Long-Term Follow-Up of Patients With Previous Coronary Artery Bypass Grafting Undergoing Percutaneous Coronary Intervention for Chronic Total Occlusion

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Successful revascularization of chronic total occlusions (CTOs) has been associated with clinical benefit. Data on outcomes in patients with previous coronary artery bypass grafting (CABG) undergoing percutaneous coronary intervention (PCI) for CTO, however, are scarce. A total of 2,002 consecutive patients undergoing PCI for CTO from January 2005 to December 2013 were divided into patients with and without previous CABG, and outcomes were retrospectively assessed. The primary outcome measure was all-cause mortality. Median follow-up was 2.6 years (interquartile range 1.1 to 3.1). A total of 292 patients (15%) had previous CABG; they were older and had a greater prevalence of comorbidities. Procedural success was achieved in 75% and 84% of patients in the previous CABG and the non-CABG groups ($p < 0.001$), respectively. All-cause mortality was 16% and 11% in the previous CABG and the non-CABG groups ($p = 0.002$), and differences were mitigated after adjustment for baseline characteristics (adjusted hazard ratio [HR] 1.22, 95% confidence interval [CI] 0.86 to 1.74, $p = 0.27$). All-cause death was significantly reduced in patients with procedural success, both in the previous CABG (11% vs 32%, adjusted HR 0.43, 95% CI 0.24 to 0.77, $p = 0.005$) and the non-CABG groups (10% vs 20%, adjusted HR 0.63, 95% CI 0.45 to 0.86, $p = 0.004$), with similar mortality benefits associated with successful revascularization in both groups (interaction $p = 0.24$). In conclusion, the relative survival benefit of successful recanalization of CTO is independent of previous CABG. However, owing to a greater baseline risk, the absolute survival benefit of successful CTO procedures is more pronounced in patients with previous CABG than in non-CABG patients. **(Am J Cardiol 2016;■:■−■)**

Chronic total occlusions (CTOs) continue to be a particularly challenging lesion subset associated with increased rates of procedural failure and complications.[1] The prevalence of CTO in patients with previous coronary artery bypass grafting (CABG) is particularly high, and percutaneous coronary revascularization has emerged as promising treatment alternative to surgery when symptomatic bypass graft failure exists. Most studies have demonstrated that PCI for CTO in patients with previous CABG is associated with lower procedural success rates compared with that in patients without previous surgical revascularization,[2–6] a finding that has mainly been attributed to the complex coronary anatomy and the heavily calcified lesions frequently encountered in these patients. However, data on clinical outcomes in patients with previous CABG are scarce and mostly limited to in-hospital events and rather small patient cohorts,[2,3] and whether lower procedural success rates translate into worse outcomes in patients with previous CABG remains unclear. Given the increasing prevalence of patients with bypass graft failure, along with the implementation of novel interventional approaches, characterization and risk stratification of these patients gained further importance. The aim of this study was therefore to assess clinical and procedural characteristics as well as long-term outcomes in patients with and without previous CABG undergoing PCI for CTO.

Methods

Data from 2,002 consecutive patients who underwent elective PCI for CTO at our institution from January 2005 to December 2013 were collected from our clinical database and retrospectively assessed.[7] The registry includes demographic, clinical, angiographic, and procedural data, along with in-hospital and long-term outcomes, of the patients. Patients were followed up by outpatient visits and telephone contacts performed at 30 days, 1 year, and 3 years after PCI for CTO. The indication for PCI for CTO was based on current guidelines on myocardial revascularization.[8] PCI for CTO was performed with contemporary techniques including double injections and anterograde/

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See page 6 for disclosure information.

