Readmission Rate After Coronary Artery Bypass Grafting Versus Percutaneous Coronary Intervention for Unprotected Left Main Coronary Artery Narrowing

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Many studies have reported comparable risk of hard end points between percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) for unprotected left main coronary artery (ULMCA) stenosis. However, there are limited data regarding the morbidity associated with ULMCA revascularization. This study sought to compare the cause and risk of readmissions after PCI and CABG for ULMCA stenosis. We evaluated the unadjusted and adjusted risk of readmissions in 1,352 patients (783 PCI treated and 569 CABG treated) who were consecutively enrolled in a multicenter registry of patients with ULMCA stenosis, named the Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease trial. Overall, 206 PCI-treated patients (26.3%) experienced at least 1 readmission after the index procedure during 48.7 ± 16.0 months of follow-up compared with 84 CABG-treated patients (14.8%, p <0.001). The most frequent causes of readmission were repeat revascularization after PCI (41%) and noncardiac readmissions after CABG (48%). Through repeated events analysis, PCI was associated with more frequent readmissions than CABG (hazard ratio 2.037, 95% confidence interval 1.542 to 2.692, p <0.001), being an independent predictor of readmission (hazard ratio 1.820, 95% confidence interval 1.420 to 2.331, p <0.001). Except for the acute period, defined as the first 3 months, when there was no significant difference in readmission rate, a higher readmission rate after PCI was consistently observed over the remainder of the follow-up period. In conclusion, PCI was shown to be associated with a higher risk of readmission than CABG in treating ULMCA disease. This higher risk was attributable to more frequent revascularization in the PCI group. © 2014 Elsevier Inc. All rights reserved. **(Am J Cardiol 2014;113:1639−1646)**

A substudy from a large randomized trial and many registry reports have shown that percutaneous coronary intervention (PCI) may be an acceptable substitute for coronary artery bypass grafting (CABG) in some patients with unprotected left main coronary artery (ULMCA) stenosis.[1−11] However, these studies were conducted with regard to the risks of "hard" end points such as cardiovascular death, myocardial infarction, or their composite. The causes and incidence of all morbidity requiring readmission after CABG or PCI have not been evaluated thoroughly, and information on potential differences in the risk of morbidity may help patients who are facing a treatment choice to decide on a revascularization strategy. The Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease (PRECOMBAT) trial randomized patients suitable for revascularization by either PCI or CABG for the treatment of ULMCA stenosis.[12] To investigate the morbidity of patients with ULMCA stenosis treated with PCI and CABG, we compared readmissions of the patients of the PRECOMBAT trial, in both the randomized group and the prespecified registry.

Methods

The study design and methods of the PRECOMBAT trial have been described previously in detail.[12] In brief, the PRECOMBAT study (n = 600) was a randomized trial with a parallel registry (n = 854) including nonrandomized patients during the same study period. To analyze the outcomes of all patients with ULMCA stenosis with minimal exclusion, this study included both the randomized

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This study was supported by the CardioVascular Research Foundation, Seoul, Korea; Cordis, Johnson and Johnson; and grant A120711 from the Korean Ministry of Health and Welfare, Korea.

See page 1644 for disclosure information.

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0002-9149/14/$ - see front matter
http://dx.doi.org/10.1016/j.amjcard.2014.02.013

