

Review

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# Multiple arterial grafting: are women being left behind?

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## Abstract

Multiple arterial grafting (MAG) has been evidenced to likely improve long-term mortality and morbidity outcomes compared with single arterial grafting during coronary artery bypass grafting (CABG), with current guidelines recommending its use. Notably, women make up less than 30% of the cohorts in the studies that inform these guidelines, and the use of MAG has not been well studied in the female population, despite the evidence that women present with more comorbidities and severe symptoms, and often perform worse after CABG compared with their male counterparts. Therefore, this comprehensive narrative review focuses on the currently available evidence examining MAG in women, and its use in on- and off-pump CABG.

**Keywords:** Coronary artery bypass grafting, multiple arterial grafting, single arterial grafting, sex-based differences, radial artery, bilateral internal mammary artery, off-pump coronary artery bypass grafting, conduit selection

## INTRODUCTION

Multiple arterial grafting (MAG) has been evidenced to likely improve long-term mortality and morbidity outcomes compared with single arterial grafting (SAG) during coronary artery bypass grafting (CABG)<sup>[1-5]</sup>. In the American College of Cardiology (ACC)/American Heart Association (AHA) joint committee report on clinical practice guidelines of the 2021 ACC/AHA/Society for Cardiovascular Angiography and Interventions (SCAI) guideline for coronary artery revascularization, a class I recommendation is to use a radial artery in preference of a saphenous vein graft (SVG) to graft the second most-important, non-left



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anterior descending (LAD) artery to ameliorate long-term cardiac outcomes during isolated CABG<sup>[6]</sup>. Additionally, the use of bilateral internal mammary artery (BIMA) grafting by experienced operators is a class IIa recommendation for patients undergoing CABG to better long-term cardiac outcomes<sup>[6]</sup>. While studies used to inform these recommendations support mid- and long-term benefits of using MAG with radial artery and/or right internal mammary artery (RIMA) over SAG, study patients were predominantly male, with females being less than 30% of included participants<sup>[7-11]</sup>. In a meta-analysis of randomized controlled trials (RCTs) comparing MAG and SAG, only 19% of patients within the MAG group were women and 17% in the SAG group were women<sup>[12]</sup>.

This gender discrepancy is problematic as outcomes in women after CABG are challenging. After CABG, women generally fare worse compared with men, presenting with more delayed diagnoses and surgical referral, and more diffuse disease<sup>[13-15]</sup>. When presenting for surgical revascularization, women are older and with a higher comorbidity profile<sup>[16]</sup>, thus facing a higher risk of mortality, major adverse cardiac and cerebrovascular events (MACCE), and postoperative graft failure<sup>[13,15]</sup>. A retrospective analysis of 1,297,204 patients in the Adult Cardiac Surgery Database (ACSD) of the Society of Thoracic Surgeons (STS), who underwent isolated CABG from 2011-2020, showed only 24% of this cohort were women. There remains significantly higher operative mortality in women compared to men, with no improvements over the last decade<sup>[14]</sup>.

The evidence of MAG improving long-term morbidity and mortality outcomes in CABG is promising, but with the caveat that women represent a substantial minority in most studies. It is of utmost importance to increase female enrollment in research and to study the application of MAG specifically in female populations undergoing CABG, in both the on- and off-pump setting. In this narrative review, we summarize the literature for MAG in women, the existing evidence comparing MAG and SAG, applications in both on- and off-pump CABG, and future directions in improving mortality and morbidity outcomes for women undergoing isolated CABG. To minimize cherry-picking articles in this narrative review, a search strategy encompassing MAG in female patients was used to obtain relevant articles discussed in this review, outlined in [Supplementary Material](#).

