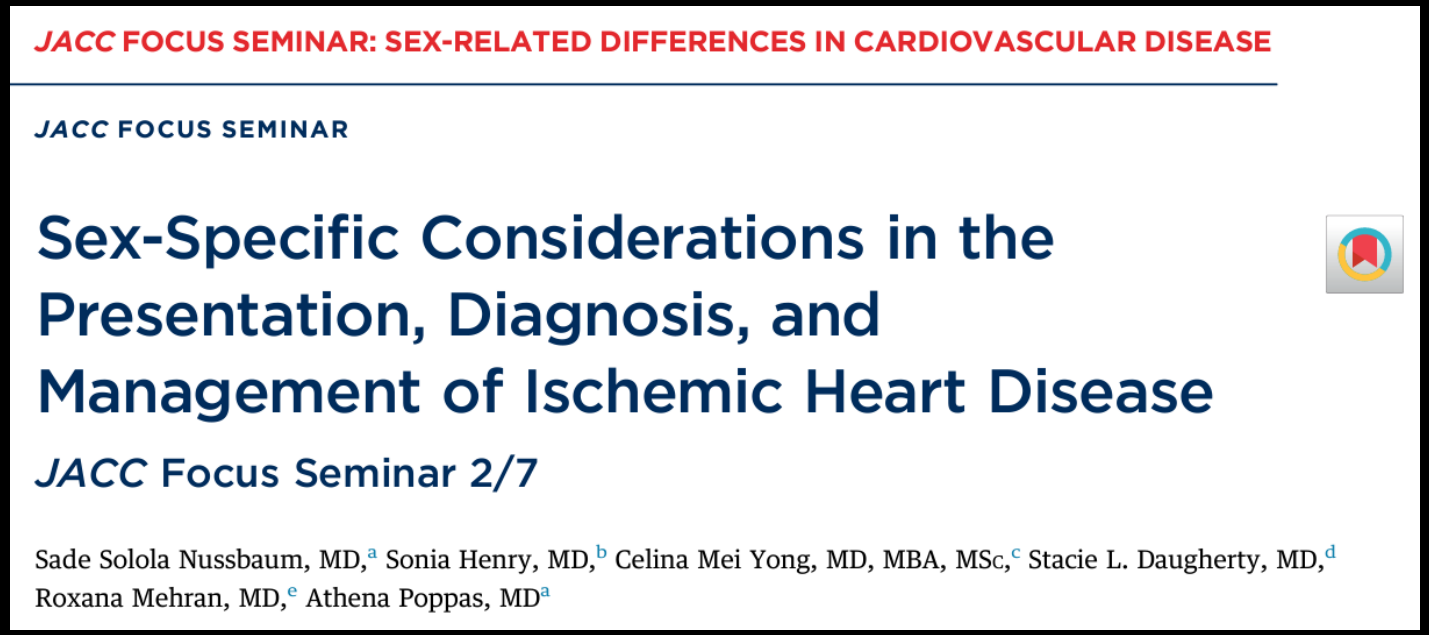
Recent issues regarding CABG in women

고려대학교 안암병원 김희중



Solola Nussbaum S, Henry S, Yong CM, Daugherty SL, Mehran R, Poppas A. Sex-Specific Considerations in the Presentation, Diagnosis, and Management of Ischemic Heart Disease: JACC Focus Seminar 2/7. Journal of the American College of Cardiology. 2022;79(14):1398-406.

- There are differences in the presentation, diagnosis, and management of IHD in men and women.
- Women more often have nonobstructive coronary disease than men but face higher morbidity and mortality.
- Initiatives to address sex-based differences in clinical research could improve outcomes for women with IHD.

TABLE 2 Female-Specific Risk Enhancing Factors

Pregnant women
Preeclampsia
Gestational hypertension
Gestational diabetes
Preterm delivery
Delivery for small for gestational age infants
Younger women (<40 y of age)
Premature ovarian failure (<40 y)
Polycystic ovarian syndrome
Hormonal contraceptive use
Menarche
Transgender
Older women (>40 y of age)
Menopause
Postmenopausal hormone therapy

TABLE 4 Sex-Specific Differences and Recommendations in Guidelines

Clinical Practice Document	Noted Sex-Specific Differences	Noted Sex-Specific Recommendations	Knowledge Gaps
2013 ACC/AHA STEMI guideline	30% are women remain undertreated	None	Prehospital delay bleeding risks
2014 ACC/AHA NSTEMI-ACS	Pregnancy: revascularization if life-threatening complications	Early invasive strategy for high risk features	Antithrombotic dosing Myocardial infarction with nonobstructive coronary arteries
2012, 2014 update ACC/AHA stable ischemic heart disease	None for PCI, medications, CABG	Avoid estrogen replacement therapy in postmenopausal women	Nonobstructive disease diagnosis, treatment
2011 ACC/AHA PCI	Higher in-hospital mortality Higher procedural complications	None	Vascular access and bleeding risks
2011 ACC/AHA CABG	Higher perioperative morbidity/mortality Similar long-term outcomes	None Most data extrapolated from men	Mitigating bleeding risks Improving complete revascularization
2020 ESC ACS without STEMI	None. Noted to follow same treatment	Careful antithrombotic dosing periprocedural	Nonobstructive disease

ACC = American College of Cardiology; ACS = acute coronary syndromes; AHA = American Heart Association; CABG = coronary artery bypass grafting; ESC = European Society of Cardiology; NSTEMI-ACS = non-ST-segment elevation myocardial infarction acute coronary syndrome; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

