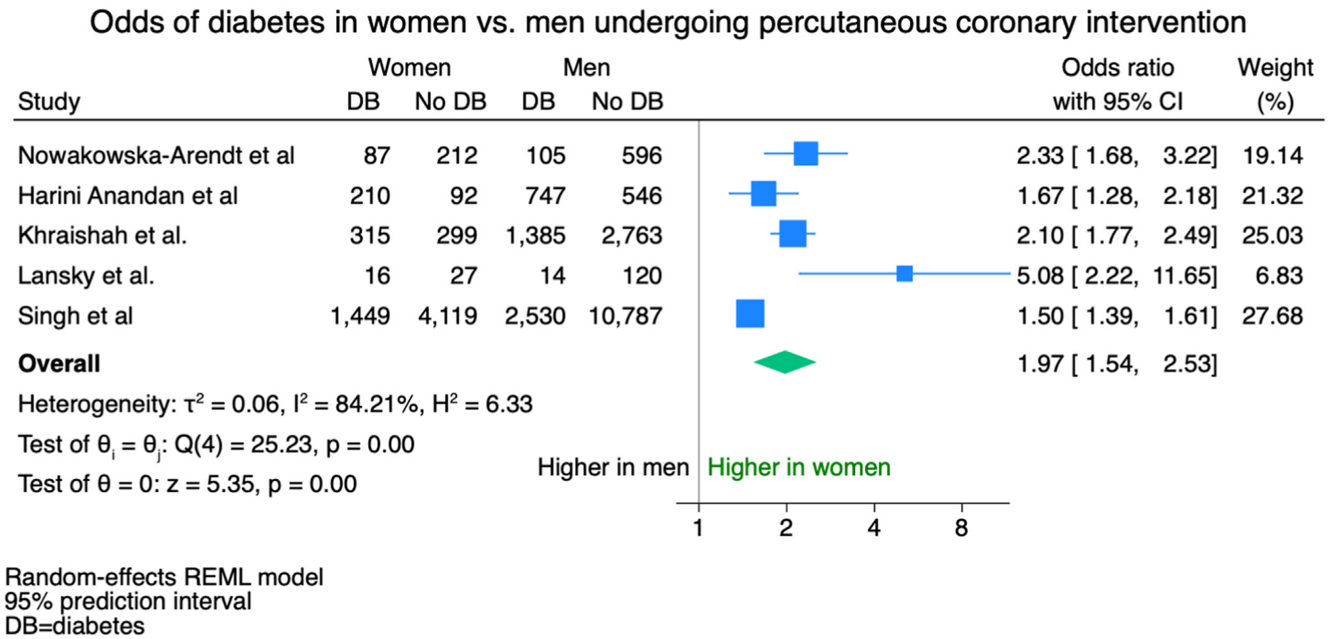

Figure 6. Odds of diabetes in women vs men undergoing percutaneous coronary intervention. REML, restricted maximum likelihood.

Ten articles compared diabetes in women vs men undergoing surgical intervention. The overall pooled prevalence of diabetes was 48% (95% CI, 38%, 57%). The odds of having concomitant diabetes were higher in women, compared to men, undergoing CABG (OR 1.94 [95% CI, 1.55-2.42], $P < 0.05$; Fig. 3).[4,5,15-18,20-23]

Six articles compared smoking in women vs men undergoing surgical intervention. The smoking overall pooled prevalence was 16% in women (95% CI, 8%, 24%). The odds of smoking were lower in women vs men (OR 0.17 [95% CI, 0.06-0.52], $P < 0.05$; Fig. 4).[15-18,21,22]

The overall pooled prevalence of hypertension in women undergoing CABG was 0.71 (95% CI, 0.62, 0.80). For diabetes, the overall pooled prevalence was 47% (95% CI, 0.41, 0.54), and finally, the smoking overall pooled prevalence was 17% (95% CI, 0.00, 0.33; Table 3).