## CURRENT USE OF MULTIPLE ARTERIAL GRAFTING FOR FEMALES

A retrospective review of the STS ACSD by Jawitz *et al.* included 1,212,487 male and female patients who underwent isolated first-time CABG from July 1, 2011, to June 28, 2019<sup>[17]</sup>. In addition to female patients being older with more comorbidities, they were more likely to present with symptoms of congestive heart failure (CHF) and cardiogenic shock. After adjusting for these baseline characteristics, women had lower odds of undergoing MAG (adjusted odds ratio, 0.78; 95%CI: 0.75-0.81) after controlling for significant interactions between sex, race, age, ejection fraction, baseline dialysis, and hematocrit. Additionally, women in this database had a significantly higher rate of incomplete revascularization compared with men.

The Cleveland Clinic also conducted a retrospective analysis of the 57,943 adult patients who underwent primary isolated CABG from January 1972 to January 2011<sup>[18]</sup>. Of these patients, only 11,009 (19%) were females. Comparable to the aforementioned studies, women who presented for CABG were older and had more severe symptoms compared with their male counterparts. These women were also more prone to have comorbidities such as pharmacologically treated diabetes mellitus, hypertension, peripheral arterial disease, and cerebrovascular disease. Even though men were more likely to undergo incomplete revascularization compared with women, women received fewer arterial grafts (including the less frequent use of BIMA and radial artery), less total arterial revascularization, increased use of the SVG to the LAD, and increased all-venous grafts. After adjusting for patient baseline characteristics and revascularization strategy differences,

female sex persisted as an independent risk factor for both early and late mortality after CABG. Women who received SVGs without any arterial grafts had low survival with 5-, 10-, and 20-year survival of 80%, 58%, and 25%, respectively, whereas women who received BIMA grafting who experienced 5-, 10-, and 20-year survivals of 90%, 77%, and 48%, respectively. This study highlighted that women are less likely to undergo MAG compared with men and that women receiving CABG with only SVGs had lower survival compared with women receiving MAG.

A similar trend was noted in the Ottawa Heart Institute CABG database in Canada. Jabagi *et al.* conducted a retrospective analysis of 19,557 patients who underwent isolated CABG with more than one distal anastomosis from January 1990 to March 2015<sup>[19]</sup>. On par with most of the existing evidence, less than one-quarter of these patients were females. The primary analysis of the unmatched cohort showed that men were statistically more likely to receive BIMA as conduits. Men also had a higher rate of use of more than one arterial conduit for revascularization. Women were more likely to receive no arterial conduits during isolated CABG. After propensity-score matching using sex in those who received BIMA as the outcome in the logistic regression model, men had a statistically significant increased use of three arteries for revascularization compared with women. While there was a trend toward increased MAG in both men and women in this retrospective analysis, a significantly decreased use of total arterial grafting remains in women compared with men.

In a study from the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZCTS) database of 54,275 patients who underwent primary isolated CABG from June 2001 to January 2020, only 10,693 (20%) were female. Females were older with more comorbidities, and they presented with more severe symptoms quantified by more severe New York Heart Association (NYHA) and Canadian Cardiovascular Society (CCS) class<sup>[20]</sup>. Women were less likely to receive MAG and received fewer grafts than men. Women may also have smaller vessel luminal diameters even when indexed to body surface area, which may be another barrier to performing multiple arterial grafting<sup>[21]</sup>.

In addition to women being less likely to receive MAG as well as fewer grafts in general compared with men, some studies also showed that women were more likely to experience graft failure and other postoperative complications. In a recently published pooled analysis of seven RCTs investigating the medical management after CABG, Sandner *et al.* investigated graft failure in women<sup>[15]</sup>. The RCTs included were as follows: Aggressive Cholesterol Therapy to Inhibit Vein Graft Events (ACTIVE), Clopidogrel After Surgery for Coronary Artery Disease (CASCADE), Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS), Different Antiplatelet Therapy Strategy after Coronary Artery Bypass Graft Surgery (DACAB), POPular CABG (POPCABG), Project of *Ex-Vivo* Vein Graft Engineering via Transfection IV trial (PREVENT-IV), and Ticagrelor Antiplatelet Therapy to Reduce Graft Events and Thrombosis (TARGET)<sup>[22-28]</sup>. Graft failure was significantly more frequent in women than men. Women also had an increased risk of myocardial infarction (MI), repeat revascularization, and all-cause mortality. Women with graft failure had more SVG grafts compared with women with no graft failure.