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0002-9149/16/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2016.08.038

Table 1
Baseline characteristics

Variable	Previous coronary artery bypass grafting		P-value
	Yes (n=292)	No (n=1710)	
Age (years)	68±9	65±11	<0.001
Women	35 (12%)	297 (17%)	0.02
Body mass index (kg/m^2)	28.5±4.4	28.1±4.4	0.10
Diabetes mellitus	113 (389%)	477 (28%)	<0.001
Current smoker	19 (7%)	382 (22%)	<0.001
Dyslipidemia	265 (91%)	1461 (85%)	0.01
Hypertension	262 (90%)	1385 (81%)	<0.001
Family history of CAD	118 (40%)	630 (37%)	0.27
Prior myocardial infarction	139 (48%)	354 (21%)	<0.001
Prior PCI	68 (23%)	242 (14%)	<0.001
Previous failed attempt	53 (18%)	317 (19%)	0.94
Left ventricular ejection fraction < 40%	67 (23%)	281 (16%)	0.009
Chronic kidney disease (stage 4)	77 (27%)	317 (19%)	0.002
Estimated glomerular filtration rate (Cockcroft, ml/min)	80±32	91±35	<0.001
Total cholesterol (mg/dl)	173±44	192±48	<0.001
High-density lipoprotein cholesterol (mg/dl)	47±13	50±15	0.004
Low-density lipoprotein cholesterol (mg/dl)	104±38	119±41	<0.001

retrograde techniques. CrossBoss and Stingray coronary (Boston Scientific Corporation; Marlborough, Massachusetts) CTO crossing and re-entry devices were not available. Coronary CTO was defined as angiographic evidence of a total occlusion with complete interruption of anterograde blood flow (Thrombolysis In Myocardial Infarction [TIMI] flow grade 0) with an estimated duration of ≥3 months (based on previous angiograms, angina symptoms, and a history of myocardial infarction).[9] Procedural success was defined angiographically as complete restoration of anterograde blood flow (TIMI flow grade 3) and <30% residual diameter stenosis by visual assessment. The primary outcome measure was all-cause mortality. The secondary outcome measure was the cumulative incidence of major adverse cardiovascular events (MACE) including all-cause death, nonfatal myocardial infarction, and clinically driven target vessel revascularization. Nonfatal myocardial infarction was defined as the presence of new Q waves in ≥2 contiguous electrocardiographic leads or an elevation of creatine kinase level or its MB isoenzyme to at least 3 times the upper limit of normal in 2 plasma samples during hospitalization.

Continuous variables are presented as mean ± SD, or median and interquartile range, and categorical variables are given as frequencies and percentages. The Kolmogorov-Smirnov test was used to test for normality of distribution. Continuous variables were tested for differences with the unpaired Student *t* test or the Mann-Whitney *U* test and categorical variables with Pearson's chi-square test or Fisher's exact test as appropriate. Logistic regression and Cox proportional hazards models were used to assess adjusted risks of the outcome variables. Models were adjusted for selected variables significantly different between groups (p <0.05). Cox proportional hazards regression test of interaction (previous CABG/non-CABG status by procedural success/failure status) was used to assess whether there was a differential effect of procedural success by previous CABG/non-CABG status. Survival curves were generated with the Kaplan-Meier method, and the log-rank test was used to provide a formal statistical assessment of the differences between groups. A 2-sided p value of <0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows Version 21.0. (IBM Corp., Armonk, New York).

Results

Baseline and procedural characteristics are summarized in Tables 1 and 2. Median follow-up was 2.6 years (interquartile range 1.1 to 3.1). Two hundred ninety-two patients (15%) had previous CABG. The prevalence of cardiovascular risk factors was high, with 86% of patients having dyslipidemia, 82% hypertension, and 29% diabetes. Procedural success was achieved in 75% and 84% of patients in the previous CABG and the non-CABG groups (p <0.001). After multivariable adjustment for baseline differences, the association between previous CABG and procedural failure remained significant (odds ratio 1.40, 95% confidence interval [CI] 1.02 to 1.93, p = 0.04). Procedural complications in the previous CABG and non-CABG groups were rare and included vascular access site complications (0.7% vs 0.4%), bleeding requiring transfusion of red packed blood cells (0.7% vs 0.6%), coronary perforation (1.0% vs 0.1%), cardiac tamponade (0.7% vs 0.5%), stroke or transient ischemic attack (0.3% vs 0.1%), and aortic dissection in 2 (0.1%) non-CABG patients.

