JAMA Cardiology | Original Investigation

Differences in Long-term Outcomes After Coronary Artery Bypass Grafting Using Single vs Multiple Arterial Grafts and the Association With Sex

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Supplemental content

IMPORTANCE Sex-related differences in the outcome of using multiple arterial grafts during coronary artery bypass grafting (CABG) remain uncertain.

OBJECTIVE To compare the outcomes of the use of multiple arterial grafts vs a single arterial graft during CABG for women and men.

DESIGN, SETTING, AND PARTICIPANTS This statewide cohort study used data from New York's Cardiac Surgery Reporting System and New York's Vital Statistics file on 63 402 patients undergoing CABG from January 1, 2005, to December 31, 2014. Statistical analysis was performed from January 10 to August 20, 2020.

EXPOSURES Multiple arterial grafting or single arterial grafting.

MAIN OUTCOMES AND MEASURES Mortality, acute myocardial infarction (AMI), stroke, repeated revascularization, major adverse cardiac and cerebrovascular event (composite of mortality, AMI, and stroke), and major adverse cardiac event (composite of mortality, AMI, or repeated revascularization) were compared among propensity-matched patients and stratified by the risk of long-term mortality.

RESULTS Of the 63 402 patients (48 155 men [76.0%]; mean [SD] age, 69.9 [10.5] years) in the study, women had worse baseline characteristics than men for most of the explored variables. Propensity matching yielded a total of 9512 male pairs and 1860 female pairs. At 7 years of follow-up, mortality was lower among men who underwent multiple arterial grafting (adjusted hazard ratio, 0.80; 95% CI, 0.73-0.87) but not women who underwent multiple arterial grafting (adjusted hazard ratio, 0.99; 95% CI, 0.84-1.15). When stratified by the estimated risk of death, the use of multiple arterial grafts was associated with better survival and a lower rate of a major adverse cardiac event among low-risk, but not high-risk, patients of both sexes, and the risk cutoff was different for men and women.

CONCLUSIONS AND RELEVANCE This study suggests that women have a worse preoperative risk profile than men. Multiple arterial grafting is associated with better outcomes among low-risk, but not high-risk, patients, and the risk cutoffs differ between sexes. These data highlight the need for new studies on the outcome of multiple arterial grafts in women.

JAMA Cardiol. doi:10.1001/jamacardio.2020.6585
Published online December 23, 2020.

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The association of sex with the outcomes of coronary artery bypass grafting (CABG) is controversial. Women presenting for CABG have different disease characteristics and worse risk profiles compared with men.[1-3] However, in most CABG observational studies and randomized clinical trials, women represent only a minority of the patient population, so the reported findings represent the predominantly male cohort and may not be applicable to women.[4-8]

The benefit associated with using multiple arterial grafts during CABG for women also remains uncertain. Although there is observational evidence demonstrating better clinical outcomes and graft patency with multiple arterial grafting (MAG) in the general population of patients undergoing CABG,[9-12] few studies have evaluated the benefit associated with MAG for women, and the results have been contradictory.[13-15] Conduits and target vessels are typically smaller in women, which may increase the complexity of MAG and probably explains some of the reported discrepancies.[16,17]

In this study, we evaluate the association of sex with the relative outcomes of MAG vs single arterial grafting (SAG) for women and men in New York state. We hypothesize that the treatment effect may be different between the 2 sexes.

Methods

Databases

This cohort study used data from New York's Cardiac Surgery Reporting System (CSRS) and New York's Vital Statistics file on patients undergoing CABG from January 1, 2005, to December 31, 2014. The CSRS database includes information on patient demographic characteristics, hospital and physician identifiers, preoperative risk factors, and outcomes. Procedural information includes the total number of conduits and the number of arterial conduits. Data from the CSRS are checked annually for completeness and accuracy by matching the records to the Statewide Planning and Research Cooperative System (SPARCS), New York's administrative acute care database. The accuracy of risk factors in the system is checked by using New York's utilization review agent to audit samples of cases from selected hospitals each year. Institutional review board approval was not required by University at Albany, State University of New York, given the retrospective nature of the study and the fact that patient identification data were encrypted.

The data from New York's Vital Statistics file were matched to the CSRS data using unique patient identifiers to obtain information on postdischarge deaths that occurred after the index procedure. The SPARCS data were used to obtain information on hospitalizations for acute myocardial infarction (AMI) or stroke after the index hospitalization. Information on repeated revascularization was obtained by matching the CABG and percutaneous coronary intervention registries and developing a longitudinal data file. The study was limited to New York state residents to minimize the chance of postdischarge outcomes occurring outside of New York. Data were also collected on surgeons' annual CABG case volumes, which were stratified as low (<75 cases), moderate (75-150 cases), and high (>150 cases). All patients with multivessel coronary artery disease who underwent nonemergency multigraft CABG with at least 1 arterial conduit and could be followed up for at least 2 years using registry data were included in the study.

