

# Determinants and Long-Term Outcomes of Percutaneous Coronary Interventions vs. Surgery for Multivessel Disease According to Clinical Presentation

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**Background:** The long-term outcome of percutaneous coronary intervention (PCI) vs. coronary artery bypass graft (CABG), particularly for patients with non-ST-elevation acute coronary syndrome (NSTEMI-ACS), remains controversial.

**Methods and Results:** We retrospectively analyzed 2,827 patients (stable coronary artery disease [SCAD], n=1,601; NSTEMI-ACS, n=1,226) who underwent either PCI (n=1,732) or CABG (n=1,095). The 8-year composite of cardiac death and myocardial infarction (MI) was compared between PCI and CABG before and after propensity matching. For patients with NSTEMI-ACS, PCI was performed more frequently for those with higher Thrombolysis in Myocardial Infarction risk score and 3-vessel disease, and PCI led to significantly higher 8-year composite of cardiac death and MI than CABG (14.1% vs. 5.9%, hazard ratio [HR]=2.22, 95% confidence interval [CI]=1.37–3.58, P=0.001). There was a significant interaction between clinical presentation and revascularization strategy (P-interaction=0.001). However, after matching, the benefit of CABG vs. PCI was attenuated in patients with NSTEMI-ACS, whereas it was pronounced in those with SCAD. Interactions between clinical presentation and revascularization strategy were not observed (P-interaction=0.574).

**Conclusions:** Although the determinants of PCI vs. CABG in real-world clinical practice differ according to the clinical presentation, a significant interaction between clinical presentation and revascularization strategy was not noted for long-term outcomes. The revascularization strategy for patients with NSTEMI-ACS can be based on the criteria applied to patients with SCAD.

**Key Words:** Coronary artery bypass graft; Percutaneous coronary intervention

The numbers of patients presenting with non-ST-elevation acute coronary syndrome (NSTEMI-ACS) are increasing and they have a poor prognosis because of multiple comorbidities.<sup>1</sup> Moreover, compared with patients with stable coronary artery disease (SCAD), there is a stronger impetus for revascularization with an early invasive approach in patients with NSTEMI-ACS, according to current guidelines.<sup>1,2</sup> Although the clinical decision between percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) can be affected by clinical presentation (SCAD vs. NSTEMI-ACS) in patients with multivessel or left main involvement, the choice of the optimal revascularization strategy with regard to clinical presentation remains controversial. Furthermore, there are no contemporary randomized clinical trials comparing PCI with CABG for patients with NSTEMI-ACS, although recent advances in PCI with drug-eluting stents have

reduced target-lesion failure, with improved outcomes, and PCI has been shown to provide an alternative treatment option to CABG for multivessel CAD.<sup>3–5</sup> Even 2 recent studies comparing PCI with CABG for NSTEMI-ACS patients showed inconsistent results over a relatively short-term follow-up.<sup>6,7</sup>

Thus, in the present study, we sought to examine (1) the clinical and angiographic determinants of PCI vs. CABG for multivessel disease according to clinical presentation in real-world clinical practice, and (2) the outcomes of PCI vs. CABG for patients with SCAD and those with NSTEMI-ACS.

## Methods

### Subjects

Between 2005 and 2011, a total of 2,827 patients who

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**Table 1. Baseline Characteristics of the Study Patients With Stable Coronary Artery Disease**

|                        | Before matching  |                 |         | After matching |                 |                        |
|------------------------|------------------|-----------------|---------|----------------|-----------------|------------------------|
|                        | PCI<br>(n=1,041) | CABG<br>(n=560) | P value | PCI<br>(n=544) | CABG<br>(n=544) | Std mean<br>difference |
| Age, years             | 65±9             | 64±9            | 0.205   | 65±10          | 65±9            | 0.065                  |
| Men                    | 713 (69)         | 411 (73)        | 0.041   | 382 (70)       | 397 (73)        | 0.105                  |
| BMI, kg/m <sup>2</sup> | 24.8±3.1         | 24.4±2.8        | 0.014   | 24.5±3.2       | 24.5±2.8        | 0.125                  |
| Hypertension           | 721 (69)         | 404 (72)        | 0.229   | 383 (70)       | 391 (72)        | -0.062                 |
| Diabetes               | 402 (39)         | 234 (42)        | 0.217   | 213 (39)       | 224 (41)        | -0.065                 |
| Dyslipidemia           | 680 (65)         | 336 (60)        | 0.035   | 335 (62)       | 330 (61)        | 0.112                  |
| Current smoker         | 192 (18)         | 101 (18)        | 0.840   | 98 (18)        | 99 (18)         | 0.011                  |
| Previous MI            | 102 (10)         | 71 (13)         | 0.077   | 60 (11)        | 64 (12)         | -0.097                 |
| Previous PCI           | 230 (22)         | 104 (19)        | 0.098   | 111 (20)       | 102 (19)        | 0.085                  |
| CKD                    | 43 (4)           | 42 (8)          | 0.004   | 35 (6)         | 38 (7)          | -0.169                 |
| LVEF, %                | 60±11            | 58±13           | 0.001   | 59±13          | 59±12           | 0.193                  |
| 3-vessel disease       | 700 (67)         | 434 (78)        | <0.001  | 401 (74)       | 426 (78)        | -0.059                 |
| Left main              | 242 (23)         | 162 (29)        | 0.013   | 139 (26)       | 156 (29)        | -0.134                 |
| Proximal LAD           | 760 (73)         | 412 (74)        | 0.808   | 411 (76)       | 405 (74)        | -0.013                 |
| LAD, mid and distal    | 828 (80)         | 420 (75)        | 0.037   | 421 (77)       | 413 (76)        | 0.112                  |
| LCX                    | 842 (81)         | 483 (86)        | 0.007   | 464 (85)       | 473 (87)        | -0.136                 |
| RCA                    | 853 (82)         | 476 (85)        | 0.120   | 466 (86)       | 466 (86)        | -0.079                 |