Crude all-cause mortality was higher in the previous CABG than in the non-CABG group (16% vs 11%, p = 0.002; Table 3 and Figure 1). After multivariable adjustment for baseline differences, all-cause mortality was similar in both groups (adjusted hazard ratio [HR] 1.22, 95% CI 0.86 to 1.74, p = 0.27). The unadjusted risk of MACE was greater in the previous CABG compared with

Table 2
Angiographic and procedural characteristics

Variable	Previous coronary artery bypass grafting		P-value
	Yes (n=292)	No (n=1710)	
CTO target vessel			
Left main	14 (5%)	1 (0.1%)	<0.001
Left anterior descending	43 (15%)	513 (30%)	<0.001
Left circumflex	107 (37%)	393 (23%)	<0.001
Right	128 (44%)	803 (47%)	0.34
No. of coronary arteries narrowed			<0.001
1	3 (1%)	365 (21%)	
2	28 (10%)	544 (32%)	
3	261 (89%)	801 (47%)	
Multivessel disease	289 (99%)	1345 (79%)	<0.001
CTO length >20 mm	222 (76%)	1302 (76%)	1.0
Moderate/severe calcifications	208 (71%)	913 (53%)	<0.001
Procedural characteristics			
Procedural success	218 (75%)	1444 (84%)	<0.001
Retrograde approach	122 (42%)	354 (21%)	<0.001
Drug-eluting stent	205 (70%)	1349 (79%)	0.001
Bare metal stent	8 (3%)	66 (4%)	0.41
Drug-eluting balloon	3 (1%)	4 (0.2%)	0.07
Number of stents	1.3±1.1	1.3±0.9	0.26
Total stent length (mm)	34.3±29.3	34.9±25.7	0.57
Contrast volume (ml)	371±170	311±152	<0.001
Fluoroscopy time (min)	53±37	33±36	<0.001
Kerma-area-product (cGy*cm^2)	17125±15080	11615±12855	<0.001

the non-CABG group (36% vs 30%, p = 0.003). After multivariable adjustments, MACE rates were similar in both groups (adjusted HR 1.08, 95% CI 0.86 to 1.35, p = 0.52). Procedural failure independently predicted all-cause mortality in the total cohort (adjusted HR 1.64, 95% CI 1.24 to 2.17, p <0.001) and affected outcomes in both the previous CABG and the non-CABG groups (Table 4 and Figure 2). All-cause mortality was significantly reduced in patients with procedural success, both in the previous CABG (11% vs 32%, p = 0.005) and the non-CABG groups (10% vs 20%, p = 0.004; Table 4). There was no significant interaction of procedural success/failure status and previous CABG/non-CABG status on all-cause mortality (interaction p = 0.24). A significant reduction in MACE rates was observed in patients with procedural success, both in the previous CABG (31% vs 50%, p = 0.01) and the non-CABG groups (28% vs 39%, p = 0.02). With respect to MACE rates, there was no significant interaction of procedural success/failure status and previous CABG/non-CABG status (interaction p = 0.36).

Discussion

This study showed substantial long-term clinical benefit of successful native-vessel PCI for CTO in patients with previous CABG. In these patients, successful compared with failed PCI for CTO was associated with a lower mortality and a lower incidence of MACE during a median follow-up of 2.6 years. The chances for success of PCI for CTO were, however, significantly less in patients with previous CABG than in those without. Nevertheless, once success was achieved, the relative risk reduction for mortality and MACE was independent of previous CABG. Owing to a greater baseline risk of patients with previous CABG, this afforded a substantially greater absolute reduction in mortality and MACE in patients with previous CABG compared with that in the non-CABG group.

