

Single-Stage Compared With Multi-Stage PCI in Multivessel NSTEMI Patients



The SMILE Trial

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ABSTRACT

BACKGROUND A lack of clarity exists about the role of complete coronary revascularization in patients presenting with non-ST-segment elevation myocardial infarction.

OBJECTIVES The aim of our study was to compare long-term outcomes in terms of major adverse cardiovascular and cerebrovascular events of 2 different complete coronary revascularization strategies in patients with non-ST-segment elevation myocardial infarction and multivessel coronary artery disease: 1-stage percutaneous coronary intervention (1S-PCI) during the index procedure versus multistage percutaneous coronary intervention (MS-PCI) complete coronary revascularization during the index hospitalization.

METHODS In the SMILE (Impact of Different Treatment in Multivessel Non ST Elevation Myocardial Infarction Patients: One Stage Versus Multistaged Percutaneous Coronary Intervention) trial, 584 patients were randomly assigned in a 1:1 manner to 1S-PCI or MS-PCI. The primary study endpoint was the incidence of major adverse cardiovascular and cerebrovascular events, which were defined as cardiac death, death, reinfarction, rehospitalization for unstable angina, repeat coronary revascularization (target vessel revascularization), and stroke at 1 year.

RESULTS The occurrence of the primary endpoint was significantly lower in the 1-stage group (1S-PCI: n = 36 [13.63%] vs. MS-PCI: n = 61 [23.19%]; hazard ratio [HR]: 0.549 [95% confidence interval (CI): 0.363 to 0.828]; p = 0.004). The 1-year rate of target vessel revascularization was significantly higher in the MS-PCI group (1S-PCI: n = 22 [8.33%] vs. MS-PCI: n = 40 [15.20%]; HR: 0.522 [95% CI: 0.310 to 0.878]; p = 0.01; p log-rank = 0.013). When the analyses were limited to cardiac death (1S-PCI: n = 9 [3.41%] vs. MS-PCI: n = 14 [5.32%]; HR: 0.624 [95% CI: 0.270 to 1.441]; p = 0.27) and myocardial infarction (1S-PCI: n = 7 [2.65%] vs. MS-PCI: n = 10 [3.80%]; HR: 0.678 [95% CI: 0.156 to 2.657]; p = 0.46), no significant differences were observed between groups.

CONCLUSIONS In multivessel non-ST-segment elevation myocardial infarction patients, complete 1-stage coronary revascularization is superior to multistage PCI in terms of major adverse cardiovascular and cerebrovascular events. (Impact of Different Treatment in Multivessel Non ST Elevation Myocardial Infarction [NSTEMI] Patients: One Stage Versus Multistaged Percutaneous Coronary Intervention [PCI] [SMILE]: [NCT01478984](https://clinicaltrials.gov/ct2/show/study/NCT01478984)) (J Am Coll Cardiol 2016;67:264-72) © 2016 by the American College of Cardiology Foundation.

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Manuscript received July 5, 2015; revised manuscript received September 28, 2015, accepted October 20, 2015.

Percutaneous coronary intervention (PCI) is the treatment of choice in patients with acute coronary syndromes (ACS). A lack of clarity exists about the role of complete coronary revascularization by PCI in patients with non-ST-segment elevation myocardial infarction (NSTEMI) (1). American College of Cardiology/American Heart Association and European Society of Cardiology guidelines are unclear as to which coronary revascularization strategy to suggest in multivessel NSTEMI patients (2,3). In this setting, identification of the culprit lesion by angiography alone could be challenging. Moreover, as suggested by histopathological, intravascular ultrasound, and optical coherence tomography analysis, secondary plaque ruptures in patients with ACS are frequent (about 25%) (4-10). Therefore, as observed in clinical observational studies, routine PCI of nonculprit arteries in NSTEMI may be of benefit (11-17). In accordance with the superiority of complete revascularization in multivessel patients, not much data exist on the difference in clinical outcomes between 1-stage percutaneous coronary intervention (1S-PCI) and multistage percutaneous coronary intervention (MS-PCI) complete coronary revascularization. The aim of our study was to compare long-term outcomes in terms of major adverse cardiovascular and cerebrovascular events (MACCE) of 2 different complete coronary revascularization strategies in patients with NSTEMI and multivessel coronary artery disease: 1S-PCI during the index procedure versus MS-PCI complete coronary revascularization during the index hospitalization.

