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Abbreviated Antiplatelet Therapy After Coronary Stenting in Patients With Myocardial Infarction at High Bleeding Risk

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ABSTRACT

BACKGROUND The optimal duration of antiplatelet therapy (APT) after coronary stenting in patients at high bleeding risk (HBR) presenting with an acute coronary syndrome remains unclear.

OBJECTIVES The objective of this study was to investigate the safety and efficacy of an abbreviated APT regimen after coronary stenting in an HBR population presenting with acute or recent myocardial infarction.

METHODS In the MASTER DAPT trial, 4,579 patients at HBR were randomized after 1 month of dual APT (DAPT) to abbreviated (DAPT stopped and 11 months single APT or 5 months in patients with oral anticoagulants) or nonabbreviated APT (DAPT for minimum 3 months) strategies. Randomization was stratified by acute or recent myocardial infarction at index procedure. Coprimary outcomes at 335 days after randomization were net adverse clinical outcomes events (NACE); major adverse cardiac and cerebral events (MACCE); and type 2, 3, or 5 Bleeding Academic Research Consortium bleeding.

RESULTS NACE and MACCE did not differ with abbreviated vs nonabbreviated APT regimens in patients with an acute or recent myocardial infarction (n = 1,780; HR: 0.83; 95% CI: 0.61-1.12 and HR: 0.86; 95% CI: 0.62-1.19, respectively) or without an acute or recent myocardial infarction (n = 2,799; HR: 1.03; 95% CI: 0.77-1.38 and HR: 1.13; 95% CI: 0.80-1.59; $P_{interaction}$ = 0.31 and 0.25, respectively). Bleeding Academic Research Consortium 2, 3, or 5 bleeding was significantly reduced in patients with or without an acute or recent myocardial infarction (HR: 0.65; 95% CI: 0.46-0.91 and HR: 0.71; 95% CI: 0.54-0.92; $P_{interaction}$ = 0.72) with abbreviated APT.

CONCLUSIONS A 1-month DAPT strategy in patients with HBR presenting with an acute or recent myocardial infarction results in similar NACE and MACCE rates and reduces bleedings compared with a nonabbreviated DAPT strategy. (Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Prolonged DAPT Regimen [MASTER DAPT]; NCT03023020) (J Am Coll Cardiol 2022;80:1220–1237) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Patients undergoing coronary stenting for acute coronary syndromes require dual antiplatelet therapy (DAPT), comprising aspirin and preferably a potent $P2Y_{12}$ receptor blocker, such as prasugrel or ticagrelor, for 12 months to reduce the risk of ischemic events, including recurrent myocardial infarction and stent thrombosis.[1-3] However, in patients at high bleeding risk presenting with acute coronary syndrome (ACS), the optimal duration and combination of DAPT or single antiplatelet therapy (SAPT) in combination with oral anticoagulant therapy (OAC) after implantation of drug-eluting coronary stents remains a matter of debate. These patients are considered to be at double-sided risk: high risk for bleeding on one hand and high risk for recurrent ischemic or thrombotic events on the other, so-called "bi-risk" patients. Little evidence exists on the optimal duration and combination of antiplatelet therapy (APT) in these bi-risk patients. European and North American guidelines recommend shortening DAPT to 3 to 6 months by stopping one antiplatelet agent in patients at high bleeding risk with ACS, respectively, although these are weak II a and b recommendations.[1,3] Considering this lack of evidence, bi-risk patients pose a clinical dilemma in daily practice, with a high degree in variation with respect to duration of DAPT and monotherapy drug of choice following DAPT around the world.[4]

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The MASTER DAPT (Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen; NCT03023020) trial was designed to investigate the safety of abbreviated vs nonabbreviated APT in patients at high bleeding risk undergoing coronary stenting, with limited exclusion criteria.[5] The trial protocol provided a stratification at randomization for patients with or without prior (≤12 months) acute myocardial infarction. In this prespecified analysis, we assessed the treatment effects of abbreviated vs nonabbreviated APT regimens in patients with or without an acute or recent (≤11 months) myocardial infarction at index percutaneous coronary intervention (PCI).

METHODS

DATA AVAILABILITY STATEMENT. The data, analytic methods, and study materials will not be made available to other researchers for the purposes of reproducing the results or replicating the procedure.

STUDY DESIGN. The MASTER DAPT trial was an investigator-initiated, randomized, open-label, noninferiority trial with sequential superiority testing in largely unselected patients at high bleeding risk who underwent PCI with a biodegradable polymer-coated Ultimaster/Ultimaster Tansei (Terumo Corporation) sirolimus-eluting stent.[5,6] The trial was performed at 140 sites in 30 countries across Europe, South America, the Middle East, Asia, and Australia. The study protocol was approved in each country and center. All patients gave written informed consent. An independent data safety monitoring board regularly reviewed the conduct of the trial and the safety of the patients. Trial organization and participating sites are detailed in the Supplemental Appendix.

PATIENTS. Patients at high risk for bleeding who underwent treatment of all planned coronary artery stenoses with Ultimaster stent implantation for acute or chronic coronary syndromes were eligible if they remained ischemic event-free until the time of randomization at 1 month after the index procedure.

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome

APT = antiplatelet therapy

BARC = Bleeding Academic Research Consortium

DAPT = dual antiplatelet therapy

MACCE = major adverse cardiac and cerebral events

NACE = net adverse clinical outcomes

NSTEMI = non-ST-segment elevation myocardial infarction

OAC = oral anticoagulation

PCI = percutaneous coronary intervention

SAPT = single antiplatelet therapy

STEMI = ST-segment elevation myocardial infarction

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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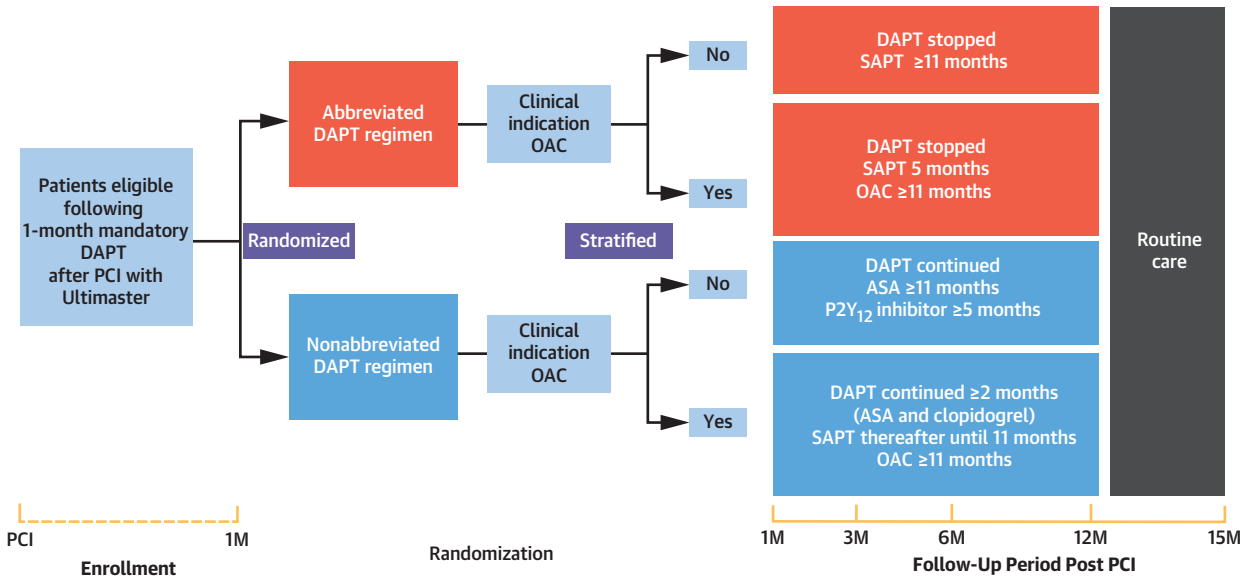
FIGURE 1 Schematic Design of the MASTER DAPT Trial

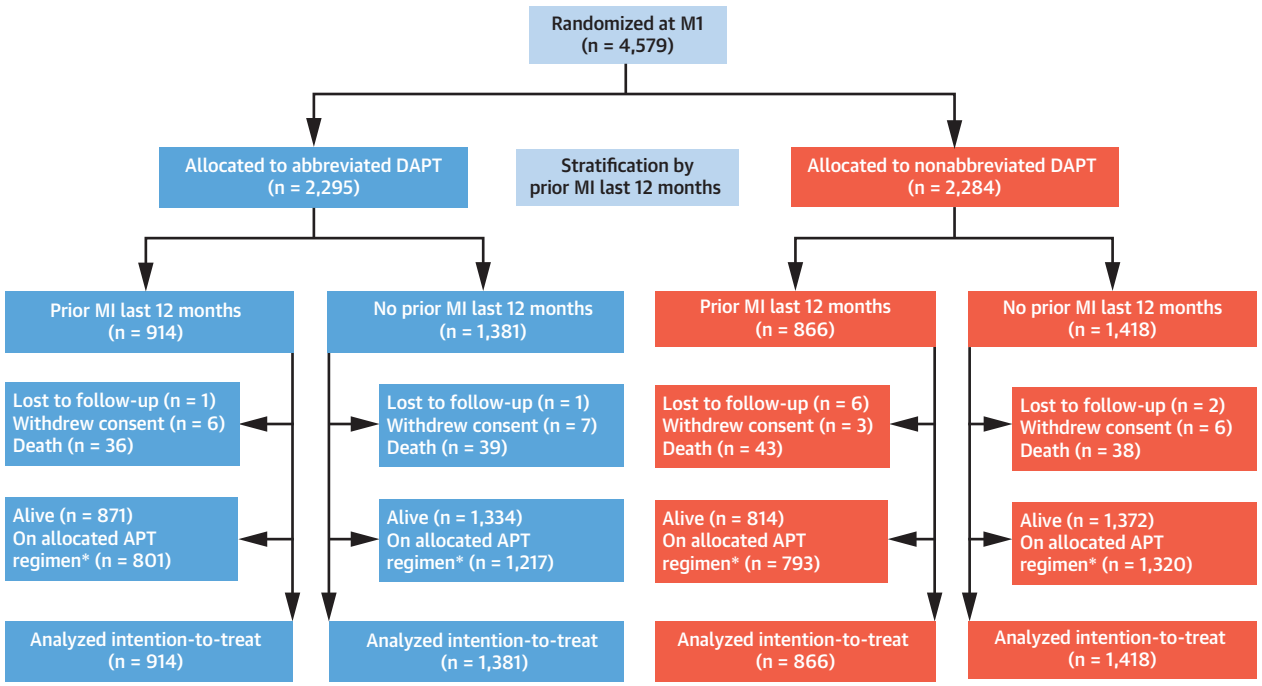


Patients were enrolled after percutaneous coronary intervention (PCI) with Ultimaster stents and randomized at 1 month if they were free of ischemic and active bleeding events. Randomization was between an abbreviated or nonabbreviated dual antiplatelet therapy (DAPT) regimen and stratified for site, clinical indication for oral anticoagulation (OAC) therapy, and prior myocardial infarction, meaning presentation with acute myocardial infarction at index PCI or recent (<11 months) myocardial infarction before index PCI. In the abbreviated DAPT arm, DAPT was immediately stopped after randomization, and single antiplatelet therapy (SAPT) continued for 5 months in patients with OAC and 11 months in patients not on OAC. In the nonabbreviated DAPT arm, DAPT was continued for a minimum of 5 months after which SAPT with acetylsalicylic acid (ASA) was continued. In patients with OAC, DAPT was continued for a minimum of 2 months, after which dual therapy (OAC and SAPT) was continued. MASTER DAPT = Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen.