- Only 38.2% were women in cardiovascular trial between 2010 and 2017
- Need for gender specific subgroup analysis

CENTRAL ILLUSTRATION Sex-Related Differences in Ischemic Heart Disease

Epidemiology
- Prevalence of IHD and angina varies by race, ethnicity, and age in women
- Women have higher mortality with IHD event and higher morbidity compared to men
- Women have high rates of angina, hospitilizations and repeat angiography

Presentation
- Women may report chest pain but more often report back pain, jaw pain, epigastric pain, palpitations and lightheadedness
- Diabetes and smoking are more potent IHD risk factors in women when compared to men
- Atypical presentation in women linked to delays in seeking care, diagnosis and life-saving treatment

Diagnostic testing
- Coronary artery calcium (CAC) is a strong predictor of subclinical CAD particularly in women
- Coronary CTA has a high diagnostic and prognostic accuracy for the detection of CAD in women

Management
- Guidelines recommending an early invasive strategy in women with NSTEMI-ACS and high-risk features
- Guidelines do not distinguish any differences in treatment for men or women in terms of use of anti-ischemic medicaltions, PCI or revascularization with CABG

Future of IHD in Women
- Focused guidelines on management and primary prevention of IHD in women
- Focus research on improving quality of clinical care in women
- Initiatives that focus on implementation science and health policy to effect the social determinants of health
- Detailed and directed research to close the gap in outcome and care

Solola Nussbaum S, et al. J Am Coll Cardiol. 2022;79(14):1398-1406.

Outcomes

Sex differences in outcomes following coronary artery bypass grafting: a meta-analysis

N. Bryce Robinson[a], Ajita Naik[a], Mohamed Rahouma [a], Mahmoud Morsi[a], Drew Wright [b], Irbaz Hameed[a], Antonino Di Franco [a], Leonard N. Girardi[a] and Mario Gaudino [a,*]

- 84 Studies
- 903346 subjects

Operative mortality	72	663 527	1.77 (1.64–1.92)	<0.001	0.56	<0.001	
After year 2000	54	280 782	1.73 (1.54–1.93)	<0.001	0.62	<0.001	0.31
Before year 2000	18	382 745	1.87 (1.69–2.06)	<0.001	0.11	0.33	0.31
Study type: regression-adjusted	52	563 900	1.75 (1.59–1.92)	<0.001	0.53	<0.001	0.56
Study type: unadjusted	9	7646	2.06 (1.54–2.75)	<0.001	0.02	0.41	0.56
Study type: PSM	11	91 981	1.82 (1.42–2.34)	<0.001	0.75	<0.001	0.56
Late mortality	33		1.16 (1.06–1.26)	<0.001	0.78	<0.001	
After year 2000	22		1.14 (1.03–1.26)	0.01	0.84	<0.001	0.60
Before year 2000	11		1.20 (1.01–1.44)	0.04	0	0.58	0.60
Study type: regression-adjusted	40		1.28 (1.14–1.44)	<0.001	0.47	<0.001	0.66
Study type: unadjusted	22		1.15 (1.03–1.28)	0.01	0.77	<0.001	0.66
Study type: PSM	8		1.35 (0.96–1.89)	0.08	0.57	0.02	0.66
Late MI	39		1.28 (1.13–1.45)	<0.001	0.48	<0.001	
Late stroke	45		1.31 (1.15–1.51)	<0.001	0.36	0.01	
Late RR	12		0.99 (0.76–1.29)	0.95	0.47	0.04	
Late MACE	8		1.4 (1.19–1.66)	<0.001	0.62	0.01	

Bryce Robinson N, Naik A, Rahouma M, Morsi M, Wright D, Hameed I, et al. Sex differences in outcomes following coronary artery bypass grafting: a meta-analysis. Interactive CardioVascular and Thoracic Surgery.

Key question

Are there differences in outcomes between the sexes following isolated coronary artery bypass grafting?

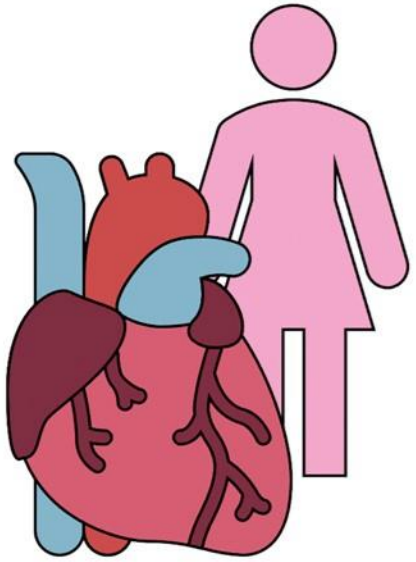
Key finding(s)

Women undergoing CABG are at higher risk for late mortality and postoperative events including MACE, MI and stroke.

Take-home message

Outcomes of women undergoing CABG remain suboptimal; studies are needed to elucidate the causes of this difference and improve women's outcomes.

CABG OUTCOMES IN WOMEN AS COMPARED TO MEN



OPERATIVE MORTALITY
OR 1.77, 95%CI 1.64-1.92

LATE MORTALITY
IRR 1.16, 95%CI 1.06-1.26

MACE
IRR 1.40, 95%CI 1.19-1.66

MYOCARDIAL INFARCTION
IRR 1.28, 95%CI 1.13-1.45

STROKE
IRR 1.31, 95%CI 1.15-1.51

Cause of sex difference in CABG

ESC European Society of Cardiology
European Heart Journal (2022) **43**, 29–31
doi:10.1093/eurheartj/ehab617

EDITORIAL

Why do women do worse after coronary artery bypass grafting?

