



# Risk of new-onset atrial fibrillation after drug-eluting stent implantation in patients with stable coronary artery disease☆☆☆

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## ABSTRACT

**Background:** New-onset atrial fibrillation (NOAF) is associated with adverse outcomes in patients with coronary artery disease (CAD). Although newer generation drug-eluting stents (NG-DESs) are more beneficial than bare-metal stents (BMSs) in reducing the risk of in-stent restenosis and revascularization, whether NG-DES implantation in patients with stable CAD reduces NOAF risk compared with BMS implantation remains unknown.

**Methods:** This population-based cohort study was conducted using data from Taiwan's National Health Insurance Research Database. Propensity score matching was used to select 18,423 pairs of patients with stable CAD receiving NG-DES implantation and BMS implantation with similar baseline characteristics for evaluation. A competing risk model was used to evaluate the risk of NOAF between the NG-DES and BMS groups in which death was considered a competing risk.

**Results:** After adjustment for patients' clinical variables, the use of NG-DESs was associated with a decreased risk of NOAF at 1-year follow-up (adjusted subdistribution hazard ratio [SHR] = 0.79, 95% confidence interval [CI] = 0.68–0.93,  $P = 0.005$ ) compared with the use of BMSs. Similar results indicated that NG-DESs were beneficial for reducing the risk of NOAF (adjusted SHR = 0.81, 95% CI = 0.67–0.97,  $P = 0.020$ ) in patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of  $\geq 2$ . These findings were also consistent with those for patients who received dual antiplatelet therapy for an undefined duration of  $>1$  month following stent implantation.

**Conclusions:** Our findings suggest that NG-DESs might reduce the risk of NOAF in patients with stable CAD.

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## 1. Introduction

Atrial fibrillation (AF) may coexist with coronary artery disease (CAD), which may be related to common risk factors including advanced age, diabetes, and hypertension [1–6]. The presence of AF is strongly associated with detrimental outcomes in patients with CAD, including heart failure, cerebrovascular events, acute kidney injury, and in-hospital mortality [7–9]. Studies have focused on AF occurrence among patients with acute myocardial infarction (AMI). Limited studies have evaluated the prevention of new-onset AF (NOAF) in patients with stable CAD.

Compared with use of bare-metal stents (BMSs), the use of newer generation drug-eluting stents (NG-DESs) in patients with stable CAD treated with percutaneous coronary intervention (PCI) is associated with a decreased risk of restenosis and repeat revascularization [10–13]. However, DES implantation requires a longer duration of dual antiplatelet therapy (DAPT) than does BMS implantation. Guidelines recommend at least 6 months and 1 month of DAPT after NG-DES and BMS implantation, respectively, to reduce the risk of stent thrombosis [14,15]. Although one meta-analysis [16] including 3 randomized clinical trials [17–19] showed that NG-DES implantation with 1 month of DAPT decreased the risks of adverse cardiac events compared with BMS implantation, this analysis focused on patients with a high risk of bleeding. Hence, these results may not be generalizable to patients with stable CAD. In addition, it remains unclear whether the use of NG-DESs, compared with the use of BMSs, is associated with a reduced risk of NOAF in patients with stable CAD receiving DAPT for an undefined duration following stent implantation.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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To address this knowledge gap, using data from Taiwan's National Health Insurance Research Database (NHIRD), this population-based retrospective cohort study investigated the association of NG-DES implantation with the risk of NOAF in patients with stable CAD treated with stent implantation at 1-year follow-up.

## 2. Methods

### 2.1. Data source

This study was approved by the Institutional Review Board of MacKay Memorial Hospital (MMH-IRB; Approval No. 19MMHIS006e). In this study, we used the NHIRD, which is a database that contains the claims data of 99% of residents in Taiwan covered by the National Health Insurance (NHI) program. Because individual identifiers in the NHIRD have been encrypted and because insurants cannot be recognized after the data are released to researchers, informed consent was waived under the full review process of the MMH-IRB. The NHIRD includes data on inpatient, outpatient, and prescription drug claims. In the NHIRD, prescribed medications are classified according to the Anatomical Therapeutic Chemical (ATC) system, and disease diagnoses are coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Death records from the National Death Registry are also be linked to the NHIRD based on patients' encrypted identifiers [20].

