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Peer-reviewed author version

Sardella, Gennaro; Spirito, Alessandro; Sartori, Samantha; Angiolillo, Dominick J.; VRANCKX, Pascal; Hernandez, Jose M. De la Torre; Krucoff, Mitchell W.; Bangalore, Sripal; Bhatt, Deepak L.; Campo, Gianluca; Cao, Davide; Chehab, Bassem M.; Choi, James W.; Feng, Yihan; Ge, Junbo; Godfrey, Katherine; Hermiller, James; Kunadian, Vijay; Makkar, Raj R.; Maksoud, Aziz; Neumann, Franz-Josef; Picon, Hector; Saito, Shigeru; Thiele, Holger; Toelg, Ralph; Varenne, Olivier; Vogel, Birgit; Zhou, Yujie; Valgimigli, Marco; Windecker, Stephan & Mehran, Roxana (2024)
1-Versus 3-Month DAPT in Older Patients at a High Bleeding Risk Undergoing PCI: Insights from the XIENCE Short DAPT Global Program. In: AMERICAN JOURNAL OF CARDIOLOGY, 214 , p. 94 -104.

DOI: 10.1016/j.amjcard.2023.12.049
Handle: http://hdl.handle.net/1942/42934

One- versus three-month DAPT in older patients at high bleeding risk undergoing PCI: insights from the XIENCE Short DAPT Global Program

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Running title: One- vs. three-month DAPT in older patients after PCI

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Funding
The study was sponsored by Abbott (Chicago, IL, USA).

Financial disclosures
Dr. Spirito received a research grant for the Swiss National Science Foundation.
Dr. Angiolillo declares that he has received consulting fees or honoraria from Abbott, Amgen, AstraZeneca, Bayer, Biosensors, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, Daiichi-Sankyo, Eli Lilly, Haemonetics, Janssen, Merck, Novartis, PhaseBio, PLx Pharma, Pfizer, Sanofi and Ventura, outside the present work. D.J.A. also declares that his institution has received research grants from Amgen, AstraZeneca, Bayer, Biosensors, CeloNova, CSL Behring, Daiichi-Sankyo, Eisai, Eli Lilly, Gilead, Janssen, Matsutani Chemical Industry Co., Merck, Novartis, Osprey Medical, Renal Guard Solutions and Scott R. MacKenzie Foundation.
Dr Bangalore received Consulting fees or been on the advisory board for Abbott Vascular, Boston Scientific, Biotronik, Amgen, Pfizer,Merck, Viatris, and REATA
Dr. Vranckx received personal fees from Daichii Sankyo, Bayer AG, Pfizer-Bristol Meyers Squibb alliance, Novartis, CSL Behring not related to this research.
Dr. Bhatt has served on advisory boards for AngioWave, Bayer,Boehringer Ingelheim, Cardax, CellProthera, Cereno Scientific,Elsevier Practice Update Cardiology, High Enroll, Janssen, Level Ex,McKinsey, Medscape Cardiology, Merck, MyoKardia, NirvaMed, NovoNordisk, PhaseBio, PLx Pharma, Regado Biosciences, and Stasys; hasserved on boards of directors for AngioWave, the Boston VA ResearchInstitute, Bristol Myers Squibb, DRS.LINQ, High Enroll, the Society ofCardiovascular Patient Care, and TobeSoft; has stock or stock optionswith AngioWave, Bristol Myers Squibb, and DRS.LINQ; has served asinaugural chair of the American Heart Association Quality OversightCommittee; has been a consultant for Broadview Ventures; hasserved on data monitoring committees for Acesion Pharma, Assis-tance Publique-Hôpitaux de Paris, the Baim Institute for ClinicalResearch (formerly Harvard Clinical Research Institute, for the POR-TICO trial, funded by St. Jude Medical, now Abbott), Boston Scientific(chair, PEITHO trial), Cleveland Clinic (including for the ExCEED trial,funded by Edwards Lifesciences), Contego Medical (chair, PERFOR-MANCE 2 trial), Duke Clinical Research Institute, Mayo Clinic, MountSinai School of Medicine (for the ENVISAGE trial, funded by Daiichi-Sankyo; and for the ABILITY-DM trial, funded by Concept Medical),Novartis, Population Health Research Institute, and Rutgers Univer-sity (for the NIH-funded MINT trial); has received honoraria from theAmerican College of Cardiology (senior associate editor, Clinical Tri-als and News, ACC.org, and chair of the ACC Accreditation OversightCommittee), Arnold and Porter law firm (work related to Sanofi/Bristol Myers Squibb clopidogrel litigation), Baim Institute for ClinicalResearch (formerly Harvard Clinical Research Institute; RE-DUAL PCIclinical trial steering committee funded by Boehringer Ingelheim;AEGIS-II executive committee funded by CSL Boehringer), BelvoirPublications (Editor-in-Chief, Harvard Heart Letter), Canadian Med-ical and Surgical Knowledge Translation Research Group (clinical trialsteering committees), Cowen and Company, Duke Clinical ResearchInstitute (clinical trial steering committees, including for the PRO-NOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global(Editor-in-Chief, Journal of Invasive Cardiology), Journal of theAmerican College of Cardiology (guest editor; associate editor), K2P(cochair, interdisciplinary curriculum), Level Ex, Medtelligence/ReachMD (CME steering committees), MJH Life Sciences, OakstoneCME (course director, Comprehensive Review of Interventional Cardi-ology), Piper Sandler, Population Health Research Institute (for theCOMPASS operations