Key Points

Question What is the association of sex with the relative outcomes of multiple vs single arterial grafting during coronary artery bypass grafting?

Findings In a statewide cohort study of 63 402 patients undergoing coronary artery bypass grafting, at 7 years' follow-up, outcomes with multiple arterial grafting were better among low-risk, but not high-risk, patients. Mortality at 7 years was lower among men, but not women, undergoing multiple arterial grafting.

Meaning Multiple arterial grafting was associated with better outcomes among low-risk, but not high-risk, men and women at different thresholds; studies of multiple arterial grafting specifically directed at women are needed.

Outcomes

The incidence rates of mortality, AMI, stroke, repeated revascularization, a major adverse cardiac and cerebrovascular event (MACCE; composite of mortality, AMI, or stroke), and a major adverse cardiac event (MACE; composite of mortality, AMI, or repeated revascularization) were compared separately for male and female patients between MAG and SAG procedures at 1 year and 7 years after the index procedure.

Statistical Analysis

Statistical analysis was performed from January 10 to August 20, 2020. Propensity score matching was used to minimize selection bias due to lack of randomization of patients to MAG and SAG by decreasing heterogeneity in baseline risk factors. Propensity matching was based on important patient risk factors, including diseased vessels, completeness of revascularization, number of conduits, total surgeon CABG volume, and type of surgery (off pump or on pump) (**Table 1**; eTables 1 and 2 in the Supplement).

The propensity scores were derived separately for male and female patients by developing nonparsimonious logistic regression models that estimated the probability of a given patient receiving multiple arterial grafts based on all of the risk factors available in the registry. Then, the propensity score was used to match patients on a 1-to-1 basis to minimize the overall distance in propensity scores between the groups. Patients were matched exactly for year of surgery to ensure similar follow-up periods for patients who underwent MAG and those who underwent SAG. Patients were also matched exactly for complete revascularization (using a proxy of number of total conduits equal to or greater than the number of diseased vessels because no better information was available), left main coronary artery disease, 3-vessel disease, 2-vessel disease with right coronary artery involvement, previous AMI within 7 days, left ventricular ejection fraction less than 50%, kidney failure (serum creatinine level >1.5 mg/dL [to convert to micromoles per liter, multiply by 88.4] or undergoing dialysis), and age (≥70 years). Patients were also matched with respect to other factors as long as their estimated log odds from the logistic regression model were no more than 0.2 SDs apart. Standardized differences in the prevalence of propensity model variables were then calculated.

The propensity-matched pairs were used to analyze differences in adverse outcomes between patients undergoing MAG and those undergoing SAG. To eliminate further differences within the matched pairs, a Cox proportional hazards regression model was used to calculate the adjusted hazard ratio (AHR) for the 2 procedures after adjusting for all risk factors in the propensity score.

Because we hypothesized that differences in MAG vs SAG outcomes by sex may be associated with differences in patients' preoperative risk profile, we performed separate propensity score–matched comparisons for men and women based on the preoperative risk factors, including a long-term mortality risk score developed by our group.[18] That risk score was developed using the New York state CSRS data from 8597 patients who underwent isolated CABG in 2000. Variables independently associated with 7-year survival at multivariable analysis (age, body mass index, ejection fraction, unstable hemodynamic state or shock, left main coronary artery disease, cerebrovascular disease, peripheral arterial disease, congestive heart failure, malignant ventricular arrhythmia, chronic obstructive pulmonary disease, type 1 or 2 diabetes, kidney failure, and history of open heart surgery) were assigned 1 to 7 points, with the maximum point total for each patient aged 28 years. Patients aged 70 to 79 years and 80 years or more had the highest weight (5 and 7 points, respectively). Female and

Table 1. Surgeon Volume and Baseline Patient Characteristics of Patients Undergoing Single Arterial and Multiple Arterial Isolated Coronary Artery Bypass Grafting Surgery in New York State From 2005 to 2014[a]

