Journal of the American Heart Association

ORIGINAL RESEARCH

Statin Use Among Women and Men Following Coronary Artery Bypass Surgery

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BACKGROUND: Limited data exist on sex differences in guideline-recommended statin therapy for secondary prevention after coronary artery bypass surgery (CABG). We examined sex differences in statin use after CABG and the association between sex-specific statin use and mortality.

METHODS AND RESULTS: Data from the Austrian national cardiac surgery registry and federal social insurance claims database for patients who underwent CABG between 2013 and 2021 were used. Multivariable logistic regression models were calculated to obtain women-to-men odds ratios for filling any statin and high-intensity statin prescriptions. Cox proportional hazards models were used to evaluate the association between statin use and mortality. A total of 15 448 patients (19% women) were included. During the 5 years after CABG, statin use decreased from 95.7% to 85.9% in men and 95.2% to 84.3% in women (P for trend <0.0001; P_{int}=0.48), high-intensity statin use decreased from 69.4% to 57.2% in men and 67.8% to 54.3% in women (P for trend <0.0001; P_{int}=0.59). The adjusted odds ratio for filling any statin prescription comparing women with men was 1.03 (95% CI, 0.92–1.16) and for filling a high-intensity statin prescription was 1.12 (95% CI, 1.02–1.23). Statin use was associated with a significantly lower mortality risk in both sexes (any statin: hazard ratio [HR], 0.56 [95% CI, 0.46–0.68]; P<0.0001, P_{int}=0.22; high-intensity statin: HR, 0.52 [95% CI, 0.42–0.63]; P<0.0001, P_{int}=0.48).

CONCLUSIONS: Women were as likely as men to fill a statin prescription after CABG and more likely to fill a high-intensity prescription. Statin use was associated with a similar mortality risk reduction among women and men.

Key Words: coronary artery bypass grafting ■ secondary prevention ■ sex differences ■ statins

While sex differences in the use of statin therapy and especially high-intensity statin therapy for secondary prevention have been reported after hospital discharge for cardiovascular events[1] and myocardial infarction,[2,3] it is unknown whether such differences exist after coronary artery bypass graft (CABG) surgery. Approximately 30% of patients undergoing CABG surgery are women. Women have worse outcomes, including a higher mortality rate, after CABG than men.[4,5] Underuse of secondary preventive therapies, including statins, has been suggested as a contributing factor to the observed differences in clinical outcomes.[6]

Here, we used integrated data from a large-scale European national cardiac surgery registry and a federal social insurance agency's medical claims database, representing a significant majority (>97%) of the population under universal health coverage, to assess the contemporary longitudinal use of any statin and high-intensity statin therapy following CABG among women compared with men. We also examined the association between sex-specific

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This manuscript was sent to Samuel S. Gidding, MD, Guest Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.124.039011

For Sources of Funding and Disclosures, see page 8.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Following coronary artery bypass surgery, women are as likely as men to claim a prescription for statin therapy and more likely to receive a high-intensity dosage once prescribed a statin.
- Continued statin use after coronary artery bypass surgery is associated with a similar mortality risk reduction among women and men, with greater benefits of high-intensity statins for both women and men.

What Are the Clinical Implications?

- Equitable use of secondary preventive therapies including high-intensity statins may narrow the mortality outcome gap between the sexes after coronary artery bypass surgery.

Nonstandard Abbreviations and Acronyms

SWEDEHEART	Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies

statin and high-intensity statin use and long-term mortality after CABG.

METHODS

Data Source

This analysis used data from the Austrian Adult Cardiac Surgery Registry, a national registry of all adult patients undergoing any cardiac surgery in Austria.[7] All cardiac surgery centers in Austria participate in the registry, and data entry is performed on-site by dedicated data managers. The registry captures demographic data, cardiac and noncardiac medical history, procedural data, discharge-related data, adverse events during the index hospital admission, 30-day and in-hospital mortality rate (if >30 days), and any readmission including reason for readmission. The registry is managed via the Austrian National Public Health Institute and audited annually for quality assurance. Annual reports are publicly available since 2021.[8] Patients are identified in the registry via their social security number, allowing for linking of registry data with national administrative databases and the national death index.