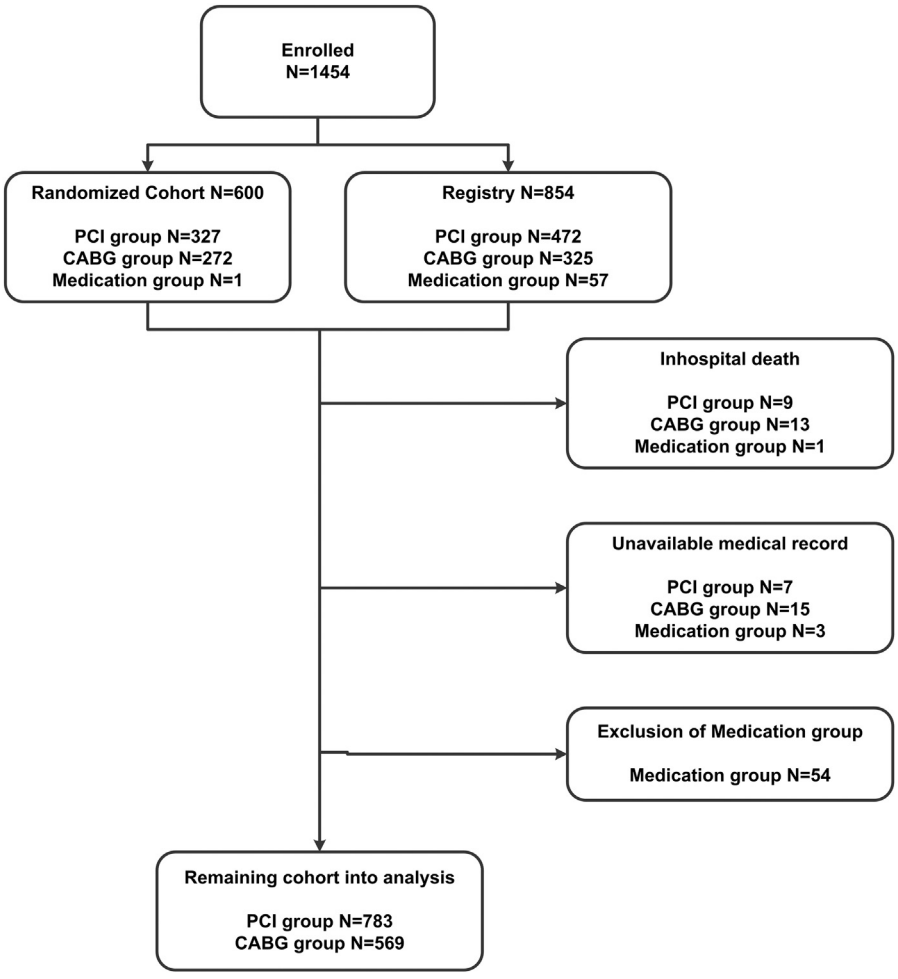

Figure 1. Patient disposition.

group and the patients from the nonrandomized registry of the PRECOMBAT study. Within this population, 799 and 597 patients received PCI and CABG, respectively. The remaining 58 patients, who were treated with medication alone, were not included in this study. Therefore, after excluding 23 cases of in-hospital death (PCI: 9 patients and CABG: 13 patients), 1,352 patients (783 PCI treated and 569 CABG treated) whose medical records were available at the time of event adjudication were included in the comparison of readmission rates (Figure 1). The institutional review board approved the protocol, and all patients provided written informed consent.

The procedures for PCI and CABG have been described previously.[10,13] During PCI, sirolimus-eluting stents were the default drug-eluting stents used. Use of intravascular ultrasound, adjunctive devices, or glycoprotein IIb/IIIa inhibitors was at the operator's discretion. All patients who underwent PCI took aspirin plus clopidogrel (loading dose 300 mg) or ticlopidine (loading dose 500 mg) before or during the procedure. After PCI, all patients were prescribed 100 mg/day aspirin indefinitely and 75 mg/day clopidogrel or 250 mg/day ticlopidine for at least 1 year. During CABG, the internal thoracic artery was preferred for bypass of the left anterior descending artery. Medications after CABG were given according to the policy of the institution or the preference of the surgeon. During the index procedure or repeated revascularization, the decision of which lesion to be revascularized was at the operator's discretion.

After PCI, all patients were asked to revisit for follow-up angiography 8 to 10 months after the procedure, or earlier if experiencing symptoms of angina. However, routine follow-up angiography was not performed for patients who underwent CABG. As a result, the patients treated with PCI (510 patients [65.1%]) underwent follow-up angiography more frequently than those with CABG (98 patients [17.2%], $p < 0.001$). All other follow-up assessments were performed at 1, 6, 9, and 12 months and yearly thereafter at a clinic visit or through a telephone interview.