### 2.2. Study cohort

This retrospective cohort study included patients who were admitted for receiving PCI and stent implantation between 2007 and 2014. The date of admission was considered the index PCI. We then excluded patients who were <20 years old; were not citizens of Taiwan; had been admitted for AMI; had died during admission; had received PCI before admission; had received first-generation DESs, polymer-free drug-coating stents, or combined DES and BMS implantation in the index PCI; or had a diagnosis of any types of AF, atrial flutter, pulmonary thromboembolism, or deep vein thrombosis with oral anticoagulant medications before and during admission. We also excluded patients who were at a high risk of AF, including those who had received coronary artery bypass grafting (CABG) [21], ventricular assist device support [22,23], valvular surgery [24], or heart transplantation [25] during the study period. Fig. 1 presents the patient selection process. Patients who had received NG-DES and BMS implantation at their index PCI comprised the NG-DES and BMS groups, respectively.

### 2.3. Propensity score matching

To reduce selection bias when estimating the effect of NG-DESs on NOAF occurrence following PCI, we used propensity score matching (PSM) to select a pair of patients who had similar baseline characteristics but different implanted stent types from the NG-DES and BMS groups. PSM has been increasingly used in studies estimating the effects of treatment by employing observational data [26,27]. In this study, we applied the most common PSM implementation: A pair of patients was matched on the logit of the propensity score by using calipers of width equal to 0.2 of the standard deviation. The covariates used to

calculate the propensity score included age, sex, the year of the index PCI, previous or coexisting medical conditions, drug prescriptions, complexity of PCI, and patients' risk profiles for developing AF (listed in Table 1).

This study included previous or coexisting medical conditions for which patients had  $\geq 2$  diagnostic claims within the 1 year prior to the date of admission; the conditions comprised diabetes mellitus, hypertension, dyslipidemia, chronic kidney disease, dialysis, congestive heart failure (CHF), cerebrovascular disease, chronic obstructive pulmonary disease or asthma, chronic liver disease, dementia, Parkinson's disease, osteoarthritis, rheumatoid arthritis, and rheumatism. Prescribed medications included angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs), beta-blockers, antiplatelets, nitrates, statins, proton pump inhibitors (PPIs), nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, amiodarone, and calcium channel blockers (CCBs). The ICD-9-CM codes for disease diagnoses and the ATC codes for medications are listed in Supplementary Table 1.

Complex PCI was defined as  $\geq 2$  coronary arteries treated in the index PCI. We also used the CHA<sub>2</sub>DS<sub>2</sub>-VASC score (the sum of risk factors for CHF, hypertension, age  $\geq 75$  years, diabetes, stroke, vascular disease, age = 65–74 years, and proportion of women) [28] as a proxy for adjusting the severity of medical conditions. The CHA<sub>2</sub>DS<sub>2</sub>-VASC score is widely used for predicting stroke and thromboembolism among patients with pre-existing AF [28], and it has been validated for use in the prediction of NOAF [29].

### 2.4. Study outcomes

The principal outcome in this study was the occurrence of NOAF (ICD-9-CM code 427.31) following stent implantation after discharge during the follow-up period. The occurrence of NOAF, including paroxysmal AF, was determined according to inpatient and outpatient claim data when patients had a diagnosis of any types of AF and received prescription of anticoagulants. The study patients were followed up for 1 year, and those who died before developing NOAF or who did not develop NOAF during the follow-up period were considered to have competing risks in this study.