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METHODS

STUDY POPULATION. This is a 2-center, unblinded, randomized clinical trial (NCT01478984). From September 1, 2011, to August 31, 2013, all consecutive NSTEMI patients scheduled to undergo an early invasive revascularization strategy (PCI within 24 h) were recruited in 2 different centers. Five hundred and forty-two patients were randomly assigned in a 1:1 manner to 1S-PCI or MS-PCI (Figure 1). In MS-PCI, the second-stage procedure was performed between 3 and 7 days after the index procedure. The inclusion criteria were the following: age ≥ 18 years; diagnosis of NSTEMI according to current guidelines, presenting with multivessel disease (3); glomerular filtration rate >60 ml/min; planned early invasive strategy; and signed informed consent. Exclusion criteria were the following: cardiogenic shock; chronic total occlusion; previous coronary artery bypass graft surgery; SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) score >32 ; candidate for bypass surgery;

and severe valvular heart disease. The protocol was accepted by the institutional ethical boards and was performed in accordance with the Declaration of Helsinki. All patients provided written informed consent.

The institutional review board defined procedure success as the achievement of an angiographic residual stenosis $<30\%$ and a TIMI (Thrombolysis In Myocardial Infarction) flow grade 3 after PCI.

STUDY DESIGN. Eligible patients were randomly allocated to receive 1-stage or multistage treatment using block allocation (block size = 8). Treatment was assigned on the basis of a 1:1 ratio.

TREATMENT. Patients randomized to 1S-PCI were completely revascularized during the index procedure, whereas patients randomized to MS-PCI underwent a culprit-only revascularization during the index procedure, followed by a deferred complete coronary revascularization of nonculprit lesions within 3 to 7 days (4.76 ± 1.23 days) during the index hospitalization. In the MS-PCI, the identification of the culprit vessel was performed according to clinical and angiographic parameters. The use of anatomic (intravascular ultrasound or optical coherence tomography) or functional (fractional flow reserve) imaging modalities to assess the culprit lesion or the presence of significant coronary stenoses was left to the operator's discretion. Radial access was strongly suggested for performance of coronary angiography and PCI. All patients were treated according to good clinical practice and the standard of care (18). Dual antiplatelet therapy was administered according to current European Society of Cardiology guidelines (18).

CLINICAL FOLLOW-UP. Telephone-based interviews and office-based direct visits were performed at 1, 6, and 12 months, respectively, for endpoint adjudication.

ENDPOINTS. Primary study endpoints were defined as the incidence of MACCE defined as cardiac death, death, reinfarction, rehospitalization for unstable angina, repeat coronary revascularization (target vessel revascularization [TVR]), and stroke at 1 year. Periprocedural myocardial infarction was not considered a MACCE. Myocardial infarction was defined as symptoms of cardiac ischemia and a troponin level above the 99th percentile value. For patients with a recurrent myocardial infarction within 14 days after randomization, the definition required new electrocardiographic evidence of ST-segment elevation, or new onset of left bundle branch block, or ST-segment

ABBREVIATIONS AND ACRONYMS

1S-PCI = 1-stage percutaneous coronary intervention

ACS = acute coronary syndrome

CI = confidence interval

HR = hazard ratio

IQR = interquartile range

MACCE = major adverse cardiovascular and cerebrovascular event(s)