For this analysis, registry data were linked to the medical claims database of the Federation of Austrian Social Insurances, which provides universal health coverage for >97% of Austrian residents, and the national death index. The medical claims database includes prescription fills from the outpatient sector for all drugs reimbursed by the insurance providers. Data are updated on a monthly basis. In creating the combined data set, patient data were pseudonymized to comply with applicable data privacy protection regulations. The study was approved by an institutional review committee (Ethics Committee of the Medical University Vienna, Protocol No. 2122-2021), and individual informed consent was not required. The data that support the findings of this study are available from the corresponding author (S.S.) upon reasonable request.

Study Design

The study population consisted of patients who underwent first-time, isolated CABG between January 1, 2013, and December 31, 2021, and who were insured with a provider within the Federation of Austrian Social Insurances at the time of admission for surgery. Longitudinal sex-specific statin use was evaluated by the proportion of women and men filling at least 2 consecutive statin prescriptions in the following time periods: within 3 months before CABG; within 6 months; months 7 to 12; and years 2, 3, 4, and 5 after CABG. Data on prescription fills and vital status were captured until loss of insurance eligibility or December 31, 2021.

Statin Use

Statin use was identified by pharmacy prescription fills using Anatomical Therapeutical Chemical codes and included simvastatin, lovastatin, pravastatin, fluvastatin, atorvastatin, cerivastatin, rosuvastatin, and pitavastatin. High-intensity statin use was defined in accordance with the 2018 American Heart Association/American College of Cardiology Guideline on the Management of Blood Cholesterol[9] and included atorvastatin 40 or 80 mg and rosuvastatin 20 or 40 mg.

Statistical Analysis

Categorical data were reported as counts and percentages. Continuous data were reported as mean±SD for normally distributed variables and median (interquartile range) for nonnormally distributed variables. The χ^2 test and 2-sample t test were used for comparison of categorical and continuous variables, respectively. Complete case data were used for all analyses and were available for 95.1% of patients. The number of observations with missing values are shown in Table S1.

Sex-Specific Use of Statins

Patients were censored at the time of loss of insurance status. The Fitzpatrick and Scott method was used to calculate simultaneous CIs for multinomial proportions.[10] Binomial univariate and multivariable logistic regression models were calculated to evaluate sex-specific differences in filling a statin prescription. The binary outcome variable discriminates between patients with or without statin prescription fills. A nominal 3-stage outcome variable (no statin, low-/moderate-intensity statin, high-intensity statin) was analyzed using multinomial logistic regression models to evaluate sex-specific differences in filling a high-intensity statin prescription. The multivariable models were adjusted for the following covariates: age, body mass index, diabetes, dyslipidemia, smoking, history of myocardial infarction, history of percutaneous coronary intervention, history of stroke, peripheral artery disease, chronic kidney disease, congestive heart failure, acute coronary syndromes, left main stenosis, multiple arterial grafting, and use of cardiopulmonary bypass. The entire 5-year observation period after CABG was analyzed by generalized estimating equations methodology with the (generalized) logit link function to evaluate adjusted sex-specific differences in filling any or a high-intensity statin prescription, respectively. The observation period was divided into the time periods described above and patients were therefore included in multiple consecutive observation periods in the generalized estimating equation analysis data set. To test for sex-specific differences in subgroups of patients, interaction terms were included in the generalized estimating equation model. Results of all models were reported as odds ratios (ORs) and 95% CIs.

Mortality After CABG by Sex and Statin Use

Landmark analyses were performed to evaluate the effect of statin use on survival after CABG. Patients filling at least 2 consecutive statin prescriptions in the time periods before the landmark were considered as using statins. The primary analysis was landmarked at 1 year; sensitivity analyses were landmarked at 30 days, 6 months, and 5 years.

Kaplan–Meier cumulative survival estimates were calculated for women and men, and univariate and multivariable Cox proportional hazards regression models were used to evaluate the association of sex and statin use with death after CABG. A potential interaction between the sex effect and the effect of statin use was tested by inclusion of an interaction term. To check the proportional hazards assumption, time-varying effects were tested and included in case of statistical significance. Treatment associations were reported as hazard ratios (HRs) and 95% CIs.

Two-sided P values <0.05 were considered statistically significant. As this is an exploratory study, no adjustments for multiplicity were made, and results are considered hypothesis generating. The software SAS version 9.4 (SAS Institute Inc., Cary, NC) was used for all analyses.

