

# One-year outcomes of percutaneous coronary intervention in native coronary arteries versus saphenous vein grafts in patients with prior coronary artery bypass graft surgery

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## Abstract

**Background:** *Patients with prior coronary artery bypass graft (CABG) surgery often require percutaneous coronary intervention (PCI). Data are still limited in regards to the outcomes of native saphenous vein graft (SVG) PCI after CABG.*

**Methods:** *We performed a retrospective study in a tertiary reference cardiac center of consecutive patients who underwent PCI after CABG. The data were collected for patients who underwent either native or graft PCI from January 2008 to December 2018. Arterial graft PCIs were excluded. Multivariable Cox regression analysis with propensity matching was performed, and major adverse cardiac events (MACE) outcomes including death or myocardial infarction (MI) or revascularization were assessed at 1-year after each index procedure.*

**Results:** *A total of 435 PCI were performed in 401 patients (209 had native PCI and 192 had graft PCI). Target lesions were classified as following: 235 (54%) native coronary arteries and 200 (46%) SVG. Propensity matching resulted in 167 matched pairs. In multivariable Cox regression graft PCI relative to native PCI was an independent risk factor for MACE (hazard ratio [HR] 1.725, 95% confidence interval [CI] 1.049–2.837) which was primarily driven by increased incidence in revascularization (HR 2.218, 95% CI 1.193–4.122) and MI (HR 2.248, 95% CI 1.220–4.142) and with no significant difference in mortality (HR 1.118, 95% CI 0.435–2.870).*

**Conclusions:** *Compared with native coronary PCI, bypass graft PCI was significantly associated with higher incidence of MACE at 1-year and this was mainly driven by MI and revascularization. (Cardiol J)*

**Key words:** acute coronary syndrome, coronary artery bypass graft, coronary artery disease, major adverse cardiac event, percutaneous coronary intervention

## Introduction

Patients with prior coronary artery bypass graft (CABG) surgery often require repeat revascularization either due to graft failure or a combination of graft failure and progression of coronary

atherosclerosis. Thrombosis, intimal hyperplasia and atherosclerosis are the main pathological processes underlying saphenous venous grafts disease [1]. Early thrombosis is the principle cause of vein graft attrition during the first month after bypass surgery, with intimal hyperplasia being an issue

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during the remainder of the first year. Thereafter, atherosclerosis predominates. The optimal revascularization strategy of patients with prior CABG and graft failure remains a subject of debate. Redo surgeries are associated with higher morbidity and mortality as well as poorer outcomes compared to initial operations [2]. Furthermore, there is limited evidence on the optimal percutaneous coronary intervention (PCI) option (i.e. native coronary artery or graft PCI) in such population. Present study was conducted to compare 1-year major adverse cardiac events (MACE) of native versus graft PCI.

## Methods

This is a retrospective study performed in a tertiary cardiac center of CABG patients who underwent subsequent PCI. The data were collected for consecutive patients who underwent either native or graft PCI from January 2008 to December 2018. Arterial graft PCI patients were excluded from the study. The procedural data for the patients who underwent PCI were collected from our local catheterization laboratory database. If a patient had more than one procedure during the study period, the first PCI was considered as the index procedure and the subsequent procedures were considered as outcomes. If a patient had undergone more than one PCI in the same first procedure during the study time period, all lesions intervened on underwent analysis. However, if those PCI involved both native and saphenous vein graft (SVG) interventions, then the patient was included in the SVG PCI study arm. The primary end point was 1-year MACE defined as a composite of death, myocardial infarction (MI) or target vessel revascularization. Secondary endpoints included angiographic complications (no-reflow, dissection and perforation). Patients' mortality was identified from the hospital clinical system which is updated regularly from the United Kingdom's Office of National Statistics. All outcomes were assessed at 1-year after each index procedure.