committee, publications committee, steeringcommittee, and USA national coleader, funded by Bayer), SlackPublications (chief medical editor, Cardiology Today's Intervention),Society of Cardiovascular Patient Care (secretary/treasurer), WebMD(CME steering committees), and Wiley (steering committee); hasother relationships with Clinical Cardiology (deputy editor), NCDR-ACTION Registry Steering Committee (chair), and VA CARTResearch and Publications Committee (chair); has been named on apatent for sotagliflozin assigned to Brigham and Women's Hospital who assigned to Lexicon (neither Dr Bhatt nor Brigham and Women'sHospital receives any income from this patent); has received researchfunding from 89Bio, Abbott, Acesion Pharma, Afimmune, Aker Bio-marine, Amarin, Amgen, AstraZeneca, Bayer, Beren, BoehringerIngelheim, Boston Scientific, Bristol Myers Squibb, Cardax, CellPro-thera, Cereno Scientific, Chiesi, CSL Behring, Eisai, Ethicon, FaradayPharmaceuticals, Ferring Pharmaceuticals, Forest Laboratories,Fractyl, Garmin, HLS Therapeutics, Idorsia, Ironwood, Ischemix,Janssen, Javelin, Lexicon, Lilly, Medtronic, Merck, Moderna, Myo-Kardia, NirvaMed, Novartis, Novo Nordisk, Owkin, Pfizer, PhaseBio,PLx Pharma, Recardio, Regeneron, Reid Hoffman Foundation, Roche,Sanofi, Stasys, Synaptic, The Medicines Company, and Youngene; hasreceived royalties from Elsevier (editor, Cardiovascular Intervention:A Companion to Braunwald's Heart Disease); has been a site coinves-tigator for Abbott, Biotronik, Boston Scientific, CSI, Endotronix, St.Jude Medical (now Abbott), Philips, SpectraWAVE, Svelte, andVascular Solutions; has been a trustee for the American College ofCardiology; and has performed unfunded research for FlowCo andTakeda.

Dr Campo received institutional research grants outside the present work.

Dr. Neumann received grants or fees from Amgen, Bayer Health Care, Biotronic, Boehringer Ingelheim, Boston Scientifc, Daiichi Sankyo, Edwards Lifesciences, Ferrer, Pfizer, Novartis, GlaxoSmithKline, Abbott Vascular, and Medtronic

Dr. Toelg received speaker honoraria from Boston Scientific, Abbott Vascular, and Biotronik.

Dr. Windecker reports research, travel or educational grants to the institution from Abbott, Abiomed, Amgen, Astra Zeneca, Bayer, Biotronik, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cardinal Health, CardioValve, Corflow Therapeutics, CSL Behring, Daiichi Sankyo, Edwards Lifesciences, Guerbet, InfraRedx, Janssen-Cilag, Johnson & Johnson, Medicure, Medtronic, Merck Sharp & Dohm, Miracor Medical, Novartis, Novo Nordisk, Organon, OrPha Suisse, Pfizer, Polares, Regeneron, Sanofi-Aventis, Servier, Sinomed, Terumo, Vifor, V-Wave.

Dr. Valgimigli reports personal fees from Astra Zeneca, grants and personal fees from Terumo, personal fees from Alvimedica/CID, personal fees from Abbott Vascular, personal fees from Daiichi Sankyo, personal fees from Opsens, personal fees from Bayer, personal fees from CoreFLOW, personal fees from IDORSIA PHARMACEUTICALS LTD, personal fees from Universität Basel | Dept. Klinische Forschung, personal fees from Vifor, personal fees from Bristol Myers Squib SA, personal fees from iVascular, personal fees from Medscape, outside the submitted work.

Dr. Windecker serves as advisory board member and/or member of the steering/executive group of trials funded by Abbott, Abiomed, Amgen, Astra Zeneca, Bayer, Boston Scientific, Biotronik, Bristol Myers Squibb, Edwards Lifesciences, Janssen, MedAlliance, Medtronic, Novartis, Polares, Recardio, Sinomed, Terumo, V-Wave and Xeltis with payments to the institution but no personal payments. He is also member of the steering/executive committee group of several investigator-initiated trials that receive funding by industry without impact on his personal remuneration.

Dr. Mehran reports institutional research payments from Abbott, Abiomed, Alleviant Medical, Amgen, AM-Pharma, Arena, AstraZeneca, Atricure, Bayer, Biosensors, Biotronik, Boston

Scientific, Bristol-Myers Squibb, CardiaWave, CeloNova, Chiesi, Concept Medical, CSL Behring, Cytosorbents, Daiichi Sankyo, Element Science, Faraday, Humacyte, Idorsia Pharmaceuticals, Janssen, Medtronic, Novartis, OrbusNeich, PhaseBio, Philips, Pi-Cardia, PLx Pharma, RenalPro, RM Global, Shockwave, Vivasure, Zoll; personal fees from Cine-Med Research, Novartis, WebMD; Equity <1% in Applied Therapeutics, Elixir Medical, Stel, ControlRad (spouse); Scientific Advisory Board for AMA, ACC (BOT Member), SCAI (Women in Innovations Committee Member), JAMA Associate Editor; Faculty CRF (no fee).

The other authors have nothing to disclose.

Abstract

Background: This analysis aims to evaluate the effect of 1- versus 3-month dual antiplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) in older patients with high bleeding risk (HBR) features.

Methods: Data from three prospective, single-arm studies (XIENCE Short DAPT Program), including HBR patients successfully treated with an everolimus-eluting stent (XIENCE, Abbott) were analyzed. Subjects were eligible for DAPT discontinuation at 1 month or at 3 months, if free from ischemic events and adherent to DAPT. Patients were stratified according to age (≥75 and <75 years). The primary endpoint was all-cause death or myocardial infarction (MI). The key secondary endpoint was Bleeding Academic Research Consortium (BARC) type 2-5 bleeding. Outcomes were assessed from 1 to 12 months after index PCI.

Results: Out of 3,364 patients, 2,241 (66.6%) were ≥75 years old. The risk of death or MI was similar with 1- vs 3-month DAPT in patients ≥75 (8.5% vs 8.0%, adj. HR 0.95, 95% CI 0.69-1.30) and <75 years old (6.9% vs 7.8%, adj. HR 0.97, 95% CI 0.60-1.57; interaction p-value 0.478). BARC type 2-5 bleeding was consistently lower with 1- than with 3-month DAPT in patients ≥75 years old (7.2% vs 9.4%, adj. HR 0.66, 95% CI 0.48-0.91) and <75 years old (9.7% vs 11.9%, adj. HR 0.86, 95% CI 0.57-1.29; interaction p-value 0.737).

Conclusion: Among HBR patients undergoing PCI, patients older and younger than 75 years derived a consistent benefit from 1- as compared with 3-month DAPT in terms of reduction of bleeding events with no increase in all-cause death or MI.

Key words

Percutaneous coronary intervention; high bleeding risk; elderly; dual antiplatelet therapy.

Commented [PV1]: Age is a high bleeding risk feature per se, should we state elderly with other HBR features?