RESULTS

Patients

In total, 2886 (18.7%) women and 12 562 (81.3%) men were included in the analysis (Figure S1). Baseline clinical and procedural characteristics are reported in the Table. Compared with men, women were older (mean age, 65.9±9.5 versus 69.0±9.3 years), had a higher prevalence of diabetes and chronic kidney disease, and more frequently presented with acute coronary syndromes (20.4% versus 23.1%). Women less often received multiple arterial grafting (17.0% versus 23.4%). The median duration of follow-up was 4.3 (interquartile range, 2.5–6.2) years. A total of 209 patients (1.4%) lost insurance status after a median of 3.2 (interquartile range, 1.3–6.5) years following surgery.

Sex-Specific Trends in the Use of Statin Therapy

Between the period before and 1 year after CABG surgery, the percentage of patients filling any statin prescription increased from 66.3% to 95.7% in men and from 65.8% to 95.2% in women (Figure 1, Table S2). The percentage of patients filling a prescription for a high-intensity statin increased from 36.2% to 69.4% in men and from 33.6% to 67.8% in women. Beyond the first year after CABG, any statin use (OR, 0.86 [95% CI, 0.84–0.87]) and high-intensity statin use (OR, 0.97 [95% CI, 0.96–0.98]) decreased (P for trend<0.0001), and the decrease in both any statin and high-intensity statin use was similar in women and men.

Between 2013 and 2021, high-intensity statin use when prescribed a statin increased from 31.4% to 70.8% in women and 33.5% to 72.5% in men (Figure S2).

Sex-specific use of nonstatin lipid-lowering medications is illustrated in Figure S3.

Sex Differences in the Use of any Statin and High-Intensity Statin Therapy

Sex differences in statin and high-intensity statin fills are shown in Figure 2. The odds of filling any statin prescription were similar among women compared with men before CABG (adjusted OR, 1.04 [95% CI, 0.94–1.14]) and during 5 years of follow-up after CABG (adjusted OR, 1.03 [95% CI, 0.92–1.16]).

Women had similar odds as men of filling a high-intensity statin prescription before CABG (adjusted OR, 1.03 [95% CI, 0.92–1.14]) but had higher odds than men of filling a high-intensity statin prescription during 5 years of follow-up after CABG (adjusted OR, 1.12 [95% CI, 1.02–1.23]; Table S3).

Table. Baseline and Procedural Characteristics of Patients Undergoing Coronary Artery Bypass Surgery

	Men (N=12 562)	Women (N=2886)	*P* value
Demographics			
Age, y, mean±SD	65.9±9.5	69.0±9.3	<0.0001
Body mass index, kg/m^2, mean±SD	28.2±4.2	27.8±5.2	0.002
Medical history, n (%)			
Diabetes*	3595 (28.6)	913 (31.6)	0.001
Hypertension	9321 (78.9)	2107 (78.6)	0.71
Dyslipidemia	8772 (70.6)	1986 (69.9)	0.49
Smoking†	4459 (35.7)	705 (24.6)	<0.0001
History of myocardial infarction	5262 (41.9)	1175 (40.7)	0.24
History of percutaneous coronary intervention	2861 (22.8)	570 (19.8)	0.0004
History of stroke	734 (5.8)	171 (5.9)	0.87
Peripheral arterial disease	2026 (16.1)	496 (17.2)	0.17
Chronic kidney disease‡	2280 (18.2)	959 (33.2)	<0.0001
Congestive heart failure§	2085 (16.7)	407 (14.2)	0.001
Left ventricular ejection fraction, %, mean±SD	52.3±11.2	53.4±10.8	<0.0001
Clinical presentation, n (%)			0.001
Chronic coronary disease	9939 (79.7)	2200 (76.9)	
Acute coronary syndrome	2540 (20.4)	661 (23.1)	
Left main stenosis,‖ n (%)	5689 (45.4)	1189 (41.2)	<0.0001
Procedural characteristics, n (%)			
Multiple arterial grafting¶	2919 (23.4)	485 (17.0)	<0.0001
Off-pump coronary artery bypass#	306 (2.5)	103 (3.6)	0.0006
Guideline-directed therapies prescribed at discharge, n (%)			
Aspirin	8199 (79.4)	1831 (79.8)	0.69
β Blocker	7374 (71.8)	1636 (71.9)	0.93
ACE inhibitor/ARB	4685 (46.8)	1030 (46.3)	0.67

ACE indicates angiotensin-converting-enzyme; and ARB, angiotensin-receptor blocker.
*Includes all medically treated diabetes (oral and insulin).
†Includes former and current smoking.
‡Creatinine ≥2 mg/dL (176 mmol/L) or dialysis.
§Clinical diagnosis or self-reported history of heart failure, New York Heart Association class ≥III, pulmonary congestion on chest radiograph, or peripheral edema on diuretics.
‖Stenosis >50%.
¶Patients receiving ≥2 arterial conduits.
#Denotes coronary artery bypass surgery performed without use of cardiopulmonary bypass.