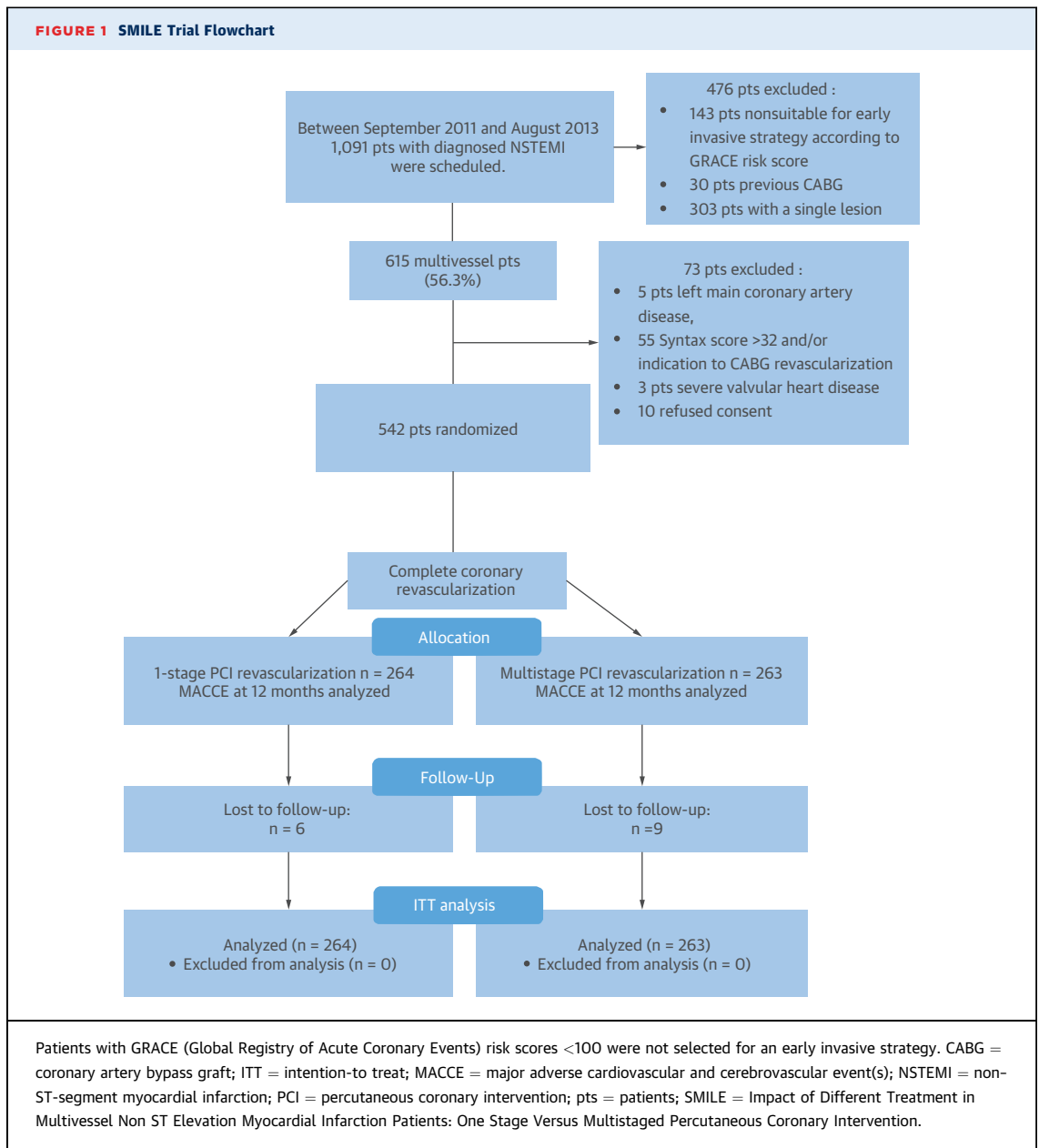
MS-PCI = multistage percutaneous coronary intervention

NSTEMI = non-ST-segment elevation myocardial infarction

PCI = percutaneous coronary intervention

TIMI = Thrombolysis In Myocardial Infarction

TVR = target vessel revascularization



depression, or transient elevation and/or T-wave changes and a rise of the troponin level above the 99th percentile, with a $\geq 20\%$ increase of the troponin value in the second sample and/or with angiographic evidence of ACS (19). Unstable angina was defined as angina despite medical therapy, supported by objective evidence of ischemia (electrocardiographic changes during a spontaneous episode of pain at rest). Stroke was defined as permanent neurological deficit adjudicated by a neurologist and confirmed by magnetic resonance imaging control. TVR was defined as any revascularization procedure, including bypass surgery, involving the initially treated artery.

Bleeding was defined according to the Academic Research Consortium definition (20).

STATISTICAL ANALYSIS. In order to assess the superiority of MS-PCI compared with 1S-PCI, we assumed the incidence of MACCE to be 9% in the MS-PCI group and 18% in the 1S-PCI group (21). On the basis of a 2-sided test size of 5% and a power of 80%, it was calculated that a minimum of 247 patients would need to be recruited in each group to detect a 9% difference in the incidence of MACCE at 1 year. All analyses were performed according to the intention-to-treat principle and per-protocol analysis (Online Appendix). All continuous variables were expressed as mean \pm SD

TABLE 1 Baseline Characteristics of the Studied Populations

	1-Stage (n = 264)	Multistage (n = 263)	p Value
Age, yrs	72 (61–78)	73 (62–78)	0.76
Sex			0.84
Male	207 (78.40)	209 (79.46)	
Female	57 (21.60)	54 (20.54)	
Medical history			
Diabetes NID	90 (34.09)	93 (35.36)	0.78
Diabetes ID	8 (3.03)	11 (4.18)	0.49
Hypertension	193 (73.10)	174 (66.15)	0.09
Hypercholesterolemia	152 (57.57)	143 (54.37)	0.48
Current smoker	120 (45.45)	107 (40.68)	0.29
Family history	139 (52.65)	136 (51.71)	0.86
Previous MI	71 (26.89)	62 (23.57)	0.68
Previous PCI	41 (15.53)	44 (16.73)	0.72
Serum creatinine, mg/dl	0.9 (0.8–1.2)	0.9 (0.8–1.2)	0.78
Troponin,* ng/ml	0.50 (0.22–1.42)	0.46 (0.16–1.36)	0.38
GRACE death-in-hospital score	176 (156–191)	175 (152–188)	0.76
CRUSADE score	22 (16–35)	23 (17–36)	0.47
Systolic blood pressure, mm Hg	130 (120–140)	125 (115–135)	0.46
Heart rate, beats/min	80 (67–90)	78 (65–88)	0.72
Left ventricular ejection fraction, %	50 (40–55)	50 (40–55)	0.87

