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RESEARCH

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# Gender differences in the incidence of saphenous vein graft intervention

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## Abstract

**Background** Saphenous vein graft percutaneous coronary intervention (SVG PCI) following coronary artery bypass grafting (CABG) is commonly used procedure for patients presenting with acute coronary syndrome (ACS). Emerging evidence suggests gender-based differences influencing SVG intervention clinical outcomes. This study aimed to analyze the impact of gender and various patient characteristics, procedural intricacies, anatomical considerations, and perioperative factors as potential risk determinants for SVG failure post-CABG surgery.

**Methods** A retrospective, single-center, analysis was conducted on post-CABG patients at Barzilai Medical Center Ashkelon from 2010 to 2023 to assess gender-based differences in SVG PCI incidence**.**

**Results** Of the 72 ACS patients undergoing SVG PCI, a notably higher incidence was observed in men. However, graft failure occurred earlier in women compared to men (13.50 ± 6.59 SD years vs. 22.13 ± 5.66 SD years). Women exhibited a 1.2 times higher likelihood of earlier PCI than men (OR 1.24 CI 1.077 to 1.487, $p = 0.0066$) after adjusting for age, smoking, diabetes, hypertension, and hyperlipidemia.

**Conclusion** Gender differences in the incidence of SVG PCI and graft failure denote the need for gender-tailored follow-up and early intervention to optimize graft patency and potentially enhance long-term clinical outcomes. Integrating gender-specific approaches into post-CABG management could significantly improve patient care and prognosis.

**Keywords** Saphenous vein graft, Gender differences, Coronary artery bypass grafting, Percutaneous coronary intervention

## Background

Over the last decade, there has been an increase in the proportion of women undergoing coronary artery bypass grafting (CABG), rising to 24.5% in 2020 [1, 2]. In addition, women tend to experience higher mortality rates and poorer prognoses than men during the 5-year post-CABG period [3]. The observed gender discrepancy in outcomes has been associated with specific patient characteristics present at the time of CABG, such as advanced age, elevated creatinine levels, peripheral vascular disease, type 2 diabetes, and heart failure, all of which have been identified as contributing factors to increased mortality rates [3]. While differences in baseline characteristics between men and women at the time of CABG are known, the extent to which post-CABG survival differences are influenced by gender or represent a confounding effect remains to be elucidated. Despite advancements in surgical techniques, pharmacological interventions, and perioperative management, interventions involving saphenous vein grafts and percutaneous coronary intervention (SVG PCI) represent 6% of all PCI procedures in the United States, despite arterial grafts being the preferred strategy [4–6]. A large-scale multicenter trial has revealed concerning rates of SVG occlusion, ranging

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from 25 to 45% within the initial 12–18 months post-surgery [7]. Moreover, a gender-based discrepancy in SVG patency failure has been identified, with women exhibiting a higher occlusion rate compared to men—16.7% versus 12.4%, respectively—at 1-year post-surgery [8]. Understanding these gender differences in post-CABG patients can lead to improved long-term clinical outcomes reducing the incidence of major adverse cardiac events in this high-risk patient population [9]. The goal of the present study was to investigate clinical outcomes in a cohort of post-CABG patients receiving SVG PCI.

## Material and methods

### Study population

For this retrospective cohort study, we analysed a gender matched group of post-CABG patients receiving urgent, SVG PCI, from 2010 to 2023, at our hospital. The study population included 72 CABG patients, 66 males and 6 females, after urgent PCI. Patients with previous CABG surgery undergoing cardiac catheterization and SVG intervention were selected for this study. Eligible patients had at least one significant de-novo SVG lesion (70–100% stenosis of a 2,25–6 mm diameter SVG) requiring PCI. Patients without complete medical record that include reports and angiograms and intervention cine were excluded from the study. Clinical and demographic characteristics were collected from hospital medical records. The study protocol adhered to the Declaration of Helsinki and was approved by the institutional review board of Barzilai Medical Center (BRZ-0080-23). Informed consent was obtained from the patients to participate in the study.