The sex-specific use of high-intensity statins during the 5 years after CABG was consistent across patient subgroups, including patients aged ≥75 years (Figure 3). Sex-specific use of high-intensity statins differed in magnitude by clinical presentation at the time of surgery, with higher use of high-intensity statins in women with chronic coronary disease and lower use in women with acute coronary syndromes compared with men (P_{int}=0.001).

Mortality After CABG by Sex and Statin Use

Use of statins after CABG was associated with a significantly lower risk of death (HR, 0.56 [95% CI, 0.46–0.68]; *P*<0.0001; Figure 4A), without a significant interaction between sex and statin use (P_{int}=0.221; Tables S4 and S5). The finding was consistent in the sensitivity models landmarked at 30 days, 6 months, and 5 years (Table S6).

The reduction in the risk of death was greater with use of high-intensity statins (HR, 0.52 [95% CI, 0.42–0.63]; *P*<0.0001) than with low-/moderate-intensity statins (HR, 0.61 [95% CI, 0.50–0.75]; *P*<0.0001) and was similar among women and men (P_{int}=0.477; Figure 4B).

When adjusted for baseline risk, procedural variables, and statin use, female sex was associated with a significantly lower risk of death versus male sex (HR, 0.70 [95% CI, 0.61–0.81]; *P*<0.0001; Table S4).

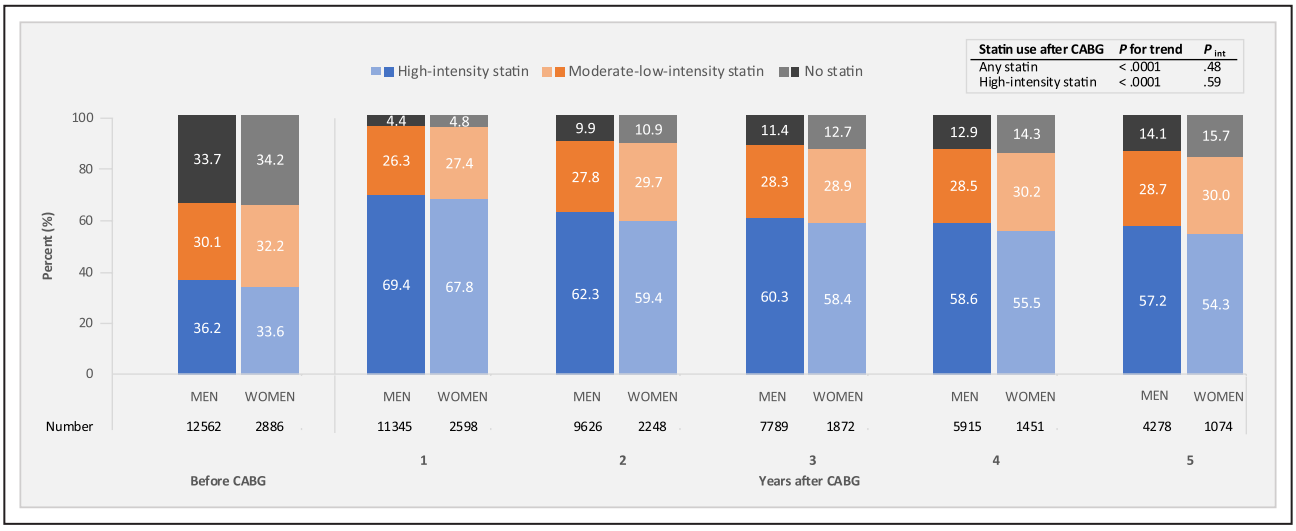

Figure 1. Trends in the use of statin therapy among women and men following CABG.
CABG indicates coronary artery bypass grafting.