Sanne A.E. Peters [1,2,3] **and Jolanda Kluin** [4]*

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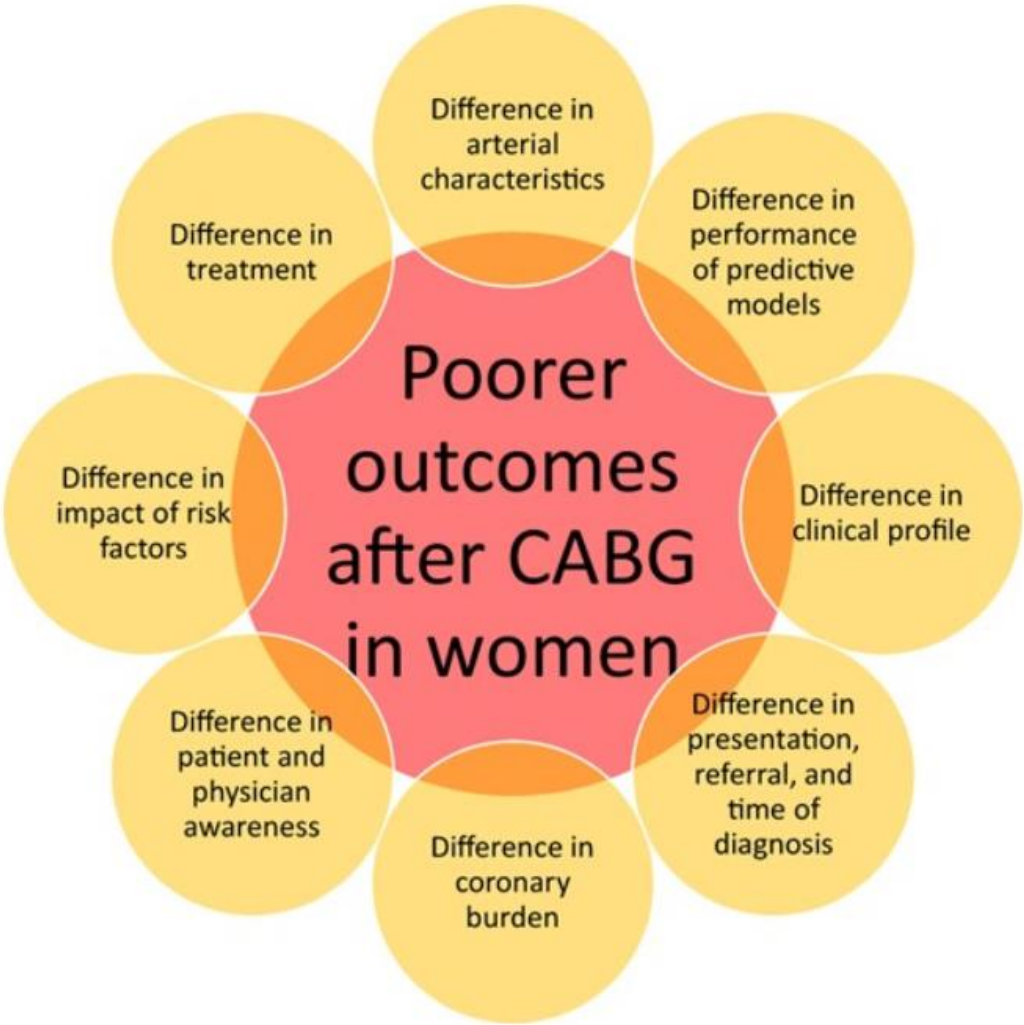
Graphical Abstract



Differ in preoperative condition

Ter Woorst JF, van Straten AHM, Houterman S, Soliman-Hamad MA. Sex Difference in Coronary Artery Bypass Grafting: Preoperative Profile and Early Outcome. J Cardiothorac Vasc Anesth. 2019;33(10):2679-84.

Original Research

Sex Difference in Coronary Artery Bypass Grafting: Preoperative Profile and Early Outcome

Table 2
Operative Data

Variables	Women N = 4,016	Men N = 13,903	p Value
Duration of CPB, min*	57.2 (±35.1)	59 (±35.5)	<0.001
Aortic cross-clamp time, min*	37.6 (±24.2)	40 (±23.7)	<0.001
ICU stay, d†	1.0 (1-56)	1.0 (1-95)	<0.001
Hospital stay, d†	7.0 (2-127)	7.0 (2-153)	0.728
Number of grafts*	3.2 (±1.1)	3.5 (±1.1)	<0.001
Aortic cross-clamp time/graft, min*	11.6 (±8.7)	11.2 (±7.0)	0.013