The primary end point of this study was readmission for any reason after discharge. Readmission related to routine angiographic surveillance of patients without ischemic symptom after PCI was not considered an event. All readmissions to hospitals participating in this trial were recorded during the follow-up period. The date of readmission and the primary reason for it were collected, with the cause of readmission judged by the Clinical Events Committee,

Table 1
Baseline characteristics of the patients

Variable	PCI (n = 783)	CABG (n = 569)	p Value
Age (yrs)	62.2 ± 10.6	63.6 ± 9.1	0.014
Men	589 (75.2)	438 (77.0)	0.46
Body mass index (kg/m^2)	24.5 ± 2.8	24.7 ± 3.0	0.33
Medically treated diabetes			
Any	269 (34.4)	215 (37.8)	0.19
Requiring insulin	23 (2.9)	41 (7.2)	<0.001
Hypertension*	437 (55.8)	315 (55.4)	0.87
Hyperlipidemia†	318 (40.6)	195 (34.3)	0.018
Current smoker	212 (27.1)	164 (28.8)	0.48
Previous PCI	149 (19.0)	73 (12.8)	0.002
Previous myocardial infarction	40 (5.1)	51 (9.0)	0.005
Previous heart failure	11 (1.4)	4 (0.7)	0.22
Chronic renal failure	12 (1.5)	2 (0.4)	0.034
Peripheral vascular disease	51 (6.5)	19 (3.3)	0.009
Chronic obstructive pulmonary disease	19 (2.4)	23 (4.0)	0.091
Clinical presentation			<0.001
Stable angina pectoris or no symptoms	422 (53.9)	230 (40.4)	
Unstable angina pectoris	304 (38.8)	311 (54.7)	
Unstable angina pectoris and recent acute myocardial infarction	57 (7.3)	28 (4.9)	
Ejection fraction (%)	60.7 ± 9.0	57.9 ± 10.7	<0.001
EuroSCORE value	2.9 ± 2.0	3.2 ± 2.0	0.001
Electrocardiographic findings			0.081
Sinus rhythm	755 (96.4)	560 (98.4)	
Atrial fibrillation	20 (2.6)	7 (1.2)	
Others	8 (1.0)	2 (0.4)	
Angiographic characteristics			
Narrowed coronary arteries			<0.001
Left main only	110 (14.0)	24 (4.2)	
Left main plus 1-vessel disease	185 (23.6)	55 (9.7)	
Left main plus 2-vessel disease	275 (35.1)	120 (21.1)	
Left main plus 3-vessel disease	213 (27.2)	370 (65.0)	
Involved location			0.78
Ostial and shaft involvement	263 (33.6)	187 (32.9)	
Distal bifurcation involvement	520 (66.4)	382 (67.1)	
Right coronary artery disease	302 (38.6)	422 (74.2)	<0.001
Restenotic lesion	6 (0.8)	3 (0.5)	0.74
Chronic total occlusion	5 (0.6)	5 (0.9)	0.75
SYNTAX score‡	23.0 ± 9.9	32.4 ± 12.5	<0.001

Data are presented as mean ± SD or n (%).

* Defined by one of the following: a history of hypertension diagnosed and treated with medication, diet, and/or exercise or blood pressure >140 mm Hg at systole or 90 mm Hg at diastole on at least 2 occasions.

† Defined by one of the following: a history of hyperlipidemia diagnosed and treated by a physician, total cholesterol >200 mg/dl, low-density lipoprotein cholesterol >130 mg/dl, high-density lipoprotein cholesterol <30 mg/dl, or triglyceride >150 mg/dl.