The proportion of patients with previous CABG of 15% observed in this registry is comparable to other series.[2,10] Patients with previous surgical revascularization undergoing PCI for CTO are known to be at a particularly high risk,[2,3,6] they were older, more frequently male, and had a greater prevalence of comorbidities compared with patients without previous CABG. Recanalization of native-vessel CTO in patients with previous CABG is often the favored revascularization strategy as redo surgery bears an increased risk of adverse events compared with initial CABG,[11] and PCI involving a diseased bypass graft is limited by an increased risk of complications such as thrombus formation and distal embolization.[12–14] Although procedural success in patients undergoing PCI for CTO has considerably improved over the last decade given the advancements in revascularization techniques and dedicated equipment, along with increasing operator experience, CTO angioplasty is still associated with reduced procedural success rates compared with PCI of nonobstructive coronary artery lesions.[1,15] Procedural success in CTO patients with previous CABG is yet further reduced in comparison to patients without previous surgical revascularization,[2–5,14,16] and the higher amount of contrast dye volume, the longer fluoroscopy time, and the greater radiation exposure, along with more frequent retrograde attempts, illustrate the overall

Table 3
Clinical outcomes in patients with and without previous coronary artery bypass grafting

Variable	Previous coronary artery bypass grafting		Crude		Adjusted*	
	Yes (n=292)	No (n=1710)	Hazard ratio (95% confidence interval)	P-value	Hazard ratio (95% confidence interval)	P-value
All-cause death	48 (16%)	193 (11%)	1.64 (1.20-2.26)	0.02	1.22 (0.86-1.74)	0.27
All-cause death and/or myocardial infarction	58 (19%)	234 (14%)	1.61 (1.21-2.14)	0.001	1.22 (0.89-1.67)	0.22
Target vessel revascularization	58 (20%)	312 (18%)	1.19 (0.90-1.58)	0.22	1.02 (0.76-1.37)	0.89
Major adverse cardiovascular events	105 (36%)	512 (30%)	1.37 (1.11-1.69)	0.003	1.08 (0.86-1.35)	0.52

* Adjusted for baseline variables showing differences ($p < 0.05$) between patients with and without previous coronary artery bypass grafting including age, gender, diabetes, smoking, dyslipidemia, hypertension, estimated glomerular filtration rate, previous myocardial infarction, left ventricular ejection fraction < 40%, multivessel disease, and moderate/severe calcifications.

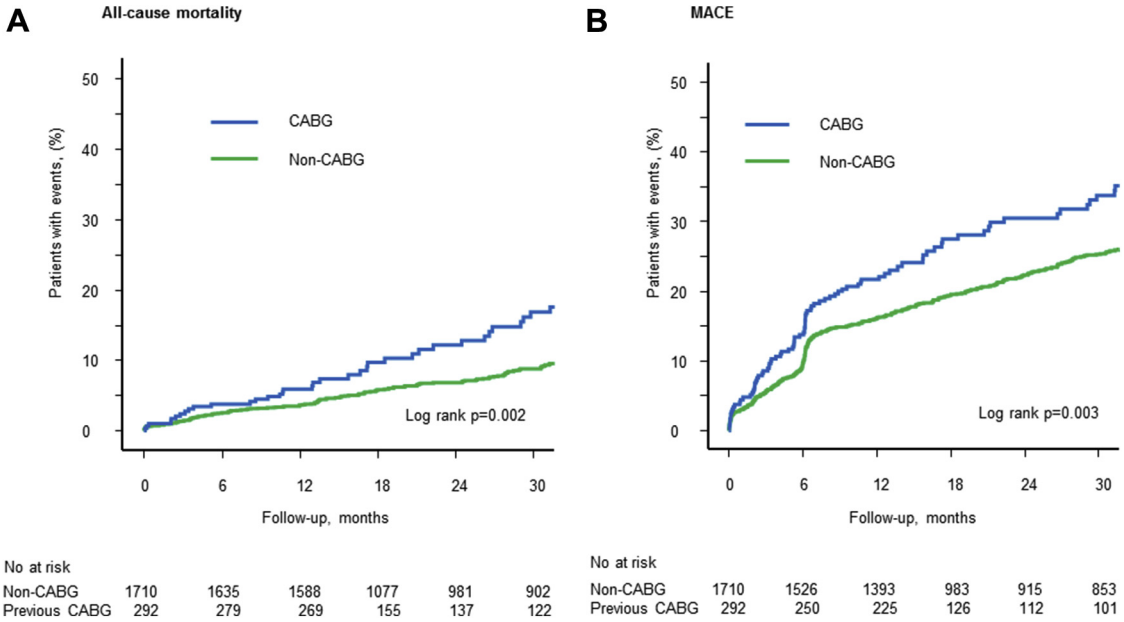

Figure 1. *(A)* Kaplan-Meier estimates for all-cause mortality events in patients with *(green line)* and without *(blue line)* previous CABG. *(B)* Kaplan-Meier estimates for MACE in patients with *(green line)* and without *(blue line)* previous CABG.