Preoperative and Demographic Characteristics

Variable	Women (n = 4,016)	Men (n = 13,903)	p Value
Age (y), mean	68.2 ± 9.6	64.4 ± 9.8	<0.001
Hypertension	2,306 (57.4%)	6,216 (44.7%)	<0.001
COPD	463 (11.5%)	1,504 (10.8%)	0.207
PVD	506 (12.6%)	1,727 (12.4%)	0.767
Prior CVA	181 (4.5%)	592 (4.3%)	0.510
Reoperation	181 (4.5%)	725 (5.2%)	0.073
Underweight	132 (3.3%)	161 (1.2%)	<0.001
Obesity	307 (7.6%)	497 (3.6%)	<0.001
Diabetes	1124 (28.0%)	2765 (19.9%)	<0.001
- Insulin-dependent (%)	385 (9.6)	816 (5.9)	
- Non-insulin-dependent (%)	621 (15.5)	1581 (11.4)	
- Diet-controlled (%)	117 (2.9)	366 (2.6)	
Emergency	109 (2.7%)	202 (1.5%)	<0.001
LVEF <35%	122 (3.0%)	504 (3.6%)	0.081
Hemoglobin level, mmol/L, mean	7.9 ± 1.1	8.8 ± 1.1	0.004
Creatinine level, μmol/L, mean	89.7 ±39.8	101.5 ±39.4	<0.001
Preoperative AF	121 (3.0%)	413 (3.0%)	0.878
3-vessel disease including main stem stenosis	2,305 (57.4%)	8,661 (62.3%)	0.085

Table 5
Multivariable Logistic Regression Analysis for Predictors of Early Mortality Stratified by Sex

	Women		Men	
Variable	OR (95% CI)	p Value	OR (95% CI)	p Value
Age	1.056 (1.029-1.084)	<0.0001	1.068 (1.050-1.086)	<0.001
Diabetes	1.433 (0.958-2.143)	0.08		
LVEF <35%	4.830 (2.610-8.937)	<0.0001	4.950 (3.490-7.021)	<0.001
COPD			1.705 (1.241-2.340)	0.001
PVD			1.529 (1.128-2.074)	0.006
Prior CVA	1.978 (0.993-3.941)	0.52	1.425 (0.891-2.280)	0.139
Prior cardiac surgery	4.733 (2.704-8.285)	<0.0001	4.747 (3.452-6.525)	<0.001
Preoperative hemoglobin, mmol/L	0.736 (0.568-0.954)	0.021	0.797 (0.685-0.927)	0.003
Serum creatinine, μmol/L	1.004 (1.001-1.006)	0.008	1.004 (1.002-1.005)	<0.001
Underweight			2.878 (1.448-5,721)	0.003
Preoperative AF			1.404 (0.834-2.363)	0.202
Cross-clamp time, min			1.006 (1.002-1.011)	0.007

Incomplete revascularization

Oertelt-Prigione S, Kendel F, Kaltenbach M, Hetzer R, Regitz-Zagrosek V, Baretti R. Detection of gender differences in incomplete revascularization after coronary artery bypass surgery varies with classification technique. Biomed Res Int.

Research Article

Detection of Gender Differences in Incomplete Revascularization after Coronary Artery Bypass Surgery Varies with Classification Technique

Sabine Oertelt-Prigione,[1] Friederike Kendel,[2] Martin Kaltenbach,[3] Roland Hetzer,[4] Vera Regitz-Zagrosek,[1,5] and Rufus Baretti[4]