Values are median (interquartile range) or n (%). *Cutoff <0.014 ng/ml in both centers.
 CRUSADE = Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines; GRACE = Global Registry of Acute Coronary Events; ID = insulin-dependent; MI = myocardial infarction; NID = noninsulin dependent; PCI = percutaneous coronary intervention.

and analyzed by the Student *t* test. Categorical variables with Gaussian distributions were analyzed by the chi-square or Fisher exact test, as appropriate. Baseline variables with non-Gaussian distributions were compared using the Mann-Whitney *U* test and summarized with medians and interquartile range (IQR). For the primary endpoint and its components, 95% confidence intervals (CIs) are reported. The event-free survival curve for MACCE was constructed using the Kaplan-Meier method, and statistical differences between curves were assessed by the log-rank test. The hazard ratio for treatment comparisons was estimated using Cox proportional hazard models. Statistical analysis was performed with SPSS (version 11.0, SPSS, Chicago, Illinois). Clinical study endpoints were adjudicated by an independent endpoints committee blinded to the randomization group.

RESULTS

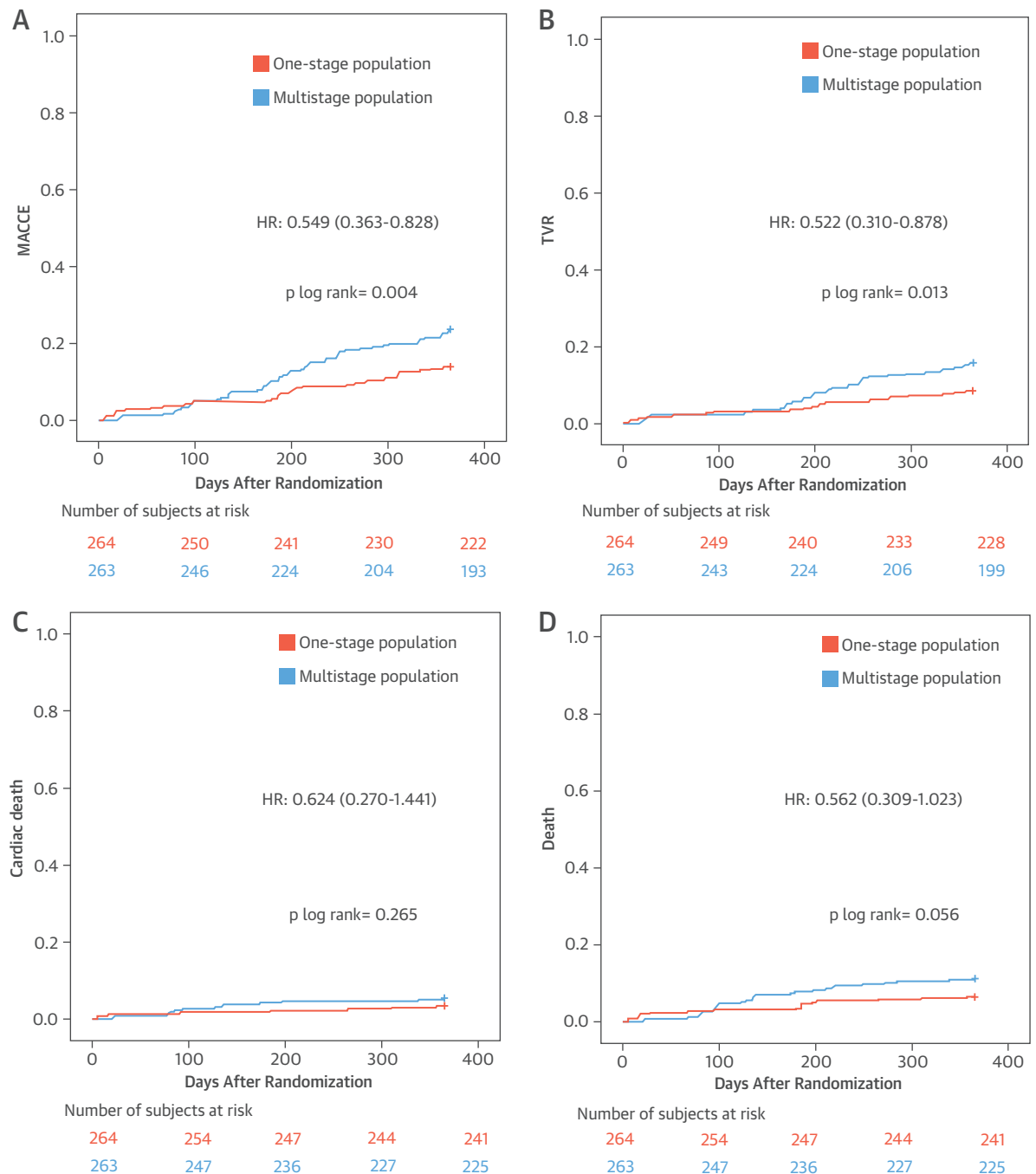
A total of 542 patients were enrolled in the study (15 patients were lost to follow-up), with 264 assigned to the 1-stage complete coronary revascularization