increased procedural complexity. As differences in procedural success rates between patients with and without previous CABG remained significant after adjustment for baseline differences, other aspects not taken into account and distinct to patients with previous surgical revascularization may come into play. Indeed, a distinct CTO morphology not only with regard to calcifications but also in terms of negative remodeling and extent of the necrotic core, along with proximal and distal tapering, has previously been reported in angiographic and histopathological comparisons of plaque characteristics between patients with and without previous CABG[2,3,17] and is assumed to affect procedural success rates. In addition, tortuous or distorted vessels and accelerated atherosclerosis progression observed in grafted arteries may further affect procedural outcomes.[3,18]

Patients with previous surgical revascularization had a 20% increased observed MACE rate after PCI for CTO, which was largely driven by a higher all-cause mortality. However, as outcomes were similar after adjustment for baseline clinical and angiographic differences, comorbidities and coronary artery disease severity may account for the increased observed adverse event rates in patients with previous surgical revascularization, and differences in outcomes do not seem to depend primarily on the CABG status per se. These results are supported by data from previous registries failing to identify previous CABG as independent predictor of mortality,[4,5] although trends toward increased in-hospital adverse events in patients with previous CABG were suggested in some studies.[2,3]

Some limitations of the study need to be noted. First, this analysis has the limitations inherent to a single-center retrospective observational study including patients undergoing PCI for CTO from 2005 to 2013. Although no independent end point adjudication committee was available,

Table 4
Clinical outcomes in patients with and without previous coronary artery bypass grafting according to procedural success

	Procedural success	Procedural failure	Crude		Adjusted*	
			Hazard ratio (95% confidence interval)	P-value	Hazard ratio (95% confidence interval)	P-value
Previous CABG						
n	218	74				
All-cause death	24 (11%)	24 (32%)	0.34 (0.20-0.61)	<0.001	0.43 (0.24-0.77)	0.005
All-cause death and/or myocardial infarction	31 (14%)	27 (37%)	0.40 (0.24-0.68)	0.001	0.53 (0.31-0.90)	0.02
Target vessel revascularization	41 (19%)	17 (23%)	0.68 (0.38-1.19)	0.18	0.65 (0.37-1.16)	0.15
Target lesion revascularization	34 (16%)	14 (19%)	0.71 (0.37-1.32)	0.27	0.71 (0.38-1.34)	0.29
MACE	68 (31%)	37 (50%)	0.55 (0.36-0.83)	0.003	0.59 (0.39-0.89)	0.01
Non-CABG						
n	1444	266				
All-cause death	139 (10%)	54 (20%)	0.48 (0.35-0.66)	<0.001	0.63 (0.45-0.86)	0.004
All-cause death and/or myocardial infarction	187 (13%)	57 (21%)	0.62 (0.46-0.83)	0.002	0.79 (0.58-1.06)	0.12
Target vessel revascularization	258 (18%)	54 (20%)	0.80 (0.60-1.08)	0.14	0.83 (0.61-1.11)	0.22
Target lesion revascularization	202 (14%)	52 (19.5%)	0.65 (0.48-0.88)	0.007	0.68 (0.49-0.92)	0.01
MACE	408 (28%)	104 (39%)	0.68 (0.54-0.61)	<0.001	0.77 (0.62-0.96)	0.02

* Adjusted for baseline variables showing differences ($p < 0.05$) between patients with and without procedural success including age, diabetes, hypertension, estimated glomerular filtration rate, previous myocardial infarction, left ventricular ejection fraction <40%, multivessel disease, and moderate/severe calcifications.