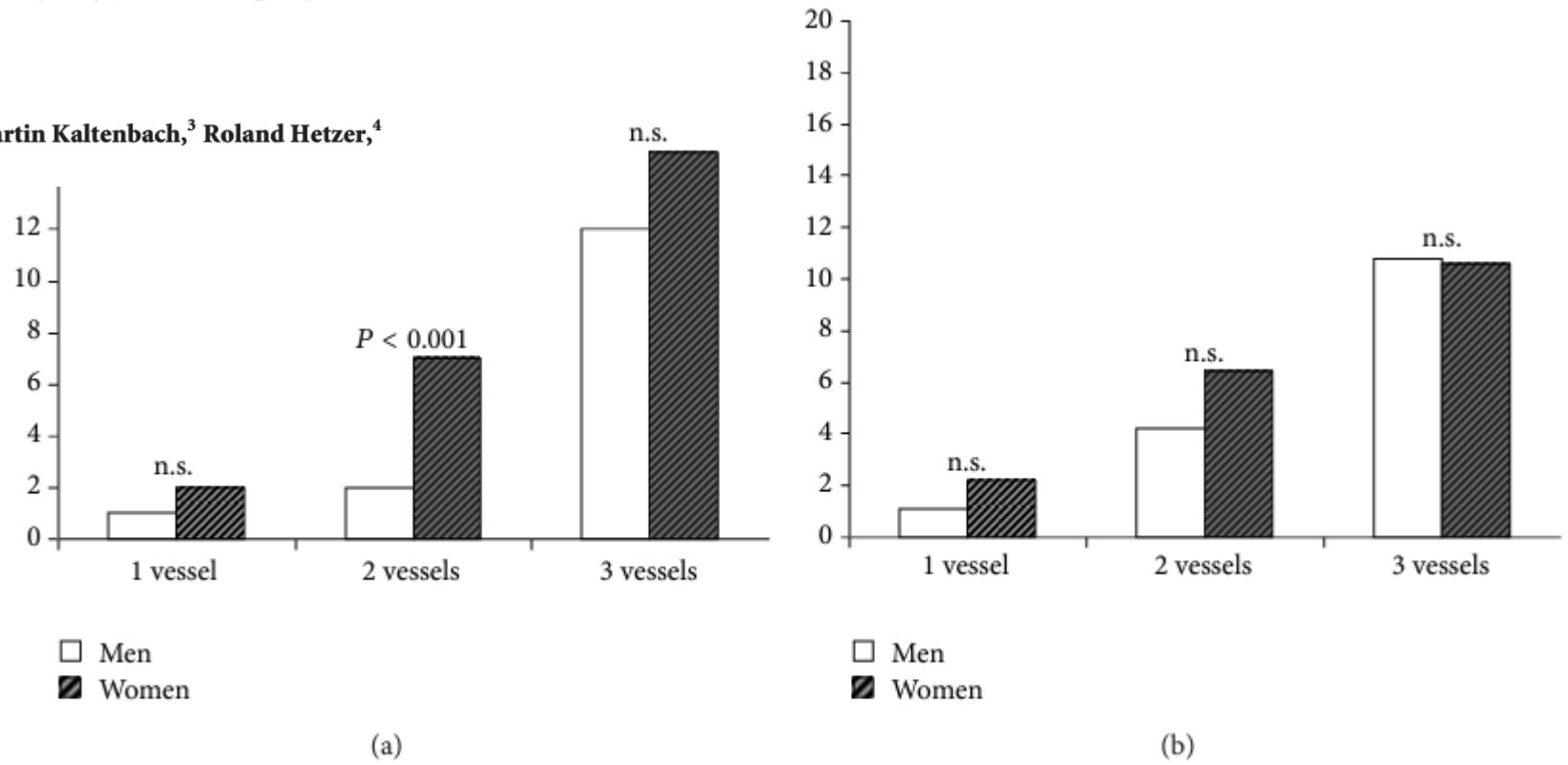


FIGURE 2: Incomplete revascularization according to the number of diseased vessels (%). According to the mathematical calculation (a), women with double-vessel disease or main stem stenosis more often receive incomplete revascularization than men, whereas the gender differences in single-vessel or triple-vessel disease are not significant. If the surgeons' classification is considered (b), a similar pattern is identified, yet with a relative overestimation of male double-vessel disease and underestimation of female triple-vessel disease.

Small coronary artery in women

Sex differences in coronary artery size assessed by intravascular ultrasound

Stuart E. Sheifer, MD,[a] Michael R. Canos, MPH,[a] Kevin P. Weinfurt, PhD,[a] Umesh K. Arora, MD,[a] Farrell O. Mendelsohn, MD,[b] Bernard J. Gersh, MB, ChB, DPhil,[c] and Neil J. Weissman, MD[a] *Washington, DC; Durham, NC; and Rochester, Minn*

Sheifer SE, Canos MR, Weinfurt KP, Arora UK, Mendelsohn FO, Gersh BJ, et al. Sex differences in coronary artery size assessed by intravascular ultrasound. Am Heart J. 2000;139(4):649-53.

Table II. Results of independent sample *t* tests comparing LM and LAD coronary artery dimensions in men and women

Dimension	Women	Men	P value
Uncorrected arterial area (mm^2)			
LM	21.53 ± 6.88	26.95 ± 5.70	<.001
LAD	14.68 ± 5.32	19.94 ± 5.38	.002
Uncorrected luminal area (mm^2)			
LM	15.94 ± 6.24	18.79 ± 4.06	.020
LAD	10.13 ± 3.48	12.71 ± 4.23	.036
Corrected arterial area (mm^2/m^2)			
LM	11.88 ± 3.89	13.33 ± 2.97	.076
LAD	8.01 ± 3.48	9.85 ± 2.41	.048
Corrected luminal area (mm^2/m^2)			
LM	8.79 ± 3.43	9.29 ± 1.98	.433
LAD	5.53 ± 2.20	6.28 ± 1.97	.291
Percent plaque area			
LM	26.0 ± 10.8	30.3 ± 11.1	.248
LAD	31.0 ± 11.2	36.2 ± 11.5	.092

Table III. Multiple linear regression models predicting LM and LAD coronary arterial area, corrected for BSA

Characteristic	β	P value
LM model		
Sex	.243	.038
Age	.238	.039
Hypertension	.122	.298
LAD model		
Sex	.287	.043
Age	.258	.070
Hypertension	.205	.150

Lower anastomosis number of arterial graft

Sex-specific disparities in patients undergoing isolated CABG☆

Table 2
Operative characteristics in patients undergoing CABG.

	Total (n = 12,736)	Male (n = 9573)	Female (n = 3163)	p-Value
Status				<0.0001
Elective	4664 (37)	3630 (38)	1034 (33)	
Urgent	7464 (59)	5522 (58)	1942 (61)	
Emergent	593 (4.6)	410 (4.3)	183 (5.8)	
Emergent salvage	15 (0.1)	11 (0.1)	4 (0.1)	
Cardiopulmonary bypass	6032 (50)	5017 (52)	1015 (41)	<0.0001
CPB time	100 (81, 123)	102 (83, 124)	94 (75, 117)	<0.0001
Aortic cross-clamp time	76 (60, 94)	78 (61, 95)	70 (55, 88)	<0.0001
Lowest temperature	34.2 (33.9, 35.5)	34.2 (33.8, 35.8)	34.3 (34.0, 35.6)	0.002
Intraoperative blood products	3013 (24)	1780 (19)	1233 (39)	<0.0001
Robot used	1401 (11)	1063 (11)	338 (11)	0.51