‡ The SYNTAX score is an angiographic model to characterize the coronary vasculature with respect to the number of lesions and their functional significance, location, and complexity, with higher scores indicative of more complex disease.

which was made up of interventional and noninterventional cardiologists who were not participating in the study. The causes were grouped based on mechanism into 7 categories, including revascularization, nonrevascularization cardiac cause, procedure related, bleeding, cerebrovascular accident, noncardiac event, and unknown cause.

A descriptive analysis was performed by presenting data as mean ± SD or number (proportion). Continuous variables were compared with the *t* test or Wilcoxon rank sum test, and categorical variables were compared with chi-square statistics or Fisher's exact test, as appropriate. When calculating the readmission rate, to adjust for the significantly different follow-up period between the 2 groups, an arbitrary unit, readmissions per patient−3 months, was derived. This was obtained by modifying the formula for person-years:

$$\text{Person} - \text{years} = \sum_{k=1}^{n} (D_k)$$

where D is the number of years each subject has been observed. To compare the interval readmission rate, follow-up dates were censored at the fixed time of 5 years because of the small number of patients with longer follow-up. In analyzing readmissions, a marginal

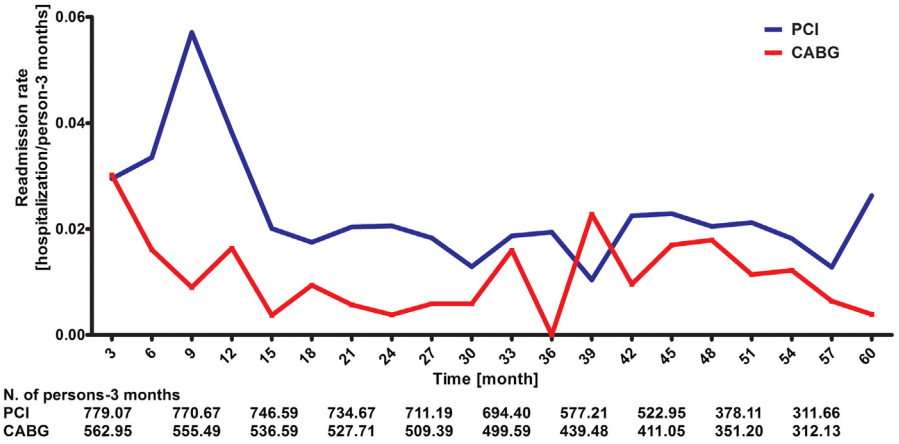

Figure 2. Readmission rate over time from the index procedure.

Table 2
Patients with repeated readmissions

No. of Readmissions	PCI (n = 783)	CABG (n = 569)
At least 1	206 (100)	84 (100)
1	140 (68.0)	64 (76.2)
2	48 (23.3)	15 (17.9)
3	12 (5.8)	3 (3.6)
4	4 (1.9)	1 (1.2)
5	1 (0.5)	—
6	1 (0.5)	—
7	—	1 (1.2)

Data are presented as n (%).

approach proposed by Wei, Lin, and Weissfeld was used to analyze recurrent events (the Wei-Lin-Weissfeld method),[14] because conventional time-to-first-event analysis excludes subsequent events after the first event.[15,16] The subgroup analysis according to the Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) trial score was performed for 1,266 patients (93.6%), using the Wei-Lin-Weissfeld method, for whom independent angiographic analysis was available.[17,18] To compare rates of revascularization-related readmission between the 2 groups, Cox proportional regression model was used. All statistical analyses were performed using SAS, version 9.3 (SAS Institute, Cary, North Carolina). A 2-tailed p value of <0.05 was considered statistically significant.

Results

Table 1 lists the baseline characteristics of the patients in each group. Patients treated with CABG were older, were more likely to have diabetes requiring insulin, had a history of myocardial infarction, and a higher EuroSCORE than those treated with PCI. Conversely, hyperlipidemia, a history of undergoing PCI, chronic renal failure, and peripheral vascular disease were more prevalent in the PCI group than in the CABG group. Hospital stay was longer in the CABG group than PCI group (2.9 ± 4.2 vs 9.5 ± 20.7, $p <0.001$). Median follow-up periods after discharge from the index procedure hospitalization were 49 months (interquartile range 37 to 60) and 58 months (interquartile range 39 to 61) for the PCI and CABG groups, respectively. During the follow-up period, 413 readmissions occurred, 299 in the PCI group and 114 in the CABG group.