Abbreviations and Acronyms:

ACS=acute coronary syndrome

ARC=Academic Research Consortium

BARC=Bleeding Academic Research Consortium

CABG=coronary artery bypass graft

CCS=chronic coronary syndrome

CKD=chronic kidney disease

CTO=chronic total occlusion

DAPT=dual antiplatelet therapy

DES=drug-eluting stent

HBR=high bleeding risk

LVEF=left ventricular ejection fraction

MI=myocardial infarction

NSTEMI=non-ST segment elevation myocardial infarction

PCI=percutaneous coronary intervention

ST=stent thrombosis

STEMI=ST-elevation myocardial infarction

TLR=target lesion revascularization

TVR=target vessel revascularization

Introduction

Given the rapidly aging population, 1 in 6 people worldwide is expected to be over the age of 65 by the year 2050 [1, 2]. Coronary artery disease (CAD) is a frequent condition and the leading cause of death in this patient group [1, 3]. Since the number of elderly patients undergoing percutaneous coronary intervention (PCI) to improve symptoms, quality of life or to reduce the recurrent ischemic events is steadily increasing [4], a better understanding of the most appropriate management for these patients is needed.

Dual antiplatelet therapy (DAPT) is the standard of care to reduce the rate of recurrent ischemic events after PCI [5-7]. However, the benefits of DAPT are offset by an increased risk of bleeding complications, which are associated with considerable morbidity and mortality [7-9]. Even though older patients are more prone to have recurrent ischemic events after PCI than their younger counterpart [10, 11], several studies demonstrated that older age is a stronger predictor of bleeding than of thrombotic events [8, 12, 13]. Accordingly, age ≥75 years was identified as a minor criterion of high bleeding risk (HBR) by the Academic Research Consortium (ARC) and it has been included in other tools for bleeding risk assessment [6, 14-16]. Even though several studies demonstrated that elderly patients may benefit from a shorter (<6 months) dual antiplatelet therapy (DAPT), the optimal DAPT duration that would provide the right amount of antithrombotic effect with minimal bleeding-related harm in this subgroup of patients is still unclear [17-19].

The aim of this study was to evaluate the effect of 1- versus 3-month DAPT among older patients with HBR features that underwent successful PCI in a large prospective multicenter series of studies.

Method

Study design

The XIENCE Short DAPT program included 3 prospective, multi-center, single-arm studies, whose rational design, and main findings have been previously reported [20, 21]. Sponsored by Abbott, the studies explored two different DAPT durations (1 and 3-month) in HBR patients undergoing PCI with implantation of a fluoropolymer-based cobalt-chromium everolimus-eluting stent (XIENCE, Abbott). The 1-month DAPT program consisted of the XIENCE 28 USA study (NCT03815175), which was conducted at 58 sites in the US and Canada, and the XIENCE 28 Global study (NCT03355742), which was conducted at 52 sites in Europe and Asia. Despite being conducted separately, the XIENCE 28 studies were prespecified as being pooled together for the statistical analysis. The 3-month DAPT program consisted of the XIENCE 90 study (NCT03218787), which was conducted at 101 sites in the United States.

The study protocols were approved by national regulatory agencies, institutional review boards, or ethics committees of participating sites. An independent data monitoring committee provided external supervision for public safety. All enrolled patients provided written informed consent [21].

Study population

The study protocols of the XIENCE 28 and XIENCE 90 were nearly identical, with the exception of DAPT duration [21]. Patients undergoing successful PCI with fluoropolymer based cobalt-chromium everolimus-eluting stent (XIENCE, Abbott) were eligible for inclusion in the XIENCE 28 and 90 studies if they met at least 1 of the following HBR criteria: age ≥75 years, clinical indication for long-term (at least 6-months) oral anticoagulation (OAC), history of major bleeding in the previous 12-months, history of ischemic or hemorrhagic stroke, renal insufficiency

(serum creatinine ≥2mg/dL) or failure (requiring renal replacement therapy), anemia (with hemoglobin <11g/dL), and systemic conditions associated with an increased bleeding risk (including thrombocytopenia or any coagulation disorder). Study protocol allowed for intervention of ≤3 target lesions, with a maximum of two lesions per epicardial vessel, and of bifurcation lesions not requiring 2-stent techniques. Patients were excluded from the XIENCE 28 and 90 studies if they presented with any of the following: acute ST-elevation myocardial infarction (STEMI) or known left ventricular ejection fraction (LVEF) <30% at time of index PCI, implantation of another drug-eluting stent (DES) (other than XIENCE) within 12-months of index-procedure, implantation of overlapping stents, or target lesion located in the left main, within an arterial or saphenous vein graft, within a previously implanted stent, or at a site of chronic total occlusion (CTO) (**Supplementary Table 1**).

Per XIENCE 28 and 90 protocols, all patients received open-label aspirin 75 to 100 mg plus a $P2Y_{12}$ inhibitor after index PCI; clopidogrel 75mg was preferred, though not mandatory, and the final decision was taken by the treating physician. Subjects were eligible for DAPT discontinuation at 1- or 3-months in XIENCE 28 and XIENCE 90, respectively, if they were adherent to DAPT and free from MI, repeat coronary revascularization, stroke, or stent thrombosis (ST). In patients meeting these criteria, one antiplatelet agent was discontinued; per-protocol requirement aspirin should have been maintained. Follow-up study visits or phone calls occurred at 1, 3, 6, and 12 months after index PCI in XIENCE 28, and at 3, 6, and 12 months in XIENCE 90. Given that eligibility to discontinue DAPT was assessed at different time points in the 2 studies, patients from XIENCE 90 who were event-free and adherent to treatment at 1 month were retrospectively identified to mimic the design of the XIENCE 28 registries.

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Endpoints

The primary endpoint was the composite of all-cause death or MI defined by the modified Academic Research Consortium definition.[22] The key secondary endpoint was BARC type 2-5 bleeding.[23] Other secondary endpoints included: individual components of the primary endpoint, cardiovascular death, definite or probable ST, stroke, target vessel revascularization (TVR), target lesion revascularization (TLR), and BARC type 3-5 bleeding. Outcomes were assessed between 1 and 12 months after index PCI, and all clinical events were adjudicated by an independent external committee. Comprehensive definitions of the primary and secondary endpoints can be reviewed in **Supplementary Table 2**.

