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Interventional Cardiology

Drug-Eluting Stents versus Bare-Metal Stents in Taiwanese Patients with Acute Coronary Syndrome: An Outcome Report of a Multicenter Registry

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***Background*:** The study aims to compare cardiovascular outcomes of using bare-metal stents (BMS) and drug-eluting stents (DES) in patients with acute coronary syndrome (ACS) through analysis of the database from the Taiwan ACS registry. Large domestic studies comparing outcomes of interventional strategies using DES and BMS in a Taiwanese population with ACS are limited.

Methods and Results: Collected data regarding characteristics and cardiovascular outcomes from the registry database were compared between the BMS and DES groups. A Cox regression model was used in an unadjusted or adjusted manner for analysis. Baseline characteristics apparently varied between DES group (n = 650) and BMS group (n = 1672) such as ACS types, Killip's classifications, or coronary blood flows. Compared with the BMS group, the DES group was associated with significantly lower cumulative incidence of all-cause mortality (3.4% vs. 5.8%, p = 0.008), target vessel revascularization (TVR) (5.2% vs. 7.4%, p = 0.035), or major adverse cardiac events (MACE) (10.2% vs. 15.6%, p < 0.001) at 1 year in a real-world setting. Cox regression analysis showed the BMS group referenced as the DES group had significantly higher risk-adjusted total mortality [hazard ratio (HR) = 1.85, p = 0.026], target vessel revascularization (TVR) (HR = 1.59, p = 0.035), and MACE (HR = 1.68, p = 0.001).

Conclusions: The data show use of DES over BMS provided advantages to patients with ACS in terms of lower 1-year mortality, TVR, and MACE. The study suggests implantation of DES compared with BMS in Taiwanese patients with ACS is safe and beneficial in the real-world setting.

Key Words: Acute coronary syndrome • Bare-metal stent • Cardiovascular outcome • Drug-eluting stent • Percutaneous coronary intervention

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INTRODUCTION

Acute coronary syndrome (ACS) is broadly presented as ST-segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), or unstable angina (UA). Cardiovascular events occurred more commonly in patients with ACS than those with stable coronary artery disease (CAD).[1-3] Drug-eluting stents (DES) have been used for patients with ACS, which were designed to locally release drugs inhibiting neointimal growth and to improve in-stent restenosis. Increasing the references to large-scale data from randomized controlled trials (RCTs)[4-15] and observational trials[16-21] have established that the

use of DES in patients with ACS is safe and efficacious compared with the use of bare-metal stents (BMS). The majority of results reveal the patients receiving DES implantations have significantly lower rates of angiographic restenosis, target vessel revascularization (TVR), and/or target lesion revascularization (TLR) during the follow-up period (8 months to 5 years) as compared to those receiving BMS implantations.[4-19] The results with regard to mortality, recurrent myocardial infarction (MI), and major adverse cardiac events (MACE) are still conflicting. A few studies have pointed out that cardiovascular outcomes partly vary between registry trials and RCTs,[22,23] or between different races.[24] In addition, no large-scale reports are available in comparison of use of DES and BMS in Taiwanese patients with ACS. The Taiwan ACS full spectrum (ACS FS) registry study is a large-scale, multicenter, prospective, observational study which was designed to evaluate real practices in ACS management.[25] The present analysis shows differences in cardiovascular outcomes between ACS participants who received either BMS alone or DES alone. The study aims were to compare patterns of use of BMS and DES in ACS patients, and further investigate the differences in cardiovascular outcomes between BMS and DES groups in a real-world setting.

METHODS

Study design

The present report is based upon the analysis of the database from the Taiwan ACS FS registry. The registry study is a multicenter, prospective, nonrandomized, observational trial. The present study was designed to detect the differences in clinical outcomes between ACS patients who received coronary stentings with any kind of DES (as the DES group) or BMS (as the BMS group). Data involving these two patient groups were collected from the case record forms of the registry. The participating sites with high annual volume of percutaneous coronary intervention (PCI) were selected and certified by the Scientific Committee of the Taiwan Society of Cardiology. Each site recruited 50-200 consecutively eligible patients who were aged 20 or older, and hospitalized within 24 hours after the onset of symptoms of ACS or transferred in from a non-participating site without a stay exceeding 12 hours. Excluded patients were those who presented as ACS secondary to co-morbidity such as trauma or bleeding, or who had been previously enrolled in the registry or in a drug study. Clinical follow-up was scheduled at 3, 6, 9 and 12 months after discharge for data collection on medication prescriptions, and clinical events such as mortality, nonfatal myocardial infarction (MI), TVR, stroke, and hospitalization. Relevant data were accumulated including characteristics, clinical presentations, PCI procedures, medication prescriptions, and adverse cardiovascular events.