Patients were considered at high bleeding risk if at least 1 of the following criteria applied: oral anticoagulant (OAC) (vitamin K antagonist or non-vitamin K antagonist) therapy for ≥12 months, recent (<12 months) nonaccess site bleeding episode(s) that required medical attention, previous bleeding episode(s) that required hospitalization if the underlying cause had not been definitively treated, age ≥75 years, systemic conditions associated with an increased bleeding risk (eg, hematological disorders or any known coagulation disorder associated with increased bleeding risk), documented anemia (defined as repeated hemoglobin levels <11 g/dL or transfusion ≤4 weeks before randomization), need for chronic treatment with steroids or nonsteroidal anti-inflammatory drugs, diagnosed malignancy (other than skin), stroke at any time or transient ischemic attack in the previous 6 months, or PRECISE DAPT (PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy) score ≥25.[7] Exclusion criteria were minimal and limited to implantation of a non-study stent within the previous 6 months or a bioresorbable scaffold at any time before the index procedure, or if they underwent treatment because of an in-stent restenosis or stent thrombosis. Detailed inclusion and exclusion criteria are provided in the Supplemental Appendix.

RANDOMIZATION, MASKING, AND PROCEDURES. Patients were centrally randomized (1:1 ratio) to an open-label abbreviated or nonabbreviated APT regimen 30 to 44 days after the index procedure. The index procedure was either a single procedure or the last installment in planned (<6 weeks) staged procedures. The Ultimaster stent had to be used in all procedures. Randomization was concealed using a web-based system; randomization sequences were computer generated; blocked with randomly selected block sizes of 2, 4, or 6; and were stratified by site, history of acute myocardial infarction (presentation with non-ST-segment elevation or ST-segment elevation myocardial infarction [NSTEMI or STEMI, respectively]) within 12 months, and indication for ≥12 months of OAC therapy. In this prespecified subgroup analysis, we report the outcomes of the populations with or without history of acute

FIGURE 2 Patient Flow



*At day 335 or on allowed alternative regimen due to, for example, prior events; if not recorded on exactly day 335, the last information on adherence is used.
APT = antiplatelet therapy; DAPT = dual antiplatelet therapy; M1 = 1 month after index coronary stent procedure; MI = myocardial infarction.

myocardial infarction within 12 months before randomization.

Figure 1 shows the trial design and the subgroups of this analysis. Patients who were randomly allocated to receive abbreviated treatment immediately discontinued DAPT after randomization and continued with SAPT until 12 months after the index procedure or 6 months in case of indication for OAC therapy. Patients who were randomly allocated to receive nonabbreviated treatment continued DAPT until ≥3 months after the index stent procedure (ie, ≥2 months after randomization) and continued thereafter with SAPT until 12 months after the index procedure. All antiplatelet and OAC treatment options were dosed according to the corresponding authorization for use and locally approved regimens. Supplemental Table 1 details the APT regimen(s) allowed after each type of event according to the presence or absence of a clinical indication for OAC.

Follow-up visits occurred at 60 ± 14 days and 150 ± 14 days after randomization, preferably as on-site visits, and at 335 ± 14 days after randomization, exclusively as an on-site visit. Two independent clinical research organizations (CERC, Massy, France, and Cardialysis, Rotterdam, the Netherlands) performed on-site and remote monitoring visits, verified the source documents, and collected source material for event adjudication. All events were adjudicated by an independent adjudication committee that was unaware of the treatment allocations. All data were stored at a central database of an academic institution (CTU, Bern, Switzerland). Nonadherence to the allocated treatment regimen was evaluated according to the Non-adherence Academic Research Consortium classification (Supplemental Table 2).[8]

OUTCOMES. Coprimary outcomes were net adverse clinical outcomes (NACE), defined as the composite of all-cause death, myocardial infarction, stroke, or Bleeding Academic Research Consortium (BARC) 3 or 5 bleeding events[1-3,9]; major adverse cardiac and cerebral events (MACCE), expressed as a composite of all-cause death, myocardial infarction, or stroke; and major or clinically relevant nonmajor bleeding, defined as a composite of type 2, 3, or 5 BARC bleeding events.

The secondary outcomes included the individual components of the 3 coprimary outcomes; the composite of cardiovascular death, myocardial infarction, and stroke; the composite of cardiovascular death,

TABLE 1 Baseline Characteristics

	Prior MI Past 12 Months		No Prior MI Past 12 Months	
	Abbreviated DAPT (n = 914)	Nonabbreviated DAPT (n = 866)	Abbreviated DAPT (n = 1,381)	Nonabbreviated DAPT (n = 1,418)
Age, y	76.1 ± 9.9	76.1 ± 9.7	76.2 ± 7.9	75.9 ± 8.2
Male	613 (67.1)	577 (66.6)	977 (70.7)	1004 (70.8)
Body mass index, kg/m^2	26.7 ± 4.7	27.0 ± 4.7	27.6 ± 4.7	27.7 ± 4.8
Family history of coronary artery disease	194 (21.2)	157 (18.1)	362 (26.2)	396 (27.9)
Arterial hypertension	679 (74.3)	666 (76.9)	1087 (78.7)	1121 (79.1)
Uncontrolled hypertension	48 (5.3)	47 (5.4)	71 (5.1)	70 (4.9)
Diabetes mellitus	291 (31.8)	316 (36.5)	463 (33.5)	468 (33.0)
Hyperlipidemia	579 (63.3)	535 (61.8)	963 (69.7)	1020 (71.9)
Smoking status	913	864	1,377	1.412
Never smoked	475 (52.0)	484 (56.0)	711 (51.6)	754 (53.4)
Previous smoker	318 (34.8)	296 (34.3)	556 (40.4)	558 (39.5)
Current smoker	120 (13.1)	84 (9.7)	110 (8.0)	100 (7.1)
Peripheral vascular disease[a]	100 (10.9)	90 (10.4)	143 (10.4)	152 (10.7)
Carotid artery disease[b]	39 (4.3)	54 (6.2)	81 (5.9)	90 (6.3)
History of heart failure	203 (22.2)	188 (21.7)	226 (16.4)	250 (17.6)
Left ventricular ejection fraction, %	51.3 ± 11.1 (870)	50.7 ± 11.2 (814)	54.9 ± 11.4 (1,299)	54.4 ± 11.9 (1,314)
Previous MI	219 (24.0)	195 (22.5)	215 (15.6)	235 (16.6)
Previous PCI	185 (20.2)	172 (19.9)	409 (29.6)	422 (29.8)
Previous cerebrovascular event reported	105 (11.5)	108 (12.5)	163 (11.8)	194 (13.7)
Stroke	80 (8.8)	79 (9.1)	113 (8.2)	138 (9.7)
TIA	30 (3.3)	32 (3.7)	56 (4.1)	52 (3.7)
Undetermined cerebrovascular event	3 (0.3)	6 (0.7)	8 (0.6)	12 (0.8)
History of arterial thromboembolism	10 (1.1)	7 (0.8)	21 (1.5)	17 (1.2)
History of venous thromboembolism	51 (5.6)	41 (4.7)	73 (5.3)	74 (5.2)
Previous CABG	62 (6.8)	54 (6.2)	108 (7.8)	117 (8.3)
Previous prosthetic mechanical heart valve	8 (0.9)	11 (1.3)	35 (2.5)	47 (3.3)
Aortic valve stenosis	23/820 (2.8)	32/777 (4.1)	68/1,249 (5.4)	72/1,274 (5.7)
Previous bleeding before/after qualifying PCI	86 (9.4)	87 (10.0)	98 (7.1)	88 (6.2)
Chronic pulmonary disease	85 (9.3)	114 (13.2)	170 (12.3)	169 (11.9)
Chronic renal failure	198 (21.7)	199 (23.0)	220 (15.9)	259 (18.3)
Liver disease	8 (0.9)	13 (1.5)	21 (1.5)	19 (1.3)
Atrial fibrillation	268 (29.3)	227 (26.2)	502 (36.4)	493 (34.8)
History of cancer	145 (15.9)	132 (15.2)	203 (14.7)	219 (15.4)
Active cancer	49 (5.4)	54 (6.2)	61 (4.4)	72 (5.1)
Hematological or coagulation disorders	163 (17.8)	156 (18.0)	127 (9.2)	132 (9.3)
Chronic treatment with steroids or NSAIDs	72 (7.9)	105 (12.1)	130 (9.4)	134 (9.4)
Previous VKA	103 (11.3)	95 (11.0)	224 (16.2)	204 (14.4)
Need for current treatment with OAC	291 (31.8)	254 (29.3)	558 (40.4)	566 (39.9)
Clinical indication for 12 months OAC	291 (31.8)	253 (29.2)	557 (40.3)	565 (39.8)
OAC treatment at randomization	287/291 (98.6)	249/253 (98.4)	555/557 (99.6)	565/565 (100.0)
PRECISE DAPT score[b]	29.0 ± 11.9	29.2 ± 12.1	25.4 ± 10.0	25.2 ± 10.1
Previous bleeding	76 (8.3)	77 (8.9)	89 (6.4)	78 (5.5)
Hemoglobin, g/L	13.0 ± 1.9	13.0 ± 2.0	13.4 ± 1.7	13.4 ± 1.7
White-cell count,[c] 10^9/L	8.8 ± 3.8	8.9 ± 3.4	7.9 ± 14.4	7.5 ± 3.3 (1,417)
Creatinine clearance,[d] mL/min/1.73 m^2	69.4 ± 26.1	69.8 ± 25.4	71.6 ± 22.5	71.7 ± 23.3

Values are mean ± SD, n (%), n, mean ± SD (n), or n/N (%). [a]Intermittent claudication, peripheral-artery bypass for insufficiency, gangrene, acute arterial insufficiency, untreated aneurysm (≥6 cm in diameter), an ankle brachial index of no more than 0.90, or aortic plaque. [b]Kidney damage (pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies) or an estimated glomerular filtration rate of <60 mL/min per 1.73 m^2 of body-surface area for ≥3 months. [c]Calculated at the screening visit. One patient in the standard-therapy group had a PRECISE DAPT score calculated without the white-cell count. [d]Calculated with the use of the Modification of Diet in Renal Disease method.