Readmission rate in readmissions per person−3 months by time after discharge from index hospitalization is shown in Figure 2. Overall, readmission rates were 0.024 readmissions per person−3 months in the PCI group and 0.011 readmissions per person−3 months in the CABG group ($p <0.001$ by chi-square test). Across the whole follow-up period, except for the first 3 months during which there was no difference in the readmission rate ($p = 0.934$ by log-rank test), a higher rate of readmission after PCI was consistently observed, with the difference being more evident between 3 months and 27 months than during the rest of the follow-up period.

The proportions of patients who experienced different numbers of readmissions are presented in Table 2. Figure 3 shows cumulative readmission rates over time; each ordered outcome (first, second, and third readmission episodes) is assigned to a separate time-dependent stratum. Data are presented up to the third readmission, because the number of patients with further episodes was too small for analysis. Patients treated with PCI had a significantly higher cumulative rate of first readmission (hazard ratio [HR] 2.09, 95% confidence interval [CI] 1.62 to 2.69, $p <0.001$) than those treated with CABG. However, the differences were not significant for the second (HR 1.12, 95% CI 0.66 to 1.90, $p = 0.68$) and third readmissions (HR 1.31, 95% CI 0.45 to 3.77, $p = 0.62$). The effect of PCI on overall readmission risk was also statistically significant (HR 2.04, 95% CI 1.54 to 2.69, $p <0.001$). Moreover, PCI (HR 1.82, 95% CI 1.42 to 2.33, $p <0.001$) and the presence of chronic renal failure (HR 2.26, 95% CI 1.06 to 4.83, $p = 0.035$) were shown to be independently associated with the occurrence of readmission after multivariate analysis.

When patients were classified into SYNTAX score terciles, with scores of each group being ≤ 22 (517 patients [41%]), 23 to 32 (361 patients [28.5%]), and ≥ 33 (388 patients [30.6%]), PCI was associated with a higher risk of

