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Use and Outcomes of Triple Therapy Among Older Patients With Acute Myocardial Infarction and Atrial Fibrillation

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ABSTRACT

BACKGROUND Antithrombotic therapy for acute myocardial infarction (MI) with atrial fibrillation (AF) among higher risk older patients treated with percutaneous coronary intervention (PCI) remains unclear.

OBJECTIVES This study sought to determine appropriate antithrombotic therapy for acute MI patients with AF treated with PCI.

METHODS We examined 4,959 patients ≥65 years of age with acute MI and AF who underwent coronary stenting (Acute Coronary Treatment and Intervention Outcomes Network Registry–Get With the Guidelines). The primary effectiveness outcome was 2-year major adverse cardiac events (MACE) comprising death, readmission for MI, or stroke; the primary safety outcome was bleeding readmission. Outcomes with dual antiplatelet therapy (DAPT) or triple therapy (DAPT plus warfarin) were compared using Cox proportional hazard modeling with inverse probability-weighted propensity adjustment.

RESULTS Among 4,959 patients, 27.6% (n = 1,370) were discharged on triple therapy. Relative to DAPT, patients on triple therapy had a similar risk of MACE (adjusted hazard ratio [HR]: 0.99 [95% confidence interval (CI): 0.86 to 1.16]) but significantly greater risk of bleeding requiring hospitalization (adjusted HR: 1.61 [95% CI: 1.31 to 1.97]) and greater risk of intracranial hemorrhage (adjusted HR: 2.04 [95% CI: 1.25 to 3.34]). Of 1,591 Medicare Part D patients, 90-day post-discharge warfarin persistence among patients discharged on warfarin was 93.2% (n = 412). Results of 90-day landmark analyses comparing triple therapy versus DAPT in patients persistently on warfarin versus those not discharged on warfarin who had not filled a warfarin prescription were similar to our primary findings.

CONCLUSIONS Approximately 1 in 4 older AF patients undergoing PCI for MI were discharged on triple therapy. Those receiving triple therapy versus DAPT had higher rates of major bleeding without a measurable difference in composite MI, death, or stroke. (J Am Coll Cardiol 2015;66:616–27) © 2015 by the American College of Cardiology Foundation.

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Selection of the optimal antithrombotic regimen for patients with acute myocardial infarction (MI) who have concomitant atrial fibrillation (AF) and are treated with percutaneous coronary intervention (PCI) presents a therapeutic challenge. Current guidelines for the management of AF recommend anticoagulation for thromboembolic prophylaxis in AF patients who are at average or higher risk for stroke but not at prohibitive risk for bleeding (1). Guidelines for the management of acute MI and

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PCI patients recommend treatment with dual antiplatelet therapy (DAPT) to reduce the risks of major adverse cardiac events (MACE) and stent thrombosis (2); however, clinicians may be reluctant to treat AF patients with concurrent indications for DAPT by using the combination of warfarin, aspirin, and clopidogrel (triple therapy) due to the high bleeding risk associated with this regimen (3,4).

Although previous studies have found that bleeding risk is higher among patients receiving triple therapy (4–6), some data also suggest a lower risk of MACE among patients treated with triple therapy relative to DAPT (7,8). Given the paucity of randomized data, studies have shown variability in anticoagulant agent use according to the predicted risks of stroke and bleeding in this patient population (8–11). Therapeutic decisions for older patients with AF and coronary artery disease may be especially challenging. Older patients in particular are at greater risk for AF-related stroke and recurrent events after acute MI but also have a higher risk for bleeding events (12). Importantly, the older population has been excluded from or underrepresented in clinical trials and, therefore, remains understudied.

By linking data from the National Cardiovascular Data Registry Acute Coronary Treatment and Intervention Outcomes Network Registry-Get With the Guidelines (ACTION Registry-GWTG) with Medicare administrative claims, we had a unique opportunity to examine a large group of older MI patients with AF undergoing PCI. We sought to: 1) describe the patterns of use of discharge triple therapy versus DAPT in older MI patients with AF treated by using PCI; 2) characterize warfarin use patterns post-discharge; and 3) compare the safety and effectiveness of triple therapy versus DAPT.

METHODS

DATA SOURCES. Clinical and procedural data for our study were obtained from the ACTION Registry-GWTG, a national quality improvement registry capturing data on consecutive MI patients treated at >500 hospitals in the United States; this registry has been described previously (13). Because patient information was collected without unique patient identifiers, we used indirect identifiers in combination (date of birth, sex, hospital identification, date of admission, and date of discharge) to link patients ≥65 years of age in the ACTION Registry-GWTG with Medicare claims data (methods previously described) (14). The linked data for our analysis were available from January 1, 2007, through December 31, 2010. We examined longitudinal outcomes by using Medicare Part A inpatient administrative data, and information regarding post-discharge warfarin and $P2Y_{12}$ receptor inhibitor use was obtained from Medicare Part D data. Warfarin was the only anticoagulant agent available for clinical use in the United States during this time period.

STUDY POPULATION. Among 123,349 patients ≥65 years of age at 683 sites identified in the ACTION Registry-GWTG during our study period, 64.7% (79,750 patients from 502 sites) were linked to Centers for Medicare & Medicaid Services data (**Figure 1**). In this linked database, there were 6,098 patients with acute MI who were eligible for Medicare

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CABG = coronary artery bypass grafting

$CHADS_2$ = congestive heart failure, hypertension, age ≥75 years, diabetes, prior stroke/transient ischemic attack

CI = confidence interval

DAPT = dual antiplatelet therapy

DES = drug-eluting stent(s)

HR = hazard ratio

MACE = major adverse cardiac event(s)

MI = myocardial infarction

NSTEMI = non-ST-segment elevation myocardial infarction

PCI = percutaneous coronary intervention

STEMI = ST-segment elevation myocardial infarction

Clinical Research Institute (clinical trial steering committee), HMP Communications (Editor in Chief, *Journal of Invasive Cardiology*), *Journal of the American College of Cardiology* (Associate Editor), Population Health Research Institute (clinical trial steering committee), Slack Publications (Chief Medical Editor, *Cardiology Today's Intervention*), WebMD (Continuing Medical Education steering committees), *Clinical Cardiology* (Deputy Editor); has received research funding from Amarin, AstraZeneca, Biotronik, Bristol-Myers Squibb, Eisai, Ethicon, Forest Laboratories, Ischemix, Medtronic, Pfizer, Roche, Sanofi, St. Jude Medical, and The Medicines Company; has served as a trustee for the American College of Cardiology; and has performed unfunded research for FlowCo, PLx Pharma, and Takeda. Dr. Saucedo is a member of the advisory board of Janssen Pharmaceuticals and Eli Lilly. Dr. Wang has received institutional research grant support from AstraZeneca, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Gilead Sciences, GlaxoSmithKline, and Regeneron; and honoraria from AstraZeneca, Eli Lilly, and PREMIER Inc. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Jonathan Tobis, MD, served as Guest Editor for this paper.

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