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ORIGINAL RESEARCH

Sex Differences and Clinical Outcomes in Patients With Myocardial Infarction With Nonobstructive Coronary Arteries: A Meta-Analysis

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BACKGROUND: Although myocardial infarction with nonobstructive coronary arteries (MINOCA) is more common in women, it is unknown whether sex is a risk factor for adverse outcomes in patients with MINOCA. We aimed to investigate the relationship between sex differences and outcomes of patients with MINOCA.

METHODS AND RESULTS: A systematic literature search was performed in PubMed, Embase, and Cochrane databases from their inception until August 2023 for relevant studies. End points were pooled using the Hartung–Knapp–Sidik–Jonkman random-effects model as odds ratio (OR) with 95% CIs. Nine studies, involving 30 281 patients with MINOCA (comprising 18 079 women and 12 202 men), were included in the study. Women were older and had a higher prevalence of hypertension, diabetes, and stroke compared with men. The median duration of follow-up was 3.5 years, with an interquartile range of 2.2 to 4.2 years. Pooled analysis revealed no statistically significant difference in the risk of all-cause mortality (OR, 1.03 [95% CI, 0.87–1.22]), major adverse cardiovascular events (OR, 1.18 [95% CI, 0.89–1.58]), heart failure (OR, 1.32 [95% CI, 0.57–3.03]), stroke (OR, 1.13 [95% CI, 0.56–2.26]), and myocardial infarction (OR, 1.04 [95% CI, 0.29–3.76]) between the 2 groups. Regarding short-term outcomes, women had a significantly higher risk of in-hospital major adverse cardiovascular events compared with men (OR, 1.33 [95% CI, 1.16–1.53]) whereas there was no significant difference in the risk of in-hospital mortality (OR, 0.90 [95% CI, 0.64–1.28]) between the 2 patient groups.

CONCLUSIONS: Despite the differences in demographics and comorbidity profiles, there was no significant difference in the long-term outcomes for patients with MINOCA between sexes. However, it is noteworthy that women experienced a higher risk of in-hospital major adverse cardiovascular events compared with men.

Key Words: female ■ male ■ MINOCA ■ mortality ■ sex differences

Cardiovascular diseases continue to be the predominant cause of mortality worldwide. In 2020 alone, an estimated 244.1 million people globally were identified with ischemic heart disease, with men showing a notably higher prevalence than women.[1] Among those with myocardial infarction (MI), up to approximately 10% have no evidence of obstructive coronary artery disease.[2] These patients with MI with nonobstructive coronary arteries (MINOCA) represent a challenge clinically because the underlying cause of their MI is frequently not apparent without additional studies.[3] Common causes of MINOCA include disruption of plaque with subsequent spontaneous recanalization of occluded coronary vessel, coronary artery

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CLINICAL PERSPECTIVE

What Is New?

- We performed an updated meta-analysis by adding 3 large, prospective, and recently published studies.
- Despite a possibly higher risk of major adverse cardiovascular events in women, there was no significant difference in the long-term all-cause mortality, major adverse cardiovascular events, heart failure, stroke, and myocardial infarction between sexes.

What Are the Clinical Implications?

- Sex alone may not be a major determinant of long-term prognosis in patients with myocardial infarction with nonobstructive coronary arteries.
- The observed increased risk of in-hospital major adverse cardiovascular events warrants further research to identify the underlying risk factors, aiming to optimize care for this patient population.

Nonstandard Abbreviations and Acronyms

MACE	major adverse cardiovascular events
MINOCA	myocardial infarction with nonobstructive coronary arteries

vasospasm, thromboembolism, and spontaneous coronary artery dissection.[4–6] Importantly, it is imperative to consider the nonischemic causes of myocardial injury in patients with MI to avoid misclassification of patients with true MINOCA.[7] Furthermore, the clinical outcomes of patients with MINOCA, in comparison to those with MI stemming from obstructive coronary artery disease, remain a controversial topic of ongoing debate. Recent meta-analyses suggest a favorable prognosis for patients with suspected MINOCA relative to their MI-coronary artery disease counterparts.[8]

Sex-specific differences in the manifestations and outcomes of cardiovascular diseases are increasingly recognized.[9] MINOCA specifically is more prevalent among young women and is associated with fewer cardiovascular risk factors.[10–12] The evidence on the impact of sex on the outcomes of patients with MINOCA remains limited and controversial, with some studies suggesting that women were at a higher risk of mortality or major adverse cardiovascular events (MACE) compared with men,[12,13] whereas others suggest otherwise.[14,15]

Given the inconclusive findings and the gaps in our understanding of sex differences in MINOCA outcomes, we conducted a systematic review and meta-analysis to synthesize currently available evidence on the outcomes of patients with MINOCA stratified by sex.