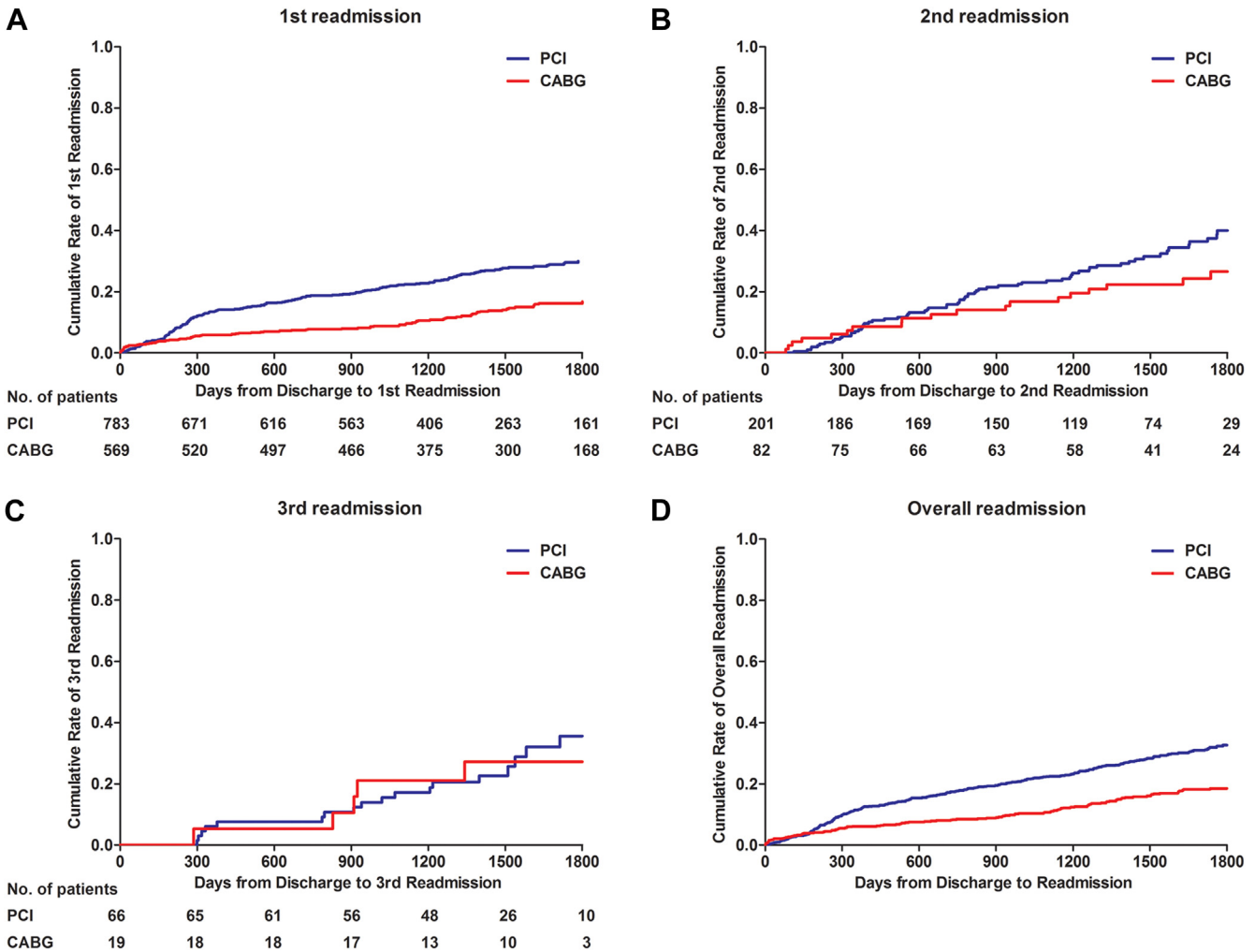

Figure 3. Kaplan-Meier estimates of repeated readmissions. Kaplan-Meier estimates of the rate of first *(A)*, second *(B)*, third *(C)*, and overall readmission *(D)*, with follow-up time starting at the time of discharge from the index hospitalization.

readmission in the low (HR 1.55, 95% CI 1.01 to 2.37, p = 0.044), intermediate (HR 2.31, 95% CI 1.34 to 3.94, p = 0.002), and high (HR 1.88, 95% CI 1.20 to 2.95, p = 0.006) tercile groups.

Table 3 lists the proportion of different causes of readmission according to index revascularization procedures. In the PCI and CABG groups, revascularization and noncardiac cause were the most common cause of readmissions, respectively. An adjusted risk of revascularization-related readmission was higher after PCI than CABG (28.9% vs 3.1%; HR 6.20, 95% CI 3.49 to 10.99, p <0.001). When it was separated according to the locations, PCI had a higher risk for revascularization of left main (8.3% vs 1.0%; HR 9.04, 95% CI 3.50 to 23.37, p <0.001) and non−left main stenosis (20.5% vs 2.1%; HR 4.87, 95% CI 2.37 to 9.99, p <0.001). Clinically driven revascularization defined as revascularization for patients with ischemic symptom or sign was 24.1% after PCI and 2.7% after CABG (HR 5.10, 95% CI 2.72 to 9.58, p <0.001). Furthermore, PCI was also related with a higher risk of non—revascularization-related readmission (HR 1.592, 95% CI 1.239 to 2.045, p <0.001).