CABG = coronary artery bypass grafting; DAPT = dual antiplatelet therapy; MI = myocardial infarction; NSAID = nonsteroidal anti-inflammatory drug; OAC = oral anticoagulant; PCI = percutaneous coronary intervention; PRECISE DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy; TIA = transient ischemic attack; VKA = vitamin K antagonist.

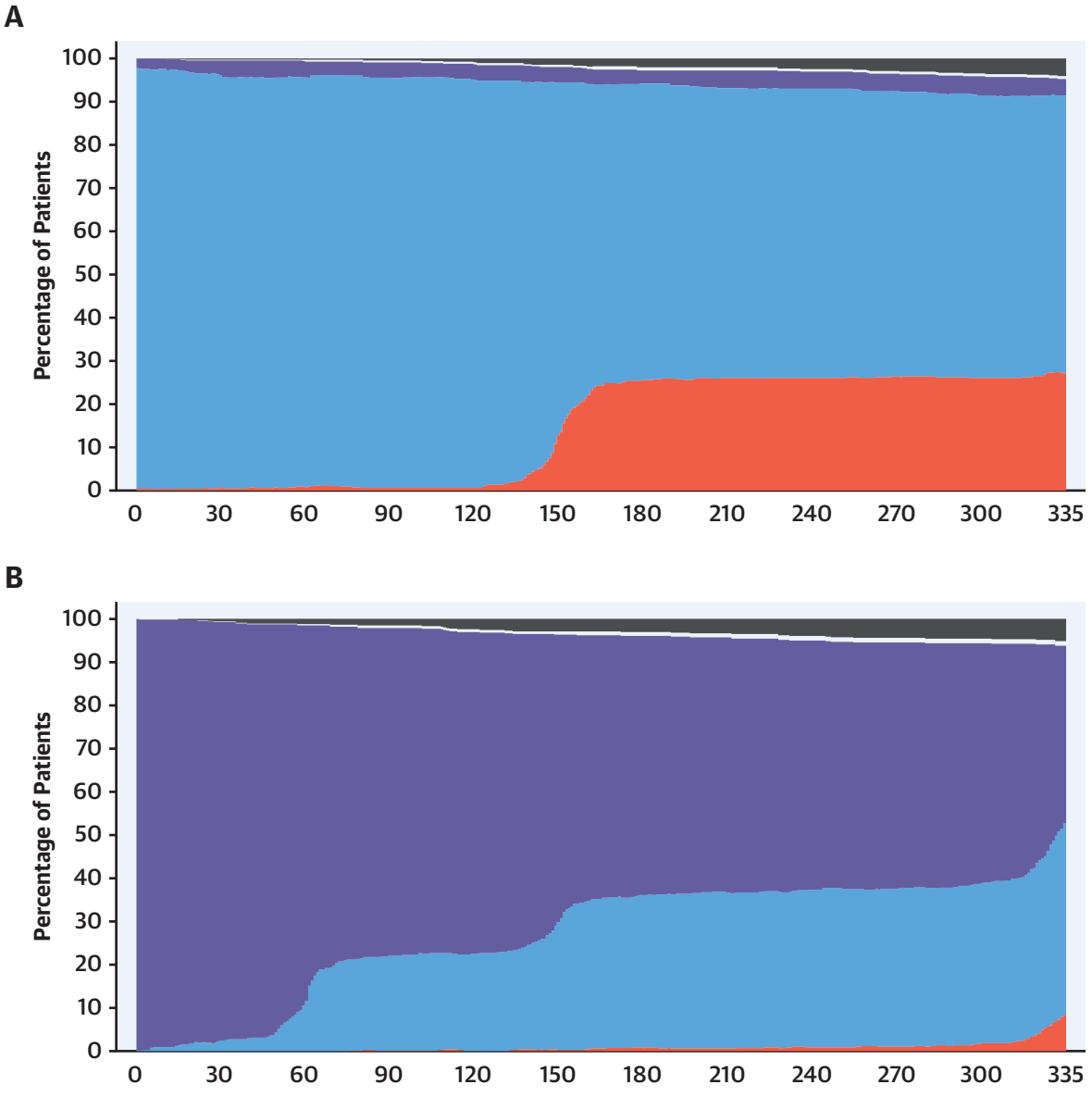
TABLE 2 Procedural Characteristics

	Prior MI Past 12 Months		No Prior MI Past 12 Months	
	Abbreviated DAPT (n = 914)	Nonabbreviated DAPT (n = 866)	Abbreviated DAPT (n = 1,381)	Nonabbreviated DAPT (n = 1,418)
Indication[a]				
Stable angina	28 (3.1)	30 (3.5)	894 (64.7)	897 (63.3)
Silent ischemia	3 (0.3)	6 (0.7)	242 (17.5)	268 (18.9)
NSTEMI	595 (65.1)	558 (64.4)	0 (0.0)	0 (0.0)
STEMI	273 (29.9)	265 (30.6)	0 (0.0)	0 (0.0)
Unstable angina	15 (1.6)	7 (0.8)	245 (17.7)	253 (17.8)
Clinical status[a]				
Killip II, III or IV	147 (16.1)	144 (16.6)	105 (7.6)	110 (7.8)
Cardiac arrest	17 (1.9)	24 (2.8)	9 (0.7)	8 (0.6)
Heart rate, beats/min	75.4 ± 16.3 (913)	76.0 ± 17.4 (865)	72.3 ± 16.4 (913)	72.4 ± 15.8 (1,415)
Systolic blood pressure, mm Hg	135.9 ± 26.7 (913)	135.9 ± 25.5 (864)	138.4 ± 25.3 (1,376)	137.5 ± 24.9 (1,414)
Procedural specifications[a]				
Arterial access site				
Femoral	153 (16.7)	119 (13.7)	207 (15.0)	174 (12.3)
Radial	759 (83.0)	746 (86.1)	1171 (84.8)	1238 (87.3)
Brachial	2 (0.2)	1 (0.1)	3 (0.2)	6 (0.4)
IABP	13 (1.4)	10 (1.2)	11 (0.8)	20 (1.4)
LVAD	0 (0.0)	1 (0.1)	2 (0.1)	5 (0.4)
Total amount of contrast, mL	171.3 ± 79.8 (902)	166.8 ± 77.3 (857)	166.1 ± 80.8 (1,373)	166.8 ± 80.7 (1,405)
Medications during the procedure[a]				1,417
Unfractionated heparin	858 (93.9)	817 (94.3)	1326 (96.0)	1355 (95.6)
Bivalirudin	3 (0.3)	1 (0.1)	2 (0.1)	1 (0.1)
Low-molecular-weight heparin	25 (2.7)	27 (3.1)	38 (2.8)	37 (2.6)
Cangrelor	1 (0.1)	1 (0.1)	7 (0.5)	2 (0.1)
Glycoprotein II/IIIa inhibitors	49 (5.4)	47 (5.4)	37 (2.7)	29 (2.0)
Total number of PCIs[b]				
1	816 (89.3)	753 (87.0)	1277 (92.5)	1313 (92.6)
2	95 (10.4)	110 (12.7)	96 (7.0)	104 (7.3)
3	3 (0.3)	3 (0.3)	8 (0.6)	1 (0.1)
Vessels treated per patient[c]				
1	667 (73.0)	621 (71.7)	1049 (76.0)	1028 (72.5)
2	201 (22.0)	204 (23.6)	282 (20.4)	337 (23.8)
3	46 (5.0)	41 (4.7)	50 (3.6)	53 (3.7)
Treated vessel(s) per patient				
Left main	52 (5.7)	46 (5.3)	74 (5.4)	88 (6.2)
Left arterial descending artery	494 (54.0)	462 (53.3)	746 (54.0)	809 (57.1)
Left circumflex artery	262 (28.7)	274 (31.6)	390 (28.2)	415 (29.3)
Right coronary artery or posterior descending right coronary	363 (39.7)	323 (37.3)	491 (35.6)	483 (34.1)
Bypass graft	17 (1.9)	19 (2.2)	21 (1.5)	19 (1.3)
Treated lesions per patient				
1	613 (67.1)	571 (65.9)	966 (69.9)	965 (68.1)
2	214 (23.4)	208 (24.0)	289 (20.9)	314 (22.1)
≥3	87 (9.5)	87 (10.0)	126 (9.1)	139 (9.8)
Total stented lesions per patient				
1	633 (69.3)	583 (67.3)	978 (70.8)	982 (69.3)
2	202 (22.1)	205 (23.7)	284 (20.6)	302 (21.3)
≥3	79 (8.6)	78 (9.0)	119 (8.6)	134 (9.4)
≥1 complex lesion B2 or C	672 (73.5)	641 (74.0)	890 (64.4)	938 (66.1)
Number of stents per patient	1.8 ± 1.1	1.8 ± 1.1	1.7 ± 1.1	1.7 ± 1.1
Total stent length per patient, mm	40.6 ± 29.4	41.1 ± 27.8	38.4 ± 29.1	38.9 ± 28.8
Any overlapping stenting	211 (23.1)	180 (20.8)	277 (20.1)	270 (19.0)
Any bifurcation or trifurcation stenting[d]	35 (3.8)	29 (3.3)	48 (3.5)	72 (5.1)

Values are n (%), mean ± SD (n), n, or mean ± SD. [a]Data from first PCI only. [b]1 PCI and up to 2 staged PCIs: the last PCI was the qualifying PCI 1 month before randomization. [c]Left main counted as 2 vessels; left internal mammary artery/right internal mammary artery/radial/ saphenous vein grafts counted as one vessel. [d]Stenting into both main and side branch(es).

IABP = intra-aortic balloon pump; LIMA = left internal mammary artery; LVAD = left ventricular assist device; NSTEMI = non-ST-segment elevation myocardial infarction; RIMA = right internal mammary artery; STEMI = ST-segment myocardial infarction; SVG = saphenous vein graft; other abbreviations as in Table 1.