Statistical analysis

For this study, patients were divided in two age groups (≥75 and age <75 years old, respectively). Baseline and procedural continuous variables were summarized by means and standard deviations, categorical variables by counts and percentages. Chi-square and Student's t-test were used to compare data, as appropriate. Outcome incidence was calculated with the Kaplan-Meier method and compared between groups using the log-rank test for the time to first event. Cox proportional hazard models were used to compare the unadjusted risk for the primary and secondary outcomes. Because treatment arms were not randomized, adjusted risks for all endpoints were estimated using propensity score stratification into quintiles, consistently with the main study design.[20] Propensity scores (patients' estimated probability of receiving 1- or 3-month DAPT) were derived using a logistic regression model that included the study group as the outcome and the following baseline demographic, clinical, and procedural covariates as the predictors: sex, body

mass index (BMI), hypertension, hypercholesterolemia, diabetes, prior PCI, prior coronary artery bypass graft (CABG), prior MI, history of stroke, history of major bleeding, baseline serum creatinine, platelet and hemoglobin counts, acute coronary syndrome (ACS), multi-vessel disease, B2/C lesion, total lesion length, mean pre-reference vessel diameter (RVD), mean pre-diameter stenosis (DS), bifurcation lesion, number of lesions treated, number of vessels treated, number of stents, total stent length, PARIS risk score, PRECISE DAPT risk score, P2Y12 at discharge, anticoagulation therapy.

The Markov Chain Monte Carlo multiple imputation method was used to handle missing data in the propensity score building. The Rubin's combination rule was used to integrate the final analysis with each of the 10 imputed data sets. The stratification weight was based on the total sample size in each stratum relative to the overall sample size for both arms. A p-value for interaction between DAPT duration (1- versus 3-month) and age was calculated and values <0.05 were considered significant. All statistical analyses were performed with Stata version 18 (StataCorp, College Station, Texas).

Results

Patient Population

The XIENCE Short DAPT program enrolled a total of 3,652 patients from July 19, 2017, to February 7, 2020. After exclusion of 213 (13.3%) patients from XIENCE 28 and 75 (3.7%) from XIENCE 90 because of adverse events, DAPT non-adherence or consent withdrawal within 1 month after PCI, the final cohort consisted of 3,364 patients, of whom 2,241 (66.6%) were ≥75 years old (**Supplementary Figure 1**). Follow-up at 12 months was completed by the great majority of patients (98.4% in XIENCE 28 and 94.7% in XIENCE 90).

Patients in the ≥75 years old group were on average 15 years older (mean age 80.5±4.3 vs 65.3±7.1 years), more likely to be women, White, to have chronic kidney disease (CKD) (eGFR <60mL/min) or prior PCI (**Supplementary Table 3**). Older patients had a higher number of fulfilled HBR criteria (1.6±0.7 vs 1.3±0.5), PARIS, and PRECISE DAPT scores (**Supplementary Table 3**); however, <50% had any of the HBR criteria other than age ≥75 years (**Figure 1**).

Among patients ≥75 years old, 949 (42.3%) received 1-month DAPT and 1,292 (57.7%) 3-month DAPT; within patients <75 years old, 443 (39.4%) and 680 (60.6%) were in the 1- and 3-month DAPT groups, respectively. Most baseline and procedural characteristics were well balanced between the 1- and 3-month groups, except for non-White race, hypertension, dyslipidemia, prior CABG (more frequent in the 1-month DAPT groups); CKD, presentation with NSTEMI, radial access, a bifurcation lesion and longer total stent length (higher in the 3-month DAPT groups) (**Table 1 and 2)**.

At discharge, Clopidogrel was the most frequently prescribed $P2Y_{12}$ inhibitor (>80% of patients) and slightly more often in the 1-month than in the 3-month DAPT cohort; use of aspirin was lower and use of OAC slightly higher in the 1-month group (**Table 2**). In about 30% of patients, the DAPT duration was shorter than the 1 or 3 months mandated by the study protocol, and in the 3-month DAPT group, early discontinuation was more frequent in older (≥75 years) than in younger patients (**Figure 2**). Conversely, longer than recommended DAPT duration occurred in only 3% patients in the 1-month DAPT group and in 14% of patients in the 3-month group.

Outcomes by age

There were no significant differences between patients ≥75 years and <75 years old concerning the rate of all-cause death or MI (8.2% vs. 7.4%, HR 1.11, 95% CI 0.85-1.45, p-value 0.464) or of the individual ischemic endpoints from 1 to 12 months after index PCI. Conversely, among patients ≥75 years compared to patients <75 years old, the risk of BARC type 2-5 bleeding (8.5% vs 10.9%; HR 0.78, 95% CI 0.61-0.99, p=0.038) and BARC type 3-5 bleeding (3.9% vs 5.3%, HR 0.70, 95% CI 0.50-0.99, p=0.043) was lower (**Figure 3 and 4**).

Effects of 1- vs 3-month DAPT

At 1-year after PCI, among patients ≥75 years the composite of all-cause death or MI occurred in 75 (8.5%) patients on 1-month DAPT and 96 (8.0%) patients on 3-months DAPT, determining a similar effect of the two regimens on this outcome (HR 0.95, 95% CI 0.69-1.30) (**Figure 5**). Similarly, there was no significant difference between 1- and 3-month DAPT concerning all-cause death (HR 0.97, 95% CI 0.65-1.44), cardiovascular death (HR 0.97, 95% CI 0.56-1.70), MI (HR 0.77, 95% CI 0.47-1.27), definite or probable ST (HR 0.43, 95% CI 0.04-4.53), target lesion failure (HR 0.96, 95% CI 0.65-1.41) or its individual components. Stroke tended to be lower with 1-month than 3-month DAPT (**Figure 5**). These effects were consistent in patients <75 years (all interaction p-values non-significant).

Among patients ≥75 years old, 63 (7.2%) and 112 (9.4%) BARC type 2-5 bleeding were observed with 1- and 3-month DAPT, respectively, and among patients <75 years, these occurred in 40 (9.7%) and 72 (11.8%) individuals. The 1-year risk of BARC 2-5 bleeding was consistently lower in patients ≥75 (Adj. HR 0.66, 95% CI 0.48-0.91) and <75 (Adj. HR 0.86, 95% CI 0.57-1.29) years old (interaction p-value 0.737) treated with 1-month DAPT as compared to 3-month DAPT (**Figure 5**). BARC type 3-5 was reduced with 1- as compared with 3-month DAPT

consistently in older (3.2% vs 4.3%, Adj. HR 0.57, 95% CI 0.35-0.94) and younger patients (5.1% vs 5.4%, Adj. HR 1.04, 95% CI 0.59-1.82, interaction p-value 0.372).