PCI

Five articles compared hypertension in women vs men undergoing PCI. The overall pooled prevalence of hypertension in women undergoing PCI was 59% (95% CI, 48%, 70%). The pooled odds ratio for hypertension suggested that women had higher odds of having hypertension, compared to men (OR 1.86 [95% CI, 1.76-1.97], $P < 0.05$; Fig. 5).[9-14]

Five articles comparing diabetes in women vs men undergoing PCI showed an overall pooled prevalence of diabetes of 43% (95% CI, 27%, 59%) in women. Women had nearly 2 times the odds of having diabetes compared to men

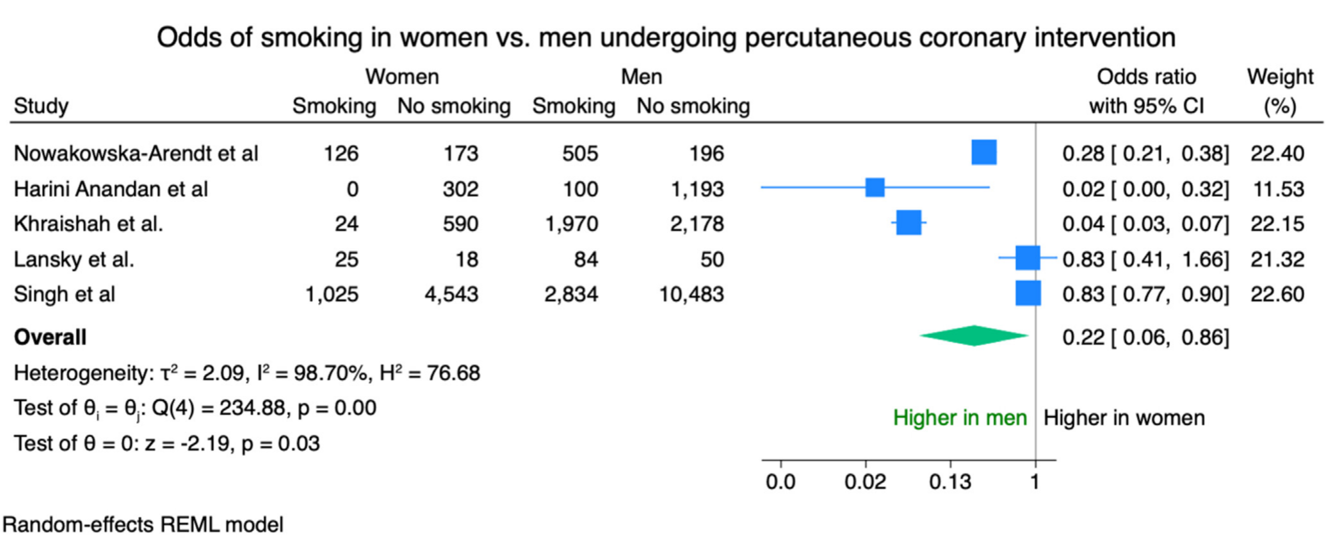

Figure 7. Odds of smoking in women vs men undergoing percutaneous coronary intervention. REML, restricted maximum likelihood.

Table 1. Comparison of risk factors in female vs male patients with percutaneous coronary intervention (PCI)