STS database, 2010 to 2021

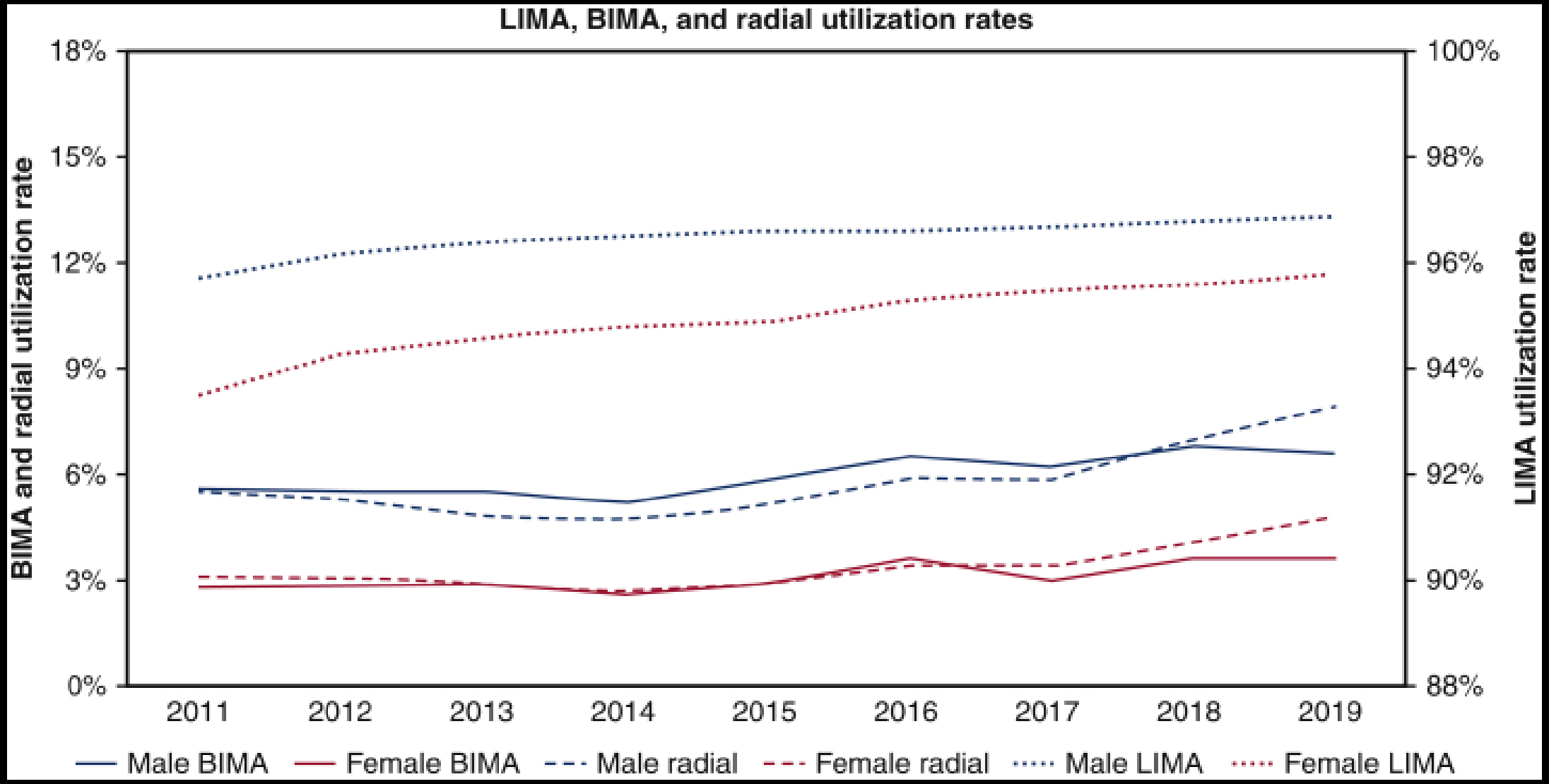
Table 3
Distal anastomoses in patients undergoing CABG.

	Total (n = 12,736)	Male (n = 9573)	Female (n = 3163)	p-Value
Distal vein anastomoses	2 (1,2)	2 (1, 2)	2 (1, 2)	<0.0001
Distal arterial anastomoses	1 (1,1)	1 (1, 1)	1 (1, 1)	<0.0001
0	270 (2.2)	166 (1.8)	104 (3.4)	
1	10,461 (85)	7742 (84)	2719 (89)	
2	1315 (11)	1118 (12)	197 (6.5)	
3	171 (1.4)	152 (1.7)	19 (0.6)	
4	21 (0.2)	20 (0.2)	1 (0.03)	

Dassanayake MT, Norton EL, Ward AF, Wenger NK. Sex-specific disparities in patients undergoing isolated CABG. Am Heart J Plus. 2023;35:100334.

Coronary surgery in women: How can we improve outcomes

Zwischenberger BA, Jawitz OK, Lawton JS. Coronary surgery in women: How can we improve outcomes. JTCVS Tech. 2021;10:122-8.



MAG vs SIMA

Single versus multiple arterial coronary artery bypass grafting in men and women: results from Polish National Registry of Cardiac Surgery Procedures

Aboul-Hassan SS, Hirnle G, Perek B, Jemielity M, Hirnle T, Brykczynski M, et al. Single versus multiple arterial coronary artery bypass grafting in men and women: results from Polish National Registry of Cardiac Surgery Procedures. International Journal of Surgery. 2024;110(4):2234-42.