Variable	Patients, No. (%)			Standardized difference
	Overall	Single arterial grafting	Multiple arterial grafting	
Men				
No. of patients	48 155 (100)	37 627 (78.1)	10 528 (21.9)	NA
Age, mean (SD), y	65.1 (10.4)	66.3 (10.2)	60.6 (9.9)	56.8
Body surface area, mean (SD), m^2	2.1 (0.2)	2.1 (0.2)	2.1 (0.2)	10.1
Risk score, mean (SD)	6.3 (3.0)	6.7 (2.9)	4.9 (2.6)	63.0
High risk (score ≥9)	10 419 (21.6)	9402 (25.0)	1017 (9.7)	41.4
Low risk (score <9)	37 736 (78.4)	28 225 (75.0)	9511 (90.3)	41.4
Off-pump surgery	10 354 (21.5)	8266 (22.0)	2088 (19.8)	5.3
Incomplete revascularization	10 554 (21.9)	8505 (22.6)	2049 (19.5)	7.7
≤3 Conduits	10 803 (22.4)	8627 (22.9)	2176 (20.7)	5.5
Aged ≥70 y	16 962 (35.2)	15 006 (39.9)	1956 (18.6)	48.2
Peripheral vascular disease	5604 (11.6)	4611 (12.3)	993 (9.4)	9.1
Cerebrovascular disease	8006 (16.6)	6746 (17.9)	1260 (12.0)	16.8
COPD	10 001 (20.8)	8561 (22.8)	1440 (13.7)	23.7
Type 1 or 2 diabetes	17 545 (36.4)	14 403 (38.3)	3142 (29.8)	17.9
Previous cardiac surgery	789 (1.6)	617 (1.6)	172 (1.6)	0.0
Women				
No. of patients	15 247 (100)	13 146 (86.2)	2101 (13.8)	NA
Age, mean (SD), y	68.6 (10.3)	69.2 (10.1)	64.8 (10.8)	42.3
Body surface area, mean (SD), m^2	1.9 (0.2)	1.9 (0.2)	1.9 (0.2)	10.6
Risk score, mean (SD)	7.4 (2.8)	7.6 (2.8)	6.2 (2.9)	48.3
High risk (score ≥9)	5022 (32.9)	4594 (34.9)	428 (20.4)	33.0
Low risk (score <9)	10 225 (67.1)	8552 (65.1)	1673 (79.6)	33.0
Off-pump surgery	3527 (23.1)	3062 (23.3)	465 (22.1)	2.8
Incomplete revascularization	3702 (24.3)	3228 (24.6)	474 (22.6)	4.7
≤3 Conduits	4210 (27.6)	3659 (27.8)	551 (26.2)	3.6
Aged ≥70 y	7599 (49.8)	6881 (52.3)	718 (34.2)	37.3
Peripheral vascular disease	2147 (14.1)	1830 (13.9)	317 (15.1)	3.3
Cerebrovascular disease	3585 (23.5)	3179 (24.2)	406 (19.3)	11.8
COPD	3863 (25.3)	3451 (26.3)	412 (19.6)	15.8
Diabetes	7389 (48.5)	6491 (49.4)	898 (42.7)	13.3
Previous cardiac surgery	198 (1.3)	166 (1.3)	32 (1.5)	2.2

Abbreviations: COPD, chronic obstructive pulmonary disease; NA, not applicable.

[a] Additional details are provided in eTables 1 and 2 in the Supplement.

male patients were divided into low-risk (<10% 1-year mortality, corresponding to a risk score of 0-8) and high-risk (≥10% 1-year mortality, corresponding to a risk score of ≥9) categories, and the outcomes were compared. The robustness of the results was tested for different risk cutoffs.

In a sensitivity analysis, a fully adjusted Cox proportional hazards regression model (including the risk score as a continuous variable) was used instead of propensity matching for risk adjustment, and the interactions between female sex and MAG and between female sex and risk score were tested.

A landmark analysis including only patients who were alive 30 days after surgery was performed. Mortality was also compared between female and male patients receiving SAG and female and male patients receiving MAG in separate fully adjusted Cox proportional hazards regression models. Gamma testing and the E-value were used to evaluate the association of unmeasured confounding with the results of the main analysis.[19-21] All *P* values were from 2-sided tests, and results were deemed statistically significant at $P < .05$. All analyses were conducted in SAS, version 9.4 (SAS Institute Inc) and R, version 3.5.2 (R Foundation for Statistical Computing).

Results

Patient Characteristics

In total, 71 706 New York state residents underwent nonemergency multigraft CABG with at least 1 arterial conduit in 42 New York state nonfederal hospitals between January 1, 2005, and December 31, 2014. Out-of-state residents (n = 2757) and patients with an invalid Social Security number (n = 5547) were excluded because their deaths or subsequent hospitalizations could not be ascertained using New York Vital Statistics and SPARCS data. The final study sample comprised 63 402 patients (48 155 men [76.0%] and 15 247 women [24.0%]; mean [SD] age, 69.9 [10.5] years) (eFigure in the Supplement).

The baseline characteristics of the male and female patients before and after propensity score matching are summarized in Table 1 and eTables 1, 2, 3, and 4 in the Supplement. Female patients had worse baseline risk profiles (overall mean [SD] risk score, 7.4 [2.8]; mean [SD] risk score for women undergoing SAG, 7.6 [2.8]; mean [SD] risk score for women undergoing MAG, 6.2 [2.9]) compared with male patients (overall mean [SD] risk score, 6.3 [3.0]; mean [SD] risk score for men undergoing SAG, 6.7 [2.9]; mean [SD] risk score for men undergoing MAG, 4.9 [2.6]).