TABLE 2 Procedural Characteristics According to Randomized Allocation

	1-Stage (n = 264)	Multistage (n = 263)	p Value
Target vessels			0.25
Left anterior descending	234 (37.6)	237 (38.5)	
Right coronary artery	155 (24.9)	159 (25.8)	
Left circumflex	210 (33.7)	204 (33.2)	
Left main	24 (3.8)	15 (2.4)	
Treated vessels	2.36 ± 0.45	2.34 ± 0.8	0.71
Lesion type			0.52
A	87 (11.5)	76 (10.1)	
B1	204 (27.0)	192 (25.6)	
B2	192 (25.4)	193 (25.7)	
C	272 (36.0)	289 (38.5)	
Baseline angiographic analysis			
RVD, mm	2.90 (2.70–3.25)	2.90 (2.67–3.12)	0.46
Lesion length, mm	20.0 (13.5–32.5)	22.0 (14.0–34.0)	0.81
MLD, mm	0.32 (0.18–0.49)	0.27 (0.10–0.43)	0.43
Diameter stenosis, %	87.5 (79.0–95.0)	90.0 (85.0–97.0)	0.17
SYNTAX score	16 (14–18)	15 (14–18)	0.63
TIMI flow pre-procedure	3 (2–3)	3 (2–3)	0.78
FFR	65 (24.62)	71 (26.99)	0.55
OCT	31 (11.745)	42 (15.96)	0.17
IVUS	39 (14.77)	27 (10.26%)	0.16
Stents per patient	3 (2–4)	3 (2–4)	0.56
Stent type			0.55
Bare metal	137 (17.0)	141 (17.6)	
Biolimus	300 (37.3)	302 (37.7)	
Zotarolimus	45 (5.5)	46 (5.7)	
Everolimus	316 (39.3)	305 (38.1)	
POBA	6 (0.8)	7 (0.9)	
Minimum stent diameter, mm	3 (2.75–3.0)	3 (2.75–3.0)	0.56
Cumulative stent length, mm	24 (16–42)	24 (16–42)	0.46
Access site			0.55
Femoral artery	44 (16.7)	39 (14.8)	
Radial artery	220 (83.3)	224 (85.2)	
Serum creatinine,* mg/dl	1.0 (0.8–1.2)	1.1 (0.9–1.2)	0.46
Serum creatinine,† mg/dl	0.9 (0.8–1.2)	1.0 (0.7–1.1)	0.65

Values are median (interquartile range), mean ± SD, or n (%). *Measured 48 h after index procedure. †Measured before discharge.
 FFR = fractional flow reserve; IVUS = intravascular ultrasound; MLD = minimum luminal diameter; OCT = optical coherence tomography; POBA = plain old balloon angioplasty; RVD = reference vessel diameter; SYNTAX = Synergy Between PCI With Taxus and Cardiac Surgery; TIMI = Thrombolysis In Myocardial Infarction.

group and 263 to the multistage complete coronary revascularization group. The characteristics of the patients at baseline were similar in the 2 groups (Table 1), as were the use of drug-eluting stents, the treated vessels, the completeness of revascularization, and medical therapies at hospital discharge (Table 2, Online Table 1).

FIGURE 2 Kaplan-Meier Curves of MACCE, TVR, Cardiac Death, and Death

The Kaplan-Meier curves show the superiority of 1-stage complete coronary revascularization in terms of MACCE (**A**) and TVR (**B**). No significant differences were observed in terms of cardiac death (**C**) and death (**D**) between the 2 complete revascularization strategies. HR = hazard ratio; MACCE = major adverse cardiovascular and cerebrovascular event(s); TVR = target vessel revascularization.

