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Duration of $P2Y_{12}$ inhibitor Prescription After Percutaneous Coronary Intervention in Patients on Oral Anticoagulants (from NCDR CathPCI Registry)

Patients on oral anticoagulation (OAC) undergoing percutaneous coronary intervention (PCI) are at high risk of bleeding while on dual antiplatelet therapy (DAPT). Recommendations on duration of antiplatelets in those patients are evolving. The purpose of this study was to examine the duration of $P2Y_{12}$ inhibitor prescription following PCI in patients on chronic OAC. The study linked the American College of Cardiology's National Cardiovascular Data Registry (ACC NCDR) CathPCI with Medicare Part D prescription claims to examine $P2Y_{12}$ inhibitor use in the 12 months following PCI in patients aged ≥65 years on chronic OAC discharged on aspirin between July 2009 and December 2013. Primary outcome was duration of $P2Y_{12}$ inhibitor use.

Analyses were stratified by stent type and clinical presentation. A total of 30,352 PCIs (29,341 patients) were included (mean age 75.6 years, 39.9% females, 30.3% with stable ischemic heart disease [SIHD], and 65.4% received drug eluting stent [DES]). Prescription duration of $P2Y_{12}$ inhibitor for any group was most often 6 to 12 months. Longer duration was observed in younger patients, females, diabetics, and patients with prior PCI ($p < 0.0005$). Duration was longer with DES vs BMS ($p < 0.0001$) but did not differ according to clinical presentation (SIHD vs ACS; $p = 0.11$). At 12 months, 39.8% of PCIs with DES and 20.5% of those with BMS were on combined therapy of $P2Y_{12}$ inhibitor and OAC. The duration of use of combined $P2Y_{12}$ inhibitor and OAC in the United States is heterogenous and suggests that opportunities to reduce duration of triple therapy and bleeding risk in this high-risk group exist.

Patients on OAC undergoing PCI are at high risk of bleeding while on DAPT. Recommendations on type and duration of antiplatelets in this population are evolving. In this study, we linked the ACC NCDR CathPCI with Medicare Part D prescription claims to examine $P2Y_{12}$ inhibitor use in the 12 months following PCI in patients aged ≥ 65 years on chronic OAC (warfarin or non−vitamin K oral anticoagulant) discharged on aspirin between July 2009 and December 2013. Patients were excluded for (1) in-hospital Coronary Artery Bypass Grafting, major bleeding or death, or (2) prior PCI within 3 months. The primary outcome was duration of $P2Y_{12}$ inhibitor prescription (defined as 80% of days covered) categorized as ≤1, >1 to 3, >3 to 6, and >6 to 12 months. Drug discontinuation was defined by a ≥30-day gap in prescription refill. Assessment of aspirin use following hospital discharge could not be captured due to incomplete prescription data in Medicare. Analyses were stratified by stent type: DES vs bare-metal stents ( ), and clinical presentation: acute coronary syndrome (ACS) versus SIHD. Pearson chi-Square and Mann-Whitney Wilcoxon rank sum tests were used to compare categorical and continuous variables, respectively. The study was exempt from Lifespan IRB as authors had no access to individual patient data.

A total of 30,352 PCIs (29,341 patients) were included. Mean age was 75.6 years, 39.9% females, 30.3% with SIHD, and 65.4% received DES. Prescription duration of $P2Y_{12}$ inhibitor for any group was most often 6 to 12 months (Figure 1). Longer duration was observed in younger patients, females, diabetics, and patients with prior PCI ($p < 0.0005$). Duration was longer with DES vs BMS ($p < 0.0001$) but did not differ according to clinical presentation (SIHD vs ACS; $p = 0.11$). At 12 months, 39.8% of PCIs with DES and 20.5% of those with BMS were on a combined therapy of $P2Y_{12}$ inhibitor and OAC.

Balancing the risk of ischemia and bleeding in PCI patients, particularly those on OAC, is challenging. We examined the practice of $P2Y_{12}$ inhibitor prescription in the time period prior to the first randomized controlled trial (RCT) demonstrating reduced bleeding with early discontinuation of aspirin in PCI patients on coumadin and clopidogrel.[1] Since that time, larger RCTs have suggested that the optimal drug combination for these patients is a non−vitamin K oral anticoagulant and $P2Y_{12}$ inhibitor for 12 months, however, a recent meta-analysis raised concern of a higher risk of stent thrombosis in patients randomized to dual versus triple therapy.[2]

The current ACC/AHA guidelines[3] recommend shorter duration of $P2Y_{12}$ inhibitors after BMS (1 and 6 months) and DES (3 and 6 months), for SIHD and ACS, respectively, in patients at higher bleeding risk. Our study revealed that longer duration of $P2Y_{12}$ inhibitors use was influenced by type of stent used (DES vs BMS) but not clinical presentation, and that the majority of patients were on longer durations of $P2Y_{12}$ inhibitors than currently recommended for patient with high bleeding risk. A significant proportion of patients with BMS continued to be on combined $P2Y_{12}$ inhibitor and OAC beyond 6 months even when PCI was performed for SIHD.