### 2.5. Statistical methods

Primary analysis was performed to examine the association between the use of the 2 stent types and the risk of NOAF in patients with stable CAD. A subgroup analysis of patients with more cardiovascular risk factors (age  $\geq 75$  years and CHA<sub>2</sub>DS<sub>2</sub>-VASC score  $\geq 2$ ) was also performed. In this study, we used a competing risk model in which death was considered a competing risk and reported the adjusted subdistribution hazard ratio (adjusted SHR). Variables used in the models were the baseline covariates listed in Table 1, including age, sex, the year of the index PCI, previous or coexisting medical conditions, drug prescriptions, complexity of PCI, and patients' CHA<sub>2</sub>DS<sub>2</sub>-VASC scores. Additionally, we calculated patients' ORBIT score (the sum of risk factors for age  $\geq 75$  years, insufficient kidney function, treatment with any antiplatelet, a positive clinical history of bleeding, and the presence of anemia or abnormal hemoglobin) [30] and included it as a variable in the regression models to account for the potential risk of bleeding complications that may influence decision-making regarding stent implantation. To confirm whether the duration of DAPT affects the risk of stent-associated NOAF, we also performed analysis in patients who received DAPT for an undefined duration of >1 month following the index PCI. All analyses were performed using SAS/STAT 9.4 software (SAS Institute Inc.,

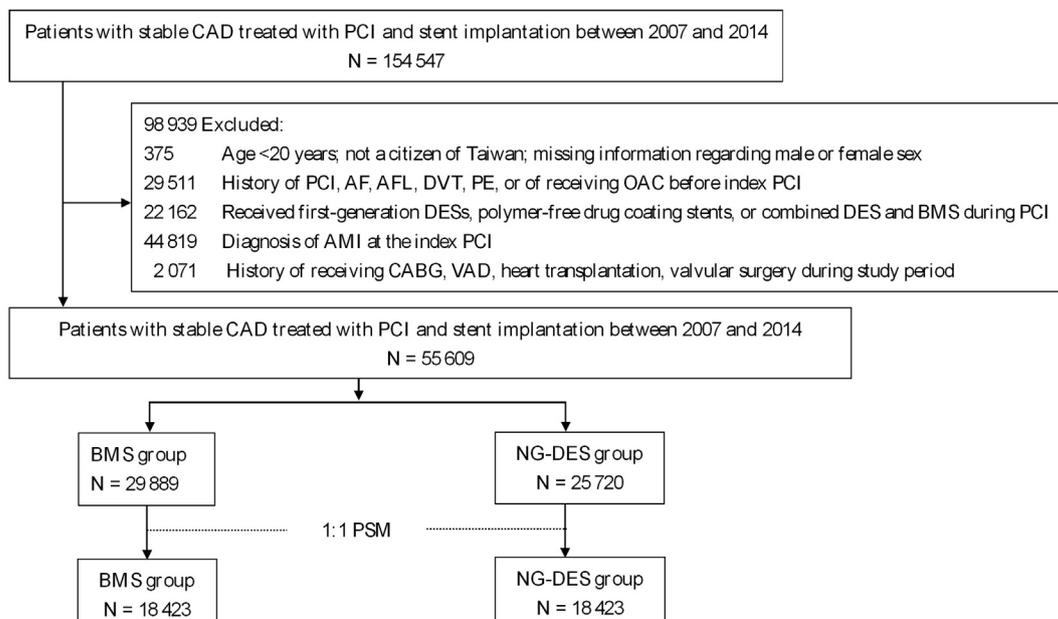


Fig. 1. Patient selection process.

**Table 1**

Baseline characteristics of patients with stable coronary artery disease receiving newer generation drug-eluting stents (NG-DESs) or bare-metal stents (BMSs) before and after PSM.