Data are presented as mean±SD or n (%). BMI, body mass index; CABG, coronary artery bypass graft; CKD, chronic kidney disease; LAD, left anterior descending; LCX, left circumflex artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery.

underwent myocardial revascularization with PCI or CABG because of multivessel disease were initially identified from the participating centers in the Korean Multicenter Angioplasty Team (KOMATE) registry.<sup>8,9</sup> Briefly, the KOMATE registry was designed for enrolling patients who underwent PCI at several centers in Korea and was based on real-world clinical practice. Demographic, clinical, procedural information and clinical outcome data were collected retrospectively using case report forms. The Institutional Review Board at the Severance Hospital of the Yonsei University Health System approved this study and waived the requirements for informed consent for this retrospective analysis.

Patients who had the following angiographic findings were defined as having multivessel disease requiring revascularization: patients with ≥2 lesions with >70% diameter stenosis in native coronary arteries with involvement of both the right and left coronary arteries (left anterior descending or circumflex) on quantitative coronary angiography, or those with coexistence of both protected and unprotected left main disease (>50% diameter stenosis). NSTEMI-ACS was defined as unstable angina and non-ST-segment elevation myocardial infarction (MI).<sup>2</sup> In the present study, patients with cardiogenic shock or ST-elevation MI were excluded. Patients whose revascularization was delayed for 2 weeks after diagnostic angiography were also excluded. Among the 2,827 patients, a total of 1,732 patients who underwent PCI, and their data regarding demographic, procedural and clinical outcomes, were identified from the KOMATE registry database. The other 1,095 patients underwent CABG, and their data were collected from medical record reviews.

### Follow-up and Study Endpoints

Clinical assessments were recorded in the hospital after revascularization by either PCI or CABG, and at 1 month,

6 months, and 1, 2, 4, and 8 years after discharge. Follow-up assessments were performed during clinic visits. All-cause death, cardiac death, MI, any revascularization, and stroke were assessed as the clinical outcomes. Also, a composite of cardiac death and MI was assessed as a hard clinical outcome. Clinical events were defined according to the Academic Research Consortium and an expert consensus document that defined the Third Universal Definition for Myocardial Infarction.<sup>10,11</sup> All deaths were considered cardiac related unless an unequivocal non-cardiac cause could be established.<sup>11</sup> After discharge, MI was defined according to the following parameters: presence of clinical symptoms, ECG changes, or abnormal imaging findings indicative of MI, and an increase in the creatine kinase myocardial band fraction above the upper normal limit or an increase in troponin-T/troponin-I above the 99th percentile of the upper normal limit. Any revascularization was defined as repeat PCI or CABG of both target lesion and non-target lesion because of either (1) angiographic diameter stenosis ≥50% according to quantitative coronary angiographic analysis with documentation of a positive stress test, or (2) angiographic diameter stenosis ≥70% irrespective of the stress test results. Stroke, as detected by the occurrence of a new neurological deficit, was confirmed using a neurological examination and imaging studies.

### Statistical Analysis

Categorical variables are reported as numbers and percentages, and compared by  $\chi^2$  test or Fisher exact test. Continuous variables are reported as mean±standard deviation and compared with Student's t-test. To reduce treatment selection bias and potential confounding factors, and to adjust for significant differences in the characteristics of patients or lesions, propensity score-matching was performed. Propensity scores were estimated using a nonparametric multiple logistic regression model for treatment

**Table 2. Baseline Characteristics of the Study Patients With Non-ST-Elevation Acute Coronary Syndrome**

|                        | Before matching |                 |         | After matching |                 |                        |
|------------------------|-----------------|-----------------|---------|----------------|-----------------|------------------------|
|                        | PCI<br>(n=691)  | CABG<br>(n=535) | P value | PCI<br>(n=287) | CABG<br>(n=287) | Std mean<br>difference |
| Age, years             | 64.8±10.8       | 64.9±9.2        | 0.883   | 64.8±11.1      | 64.9±8.9        | −0.003                 |
| Men                    | 462 (67)        | 377 (71)        | 0.178   | 199 (69)       | 206 (72)        | 0.052                  |
| BMI, kg/m <sup>2</sup> | 24.6±3.2        | 24.3±3.0        | 0.094   | 24.6±3.2       | 24.5±3.0        | 0.019                  |
| Hypertension           | 477 (69)        | 358 (67)        | 0.431   | 203 (71)       | 201 (70)        | 0.015                  |
| Diabetes               | 258 (37)        | 241 (45)        | 0.006   | 127 (44)       | 121 (42)        | 0.043                  |
| Dyslipidemia           | 411 (60)        | 300 (56)        | 0.231   | 174 (61)       | 172 (60)        | 0.014                  |
| Current smoker         | 203 (29)        | 140 (26)        | 0.214   | 76 (27)        | 82 (29)         | −0.046                 |
| Previous MI            | 72 (10)         | 72 (14)         | 0.101   | 47 (16)        | 43 (15)         | 0.046                  |
| Previous PCI           | 165 (24)        | 114 (21)        | 0.287   | 79 (28)        | 78 (27)         | 0.008                  |
| CKD                    | 54 (8)          | 47 (9)          | 0.540   | 25 (9)         | 22 (8)          | 0.039                  |
| Clinical presentation  |                 |                 | 0.933   |                |                 | 0.079                  |
| Unstable angina        | 422 (61)        | 328 (61)        |         | 181 (63)       | 192 (67)        |                        |
| NSTEMI                 | 269 (39)        | 207 (39)        |         | 106 (37)       | 95 (33)         |                        |
| TIMI risk score        | 3.82±1.12       | 3.06±1.13       | <0.001  | 3.65±1.10      | 3.40±1.10       | 0.218                  |
| LVEF, %                | 56.4±12.6       | 52.5±14.1       | <0.001  | 55.2±13.4      | 55.2±13.3       | −0.001                 |
| 3-vessel disease       | 488 (71)        | 352 (66)        | 0.071   | 186 (65)       | 210 (73)        | −0.082                 |
| Left main              | 144 (21)        | 163 (31)        | <0.001  | 68 (24)        | 71 (25)         | −0.026                 |
| Proximal LAD           | 502 (73)        | 277 (52)        | <0.001  | 192 (67)       | 197 (69)        | 0.039                  |
| LAD, mid and distal    | 542 (78)        | 262 (49)        | <0.001  | 199 (69)       | 202 (70)        | −0.025                 |
| LCX                    | 569 (82)        | 338 (63)        | <0.001  | 228 (79)       | 234 (82)        | −0.055                 |
| RCA                    | 597 (86)        | 348 (65)        | <0.001  | 238 (83)       | 238 (83)        | 0.000                  |