Discussion

In this study, we compared the effects of 1- vs 3-month DAPT on 1-year outcomes in HBR patients ≥75 years old undergoing PCI with XIENCE stent implantation using a series of prospective studies with data on antiplatelet adherence and adjudicated outcomes. The main findings can be summarized as follows:

1) Patients ≥75 years comprised about two thirds of the study population and were more likely to be women, to have comorbidities, but less likely to have other HBR features in addition to advanced age as compared to patients <75 years old.
2) One as compared to 3-month DAPT was associated with a similar risk of the composite of all-cause death or MI and of other ischemic complications, and fewer BARC type 2-5 bleeding consistently in patients ≥75 years and <75 years old; bleeding reduction tended to be greater in the patients ≥75 years old.

Elderly patients are more likely to experience complications after PCI than younger individuals [8, 10-13]. Shorter (i.e. <6 months) or less potent DAPT has been shown to reduce bleeding events without significantly increasing ischemic harm, especially in patients with advanced age or other HBR features [17-19, 24, 25]. However, the most appropriate antiplatelet regimen or DAPT duration in elderly are still unclear, since no study directly compared these new antiplatelet strategies against each other and because elderly are frequently underrepresented in clinical trials [17-19, 24, 25].

Age ≥75 years was one of the HBR criteria making subjects eligible for inclusion in the XIENCE short DAPT program - a series of prospective studies focusing on HBR patients who

underwent XIENCE stent implantation. Patients ≥75 years old comprised around two thirds of the study population, and <50% of them had at least one of the other HBR criteria (e.g. long term OAC, anemia, prior bleeding or stroke). While older and younger patients had a similar risk of death, MI, or other ischemic complications, the former were at lower risk of bleeding. Particularly, the 1-year rate of major bleeding (BARC 3 or 5) in patients ≥75 years was slightly below the 4% threshold established by the ARC-HBR consensus to define HBR, while it exceeded 5% in younger patients. These observations validate the ARC-HBR definition, in which age ≥75 years alone is considered a minor criterion and most of the other HBR features, which were significantly more prevalent among young patients, major HBR criteria [26].

We found that 1- as compared to 3-month DAPT followed by antiplatelet monotherapy (aspirin in >90% of patients) was associated with a similar hazard of the composite of all-cause death or MI and of any individual ischemic events, and with a consistent reduction of BARC 2-5 bleeding irrespective of age. The bleeding-related benefits of 1-month DAPT seem to extend also to more severe BARC 3-5 bleeding, even though the risk reduction for this outcome was only numerical and not statistically significant.

In aggregate, these results confirm the findings of the main analysis of the XIENCE short DAPT program [21], and suggest that an earlier transition (i.e. at 1-month) to a regimen with a single antiplatelet agent may reduce bleeding-related harm without increasing the ischemic risk in both older and younger HBR patients.

Two prior studies demonstrated that respectively 1- and 3-month DAPT followed by aspirin monotherapy were non inferior to 12-month DAPT for the prevention of ischemic events and net adverse clinical events in both patients ≥65 and <65 years old [27, 28]. Other clinical trials showed that 1-month DAPT followed by aspirin monotherapy after DES implantation might be an

appropriate option in elderly; however, the comparison group in these studies consisted of patients treated with another stent type and not with a different antiplatelet regimen [29-31]. A larger amount of evidence support the use of a short (1- or 3-month) DAPT followed by $P2Y_{12}$ monotherapy after PCI, with several studies demonstrating that this regimen significantly reduces bleeding without ischemic harm consistently in elderly [11, 32, 33]; and HBR patients [34-36].

At variance with prior studies, the current analysis showed that 1-month DAPT followed by aspirin monotherapy is not only non-inferior to 3-month DAPT, but it might provide additional benefits in terms of bleeding reduction without a significant increase of ischemic complications.

Current guidelines do not provide specific recommendation concerning antiplatelet therapy for elderly undergoing PCI. The American College of Cardiology/American Heart Association (ACC/AHA) recommend that in presence of HBR features $P2Y_{12}$ inhibitor might be discontinued after 3 months of DAPT if the indication of PCI was a CCS and at 6 months in case of ACS (level of recommendation 2b) [6]. Conversely, according to European Society of Cardiology (ESC) guidelines, transition from DAPT to aspirin monotherapy can occur already at 1-month in patients at very high risk of bleeding [5].

Larger randomized studies are needed to confirm the findings of the current analysis and to compare the effects of $P2Y_{12}$ versus aspirin discontinuation in patients with advanced age or other HBR features.

Study Limitations

The results of this study may be limited by the nonrandomized study design, although confounding factors were attenuated by nearly identical protocols for both XIENCE 28 and 90 and by propensity score stratification. Moreover, adherence rates slightly differed between patients

receiving 1- vs 3-month DAPT, with about 30% of patients transitioning from DAPT to single antiplatelet agent before the mandated 1 o 3 months, and about 15% of patients of XIENCE 90 continuing DAPT beyond 3 months. The results should be considered exploratory, since the study was underpowered to detect small differences for single ischemic endpoints such as MI, stent thrombosis or stroke.

In addition, the results apply only to patients meeting the inclusion and exclusion criteria of this analysis, namely patients that did not experience major ischemic adverse events in the first month after PCI, that were adherent to DAPT treatment and without some high-risk characteristics for ischemic complications, such as presentation with STEMI or complex PCI features (e.g. bifurcations lesions with double stenting, treatment of in-stent restenosis, or CTO).

Conclusions

Among HBR patients undergoing successful PCI with a cobalt-chromium everolimus-eluting stent, patients older and younger than 75 years derived a consistent benefit from 1- as compared to 3-month DAPT in terms of reduction of bleeding events with no increase in all-cause death or MI.

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Figure Legends

Figure 1. Distribution of the study specific HBR criteria in patients ≥75 or <75 years old.
OAC: oral anticoagulation

Figure 2. Proportion of patients on DAPT at different timepoints. DAPT discontinuation was mandated at 1-month post-index PCI in XIENCE 28 (A), and 3-month post-PCI in XIENCE 90 (B). Reported rates reflect the number of patients remaining on study-mandated DAPT at follow-up, stratified by age ≥75 or <75 years old.