	Before PSM					After PSM				
	BMS		NG-DES		SMD <sup>a</sup>	BMS		DES		SMD <sup>a</sup>
	N	(%)	N	(%)		N	(%)	N	(%)	
Sample size	29,889		25,720		0.089	18,423		18,423		<0.001
Male	20,714	(69.3)	18,856	(73.3)		13,171	(71.5)	13,171	(71.5)	
Age [mean, SD]	[66.9, 12.2]		[64.8, 11.3]			[65.9, 11.5]		[65.9, 11.5]		
20–44	1126	(3.8)	930	(3.6)	0.008	599	(3.3)	590	(3.2)	0.003
45–64	11,393	(38.1)	11,959	(46.5)	0.170	7771	(42.2)	7789	(42.3)	0.002
65–74	8218	(27.5)	7211	(28.0)	0.012	5296	(28.7)	5257	(28.5)	0.005
≥75	9152	(30.6)	5620	(21.9)	0.200	4757	(25.8)	4787	(26.0)	0.004
Year of the index PCI										
2007–2009	10,980	(36.7)	3364	(13.1)	0.569	3299	(17.9)	3299	(17.9)	<0.001
2010–2012	11,338	(37.9)	11,135	(43.3)	0.109	8625	(46.8)	8625	(46.8)	<0.001
2013–2014	7571	(25.3)	11,221	(43.6)	0.392	6499	(35.3)	6499	(35.3)	<0.001
Number of stents [mean, SD]	[1.4, 0.7]		[1.4, 0.7]			[1.5, 0.7]		[1.4, 0.7]		
Complex PCI (≥2 vessels)	9401	(31.5)	8596	(33.4)	0.042	5873	(31.9)	5937	(32.2)	0.007
Comorbidity, yes										
DM	8925	(29.9)	7080	(27.5)	0.052	5421	(29.4)	5225	(28.4)	0.023
HTN	11,934	(39.9)	10,334	(40.2)	0.005	7422	(40.3)	7542	(40.9)	0.013
Dyslipidemia	1406	(4.7)	1795	(7.0)	0.097	1009	(5.5)	1007	(5.5)	<0.001
CVD	3444	(11.5)	2258	(8.8)	0.091	1829	(9.9)	1863	(10.1)	0.006
CRD	3703	(12.4)	1746	(6.8)	0.191	1714	(9.3)	1535	(8.3)	0.034
Dialysis	137	(0.5)	30	(0.1)	0.064	29	(0.2)	19	(0.1)	0.015
CHF	3115	(10.4)	1353	(5.3)	0.193	1265	(6.9)	1220	(6.6)	0.010
COPD and Asthma	2689	(9.0)	1593	(6.2)	0.106	1329	(7.2)	1346	(7.3)	0.004
Dementia and Parkinsonism	920	(3.1)	498	(1.9)	0.073	451	(2.4)	438	(2.4)	0.005
OA, RA, and Rheumatism	5277	(17.7)	3758	(14.6)	0.083	3027	(16.4)	3029	(16.4)	<0.001
CHA <sub>2</sub> DS <sub>2</sub> -VASC [mean, SD]	[2.3, 1.5]		[2.0, 1.5]			[2.1, 1.5]		[2.1, 1.5]		
0–1	10,138	(33.9)	11,447	(44.5)	0.218	7210	(39.1)	7187	(39.0)	0.003
≥2	19,751	(66.1)	14,273	(55.5)	0.218	11,213	(60.9)	11,236	(61.0)	0.003
Medication use										
ACEI/ARB	20,074	(67.2)	16,025	(62.3)	0.102	12,011	(65.2)	12,037	(65.3)	0.003
Beta-blocker	18,594	(62.2)	15,771	(61.3)	0.018	11,338	(61.5)	11,374	(61.7)	0.004
Nitrate	27,319	(91.4)	23,327	(90.7)	0.025	16,835	(91.4)	16,766	(91.0)	0.013
Statin	15,260	(51.1)	15,493	(60.2)	0.186	10,457	(56.8)	10,206	(55.4)	0.027
PPIs	4956	(16.6)	2664	(10.4)	0.183	2315	(12.6)	2205	(12.0)	0.018
Steroid	6648	(22.2)	3450	(13.4)	0.232	3050	(16.6)	2990	(16.2)	0.009
NSAID	16,410	(54.9)	11,745	(45.7)	0.186	9224	(50.1)	9356	(50.8)	0.014
Amiodarone	2317	(7.8)	845	(3.3)	0.197	800	(4.3)	735	(4.0)	0.018
DHP CCB	14,777	(49.4)	11,096	(43.1)	0.127	8374	(45.5)	8613	(46.8)	0.026
Non-DHP CCB	7079	(23.7)	5228	(20.3)	0.081	3878	(21.0)	4031	(21.9)	0.020
Follow-up period [mean, SD]	[10.9, 3.3]		[11.7, 1.8]			[11.1, 2.7]		[11.6, 1.9]		