Data are presented as mean±SD or n (%). NSTEMI, non-ST-elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction. Other abbreviations as in Table 1.

with PCI vs. CABG for patients with SCAD and for those with NSTEMI-ACS. For SCAD, all the clinical and angiographic variables shown in **Table 1** were entered to calculate the propensity score. Similarly, for NSTEMI-ACS, all the variables shown in **Table 2** were entered. New propensity scores were incorporated to assess the efficacy of CABG. For the development of propensity score-matched pairs without replacement (1:1 match), a local optimal algorithm with the caliper method was used. The Hansen and Bowers overall balance test was performed (for SCAD patients,  $\chi^2=10.95$ ,  $P=0.859$ ; for NSTEMI-ACS patients,  $\chi^2=16.15$ ,  $P=0.648$ ). A matching caliper of 0.2 standard deviations of the logit of the estimated propensity score was enforced to ensure that matches of poor fit were excluded. The matching procedure was performed by using the R package, including Matchit, Rtools, and CEM. After propensity score-matching, covariates were compared with the paired t-test for continuous variables and the McNemar test for categorical variables.

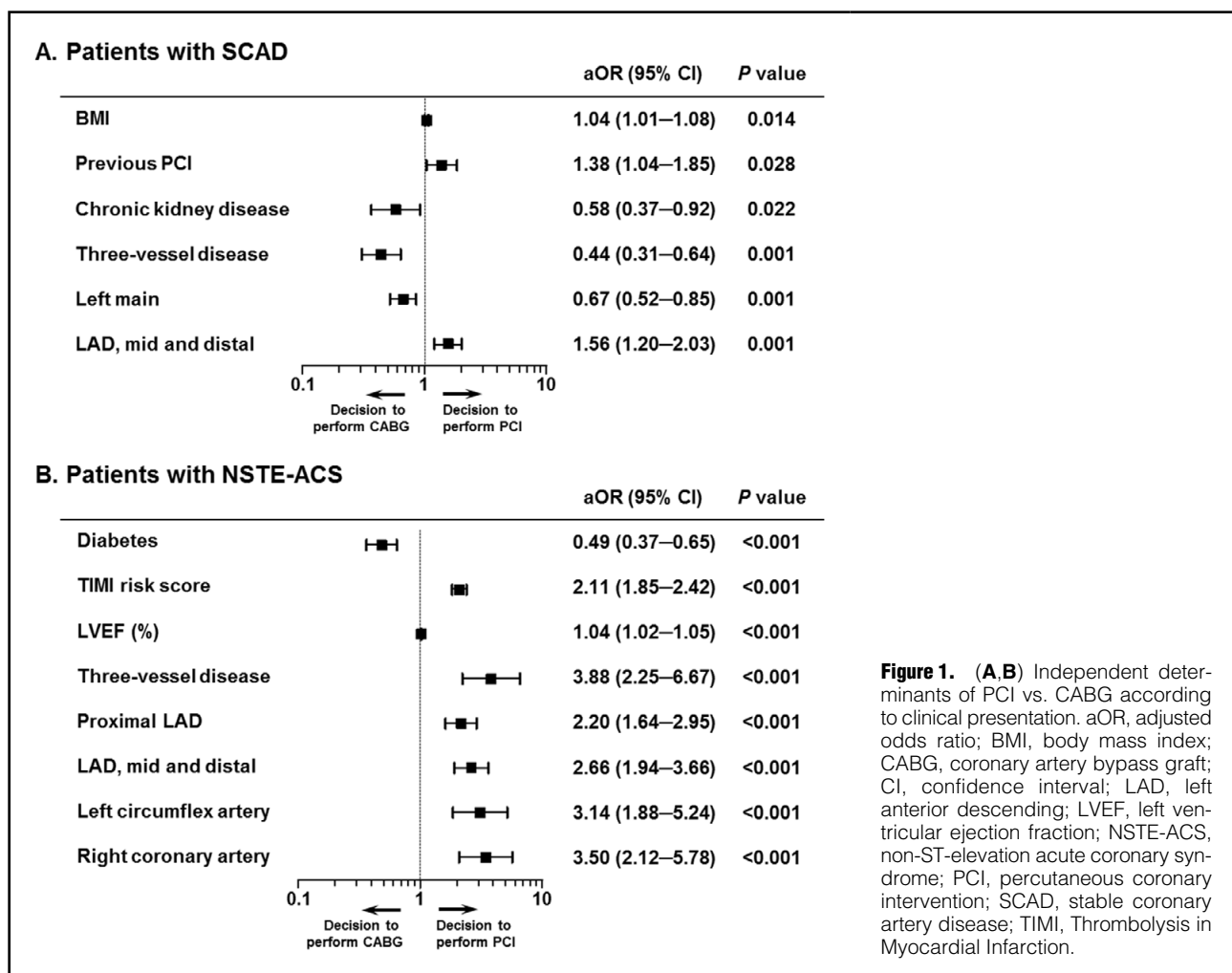
The cumulative incidences of clinical outcomes were calculated with Kaplan-Meier estimates and compared by log-rank test. Statistical analyses were performed with IBM SPSS, version 19.0 (IBM Corporation, New York, NY, USA). All tests were 2-sided, and  $P<0.05$  was considered statistically significant.