The causes of readmission during specific time intervals after discharge are presented in Figure 4. For the first 3 months, revascularization (8.7% in the PCI vs 0% in the CABG groups) contributed little to patients' readmissions in both groups. Noticeably, readmissions caused by adverse events related to the index procedure were causative of 20% of all readmissions for the first 3 months in the CABG group but did not arise in the PCI group. The difference in the proportion of revascularization as the cause of readmission between the 2 groups was most obvious in the 3- to 12-month period (34.9%) compared with 0 to 3 months (8.7%), 12 to 27 months (7.9%), and 27 to 60 months (18%).

Discussion

In this long-term prospective observational study of consecutive patients with ULMCA disease, we found that

Table 3
Causes of readmission

Variable	PCI (n = 299)	CABG (n = 114)	p Value
Revascularization	121 (40.5)	15 (13.2)	<0.001*
Nonrevascularization cardiac	62 (20.7)	34 (29.8)	
Procedure related	0	4 (3.5)	
Bleeding	13 (4.3)	3 (2.6)	
Cerebrovascular accident	6 (2)	2 (1.8)	
Noncardiac	96 (32.1)	55 (48.2)	0.13†
Malignancy	12 (12.5)	13 (23.6)	
Gastrointestinal	11 (11.5)	5 (9.1)	
Related to bone and soft tissue	11 (11.5)	3 (5.5)	
Pulmonary	12 (12.5)	1 (1.8)	
Peripheral vascular disease	6 (6.3)	4 (7.3)	
General weakness	3 (3.1)	6 (10.9)	
Neurologic	5 (5.2)	3 (5.5)	
Related to diabetes mellitus	3 (3.1)	5 (9.1)	
Infection	4 (4.2)	2 (3.6)	
Ophthalmologic	5 (5.2)	1 (1.8)	
Related to urogenital organ	3 (3.1)	1 (1.8)	
Other	21 (21.9)	11 (20.0)	
Unknown	1 (0.3)	1 (0.9)	

Data are presented as n (%).

* A value derived from a comparison of the proportions of the 7 major causes of readmissions between the PCI and CABG groups.

† A value derived from a comparison of the proportions of noncardiac causes of readmissions between the PCI and CABG groups.

the long-term risk of readmission was significantly higher in patients initially treated with PCI than in those who underwent CABG as the index procedure. Although the readmission rate of the PCI group was higher during the entire follow-up period, the difference was most conspicuous from 3 to 27 months, with the first 9 months of this period showing the greatest difference. The causes of readmission other than repeated revascularization were not different between the 2 groups, confirming that the difference in the readmission rates between PCI and CABG was primarily driven by a higher rate of repeated revascularization after PCI.

Many registries and randomized studies have shown that PCI and CABG for patients with ULMCA disease have similar mortality, nonfatal myocardial infarction, or composite outcomes. Nevertheless, a higher tendency for repeated revascularization was seen for PCI group compared with CABG group, and it is not clear whether this similar risk of hard end points and higher risk of repeated revascularization between the 2 procedures can be translated into similar morbidity requiring readmission. In addition, conventional time-to-event studies considered the first event as a target end point in a hierarchical order and neglected the repeated episode of events in the final analysis. Therefore, on this background, the present study compared the rates and causes of readmissions between the 2 groups of the PRECOMBAT registry, one of the largest cohorts of patients with ULMCA disease.

Analysis of readmissions after revascularization therapy for coronary artery disease has been conducted to evaluate the quality of care provided during index hospitalization and to find ways to reduce readmission.[19–23] All these studies used 30-day readmissions, showing a readmission rate of around 10% regardless of revascularization procedure. However, the PRECOMBAT registry showed a relatively low 30-day readmission rate, which was 0.9% in the PCI group and 2.1% in the CABG group, compared with previous studies. First, patients enrolled in the PRECOMBAT study may have been healthier compared with those enrolled in the other studies.[19–23] Second, inclusion of the relatively healthier randomized group might have resulted in a low 30-day readmission rate.[24] Thirdly, the procedural factors, such as a high utilization rate of intravascular ultrasound, single-stent technique, or off-pump surgery, may be related with low readmission rate. Finally, our study only involved an Asian population, which might have different propensities for ischemic or thrombotic complications from patients of other ethnic origin.[25,26]