Among male patients, 37 627 (78.1%) received a single arterial graft, and 10 528 (21.9%) received multiple arterial grafts (Table 1; eTable 1 in the Supplement). The median follow-up was 6.5 years (range, 3.9-9.2 years) for all male patients, 6.4 years (range, 3.8-9.0 years) for men undergoing SAG, and 7.2 years (range, 4.4-9.6 years) for men undergoing MAG. The median number of grafts per male patient was 3 (interquartile range, 3-4), and the median number of arterial grafts per male patient was 1 (interquartile range, 1-1). Male patients undergoing MAG were younger than those undergoing SAG and had a lower prevalence of diabetes, cerebrovascular disease, congestive heart failure, chronic obstructive pulmonary disease, kidney dialysis, elevated serum creatinine level (>1.5 mg/dL), and/or low left ventricular ejection fraction (<40%). Men receiving multiple arterial grafts were also more likely than those receiving a single arterial graft to be undergoing an elective procedure and to have a higher body surface area. Patients undergoing off-pump SAG and patients undergoing off-pump MAG had similar rates of incomplete revascularization (2121 of 8266 [25.7%] vs 504 of 2088 [24.1%]; P = .15). Surgeons with low (<75 cases), moderate (75-150 cases), or high (>150) annual CABG volumes were all more likely to perform SAG than MAG for male patients (low, 14 358 of 17 477 [82.2%] vs 3119 of 17 477 [17.8%]; moderate, 16 075 of 22 329 [72.0%] vs 6254 of 22 329 [28.0%]; high, 7194 of 8349 [86.2%] vs 1155 of 8349 [13.8%]).

Among female patients, 13 146 (86.2%) received a single arterial graft, and 2101 (13.8%) received multiple arterial grafts (Table 1; eTable 2 in the Supplement). The median follow-up was 6.3 years (range, 3.7-8.8 years) for all female patients, 6.2 years (range, 3.6-8.7 years) for women undergoing SAG, and 6.8 years (range, 4.1-9.4 years) for women undergoing MAG. The median number of grafts per female patient was 3 (interquartile range, 2-3), and the median number of arterial grafts per female patient was 1 (interquartile range, 1-1). Female patients undergoing MAG were younger than those undergoing SAG and had lower a prevalence of diabetes, cerebrovascular disease, congestive heart failure, chronic obstructive pulmonary disease, and/or kidney dialysis. Female patients undergoing MAG also had higher body surface areas and higher left ventricular ejection fraction (≥40%) compared with those undergoing SAG. Patients undergoing off-pump SAG and patients undergoing off-pump MAG had similar rates of incomplete revascularization (899 of 3062 [29.4%] vs 139 of 465 [29.9%]; P = .81). Surgeons with low (<75 cases), moderate (75-150 cases), or high (>150 cases) annual CABG volumes were all more likely to perform SAG than MAG for female patients (low, 4976 of 5555 [89.6%] vs 579 of 5555 [10.4%]; moderate, 5716 of 7050 [81.1%] vs 1334 of 7050 [18.9%]; high, 2454 of 2642 [92.9%] vs 188 of 2642 [7.1%]).

Propensity Matching

Propensity matching yielded a total of 9512 propensity-matched male pairs and 1860 propensity-matched female pairs. Both the male and female propensity-matched pairs were similar with respect to prevalence of risk factors, with no patient characteristic having a standardized difference exceeding 10% (eTables 3 and 4 in the Supplement). There were no significant differences by sex in mortality between patients undergoing SAG and those undergoing MAG (eTable 5 in the Supplement).

Outcomes in Propensity-Matched Male Patients by Number of Arterial Grafts

The 1-year and 7-year outcomes of propensity-matched male patients who underwent MAG or SAG are summarized in **Table 2**. At 1 year, the incidence of mortality was similar for male patients who underwent MAG and those who underwent SAG (Kaplan-Meier estimates: 195 of 9512 [2.1%] vs 185 of 9512 [1.9%]; AHR, 1.06; 95% CI, 0.87-1.30). The incidences of AMI, stroke, and MACCE were also not different, but male patients who underwent MAG had lower incidences of repeated revascularization (Kaplan-Meier estimates: 220 of 9512 [2.3%] vs 310 of 9512 [3.3%]; AHR, 0.72; 95% CI, 0.61-0.86) and MACE (Kaplan-Meier estimates: 500 of 9512 [5.3%] vs 601 of 9512 [6.3%]; AHR, 0.84; 95% CI, 0.75-0.94) than those who underwent SAG.

At 7 years, the incidence of mortality was significantly lower for male patients who underwent MAG (Kaplan-Meier estimates: 933 of 9512 [11.6%] vs 1133 of 9512 [14.1%]; AHR, 0.80; 95% CI, 0.73-0.87) (**Figure 1**A). The incidences of AMI, repeated revascularization, MACCE, and MACE were also lower for male patients who underwent MAG (Kaplan-Meier estimates: AMI, 430 of 9512 [5.3%] vs 498 of 9512 [6.3%]; AHR,0.84; 95% CI, 0.74-0.96; repeated revascularization, 890 of 9512 [11.3%] vs 1111 of 9512 [14.2%]; AHR, 0.80; 95% CI, 0.73-0.87; MACCE, 1565 of 9512 [19.1%] vs 1804 of 9512 [21.9%]; AHR, 0.85; 95% CI, 0.80-0.91; MACE, 1930 of 9512 [23.4%] vs 2336 of 9512 [28.2%]; AHR, 0.81; 95% CI, 0.76-0.86). The incidence of stroke was similar for male patients who underwent MAG and those who underwent SAG.