Abbreviations: ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; BMS = bare-metal stent; CAD = coronary artery disease; CCB = calcium channel blocker; CHA<sub>2</sub>DS<sub>2</sub>-VASC score = congestive heart failure, hypertension, age ≥ 75 years, diabetes, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category (female); CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CRD = chronic renal disease; CVD = cerebrovascular disease; DHP = dihydropyridine; DM = diabetes mellitus; HTN = hypertension; NSAID = nonsteroidal anti-inflammatory drug; NG-DES = newer generation drug-eluting stent; OA = osteoarthritis; PCI = percutaneous coronary intervention; PPIs = proton pump inhibitors; PSM = propensity score matching; RA = rheumatoid arthritis; SD = standard deviation; SMD = standardized mean difference.

<sup>a</sup> Difference in means or proportions divided by SE; an imbalance was defined as an absolute value > 0.1.

Cary, NC, US) and STATA 14 software (Stata Corp LP, College Station, TX, US). A *P* value of <0.05 was considered significant.

### 3. Results

Of the 55,609 patients with stable CAD receiving PCI and stent implantation in this study, 25,720 (46.3%) received NG-DESs in the index PCI. The use of NG-DESs gradually increased over time. Patients in the BMS group were older, had more comorbidities, and had a higher CHA<sub>2</sub>DS<sub>2</sub>-VASC score than did those in the NG-DES group. Compared with patients in the NG-DES group, those in the BMS group more frequently used ACEIs or ARBs, PPIs, steroids, NSAIDs, amiodarone, and CCBs (Table 1). After PSM, 18,423 patient pairs were selected, and the baseline characteristics in the NG-DES and BMS groups were markedly similar (Table 1).

The rates of cumulative incidence competing risk (CICR) of NOAF following stent implantation at 3-month, 6-month, 9-month, and 1-year follow-up were lower in the NG-DES group (0.66%, 0.92%, 1.17%, and 1.46%, respectively) than in the BMS group (0.82%, 1.25%, 1.56%, and 1.82%, respectively) (Fig. 2). After adjustment for clinical variables, including age, sex, the year of the index PCI, previous coexisting

medical conditions, drug prescriptions, complexity of PCI, and patients' CHA<sub>2</sub>DS<sub>2</sub>-VASC and ORBIT scores, NG-DES implantation in patients with stable CAD was associated with a decreased risk of NOAF at 1-year follow-up compared with BMS implantation, with an adjusted SHR of 0.79 (95% CI = 0.68–0.93, *P* = 0.005) (Table 2). In patients aged ≥75 years, the use of NG-DESs was not associated with a decreased risk of NOAF (Table 2). However, in patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASC score of ≥2, the use of NG-DESs was associated with a decreased risk of NOAF at 1-year follow-up (adjusted SHR = 0.81, 95% CI = 0.67–0.97, *P* = 0.020) (Table 2).

