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Sex-Based Differences in Cessation of Dual-Antiplatelet Therapy Following Percutaneous Coronary Intervention With Stents

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ABSTRACT

OBJECTIVES The aim of this study was to compare the incidence and impact of cessation of dual-antiplatelet therapy (DAPT) in women and men treated with percutaneous coronary intervention.

BACKGROUND Nonadherence to cardiovascular medications and female sex are associated with worse outcomes. However, the patterns and impact of DAPT cessation in women compared with men following percutaneous coronary intervention have not been studied.

METHODS Baseline characteristics, patterns of DAPT cessation, and 2-year clinical outcomes were compared in 5,031 patients (1,279 women, 3,739 men) enrolled following successful percutaneous coronary intervention with stents in the PARIS (Patterns of Non-Adherence to Antiplatelet Regimens in Stented Patients) study. DAPT cessation was adjudicated as physician-guided discontinuation, interruption for surgery, or disruption due to bleeding or noncompliance. Clinical endpoints were major adverse cardiac events (a composite of cardiac death, definite or probable stent thrombosis, spontaneous myocardial infarction, or clinically indicated target lesion revascularization), a second restricted definition of major adverse cardiac events excluding target lesion revascularization, and bleeding.

RESULTS DAPT cessation was more common in women than men (59.1% vs. 55.9%, $p = 0.007$) and comprised increased rates of discontinuation, disruption for bleeding, and disruption due to noncompliance. The impact of DAPT cessation was similar regardless of sex and varied according the mode; in particular, disruption was associated with increased risk for both ischemic and bleeding events. After adjusting for differences in baseline and treatment characteristics as well as DAPT cessation events, female sex remained an independent predictor of bleeding but not of ischemic events.

CONCLUSIONS DAPT cessation was more common in women, but its impact was similar in women and men. Female sex was an independent predictor of bleeding but not of ischemic events after adjustment for differences in DAPT cessation and baseline and treatment characteristics. (J Am Coll Cardiol Intv 2016;9:1461–9) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

BARC = Bleeding Academic Research Consortium

CI = confidence interval

DAPT = dual-antiplatelet therapy

HR = hazard ratio

MACE = major adverse cardiac event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

ST = stent thrombosis

Dual-antiplatelet therapy (DAPT) is almost universally prescribed following percutaneous coronary intervention (PCI) in the absence of contraindications (1). Previous studies have suggested lower medication adherence among women compared with men, as well as worse long-term outcomes in nonadherent patients (2–4). Furthermore, women have been shown to have increased adverse events following PCI, including increased risk for bleeding (5,6), which arguably affects both the duration of DAPT prescribed by physicians as well as patient adherence to DAPT. However, the patterns of DAPT cessation among women and men and the contribution of DAPT cessation to the observed risks associated with female sex post-PCI are not known.

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The PARIS (Patterns of Non-Adherence to Antiplatelet Regimens in Stented Patients) study demonstrated significant variation in the risk for DAPT cessation according to the specific mode of cessation, with disruptions in therapy (for bleeding or noncompliance) being associated with markedly increased risk for major adverse cardiac events (MACE =) compared with no increased risk with temporary interruptions or physician-guided discontinuations of DAPT (7). We therefore sought to compare the patterns and impact of cessation of DAPT in women and men who have undergone PCI with stents.

METHODS

The methods and main findings of the prospective, multicenter PARIS study were previously published (7). In brief, patients who were prescribed DAPT following successful PCI with placement of at least 1 stent between July 2009 and December 2010 were eligible for enrollment. Patients were excluded if they underwent PCI for stent thrombosis (ST) or if they were participants in an investigational drug or device trial. Patients were followed for 2 years, with contact at 1, 6, 12, and 24 months to ascertain the occurrence of any clinical adverse events as well as any cessations of DAPT. All events, including cessations of DAPT, were adjudicated by an external clinical events committee.

In the present study, we compared the baseline characteristics, treatment, DAPT cessation, and clinical outcomes of the women and men enrolled in the PARIS study.

STUDY DEFINITIONS. In the present analysis, MACE included cardiac death, definite or probable ST, spontaneous myocardial infarction (MI), or clinically indicated target lesion revascularization. A secondary restricted MACE endpoint comprised cardiac death, definite or probable ST, and spontaneous MI only. Bleeding, unless otherwise specified, referred to bleeding events meeting criteria for Bleeding Academic Research Consortium (BARC) type ≥3 (8).

ST was adjudicated according to the Academic Research Consortium definition (9). Spontaneous MI was defined as raised biomarkers in the presence of supportive clinical or electrocardiographic indicators per the (first) universal definition published in 2007 (10). In addition the BARC criteria, all bleeding events were also adjudicated using the TIMI (Thrombolysis in Myocardial Infarction) and ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) definitions (11,12).

Each episode of DAPT cessation was adjudicated as 1 of the following 3 "modes": 1) discontinuation, including cessation of 1 or both components of DAPT by a treating physician because of lack of benefit or increased harm from ongoing therapy; 2) interruption, cessation of ≤14 days' duration of 1 or both components of DAPT for surgery or an invasive procedure; and 3) disruption, further adjudicated as physician-recommended cessation of antiplatelet treatment (i.e., because of bleeding) or non-recommended (i.e., patient noncompliance, not directed by the physician). In patients with multiple episodes of DAPT cessation during the 2-year follow-up period, each episode of cessation was considered individually. All episodes of DAPT cessation and

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