## Results

The baseline characteristics of patients undergoing PCI vs. those undergoing CABG are presented for those with SCAD in **Table 1** and for NSTEMI-ACS in **Table 2**. Among patients with NSTEMI-ACS ( $n=1,226$ ), 476 (39%) had acute MI and 691 (56.4%) underwent PCI. For CABG-treated

patients, timing from diagnostic angiography to CABG is presented in **Figure S1**. CABG was performed in  $4.2\pm3.3$  days after diagnostic angiography for patients with SCAD, and in  $3.8\pm3.5$  days for those with NSTEMI-ACS. For PCI-treated patients, timing from diagnostic angiography to PCI was significantly shorter than for CABG-treated patients for both patients with SCAD ( $0.1\pm0.1$  days,  $P<0.001$ ) and those with NSTEMI-ACS ( $0.1\pm0.1$  days,  $P<0.001$ ). The European System for Cardiac Operative Risk Evaluation (EuroSCORE) II was not different between groups for patients with SCAD (PCI vs. CABG;  $1.0\pm0.8\%$  vs.  $1.1\pm1.1\%$ ,  $P=0.093$ ), or for those with NSTEMI-ACS ( $1.2\pm1.0\%$  vs.  $1.3\pm1.1\%$ ,  $P=0.077$ ). After propensity score-matching for the clinical and angiographic findings, 544 matched pairs for patients with SCAD were created. For patients with NSTEMI-ACS, 287 matched pairs were created because of the relatively much greater differences between the PCI- and CABG-treated patients. All variables were well balanced for patients with SCAD and those with NSTEMI-ACS (**Figure S2**).

The independent determinants of PCI vs. CABG were different for patients with SCAD and those with NSTEMI-ACS (**Figure 1**). For patients with SCAD, PCI treatment was performed less frequently for those with more severe CAD such as 3-vessel disease (adjusted odds ratio [aOR]=0.44, 95% confidence interval [CI]=0.31–0.64,  $P=0.001$ ). By contrast, for patients with NSTEMI-ACS, PCI treatment was performed more frequently for those with the same severity of CAD (aOR=3.88, 95% CI=2.25–6.67,  $P<0.001$ ). The other independent determinants of PCI vs. CABG for SCAD were greater body mass index, previous PCI, absence of chronic kidney disease, no involvement of a left main lesion, and involvement of a mid to distal left



anterior descending artery lesion. For patients with NSTEMI-ACS, the independent predictors of PCI vs. CABG were absence of diabetes, higher Thrombolysis in Myocardial Infarction (TIMI) risk score, greater left ventricular ejection fraction, and involvement of a left anterior descending artery, left circumflex artery, and right coronary artery lesion (**Figure 1**).

With a median follow-up of 6.8 years (interquartile range, 5.1–8.3 years), the clinical outcomes at 4 and 8 years are summarized in **Table 3** for patients with SCAD, and in **Table 4** for those with NSTEMI-ACS. For patients with SCAD, those treated with PCI experienced a significantly higher composite endpoint of cardiac death and MI vs. those treated with CABG at 4 years (2.8% vs. 0.7%, hazard ratio [HR]=4.54, 95% CI=1.38–14.90,  $P=0.006$ ), mainly driven by higher rates of MI (2.1% vs. 0.5%, HR=4.88, 95% CI=1.14–20.80,  $P=0.018$ ). However, at 8 years, these differences had decreased without statistical significance (5.5% vs. 3.6%, HR=1.67, 95% CI=0.90–3.10,  $P=0.100$ ) (**Figure 2A**). After propensity score-matching, these findings were again more pronounced in patients with SCAD, with a borderline statistical significance (**Figure 2B**). Patients treated with PCI had significantly higher rate of repeat revascularizations compared with those treated with CABG (30.4% vs. 12.7%, HR=2.76, 95% CI=2.03–3.77,  $P<0.001$ ) (**Figure 2G**). As for the revascularization strategy for repeat

revascularization, 11.8% (29/246) among the PCI group were treated with CABG, and 6.3% (3/48) among the CABG group were treated with CABG.