METHODS

We conducted this study according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (Table S1). The study protocol was registered in the International Prospective Register of Systematic Reviews under the registration number CRD42023491540. This study involved analysis of previously published studies and there is no use of identified personal data. Thus, approval from institutional review board was not required. The authors declared that all data are available within the article and its supplementary material.

Search Strategy

We performed a systematic literature search in online databases including PubMed, Embase, and Cochrane Library from their respective date of inception until August 10, 2023. Briefly, our search focused on keywords including “myocardial infarction,” “nonobstructive,” “MINOCA,” “outcomes,” and “mortality” with the search terms being modified for each database. In addition, the reference lists of all potentially eligible studies were screened to identify any additional relevant studies. Details of the search strategy are available in Table S2.

Study Selection

We included 2-arm studies that compared the clinical outcomes between men and women with MINOCA. MINOCA was defined as <50% stenosis in coronary arteries on coronary angiography.[16] Studies that evaluated outcomes in patients with MINOCA without stratification by sex were excluded. In terms of study design, case–control, cross-sectional, cohort studies, and randomized controlled trials were included. We excluded nonhuman studies, single-arm studies, case reports, case series, and review articles. No restrictions were applied on age, language, or geographical location.

Data Extraction and Quality Assessment

Screening of studies was performed independently by 2 authors (J.E.C. and S.P.A.), with any disagreements being resolved by a third author (J.I.). Data on patients’ demographics, comorbidities, angiographic findings, percutaneous coronary intervention characteristics, medications, and relevant outcomes were also extracted. We evaluated both short- and long-term outcomes. Short-term outcomes included in-hospital

mortality and in-hospital MACE, and long-term outcomes included all-cause mortality, MACE, stroke, and MI. Two authors (J.E.C. and K.M.) independently assessed the quality and risk of bias of the included studies using the Newcastle-Ottawa Scale for observational studies and the certainty of evidence for each outcome using the Grading of Recommendations Assessment, Development, and Evaluation approach. Any discrepancies were resolved by a third author (S.P.A.).

Statistical Analysis

Patients' demographics, comorbidities, and clinical characteristics were summarized using descriptive statistics. For binary data, frequencies or percentages were used, while continuous data were presented as either median with interquartile range or mean±SD, where appropriate. The primary and secondary outcomes were analyzed quantitatively using the random-effects model with the Hartung–Knapp–Sidik–Jonkman method, to account for variations between studies.[17–19] The results were presented as odds ratios (OR) with a 95% CI. Outcomes with a 2-tailed *P* value <0.05 were statistically significant. Sensitivity analyses were conducted using 2 approaches. Initially, we employed the leave-one-out method, recalculating the pooled effect sizes by sequentially excluding each study. Additionally, Firth's bias-reduced logistic regression was used for studies with zero or fewer than 5 events in either arm. Subsequently, a conventional meta-analysis was performed using a fixed-effects model.

Subgroup analyses were conducted based on age (<60 versus ≥60 years), follow-up duration (<3 versus ≥3 years), study methodology (prospective versus retrospective), and data source (single center versus multicenter or registry based). The study's heterogeneity was evaluated using the Higgins I^2 model, with I^2 values of 75% or higher indicating high heterogeneity.[20] Publication bias was assessed using funnel plots. All statistical analyses were done using STATA v17 software (College Station, TX).

RESULTS

Baseline Characteristics of Studies and Patients

Our systematic electronic search retrieved 4751 studies, with 1249 studies electronically identified as duplicates. After the initial screening of titles and abstracts, 89 studies were selected for full-text screening. Finally, a total of 9 studies, involving 30 281 patients with MINOCA (comprising 18 079 women and 12 202 men), were incorporated into this study.[12–15,21–25] Of these, 6 studies[13,15,21,22,24,25] adopted a prospective methodology, whereas 3 were retrospective in design.[12,14,23] In terms of data sources, 4 studies were based on single-center data, and the remaining 5 used multicenter or registry-based data. Details of screening of literature are depicted in Figure S1.