DISCUSSION

In this nationwide study involving 15448 patients who underwent CABG over 9 years, women were as likely as men to receive statin therapy for secondary prevention after CABG, and more likely than men to receive a high-intensity dosage when prescribed a statin. Use of statins was associated with a similar reduction in mortality rate after CABG among women and men with a greater benefit of high-intensity statins in both sexes.

This study used a comprehensive data set created by merging records from a national cardiac surgery registry with the Austrian Federation of Social Insurances' medical claims database, encompassing >97% of residents under universal health coverage. More than 95% of both women and men filled consecutive statin

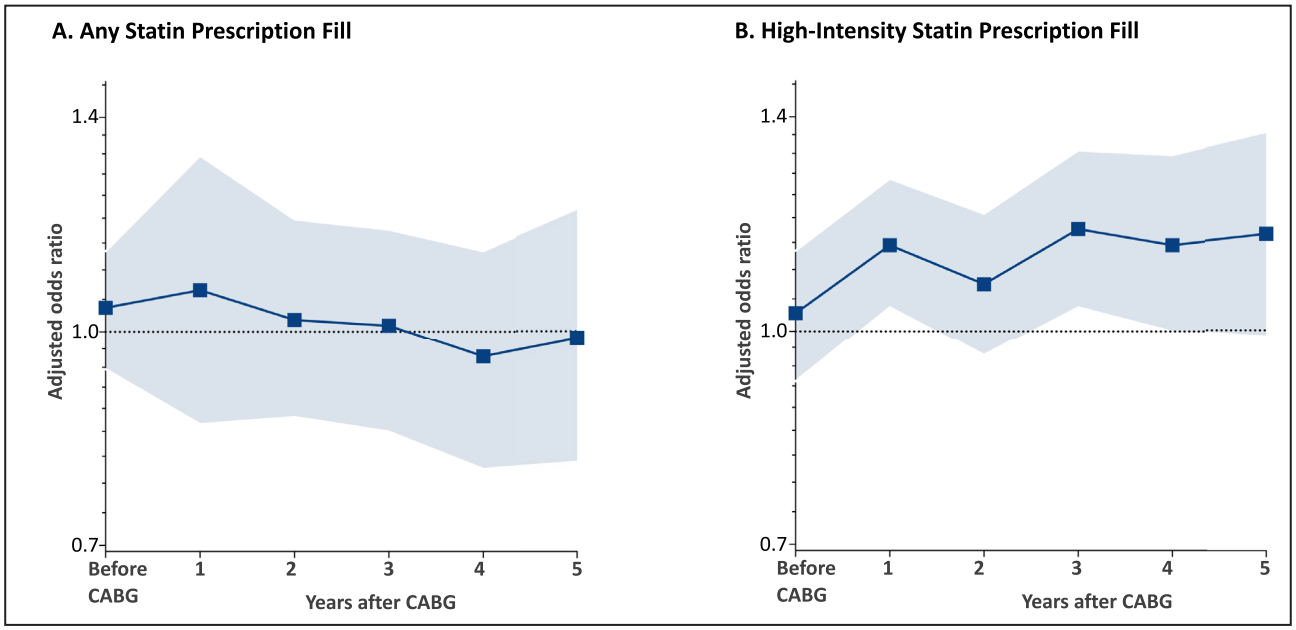

Figure 2. Statin prescription fills among women versus men after CABG.
A, Any statin prescription fill. **B**, High-intensity statin prescription fill. The line represents the adjusted odds ratio (95% CI) for filling any statin or a high-intensity statin prescription comparing women with men (reference). The shaded region depicts the 95% CIs. The model includes adjustment for age, body mass index, diabetes, dyslipidemia, smoking, history of myocardial infarction, history of percutaneous coronary intervention, history of stroke, peripheral artery disease, chronic kidney disease, congestive heart failure, acute coronary syndromes, left main stenosis, multiple arterial grafting, and use of cardiopulmonary bypass (see Table). CABG indicates coronary artery bypass grafting.