For patients with NSTEMI-ACS, the rate of the composite of cardiac death and MI at 8 years was significantly higher in PCI-treated patients than in CABG-treated patients (14.1% vs. 5.9%, HR=2.22, 95% CI=1.37–3.58,  $P=0.001$ ) (**Figure 3A**), mainly driven by a higher rate of MI in PCI-treated patients (12.3% vs. 3.9%, HR=3.45, 95% CI=1.85–6.42,  $P<0.001$ ) (**Figure 3E**). However, after matching the clinical and angiographic findings (287 matched pairs), these differences were attenuated for composite of cardiac death and MI (9.7% vs. 6.8%, HR=1.46, 95% CI=0.75–2.86,  $P=0.264$ ) (**Figure 3B**) and MI (7.2% vs. 3.7%, HR=2.13, 95% CI=0.88–5.19,  $P=0.088$ ) (**Figure 3F**). Similar to the patients with SCAD, patients treated with PCI had significantly higher rate of repeat revascularizations compared with those treated with CABG; 11.5% (20/173) among the PCI group were treated with CABG, and 7.3% (4/55) among the CABG group were treated with CABG.

Although there was a significant interaction between clinical presentation (SCAD vs. NSTEMI-ACS) and revascularization strategy (PCI vs. CABG) for an 8-year composite of cardiac death and MI before matching ( $P$ -interaction=0.001), significant interactions were not observed after matching ( $P$ -interaction=0.574).

**Table 3. Clinical Outcomes for the Study Patients With Stable Coronary Artery Disease**

|                                   | Before matching  |                 |                      |         | After matching |                 |                      |         |
|-----------------------------------|------------------|-----------------|----------------------|---------|----------------|-----------------|----------------------|---------|
|                                   | PCI<br>(n=1,041) | CABG<br>(n=560) | HR<br>(95% CI)       | P value | PCI<br>(n=544) | CABG<br>(n=544) | HR<br>(95% CI)       | P value |
| <b>4-year outcome</b>             |                  |                 |                      |         |                |                 |                      |         |
| Composite of cardiac death and MI | 29 (2.8%)        | 3 (0.7%)        | 4.54<br>(1.38–14.90) | 0.006   | 18 (3.4%)      | 3 (0.7%)        | 5.30<br>(1.56–17.99) | 0.003   |
| Death                             | 26 (2.5%)        | 15 (3.2%)       | 0.80<br>(0.42–1.51)  | 0.491   | 19 (3.6%)      | 15 (3.2%)       | 1.11<br>(0.56–2.18)  | 0.770   |
| Cardiac death                     | 12 (1.2%)        | 1 (0.2%)        | 5.68<br>(0.74–43.71) | 0.059   | 10 (1.9%)      | 1 (0.2%)        | 8.91<br>(1.14–69.65) | 0.012   |
| MI                                | 21 (2.1%)        | 2 (0.5%)        | 4.88<br>(1.14–20.80) | 0.018   | 10 (1.9%)      | 2 (0.5%)        | 4.33<br>(0.95–19.78) | 0.039   |
| Any revascularization             | 151 (14.9%)      | 19 (3.9%)       | 3.90<br>(2.42–6.29)  | <0.001  | 84 (16.1%)     | 19 (4.0%)       | 4.08<br>(2.48–6.71)  | <0.001  |
| Stroke                            | 27 (2.7%)        | 7 (1.5%)        | 1.78<br>(0.77–4.07)  | 0.172   | 18 (3.5%)      | 7 (1.6%)        | 2.25<br>(0.94–5.39)  | 0.061   |
| <b>8-year outcome</b>             |                  |                 |                      |         |                |                 |                      |         |
| Composite of cardiac death and MI | 45 (5.5%)        | 13 (3.6%)       | 1.67<br>(0.90–3.10)  | 0.100   | 27 (6.4%)      | 13 (3.7%)       | 1.89<br>(0.98–3.67)  | 0.055   |
| Death                             | 45 (5.5%)        | 36 (9.3%)       | 0.59<br>(0.38–0.92)  | 0.018   | 28 (6.6%)      | 35 (9.2%)       | 0.72<br>(0.44–1.18)  | 0.189   |
| Cardiac death                     | 14 (1.4%)        | 8 (2.3%)        | 0.81<br>(0.34–1.94)  | 0.641   | 11 (2.3%)      | 8 (2.2%)        | 1.21<br>(0.49–3.02)  | 0.678   |
| MI                                | 36 (4.7%)        | 7 (1.8%)        | 2.49<br>(1.11–5.61)  | 0.022   | 19 (5.0%)      | 7 (1.9%)        | 2.48<br>(1.04–5.91)  | 0.034   |
| Any revascularization             | 246 (30.4%)      | 48 (12.7%)      | 2.76<br>(2.03–3.77)  | <0.001  | 127 (30.8%)    | 46 (12.6%)      | 2.82<br>(2.01–3.95)  | <0.001  |
| Stroke                            | 44 (5.6%)        | 18 (4.9%)       | 1.18<br>(0.68–2.04)  | 0.559   | 26 (5.9%)      | 17 (4.7%)       | 1.39<br>(0.75–2.57)  | 0.288   |