Study (year), intervention	Aim of the study, intervention, and/or treatment	Sample size, age and ethnicity	Risk factors
Singh et al.[9] (2008) Retrospective study	To examine whether sex-based differences in mortality after PCI have changed in the past 25 years	1979–1995 N = 7904 W: 2203 (27.9%) Mean age, y: 67.3 ± 11.1 M: 5701 (72.1%) Mean age, y: 62.4 ± 11.2 1996–2004 N = 10,981 W: 3365 (30.6%) Mean age, y: 69.4 ± 12.0 M: 7616 (69.4%) Mean age, y: 64.7 ± 11.8 Ethnicity: NA Origin of the study: US	1979–1995 DB: **W: 23%,** M: 15% HTN: **W: 60%,** M: 44% Smoking: W: 19%, **M: 23%** HTN > DB 1996–2004 DB: **W: 28%,** M: 22% HTN: **W: 73%,** M: 60% Smoking: W:18%, **M: 20%** DB: $P = 0.007$ HTN: $P = 0.46$ Smoking: $P = 0.34$
Gurm et al.[10] (2021) Prospective study	Examination of the prevalence of RFs	N = 108,501 W: 38,930 (35.9%) Age, y: ≤ 45: 5.8% 46–55: 14.98% 56–65: 25.8% 66–75: 27.37% ≥ 75: 26.47% (+ W aged ≥ 65 y) M: 69,571 (64.1%) Ethnicity: White: W (83.3%), M (87.3%) Black: W (14.1%), M (9.5%) Asian: W (0.9%), M (1.2%) American Indian or Alaskan native: W (0.3%), M (0.3%) Origin of the study: US	Age ≤ 45 y: Smoking: **W: 66%,** M: 62.1% HTN: **W: 62.3%,** M: 56.4% OB: **W: 62.3%,** M: 56.9%, DLP**:** W: 47.2%, **M: 50.2%** DB: **W: 35.8%,** M: 20.5%. No P-value Age 46–55 y: Smoking: **W: 61.1%,** M: 52.4% HTN: **W: 70%,** M: 63.8% OB: **W: 55.5%,** M: 50.5% DLP: **W: 61.1%,** M: 59.2% DB: **W: 33.5%,** M: 23.7%. No P value Age 56–65 y: Smoke: **W: 41.1%,** M: 36.7% HTN: **W: 78.1%,** M: 71.1% OB: **W: 54.4 %,** M: 46.9% DLP: **W: 68.2%,** M: 65.6% DB: **W: 37.5%,** M: 28%. No P value Age 66–75 y: Smoking: **W: 21.3%,** M: 19.9% HTN: **W: 84.5%,** M: 79.1% OB: **W: 49.8%,** M: 42.6% DLP: **W: 74.7%,** M: 72% DB: **W: 39%,** M: 32.6% No P value Age ≥ 75 y: Smoking: W: 6.8%, **M: 8.4%** HTN: **W: 89%,** M: 83.6% OB: **W:32.7%,** M: 27.3% DLP: **W: 72.6%,** M: 70.1% DB: **W: 31.2%,** M: 30.1% No P value Number of RFs 0: W: 3.4%, **M: 5.1%** 1: W: 13.5%, **M: 17.4%** 2: W: 27.8%, **M: 28.6%** 3: **W: 30.1**%, M: 28.9% 4: **W: 21.2%,** M: 16.8% 5: **W: 3.9%,** M: 3%
Nowakowska-Arendt et al.[11] (2008) Retrospective study	To compare direct results of PCI in M and W	N = 1000 W: 299 (29.9%) Mean age, y: 63.7 ± 11.2 M: 701 (70.1%) Mean age, y: 58.5 ± 10.4 Ethnicity: NA Origin of the study: Poland	HTN: **W: 70.2%,** M: 56.5%, $P < 0.0001$ Smoking: W: 42.1%, **M: 72.0%**, $P < 0.0001$ DB: **W: 29.1%,** M: 15%, $P < 0.0001$

Table 1. Continued.

Study (year), intervention	Aim of the study, intervention, and/or treatment	Sample size, age and ethnicity	Risk factors
Anandan et al.[12] (2021) Retrospective study	Compare gender-based differences in patients who underwent PCI	N = 1595 W: 302 (18.9%) Mean age, y: 60.8 ± 9.1 M: 1293 (81.1%) Mean age, y: 58 ± 10.9 Ethnicity: NA Origin of the study: India	DB: **W: 69.5%,** M: 57.8%, $P < 0.001$ HTN: **W: 65%,** M: 50.2%, $P < 0.001$ DLP: W: 19.3%, M: 16.7%, $P = 0.3$ Smoking: **W: 0%,** M: 7.7%, $P < 0.001$ BMI, kg/m^2: **W: 27.2 ± 4,** M: 26.2 ± 6.7, $P < 0.001$
Khraishah et al.[13] (2022) Prospective study	Exploring differences (clinical, medical care, outcomes of AMI) in young adults age < 50 y PCI Thrombolyses	N = 4762 W: 614 (12.89%) M: 4148 (87.11%) Age of W and M, y: ≤ 50 Ethnicity: NA Origin of the study: India	HTN: **W: 47.7%,** M: 31.7%, $P < 0.001$ DB: **W: 51.3%,** M: 33.4%, $P < 0.001$ History of tobacco use: **W: 3.9%,** M: 47.5%, $P < 0.001$
Lansky et al.[14] (2004) Prospective study	Assess the gender differences in RFs and clinical outcomes among patients with premature (age 40 y) CAD undergoing PCI	N = 177 W: 43 (24.3%) Mean age, y: 35 ± 4 M:134 (75.7%) Mean age, y: 36 ± 4 Ethnicity: NA Origin of the study: US	DB: **W: 37.5%,** M: 10.3%, $P < 0.001$ DLP: **W: 57.8%,** M: 75.3%, $P < 0.001$ HTN: W: 39.1%, M: 40.2%, $P = 0.87$ Smoking: W: 58.8%, M: 62.6%, $P = 0.49$

Boldface the sex with the highest percentage of RFs.