DAPT: dual antiplatelet therapy; PCI: percutaneous coronary intervention

Figure 3. Cumulative incidence of the composite of all-cause death or MI and of BARC 2-5 bleeding.

BARC: Bleeding Academic Research Consortium; DAPT: dual antiplatelet therapy; MI: myocardial infarction

Figure 4. Unadjusted risk of adverse outcomes between 1 and 12 months after PCI in patients ≥75 vs. <75 years old. Adverse events are reported as Kaplan-Meier (K-M) rates.

BARC: Bleeding Academic Research Consortium; MI: myocardial infarction; ST: stent thrombosis; TLR: target lesion revascularization; TVR: target vessel revascularization

Figure 5. Effects of 1- vs. 3-month DAPT duration outcomes from 1 to 12-months after PCI in patients ≥75 (red) and <75 years old (blue)

BARC: bleeding academic research consortium; DAPT: dual-antiplatelet therapy; MI: myocardial infarction; ST: stent thrombosis; TLR: target lesion revascularization; TVR: target vessel revascularization

* 2241 patients ≥75 years old, of which 949 were assigned to 1-month DAPT, and 1292 were assigned to 3-month DAPT
# 1123 patients <75 years old, of which 443 were assigned to 1-month DAPT, and 680 were assigned to 3-month DAPT

Figure 1.

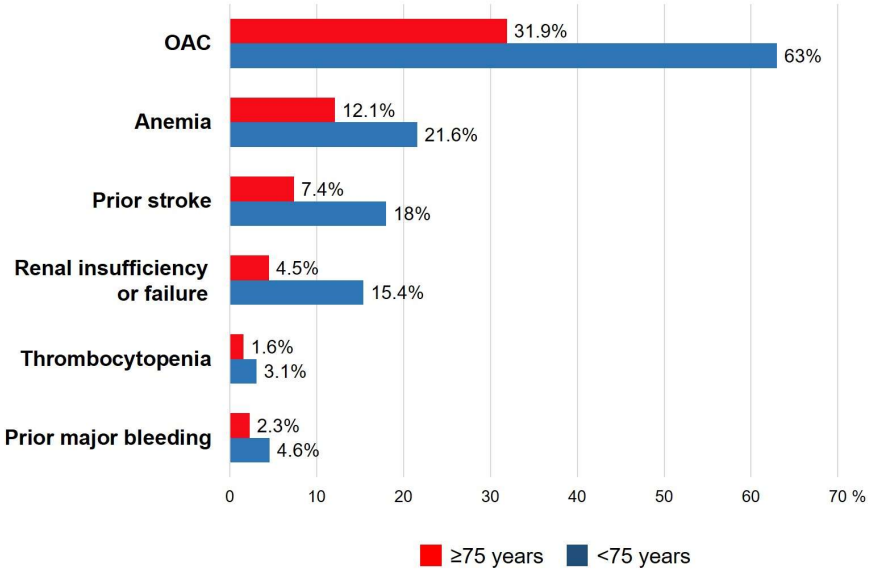
OAC
31.9%
63%
Anemia
12.1%
21.6%
Prior stroke
7.4%
18%
Renal insufficiency or failure
4.5%
15.4%
Thrombocytopenia
1.6%
3.1%
Prior major bleeding
2.3%
4.6%
0
10
20
30
40
50
60
70 %
≥75 years
<75 years

Figure 2.

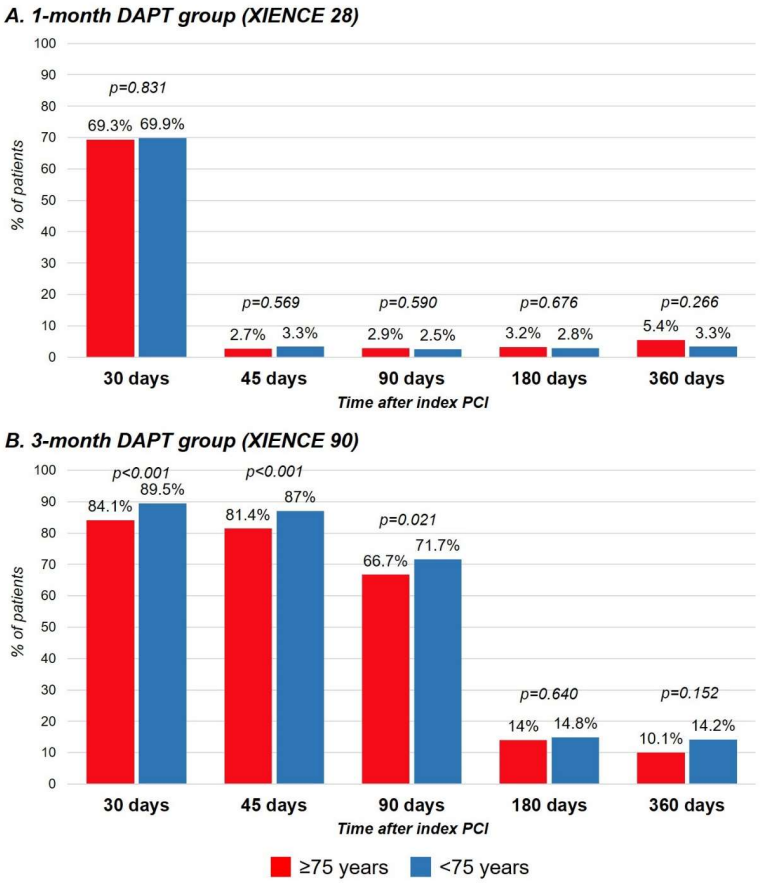
A. 1-month DAPT group (XIENCE 28)
% of patients
p=0.831
69.3% 69.9%
p=0.569
2.7% 3.3%
p=0.590
2.9% 2.5%
p=0.676
3.2% 2.8%
p=0.266
5.4% 3.3%
30 days
45 days
90 days
180 days
360 days
Time after index PCI
B. 3-month DAPT group (XIENCE 90)
% of patients
p<0.001
84.1% 89.5%
p<0.001
81.4% 87%
p=0.021
66.7% 71.7%
p=0.640
14% 14.8%
p=0.152
10.1% 14.2%
30 days
45 days
90 days
180 days
360 days
Time after index PCI
≥75 years
<75 years

Figure 3.