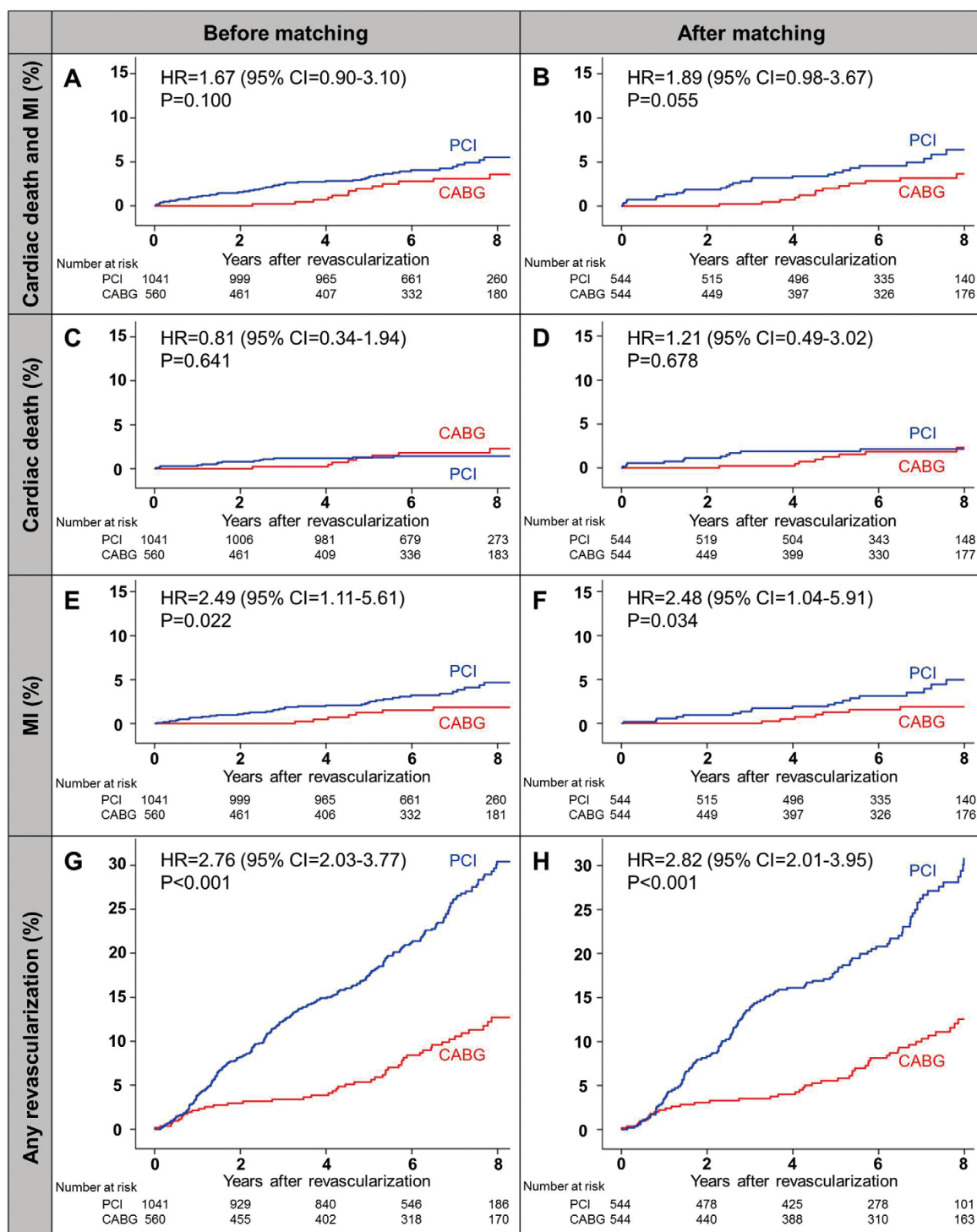
Data are presented as n (% of the cumulative rates according to Kaplan-Meier event rates). P values are from the log-rank test. CI, confidence interval; HR, hazard ratio. Other abbreviations as in Table 1.

**Table 4. Clinical Outcomes for the Study Patients With Non-ST-Elevation Acute Coronary Syndrome**

|                                   | Before matching |                 |                     |         | After matching |                 |                     |         |
|-----------------------------------|-----------------|-----------------|---------------------|---------|----------------|-----------------|---------------------|---------|
|                                   | PCI<br>(n=691)  | CABG<br>(n=535) | HR<br>(95% CI)      | P value | PCI<br>(n=287) | CABG<br>(n=287) | HR<br>(95% CI)      | P value |
| <b>4-year outcome</b>             |                 |                 |                     |         |                |                 |                     |         |
| Composite of cardiac death and MI | 45 (6.8%)       | 15 (3.4%)       | 1.97<br>(1.10–3.54) | 0.020   | 15 (5.4%)      | 8 (3.2%)        | 1.70<br>(0.72–4.01) | 0.221   |
| Death                             | 47 (6.9%)       | 22 (4.9%)       | 1.38<br>(0.83–2.29) | 0.210   | 20 (7.1%)      | 10 (4.0%)       | 1.77<br>(0.83–3.79) | 0.134   |
| Cardiac death                     | 16 (2.4%)       | 11 (2.4%)       | 0.94<br>(0.44–2.02) | 0.871   | 5 (1.8%)       | 6 (2.4%)        | 0.74<br>(0.23–2.44) | 0.624   |
| MI                                | 35 (5.3%)       | 7 (1.7%)        | 3.30<br>(1.46–7.43) | 0.002   | 11 (4.0%)      | 4 (1.7%)        | 2.49<br>(0.79–7.83) | 0.106   |
| Any revascularization             | 124 (18.6%)     | 34 (12.5%)      | 2.48<br>(1.70–3.62) | <0.001  | 51 (18.6%)     | 19 (7.6%)       | 2.46<br>(1.45–4.17) | 0.001   |
| Stroke                            | 10 (1.5%)       | 11 (2.8%)       | 0.56<br>(0.24–1.33) | 0.185   | 5 (1.8%)       | 8 (3.6%)        | 0.53<br>(0.17–1.63) | 0.263   |
| <b>8-year outcome</b>             |                 |                 |                     |         |                |                 |                     |         |
| Composite of cardiac death and MI | 71 (14.1%)      | 22 (5.9%)       | 2.22<br>(1.37–3.58) | 0.001   | 22 (9.7%)      | 14 (6.8%)       | 1.46<br>(0.75–2.86) | 0.264   |
| Death                             | 70 (12.7%)      | 39 (11.1%)      | 1.19<br>(0.81–1.76) | 0.381   | 28 (12.5%)     | 22 (11.2%)      | 1.19<br>(0.68–2.09) | 0.540   |
| Cardiac death                     | 21 (3.7%)       | 16 (4.6%)       | 0.87<br>(0.45–1.66) | 0.665   | 7 (3.0%)       | 10 (5.1%)       | 0.64<br>(0.24–1.69) | 0.367   |
| MI                                | 59 (12.3%)      | 12 (3.9%)       | 3.45<br>(1.85–6.42) | <0.001  | 16 (7.2%)      | 7 (3.7%)        | 2.13<br>(0.88–5.19) | 0.088   |
| Any revascularization             | 173 (30.5%)     | 55 (14.5%)      | 2.24<br>(1.65–3.03) | <0.001  | 75 (35.9%)     | 33 (16.5%)      | 2.26<br>(1.50–3.41) | <0.001  |
| Stroke                            | 20 (3.9%)       | 22 (6.8%)       | 0.59<br>(0.32–1.08) | 0.080   | 10 (4.7%)      | 14 (7.4%)       | 0.64<br>(0.29–1.45) | 0.281   |