Outcomes in Propensity-Matched Female Patients by Number of Arterial Grafts

The 1-year and 7-year outcomes for MAG and SAG propensity-matched female patients are summarized in Table 2. At 1 year, the incidence of mortality was similar for female patients who underwent MAG vs those who underwent SAG (91 of 1860 [4.9%] vs 66 of 1860 [3.5%]; AHR, 1.34; 95% CI, 0.97-1.84). The incidences of AMI, stroke, MACE, repeated revascularization, and MACCE were also similar between groups.

At 7 years, the incidence of mortality was similar for female patients who underwent MAG and those who underwent SAG (Kaplan-Meier estimates: 316 of 1860 [19.6%] vs 310 of 1860 [19.5%]; AHR, 0.99; 95% CI, 0.84-1.15) (Figure 1B). The incidences of stroke, repeated revascularization, MACCE, and MACE were also similar for female patients who underwent

Table 2. One- and 7-Year Outcomes of Propensity-Matched Patients Undergoing Multiple Arterial vs Single Arterial Isolated Coronary Artery Bypass Grafting in New York State From 2005 to 2014

Outcome	Multiple arterial grafting		Single arterial grafting		AHR (95% CI)	*P* value
	Patients at risk at the end of the follow-up period, No.	Adverse event, No. (%)[a]	Patients at risk at the end of the follow-up period, No.	Adverse event, No. (%)[a]		
Men						
1-y Outcome						
Mortality	9317	195 (2.1)	9327	185 (1.9)	1.06 (0.87-1.30)	.56
AMI	9182	142 (1.5)	9160	179 (1.9)	0.80 (0.64-1.00)	.05
Stroke	9184	156 (1.6)	9205	146 (1.5)	1.06 (0.85-1.33)	.60
Repeated revascularization	9098	220 (2.3)	9020	310 (3.3)	0.72 (0.61-0.86)	<.001
MACCE	9053	459 (4.8)	9041	471 (5.0)	0.99 (0.87-1.12)	.83
MACE	9012	500 (5.3)	8911	601 (6.3)	0.84 (0.75-0.94)	.004
7-y Outcome						
Mortality	4892	933 (11.6)	4741	1133 (14.1)	0.80 (0.73-0.87)	<.001
AMI	4685	420 (5.3)	4490	498 (6.3)	0.84 (0.74-0.96)	.01
Stroke	4705	421 (5.3)	4555	418 (5.2)	0.99 (0.86-1.13)	.89
Repeated revascularization	4411	890 (11.3)	4141	1111 (14.2)	0.80 (0.73-0.87)	<.001
MACCE	4513	1565 (19.1)	4320	1804 (21.9)	0.85 (0.80-0.91)	<.001
MACE	4301	1930 (23.4)	4023	2336 (28.2)	0.81 (0.76-0.86)	<.001
Women						
1-y Outcome						
Mortality	1769	91 (4.9)	1794	66 (3.5)	1.34 (0.97-1.84)	.07
AMI	1732	43 (2.4)	1745	54 (2.9)	0.80 (0.53-1.19)	.27
Stroke	1725	55 (3.0)	1757	46 (2.5)	1.18 (0.80-1.74)	.41
Repeated revascularization	1707	62 (3.4)	1738	57 (3.1)	1.06 (0.74-1.52)	.74
MACCE	1688	172 (9.2)	1711	149 (8.0)	1.13 (0.91-1.41)	.25
MACE	1681	179 (9.6)	1705	15 (8.3)	1.14 (0.92-1.41)	.24
7-y Outcome						
Mortality	886	316 (19.6)	881	310 (19.5)	0.99 (0.84-1.15)	.85
AMI	836	120 (8.0)	807	154 (10.2)	0.77 (0.60-0.97)	.03
Stroke	834	126 (8.2)	835	106 (6.9)	1.19 (0.92-1.54)	.18
Repeated revascularization	774	222 (14.8)	755	250 (16.6)	0.90 (0.75-1.08)	.25
MACCE	789	478 (29.0)	765	486 (29.9)	0.97 (0.86-1.10)	.65
MACE	745	560 (33.9)	713	585 (35.8)	0.94 (0.84-1.06)	.29

Abbreviations: AHR, adjusted hazard ratio; AMI, acute myocardial infarction; MACCE, mortality, AMI, stroke, repeated revascularization, major adverse cardiac event, and cerebrovascular event (composite of mortality, AMI, and stroke); MACE, major adverse cardiac event (composite of mortality, AMI, or repeated revascularization).

[a] Kaplan-Meier estimate at the end of 1- and 7- year periods.