Polish National Registry of Cardiac Surgery Procedures database

January 2012 and December 2020

22.9 were women

MAG was performed in 8.3 and 11.7% of female and male patients, respectively

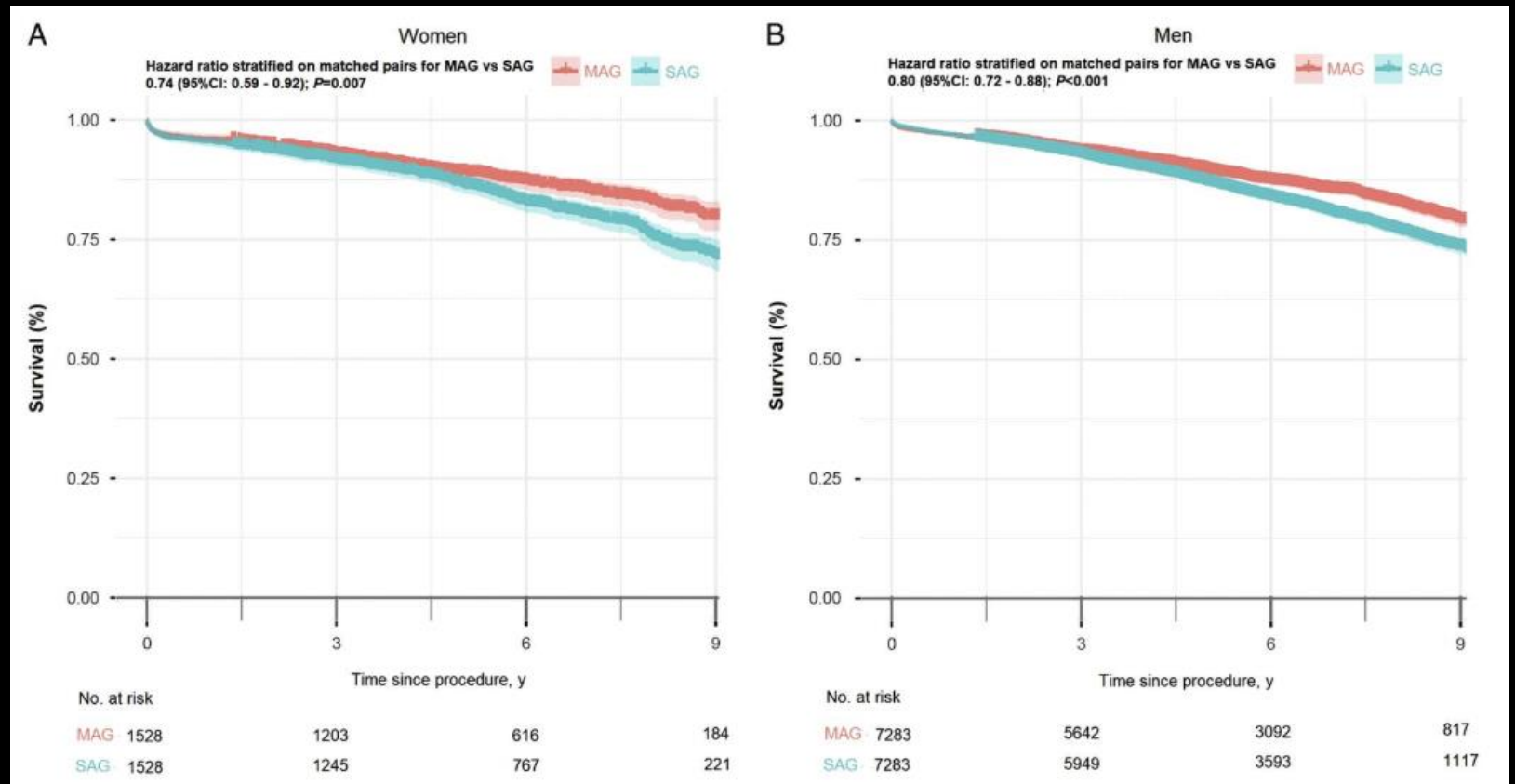


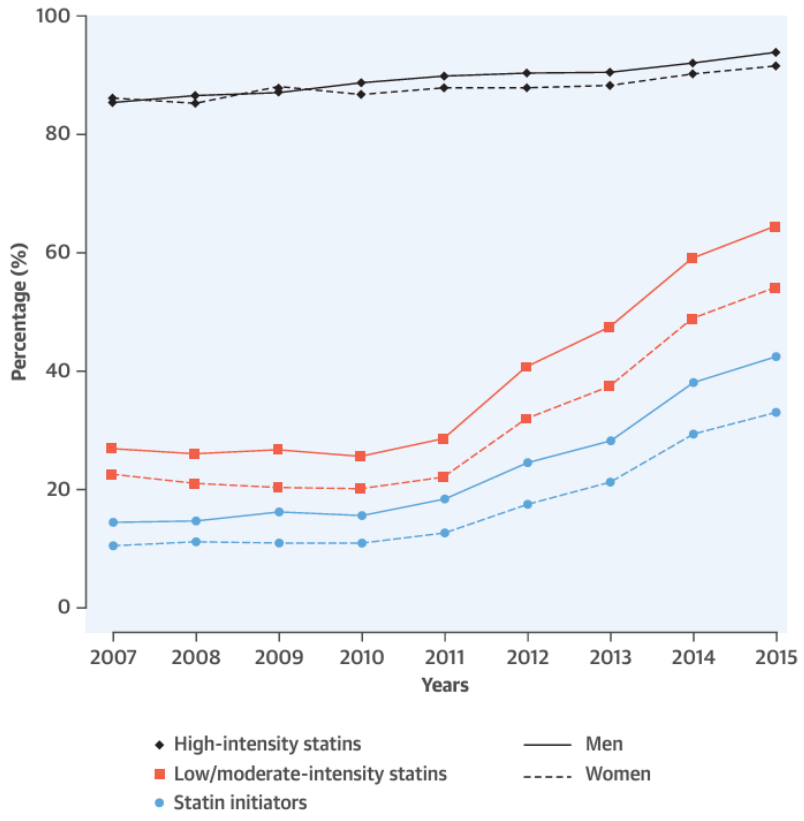
Figure 2. Risk of mortality in women and men who underwent multiple arterial graft (MAG) versus single arterial graft (SAG) in the propensity score matched patients and in the propensity matched subgroup of patients younger than age 70 years and aged 70 years or older, diabetic and non diabetic patients, obese and nonobese patients, ejection-fraction (EF) above 40% and equal or below 40%, with and without peripheral artery disease (PAD), and with and without chronic lung disease (CLD), separately in women and men.