## Statistical analysis

Continuous variables are presented as means (SD) or medians (IQR). For normally distributed variables, Student's t-test was used, whereas in samples with non-normal distribution Mann-Whitney U test was used. Categorical variables were compared with the use of Fisher's exact tests (2-sided). To best control for the non-random assignment of patients to 1 of 2 PCI approaches, we have used a combination of matching methods: it

is matched exactly on the categorical variables (gender, diabetes, chronic kidney disease, hypertension, urgency of procedures and clinical presentation [angina or acute coronary syndrome; ACS]) and used a propensity score on the age variable. So, in each matched pair the age may vary slightly but the other covariates all take exactly the same value. Matching resulted in 167 matched pairs. Kaplan-Meier curves for outcomes and compared with the use of the log-rank test. For multivariable analysis, the Cox regression model was applied. Estimated hazard ratios (HR) and their 95% confident intervals (CI) were calculated. Two-sided statistics were performed with a p-value less than 0.05 determining significance. Statistical analysis was performed using SPSS v.25.0 (IBM Corp., Armonk, New York, United States).

## Results

A total of 435 PCI were performed to 401 patients during the study period. They were classified as following: native coronary artery (235 [54%]), SVG (200 [46%]). The native vessel and SVG intervention had comparable baseline characteristics, left ventricular ejection fraction and clinical presentation (angina and ACS) as shown in Table 1. Graft age was greater in patients who underwent graft PCI. Femoral access was used in over half of both groups with no statistical difference between two groups. Most bypass graft target lesions were located at the body of the graft 58.6%. Compared with patients who underwent bypass graft PCI, those who underwent native coronary artery PCI were more likely to undergo PCI of a chronic total occlusion (CTO) or to an in-stent restenosis (ISR). In native vessel PCI, there was a greater likelihood of requiring more than one stent. However, in graft PCI stent diameters were larger. Regarding the length of the stents, there was no statistical difference between the two groups. In comparison to native coronary lesions, graft lesions were more likely to be treated with bare-metal stents (BMS) and drug eluting balloon. Patients in native PCI group were more likely to have post-procedural Thrombolysis in Myocardial Infarction III flow. Statistically, there was no difference in fluoroscopy time and contrast amount between both groups (Table 2). No reflow phenomenon was significantly more frequent in patients undergoing graft PCI compared to patients with native artery PCI (10% vs. 0.4%,  $p < 0.001$ ) (Table 3). Matched groups analysis resulted in a significant difference in age between both groups

**Table 1.** Baseline characteristics and presentation of patients undergoing native and graft percutaneous coronary intervention, before and after matching.

Parameter	Before matching			After matching		
	Native coronary PCI (209)	SVG PCI (192)	P	Native coronary PCI (167)	SVG PCI (167)	P
<b>Demographics</b>						
Age, median (IQR)	70 [62–76]	70 [65–78]	0.090	71 [63–76]	71 [66–79]	0.023
Female	28 (13%)	29 (15%)	0.669	23 (14%)	23 (14%)	1
<b>Comorbidities</b>						
Diabetes	84 (40%)	77 (40%)	1	67 (40%)	67 (40%)	1
Hypertension	148 (71%)	123 (64%)	0.166	112 (67%)	112 (67%)	1
Hyperlipidemia	99 (47%)	87 (45%)	0.690	78 (47%)	80 (48%)	0.913
Chronic kidney disease	30 (14%)	28 (15%)	1	23 (14%)	23 (14%)	1
Dialysis	3 (1%)	4 (2%)	0.714	3 (2%)	4 (2%)	1
Previous MI	156 (75%)	130 (68%)	0.151	122 (73%)	113 (68%)	0.338
Previous PCI	53 (25%)	47 (25%)	0.908	40 (24%)	40 (24%)	1
Reduced left ventricular systolic function (LVEF ≤ 40%)	60 (29%)	45 (23%)	0.256	50 (30%)	36 (22%)	0.103
Years from CABG, median (IQR)	10 [7–14]	12 [9–15]	0.002	10 [7–14]	12 [9–15]	0.003
<b>Presentation</b>						
Urgent procedure	102 (49%)	116 (60%)	0.021	97 (58%)	97 (58%)	1
Angina	106 (51%)	76 (40%)	0.061	70 (42%)	70 (42%)	0.899
NSTEMI	66 (32%)	80 (42%)		63 (38%)	66 (40%)	
STEMI	37 (18%)	36 (19%)		34 (20%)	31 (19%)	