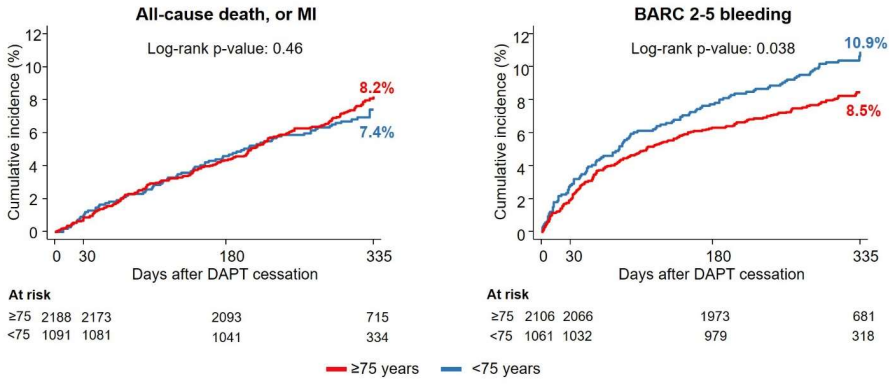
All-cause death, or MI
Log-rank p-value: 0.46
8.2%
7.4%
Cumulative incidence (%)
0
2
4
6
8
10
12
0
30
180
335
Days after DAPT cessation
At risk
≥75 2188 2173 2093 715
<75 1091 1081 1041 334
BARC 2-5 bleeding
Log-rank p-value: 0.038
10.9%
8.5%
Cumulative incidence (%)
Days after DAPT cessation
At risk
≥75 2106 2066 1973 681
<75 1061 1032 979 318
≥75 years
<75 years

Figure 4

Outcomes	≥75 years N=2241	<75 years N=1123	Hazard ratio (95% CI)	p-value
All-cause death, or MI	171 (8.2%)	77 (7.4%)	1.11 (0.85-1.45)	0.464
All-cause death	110 (5.3%)	42 (4.1%)	1.31 (0.92-1.87)	0.135
Cardiovascular death	55 (2.7%)	26 (2.5%)	1.06 (0.66-1.69)	0.814
MI	72 (3.5%)	41 (4.0%)	0.87 (0.60-1.28)	0.495
Definite or probable ST	4 (0.2%)	6 (0.6%)	0.34 (0.09-1.19)	0.091
Stroke	27 (1.4%)	17 (1.6%)	0.80 (0.44-1.47)	0.476
TVR	45 (2.3%)	30 (3.0%)	0.75 (0.47-1.19)	0.217
TLR	28 (1.4%)	16 (1.6%)	0.87 (0.47-1.62)	0.669
BARC 2-5 bleeding	175 (8.5%)	112 (10.9%)	0.78 (0.61-0.99)	0.038
BARC 3-5 bleeding	79 (3.9%)	56 (5.3%)	0.70 (0.50-0.99)	0.043

Figure 5.

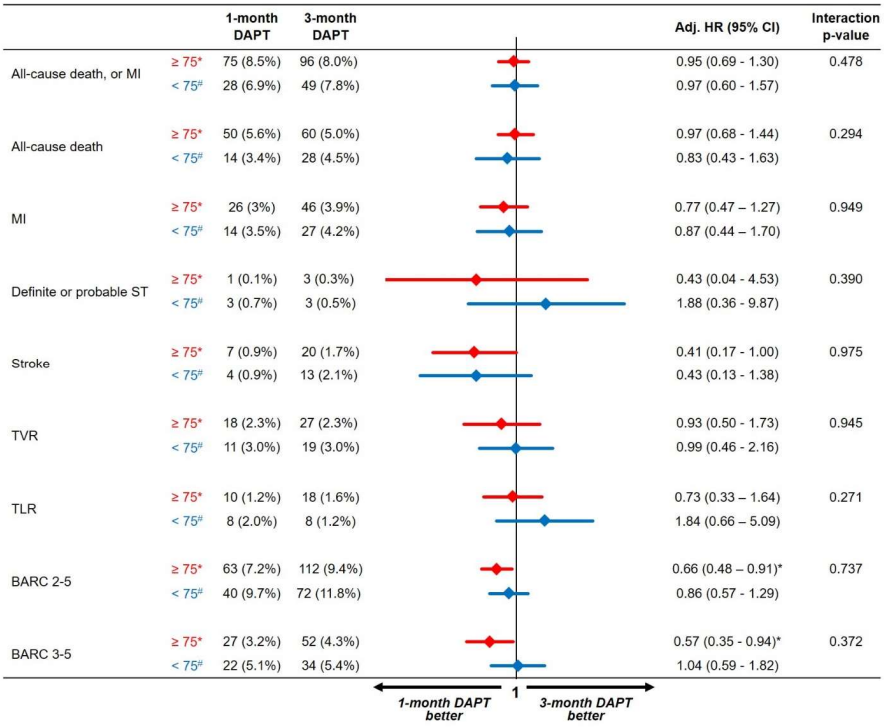
1-month DAPT
3-month DAPT
Adj. HR (95% CI)
Interaction p-value
All-cause death, or MI
≥ 75* 75 (8.5%) 96 (8.0%) 0.95 (0.69 - 1.30) 0.478
< 75# 28 (6.9%) 49 (7.8%) 0.97 (0.60 - 1.57)
All-cause death
≥ 75* 50 (5.6%) 60 (5.0%) 0.97 (0.68 - 1.44) 0.294
< 75# 14 (3.4%) 28 (4.5%) 0.83 (0.43 - 1.63)
MI
≥ 75* 26 (3%) 46 (3.9%) 0.77 (0.47 – 1.27) 0.949
< 75# 14 (3.5%) 27 (4.2%) 0.87 (0.44 – 1.70)
Definite or probable ST
≥ 75* 1 (0.1%) 3 (0.3%) 0.43 (0.04 - 4.53) 0.390
< 75# 3 (0.7%) 3 (0.5%) 1.88 (0.36 - 9.87)
Stroke
≥ 75* 7 (0.9%) 20 (1.7%) 0.41 (0.17 - 1.00) 0.975
< 75# 4 (0.9%) 13 (2.1%) 0.43 (0.13 - 1.38)
TVR
≥ 75* 18 (2.3%) 27 (2.3%) 0.93 (0.50 - 1.73) 0.945
< 75# 11 (3.0%) 19 (3.0%) 0.99 (0.46 - 2.16)
TLR
≥ 75* 10 (1.2%) 18 (1.6%) 0.73 (0.33 – 1.64) 0.271
< 75# 8 (2.0%) 8 (1.2%) 1.84 (0.66 – 5.09)
BARC 2-5
≥ 75* 63 (7.2%) 112 (9.4%) 0.66 (0.48 – 0.91)* 0.737
< 75# 40 (9.7%) 72 (11.8%) 0.86 (0.57 - 1.29)
BARC 3-5
≥ 75* 27 (3.2%) 52 (4.3%) 0.57 (0.35 - 0.94)* 0.372
< 75# 22 (5.1%) 34 (5.4%) 1.04 (0.59 - 1.82)
1
1-month DAPT better
3-month DAPT better

Table 1. Baseline clinical characteristics in HBR patients receiving 1- vs 3-month DAPT stratified by age.