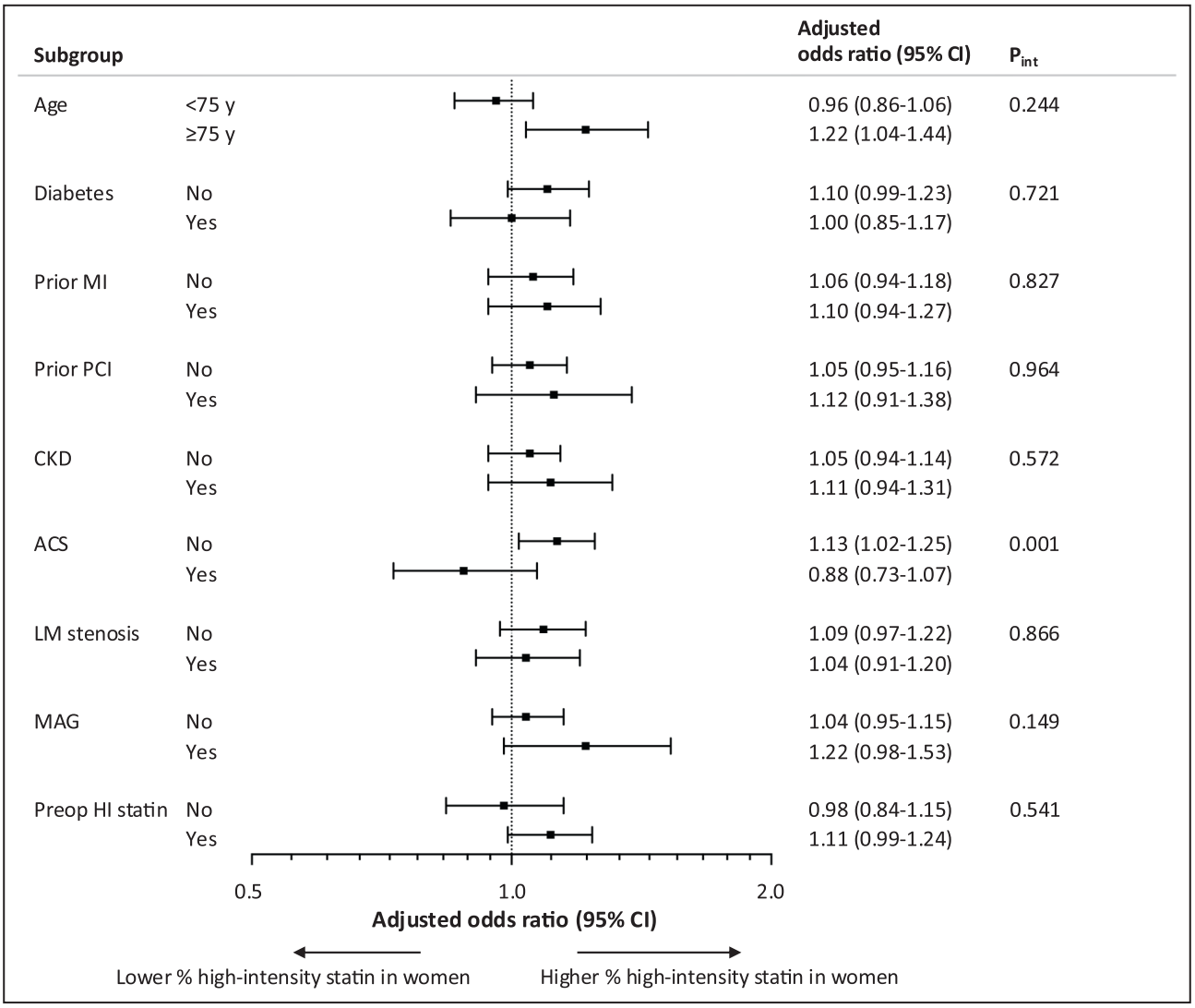

Figure 3. Adjusted odds ratios (95% CIs) for filling a high-intensity statin prescription among women versus men (reference) across patient subgroups in a 5-year period after CABG.
The *P*-values correspond to the sex-related interaction terms tested in the multivariable generalized estimating equation models. ACS indicates acute coronary syndromes; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; HI, high-intensity; LM, left main; MAG, multiple arterial grafting; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

prescriptions within the first year after CABG surgery, and ≈70% of these were prescriptions for a high-intensity statin. Although statin and high-intensity statin use decreased during the 5 years after surgery, the decrease was similar for both sexes. A previous analysis from the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) registry in a CABG population reported similarly high statin use early after surgery, but a greater subsequent decrease among women, with high-intensity statins used in only 36% of patients.[11] Our study, which includes patients who underwent CABG nearly a decade later, suggests a greater use of guideline-recommended statin treatment strategies, especially among women.