In the pooled cohort of patients with MINOCA, a predominance of women was observed, constituting 59.5% of the cohort. The female patients were, on average, older with a mean age of 64 years compared with 55 years for male patients (*P*<0.01). Additionally, women had a higher prevalence of certain comorbidities, including hypertension (66% in women versus 56% in men, *P*<0.01), diabetes (20% in women versus 18% in men, *P*<0.01), and a history of heart failure (8.3% in women versus 7.4% in men, *P*=0.02). Conversely, smoking was more prevalent among men (22% in women versus 36% in men, *P*<0.01). Clinically, the presentation of ST-segment–elevation MI was less common in women (14% in women versus 24% in men, *P*<0.01). Furthermore, aggregate data from 5 studies indicated that, upon discharge, women diagnosed with MINOCA were less frequently prescribed statins, angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB), and beta blockers but were more likely to receive aspirin in comparison to their male counterparts. Details of characteristics of studies and patients are summarized in Table 1.

Quality Assessment and Certainty of Evidence

The methodological quality of the studies included in the analysis was assessed using the Newcastle-Ottawa Scale. The results were quantified by assigning stars, which were then translated into the Agency for Healthcare Research and Quality standards as "good," "fair," or "poor" (Table S3). The quality scores of the studies ranged from 6 to 8 stars. Of these, 5 studies were rated as "good" and 4 as "fair." The certainty of evidence for each outcome varied from moderate to low and is detailed in Table S4.

Meta-Analysis of Outcomes

The median duration of follow-up was 3.5 years, with an interquartile range of 2.2 to 4.2 years. Six studies reported data on all-cause mortality, with a higher crude rate of all-cause mortality observed in women compared with men (11.3% versus 9.7%, respectively).[12,13,15,23–25] Results of meta-analysis showed that there was no statistically significant difference between women and men in all-cause mortality (OR, 1.03 [95% CI, 0.87–1.22]) (Figure 1A). The CI indicates that the data are compatible with women having a 13% lower risk to a 22% higher risk of all-cause mortality compared with men. The low heterogeneity (I^2=12.48%) and overlapping CIs suggest that the differences in

Table. Baseline Study Characteristics, Patients' Demographics, Comorbidities, Clinical Presentation, and Discharge Medications

Study	Year	Design	Sex	Sample size	Total	Age, y	Hypertension	Diabetes	Heart failure	Prior MI	Peripheral arterial disease	Smoking	Stroke	ST-segment–elevation MI presentation	Statin	Angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers	Beta blocker	Aspirin
Jung el al.[21]	2020	Prospective	Men	346	645	60.1±12	56.4	19.65	1.73	5.49	1.16	23.70	N/A	12.43	68.21	41.33	28.32	67.92
			Women	299		64.4±12	55.5	17.06	2.68	2.34	2.34	19.06	N/A	5.69	66.22	35.12	20.40	68.23
Gao et al.[15]	2021	Prospective	Men	867	1179	54.1±11.7	50.6	14.19	N/A	5.54	N/A	53.29	N/A	43.71	95.85	65.86	72.90	N/A
			Women	312		58.8±10.3	61.2	20.51	N/A	3.21	N/A	6.73	N/A	30.77	95.83	60.26	73.08	N/A
Mohammed et al.[22]	2022	Prospective	Men	132	259	58.8±10.3	43.9	13.64	3.79	N/A	6.82	63.64	9.85	48.48	73.85	42.31	50.77	66.15
			Women	127		67.8±11.5	54.3	13.39	0.79	N/A	11.81	15.75	17.32	31.50	79.20	46.40	48.00	50.40
Smilowitz et al.[14]	2017	Retrospective	Men	7155	18918	54±14.82	59.4	18.67	8.25	6.93	3.20	36.00	4.93	22.26	N/A	N/A	N/A	N/A
			Women	11763		63.3±15.57	68.9	21.15	8.79	7.90	3.79	22.77	5.42	13.70	N/A	N/A	N/A	N/A
Jędrychowska et al.[23]	2019	Retrospective	Men	56	134	66.6±13.7	23.2	19.64	N/A	12.50	N/A	33.93	1.79	N/A	N/A	N/A	N/A	N/A
			Women	78		54.5±17.4	42.3	23.08	N/A	16.67	N/A	21.79	8.97	N/A	N/A	N/A	N/A	N/A
Eggers et al.[12]	2018	Retrospective	Men	2677	7266	Overall 66 (58–74)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
			Women	4589			N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lawless et al.[24]	2023	Prospective	Men	795	1439	64±14.6	38.7	15.47	2.52	17.99	6.04	14.72	3.40	18.36	51.70	47.42	47.92	39.75
			Women	644		69±12.9	38.2	12.89	2.48	10.40	4.50	11.34	1.86	14.13	48.91	48.60	45.03	32.92
Canton et al.[13]	2023	Prospective	Men	87	255	57.7±14.6	59.8	6.90	N/A	N/A	2.30	55.17	4.60	14.94	73.56	56.32	72.41	75.86
			Women	168		69.5±12.6	70.2	11.90	N/A	N/A	2.38	34.52	7.74	11.31	72.62	66.07	76.19	75.60
Williams et al.[25]	2023	Prospective	Men	87	186	58±11	27.2	14.81	N/A	8.75	N/A	22.08	N/A	18.18	N/A	N/A	N/A	N/A
			Women	99		63±12	27.2	6.59	N/A	5.43	N/A	18.68	N/A	23.81	N/A	N/A	N/A	N/A
Summary			Men	12202	30281	55.27±14.68	56.0	17.8	7.37	7.67	3.43	35.79	4.84	23.88	73.62	53.70	55.73	51.79
			Women	18079		63.56±15.29	66.4	20.4	8.25	7.72	3.85	21.82	5.41	14.19	66.75	50.06	49.55	49.03
P value						<0.01	<0.01	<0.01	0.02	0.91	0.11	<0.01	0.07	<0.01	<0.01	<0.01	<0.01	<0.01