FIGURE 3 **Daily Antiplatelet Use Since Randomization**



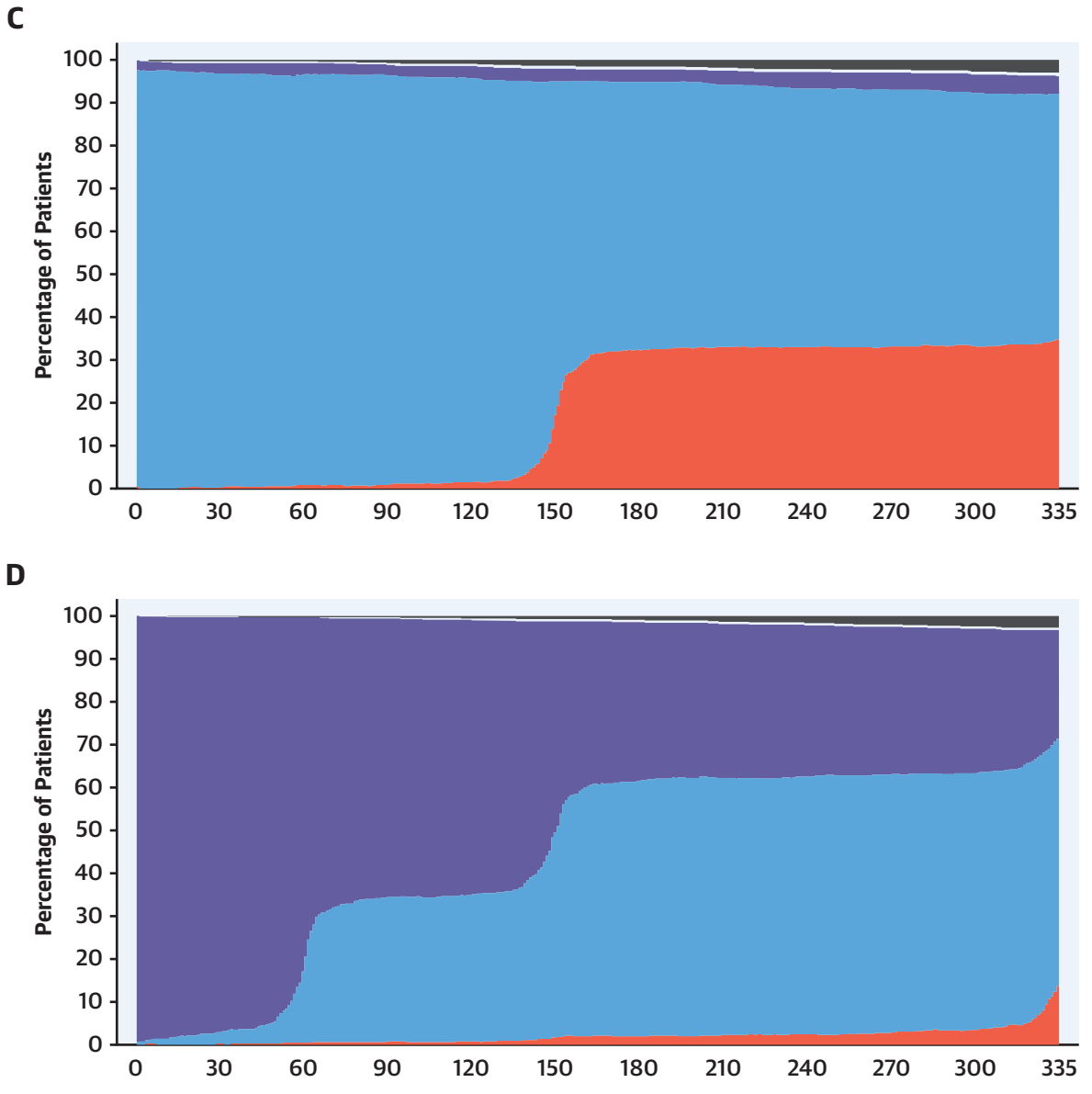
Depicted is antiplatelet use on a daily basis since randomization in the 4 groups. **(A)** Patients with prior myocardial infarction on abbreviated antiplatelet therapy (APT). **(B)** Patients with prior myocardial infarction on nonabbreviated APT. **(C)** Patients without prior myocardial infarction on abbreviated APT. **(D)** Patients without prior myocardial infarction on nonabbreviated APT. **Purple** illustrates the period and percentage of patients on dual APT (DAPT), **blue** illustrates the period and percentage of patients on single APT (SAPT), **red** illustrates the period and percentage of patients without APT, **black** illustrates the period and percentage of deceased patients, and **white** illustrates the period and percentage with no information of patients.

Continued on the next page

myocardial infarction, and definite or probable stent thrombosis, the composite of stroke and transient ischemic attack; and all bleeding events, adjudicated according to the BARC classifications.[9] All outcomes were prespecified.[5] All analyses evaluated the occurrence of the adjudicated outcomes between randomization and 335 days.

STATISTICAL ANALYSIS. The data were analyzed according to the intention-to-treat principle. Outcomes were assessed separately for patients with and

FIGURE 3 Continued



without a history of myocardial infarction ≤12 months before randomization by calculating HRs with 95% CIs. We report cause-specific estimates throughout the paper. For patients with a primary outcome, time-to-event was calculated as the difference between the date of occurrence of the outcome event and the date of randomization plus 1. For patients with an outcome event and complete follow-up until the end of day 335, time to censoring was calculated as 335 days. For patients with incomplete clinical follow-up, time to censoring was defined as the difference between the dates of last known clinical status and randomization plus 1. For the third coprimary outcome, the occurrence of death was defined as a competing risk event, and follow-up was censored at the time of the occurrence of death. Kaplan-Meier curves were created for the first 2 (time-to-event) coprimary outcomes, and cause-specific Kaplan-Meier curves for the third coprimary outcome (with censoring at the time of the competing risk event of unrelated death). Kaplan-Meier calculations included all (first) adjudicated outcome events that occurred between randomization and 335 days thereafter according to the randomized treatment assignment, irrespective of the dual

antiplatelet regimen received at the time of the outcome event. Cause-specific HR and 95% CI were generated for primary and secondary outcomes with the use of Cox proportional hazards regression analysis with censoring at end of study and at the time of the competing risk event of unrelated death as defined previously. The landmark analyses are based on the timepoints patients were allowed to reduce APT per protocol.

P values for testing homogeneity of the HR in subgroups of patients were derived in Cox proportional hazards models with interaction terms for treatment group and subgroup membership.

RESULTS

From February 28, 2017, to December 5, 2019, 5,204 patients were screened and 4,579 (88.1%) were randomized a median of 34 days (IQR: 32-39 days) post stenting, of which 2,295 patients were randomized to an abbreviated APT and 2,284 to a nonabbreviated APT strategy. In the abbreviated arm, 914 patients had a myocardial infarction in the 12 months before randomization and 1,381 had no myocardial infarction in the 12 months before randomization. In the nonabbreviated arm, the corresponding numbers of patients were 866 and 1,418, respectively (**Figure 2**). Complete follow-up in the prior (≤12 months) myocardial infarction group was 99.2% for the abbreviated APT arm and 99.0% for the nonabbreviated APT arm, and 99.4% and 99.4%, respectively, in the subgroup with no myocardial infarction in the 12 months before randomization.

Baseline and procedural characteristics are described in **Tables 1 and 2** and Supplemental Table 3. The mean age was 76.0 ± 8.7 years, 33.6% of patients received treatment for diabetes, and 36.4% were on OAC therapy. The indication for coronary stenting was ACS for 48.3% of patients, of whom 25.2% had NSTEMI and 11.7% had STEMI. In the 1,780 patients with a prior (≤12 months) myocardial infarction at randomization, 1,691 (95.0%) presented with an acute myocardial infarction (NSTEMI or STEMI) at the index PCI (or first PCI in case of staged procedures). Eighty-nine patients (5.0%) had no indication for acute myocardial infarction at index or first PCI, but had a history of myocardial infarction during the 11 months before the index or first PCI.

Medication use and detailed information on APT at each visit are shown in Supplemental Tables 4 and 5. In the prior (≤12 months) myocardial infarction groups, 33.0% and 34.2%, respectively, of the patients received ticagrelor in the abbreviated and nonabbreviated groups at randomization, whereas only 3.0% and 3.2%, respectively, received prasugrel. In both the no prior (≤12 months) myocardial infarction groups, aspirin plus clopidogrel (90.1% and 89.0%) was the most frequently implemented regimen. Median durations of DAPT since coronary stenting in the abbreviated arm were both 35 days (IQR: 32-40 days) in the prior myocardial infarction and no prior myocardial infarction groups. In the nonabbreviated arm, the median DAPT durations were 363 days (IQR: 153-369 days) and 186 days (IQR: 98-366 days) for the prior myocardial infarction and no prior myocardial infarction groups, respectively.

Adherence to the allocated antiplatelet regimen decreased over time and was lower in the abbreviated vs nonabbreviated groups at 12 months in the prior (≤12 months) myocardial infarction groups (88.6% vs 98.4%; $P < 0.001$, respectively) and in the no prior (≤12 months) myocardial infarction groups (88.5% vs 96.9%, $P < 0.001$, respectively). Detailed information on adherence is shown in **Figure 3** and Supplemental Table 6.

OUTCOMES AMONG PATIENTS WITH PRIOR (≤12 MONTHS) MYOCARDIAL INFARCTION. Clinical outcomes at 11 months post randomization in patients with prior (≤12 months) myocardial infarction are shown in **Table 3**. NACE occurred in 81 (8.9%) patients in the abbreviated group vs 91 (10.6%) patients in the nonabbreviated group (HR: 0.83; 95% CI: 0.61-1.12; $P = 0.22$) (**Figure 4A**). MACCE did not differ, occurring in 69 (7.6%) patients in the abbreviated arm vs 75 (8.7%) patients in the nonabbreviated arm (HR: 0.86; 95% CI: 0.62-1.19; $P = 0.36$) (**Figure 4B**). BARC 2, 3, or 5 bleeding occurred in 56 (6.2%) patients in the abbreviated arm vs 79 (9.3%) patients in the nonabbreviated arm (HR: 0.65; 95% CI: 0.46-0.91; $P = 0.01$) (**Figure 4C**). This difference was mainly driven by a reduction in BARC 2 bleeds 3.9% vs 6.3%, respectively (HR: 0.61; 95% CI: 0.40-0.93; $P = 0.022$). Other outcomes did not differ between groups, including definite and definite or probable stent thromboses.

Landmark analyses at 150 days after randomization showed consistent treatment effects with an abbreviated APT strategy for the coprimary and secondary outcomes with respect to time among patients with prior (≤12 months) myocardial infarction (**Table 4**). However, the reduction in BARC 2, 3, or 5 bleeding with an abbreviated APT strategy was more prominent in the first 150 days compared with the latter 6 months.