### Degeneration score

SVG degeneration score is an ordinal metric of the extent of lumen irregularities and ectasia. Two scores were used for this study. The first score, the classical two categories score for SVG degeneration indicating more than 50% of the length is affected containing multiple plaques. The second score is subdividing SVG degeneration into 4 categories 25% (SVG degeneration score, 0), 26–50% (SVG degeneration score, 1), 51–75% (SVG degeneration score, 2), or 75% (SVG degeneration score, 3) of the total SVG length [10]. In this study, the majority of patients underwent left internal mammary artery (LIMA) or right internal mammary artery (RIMA) graft to the left anterio descending artery (LAD).

### Statistical analysis

The results were presented as the mean ± Standard Deviation (SD) for continuous variable with normal distribution, and as the number and percentage for categorical data. T test was performed for comparison of continuous variables. X2 test and Fisher's exact test were used for categorical data. A two-sided *P*-value < 0.05 was considered statistically significant. Logistic regression analysis was used to determine the variables associated with gender and to calculate the adjusted odd ratios (OR) for significant comorbidities. Statistical analysis was performed with Prism Graphpad.

## Results

Between 2010 and 2023, 72 consecutive CABG patients were subjected to urgent PCI in our hospital. The percentage of SVG intervention was 2.01% of STEMI/NSTEMI patients and the number of CABG patients undergoing urgent PCI was 0.84% of total PCI patients. No significant differences were observed in baseline characteristics, comorbidities and pharmacological treatment in women undergoing PCI and CABG compared to males (Table 1).

PVD, peripheral vein disease, ACEI/ARBs, angiotensin converting enzyme inhibitors/angiotensin receptor blockers. AP, angina pectoris. NSTEMI, Non-ST-Elevation Myocardial Infarction. STEMI, ST-Elevation Myocardial Infarction.

**Table 1** Clinical characteristics of the cohort

| | Male | Female | *p* value |
|---|---|---|---|
| Age (years), mean ± SD | 72.20 (9.16 SD) | 68.5 (13.78 SD) | ns |
| Gender | 66 | 6 | |
| Comorbidities | | | |
| Renal disease, n (%) | 17 (26%) | 0 (0%) | ns 0.32 |
| PVD, n (%) | 12 (18%) | 0 (0%) | ns 0.58 |
| Previous Stroke, n (%) | 9 (13%) | 2 (33%) | ns 0.19 |
| Previous MI, n (%) | 35 (53%) | 1 (16%) | ns 0.08 |
| Obesity, n (%) | 27 (40%) | 4 (66%) | ns 0.09 |
| Hyperlipidaemia, n (%) | 62 (93%) | 6 (100%) | ns 0.53 |
| Hypertension, n (%) | 58 (87%) | 6 (100%) | ns 0.36 |
| Diabetes, n (%) | 42 (63%) | 4 (66%) | ns 0.88 |
| Smoking status, n (%) | 16 (24%) | 2 (33%) | ns 0.62 |
| Ex-smoker, n (%) | 8 (12%) | 1 (16%) | ns 0.36 |
| Pharmacological treatment | | | |
| Aspirin, n (%) | 51 (77%) | 6 (100%) | ns 0.30 |
| Statins, n (%) | 57 (86%) | 6 (100%) | ns 0.57 |
| Beta blockers, n (%) | 51 (77%) | 6 (100%) | ns 0.25 |
| ACEI/ARBs, n (%) | 42 (64%) | 6 (100%) | ns 0.12 |
| Presentation symptoms | | | |
| Stable AP, n (%) | 2 (3%) | 0 (0%) | ns > 0.9999 |
| Unstable AP, n (%) | 16 (24%) | 2 (33%) | ns 0.6081 |
| NSTEMI, n (%) | 36 (54%) | 2 (33%) | ns 0.6432 |
| STEMI, n (%) | 7 (10%) | 1 (16%) | ns 0.4873 |
| Low compliance, n (%) | 5 (7%) | 0 (0%) | ns 0.9999 |

Graft patency failure was observed to occur earlier in women than in men (13.50 ± 6.59 SD vs. 22.13 ± 5.66 SD). Women underwent urgent PCI treatment earlier than men (7.66 ± 7 SD years vs. 15.45 ± 6.3 SD years). In addition, women had 1.2 times higher than males to undergo PCI earlier than men (OR 1.24 CI 1.077–1.487, $p = 0.0066$) after adjusting for age, smoking, diabetes, hypertension, and hyperlipidaemia (Table 2). 30-day mortality and 1-year mortality was limited to 1 patient. The majority of the coronary arteries supplied by the intervened SVG's presented chronic total occlusion (92.5%) in both genders, and presented a degeneration score of ≤ 25% (Table 2).