After excluding patients who received <1 month of DAPT or no DAPT, we generated a second cohort comprising those who received DAPT for an undefined duration of >1 month following stent implantation (Supplementary Fig. 1). Baseline characteristics of the NG-DES and BMS groups in the second cohort were similar after PSM (Supplementary Table 2). Among patients who received DAPT for an undefined duration of >1 month following stent implantation, the CICR of NOAF at 3-month, 6-month, 9-month, and 1-year follow-up were still lower in the NG-DES group (0.28%, 0.49%, 0.76%, and 1.04%, respectively) than in the BMS group (0.58%, 0.94%, 1.16%, and 1.41%, respectively) (Supplementary Fig. 2). After adjustment for clinical variables (listed in

Supplementary Table 2), NG-DES implantation was associated with a decreased risk of NOAF at 1-year follow-up compared with BMS implantation, with an adjusted SHR of 0.72 (95% CI = 0.57–0.90,  $P = 0.004$ ) (Supplementary Table 3). The results for 2 subgroups (patients aged  $\geq 75$  years and those with a  $\text{CHA}_2\text{DS}_2\text{-VASc}$  score of  $\geq 2$ ) were similar to those for the first cohort (Supplementary Table 3).

#### 4. Discussion

Limited information exists on the incidence of NOAF following PCI in patients with stable CAD. In the EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial [31], NOAF developed at a mean of  $2.7 \pm 2.5$  days after revascularization and was common after CABG but was extremely rare after PCI. However, this analysis was based on in-hospital observation, not on a long-term follow-up after discharge, potentially resulting in underestimation. In addition, the EXCEL trial [31] was conducted in patients with left main disease implanted with a specific DES; the results could not be generalized to patients with stable CAD. To the best of our knowledge, our data represent the first large-scale population-based evidence demonstrating that NG-DES use, compared with BMS use, might be associated with reduced NOAF risk in patients with stable CAD. Some mechanisms might explain our findings. Atrial and ventricular ischemia from CAD tends to increase atrial pressure, cause atrial dilation, and result in structural and electrophysiological abnormalities, increasing the risk of AF [32,33]. A lower risk of restenosis-related ischemia and revascularization associated with NG-DES implantation might decrease recurrent ischemia and limit atrial remodeling, thereby decreasing the risk of NOAF. A reduced risk of stent thrombosis (ST) associated with the use of NG-DES might be another potential mechanism. In the Swedish Coronary Angiography and Angioplasty Registry (SCAAR), PCI with NG-DES placement was related to a lower risk of ST compared to that with BMS placement [34]. Additionally, the superiority of NG-DES over BMS for a lower risk of ST became obviously in early months during the follow-up period in the SCAAR data [34]. Therefore, a reduced risk of ST-related myocardial ischemia and atrial arrhythmia associated with NG-DES

**Table 2**

One-year cumulative incidence of NOAF occurrence in patients with stable CAD receiving NG-DESs or BMSs.