CABG — coronary artery bypass graft; IQR — interquartile range; LVEF — left ventricular ejection fraction; MI — myocardial infarction; NSTEMI — non-ST-segment elevation myocardial infarction; PCI — percutaneous coronary intervention; STEMI — ST-segment elevation myocardial infarction; SVG — saphenous vein graft

**Table 2.** Lesion characteristics and procedural details, before and after matching.

Parameter	Before matching			After matching		
	Native coronary PCI (235)	SVG PCI (200)	P	Native coronary PCI (189)	SVG PCI (176)	P
Femoral access	121 (52%)	111 (56%)	0.441	93 (49%)	97 (55%)	0.295
<b>Targeted vessel</b>						
LM	28 (12%)	–	–	25 (13%)	–	–
LAD/diagonal	45 (19%)	48 (24%)		37 (20%)	42 (24%)	
LCX/OM	76 (32%)	83 (42%)		59 (31%)	76 (42%)	
RCA/PDA/PLV	86 (37%)	69 (33%)		68 (36%)	58 (33%)	
<b>Lesion characteristic</b>						
In-stent restenosis	26 (11%)	12 (6%)	0.087	18 (10%)	11 (6%)	0.245
True bifurcation	5 (1%)	–	–	5 (3%)	0	–
Graft aortic anastomosis	–	63 (31.5%)	–	–	58 (33%)	–
Graft body	–	119 (59.5%)	–	–	102 (58%)	–
Graft distal anastomosis	–	18 (9.0%)	–	–	16 (9%)	–

→

**Table 2 (cont.).** Lesion characteristics and procedural details, before and after matching.

Parameter	Before matching			After matching		
	Native coronary PCI (235)	SVG PCI (200)	P	Native coronary PCI (189)	SVG PCI (176)	P
<b>Stents characteristics and TIMI flow</b>						
Number of stents, median (IQR)	1 [1–2]	1 [1–1]	< 0.001	1 [1–2]	1 [1–1]	< 0.001
Length of stents [mm], median (IQR)	23 [16–32]	22 [16–28]	0.114	23.5 [17–32]	22 [16–28]	0.138
Diameter of stents [mm], median (IQR)	3 [2.75–3.5]	3.5 [3.0–4.0]	< 0.001	3.0 [2.75–3.5]	3.5 [3.0–4.0]	< 0.001
Bare metal stents	22 (10%)	42 (20%)	< 0.001	15 (8%)	37 (21%)	< 0.001
Drug eluting stents	201 (87%)	138 (69%)		164 (88%)	121 (69%)	
Drug eluting balloons	9 (4%)	19 (10%)		7 (4%)	17 (10%)	
<b>Pre-procedural TIMI flow</b>						
TIMI III flow	165 (70%)	135 (68%)	0.136	129 (68%)	120 (68%)	0.154
TIMI II flow	20 (9%)	14 (7%)		18 (10%)	10 (6%)	
TIMI I flow	7 (3%)	16 (8%)		7 (4%)	15 (9%)	
TIMI 0 flow	43 (18%)	35 (18%)		35 (19%)	31 (18%)	
<b>Post-procedural TIMI flow</b>						
TIMI III flow	233 (99%)	179 (90%)	< 0.001	187 (99%)	157 (89%)	< 0.001
TIMI II flow	1 (0.4%)	7 (4%)		1 (0.5%)	7 (4%)	
TIMI I flow	1 (0.4%)	6 (3%)		1 (0.5%)	5 (3%)	
TIMI 0 flow	0	8 (4%)		0	7 (4%)	
Contrast amount, median (IQR) [mL]	230 [170–320]	230 [160–310]	0.643	230 [175–320]	230 [160–300]	0.422
Fluoroscopy time, median (IQR) [min]	16.5 [11–25]	16.5 [11–24.5]	0.824	17.5 [11.5–25.75]	18 [11–26]	0.951