PCI, percutaneous coronary intervention. CABG, coronary artery bypass graph. LVEF, left ventricular ejection fraction. SVG, saphenous venous graft. LAD, left anterior descending artery. LCX, circumflex branch of the left coronary artery. OM, obtuse marginal arteries. PDA, posterior descending artery.

## Discussion

In this study, we have observed a gender difference at the time for elective CABG surgery, as well as for urgent PCI management. In addition, women referred for urgent PCI treatment presented at a younger age graft than men. CABG surgery, and graft patency failure increases the risk of morbidity and mortality with PCI being the only option with an incidence of SVG intervention at 6% [11], or 0.84% as observed in our hospital. In addition, several studies indicate that the percentage of women undergoing CABG range from 26.1% to 33.6% [1, 8–10], with limited number of women undergoing urgent PCI [12, 13]. Interestingly, the time interval between CABG and urgent PCI was notably shorter in women compared to men, suggesting a potentially faster progression of graft issues in female patients. Furthermore, women with SVG failure represent small percentage of patients undergoing urgent PCI from the predicted number based of the CABG prevalence. Several explanations have been offered in order to explain this gender differences some including in-hospital mortality, differences in disease severity, health care seeking behaviour leading to undertreatment relative to men, physician referral patterns for both CABG and/or PCI and the type of graft (vein vs. artery) [14]. Early mortality differences in women may explain the observed results in this study. Sex differences have been suggested to affect CABG clinical outcomes with women presenting with more stable and diffuse atherosclerotic disease, as well as a distinct difference in patency and occlusion rates with women more prone to SVG, and a more silent closure course [1, 15–17]. In a retrospective study by Tan et al. the one-year occlusion rates of SVG and IMA grafts were comparable in women and men [8]. Clinical outcome was related to graft patency and was less favourable in women owing to their uneven distribution of risk factors among both groups. Nevertheless, the highest rates were observed for SVG onto small-sized coronary arteries (lumen diameter ≤ 1.0 mm). In another study by Fukui evaluated patency rates of both arterial and vein grafts, the results indicate that arterial graft patency were not significantly different between the genders; however, SVG in females presented with significantly lower patency rate than those in males suggesting a more silent closure course [18]. Interestingly, the authors performed the angiography 12.5 days after surgery which may relate to the surgical follow-up but not to the long-term influence of gender on SVG over time. In addition, McLean et al. 2011 assessed the patency of 611

**Table 2** Angiographic, and procedural variables

| | Male | Female | *P* value |
|---|---|---|---|
| Graft age patency (years), mean ± SD | 22.13 (5.66 SD) | 13.50 (6.59 SD) | < 0.001 |
| Previous PCI (years), n (%) | 25 (38%) | 1 (1.4%) | ns 0.4043 |
| Time from CABG to PCI (years), mean ± SD | 15.45 (6.3 SD) | 7.66 (7.0 SD) | < 0.006 |
| LVEF (%), mean ± SD | 46.41 (10.68 SD) | 52.5 (8.21 SD) | ns 0.18 |
| SVG Degeneration score, n | | | |
| < 25% | 56 | 6 | 0.30 |
| 25–50% | 10 | 0 | |
| 51–75% | 0 | 0 | |
| > 75% | 0 | 0 | |
| SVG Graft Territories, n | | | |
| PCI to SVG to LAD | 7 | 1 | |
| PCI to SVG to LCX territory (OM or Ramus) | 42 | 2 | |
| PCI to SVG to right PDA | 17 | 3 | |