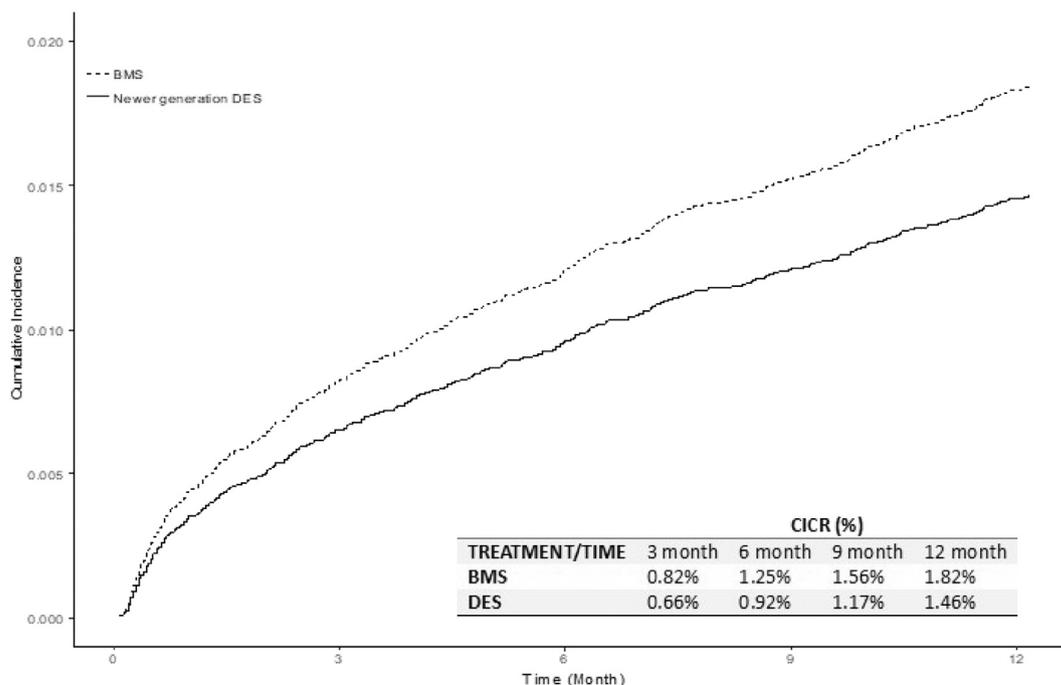
Group	Treatment	CICR (%)	Adjusted <sup>a</sup> SHR (95% CI)	<i>P</i>
Overall	BMS	1.82	1.00 (Ref.)	0.005
	NG-DES	1.46	0.79 (0.68–0.93)	
Age $\geq 75$	BMS	3.32	1.00 (Ref.)	0.311
	NG-DES	3.01	0.89 (0.71–1.16)	
$\text{CHA}_2\text{DS}_2\text{-VASc} \geq 2$	BMS	2.33	1.00 (Ref.)	0.020
	NG-DES	1.91	0.81 (0.67–0.97)	

Abbreviations: BMS = bare-metal stent; CAD = coronary artery disease;  $\text{CHA}_2\text{DS}_2\text{-VASc}$  score = congestive heart failure, hypertension, age  $\geq 75$  years, diabetes, stroke or transient ischemic attack, vascular disease, age 65 to 74 years, sex category (female); CI = confidence interval; CICR = cumulative incidence competing risks; NG-DES = newer generation drug-eluting stent; ORBIT score = the sum of risk factors for age  $\geq 75$  years, insufficient kidney function, treatment with any antiplatelets, a positive clinical history for bleeding, and the presence of anemia or abnormal hemoglobin; Ref. = reference; SHR = subdistribution hazard ratio.

<sup>a</sup> Adjusted for all covariates listed in Table 1 and patients' ORBIT scores.

implantation might also explain our findings [34,35]. However, ST still remains a multifactorial issue with many variables, including the vascular healing, kinetics of drug release, the type of polymer, and strut thickness [34,35]. Further investigation is needed to address and clarify this issue.

The optimal PCI strategy for elderly patients remains ill-defined in terms of both the stent type and the appropriate duration of DAPT after intervention [18]. Because elderly patients have a high risk of bleeding complications from prolonged DAPT, a significant number of elderly patients receive BMSs instead of DESs to shorten the duration of DAPT [16,18]. The SENIOR trial (DESs in elderly patients with CAD)—in which 55% of patients had stable CAD and 45% of patients had acute coronary syndrome [18]—indicated that, for a similar duration of DAPT, DESs reduced the risk of adverse outcomes (i.e., all-cause mortality, myocardial infarction, ischemia-driven target lesion revascularization, or stroke) among patients aged  $\geq 75$  years more than did BMSs. In contrast to the SENIOR trial [18], the primary outcome in the present study was the occurrence of NOAF, for which aging is the most important risk factor [36,37], and the risk factor could not be modified by



**Fig. 2.** Competing risk (cumulative incidence function curve) of BMS versus NG-DES in patients with stable CAD.

implanted stents or DAPT. This might explain why the use of NG-DESs with an undefined duration of DAPT was not associated with a reduced NOAF risk compared with the use of BMSs in patients aged  $\geq 75$  years. Additional randomized clinical trials are required to clarify the effect of NG-DES implantation as well as the influence of shortened DAPT among elderly patients with stable CAD.