OUTCOMES AMONG PATIENTS WITHOUT PRIOR (≤12 MONTHS) MYOCARDIAL INFARCTION. Clinical outcomes at 12 months in patients without prior

TABLE 3 Clinical Outcomes at 11 Months Post Randomization in the ITT Population

	Prior MI Past 12 Months				No Prior MI Past 12 Months				
	Abbreviated DAPT (n = 914)	Nonabbreviated DAPT (n = 866)	HR (95% CI)[a]	*P* Value	Abbreviated DAPT (n = 1,381)	Nonabbreviated DAPT (n = 1,418)	HR (95% CI)[a]	*P* Value	Interaction *P* Value[b]
NACE	81 (8.9)	91 (10.6)	0.83 (0.61–1.12)	0.22	91 (6.6)	91 (6.4)	1.03 (0.77–1.38)	0.85	0.31
MACCE	69 (7.6)	75 (8.7)	0.86 (0.62–1.19)	0.36	69 (5.0)	63 (4.5)	1.13 (0.80–1.59)	0.48	0.25
MCB	56 (6.2)	79 (9.3)	0.65 (0.46–0.91)	0.01	92 (6.7)	132 (9.4)	0.71 (0.54–0.92)	0.010	0.72
Death	36 (4.0)	43 (5.0)	0.78 (0.50–1.22)	0.28	39 (2.8)	38 (2.7)	1.06 (0.68–1.65)	0.81	0.35
Cardiovascular death	17 (1.9)	23 (2.7)	0.69 (0.37–1.29)	0.25	20 (1.5)	21 (1.5)	0.98 (0.53–1.81)	0.95	0.43
Noncardiovascular death	15 (1.7)	14 (1.7)	1.00 (0.48–2.07)	0.998	14 (1.0)	14 (1.0)	1.03 (0.49–2.16)	0.94	0.96
Cerebrovascular accident	8 (0.9)	15 (1.8)	0.50 (0.21–1.17)	0.11	9 (0.7)	17 (1.2)	0.54 (0.24–1.22)	0.14	0.88
Stroke[c]	5 (0.6)	10 (1.2)	0.47 (0.16–1.37)	0.17	7 (0.5)	13 (0.9)	0.56 (0.22–1.39)	0.21	0.81
Ischemic	4 (0.5)	7 (0.8)	0.53 (0.16–1.83)	0.32	7 (0.5)	11 (0.8)	0.66 (0.25–1.69)	0.38	0.80
Hemorrhagic	1 (0.1)	3 (0.4)	0.31 (0.03–2.99)	0.31	0 (0.0)	2 (0.1)	0.21 (0.01–4.37)	0.50	-
TIA	3 (0.3)	5 (0.6)	0.56 (0.13–2.35)	0.43	2 (0.2)	4 (0.3)	0.51 (0.09–2.81)	0.44	0.94
MI	34 (3.8)	31 (3.7)	1.03 (0.63–1.67)	0.92	26 (1.9)	18 (1.3)	1.49 (0.82–2.72)	0.19	0.34
Definite or probable stent thrombosis	10 (1.1)	7 (0.8)	1.34 (0.51–3.52)	0.55	4 (0.3)	2 (0.1)	2.06 (0.38–11.27)	0.40	0.66
Definite	7 (0.8)	5 (0.6)	1.31 (0.42–4.13)	0.64	4 (0.3)	2 (0.1)	2.06 (0.38–11.27)	0.40	0.66
Probable	3 (0.3)	2 (0.2)	1.40 (0.23–8.40)	0.71	0 (0.0)	0 (0.0)	-	-	-
Bleeding BARC classification									
Type 1	25 (2.8)	44 (5.2)	0.53 (0.32–0.86)	0.01	40 (2.9)	65 (4.6)	0.63 (0.42–0.93)	0.021	0.58
Type 2	35 (3.9)	53 (6.3)	0.61 (0.40–0.93)	0.022	67 (4.9)	99 (7.1)	0.69 (0.50–0.94)	0.018	0.65
Type 3	21 (2.3)	24 (2.8)	0.82 (0.45–1.47)	0.50	32 (2.4)	35 (2.5)	0.94 (0.58–1.52)	0.79	0.72
Type 3a	12 (1.3)	16 (1.9)	0.70 (0.33–1.48)	0.35	14 (1.0)	14 (1.0)	1.03 (0.49–2.16)	0.94	0.47
Type 3b	8 (0.9)	7 (0.8)	1.07 (0.39–2.94)	0.90	13 (1.0)	13 (0.9)	1.03 (0.48–2.22)	0.94	0.96
Type 3c	1 (0.1)	1 (0.1)	0.93 (0.06–14.93)	0.96	6 (0.4)	8 (0.6)	0.77 (0.27–2.22)	0.63	0.90
Type 4	0 (0.0)	0 (0.0)	-	-	0 (0.0)	0 (0.0)	-	-	-
Type 5	2 (0.2)	5 (0.6)	0.37 (0.07–1.93)	0.24	0 (0.0)	3 (0.2)	0.15 (0.01–2.90)	0.25	-
Type 5a	0 (0.0)	1 (0.1)	0.32 (0.01–7.84)	0.49	0 (0.0)	1 (0.1)	0.34 (0.01–8.34)	1.00	1.00
Type 5b	2 (0.2)	4 (0.5)	0.47 (0.09–2.54)	0.38	0 (0.0)	2 (0.1)	0.21 (0.01–4.37)	0.50	-
Type 3 or 5	23 (2.6)	29 (3.4)	0.74 (0.43–1.28)	0.28	32 (2.4)	38 (2.7)	0.86 (0.54–1.38)	0.54	0.67

Values are n (% from Kaplan-Meier estimate) unless otherwise indicated. [a]HRs and 95% CIs from Cox's time-to-first event analyses. Continuity corrected RRs (95% CIs) in case of zero events with Fisher's exact test *P* value. [b]Interaction *P* value testing for the modifying effect of prior MI in past 12 months (yes or no). [c]Includes undetermined strokes.

BARC = Bleeding Academic Research Consortium; ITT = intention-to-treat; MACE = major adverse cardiovascular events (coprimary composite endpoint of all-cause death, MI, stroke); MCB = major or clinically relevant nonmajor bleeding (coprimary composite endpoint of bleeding BARC 2, 3, or 5); NACE = net adverse clinical events (coprimary composite endpoint of all-cause death, MI, stroke, and bleeding BARC 3 or 5); RR = risk ratio; other abbreviations as in Table 1.

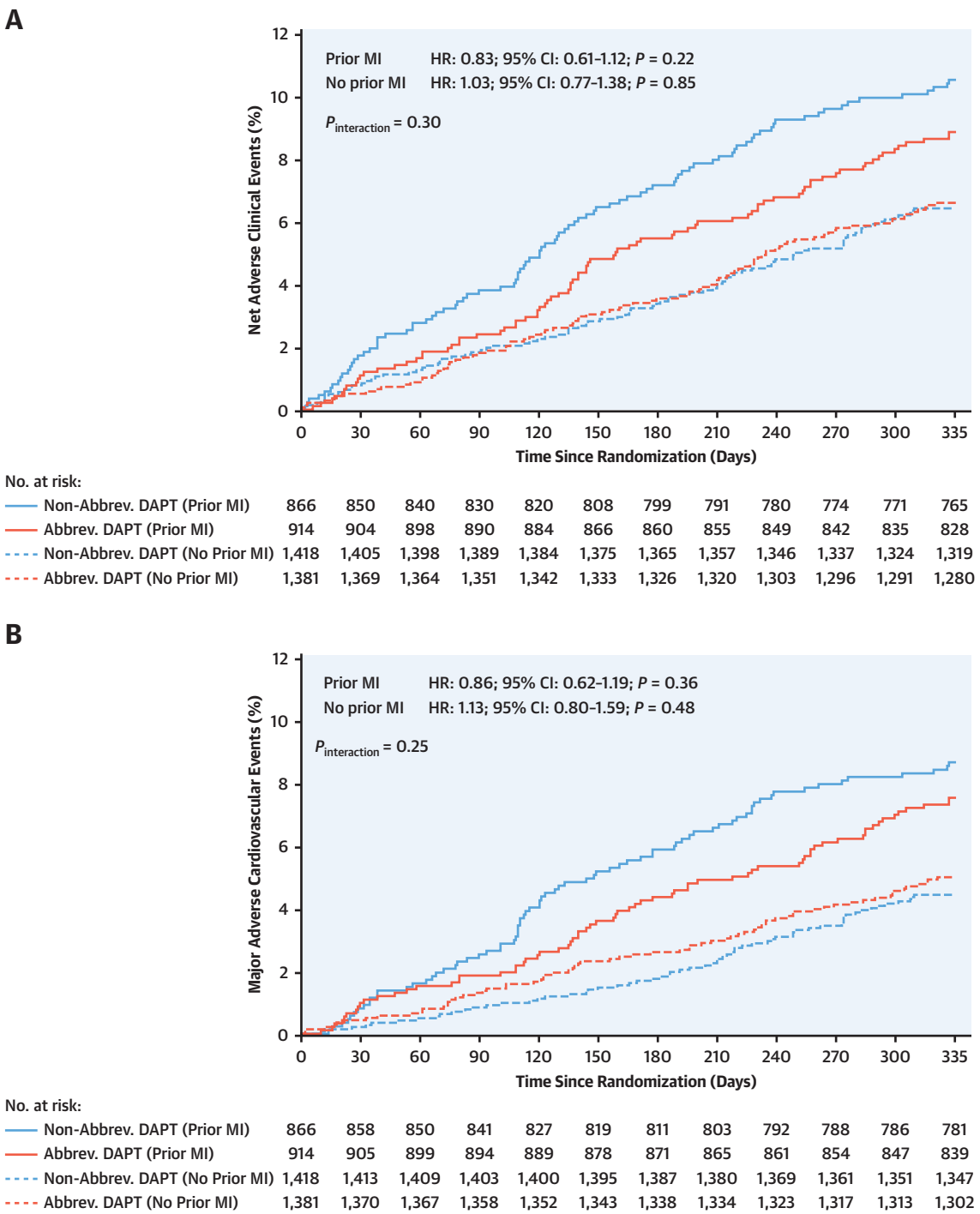
(≤12 months) myocardial infarction are shown in Table 3. NACE did not differ between the abbreviated and nonabbreviated APT groups (91 [6.6%] vs 91 [6.4%], respectively; HR: 1.03; 95% CI: 0.77-1.38; $P = 0.85$) (Figure 4A). MACCE also did not differ between the treatment groups (69 [5.0%] vs 63 [4.5%]; HR: 1.13; 95% CI: 0.80-1.59; $P = 0.48$) (Figure 4B). BARC 2, 3, or 5 bleeding occurred less frequently in the abbreviated arm (92 [6.7%] vs 132 [9.4%]; HR: 0.71; 95% CI: 0.54-0.92; $P = 0.010$) (Figure 4C). Fewer BARC 1 and BARC 2 bleedings occurred in the abbreviated APT arm ($P = 0.021$ and $P = 0.018$, respectively).

Landmark analyses at 150 days after randomization showed consistent treatment effects with respect to time for the coprimary outcomes and secondary outcomes among patients without prior (≤12 months) myocardial infarction, except for BARC 3 bleeding and stroke (Table 4).

TREATMENT EFFECTS AND EVENT RATES BETWEEN PATIENTS WITH OR WITHOUT PRIOR (≤12 MONTHS) MYOCARDIAL INFARCTION. The treatment effects between abbreviated and nonabbreviated APT were consistent in patients with or without prior (≤12 months) myocardial infarction for all coprimary outcomes and secondary outcomes, with a similar magnitude of reduction in BARC 2, 3, or 5 bleedings in the abbreviated groups of both populations.