Data are presented as n (% of the cumulative rates according to Kaplan-Meier event rates). P values are from the log-rank test. Abbreviations as in Tables 1,3.



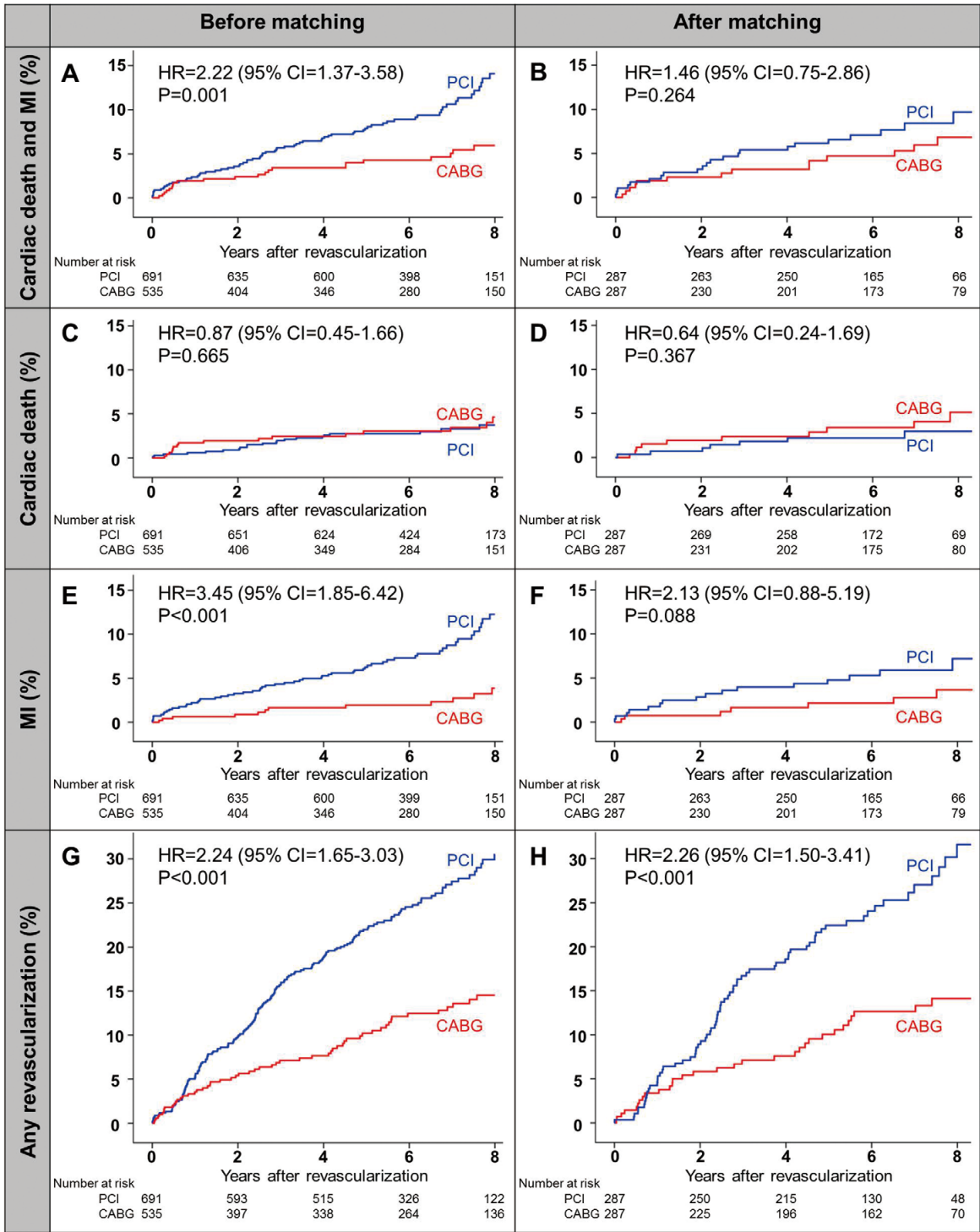


**Figure 2.** (A–H) Clinical outcomes for patients with stable coronary artery disease. HR, hazard ratio; MI, myocardial infarction. Other abbreviations as in Figure 1.