AMI, acute myocardial infarction; BMI, body mass index; CAD, coronary artery disease; DB, diabetes; DLP, dyslipidemia; HTN, hypertension; M, men; NA, not available; OB., obese; RF, risk factor; W, women

undergoing PCI (OR 1.97 [95% CI, 1.54-2.53], $P < 0.05$; Fig. 6).[9-14]

In the 5 articles reporting smoking in patients undergoing PCI, the pooled prevalence of smoking in women was 16% (95% CI, 8%, 24%). Similar to the odds for patients undergoing CABG, the odds of smoking were lower in women undergoing PCI, compared to men (OR 0.22 [95% CI, 0.06-0.86], $P < 0.03$; Fig. 7).[9-14]

The overall pooled prevalence of hypertension in women undergoing PCI was 0.59 (95% CI, 0.50, 0.69). For the diabetes RF, the overall pooled prevalence was 0.43 (95% CI, 0.25, 0.60); finally, the overall pooled prevalence of smoking was 0.24 (95% CI, 0.02, 0.45; Table 3).

Table 4 presented two articles comparing RFs in female vs. male patients with medical, percutaneous, or surgical intervention.[6,24] These two articles reported higher percentage of DB, HTN and OB in women compared to men. In Bhatt et al. article, men presented with higher percentage of smoking compared to women.[6]

The graphical abstract shows a generalization of all the results (Fig. 8).

Only 7 of 18 studies reported the ethnicity of patients.[6,10,15,18-20,24] The majority of participants in studies included in the present meta-analysis were Caucasian (roughly 70% of the cohorts), and around 15% of patients were African American or Afro-Caribbean. A small minority of participants were Hispanic or Asian. Most of the studies were carried out in North America.[6] Three studies were conducted in India, and 3 were conducted in Europe.

Discussion

The main objective of this review was to investigate the prevalence of cardiovascular RFs in women compared to men who undergo surgical or percutaneous revascularization. Indeed, an understanding of the impact of RFs is important, as the literature demonstrates that women have more RFs, compared to men, when they present with obstructive CAD, and that these probably lead to a higher incidence of mortality and morbidity, in comparison to that for men.

This review also showed that, at this time, no good-quality studies have been done comparing women to each other in terms of the effect of cardiovascular RFs on the incidence of coronary heart disease requiring cardiac surgery. In contrast, many comparisons have been conducted of men vs women in terms of coronary heart disease requiring surgery; however, all articles evaluated a mixed population in which the percentage of men was, in every article, much higher than the percentage of women. In addition, a large number of cohort studies present findings in which the results are mixed, without separation by sex.

These significant differences between women and men have several causes. First, women are underrepresented in clinical trials; the sex disparity in the studies means that results are from predominantly male samples, resulting in suboptimal treatment, development, and management of cardiovascular disease that is not specific to women. This factor is one of the reasons that the gaps in knowledge and understandings, and inappropriate treatment, for women are predominant. In fact, since only 1997 has Health Canada mandated the consideration of sex when conducting clinical trials; and this gap has clearly had an impact on women's health, as evidenced by the fact that many treatments do not have the same effect in men and women, owing to anatomic, hormonal and physiological differences.[24]

If we look at the physiological and anatomic aspects of this issue, women have a smaller body surface area and therefore smaller coronary arteries, resulting in more incomplete coronary revascularization compared to that for men.[4] The revascularization procedure is known to be potentially more complex in patients with smaller arteries, which could explain the fact that women have fewer arterial grafts and less

Table 2. Comparison of risk factors in female vs male patients with surgical cardiac intervention (coronary artery bypass grafting [CABG])