According to Kaplan-Meier curves, the primary endpoint was significantly lower in the 1-stage group, ($p = 0.004$, log-rank test) (**Figure 2**). The 1-year primary outcome occurred significantly more frequently

in the MS-PCI group (1S-PCI: $n = 36$ [13.63%] vs. MS-PCI: $n = 61$ [23.19%]; hazard ratio [HR]: 0.549 [95% CI: 0.363 to 0.828]; $p = 0.004$) (**Table 3**; the events rate at 1 month and 6 months are reported in the

Online Tables 2 and 3). The 1-year rate of TVR was significantly higher in the MS-PCI group (1S-PCI: n = 22 [8.33%] vs. MS-PCI: n = 40 [15.20%]; HR: 0.522 [95% CI: 0.310 to 0.878]; p = 0.01; p log-rank = 0.013) (Online Table 4 reports the main characteristics of patients who experienced TVR). A higher rate of 6-month stress test was observed in the MS-PCI group during the follow-up period (1S-PCI: n = 71 [26.89%] vs. MS-PCI: n = 93 [35.36%]; p = 0.048). The analyses of the 2 main components of the primary outcome, cardiac death (1S-PCI: n = 9 [3.41%] vs. MS-PCI: n = 14 [5.32%]; HR: 0.624 [95% CI: 0.270 to 1.441]; p = 0.27) and myocardial infarction (1S-PCI: n = 7 [2.65%] vs. MS-PCI: n = 10 [3.80%]; HR: 0.678 [95% CI: 0.156 to 2.657]; p = 0.46), showed no significant differences between the groups (Figure 2, Table 3). The rate of overall death did not differ significantly between the 2 study groups, but it presented a trend in favor of 1S-PCI (Figure 2, Table 3). No significant differences were observed between the 2 groups in terms of stroke and rehospitalization for unstable angina (Table 3), or in types 2, 3, 4, and 5 bleeding. However, the 1-year rate of type 1 bleeding was significantly higher in the MS group (1S-PCI: n = 2 [0.76%] vs. MS-PCI: n = 9 [3.42%]; HR: 0.528 [95% CI: 0.332 to 0.897]; p = 0.03). No significant differences in definite stent thrombosis were observed (1S-PCI: n = 1 [0.38%] vs. MS-PCI: n = 1 [0.38%]; HR: 0.437 [95% CI: 0.032 to 5.456]; p = 1).

Radial access was performed with a rate of 84.2%, with no differences between the groups (Table 2). In the MS-PCI group, the rate of radial access during the second procedure decreased to 64.6% (p < 0.001) (Online Table 5) compared with 1S-PCI. Troponin T values during the hospitalization decreased rapidly in the 1S-PCI group, whereas a significant increase of troponin T was observed in the MS-PCI group (median: MS-PCI baseline: [0.46 (IQR: 0.16, 1.36)] vs. MS-PCI 12 h: [0.96 (IQR: 0.44, 1.76)]; p < 0.001). Creatine kinase-myocardial band showed similar kinetics to troponin (Online Table 6). No cases of contrast-induced nephropathy requiring dialysis were observed in the studied population (Online Table 7). The per-protocol analysis is reported in the Online Appendix.

DISCUSSION

The major findings of SMILE (Impact of Different Treatment in Multivessel Non ST Elevation Myocardial Infarction Patients: One Stage Versus Multistaged Percutaneous Coronary Intervention) trial are as follows: 1) 1-stage complete coronary revascularization is superior to multistage complete coronary