These large studies highlight the pattern of decreased MAG use in women undergoing CABG, as well as the challenges inherent to treating women as they are older, suffering more comorbidities, and presenting with more severe symptoms such as CHF and cardiogenic shock.

## EVIDENCE FOR MULTIPLE VERSUS SINGLE ARTERIAL GRAFTING FOR WOMEN

There have been several key observational studies focusing on outcomes in undergoing CABG with single or multiple arterial grafting that have provided some insight as to the value of this strategy in women.

Rubens *et al.* published a retrospective population-based cohort study from October 2008–September 2019 using the Institute of Clinical Evaluative Sciences (ICES) database encompassing population-health data for all 11 Ontario cardiac surgery centers<sup>[29]</sup>. They included 9,135 female patients and 36,748 male patients undergoing primary isolated CABG with either double arterial grafting or SAG. After propensity-score matching with double arterial grafting as the dependent variable, this study showed that there was a lower risk of medium-term mortality (mean follow-up  $4.4 \pm 2.6$  years) in women who underwent double arterial grafting compared with SAG [hazard ratio (HR) 0.87; 95%CI: 0.81–0.94]. Additionally, females who underwent double arterial grafting were associated with a lower risk of repeat revascularization (HR 0.76; 95%CI: 0.68–0.85), decreased risk of MI (HR 0.78; 95%CI: 0.69–0.89), and heart failure requiring hospitalization (HR 0.88; 95%CI: 0.80–0.97) compared with SAG at medium-term follow-up. Furthermore, the incremental improvement in the 9-year survival was 4.0% in women who underwent double arterial grafting compared with 0.9% in men.

Tam *et al.* conducted a similar retrospective propensity score-matched comparison of MAG compared with SAG for women from October 2008–March 2019, also using data from the ICES<sup>[30]</sup>, including 10,915 female patients who underwent multivessel CABG with either MAG ( $n = 2,961$ ) or SAG ( $n = 7,954$ ). Patients undergoing MAG were significantly younger, with fewer cardiac comorbidities, lower body mass index, and higher renal function compared with patients undergoing SAG. Propensity score matching yielded 2,446 matched pairs, and no statistically significant differences were noted in in-hospital complications of MI, stroke, or early mortality between the MAG and SAG groups. MAG group was associated with longer 10-year survival and greater freedom from MACCE at 10 years. Additionally, a lower incidence of repeat revascularization was found in the MAG group compared with SAG.

Gaudino *et al.* used the New York State registry data and performed a retrospective analysis of patients who underwent CABG from January 2005 to December 2014<sup>[31]</sup>. Of the 63,402 included patients who underwent nonemergency multigraft CABG with at least one radial artery conduit, 15,247 were women. Females who underwent MAG were younger in age, as well as had fewer comorbidities of diabetes, cerebrovascular disease, CHF, chronic pulmonic disease, and renal failure. It was also noted that regardless of surgeon case volumes, females were more likely to receive SAG than MAG when undergoing CABG. Propensity matching was completed using MAG as the dependent variable. No significant differences were found in 1-year and 7-year outcomes of mortality, MACCE, stroke, major adverse cardiac event (MACE), and repeated revascularization. Secondary outcomes showed that females who underwent MAG had a lower incidence of acute MI at 7-year follow-up. A statistically significant decreased incidence of mortality and MACE at 7 years was reported in low-risk patients undergoing MAG. High-risk patients showed no significant difference in these outcomes. Given these results being secondary outcomes, it was only hypothesis-generating, and the primary outcome of this study showed no significant differences between MAG and SAG in women. Further exploration is warranted.