Study (year), intervention	Aim of the study, intervention, and/or treatment	Sample size, age, and ethnicity	Risk factors
Hosseini et al.[5] (2021) Retrospective study	Evaluate RFs in young patients undergoing CABG	N = 6917 W: 1449 (20.9%) Mean age, y: 50.11 ± 4.45 M: 5768 (79.1%) Mean age, y: 49.39 ± 4.8 Ethnicity: NA Origin of the study: Iran	DB: **W: 58.3%,** M: 28.6%, $P < 0.0001$ HTN: **W: 64.2%,** M: 38.5%, $P < 0.0001$ DLP: **W: 69.7%,** M: 55.3%, $P < 0.0001$ BMI, kg/m^2, > 30: **W: 44.7%,** M:23.9%, $P < 0.0001$
Kasliwal et al.[15] (2006) Cross-sectional study	Measure the cardiovascular RFs in patients undergoing CABG	N = 1000 W: 116 (11.6%) M: 884 (88.4%) Mean age of W and M, y: 59.73 ± 9.5 Ethnicity: Indian Origin of the study: India	HTN: W: 71.6%, M: 70.8%, $P = 0.869$ DB: W: 55.2%, M: 46.5%, $P = 0.078$ Smoking: W: 5.2%, **M: 44.1%**, $P < 0.001$ DLP: **W: 93.9%,** M: 84.5%, $P = 0.023$ Number of RFs: 0: **W: 4.3%,** M: 4.1% 1: **W: 16.4%,** M: 15.3% 2: **W: 38.8%,** M: 30.9% 3: W: 25.9%, M: **35.4%** 4: **W: 13.8%,** M: 12.4% 5: W: 0.9%, **M: 1.9%**
Abramov et al.[16] (2000) Prospective study	To assess the impact of gender as an independent RF for early and late morbidity and mortality following CABG	N = 4823 W: 932 (19.3%) Mean age, y: 65.2 ± 9 Age > 70 y: 31.3% M: 3891 (80.7%) Mean age, y: 61.9 ± 10 Age > 70 y: 19.2% Ethnicity: NA Origin of the study: Canada	DB: **W: 31.4%,** M: 21.8%, $P < 0.001$ HTN: **W: 59.7%,** M: 45%, $P < 0.001$ Smoking: W: 14.5%, M: 17.1%, $P = 0.057$
Ahmad et al.[17] (2010) Retrospective analysis of prospectively collected data	Investigate the gender disparity in the distribution of patient-related RFs and their effect on the surgical management and clinical outcome of CAD	N = 971 W: 184 (19%) Mean age, y: 63.4 M: 787 (81%) Mean age, y: 59.5 Ethnicity: NA Origin of the study: Saudi Arabia	DB: **W: 78.8%;** M: 61.2%, $P < 0.0001$ HTN: **W: 79.9%** M: 61.9%, $P < 0.0001$ Morbid OB: **W: 45.1%** M:24.7%, $P < 0.0001$ Smoking: W: 2.2%, **M: 44.2%,** $P < 0.0001$
Karimi et al.[18] (2009) Retrospective study	Detect the prevalence of these RFs of premature CAD in a population undergoing CABG	N = 10,622 W: 2720 (25.6%) M: 7902 (74.4%) Mean age of W and M, y: 58.75 ± 9.72 Ethnicity: Iranian Origin of the study: Iran	HTN: **W: 66.2%,** M: 46.9%, $P < 0.001$ DB: **W: 50.5%,** M: 28.7%, $P < 0.001$ HLP: **W: 74.5%.** M: 60.3%, $P < 0.001$ Smoking: W: 8.2%, **M: 48%,** $P < 0.001$ Overweight: **W: 77.9%,** M: 64.6%, $P < 0.001$ OB: **W: 34.8%,** M: 16.4%, $P < 0.001$ Number of RFs: 0: W: 3.9%, **M: 10%** 1: W: 17.3%, **M: 27.5%** 2: W: 32.6%, **M: 34%** 3: **W: 34.8%,** M:21.5% 4: **W: 11.1%,** M: 6.4% 5: W: 0.3%, **M: 0.7%**