Categorical variables are presented as percentages (%). Continuous variables are presented as mean±SD. MI indicates myocardial infarction.
*Muhammad et al[22] reported missing/unavailable data at time of discharge (2 men, 2 women) and during follow-up (10 men, 8 women).

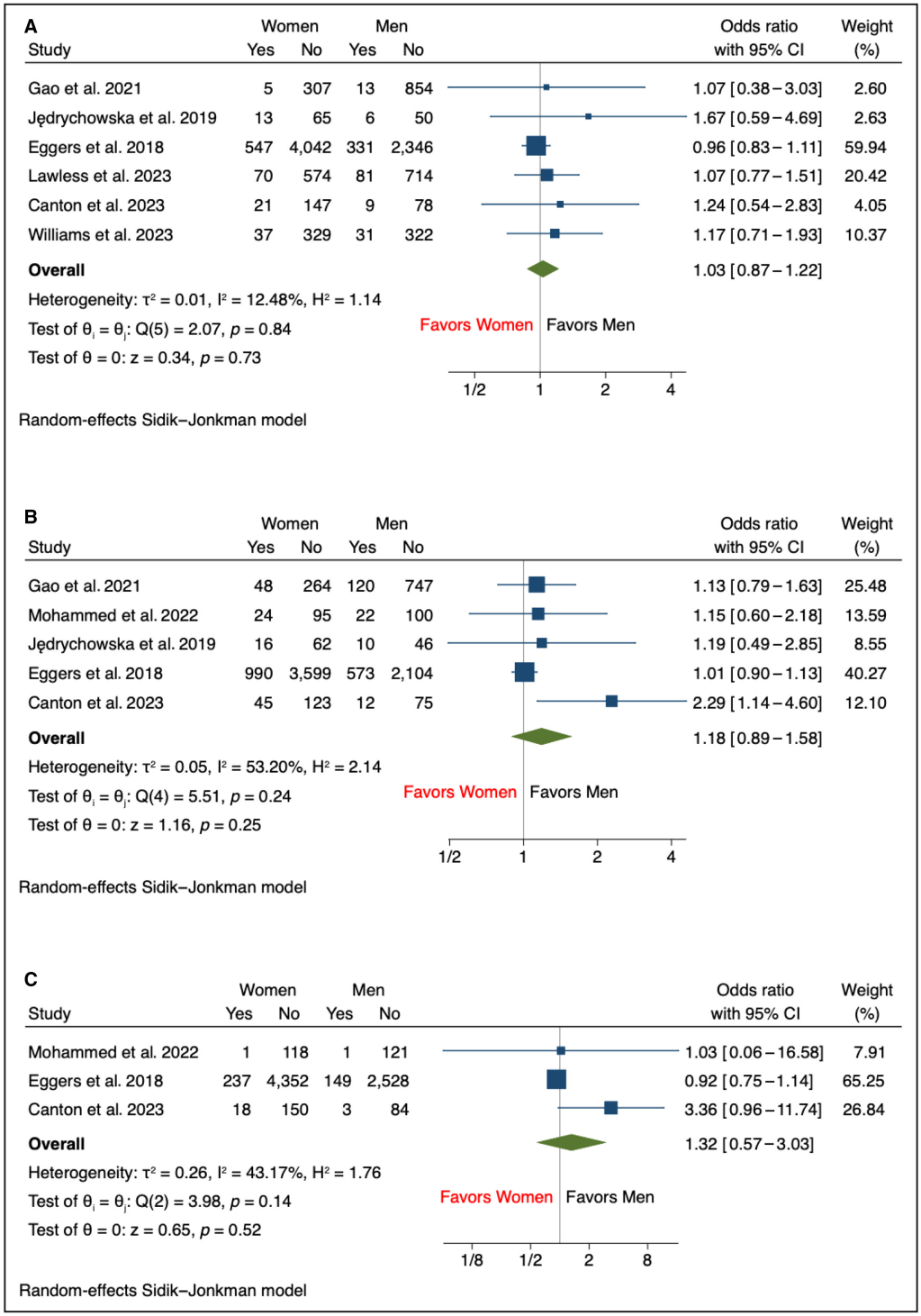

Figure 1. Forest plots of long-term outcomes including (A) all-cause mortality,[12,13,15,23–25] (B) major adverse cardiovascular events,[12,13,15,22,23] and (C) heart failure.[12,13,22]

effect sizes are not practically relevant, and the overall effect is consistent across studies. The