The rate of myocardial infarction was 2-fold higher in the prior (≤12 months) vs no prior (≤12 months)

FIGURE 4 Kaplan-Meier Curves of the 3 Coprimary Outcomes and Myocardial Infarction



(A to D) Kaplan-Meier curves of the major outcomes at 11 months post randomization. **(A)** Net adverse clinical events, **(B)** major cardiovascular events, **(C)** major or clinically relevant nonmajor bleeding, and **(D)** myocardial infarction (MI) events rates over time for patients with (prior MI) or without (no prior MI) an acute or recent (<11 months) MI at index percutaneous coronary intervention (PCI). Net adverse clinical outcomes events (NACE) (composite of death, MI, stroke, or Bleeding Academic Research Consortium [BARC] 3 or 5), major adverse cardiac and cerebral events (MACCE) (death, MI, or stroke), and MI rates did not differ between abbreviated and nonabbreviated antiplatelet (APT) strategy arms in both the prior MI and no prior MI subgroups. BARC 2, 3, or 5 bleedings rates were significantly lower in the abbreviated APT arms in both the prior and no prior MI subgroups. Abbrev. = abbreviated; DAPT = dual antiplatelet therapy.

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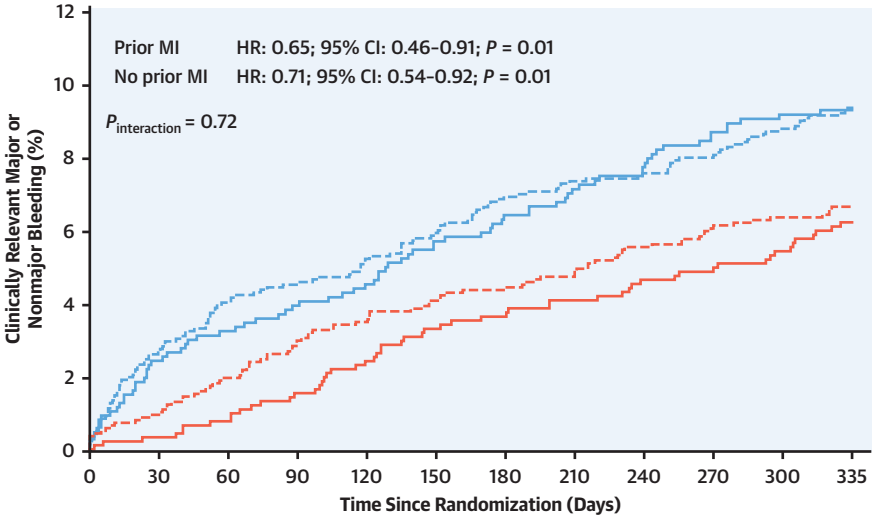
FIGURE 4 Continued

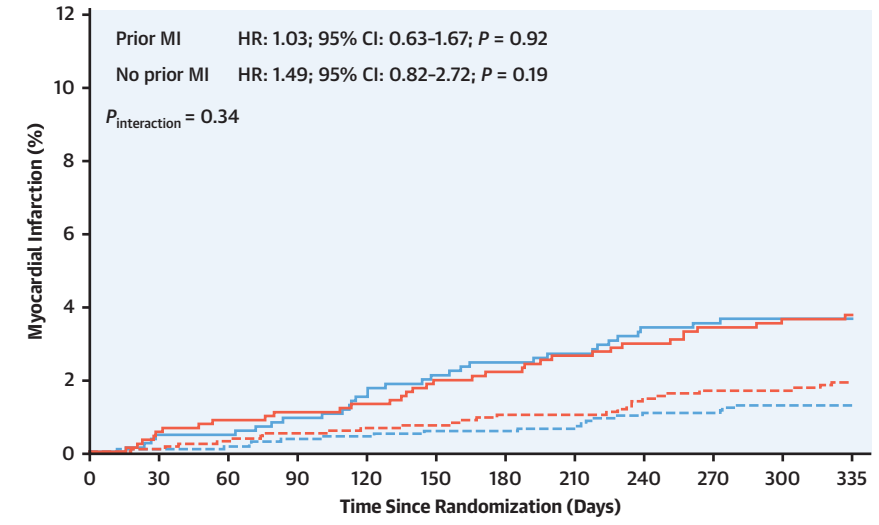
C



No. at risk:

Non-Abbrev. DAPT (Prior MI)	866	842	829	819	810	797	788	779	768	756	751	745
Abbrev. DAPT (Prior MI)	914	908	902	893	883	867	861	857	852	845	838	826
Non-Abbrev. DAPT (No Prior MI)	1,418	1,378	1,357	1,347	1,337	1,325	1,306	1,298	1,292	1,279	1,264	1,254
Abbrev. DAPT (No Prior MI)	1,381	1,361	1,347	1,330	1,319	1,306	1,300	1,293	1,278	1,272	1,264	1,252

D



No. at risk:

Non-Abbrev. DAPT (Prior MI)	866	858	851	843	830	822	814	809	799	794	792	787
Abbrev. DAPT (Prior MI)	914	906	901	896	891	880	873	867	863	856	850	842
Non-Abbrev. DAPT (No Prior MI)	1,418	1,414	1,411	1,405	1,402	1,398	1,391	1,386	1,376	1,368	1,359	1,355
Abbrev. DAPT (No Prior MI)	1,381	1,372	1,369	1,361	1,355	1,347	1,341	1,338	1,327	1,321	1,318	1,307

myocardial infarction populations, with similar event rates between abbreviated and nonabbreviated APT groups in both populations (Figure 4D). The rates of NACE, MACCE, and all-cause death were numerically higher in the prior (≤12 months) myocardial infarction population.

CONSISTENCY IN PER-PROTOCOL POPULATION AND SENSITIVITY ANALYSES. The coprimary findings

TABLE 4 Clinical Outcomes Using a Landmark at 150 Days (6-Month Visit)

	Prior MI Past 12 Months					No Prior MI Past 12 Months				
	Abbreviated DAPT	Nonabbreviated DAPT	HR (95% CI)[a]	*P* Value	$P_{interaction}$[b]	Abbreviated DAPT	Nonabbreviated DAPT	HR (95% CI)[a]	*P* Value	$P_{interaction}$[b]
ITT population										
NACE, d					0.44					0.77
0–150	44/914 (4.8)	55/866 (6.4)	0.75 (0.50–1.11)	0.15		42/1381 (3.1)	40/1418 (2.8)	1.08 (0.70–1.66)	0.73	
151–335	37/866 (4.3)	36/806 (4.5)	0.95 (0.60–1.50)	0.82		49/1333 (3.7)	51/1374 (3.7)	0.99 (0.67–1.46)	0.96	
MACE, d					0.15					0.09
0–150	32/914 (3.5)	44/866 (5.1)	0.68 (0.43–1.08)	0.10		32/1381 (2.3)	20/1418 (1.4)	1.65 (0.95–2.89)	0.08	
151–335	37/878 (4.2)	31/817 (3.8)	1.11 (0.69–1.78)	0.68		37/1343 (2.8)	43/1394 (3.1)	0.89 (0.57–1.38)	0.60	
MCB, d					0.53					0.79
0–150	30/914 (3.3)	47/866 (5.5)	0.59 (0.37–0.93)	0.02		56/1381 (4.1)	83/1418 (5.9)	0.69 (0.49–0.96)	0.029	
151–335	26/867 (3.0)	32/796 (4.1)	0.73 (0.44–1.23)	0.24		36/1306 (2.8)	49/1323 (3.7)	0.74 (0.48–1.14)	0.17	
Bleeding BARC 3 or 5, d					0.94					0.09
0–150	14/914 (1.6)	18/866 (2.1)	0.73 (0.36–1.46)	0.37		12/1381 (0.9)	22/1418 (1.6)	0.56 (0.28–1.13)	0.11	
151–335	9/883 (1.0)	11/824 (1.4)	0.76 (0.31–1.83)	0.54		20/1347 (1.5)	16/1383 (1.2)	1.28 (0.67–2.48)	0.46	
Bleeding BARC 3, d					0.99					0.040
0–150	14/914 (1.6)	16/866 (1.9)	0.82 (0.40–1.68)	0.58		12/1381 (0.9)	22/1418 (1.6)	0.56 (0.28–1.13)	0.11	
151–335	7/883 (0.8)	8/824 (1.0)	0.81 (0.29–2.24)	0.69		20/1347 (1.5)	13/1383 (1.0)	1.58 (0.79–3.18)	0.20	
Bleeding BARC 2, d					0.49					0.5
0–150	17/914 (1.9)	30/866 (3.5)	0.53 (0.29–0.96)	0.035		45/1381 (3.3)	62/1418 (4.4)	0.74 (0.50–1.09)	0.13	
151–335	18/879 (2.1)	23/808 (2.9)	0.71 (0.38–1.32)	0.28		22/1315 (1.7)	37/1343 (2.8)	0.60 (0.35–1.02)	0.06	
All-cause death, d					0.14					0.07
0–150	14/914 (1.5)	24/866 (2.8)	0.55 (0.28–1.06)	0.07		18/1381 (1.3)	10/1418 (0.7)	1.86 (0.86–4.02)	0.12	
151–335	22/896 (2.5)	19/837 (2.3)	1.08 (0.58–1.99)	0.81		21/1357 (1.6)	28/1404 (2.0)	0.77 (0.44–1.36)	0.37	
Cerebrovascular accident, d					0.69					0.20
0–150	3/914 (0.3)	7/866 (0.8)	0.40 (0.10–1.56)	0.19		5/1381 (0.4)	5/1418 (0.4)	1.03 (0.30–3.56)	0.96	
151–335	5/893 (0.6)	8/831 (1.0)	0.58 (0.19–1.77)	0.34		4/1353 (0.3)	12/1399 (0.9)	0.34 (0.11–1.06)	0.06	
Stroke,[c] d					0.99					0.046
0–150	2/914 (0.2)	4/866 (0.5)	0.47 (0.09–2.57)	0.38		5/1381 (0.4)	3/1418 (0.2)	1.72 (0.41–7.20)	0.46	
151–335	3/894 (0.3)	6/834 (0.7)	0.47 (0.12–1.86)	0.28		2/1353 (0.1)	10/1401 (0.7)	0.21 (0.05–0.94)	0.04	
MI, d					0.53					0.69
0–150	17/914 (1.9)	18/866 (2.1)	0.89 (0.46–1.72)	0.72		10/1381 (0.7)	8/1418 (0.6)	1.29 (0.51–3.27)	0.59	
151–335	17/880 (1.9)	13/820 (1.6)	1.22 (0.59–2.50)	0.60		16/1347 (1.2)	10/1397 (0.7)	1.66 (0.75–3.65)	0.21	
Definite stent thrombosis, d					0.92					0.55
0–150	3/914 (0.3)	2/866 (0.2)	1.42 (0.24–8.47)	0.70		1/1381 (0.1)	1/1418 (0.1)	1.03 (0.06–16.47)	0.98	
151–335	4/893 (0.5)	3/835 (0.4)	1.24 (0.28–5.55)	0.78		3/1356 (0.2)	1/1403 (0.1)	3.10 (0.32–29.79)	0.33	

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remained unchanged in the per-protocol population (Supplemental Table 7). An overview of protocol violations used to define the per-protocol population are summarized in Supplemental Table 8.