Blankstein et al.[19] (2005) Retrospective study	We attempted to determine whether, all other factors being equal, there is a significant difference in operative mortality between M and W undergoing CABG	N = 15,440 W: 5023 (32.53%) M: 10 447 (67.47%) Age, y < 55: W: 15.4%, M: 22.8% Age 55−64 y: W: 23.9%, M: 29.6% Age 65−74 y: W: 34.6%, M: 30.6% Age 75−84 y: W: 24.5%, M: 16.0% Age, y > 85: W: 1.5%, M: 1.0% Ethnicity: US Midwestern Origin of the study: US Midwest	DB: W: 40.6%, M: 30.7%, $P = 0.000$
Bukkapatnam et al.[20] (2010) Prospective study	Evaluation of factors related to operative mortality in a large cohort of W and M undergoing isolated CABG	N = 30,747 W: 10,708 (34.8%) M: 29,669 (65.2%) Age, y < 65: W: 33.46%, M: 45.53% Age 65−74 y: W: 34.40%, M: 32.06% Age > 75 y: W: 32.13%, M: 22.41% Ethnicity: Caucasian: W (66.32%), M (71.28%) African American: W (13.88%), M (11.49%) Hispanic: W (5.66%), M (2.97%) Asian: W (8.93%), M (8.78%) Origin of the study: US	DB: **W: 46.82%,** M: 35.88%, $P < 0.0001$ HTN: **W: 85.14%,** M: 76.51%, $P < 0.0001$
Kasirajan et al.[21] (2009) Prospective study	Create a risk profile based on gender, and look at outcomes in propensity-matched groups with similar factors differing by gender	N = 538 W: 269 (50%) Mean age, y: 65.8 ± 11 M: 269 (50%) Mean age, y: 61.8 ± 10.7 Ethnicity: NA Origin of the study: US	DB: W: 48.7%, M: 48.33%, $P = 0.93$ HTN: W: 87.73%, M: 86.62%, $P = 0.70$ Smoking: W: 58.36%, M: 58.74%, $P = 0.93$
Mandegar et al.[22] (2008) Prospective study	Analyze the RFs on patients undergoing CABG	N = 1258 W: 321 (25.5%) M: 937 (74.5%) Mean age, y, W and M: 58.7 Ethnicity: NA Origin of the study: Iran	HTN: **W: 64.2%,** M: 31.4%, $P < 0.001$ Smoking: W: 12.5%, **M: 52.6%**, $P < 0.001$ DB: **W: 44.2%,**M: 22.2%, $P < 0.001$
Cloin and Noyez[23] (2006) Cross-sectional study	Evaluate the influence of gender on hospital mortality and morbidity after CABG	N = 8578 W: 2083 (24.3%) Mean age, y: 66.5 ± 9.0 M: 6495 (75.7%) Mean age, y: 62.2 ± 9.6 Ethnicity: NA Origin of the study: Netherlands	DB: **W: 24.5%,** M: 13.2%, $P = 0.001$ HLP: **W:55.5%,** M: 52.1%, $P = 0.008$ HTN: **W: 61.7%,** M: 53.2%, $P = 0.001$

Boldface indicates the sex with the highest percentage of RFs.

DB, diabetes; BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; DLP, dyslipidemia; HLP, hyperlipidemia; HTN, hypertension; M, men; NA, not available; OB, obesity; RF, risk factor; W, women.

Table 3. Overall pooled prevalence of risk factors in women undergoing PCI and CABG

Risk factor	PCI	CABG
Hypertension	0.59 (0.48, 0.70)	0.71 (0.64, 0.78)
Diabetes	0.43 (0.27, 0.58)	0.48 (0.38, 0.57)
Smoking	0.24 (0.02, 0.45)	0.17 (0.00, 0.33)

Values are the pooled prevalence with the 95% confidence interval.

CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

complete revascularization. But from the literature, arterial grafts also are known to be a more effective procedure in the long term, with fewer complications and a lower mortality rate. Finally, sex bias has been shown to impact the identification and management of acute myocardial infarction, affecting survival rates in women. Indeed, women express their symptoms differently, they present late to the emergency and often with atypical symptoms.[4]

RFs play a major role in the development of CVD, as shown in this review and in the literature; traditional RFs are known to have an impact in the development of CVD. In fact, we can see from the results not only that DB, HTN, and DLP are the most predominant RFs in women, compared to men, but also,that these factors have a greater cumulative effect on women (Supplemental Fig. S1-S6).