Aboul-Hassan *et al.* published a retrospective analysis of the impact of sex on long-term outcomes in patients undergoing CABG with MAG compared with SAG of the Polish National Registry of Cardiac Surgery Procedures database from January 2012 to December 2020<sup>[32]</sup>. Of the 81,136 patients included, 18,528 (23%) were women. Only 1,532 (8.3%) of females who underwent CABG in this database received MAG, with the rest of the 16,994 patients receiving SAG. Patients undergoing MAG were younger, with fewer comorbidities. Short-term outcomes of 30-day mortality, in-hospital MI, in-hospital cerebrovascular adverse events, new-onset renal replacement therapy, reopening due to bleeding, incidence of sternal wound infection, and mechanical circulatory device implantation were similar between the MAG and SAG groups. MAG use was associated with improved long-term survival in patients under 70 years of age (HR

0.70; 95%CI: 0.52-0.92), in patients with diabetes (HR 0.67; 95%CI: 0.47-0.96), and in those with a left ventricular ejection fraction (LVEF) greater than 40% (HR 0.76; 95%CI: 0.60-0.96) compared with patients who underwent SAG.

Additionally, Ren *et al.* did a retrospective analysis of 10,693 female patients in the ANZSCTS database who underwent primary isolated CABG from June 2001 to January 2020<sup>[20]</sup>. After balancing baseline characteristics, MAG was associated with a significantly lower incidence of late mortality compared with SAG in the female population at a median follow-up of 5.2 years (adjusted HR 0.83; 95%CI: 0.76-0.91).

While there are robust, large-sized observational studies supporting the use of MAG for female patients, it is important to note these mentioned studies are all retrospective, which comes with its own limitations of selection bias and use of registry data that was not collected for the intention of research. There could be potentially unmeasured confounders leading to bias in results. Additionally, there was a lack of granularity in the data reported, such as the location and quality of the target coronary vessels for both MAG and SAG groups, how many SVGs were used in both groups, and the conduit quality of either MAG or SAG groups.

Robinson *et al.* published a meta-analysis of six propensity-matched observational studies that compared MAG vs. SAG in CABG that reported outcomes by sex from inception until October 29, 2020, with a total of 32,793 female patients included in these pooled analyses<sup>[33]</sup>. The propensity sample size was less than 1,000 in four of the six included studies<sup>[30,31,34-37]</sup>. Women who received MAG compared with SAG had lower long-term mortality and decreased incidence of spontaneous MI. However, when only the largest three studies were included in sensitivity analyses, no differences were noted in long-term mortality between MAG and SAG groups. When including the studies that only used radial arteries for MAG, the use of MAG was associated with a statistically significant improved long-term survival. Table 1 summarizes all the primary research studies that compare MAG vs. SAG in females.

## **MULTIPLE ARTERIAL GRAFTING DURING ON- VS . OFF-PUMP CORONARY ARTERY BYPASS GRAFTING**

Observational studies have shown improved survival and freedom from MACCE in women who undergo off-pump CABG compared with on-pump CABG, with a few studies suggesting that women may benefit from off-pump CABG to a greater extent than men<sup>[38-41]</sup>. However, other studies have shown that off-pump CABG may be associated with an increased risk of graft failure in female patients<sup>[15]</sup>. The debate of on- vs. off-pump CABG remains controversial, and there are no current RCTs comparing MAG in on- vs. off-pump CABG for women, to the best of our knowledge. There exists a large knowledge gap in the applicability of MAG in off-pump surgery, especially in the context of decreased total revascularization in off- compared with on-pump CABG groups.

Rubens *et al.* conducted a retrospective population-based cohort study using the ICES database that focused on the effect of on- vs. off-pump strategies in CABG patients undergoing MAG<sup>[21]</sup>. The patients were pre-stratified by sex and then propensity scores were derived based on the use of off-pump CABG. Before propensity matching, women had a higher crude mortality rate of 2.55%/year compared with 1.70%/year in men, with no significant differences between on- or off-pump status. Women also had a higher event rate of MACCE, stroke hospitalization, MI hospitalization, CHF hospitalization, and revascularization compared with men. After propensity matching, there were no significant differences in all-cause mortality between on- and off-pump groups, in both male and female groups. However, women had an increased risk of MACCE in the off-pump group. The authors hypothesized that these outcomes could be attributed to a variety of factors, such as the increased technical challenge of smaller vessel targets. They recommended