TABLE 3 1-Year Clinical Events According to Randomized Allocation

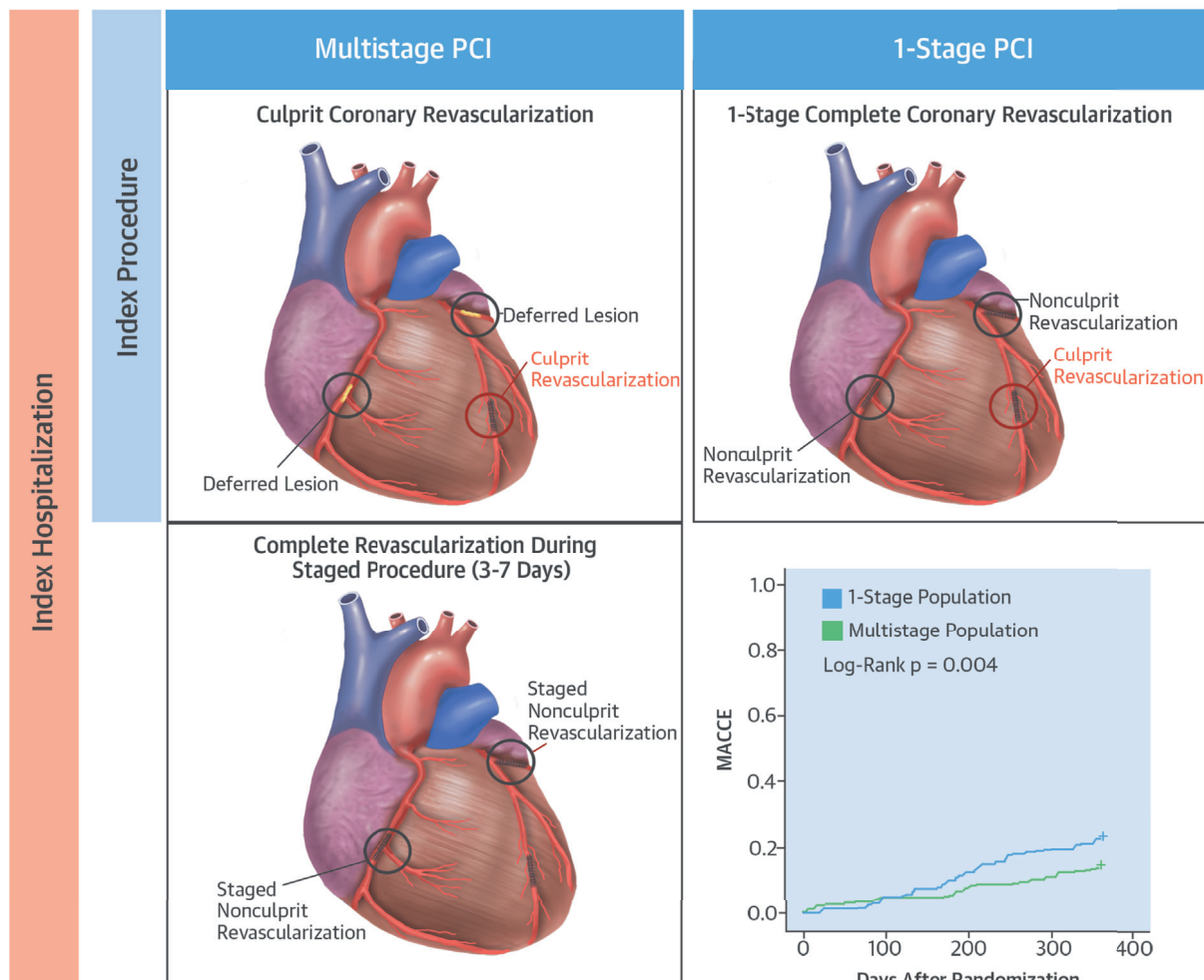
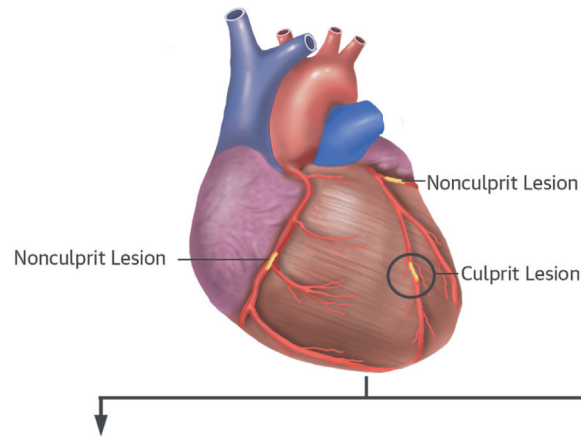
	1-Stage (n = 264)	Multistage (n = 263)	Hazard Ratio (95% CI)	p Value
MACCE	36 (13.63)	61 (23.19)	0.549 (0.363-0.828)	0.004
Death	17 (6.43)	29 (11.02)	0.562 (0.309-1.023)	0.06
Cardiac death	9 (3.41)	14 (5.32)	0.624 (0.270-1.441)	0.27
Stroke	1 (0.38)	2 (0.76)	0.487 (0.044-5.368)	0.54
Myocardial infarction	7 (2.65)	10 (3.80)	0.678 (0.156-2.657)	0.46
STEMI	2 (0.76)	4 (1.52)	0.486 (0.089-2.654)	0.39
NSTEMI	5 (1.89)	6 (2.28)	0.812 (0.248-2.661)	0.73
UA needing hospitalization	11 (4.16)	13 (4.94)	0.797 (0.068-4.276)	0.68
TVR	22 (8.33)	40 (15.20)	0.522 (0.310-0.878)	0.01

Values are n (%) unless otherwise indicated. MACCE include cardiac death, death, reinfarction, rehospitalization for unstable angina, repeat coronary revascularization (TVR), and stroke at 1 year.
 CI = confidence interval; MACCE = major adverse cardiovascular and cerebrovascular events; NSTEMI = non-ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction, TVR = target vessel coronary revascularization; UA = unstable angina.

revascularization in terms of MACCE; 2) this is mainly due to an unexplained higher incidence of TVR; 3) the intention-to-treat analysis showed a net trend in favor of 1S-PCI in terms of overall death; 4) the 1-stage strategy, as compared with MS-PCI complete coronary revascularization, is associated with a significantly lower incidence of minimal bleeding and a rapid decrease in myocardial enzymes.