crude rate of MACE was higher in women compared with men (5.3% versus 4.0%, respectively). The pooled analysis of 5 studies showed that women are associated with an 18% excess risk of MACE compared with men (OR, 1.18 [95% CI, 0.89–1.58]; Figure 1B).[12,13,15,22,23] The CI indicates that the data are compatible with women having an 11% lower risk to a 58% higher risk of MACE compared with men. The moderate heterogeneity

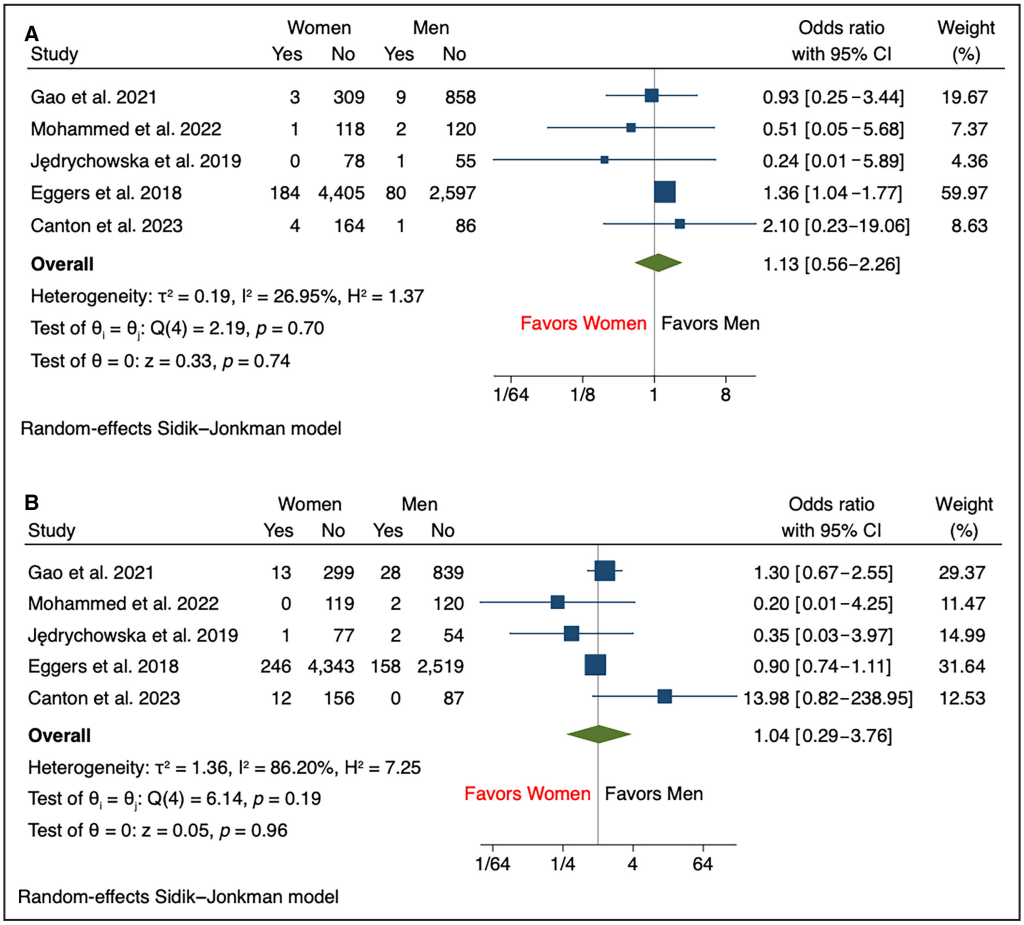

Figure 2. Forest plots of long-term outcomes including (A) stroke[12,13,15,22,23] and (B) myocardial infarction.[12,13,15,22,23]