As demonstrated by Hosseini et al. and Vikulova et al., respectively, "women carried a higher risk of events and mortality after CABG at a young age (< 55 years)"[5] and "the prevalence of major cardiovascular RFs increased between 2000 and 2016."[25] Together, these results demonstrate a potential relationship between not only the burden of RFs but also the cumulative effect of RFs and the higher incidence of comorbidity and mortality in women. Gurm et al. found very interesting results; although women might be expected to have more risk factors because they are older, this article shows that in all age groups, women have a higher prevalence of risk factors than men.[18]

Finally, for some sex-specific factors, data are limited on their effect in revascularized patients. Nontraditional RFs in women's life trajectory, are even less well understood, according to the literature, and have not been well studied. For example, early menopause and hormonal therapy, gestational diabetes, preeclampsia, and other conditions that are major factors in some women's lives have been shown to be associated with CVD, yet little is known about the follow-up and management of nontraditional RFs.

With the current findings, we observed that DB, HTN, smoking, and DLP were the main RFs present in women who are affected by CAD and are undergoing surgical intervention or PCI for CAD. Prevention of and education relating to those RFs have potential to decrease the risk of CVD development, especially in women who present with disease that has a greater likelihood of being fatal and who have a worse prognosis following an event.[1] More studies are needed to assess the impact of different cardiovascular RFs in women, especially across the lifetime trajectory, which differs from that of men.

Several limitations of this review can be noted. First, in all the studies, women are underrepresented, compared to men. In the majority of the articles, they represent 30% of the cohort. These results impact our findings regarding the prevalence of RFs that are subject to selection bias. Another potential source of bias is the way in which RFs were measured, with the ascertainment of RFs being variable or under-described in some studies, and assessed from medical records or by self-reporting in others. Both methods can lead to misclassification. In the majority of studies, missing information regarding patients' ethnicity may represent an additional confounding factor, as specific populations are more likely to develop certain RFs and CVD.

Future directions

Currently, hormonal therapy is used in different treatments, such as relief of vasomotor symptoms during menopause, but the impact of this therapy on cardiovascular health is poorly understood.[26] The medical community needs to be aware of the identification of "new risk factors" in women who are at highest risk of CVD, and to better understand their association with CVD risk. Also, women who have early

Table 4. Comparison of risk factors in female vs male patients with medical, percutaneous, or surgical cardiac intervention

Study (year), intervention	Aim of the study, intervention, and/or treatment	Sample size, age, and ethnicity	Risk factors
Aguilar et al.[24] (2002) Retrospective study	To study gender differences in clinical status at the time of coronary revascularization PTCA, CABG	N = 3645 W: 671 (18.4%) Mean age, y: 68 M: 2974 (81.6%) Mean age, y: 62 Ethnicity: Spanish Origin of the study: Spain	DB: **W: 37%,** M: 21%, $P < 0.001$ HTN: **W: 69%,** M: 44%, $P < 0.001$ OB: **W: 27%** M: 17%, $P < 0.001$
Bhatt et al.[6] (2015) Observational study	Gender-related differences in prevalence of conventional and nonconventional RFs CABG, PCI, medication	N = 6867 M: 5678 (82.7%) W: 1189 (17.3%) Age of W and M, y: > 41 Ethnicity: Indian Origin of the study: India	Smoking: W: 5%, **M**: **17.34**%, $P < 0.001$ DB: **W**: **27.84 %,** M: 25.93%, $P < 0.001$ OB: **W**: **8.66%,** M: 6.11%, $P < 0.001$ HTN: **W**: **41.38**%, M: 34.69%, $P < 0.001$

Boldface indicates the sex with the highest percentage of RFs.

CABG, coronary artery bypass graft; DB, diabetes; HTN, hypertension; M, men; OB, obesity; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; W, women.