IQR — interquartile range; PCI — percutaneous coronary intervention; SVG — saphenous vein graft; TIMI — Thrombolysis in Myocardial Infarction

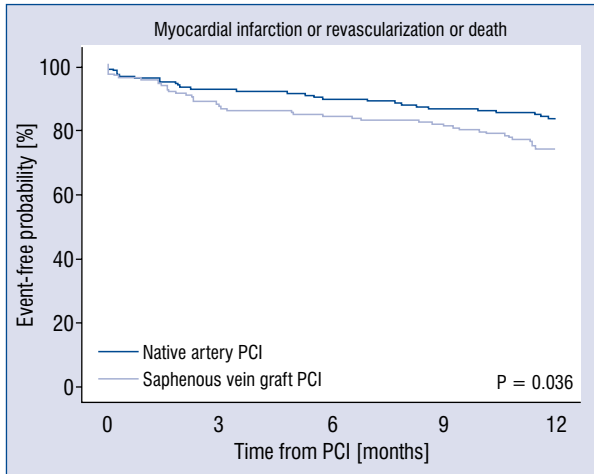
**Table 3.** Peri-procedural complications before and after matching.

Parameter	Before matching			After matching		
	Native coronary PCI (235)	SVG PCI (200)	P	Native coronary PCI (189)	SVG PCI (176)	P
No reflow	1 (0.4%)	19 (10%)	< 0.001	1 (0.5%)	16 (9%)	< 0.001
Dissection	7 (3%)	2 (1%)	0.188	6 (3%)	2 (1%)	0.286
Perforation	3 (1%)	0	–	2 (1%)	0	–
Intra-aortic balloon pump	6 (3%)	3 (2%)	0.337	6 (3%)	3 (2%)	0.505

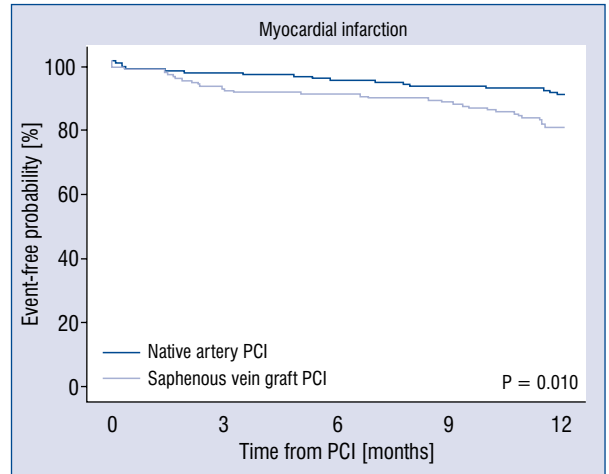
PCI — percutaneous coronary intervention; SVG — saphenous vein graft

( $p = 0.023$ ), however the size of the difference was not large (median age 71 [63–76] vs. 71 [66–79] in native PCI and SVG PCI groups, respectively). On the other hand, after matching the presentation (stable angina or ACS) was equally distributed