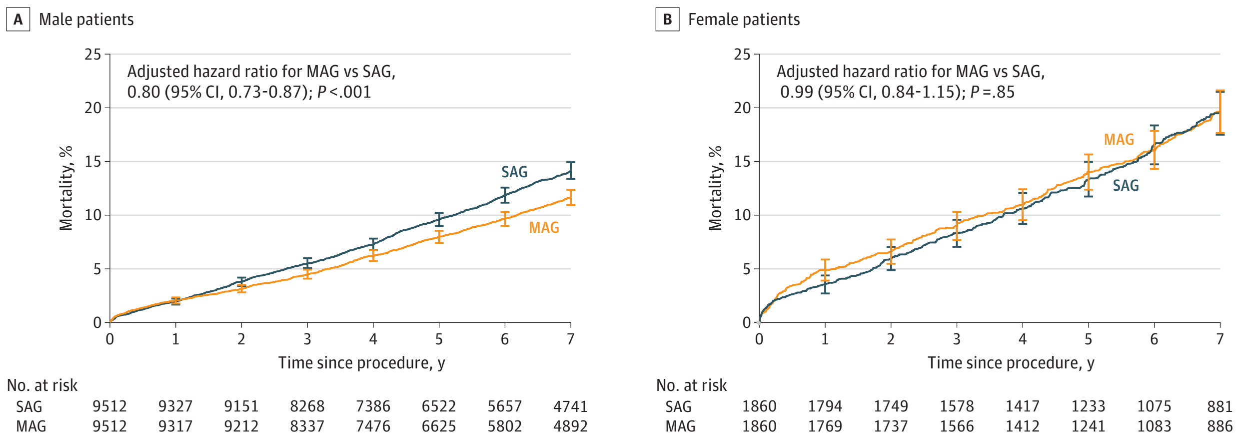
MAG and those who underwent SAG (Kaplan-Meier estimates: stroke, 126 of 1860 [8.2%] vs 106 of 1860 [6.9%]; AHR, 1.19; 95% CI, 0.92-1.54; repeated revascularization, 222 of 1860 [14.8%] vs 250 of 1860 [16.6%]; AHR 0.90; 95% CI, 0.75-1.08; MACCE, 478 of 1860 [29.0%] vs 486 of 1860 [29.9%]; AHR, 0.97; 95% CI, 0.86-1.10; MACE, 560 of 1860 [33.9%] vs 585 of 1860 [35.8%]; AHR, 0.94; 95% CI, 0.84-1.06). Female patients who underwent MAG had a significantly lower incidence of AMI at 7 years follow-up (Kaplan-Meier estimates: 120 of 1860 [8.0%] vs 154 of 1860 [10.2%]; AHR, 0.77; 95% CI, 0.60-0.97).

Analysis by Estimated Risk of Mortality

At 7 years, the incidence of mortality was lower for MAG vs SAG among low-risk male and female patients (Kaplan-Meier estimates: male, 681 of 9467 [8.6%] vs 882 of 9467 [11.1%]; AHR, 0.80; 95% CI, 0.73-0.89; female, 183 of 1669 [13.0%] vs 233 of 1669 [16.3%]; AHR, 0.80; 95% CI, 0.65-0.97) (**Table 3**, **Figure 2**A and B). Among high-risk male and female patients, the incidence of 7-year mortality was similar for MAG vs SAG (Kaplan-Meier estimates: male, 377 of 1013 [43.7%] vs 381 of 1013 [44.3%]; AHR, 0.95; 95% CI, 0.82-1.10; female, 179 of 424 [47.9%] vs 153 of 424 [42.3%]; AHR, 1.14; 95% CI, 0.91-1.42) (Table 3; Figure 2C and D).

Similar to mortality, at 7 years, low-risk male and female patients undergoing MAG had a significantly lower incidence of MACE compared with those undergoing SAG (Kaplan-Meier estimates: male, 1693 of 9467 [20.7%] vs 2139 of 9467 [25.8%]; AHR, 0.79; 95% CI, 0.74-0.84; female, 421 of 1669 [28.6%] vs 495 of 1669 [33.6%]; AHR, 0.84; 95% CI, 0.74-0.98). For high-risk patients, the incidence of 7-year MACE was similar for MAG and SAG for both male and female patients

Figure 1. Seven-Year Mortality of Propensity-Matched Patients Undergoing Multiple Arterial Grafting (MAG) vs Single Arterial Grafting (SAG) for Coronary Artery Bypass Grafting in New York State From 2005 to 2014



A, Male patients. B, Female patients. Vertical lines indicate 95% CIs.