(I^2=53.2%) reflects variability in effect sizes, but the overall pooled estimate suggests no statistically significant difference in MACE risk between sexes. Data on heart failure were derived from 3 studies, with women having a higher crude rate of heart failure compared with men (4.9% versus 4.7%, respectively).[12,13,22] The pooled analysis of 3 studies suggested that women have a 32% higher risk of heart failure compared with men, but results did not reach statistically significance (OR, 1.32 [95% CI, 0.57–3.03]; Figure 1C). The CI indicates that the data are compatible with women having a 43% lower risk to more than 3 times the risk of heart failure compared with men. Moderate heterogeneity (I^2=43.17%) indicates variability in effect sizes, but the overall pooled estimate suggests no statistically significant difference in the risk of heart failure between the 2 sexes.

The pooled effect size for stroke and MI was derived from 5 studies, respectively.[12,13,15,22,23] Women had a higher crude rate of stroke compared with men (3.6% versus 2.4%, respectively). Results of the meta-analysis showed that female sex was associated with a 13% excess in risk of stroke compared with men, but the results did not reach statistical significance (OR, 1.13 [95% CI, 0.56–2.26]; *P*=0.74) (Figure 2A). The CI indicates that the data are compatible with women having a 44% lower risk (OR, 0.56) to more than twice the risk (OR, 2.26) of stroke compared with men. Low heterogeneity is observed across studies (I^2=26.95%), indicating variability in effect sizes. The overlapping CIs suggest that the differences in effect sizes are not practically relevant. Although women had a slightly numerically higher crude rate of MI compared with men (5.2% versus 5.0%, respectively), we observed no significant difference between women and men in the risk of MI between the 2 sexes (OR, 1.04 [95% CI, 0.29–3.76]; *P*=0.96) (Figure 2B). The CI indicates that the data are compatible with women having a 71% lower risk to more than 3 times the risk of MI compared with men. However, the heterogeneity is high (I^2=86.2%), indicating significant differences in the effect sizes between studies. Despite this high heterogeneity, the pooled estimate suggests no significant difference in MI risk between sexes.