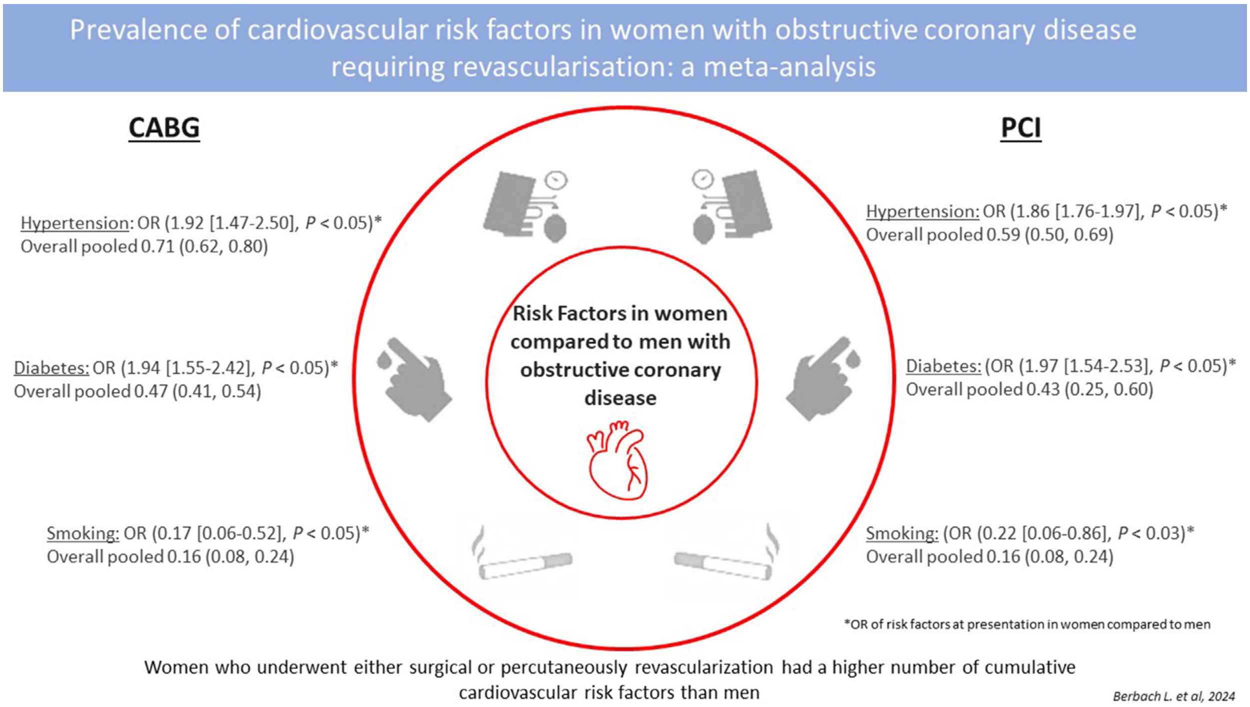

Figure 8. Prevalence of cardiovascular risk factors in women with obstructive coronary disease requiring revascularization. REML, restricted maximum likelihood.

menopause (at age < 45 years) have an increased risk of developing hypertension, compared to those who have menopause at a normal age, which could also be related to eventual development of CVD.[26]

Women with gestational diabetes mellitus (GDM) are mainly young patients and have twice the risk of cardiovascular events after childbirth compared to their peers.[27] This risk appears within the first 10 years after pregnancy. Women with GDM are an at-risk population for CVD and need to be evaluated early for this RF.[27] An important point to note is that unrecognized factors may have an impact during and after pregnancy that contributes to the observed association between GDM and later CVD. These factors could be pregnancy-associated conditions such as preeclampsia or eclampsia or latent or unidentified determinants of cardiovascular risk.

Last, further research is important to better understand these factors. Further studies are needed to better understand the role of such novel RFs and improve screening and treatment, including case-control and cohort studies aimed at identifying markers of increased risk, and optimal intervention trials aimed at improving follow-up and management strategies in these populations. The higher odds of certain traditional RFs in women, once they require revascularization, indicates that improvement of sex-specific strategies for screening and RF control is clearly needed. Trials aimed at testing sex-specific thresholds for optimal blood pressure control or incorporating sex-specific considerations into primary prevention programs are examples of the many potential research avenues for closing this persistent gap in women's care.

Conclusion

The majority of studies conclude that women undergoing surgical or percutaneous revascularization have higher odds of hypertension and diabetes than do men with CAD. According to the characteristics of the patients admitted, the cardiovascular RFs most present before cardiac surgery and PCI in women are HTN first, followed by DB and DLP. More studies are needed to better understand the effects of both traditional and nontraditional RFs for women throughout their lifespan. The ultimate goal is to engage women and educate them about their RFS, to promote better lifestyle and health choices and ultimately prevent CAD.

Ethics Statement

The research reported has adhered to the relevant ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article. This is a review article using de-identified data; therefore the IRB did not require consent from the patient.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2023.10.016.