**Table 1. Summary of the included primary research studies comparing multiple arterial grafting to single arterial grafting in females**

| Author (year)                               | Study design (database used if applicable)                                          | MAG definition                                                               | Number of female patients                                     | Mean age (SD) of MAG group                                      | Mean age (SD) of SAG group                                      | Propensity-score matching dependent variable | Follow-up duration                                 | Primary outcome (s)                                                                                                                                                                                                                                           | Additional results                                                                                                                                                                                                                                                                                                                                               |
|---------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------------------|---------------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|----------------------------------------------|----------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ren et al., (2024) <sup>[20]</sup>          | Retrospective cohort study (ANZSCTS)                                                | Two or more arterial grafts used                                             | 10,693 (MAG 5,494; SAG 5,199; 4,240 propensity-matched pairs) | 68.5 (10.0)                                                     | 68.6 (10.5)                                                     | MAG                                          | Median 5.2 (IQR 2.4-8.7) years                     | Lower long-term mortality (adjusted HR 0.83; 95%CI: 0.76-0.91; $P < 0.001$ )                                                                                                                                                                                  | Only incident of congestive HF was increased in MAG patients, but no significant differences in 30-day mortality, readmission to the hospital due to a composite of MI, deep sternal wound infection, arrhythmia, or recurrent angina                                                                                                                            |
| Tam et al., (2021) <sup>[30]</sup>          | Retrospective cohort study (ICES Database)                                          | Two or more arterial grafts used                                             | 10,915 (2,446 propensity-matched pairs)                       | 66.0 (9.9) before propensity-score matching; 66.7 (9.9) after   | 68.9 (9.3) before propensity-score matching; 66.7 (9.9) after   | MAG                                          | Median 5.0 (IQR 2.6-7.8) years; maximum 11.0 years | Long-term survival at 10 years better in MAG patients (HR 0.85; 95%CI: 0.84-0.98)                                                                                                                                                                             | Freedom from MACCE at 10 years higher in MAG group (HR 0.85; 95%CI: 0.76-0.95); incidence of repeat revascularization lower in MAG (HR 0.77; 95%CI: 0.64-0.93); no differences in 10-year MI, incidence of stroke; early mortality, in-hospital complications of MI, stroke; readmission for sternal complications at 1 year (MAG 1.5%; SAG 0.74%; $P = 0.009$ ) |
| Gaudino et al., (2021) <sup>[31]</sup>      | Retrospective cohort study (New York's CSRS and New York's Vital Statistics file)   | Use of more than one arterial conduit                                        | 15,247 (1,860 propensity-matched pairs)                       | 64.8 (10.8) before propensity-score matching; 65.2 (10.3) after | 69.2 (10.1) before propensity-score matching; 65.0 (10.3) after | MAG                                          | Median 6.3 (range 3.7-8.8) years                   | No significant difference in mortality at 1 year and at 7 years                                                                                                                                                                                               | No significant difference in acute MI, stroke, MACE, repeated revascularization, and MACCE at 1 year; female patients who underwent MAG had lower incidence of acute MI at 7 years (adjusted HR 0.88; 95%CI: 0.60-0.97); no significant differences for stroke, repeated revascularization, MACCE, and MACE                                                      |
| Aboul-Hassan et al., (2024) <sup>[32]</sup> | Retrospective cohort study (Polish National Registry of Cardiac Surgery Procedures) | More than one arterial conduit (60.8% of patients received BITA ± RA or SVG) | 18,528 (1,528 propensity-matched pairs)                       | 64.0 (9.17)                                                     | 64.1 (9.01)                                                     | MAG                                          | Median 5.7 (IQR 3.4-7.9) years                     | Lower long-term mortality in MAG patients age < 70 years (HR 0.70; 95%CI: 0.52-0.92), with diabetes (HR 0.67; 95%CI: 0.47-0.96), LVEF > 40% (HR 0.76; 95%CI: 0.60-0.96), without PAD (HR 0.76; 95%CI: 0.59-0.99), and without CLD (HR 0.79; 95%CI: 0.63-0.99) | No significant differences in 30-day mortality, in-hospital MI, new-onset RRT, reoperation for bleeding, postoperative MCS, or sternal wound infection                                                                                                                                                                                                           |