Guideline oriented optimal management following CABG

Peters SAE, Colantonio LD, Zhao H, Bittner V, Dai Y, Farkouh ME, et al. Sex Differences in High-Intensity Statin Use Following Myocardial Infarction in the United States. J Am Coll Cardiol. 2018;71(16):1729-37.

Sex Differences in High-Intensity Statin Use Following Myocardial Infarction in the United States

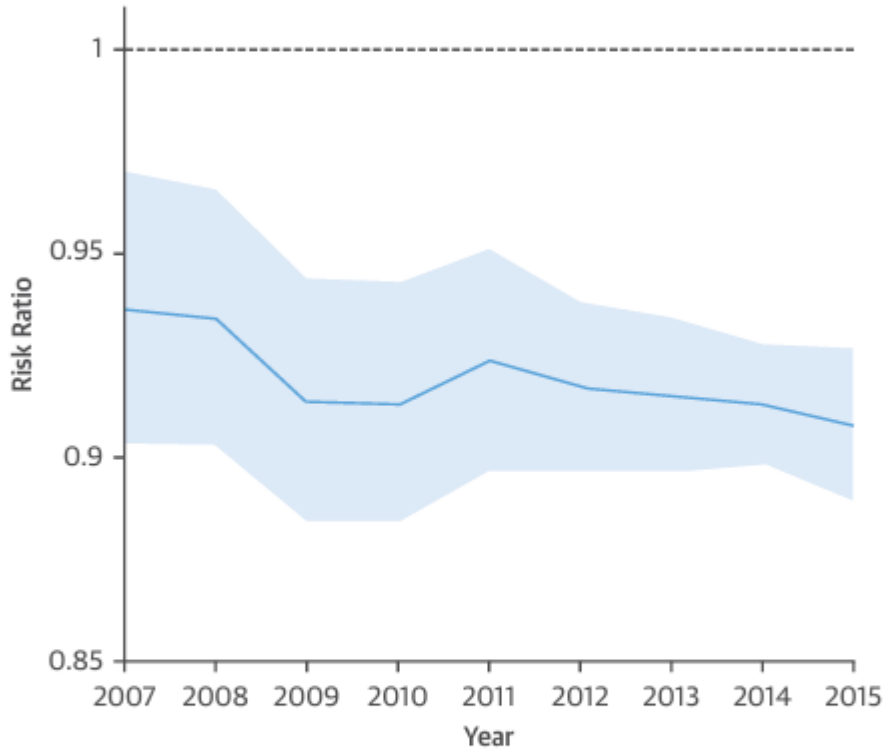
CENTRAL ILLUSTRATION Trends in the Percentage of Women and Men Filling a High-Intensity Statin Prescription After Hospital Discharge for Myocardial Infarction Between 2007 and 2015



Peters, S.A.E. et al. J Am Coll Cardiol. 2018;71(16):1729-37.

Black diamonds indicate those taking high-intensity statins prior to their myocardial infarction. **Orange squares** indicate those taking low/moderate-intensity statins prior to their myocardial infarction. **Blue circles** indicate statin initiators. **Solid lines** indicate men, **dashed lines** indicate women.

FIGURE 2 Risk Ratios (95% Confidence Intervals) for Filling a High-Intensity Statin Prescription Among Women Versus Men Between 2007 and 2015



The **line** represents the RR for filling a high-intensity statin prescription comparing women with men, and the **shaded region** shows the 95% CIs. Models include adjustment for age; race; prior statin use; history of diabetes, CHD, stroke, PAD, heart failure, and CKD; depression; Charlson comorbidity index; any hospitalization; cardiologist care; nonstatin lipid-lowering medication use; total number of medications taken; and data from 30 days post-discharge (see Table 1). Abbreviations as in Figure 1.

Summary

- Women in CABG

- Lower refer rate to CABG

- High co-morbidity,

- Technical demanding coronary anatomy

- Low multiple arterial grafts

- Poor guideline oriented management

- Lack of evidence of the women undergoing CABG due to small number of the participants in studies

Future direction of the CABG in women

- Include animals of both sexes in basic science research to understand physiologic differences
- Use guideline-directed optimal medical care
- Use guideline-directed revascularization strategies including use of arterial conduits
- Enroll more women in clinical trials
- Surgeon specialization in coronary surgery for women
- Establish centers for specialization in the treatment of women with cardiovascular disease

Zwischenberger BA, Jawitz OK, Lawton JS. Coronary surgery in women: How can we improve outcomes. JTCVS Tech. 2021;10:122-8.

경청해주셔서 감사합니다.