Sensitivity analyses by extending the prior myocardial infarction period to indefinite or by limiting it to presentation at first PCI or by including unstable angina population at first PCI showed consistent findings as in the primary analysis, apart from a significant reduction in cerebrovascular accidents in the abbreviated APT group in the any prior myocardial infarction population (Supplemental Tables 9 to 11).

DISCUSSION

The main findings of this subgroup analysis from the MASTER DAPT trial are 2-fold. First, compared with a nonabbreviated APT strategy, an abbreviated APT strategy, whereby DAPT was stopped 1 month post coronary stenting with a biodegradable polymer-coated sirolimus-eluting stent, was not associated with higher ischemic and net events in patients at high bleeding risk presenting with or without an acute or recent myocardial infarction. Second, stopping DAPT at 1 month and continuing with SAPT significantly reduced clinically relevant bleedings in

TABLE 4 Continued

	Prior MI Past 12 Months					No Prior MI Past 12 Months				
	Abbreviated DAPT	Nonabbreviated DAPT	HR (95% CI)[a]	*P* Value	$P_{interaction}$[b]	Abbreviated DAPT	Nonabbreviated DAPT	HR (95% CI)[a]	*P* Value	$P_{interaction}$[b]
PP population										
NACE, d					0.47					0.54
0–150	42/874 (4.8)	52/847 (6.2)	0.77 (0.52–1.16)	0.22		41/1330 (3.1)	36/1383 (2.6)	1.19 (0.76–1.86)	0.45	
151–335	36/830 (4.3)	35/791 (4.4)	0.97 (0.61–1.55)	0.91		46/1284 (3.6)	49/1343 (3.7)	0.98 (0.66–1.47)	0.92	
MACE, d					0.23					0.08
0–150	31/874 (3.6)	41/847 (4.9)	0.73 (0.46–1.16)	0.18		31/1330 (2.3)	19/1383 (1.4)	1.71 (0.96–3.02)	0.07	
151–335	36/841 (4.3)	31/802 (3.9)	1.10 (0.68–1.78)	0.69		35/1294 (2.7)	41/1360 (3.0)	0.89 (0.57–1.40)	0.63	
MCB, d					0.59					0.79
0–150	28/874 (3.2)	45/847 (5.4)	0.59 (0.37–0.94)	0.028		53/1330 (4.0)	79/1383 (5.7)	0.69 (0.49–0.98)	0.036	
151–335	24/831 (2.9)	31/780 (4.0)	0.72 (0.42–1.22)	0.22		35/1259 (2.8)	48/1292 (3.7)	0.74 (0.48–1.15)	0.18	
Bleeding BARC 3 or 5, d					0.95					0.21
0–150	13/874 (1.5)	17/847 (2.0)	0.73 (0.36–1.51)	0.40		12/1330 (0.9)	19/1383 (1.4)	0.66 (0.32–1.35)	0.25	
151–335	8/846 (1.0)	10/807 (1.3)	0.76 (0.30–1.92)	0.56		18/1297 (1.4)	15/1351 (1.1)	1.25 (0.63–2.48)	0.52	
Bleeding BARC 3, d					0.95					0.10
0–150	13/874 (1.5)	16/847 (1.9)	0.78 (0.37–1.62)	0.50		12/1330 (0.9)	19/1383 (1.4)	0.66 (0.32–1.35)	0.25	
151–335	6/846 (0.7)	7/807 (0.9)	0.81 (0.27–2.41)	0.71		18/1297 (1.4)	12/1351 (0.9)	1.56 (0.75–3.24)	0.23	
Bleeding BARC 2, d					0.55					0.64
0–150	16/874 (1.8)	29/847 (3.5)	0.53 (0.29–0.97)	0.039		42/1330 (3.2)	61/1383 (4.4)	0.71 (0.48–1.05)	0.09	
151–335	17/842 (2.0)	23/792 (2.9)	0.69 (0.37–1.28)	0.24		22/1268 (1.8)	37/1309 (2.9)	0.61 (0.36–1.03)	0.06	
All-cause death, d					0.21					0.06
0–150	14/874 (1.6)	23/847 (2.7)	0.59 (0.30–1.14)	0.11		18/1330 (1.4)	10/1383 (0.7)	1.88 (0.87–4.07)	0.11	
151–335	21/858 (2.5)	19/820 (2.3)	1.05 (0.57–1.95)	0.88		19/1307 (1.5)	27/1369 (2.0)	0.73 (0.41–1.32)	0.30	
Cerebrovascular accident, d					0.44					0.14
0–150	2/874 (0.2)	7/847 (0.8)	0.28 (0.06–1.32)	0.11		5/1330 (0.4)	4/1383 (0.3)	1.30 (0.35–4.85)	0.69	
151–335	5/856 (0.6)	8/814 (1.0)	0.59 (0.19–1.81)	0.36		4/1303 (0.3)	12/1365 (0.9)	0.35 (0.11–1.08)	0.07	
Stroke,[c] d					0.61					0.03
0–150	1/874 (0.1)	4/847 (0.5)	0.24 (0.03–2.15)	0.20		5/1330 (0.4)	2/1383 (0.1)	2.61 (0.51–13.45)	0.25	
151–335	3/857 (0.4)	6/817 (0.7)	0.48 (0.12–1.90)	0.29		2/1303 (0.1)	10/1367 (0.7)	0.21 (0.05–0.95)	0.043	
MI, d					0.70					0.47
0–150	17/874 (2.0)	16/847 (1.9)	1.02 (0.52–2.03)	0.95		9/1330 (0.7)	8/1383 (0.6)	1.18 (0.45–3.05)	0.74	
151–335	17/842 (2.0)	13/805 (1.6)	1.25 (0.61–2.57)	0.55		16/1298 (1.2)	9/1362 (0.7)	1.86 (0.82–4.22)	0.14	
Definite stent thrombosis, d					0.91					-
0–150	3/874 (0.4)	2/847 (0.2)	1.45 (0.24–8.68)	0.68		1/1330 (0.1)	1/1383 (0.1)	1.04 (0.07–16.66)	0.98	
151–335	4/855 (0.5)	3/818 (0.4)	1.27 (0.28–5.67)	0.76		3/1306 (0.2)	0/1368 (0.0)	-	-	

Values are n/N (% from Kaplan-Meier estimate) unless otherwise indicated. [a]HRs and 95% CIs from Cox's time-to-first event analyses, using a Landmark at 150 days post randomization. [b]Interaction *P* value for randomization (abbreviated vs standard DAPT) × period (0–150 days vs 151–335 days) modifying effect. Interaction *P* value testing for the modifying effect of prior MI in last 12 months (yes or no). [c]Includes undetermined strokes.

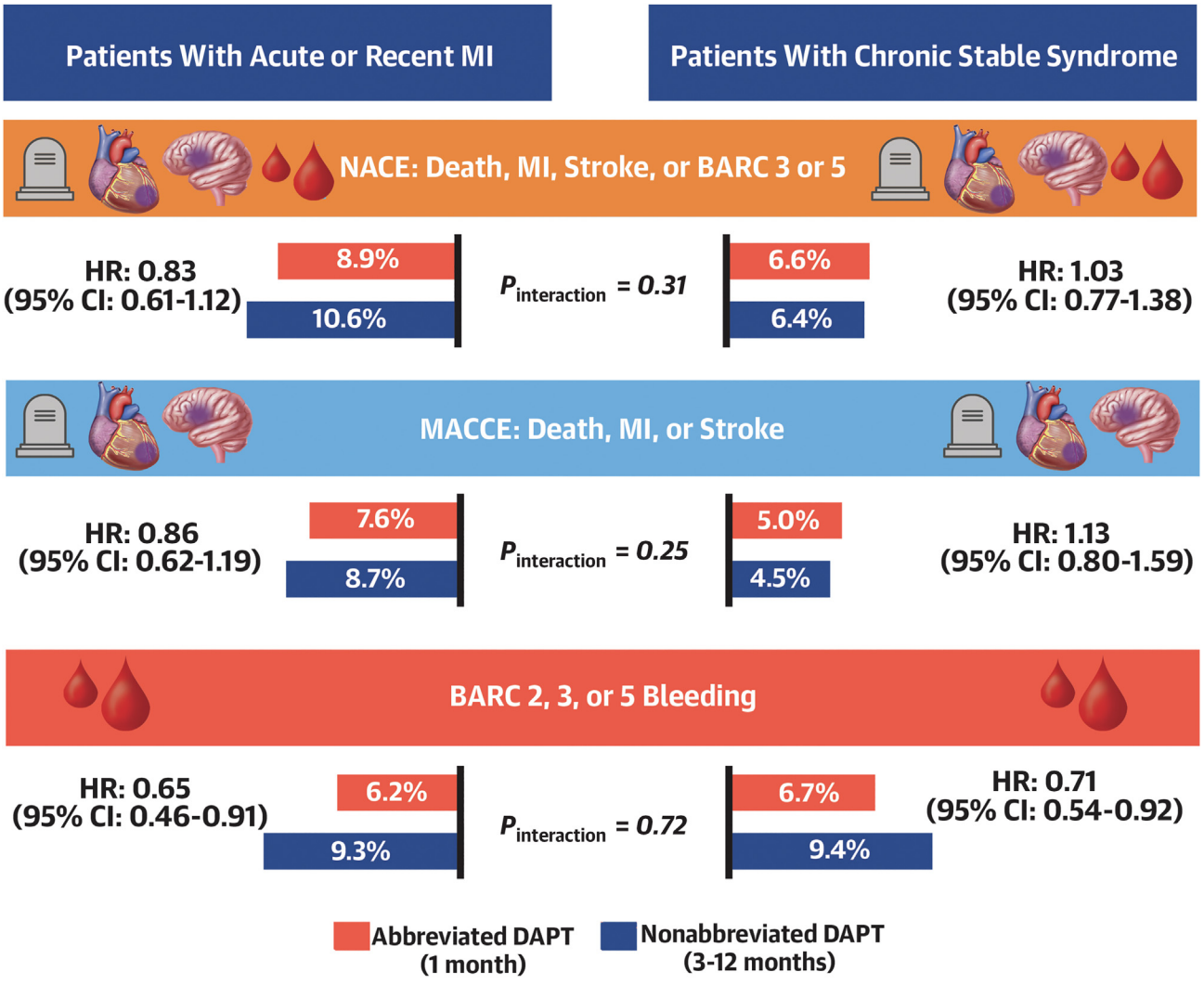
PP = per-protocol; other abbreviations as in Tables 1 and 3.

patients at high bleeding risk with or without an acute or recent myocardial infarction. These observations are supported by negative interaction testing for the 3 ranked primary or major secondary endpoints (**Central Illustration**).