Patients with a high CHA<sub>2</sub>DS<sub>2</sub>-VASc score are at a high risk of bleeding [38], potentially influencing the decision-making of DES implantation. Lower hemoglobin levels and history of bleeding are associated with a lower likelihood of receiving DESs [39]. To address these potentially confounding factors in our analysis, we included the CHA<sub>2</sub>DS<sub>2</sub>-VASc and ORBIT scores [30] as variables in the regression model. In this study, we still observed that NG-DES implantation was associated with a decreased risk of NOAF in patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score  $\geq 2$ . This finding is critical for this specific group, because they are at a high risk of ischemic stroke and frequently need oral anticoagulant therapy in addition to DAPT once NOAF occurs after stent implantation [32,33], potentially increasing the risk of bleeding complications [38]. In addition, studies have reported that the CHA<sub>2</sub>DS<sub>2</sub>-VASc score is useful for predicting in-stent restenosis among patients receiving PCI and BMS implantation [40,41]. Our findings, as well as those of other studies [40,41], indicate that the CHA<sub>2</sub>DS<sub>2</sub>-VASc score might assist clinicians in identifying high-risk patients with CAD who can benefit from NG-DES implantation to prevent the occurrence of in-stent restenosis and NOAF following PCI. Furthermore, the use of decision aids, such as risk prediction models for individualized risk of bleeding and restenosis, may help clinicians and patients weigh the potential risks and benefits of competing stent types [37–39].

An advantage of this study is its use of nationwide data, including data from all PCI-capable institutions in Taiwan, although in-stent selection varied markedly between patients, clinicians, and institutions [38]. Additionally, few structural differences exist in Taiwan, because the NHI program covers 99% of residents and necessary invasive cardiac procedures for CAD. Thus, our findings are likely to be representative of real-world evidence.

This study has limitations. First, the NHIRD does not provide certain clinical information, such as information on angiographic findings and complexity of PCI (e.g., PCI for bifurcation lesions or chronic total occlusion, and procedural time), the extent of a patient's CAD, which might also influence the occurrence of AF. We recognized this limitation since we were unable to control these mentioned factors which might bias our findings. To reduce the bias as much as possible, we alternatively defined the complex PCI as PCI for  $\geq 2$  coronary arteries. Second, PSM in observational studies considers only observed variables; therefore, a hidden bias of stent selection introduced by unobserved variables, such as frailty of patients, may occur. Although the NHIRD does not provide information on patients' frailty, we still noted that patients in the BMS group had poorer health statuses than those in the NG-DES group before PSM. In the present study, we used PSM to reduce the bias after accounting for most observed variables, however, some unobserved variables still existed to be impossible to account. Despite its limitations, PSM is still an acceptable approach that has been validated in randomized clinical trials [27,42]. Third, we did not compare the effects of the different types of NG-DES (i.e., durable polymer DES and biodegradable polymer DES). Finally, Taiwanese patients were included in this study; therefore, the results might not be generalizable to other populations. Future prospective randomized studies are warranted to confirm our findings.

## 5. Conclusions

At 1-year follow-up, patients with stable CAD who had received PCI and NG-DES implantation exhibited a lower risk of NOAF following PCI than did those who had received BMS implantation; these results are consistent with those for patients who had a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of

$\geq 2$ . Overall, our findings suggest that NG-DESs significantly prevent NOAF following PCI.

## Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2019.05.053>.

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