	≥75 years old			<75 years old		
	1-month DAPT N= 949	**3-month DAPT N=1292**	**p-value**	**1-month DAPT N= 443**	**3-month DAPT N= 680**	**p-value**
Age, years	80.5±4.1	80.6±4.4	0.560	66.3±6.8	64.6±7.2	<0.001
Female sex	330 (34.8%)	504 (39.0%)	0.040	123 (27.8%)	197 (29.0%)	0.662
Race						
Asian	75 (11.8%)	32 (2.5%)	<.001	51 (15.3%)	13 (1.9%)	<0.001
Black or African American	16 (2.5%)	57 (4.4%)	0.039	20 (6.0%)	60 (8.8%)	0.118
Hispanic or Latino ethnicity	99 (11.1%)	30 (2.3%)	<.001	39 (9.2%)	26 (3.8%)	<0.001
Native Hawaiian or Pacific Islander	0 (0.0%)	3 (0.2%)	0.555	0 (0.0%)	2 (0.3%)	1.000
American Indian or Alaskan Native	0 (0.0%)	5 (0.4%)	0.178	2 (0.6%)	6 (0.9%)	1.000
White	547 (85.7%)	1157 (89.6%)	0.014	260 (78.1%)	582 (85.6%)	0.003
Hypertension	800 (84.3%)	1152 (89.2%)	<.001	379 (85.6%)	619 (91.0%)	0.004
Dyslipidemia	633 (66.7%)	1071 (82.9%)	<.001	306 (69.1%)	551 (81.0%)	<0.001
Diabetes mellitus	307 (32.6%)	436 (33.8%)	0.550	205 (46.6%)	351 (51.6%)	0.100
Prior PCI	279 (29.4%)	423 (32.7%)	0.092	111 (25.1%)	184 (27.1%)	0.456
Prior CABG	75 (7.9%)	157 (12.2%)	0.001	37 (8.4%)	89 (13.1%)	0.014
Prior MI	151 (16.0%)	196 (15.4%)	0.711	76 (17.3%)	121 (18.0%)	0.767
Chronic kidney disease	507 (56.1%)	639 (49.9%)	0.004	124 (29.0%)	162 (24.0%)	0.061
Clinical presentation						
Chronic coronary syndrome	641 (67.5%)	845 (65.4%)	0.289	276 (62.3%)	438 (64.4%)	0.473
Unstable angina	144 (15.2%)	374 (28.9%)	<.001	86 (19.4%)	198 (29.1%)	<0.001
NSTEMI	164 (17.3%)	88 (6.8%)	<.001	81 (18.3%)	53 (7.8%)	<0.001
PARIS bleeding risk score	6.3±2.2	6.3±2.3	0.406	5.6±2.3	5.5±2.3	0.626
PRECISE-DAPT risk score	30.2±9.8	29.3±9.9	0.027	22.2±12.3	20.3±12.6	0.017
Number of HBR criteria	1.6±0.8	1.6±0.7	0.090	1.3±0.5	1.3±0.6	0.757

Values are n/N (%), mean ± SD, or median (interquartile range [IQR]).

CABG = coronary artery bypass grafting; DAPT = dual antiplatelet therapy; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; PARIS = Patterns of Non-Adherence to Dual Anti-Platelet Regimen in Stented Patients; PCI = percutaneous coronary intervention.

Table 2. Procedural characteristics in HBR patients receiving 1- vs 3-month DAPT stratified by age.

	≥75 years old			<75 years old		
	1-month DAPT N= 949	**3-month DAPT N=1292**	**p-value**	**1-month DAPT N= 443**	**3-month DAPT N= 680**	**p-value**
Procedural characteristics						
Multivessel disease	378 (39.8%)	617 (47.8%)	<.001	195 (44.0%)	301 (44.3%)	0.935
Number of lesions treated [IQR]	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.906	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.992
Number of vessels treated [IQR]	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.309	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.217
B2/C lesion	313 (33.0%)	459 (35.5%)	0.210	185 (41.8%)	228 (33.5%)	0.005
Bifurcation	107 (11.3%)	107 (8.3%)	0.017	54 (12.2%)	46 (6.8%)	0.002
Radial access	660 (69.5%)	673 (52.1%)	<.001	326 (73.6%)	355 (52.2%)	<.001
Number of stents per subject [IQR]	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.838	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.935
Total stent length, mm	26.8±14.5	25.2±14.2	0.010	28.1±14.3	26.2±13.1	0.026
Pre-procedure RVD, mm	3.0±0.5	3.0±0.5	0.887	3.0±0.5	3.0±0.5	0.054
Pre-procedure % DS	82.4±10.3	84.2±9.5	<.001	82.7±10.4	83.4±9.6	0.260
Antiplatelet therapy at discharge						
Aspirin	787 (82.9%)	1199 (92.8%)	<.001	345 (77.9%)	602 (88.5%)	<.001
Clopidogrel	818 (86.2%)	1062 (82.2%)	0.011	386 (87.1%)	550 (80.9%)	0.006
Prasugrel	7 (0.7%)	30 (2.3%)	0.004	7 (1.6%)	16 (2.4%)	0.372
Ticagrelor	124 (13.1%)	200 (15.5%)	0.108	50 (11.3%)	117 (17.2%)	0.006
Oral anticoagulation	317 (33.4%)	398 (30.8%)	0.192	300 (67.9%)	407 (59.9%)	0.007

DAPT = dual antiplatelet therapy; DS = diameter stenosis; RVD = reference vessel diameter.