## Discussion

The principal findings of the present study were as follows. (1) The determinants of PCI vs. CABG for multivessel CAD were different between patients with SCAD and those

with NSTEMI-ACS. For patients with SCAD, PCI treatment was performed less often for those with 3-vessel disease or left main lesion involvement. For patients with NSTEMI-ACS, PCI treatment was performed more frequently for those with higher TIMI risk score and greater incidence of



**Figure 3.** (A–H) Clinical outcomes for patients with non-ST-elevation acute coronary syndrome. Abbreviations as in Figures 1,2.

3-vessel disease. (2) For patients with NSTEMI-ACS, those treated with PCI had significantly higher rate of the composite of cardiac death and MI at 8 years than those treated with CABG, mainly driven by MI, although the benefit of CABG vs. PCI was attenuated after matching. By contrast, the benefit of CABG vs. PCI was pronounced

in patients with SCAD after matching. Notably, a significant interaction between clinical presentation and revascularization strategy was noted before matching, but not after matching.

Although the current guideline recommends that the choice of PCI or CABG for multivessel CAD needs to be

based on the clinical status as well as the severity and distribution of CAD, there are no randomized clinical trials comparing PCI with CABG, particularly for patients with NSTEMI-ACS. Although not randomized, 2 recent prospective studies reported conflicting results regarding the outcomes between PCI and CABG in patients with NSTEMI-ACS.<sup>6,7</sup> According to a posthoc analysis of the ACUTY (Acute Catheterization and Urgent Intervention Triage Strategy) trial of 5,627 patients with NSTEMI-ACS with multivessel CAD, a total of 4,412 (78%) underwent PCI while the remaining patients were treated surgically.<sup>6</sup> After propensity score-matching (528 matched pairs), there were no significant differences between PCI-treated patients and CABG-treated patients in all-cause death (5.7% vs. 4.4%,  $P=0.58$ ) and cardiac death (4.7% vs. 3.1%,  $P=0.26$ ) at 1 year. PCI-treated patients had higher rates of unplanned revascularization (12% vs. 0.2%,  $P<0.0001$ ) and tended to more frequently experience major adverse cardiac event (25.0% vs. 19.2%;  $P=0.053$ ) at 1 year. In another prospective registry study (from the Milestone Registry), 4,566 patients with NSTEMI-ACS and multivessel CAD, including left main disease, were analyzed.<sup>7</sup> A total of 3,033 patients were selected for stenting (10.3% received drug-eluting stents) and 1,533 for CABG. For the 929 well-matched pairs after propensity score-matching, the 3-year survival was higher in patients treated with PCI than in those treated with surgery (86% vs. 82%,  $HR=1.33$ ,  $P=0.01$ ). According to those studies, the 1- and 3-year outcomes were comparable between PCI and CABG for patients with NSTEMI-ACS. In the present study, a longer-term follow-up (8 years) was performed, and comparable outcomes were found between PCI and CABG after matching, although the composite of cardiac death and MI was significantly higher in PCI-treated patients than in CABG-treated patients before matching.

Furthermore, for patients with SCAD, CABG was more beneficial than PCI after matching. Although the benefit of CABG was attenuated, particularly for patients with NSTEMI-ACS, our finding of the superiority of CABG particularly for multivessel disease was consistent with previous studies. A recent meta-analysis of individual patient data from 3 randomized clinical trials included a total of 3,280 patients with multivessel disease or left main disease.<sup>12</sup> Among the patients, 1,282 (39%) presented with NSTEMI-ACS. The rate of the primary outcome, a composite of all-cause death, MI or stroke, was significantly lower with CABG than with PCI (13.0% vs. 16.0%;  $P=0.046$ ).<sup>12</sup> Our findings also support the current guideline recommendation of performing CABG for more severe complex CAD,<sup>3-5</sup> based on recent randomized trials.<sup>13-16</sup>

### Study Limitations

First, the patients were not randomized, although we matched PCI- and CABG-treated patients for SCAD and NSTEMI-ACS. Second, a detailed anatomic analysis of CAD (i.e., SYNTAX score) was not performed. Third, even though the patients were followed long-term, the number of patients was relatively small. Fourth, particularly for the patients with NSTEMI-ACS, the timing of revascularization from diagnostic angiography to revascularization might have affected early and long-term results. Although this interaction analysis for the timing of revascularization and the revascularization strategies was not performed in the present study, further studies evaluating the benefit of the faster PCI are required.

In conclusion, the determinants of PCI vs. CABG were different between patients with SCAD and those with NSTEMI-ACS in real-world clinical practice. For patients with NSTEMI-ACS, PCI treatment was performed more frequently for those with higher TIMI risk score and greater incidence of 3-vessel disease, which was related to worse outcomes at 8 years. However, after matching, the benefit of CABG vs. PCI was attenuated in patients with NSTEMI-ACS and there were no significant interactions between the revascularization strategies and clinical presentation for long-term outcomes. Thus, the revascularization strategy for patients with NSTEMI-ACS can be based on the criteria applied to patients with SCAD.

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### Disclosures

The authors have no conflicts of interest to disclose.

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### Supplementary Files

#### Supplementary File 1

**Figure S1.** Timing from diagnostic angiography to surgery for CABG-treated patients.

**Figure S2.** Love plots for absolute standardized difference for baseline covariate between PCI-treated patients and CABG-treated patients, before and after propensity score-matching.

Please find supplementary file(s);  
<http://dx.doi.org/10.1253/circj.CJ-17-1173>