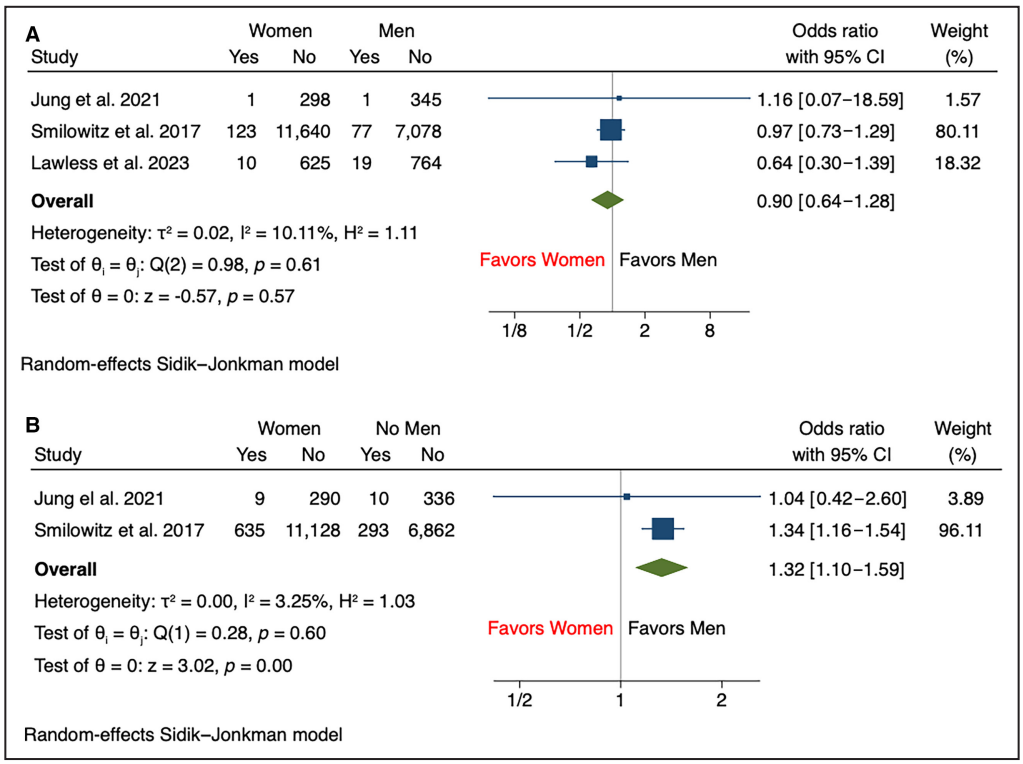

Figure 3. Forest plots of short-term outcomes including (A) in-hospital mortality[14,21,24] and (B) in-hospital major adverse cardiovascular events.[14,21]

Regarding short-term outcomes, 3 studies reported data on in-hospital mortality[14,21,24] and 2 studies reported on in-hospital MACE.[14,21] Women had a slightly lower numerically crude rate of in-hospital mortality compared with men (1.1% versus 1.2%). Results of meta-analysis suggested no statistically significant difference in the risk of in-hospital mortality between women and men (OR, 0.90 [95% CI, 0.64–1.28]; *P*=0.58; Figure 3A). The heterogeneity across the studies is low (I^2=10.11%), indicating that most of the variability in the effect size is due to chance rather than actual differences between studies. Furthermore, the crude rate of in-hospital MACE was higher in women compared with men (5.3% versus 4.0%, respectively). Results of meta-analysis suggested women had a 33% increased risk of in-hospital MACE compared with men, and the results are statistically significant (OR, 1.33 [95% CI, 1.16–1.53]; Figure 3B). The CI indicates that the increased risk of in-hospital MACE ranged from 16% to 53% in women compared with men. There is low heterogeneity across the studies (I^2=3.25%), with both studies showing higher risk of in-hospital MACE in women.

Subgroup and Sensitivity Analyses

Subgroup analyses were undertaken to evaluate all-cause mortality, MACE, and MI based on various criteria: age, follow-up duration, study methodology, and data source as specified in methods. When stratified by follow-up duration, the risk of all-cause mortality, MACE, and MI were found to be consistent with primary analyses, with no statistically significant difference between both groups (Figures S2–S5). A similar consistency in risk was observed when analyses were stratified by study design (Figures S6–S9) and data source (Figures S10–S13), indicating that both sexes exhibited no significant difference in the risks for all-cause mortality, MACE, and MI, with no significant subgroup differences (*P*>0.05).

Sensitivity analyses were conducted for outcomes such as all-cause mortality, MACE, heart failure, MI, and stroke. By omitting 1 study sequentially, the outcomes were consistent with the primary analysis, demonstrating no notable differences in all-cause mortality, MACE, heart failure, and MI between female and male patients (Figures S14–S18). In addition, we implemented Firth's bias-reduced logistic regression for small studies and conducted a secondary analysis using fixed effects model. The sensitivity analysis revealed no statistically significant difference between women and men regarding the risk of all-cause mortality, MACE, heart failure, MI, in-hospital mortality, and in-hospital MACE (Figures S19–S24). However, when using a fixed-effects model for the meta-analysis,

women had a higher risk of stroke compared with men (OR, 1.32 [95% CI, 1.02–1.69]) (Figure S25). It is important to note that this effect size is predominantly influenced by 1 study (Eggers et al),[12] which accounted for >90% of the weight in the analysis.

Publication Bias

Visualization of funnel plots showed that there was minimal asymmetry for all-cause mortality, MACE, heart failure, and MI, suggesting the absence of publication bias (Figures S26–S30).

DISCUSSION

In the present systematic review and meta-analysis, we observed that there was no significant sex difference in the long-term outcomes, including all-cause mortality, MACE, stroke, and MI in patients diagnosed with MINOCA. These results remained consistent and unaltered after sensitivity analysis and subgroup analyses based on age, follow-up period, study design, and data source, confirming robustness of results. Lastly, there was no significant difference in terms of in-hospital mortality between both groups of patients.