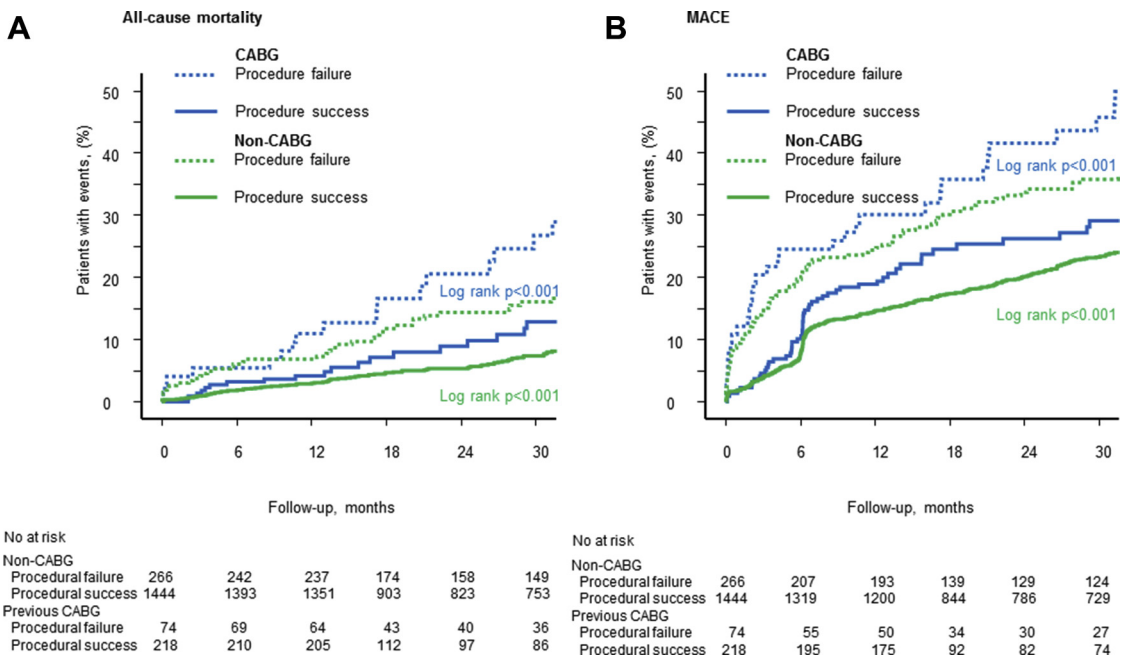

Figure 2. *(A)* Kaplan-Meier estimates for all-cause mortality events in patients with and without previous CABG stratified for procedural success. *Green dotted line* indicates procedural failure in CABG, *green line* indicates procedural success in CABG, *blue dotted line* indicates procedural failure in non-CABG, and *blue line* indicates procedural success in non-CABG. *(B)* Kaplan-Meier estimates for MACE in patients with and without previous CABG stratified for procedural success. *Green dotted line* indicates procedural failure in CABG, *green line* indicates procedural success in CABG, *blue dotted line* indicates procedural failure in non-CABG, *blue line* indicates procedural success in non-CABG.

coronary lesion assessment based on operator estimates and comprehensive clinical, angiographic, and procedural data, along with complete long-term follow-up, in a large patient cohort undergoing PCI for CTO are presented. However, data on angina severity at follow-up were not available. Second, we cannot exclude that additional confounding factors not incorporated in the multivariate models may have influenced the outcome measures. Third, the use of a different definition of nonfatal myocardial infarction may affect the results. Fourth, specific aspects of CTO revascularization such as ischemic burden and complete revascularization were not taken into account in this study.

In this registry, successful PCI for CTO was linked to improved survival in both patients with and without previous CABG, associations which remained significant after adjustment for baseline differences, and interaction analyses suggested a similar revascularization benefit in both patient groups. These findings extend our knowledge about mortality benefits associated with successful CTO revascularization to the high-risk patient subgroup with previous CABG[5,19–22] and underline the importance to offer PCI for CTO to this complex lesion and patient subgroup, particularly as procedural success rates in patients with and without previous CABG may further converge in near future.

Disclosures

The authors have no conflicts of interest to disclose.

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