As previously reported, no randomized data exist about the role of complete coronary revascularization in NSTEMI patients. In this setting, guidelines are also ambiguous and inconclusive (3-4). Recently published Italian data reported on the treatment of 43,645 multivessel patients, of whom 58.6% (n = 25,575) underwent complete coronary revascularization in a single-stage procedure (22). Our hypothesis was that a longer procedure duration, higher contrast volume administered during the index procedure, a possible major rate of complications (periprocedural myocardial infarction, procedure-related stroke, bleeding requiring transfusion, and contrast-induced nephropathy requiring dialysis) could have an impact on MACCE at long-term follow-up. However, our data showed the opposite results, mainly due to a higher rate of TVR. A possible explanation for this finding could be the observed higher rate of 6-month stress tests in the MS-PCI group during the follow-up period (1S-PCI: n = 71 [26.89%] vs. MS-PCI: n = 93 [35.36%]; p = 0.0479). Cardiac enzyme levels (in particular, troponin T), promptly decreased in the 1S-PCI group, whereas a significant increase of troponin T was observed in the MS-PCI group after the index procedure (median: MS-PCI baseline [0.46 (IQR: 0.16 to 1.36)] vs. [0.96 (IQR: 0.44 to 1.76)] 12 h; p < 0.001); these results could be related to a longer

CENTRAL ILLUSTRATION Complete Coronary Revascularization Strategies in NSTEMI Patients with Multivessel Coronary Artery Disease



Sardella, G. et al. J Am Coll Cardiol. 2016; 67(3):264-72.

The SMILE (Impact of Different Treatment in Multivessel Non ST Elevation Myocardial Infarction Patients: One Stage Versus Multistaged Percutaneous Coronary Intervention) trial is a randomized study comparing 2 complete coronary revascularization strategies in patients presenting with non-ST-segment elevation myocardial infarction (NSTEMI) and multivessel coronary artery disease. In the 1-stage percutaneous coronary intervention (PCI) group, complete coronary revascularization was performed during the index procedure. In the multistage PCI group, culprit-only revascularization was performed during the index procedure and completed revascularization was achieved during a staged procedure. The major finding of the study was that 1-stage PCI was superior to multistage PCI in terms of major adverse cardiovascular and cerebrovascular events (MACCE).

time of ischemia in the MS-PCI. A longer time of myocardial ischemia in MS-PCI group could be also due to a possible erroneous identification of the culprit lesion during coronary angiography or to the presence of multiple culprit lesions and, consequently, to incomplete ischemia resolution (4-11). Finally, in the MS-PCI group, a higher rate of minimal bleeding was observed, probably due to a higher rate of access site switching in the second procedure.

The SMILE trial is a randomized study that assumed complete coronary revascularization as preferred strategy in ACS multivessel patients. Comparing the SMILE trial to previously published nonrandomized studies is difficult. Shishehbor et al. (12), in a prospective propensity-matched analysis on 1,240 ACS patients with multivessel coronary artery disease, observed that complete coronary revascularization is associated with a lower rate of the composite endpoint (death, myocardial infarction, or revascularization). If we compare the rate of MACCE in the SMILE trial (1S-PCI: 13.63% vs. MS-PCI: 23.19%) with the propensity-matched composite endpoint of Shishehbor et al. (complete revascularization: 30.0% vs. culprit-only strategy: 40.0%), a lower event rate was observed, independent of the revascularization strategy in complete revascularization (12). These results suggest that complete coronary revascularization should be the preferred strategy in multivessel patients, independent of the timing of revascularization.

In contrast, recently published data strongly suggest that complete coronary revascularization is associated with a significant reduction in major adverse cardiovascular events in the setting of STEMI in multivessel patients (23-25).

STUDY LIMITATIONS. The SMILE trial had several limitations: the primary endpoint is a combined one; the trial is not powered for secondary endpoints; the trial had an open-label design. Culprit-vessel-only PCI was excluded as a possible revascularization

strategy in our population. However, the mean GRACE (Global Registry of Acute Coronary Events) in-hospital score was >140, patients enrolled in the study were at low risk, considering their SYNTAX scores and preserved left ventricular ejection function. Fractional flow reserve and other imaging modalities were not routinely used to assess the severity of coronary lesions.

CONCLUSIONS

In multivessel NSTEMI patients, 1S-PCI during the index procedure is superior to MS-PCI complete coronary revascularization during the index hospitalization in terms of MACCE (Central Illustration).

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL

SKILLS: On the basis of near-term outcomes in patients with NSTEMI and multivessel coronary artery disease, single-session complete coronary interventional procedures are preferred over multistage methods of percutaneous revascularization.

TRANSLATIONAL OUTLOOK: Longer-term follow-up studies are needed to assess the comparative mortality benefit of performing complete coronary revascularization during index procedures, rather than delaying intervention on lesions in nonculprit vessels in patients with NSTEMI.

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KEY WORDS acute coronary syndrome, coronary artery disease, intention-to-treat analysis, myocardial infarction, myocardial ischemia, troponin

APPENDIX For supplemental tables, please see the online version of this paper.