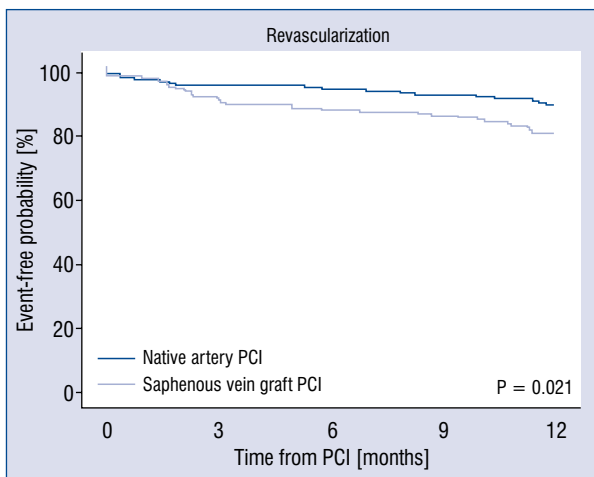
across the two groups. The lesion characteristics of matched patient groups were comparable to those prior to matching. Patients who underwent graft PCI had a significantly higher incidence of MACE (Fig. 1), principally driven by MI (Fig. 2)



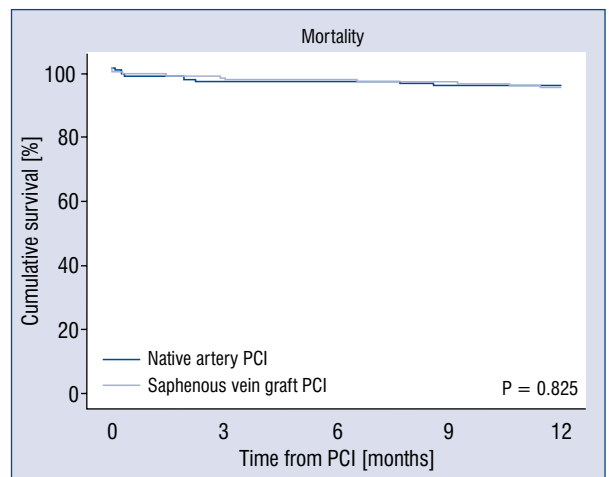
**Figure 1.** Myocardial infarction or revascularization or death after index percutaneous coronary intervention (PCI) in matched groups.



**Figure 2.** Myocardial infarction after index percutaneous coronary intervention (PCI) in matched groups.



**Figure 3.** Revascularization after index percutaneous coronary intervention (PCI) in matched groups.



**Figure 4.** Mortality after index percutaneous coronary intervention (PCI) in matched groups.

and revascularization rate (Fig. 3), while there was no significant difference in mortality (Fig. 4).

In multivariable Cox regression analysis (Table 4) the only factor associated with MACE was graft PCI compared to native PCI (HR 1.725, 95% CI 1.049–2.837,  $p = 0.032$ ). Age, urgency of the procedure, history of MI, diabetes, hypertension, hyperlipidemia, previous PCI, left ventricular ejection fraction, contrast amount used and fluoroscopy time were not significantly associated with MACE. Detailed Cox regression analyses on mortality, MI and revascularization are presented in Tables 5–7, respectively.

## Discussion

This single-center study which compares outcomes of PCI in patients with previous CABG has a number of interesting findings. Although there was no statistical difference in the baseline demographics of the two patient groups (Table 1), SVG PCIs were more likely to be urgent procedures. To reduce selection bias, there was a preponderance of males in the present study (86%). There was an even greater disproportion as reported by Brilakis et al. (99% of males) [3]. This significant underrepresentation of females with prior CABG

**Table 4.** Multivariate Cox regression with regard to major adverse cardiac events in matched groups.

Parameter	Hazard ratio	95% CI	P
Age [years]	0.990	0.964–1.017	0.467
Type of procedure (urgent vs. elective)	0.913	0.551–1.513	0.724
Graft PCI vs. native PCI	1.725	1.049–2.837	0.032
History of MI	1.444	0.759–2.746	0.263
Previous PCI	1.677	0.966–2.912	0.066
Diabetes	0.972	0.536–1.761	0.925
Hypertension	1.440	0.728–2.847	0.294
Hyperlipidemia	1.240	0.713–2.157	0.446
Chronic kidney disease	1.403	0.741–2.656	0.299
Fluoroscopy time (1 min increase)	0.999	0.983–1.015	0.878
Contrast amount (1 mL increase)	1.001	0.999–1.004	0.254
LVEF ( $\leq 40\%$ )	0.839	0.465–1.516	0.562