|                                                |                                                                                                                 |                                       |                              |                                                                        |                                                             |                         |                                                                         |                                                                                                                                                                 |                                                                                                                                  |
|------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------------------|------------------------------|------------------------------------------------------------------------|-------------------------------------------------------------|-------------------------|-------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|
| Rubens <i>et al.</i> , (2022) <sup>[29]</sup>  | Retrospective (Clinical Registry Data from CorHealth Ontario and ICES Database)                                 | Two arterial conduits used            | 9,135 (MAG 1,975; SAG 7,160) | 65.65 (9.98); post weighting 68.15                                     | 68.75 (9.45); post weighting 68.01                          | Double arterial conduit | Mean 4.4 ± 2.6 years; median 4.2 (IQR 2.1-6.6) years, maximum 9.3 years | Higher risk of death after MAG (HR 1.48; 95%CI: 1.23-1.79); higher risk of 30-day mortality in women whose MAG comprised of LITA + RA compared with BITA grafts | Higher risk of MACCE after MAG (HR 1.32; 95%CI: 1.14-1.51), higher rates of revascularization and readmission for HF at 30 days; |
| Saraiva <i>et al.</i> , (2018) <sup>[42]</sup> | Retrospective cohort study (Database of the Department of Cardiothoracic Surgery at Centro Hospitalar São João) | Patients who underwent CABG with BITA | 460 (MAG 124; SAG 336)       | 58.6 (9.6) for all male and female patient (did not report separately) | 67.3 (8.6) for males and female (did not report separately) | BIMA                    | Median 5.8 years (did not report IQR), maximum 12 years                 | Females undergoing MAG had worse survival rates compared with SAG (HR 2.00; 95%CI: 1.03-3.89)                                                                   | No statistically significant early mortality or reoperation due to sternal wound complications                                   |

SD: Standard deviation; MAG: multiple arterial grafting; SAG: single arterial grafting; ANZSCTS: Australian and New Zealand society of cardiac and thoracic surgeons; IQR: interquartile range; HR: hazard ratio; CI: confidence interval; ICES: institute for clinical evaluative sciences; CSRS: cardiac surgery reporting system; LITA: left internal thoracic artery; RITA: right internal thoracic artery; MAG: multiple arterial grafting; MACCE: major adverse cardiac and cerebrovascular event; MI: myocardial infarction; CAE: cerebral adverse event; RRT: renal replacement therapy; MCS: mechanical circulatory support; BITA: bilateral internal thoracic artery; RA: radial artery; SVG: saphenous vein graft; LVEF: left ventricular ejection fraction; PAD: peripheral artery disease; CLD: chronic lung disease; HF: heart failure; MACE: major adverse cardiac event; NACSA: national institute for cardiovascular outcomes research; CVA: cerebrovascular accident; IABP: intra-aortic balloon pump; CABG: coronary artery bypass grafting.

that one should proceed with caution when performing off-pump CABG for women requiring multivessel revascularization, as the risks may outweigh any potential benefits.

## THE POTENTIAL RISKS OF MULTIPLE ARTERIAL GRAFTING

There remain several potential issues that deter surgeons from expanding the use of MAG in women. A meta-analysis conducted by Chngal *et al.* included 10 contemporary RCTs that compared MAG vs. SAG with at least one year of follow-up<sup>[12]</sup>. The MAG group had a significantly higher incidence of sternal wound complications [relative risk (RR) 1.75; 95%CI: 1.19-2.55]. Subgroup analysis showed that the MAG group who received RITA drove the statistically significant higher incidence of sternal wound complications compared with the SAG group (RR 1.75; 95%CI: 1.17-2.60). This finding was also demonstrated by Tam *et al.*, who concluded that patients who underwent MAG had a statistically significantly higher one-year sternal complication rate compared with patients undergoing SAG<sup>[30]</sup>. Similarly, Attia *et al.* found women were more likely to experience postoperative deep sternal wound infections and septicemia than men in their large retrospective analysis<sup>[18]</sup>.