In the contemporary era, sex-specific differences in the manifestations and outcomes of cardiovascular diseases are increasingly recognized, owing to increased awareness. Compared with men, women with coronary artery disease tend to present later and with a much larger burden of comorbidities.[26–32] They are also less likely to be referred or treated with guideline-directed medical therapy.[27,32–36] However, data with regard to mortality after acute coronary syndrome remain controversial, with some studies suggesting higher risk among women[34,37] and others showing similar outcomes.[36,38,39]

The current study expanded on the findings of a recent meta-analysis of 7 observational studies. Specifically, Chaudhary et al investigated the sex-specific clinical outcomes in patients with MINOCA and observed that women had a significantly higher incidence of MACE and stroke compared with men whereas there was no significant difference in all-cause mortality, nonfatal MI, and cardiovascular readmission between women and men.[40] Of note, whether these outcomes would differ based on time of assessment of outcomes or follow-up period was not examined. The included studies, specifically by Jung et al and Smilowitz et al, evaluated the in-hospital outcomes whereas the remainder of the studies evaluated the mid- and long-term outcomes in these patients. To further clarify the question, we separated in-hospital and long-term periods and found that over the in-hospital period, women continued to have a significantly higher risk of MACE compared with men. However, over the follow-up period, the difference in the risk of MACE attenuated and was nonsignificant between both groups of patients. The results of the stroke analysis also varied between the 2 methodological approaches. In our primary analysis using a random-effects model, we found no statistically significant difference in stroke risk between sexes. Conversely, our secondary analysis using a fixed-effects model indicated a higher risk of stroke in women, consistent with the findings of Chaudhary et al. It is important to note that the fixed-effects results were heavily influenced by a single study. Given the heterogeneity in patient populations and the variability in the inclusion criteria for patients with MINOCA, we believe that a random-effects model may be more appropriate for this analysis. To refine these findings, more studies with precise, longitudinal data will be needed to better account for variability and ensure robust conclusions. Consistent with prior studies comparing MINOCA and MI-coronary artery disease, we found that there was no sex difference in terms of mortality in patients with MINOCA either in hospital or long term and that the higher risk of post-MI mortality among women compared with men was restricted to the MI-coronary artery disease group.

An interesting observation was that despite the relative disparities in terms of prescription medications at discharge, with women receiving relatively less frequent statins, beta blockers, and ACEIs/ARBs compared with men, the long-term outcomes including all-cause mortality, MACE, and MI appeared to be similar between both sexes. This may be related to the prevalence of nonatherosclerotic underlying causes of MINOCA. In a multicenter registry-based retrospective study, Ciliberti et al observed that the use of beta blockers was associated with a significant reduction in the incidence of a composite outcome of all-cause mortality, acute MI, acute coronary syndrome, heart failure hospitalization, or stroke.[41] However, no significant difference in the composite outcome was observed in those who were taking statins or ACEIs/ARBs. Choo et al, on the other hand, examined several prognostic factors and their association with mortality in patients with MINOCA using a nationwide registry and concluded that the use of ACEIs/ARBs and statins was related to reduced mortality in patients with MINOCA.[42] Importantly, the use of cardiac magnetic resonance or other noninvasive imaging techniques to evaluate the underlying cause of MINOCA was limited in these studies. The ongoing multicenter pragmatic randomized controlled trial, MINOCA BAT (Randomized Evaluation of β-Blocker and ACEI/ARB Treatment in MINOCA Patients; ClinicalTrials.gov Identifier: NCT03686696) study will provide additional insights on the effects of these routinely used cardioprotective medications in patients with MINOCA.[43]

Strengths and Limitations

Our study derives its strength from being the most comprehensive and updated meta-analysis thus far, notably with the inclusion of 3 additional studies published in 2023. Several limitations should be taken into consideration upon interpretation of the study. First, the majority of included studies were observational in nature, thus the risk of confounding bias could not be ruled out. The distribution of weight was notably uneven in outcomes such as long-term MACE and all-cause mortality. However, after excluding the study with the largest weight, these outcomes remained consistent with primary analyses, proving the robustness of results. In addition, the definition of MINOCA varied slightly across included studies. Particularly, 4 studies did not include the underlying causes of MINOCA, hence the potential of the inclusion of nonischemic causes such myocarditis and Takotsubo syndrome could not be entirely excluded (Table S5).

CONCLUSIONS

Our study suggests that there was no significant difference in the long-term outcomes for patients with MINOCA across sexes, suggesting that sex by itself may not be associated with long-term prognosis in patients with MINOCA. The observed increased risk of in-hospital MACE in women calls for additional research to identify specific risk factors contributing to this disparity. Understanding these risk factors is essential for developing targeted strategies to improve short-term outcomes in these patients.

ARTICLE INFORMATION

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None.

Supplemental Material

Tables S1–S5.
Figures S1–S30.

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