CI — confidence interval; MI — myocardial infarction; LVEF — left ventricular ejection fraction; PCI — percutaneous coronary intervention

**Table 5.** Multivariate Cox regression with regard to revascularization in matched groups.

Parameter	Hazard ratio	95% CI	P
Age [years]	0.964	0.933–0.995	0.025
Type of procedure (urgent vs. elective)	0.684	0.374–1.252	0.218
Graft PCI vs. native PCI	2.218	1.193–4.122	0.012
History of MI	1.650	0.737–3.691	0.223
Previous PCI	1.824	0.953–3.493	0.070
Diabetes	0.972	0.581–2.487	0.925
Hypertension	1.003	0.453–2.222	0.994
Hyperlipidemia	0.994	0.498–1.983	0.986
Chronic kidney disease	1.257	0.741–2.656	0.582
Fluoroscopy time (1 min increase)	0.998	0.977–1.020	0.867
Contrast amount (1 mL increase)	1.000	0.997–1.004	0.853
LVEF ( $\leq 40\%$ )	0.953	0.472–1.923	0.893

CI — confidence interval; MI — myocardial infarction; LVEF — left ventricular ejection fraction; PCI — percutaneous coronary intervention

**Table 6.** Multivariate Cox regression with regard to myocardial infarction in matched groups.

Parameter	Hazard ratio	95% CI	P
Age [years]	0.996	0.964–1.028	0.791
Type of procedure (urgent vs. elective)	1.349	0.715–2.544	0.355
Graft PCI vs. native PCI	2.248	1.220–4.142	0.009
History of MI	1.226	0.600–2.506	0.576
Previous PCI	1.425	0.732–2.772	0.297
Diabetes	0.910	0.455–1.821	0.790
Hypertension	2.112	0.913–4.883	0.081
Hyperlipidemia	0.885	0.472–1.656	0.701
Chronic kidney disease	1.667	0.804–3.454	0.169
Fluoroscopy time (1 min increase)	1.001	0.984–1.018	0.924
Contrast amount (1 mL increase)	1.001	0.998–1.004	0.413
LVEF ( $\leq 40\%$ )	1.152	0.593–2.238	0.675

CI — confidence interval; MI — myocardial infarction; LVEF — left ventricular ejection fraction; PCI — percutaneous coronary intervention

**Table 7.** Multivariate Cox regression with regard to mortality in matched groups.

Parameter	Hazard ratio	95% CI	P
Age [years]	1.047	0.990–1.107	0.107
Type of procedure (urgent vs. elective)	0.684	0.537–5.495	0.361
Graft PCI vs. native PCI	1.118	0.435–2.870	0.817
History of MI	1.327	0.403–4.370	0.642
Previous PCI	0.913	0.282–2.954	0.879
Diabetes	0.900	0.303–2.674	0.850
Hypertension	4.859	0.564–4.829	0.150
Hyperlipidemia	1.942	0.660–5.719	0.228
Chronic kidney disease	2.296	0.809–6.513	0.118
Fluoroscopy time (1 min increase)	1.005	0.983–1.028	0.642
Contrast amount (1 mL increase)	1.004	1.000–1.008	0.060
LVEF ( $\leq 40\%$ )	0.840	0.262–2.694	0.769