A single-center retrospective cohort study specifically comparing BIMA with single IMA CABG in 2,424 patients, of which 460 were females, showed no significant difference in survival between these two groups<sup>[42]</sup>. Females had significantly higher mortality when undergoing BIMA compared to males, with a median follow-up of 5.5 years (HR 2.00; 95%CI: 1.03-3.89;  $P = 0.039$ ). Ren *et al.* demonstrated a statistically significant increased incidence of CHF at 30 days in

women undergoing MAG compared with SAG for isolated CABG<sup>[20]</sup>. Additionally, a retrospective cohort study using the ICES database conducted by Rubens *et al.* compared patient outcomes when they underwent primary isolated CABG with either a single arterial conduit or double arterial conduits found that a double arterial conduit was associated with an increased rate of 30-day mortality (HR 1.48; 95%CI: 1.23-1.79) and increased postoperative MACCE (HR 1.32; 95%CI: 1.44-1.51)<sup>[29]</sup>. The increased morbidity and mortality in female patients undergoing MAG should be further investigated through research.

## WHAT IS ON THE HORIZON FOR MULTIPLE ARTERIAL GRAFTING FOR WOMEN?

To the best of our knowledge, there are currently no RCTs comparing MAG and SAG for women that can be used to direct practice. The Randomized Comparison of the Outcome of Single Versus Multiple Arterial Grafts trial (ROMA): Women, a large, multi-center, international RCT led by Gaudino *et al.*, aims to address this gap<sup>[43]</sup>. This study involves the randomization of female patients undergoing isolated, primary CABG in a non-emergent setting to receive either MAG or SAG. Patients in both groups will receive a left internal mammary artery to LAD anastomosis, and patients in the MAG group will receive a graft with either a radial artery or a RIMA to a major vessel to the lateral wall. This RCT will not only help gain a better understanding of MAG *vs.* SAG for women specifically but will also help shape guidelines for coronary revascularization in women. We anticipate it will also provide insights as to how we can address the sex-based disparities in CABG outcomes so that women can expect identical early and late outcomes as their male counterparts.

## CONCLUSION

While MAG has been shown to improve mortality and morbidity compared with SAG during CABG and has been integrated into recent coronary artery revascularization guidelines, there remains a scarcity of data on the effects of MAG *vs.* SAG on CABG outcomes for women. Females remain under-represented and under-studied in observational studies and RCTs, although we have known for decades that women fare worse post-CABG due to a multitude of potential factors. In the evidence used to inform guidelines for MAG in CABG, females were less than 30% of the included population in these studies. Additionally, females were older in age with more comorbidities, and had more severe symptoms in their initial presentation for CABG. Women were also less likely to receive MAG compared with their male counterparts, perhaps due to these preoperative factors, in combination with preconceived surgeon biases, and the culture of practice at various institutions. The studies that examined the effect of MAG *vs.* SAG for females specifically showed that MAG in females may be associated with improved long-term survival and freedom from MACCE, with decreases in other morbidity outcomes. While on- *vs.* off-pump CABG remains a controversial topic, there was some evidence that showed the potential benefits of MAG in women may be undermined by the potential risks of off-pump surgery. There were also concerns for the increased risk of sternal wound infection, increased mortality, and CHF post-CABG for women who undergo MAG (specifically with BIMA) *vs.* SAG.

While there remains a necessity to gather more data, results from large-sized observational studies show the benefits of MAG in women, and this revascularization strategy should be employed when appropriate and safe for the patient. Overall, there remains uncertainty about the true effect of MAG for women undergoing CABG, and data from a large multi-center RCT investigating MAG *vs.* SAG in a female population undergoing isolated, primary CABG will help address this knowledge gap.

## DECLARATIONS

### Authors' contributions

Made substantial contributions to the conception, writing, and editing of the manuscript: Qiu Y, Rubens FD

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Both authors declared that there are no conflicts of interest.

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