Table 3. Seven-Year Mortality Rates of Propensity-Matched Risk-Stratified Patients After Multiple Arterial vs Single Arterial Coronary Artery Bypass Grafting in New York State From 2005 to 2014

	Multiple arterial grafting		Single arterial grafting			
Patient group	Patients at risk at the end of the follow-up period, No.	Adverse event, No. (%)[a]	Patients at risk at the end of the follow-up period, No.	Adverse event, No. (%)[a]	AHR (95% CI)	*P* value
Women						
Overall	999	362 (20.0)	972	386 (21.5)	0.92 (0.80-1.07)	.29
Low risk (score <9)	869	183 (13.0)	834	233 (16.3)	0.80 (0.65-0.97)	.02
High risk (score ≥9)	130	179 (47.9)	138	153 (42.3)	1.14 (0.91-1.42)	.26
Men						
Overall	5408	1058 (11.9)	5301	1263 (14.2)	0.83 (0.77-0.90)	<.001
Low risk (score ≤8)	5081	681 (8.6)	4980	882 (11.1)	0.80 (0.73-0.89)	<.001
High risk (score ≥9)	327	377 (43.7)	321	381 (44.3)	0.95 (0.82-1.10)	.47

Abbreviation: AHR, adjusted hazard ratio.

[a] Kaplan-Meier estimate.

(Kaplan-Meier estimates: male, 459 of 1013 [52.0%] vs 457 of 1013 [52.3%]; AHR, 0.97; 95% CI, 0.85-1.11; female, 215 of 424 [56.1%] vs 184 of 424 [49.1%]; AHR, 1.20; 95% CI, 0.98-1.46).

Results of the analysis using different low-risk cutoffs showed that MAG was associated with lower mortality for all the explored low-risk levels in men, while for women, no differences between MAG and SAG were seen when cases with a risk score higher than 11 (corresponding to a 1-year mortality of 17.5%) were included (eTable 6 in the Supplement). In a fully adjusted model (including the risk score), MAG was inversely associated with mortality (AHR, 0.53; 95% CI, 0.46-0.61), while female sex (AHR, 1.44; 95% CI, 1.26-1.64; $P < .001$) and the risk score (AHR, 1.28; 95% CI, 1.27-1.29; $P < .001$) were positively associated with it (eTable 7 in the Supplement).

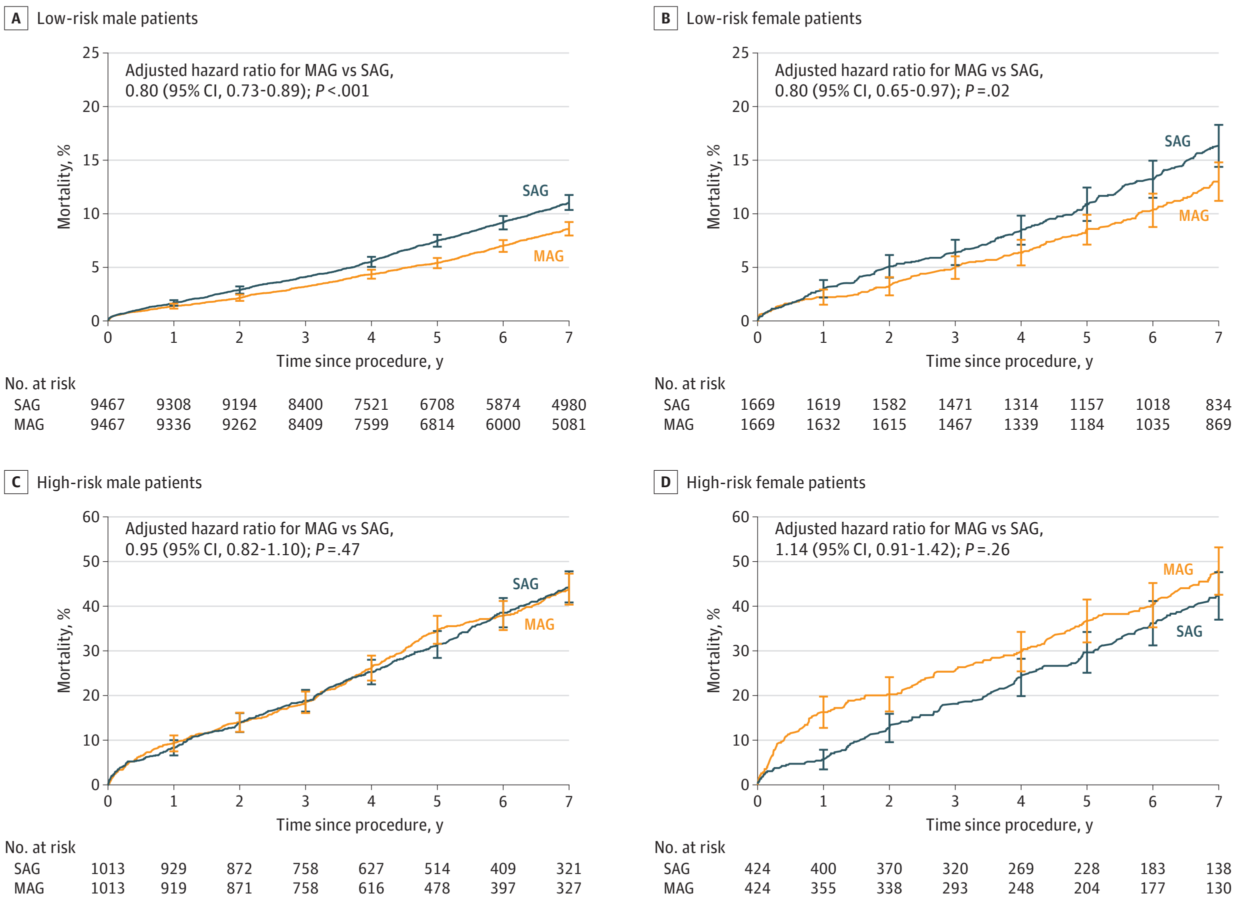
The results of the landmark analysis were consistent with the results of the main analysis (eTable 8 in the Supplement). Results of the analysis using gamma testing and the E-value are reported in eTable 9 and eTable 10 in the Supplement and show that only unmeasured confounders with moderate to high association with the treatment and the outcome would explain the reported results. Female patients receiving a single arterial graft and female patients receiving multiple arterial grafts had higher mortality than their male counterparts in separate fully adjusted Cox proportional hazards regression models (eTable 11 in the Supplement).