CI — confidence interval; MI — myocardial infarction; LVEF — left ventricular ejection fraction; PCI — percutaneous coronary intervention

in need of subsequent PCI reported in studies to date warrants further prospective assessment. In the current study there was a relatively high percentage of radial approach (47%) in comparison to the other reported studies [4]. RADIAL-CABG Trial [5] was a randomized prospective study which suggested that diagnostic angiography using radial access compared with femoral access was associated with greater contrast use, longer procedure and fluoroscopy time as well as greater patient and operator radiation exposure. However, no significant differences in these parameters were observed among patients undergoing PCI in the present study. Other studies suggested that a radial approach is feasible and is as fast as the femoral approach [6, 7]. It was noted that venous grafts were more likely to be the PCI target vessel with increasing time after CABG, consistent with the accelerated pace of late saphenous venous graft failure [8]. Nearly all target bypass grafts were SVG, a reflection of the excellent outcomes achieved with use of internal mammary arteries [9, 10]. Radial-artery grafts have a lower rate of graft occlusion at 1-year than SVGs [11]. We would thus advocate a randomized study to compare the outcomes of conventional CABG versus a hybrid approach where only arterial grafts would be used, plus PCI for the other vessels. It was found that patients who underwent bypass graft rather than native coronary PCI were more likely to receive BMS. The benefits of drug eluting stents (DES) over BMS in venous graft interventions are still controversial. The DIVA study [12], which is the most recent randomized trial included 597 patients undergoing PCI of de-novo SVG lesions. There was

no significant difference in 12-month and long-term (median 2.7 years) incidence of cardiac death, target vessel MI or target vessel revascularization (TVR). DES implantation was associated with improved results in ISAR-CABG trial which randomized 610 patients with diseased SVG to DES or BMS and reported that DES were associated with favorable hard endpoint outcomes (15.4% vs. 22.1%;  $p = 0.03$ ) [13]. The stenting of saphenous vein grafts trial (SOS), also demonstrated a significant reduction in MACE rates with paclitaxel-eluting stents compared with BMS, which was mainly driven by lower target lesion revascularization (TLR) rates [14]. Sirolimus-eluting stents were studied in the Reduction of Restenosis In Saphenous Vein Grafts With Cypher Sirolimus-eluting Stent RRISC trial [15], which demonstrated a reduction in TLR and TVR, and late stent loss in the DES group compared with the BMS group at 6 months. Conversely, the DELAYED RRISC study [16] found the TVR benefit was lost at 3-year follow-up and BMS was associated with lower long-term mortality. In the present study, no-reflow was significantly higher in graft PCI compared to native artery PCI (10% vs. 0.4%;  $p < 0.001$ ). Venous graft PCI was an independent risk factor for the peri-procedural complications including no-reflow [17], especially if the presentation was ST-segment elevation MI [18]. From our real-world data, SVG PCI carried a higher risk of MACE at 1 year when compared with native coronary PCI, that was mainly driven by MI and TVR. All of the efforts need to be taken into consideration to attempt native coronary revascularization. Percutaneous revascularization of CTO continues to gain popularity and accept-

ance despite its risk and complexity. Techniques have improved with the increasing availability of new equipment as previous studies showed favorably high success rates for CTO PCI even in previously bypassed patients [19–21]. SVG can be used to attempt CTO PCI via the retrograde approach as shown in a previous study [22]. Anatomic complexity in patients with previous CABG might adversely impact in the outcome of chronic coronary occlusions PCI [23]. Redo CABG carries a higher mortality rate compared with first-time CABG [24, 25]. In post-CABG patients, PCI was associated with better survival compared to redo CABG [26]. Another study suggested no difference in survival between redo CABG and PCI, however, PCI was associated with a higher revascularization rate [27]. Overall, redo CABG could be considered as an option for revascularization especially if the arterial graft (i.e. left anterior mammary artery; LIMA) was not used during the first CABG.

### Limitations of the study

Firstly, it was a retrospective study and not a prospective randomized trial and hence was subject to all the limitations of observational studies. Secondly, the choice of PCI target was dependent on the judgement of the operator. Thirdly, some patient data may have been missed since not all patients were routinely followed up at 12 months post-procedure.

### Conclusions

The present study findings would currently support considering PCI in the native vessel rather than the failing venous graft in patients with previous CABG. Further work however is needed and, in this respect, the currently ongoing PROCTOR study, a multi-center, prospective trial is randomizing patients to native vessel versus venous graft PCI [28].

**Conflict of interest:** None declared

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