In this study, PCI was related to more frequent readmission compared with CABG, which was shown across all 3 SYNTAX terciles. Nevertheless, as the previous randomization studies had shown, the gap in readmission rate between the 2 groups was more prominent in the high SYNTAX tercile having multivessel disease compared with the low SYNTAX tercile because of the higher revascularization rate of the former.[27,28] The trend of readmission rate over time indicated that across the whole follow-up period except for the first 3 months, a higher rate of readmission after PCI was consistently observed over 5 years after discharge. In particular, the difference in readmission rate between the 2 groups was most pronounced at 9 months, driven by a greater incidence of revascularization after PCI. This pattern was not different in the randomized and nonrandomized patients. In contrast, the risk of non-revascularization-related readmission was smaller than that of revascularization-related readmission after PCI. Therefore, these findings confirmed that a higher revascularization rate may still be the unique Achilles of PCI compared with CABG surgery in the treatment of ULMCA stenosis.[1–11] On the contrary, CABG carries a greater degree of invasiveness as its inherent weakness, which was shown as a greater proportion of procedure-related readmission after this procedure for the first 3 months in the present study.

Our study had several limitations. The first-generation sirolimus-eluting stent, which was the default stent in this study, may be associated with higher risk of readmission after PCI. In addition, despite exclusion of readmissions for a routine angiographic surveillance out of the analysis, the higher rate of angiographic follow-up after PCI might have inflated the revascularization-related readmission rate. Global utilization of fractional flow reserve may prevent unnecessary revascularization of nonischemic restenosis and subsequently decrease the readmission rate in patients receiving PCI.

Disclosures

The authors have no conflicts of interest to disclose.

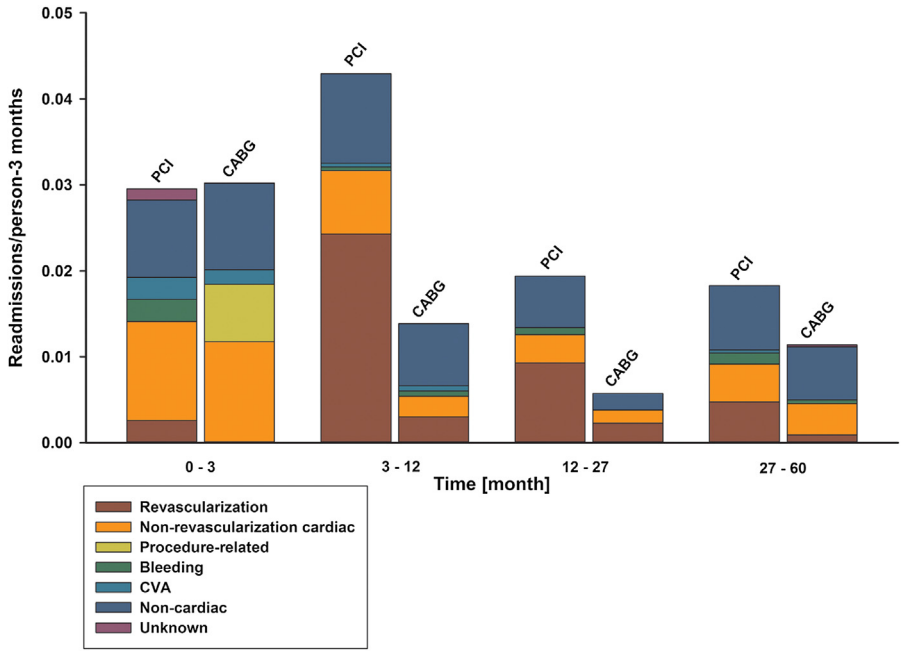

Figure 4. Causes of readmission during specific time intervals. CVA = cerebrovascular accident.

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