These findings have the following implications: our results show that it is safe and beneficial to stop DAPT after 1 month following biodegradable polymer-coated sirolimus-eluting coronary stent implantation in patients at high bleeding risk presenting with or without an acute or recent (≤12 months) myocardial infarction.

Our results are in line with recent findings from meta-analyses of PCI trials analyzing outcomes with different DAPT regimens or examining the temporal bleeding or ischemic risk post PCI.[10-13] The network meta-analysis in 79,008 patients in 24 randomized trials by Khan et al[10] compared short-term (<6 months) DAPT, followed by SAPT with aspirin or a $P2Y_{12}$ inhibitor; midterm (6 months) DAPT; 12-month DAPT; and extended-term (>12 months) DAPT after PCI with drug-eluting stents. They found that short-term DAPT followed by $P2Y_{12}$ inhibitor monotherapy, in comparison with 12-month DAPT,

CENTRAL ILLUSTRATION **Abbreviated Antiplatelet Therapy in Patients With High Bleeding Risk With or Without Myocardial Infarction**



Smits PC, et al. J Am Coll Cardiol. 2022;80(13):1220–1237.

In the stratified subgroup analysis of the multicenter randomized controlled MASTER DAPT (Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen) trial, net adverse clinical outcomes events (NACE) and major adverse cardiac and cerebral events (MACCE) rates did not differ between a 1-month abbreviated dual therapy (DAPT) strategy compared with a nonabbreviated DAPT strategy (3-12 months DAPT) in both subgroups in which patients presented with or without an acute myocardial infarction (MI) or recent history (<11 months) of MI at index percutaneous coronary intervention. The major and nonmajor clinical relevant bleeding rates (Bleeding Academic Research Consortium [BARC] 2, 3, or 5) were significantly lower with the abbreviated DAPT strategy compared with the nonabbreviated DAPT strategy in both subgroups. NACE was defined as the composite of all-cause death, MI, stroke, and BARC 3 or 5 bleeding. MACCE was defined as the composite of all-cause death, MI, and stroke. BARC is bleeding according to the Bleeding Academic Research Consortium endpoints.

was noninferior for myocardial infarction, major adverse cardiovascular event, and death, and superior for major bleeding and NACE. Furthermore, sensitivity analysis favored 1 to 3 months of DAPT followed by $P2Y_{12}$ inhibitor monotherapy for reducing bleeding and having comparable cardiovascular outcomes in comparison with 12 months of DAPT.

These results are similar to our findings, although our study specifically focused on patients at high bleeding risk with acute or recent myocardial

infarction, a specific complex population, as these bi-risk patients simultaneously carry features that increase bleeding and ischemic risk. Other meta-analyses examining the temporal bleeding and ischemic risk post PCI indicate that in patients with ACS, ischemic risk exceeds bleeding in the first 3 months post PCI, whereas after this, the bleeding risk exceeds ischemia,[11,12] although in our study in patients with ACS at high bleeding risk, we found no difference in ischemic risk after 1 month and a significant reduction in bleeding risk.

Our results are discordant with the recently presented STOPDAPT-2 ACS (ShorT and OPtimal duration of Dual AntiPlatelet Therapy after everolimus-eluting cobalt-chromium stent) trial results.[14] The STOPDAPT-2 ACS trial enrolled 2,988 patients with ACS and pooled the results with the 1,148 patients with ACS from the STOPDAPT-2 trial,[15] for a total of 4,136 patients. Both trials used the same protocol. Participants were randomly assigned in a 1:1 ratio to 1-month DAPT followed by clopidogrel monotherapy or 12 months DAPT after PCI with cobalt-chromium everolimus-eluting stents. STOPDAPT-2 ACS showed that 1-month DAPT followed by clopidogrel monotherapy for 11 months did not meet criteria for non-inferiority compared with a standard 12-month duration of DAPT for the composite NACE outcome, because a trend toward increased ischemic events occurred in the 1-month DAPT group despite a reduction in major bleeds. These differences in ischemic and NACE outcomes can be explained by several reasons. In comparison with STOPDAPT-2 ACS, the MASTER DAPT trial left the choice of SAPT at the discretion of the operator. In the prior myocardial infarction subgroups, 25% to 32% of patients continued with ticagrelor as monotherapy, whereas in the abbreviated DAPT group of STOPDAPT-2 ACS, all patients were treated with monotherapy clopidogrel, a less potent $P2Y_{12}$ receptor blocker and less protective against ischemic events in patients with ACS compared with ticagrelor or prasugrel.[16,17] Second, STOPDAPT-2 ACS was conducted in Japan, and the prevalence of clopidogrel non-responders in Japan is approximately 14%.[18] Furthermore, in contrast to STOPDAPT-2 ACS, MASTER DAPT selected exclusively patients at high bleeding risk in whom the reduction in bleeding events by an abbreviated DAPT strategy is likely more prominent. On the other hand, an abbreviated DAPT strategy has the potential to increase ischemic events. These opposite effects can potentially equalize NACE rates between abbreviated and prolonged DAPT strategies. However, this was not observed in this prior myocardial infarction substudy of MASTER DAPT, as no increase in ischemic events but a significant reduction in bleeding events occurred, resulting in a numerically lower NACE rate for the abbreviated APT group in the population with an acute or recent myocardial infarction.

In the population with an acute or recent myocardial infarction, numerically fewer ischemic events occurred with the abbreviated vs nonabbreviated APT strategy. This was caused primarily by numerically lower all-cause death and stroke rates in the abbreviated APT arm, as myocardial infarction rates were similar in both APT strategy arms. This observation cannot be explained by differences in use of more potent $P2Y_{12}$ receptor blockers in the abbreviated APT group. At 1, 3, and 6 months, the use of ticagrelor as monotherapy in the abbreviated APT arm was 26%, 25%, and 24%, respectively, whereas the use of ticagrelor in combination with aspirin in the non-abbreviated APT arm was 34%, 32%, and 30%, respectively. The use of prasugrel was low (between 1% and 3%) in both arms. Likely the reduced bleeding risk and its positive effect on cardiovascular death and the observed occurrence of fewer ischemic strokes in an abbreviated APT strategy in the OAC population may explain this apparently paradoxical observation.[19] On the other hand, play of change cannot be ruled out.

Our study compared a 1-month vs a predominantly 12-month DAPT strategy in this ACS population. Whether a 3-month DAPT strategy followed by SAPT with ticagrelor-only strategy, as in the TWILIGHT (Ticagrelor With Aspirin or Alone in High-Risk Patients After Coronary Intervention)[20] and TICO (Ticagrelor Monotherapy After 3 Months in the Patients Treated With New Generation Sirolimus Stent for Acute Coronary Syndrome)[21] trials, in terms of NACE and MACCE, is better without compromising the reduction in bleeding remains to be explored. Only the TWILIGHT trial has reported the outcomes in a population at high bleeding risk, showing a significant reduction in major bleedings and no differences in the composite ischemic outcomes between the abbreviated and nonabbreviated aspirin groups in conjunction with the use of ticagrelor. Contrary to the TWILIGHT high bleeding risk subgroup analysis, our subgroup analysis showed no differences in BARC 3 or 5 bleedings between the abbreviated and non-abbreviated DAPT strategies. Despite differences between the TWILIGHT and MASTER DAPT populations (TWILIGHT excluded patients at very high bleeding risk, including those with a clinical indication for OAC and dialysis), the rates of BARC 3 or 5 bleedings in the TWILIGHT trial were significantly lower in the abbreviated DAPT arm (1.6% vs 5.0%; HR: 0.31;

95% CI: 0.14-0.67), whereas this was only 2.6% vs 3.4% in the MASTER DAPT prior myocardial infarction group and 2.4 vs 2.7% in the no prior myocardial infarction group (abbreviated vs nonabbreviated, respectively). The on-average lower rates of BARC 3 or 5 bleeding in MASTER DAPT, despite the higher bleeding risk compared with TWILIGHT, can be explained by a more personalized approach by the treating physician, in which a $P2Y_{12}$ receptor blocker in combination with aspirin or as monotherapy should be prescribed for each individual patient. In that respect, shortening DAPT to 1 month and selecting the type of $P2Y_{12}$ receptor blocker based on history and clinical presentation, together with coronary patho-anatomy and treatment parameters, appears to be the best way to treat patients with high bleeding risk post PCI for now.

STUDY LIMITATIONS. This was a subgroup analysis (albeit the subgroups were prespecified and stratified at randomization). The subgroups were not powered for the coprimary and individual outcomes, such as myocardial infarction and stent thrombosis, therefore the results should therefore be interpreted with caution. In addition, the stratified subgroup of patients with acute or recent myocardial infarction consisted mainly of patients with NSTEMI (65.1%) and less of patients with STEMI (29.9%) at first PCI, limiting the interpretation for patients with STEMI. Furthermore, the 95% CI and *P* values for interaction were not adjusted for multiplicity and the results should not be used to infer definitive treatment effects.

Treatment allocation was open label, which reflects a treatment-strategy trial and the impossibility of masking treatment for 3 oral $P2Y_{12}$ inhibitors and aspirin. Randomization was done at 1 month if the patient was free of ischemic and active bleeding events. This could indicate that patients at lower ischemic risk were selected; however, allowing patients to enter the trial only after 30 days of uneventful follow-up mimics clinical practice and prevents the inclusion of patients in whom the clinical equipoise between DAPT continuation or discontinuation is questionable and unethical. Our trial included patients at high risk for bleeding who underwent biodegradable polymer sirolimus-eluting stent implantation; consequently, our results may not extend to patients who are not at high bleeding risk or received other stent types or to countries where this stent is not available. Furthermore, this subgroup analysis focused on patients presenting with or without an acute or recent myocardial infarction and not on complex or noncomplex PCI. For these results, we refer to the recent published complex PCI substudy of the MASTER DAPT trial.[22]

CONCLUSIONS

In patients at high bleeding risk presenting with or without acute or recent myocardial infarction, stopping DAPT 1 month after coronary stenting was associated with lower bleeding risk and no increased ischemic risk in comparison with continuing DAPT for 2 to 11 months.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS:

Patients with myocardial infarction at high risk of bleeding after coronary stenting may stop DAPT after 1 month to avoid bleeding. Although this might increase the risk of ischemic events, no increase was observed in the MASTER-DAPT trial.

TRANSLATIONAL OUTLOOK: More research is needed to delineate specific clinical and angiographic features that identify patients optimally treated with shorter or longer period of DAPT following PCI.

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KEY WORDS acute coronary syndrome, antiplatelet therapy, dual antiplatelet therapy, percutaneous coronary intervention

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