Despite limitations of our study, including absence of information about aspirin use and more recent Medicare linking to assess changes in prescribing patterns, our analysis provides important observations. First, duration of combined $P2Y_{12}$ inhibitor and OAC

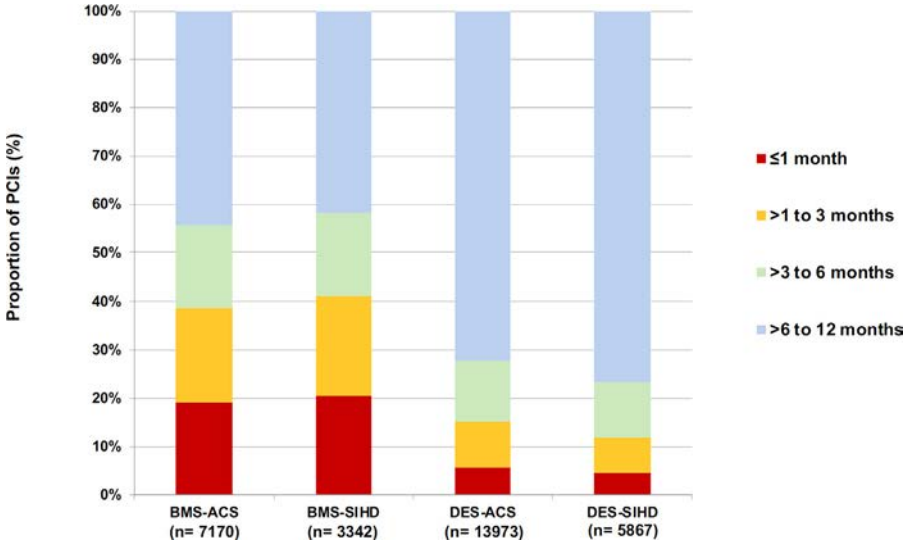

Figure 1. Duration of $P2Y_{12}$ inhibitor among PCI patients on OAC.

use in the United States is heterogeneous. Second, physicians tend to prescribe longer durations of $P2Y_{12}$ inhibitor in SIHD than currently recommended, especially with DES. This finding is particularly relevant given studies supporting DES use over BMS in patients at high bleeding risk. The ability to determine drug prescription patterns and adoption of findings from RCTs rely on an accurate mechanism to assess medication use. Our study highlights that over-the-counter aspirin limits the ability to examine DAPT using claims data. This is becoming increasingly germane in current era as more evidence mounts for reducing aspirin duration in PCI patients at high bleeding risk, including those not on an OAC.[4]

Disclosures

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Trends of Co-morbidities in Clinical Trials of Lipid Lowering Therapies

Dyslipidemia is an established risk factor for cardiovascular disease.[1] Although optimal management of dyslipidemia can reduce cardiovascular risk burden,[2] a significant proportion of patients with dyslipidemia carry significant co-morbidity burden, influencing the quality of life, and outcomes.[1] Hence, it is imperative that randomized controlled trials examining the efficacy of lipid-lowering therapy should recruit patients reflective of the real-world multimorbid population. Accordingly, we systematically reviewed the prevalence and temporal changes in comorbidities reported in lipid-lowering therapy trials to gain further insights on this issue.[3]

A total of 61 randomized controlled trials (n = 485,678) with follow-up of ≥3 months were identified using MEDLINE and Clinicaltrials.gov (January 1993-December 2018).[4] Categorical variables were reported as No. (%) and were compared using Chi-square testing. Trends of co-morbidities were tested using simple linear regression model using the publication year as an independent variable. SPSS V-24 (IBM Corporation) was used for all analyses.

The median number of participants per trial was 5,011 (IQI, 2,805 to 10,944). Mean age ± SD was 62.4 ± 4.33 years with 31.7% of participants being females. 33 trials used statins, 3 trials used ezetimibe, 6 trials used PCSK9 inhibitors, 5 trials fibrates, 2 niacin trials, and 12 trials used omega 3 fatty acids. A total of 47.5% were primary prevention trials and 52.5% were secondary prevention trials. Diabetes mellitus was reported by 86.9% of trials, hypertension 73.6%, stroke 42.6%, coronary artery disease (CAD) 42.6%, and peripheral artery disease (PAD) by 39.3% of trials. A total of 83.6% reported smoking status while body mass index was reported by 55.7% trials. Only 3.3% trials reported chronic kidney disease (CKD) and cancer or chronic obstructive pulmonary disease (COPD) were reported by only 6.6% of trials, each. The prevalence of CAD (from 57.1% in 1993-1998 to 30.9% in 2014-2018) and PAD (from 11.6 % in 1999-2003 to 4.2 % in 2014-2018) decreased, and enrollment of hypertensives (from 23.8% in 1993-1998 to 59.2% in 2014-2018), diabetics (6.2% in 1993-1998 to 35.8% in 2014-2018), and patients with cerebrovascular accident (CVA) (from 2.1% in 1993-1998 to 7.2% in 2014-2018) increased (Table 1). Enrollment of patients with CKD, COPD and cancer remained consistently low. Compared with primary prevention trials, enrollment of active smokers (21.3% vs 13.9%) and hypertensives (54.1% vs 43.6%) was higher in secondary prevention trials, whereas, diabetics (30.9% vs 26.9%) were more prevalent in primary versus secondary prevention trials.

Between 1993 and 2018, the enrollment of patients with cardiovascular and noncardiovascular comorbidities varied over time in trials of lipid-lowering therapy. The prevalence of cardiovascular risk factors, such as smoking or hypertension, and of non-cardiovascular diseases such as CKD, COPD, and cancer remained consistently low. Interestingly, the enrollment of patients with CAD and PAD also declined over the years in trials