Previous studies have consistently shown underuse of statins among women compared with men for secondary prevention of cardiovascular disease.[12–14] In a retrospective cohort analysis of 284 952 US patients (128 422 women), women were less likely to receive statins than men within 30 days of discharge from hospitalization for a new cardiovascular event including myocardial infarction, revascularization, or stroke (adjusted OR, 0.81 [95% CI, 0.80–0.82]; *P*<0.001).[1] Similarly, another study including 88 256 US adults (39 256 women) who filled a statin prescription following hospital discharge after myocardial infarction further showed that once prescribed a statin, the intensity of the dosage was lower in women than in men, with an adjusted risk ratio for filling a high-intensity statin

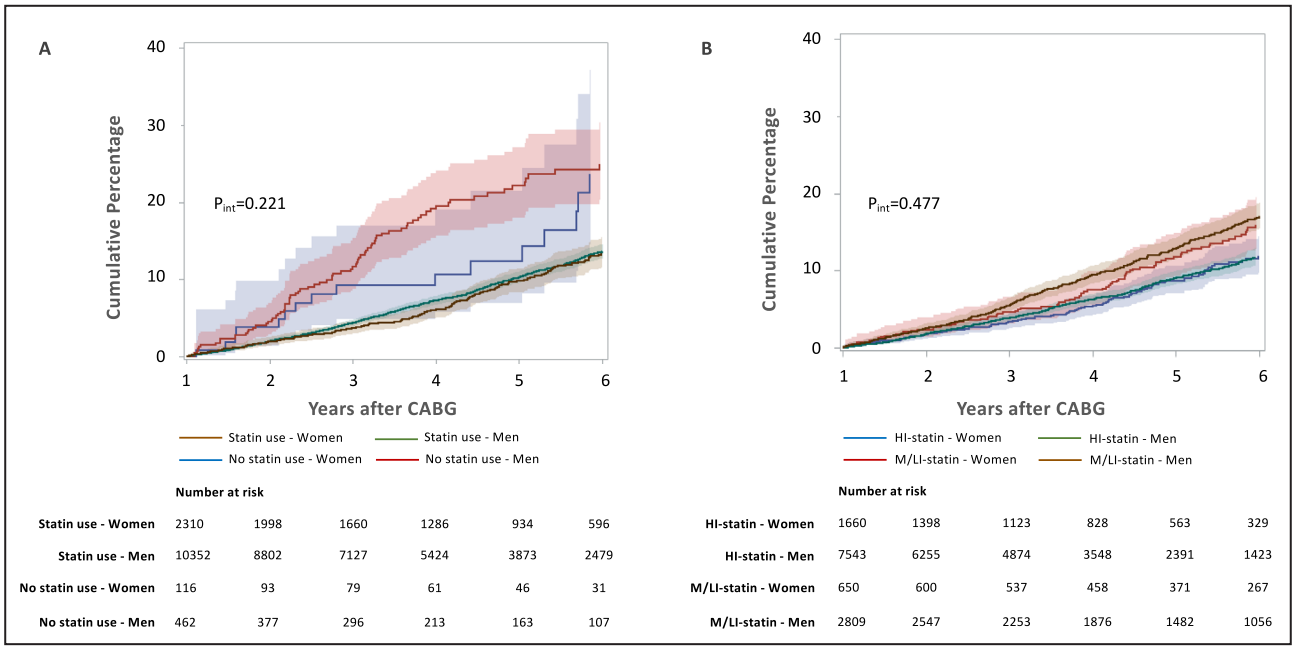

Figure 4. Death after CABG in women and men by statin use.
A, Statin vs no statin use. **B**, HI vs M/LI statin use. The primary analysis was landmarked at 1 y after CABG surgery. Time 0 represents the landmark time (1 y after CABG). *P* values correspond to the sex-related interaction terms tested in the Cox models. CABG indicates coronary artery bypass grafting; HI, high-intensity; and M/LI, moderate-/low-intensity.

prescription of 0.91 (95% CI, 0.90–0.92) comparing women with men.[2] In our contemporary CABG population, the odds of filling any statin prescription during the 5-year period after CABG surgery were similar between women and men, with women having higher odds of filling a high-intensity statin prescription.