Discussion

In this study of patients undergoing CABG in New York state from 2005 to 2014, MAG was associated with longer survival and a lower rate of MACE for low-risk, but not high-risk, men and women. The risk thresholds at which the association of MAG with improved outcomes was lost differed between men and women.

Although a large body of observational evidence has compared follow-up data of patients undergoing SAG vs MAG, few studies, to our knowledge, have examined sex-related differences or have stratified the outcomes based on the preoperative risk profile of the patients. Our findings of a clear differ-

Figure 2. Seven-Year Mortality of Propensity-Matched Patients Undergoing Multiple Arterial Grafting (MAG) vs Single Arterial Grafting (SAG) Coronary Artery Bypass Grafting in New York State From 2005 to 2014



A, Low-risk male patients. B, Low-risk female patients. C, High-risk male patients. D, High-risk female patients. Vertical lines indicate 95% CIs.

ence in the outcome of MAG between high-risk and low-risk patients is consistent with studies that have reported an age cutoff for the survival advantage associated with MAG[11,22-24] and is biologically plausible because a shorter life expectancy may minimize any cardiac survival benefit associated with MAG.

The current literature on the sex-specific outcomes of MAG is based mainly on subanalyses of studies with a predominantly male population. The few observational studies that have focused specifically on women have reported conflicting results.[13,14,25,26]

In our study, similar to most previous literature, women had more baseline comorbidities than men, and the apparent lack of benefit associated with MAG in the overall female cohort may be due to the higher percentage of women in the high-risk category (13.0% vs 6.0% of men). However, we cannot exclude that other factors associated with sex and not measured in our database may have played a role in determining the observed differences. Also, women have a higher rate of postoperative sternal complications after bilateral internal thoracic artery grafting.[14]

Limitations

This analysis has important limitations. The granularity of the data in our database is limited for the purposes of this study. We had no data on the type and quality of the conduit used, the severity of target-vessel stenosis, or the location and quality of the target vessel. These data and other unmeasured variables may be important determinants of MAG outcomes, so our analysis cannot clarify whether the differences found between men and women are associated entirely with differences in baseline characteristics or with other sex-related confounders. Further investigations using more granular data sources are needed to address this important question.

In addition, we used a score developed from our database and not one of the more widely adopted surgical scores for risk stratification, which limits the generalizability of our findings. As in most observational comparative studies in surgery, it is possible that, despite extensive adjustment, unmeasured confounders and treatment allocation bias were present.[27] Data on postoperative adherence with medical therapy were not available, and prescription and medication adherence may be different between men and women. Clinical follow-up data were limited to hospital visits and deaths within the state, which could have introduced a bias. Finally, the percentage of patients included in the high-risk group was relatively small, so an inability to identify significant treatment differences among the high-risk patients may be due to power limitations.

Conclusions

In this analysis of New York's CSRS from 2005 to 2014, MAG was associated with longer survival and lower incidence of MACE among low-risk, but not high-risk, men and women. The threshold at which MAG was not associated with improved outcome was different in the 2 sexes, suggesting that important differences in the association of MAG may exist between sexes and that data derived from studies with a predominantly male population may not be applicable to women.

New studies, including randomized clinical trials, specifically designed to test the outcome of MAG vs SAG for women are needed. Our data also highlight the importance of a grafting strategy tailored to the risk profile of the individual patient.

ARTICLE INFORMATION

Accepted for Publication: October 16, 2020.

Published Online: December 23, 2020. doi:10.1001/jamacardio.2020.6585

Author Contributions: Dr Samadashvili had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Gaudino and Samadashvili contributed equally to this work.
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Acquisition, analysis, or interpretation of data: All authors.
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Supervision: Girardi, Hannan.

Conflict of Interest Disclosures: None reported.

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