SVG in 291 patients enrolled in the Reduction in Graft Occlusion Rates (RIGOR) study. The results indicated that female gender and low mean graft blood flow are significant risk factors for SVG thrombosis within six months of CABG surgery [19]. In terms of anatomical variables, a study by Mclean showed that SVG failure within six months of CABG surgery was predominantly an all-or-none phenomenon with 126 (20.1%) SVGs totally occluded, 485 (77.3%) widely patent and only 16 (2.5%) containing high-grade stenoses. The study showed that a target vessel diameter $\leq 1.5$ mm (OR 2.37, P = 0.003) and female gender (OR 2.46, $P = 0.01$) were strongly associated with early SVG occlusion. Additionally, small vessel diameter, female gender and low mean graft blood flow are significant risk factors for SVG thrombosis within six months of CABG surgery in patients on postoperative aspirin therapy [19].

Gender differences in the incidence of SVG PCI and graft failure require for gender-tailored follow-up and early intervention to optimize graft patency and potentially enhance long-term clinical outcomes. We propose several interventions aimed at maintaining graft patency, encompassing both diagnostic and therapeutic perspectives. Women are often underdiagnosed and less frequently referred to cardiology specialists. Consequently, we recommend a closer follow-up protocol in post-CABG female patients, even in the absence of apparent symptoms, including regular scheduled consultation, and cardiac CT referrals after CABG to detect early signs of SVG stenosis. In addition, the implementation of an intensive statin therapy should be considered. In a multicenter study, the use of an aggressive lowering of LDL cholesterol levels to below 100 mg/dl was shown to reduce the progression of atherosclerosis in grafts [20]. Specifically, the rate of revascularization over a four-year period was reduced by 29% in the group with the aggressive LDL lowering approach. We recommend much aggressive LDL lowering to less than 55 mg/dl.

Nevertheless, a multicenter study on a larger post-CABG is required to evaluate the use of high dose statins, proprotein convertase subtilisin kexin type 9 inhibitors (PCSK9-I) and the newly added inclisiran, or combination of the above in the reduction of adverse cardiovascular outcomes in post-CABG patients and SVG patency failure prevention, especially women [21].

The main limitations of this study are the single-center nature of the cohort, the small sample size and selection bias included in the analysis. To conclude, the results of our study indicate that women have higher SVG failure rates compared to men, possibly due to silent closure courses associated with increased in mortality. Consequently, we recommend a close follow-up course for women even in the absence of apparent symptoms, including evaluation of troponin levels which may potentially indicate significant SVG lesions or graft patency failure.

In conclusion, our research provides new insights into gender differences indicating that women are more likely to undergo SVG PCI earlier post-CABG compared to men. In addition, men and women are known to present with different patient characteristics at the time of CABG, and it remains to be seen if post-CABG survival difference can be attributed to sex itself, or rather to risk-factor mediation. Consideration for performing cardiac CT in women after bypass surgery is recommended to enhance the detection of potential graft failure early on. Consequently, further studies are needed to investigate the observed gender differences and revascularization strategies in selected patients.

#### Abbreviations

| | |
|---|---|
| ACS | Acute coronary syndrome |
| CABG | Artery bypass grafting |
| CI | Confidence interval |
| CT | Computed tomography |
| IMA | Internal mammary artery |
| OR | Odd ratio |
| RIGOR | Reduction in graft occlusion rates |
| SD | Standard deviation |
| SVG PCI | Saphenous vein graft percutaneous coronary intervention coronary |

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#### Author contributions
Conception and Design of the work (A.O. and E. G-C.), Data Acquisition (I. A., D.N., and I.O), Analysis and interpretation of data (A.O., E. G-C. and J.J.), Draft and Revised (all authors).

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#### Availability of data and materials
No datasets were generated or analysed during the current study.

### Declarations

#### Ethics approval and consent to participate
The study protocol adhered to the Declaration of Helsinki and was approved by the institutional review board of Barzilai Medical Center (BRZ-0080-23). Informed consent was obtained from the patients to participate in the study.

#### Consent for publication
Not applicable.

#### Competing interests
The authors declare no competing interests.

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