Our finding that women were more likely than men to fill high-intensity statin prescriptions after CABG warrants careful consideration. Several factors may explain this observation. CABG surgery is often perceived as a pivotal event in a patient's health journey, particularly for women who may undergo revascularization less frequently than men.[15] This context may amplify the emphasis on optimizing secondary prevention strategies after CABG, among both patients and health care providers. Women in this setting may be more likely to perceive high-intensity statins as an integral part of maintaining the benefits of surgery, thereby increasing acceptance of these therapies.

Moreover, the extensive coverage provided by the Austrian health care system, which minimizes financial barriers to accessing high-cost medications, could facilitate equitable prescribing and adherence to guideline-recommended therapies. This system may have mitigated some of the socioeconomic disparities that have historically led to lower use of high-intensity statins among women in other settings.[16]

Finally, there may have been an evolution in clinical practice patterns over the past decade. Growing awareness of sex disparities in cardiovascular care, coupled with targeted efforts to address these gaps, may have led to increased prescribing of high-intensity statins for women in recent years. These efforts likely reflect the influence of updated guidelines and educational campaigns emphasizing the importance of high-intensity statins for both sexes in secondary prevention.[17] Women undergoing CABG are often older and have a higher burden of comorbidities than their male counterparts,[18] potentially leading clinicians to prioritize high-intensity statins to manage elevated cardiovascular risk more aggressively.

Early postdischarge statin therapy is associated with reduced all-cause death and major adverse cardiovascular events after CABG.[19] An analysis from the SWEDEHEART registry[11] reported that ongoing statin treatment after CABG was associated with reduced risk of major adverse cardiovascular events (adjusted HR, 0.56 [95% CI, 0.53–0.59]) with a larger treatment effect in men (P_{int}=0.046). Our study expands on these findings by showing an association between statin use and significant mortality risk reduction after CABG, irrespective of statin intensity, with consistent findings across sensitivity analyses. It is important to note that the magnitude of the mortality risk reduction after CABG in our analysis was similar among women and men, consistent with prior research.[20] Our data also suggest that equitable use of statins for secondary prevention may narrow the mortality outcome gap between the sexes after CABG.

Limitations

Our analysis has several limitations. First, while we used a comprehensive national data set from the Federation of Austrian Social Insurances, it captures only prescription fills and does not provide information on whether medications were actually taken or the degree of patient adherence. Additionally, we could not account for prescriptions that may have been written but not filled, introducing potential bias, particularly if sex-specific differences in adherence or initiation behaviors exist. Second, our data set lacked clinical factors that could influence statin prescription, dosage, and continuation, such as low-density lipoprotein cholesterol levels, which are critical for assessing baseline cardiovascular risk, monitoring therapeutic response, and evaluating adherence to guideline-directed targets. The absence of such information limits our ability to contextualize the observed sex differences in statin use or determine the extent to which patients achieved recommended low-density lipoprotein cholesterol thresholds. Third, we were unable to identify patients who discontinued statins due to intolerance or side effects, which may vary by sex, limiting the interpretation of sex-specific differences in long-term statin use. Fourth, other potential confounders, including renal or hepatic impairment, and adherence to other guideline-directed therapies, were not captured in the administrative data set. These factors could influence both the decision to prescribe statins and the clinical outcomes associated with their use. Fifth, although the extensive coverage of the Austrian health care system likely reduces socioeconomic disparities in access to medications, our findings may not be fully generalizable to health care systems with differing levels of coverage or socioeconomic diversity. Finally, while our study included nearly all patients undergoing CABG in Austria over a 9-year period, the sample size remains modest compared with the global burden of CABG procedures. Variations in clinical practices, patient demographics, and health system structures across countries may limit the applicability of our findings to other populations.

Conclusions

In a nationwide European study of patients undergoing CABG, women were as likely as men to fill a prescription for statins and more likely to fill a high-intensity dosage when prescribed. Continued statin use after CABG was associated with similar mortality risk reductions for both sexes, with high-intensity statins providing greater benefits for both women and men.

ARTICLE INFORMATION

Received September 24, 2024; accepted December 19, 2024.

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Acknowledgments

The authors thank Professor Emeritus Dr Ernst Wolner and the Austrian Society for Cardiac and Thoracic Vascular Surgery for their support.

Sources of Funding

None.

Disclosures

None.

Supplemental Material

Tables S1–S6
Figures S1–S3

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