We were authorized to conduct the analysis of the registry database regarding clinical outcome of BMS and DES groups. The study protocol had been examined and accepted by the Publication Committee of the registry. The ACS participants who received coronary stentings with 1 or more BMS or DES were respectively accumulated as the BMS group or the DES group. Participants who did not receive coronary stenting or received hybrid implantations with both BMS and DES or died during procedures were excluded for analysis. Any kind of BMS or DES was allowed at the individual interventionist's discretion. Available classes of DES included sirolimus- (SES), paclitaxel- (PES), zotarolimus- (ZES), and everolimus-eluting stent (EES) during the registry period. Patient data relevant to classic risk factors for CAD, the index PCIs, the subsequent events, and prescribed medications were gathered from the case report forms. Prescriptions of aspirin, clopidogrel, aspirin plus clopidogrel as dual anti-platelet therapy (DAPT), beta-blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, and statins were compared between the two groups. Newer anti-platelet agents, such as prasugrel and ticagrelor were not marketed at the registry period in Taiwan.

The registry and the present study were performed in accordance with the Declaration of Helsinki and the local regulatory guidelines. The medical ethics committee approved the study protocol at each participating site. Written informed consent was obtained from all participants.

Adverse events in hospital and at 1 year

The cardiovascular endpoints included all-cause mortality, nonfatal MI, hemorrhagic or ischemic stroke, and ischemia-driven TVR during the 1-year follow-up.

MACE was defined as a composite of all-cause mortality, nonfatal MI, and TVR. A cardiovascular event was confirmed by physicians according to the clinical symptoms and signs, electrocardiographic findings, levels of cardiac enzymes, and/or diagnostic images. In-hospital adverse events were assessed including mortality, nonfatal MI, unplanned TVR, stroke, cardiogenic shock, ventricular arrhythmia, atrial fibrillation, and acute renal failure. The event of ventricular arrhythmia was defined as ventricular fibrillation, sustained or non-sustained ventricular tachycardia. Acute renal failure indicated a rise in serum creatinine beyond 0.56 microgram per deciliter above the baseline value.

Statistical analysis

All variables were analyzed using SAS software version 9.2 (SAS Institute Inc., Cary, NC, USA) in the analytic center of the registry. All categorical data and rates are displayed as percentages and numbers, and the continuous data are shown as means ± standard deviation. Baseline and outcome data were compared between groups using chi-square test or Fisher's exact test for categorical variables, and ANOVA test for continuous variables. Kaplan-Meier analysis with log-rank test was used to detect differences in cumulative event-free survival at 1 year between the BMS and DES groups. Hazard ratios (HRs) and 95% confidence interval (CI) were calculated from a Cox regression model in an unadjusted or adjusted manner for other covariates. Demographic characteristics (age, gender and body mass index), stent type, Killip class, classical cardiac risk factors (the presence of hypertension, diabetes, history of smoking or smoke, family history of atrial fibrillation, history of heart failure, and cerebrovascular accident), vascular history (previous MI, previous PCI, or previous bypass surgery), insulin, and ACS type were included for analysis. Each of the above variables was used for its univariate association with 1-year mortality in the Cox regression. Covariates that were significantly associated with 1-year mortality with a significance level of $p < 0.05$ were selected for multivariate Cox model. Stepwise model selection with critical value of $p < 0.15$ and $p > 0.25$ was implemented for variable selection and for variable elimination. Cox regression analysis was adjusted for the selected variables including age, Killip class, diabetes mellitus, heart failure and ACS type. A p value < 0.05 with two-sided 95% CI was considered statistically significant for all tests. Analysis was conducted as time to first event without double counting of events within analysis involving composite endpoints. In the registry, patients who were lost to follow up were censored at the time of last contact with their vital status deemed as alive and event-free at that time.

RESULTS

Patient demographic data and characteristics

The registry study recruited 3183 participants with ACS from 39 participating sites between October 2008 and January 2010. A total of 2659 participants (83.5%) received PCI. Among them, 2322 participants with a mean age of 62.3 ± 13.4 years who received 1 or more BMS (as the BMS group, n = 1672) or DES (as the DES group, n = 650) were included for analysis (Figure 1). Demographic and characteristic variations were apparent between the groups. Dyslipidemia, known CAD, family history of vascular disease, presentation as non-ST segment elevation acute coronary syndrome (NSTEACS), and stentings at the left main trunk and at the left anterior descending artery were more common in the DES group ($p < 0.05$) as compared to the BMS group. Cigarette smoking, history of cerebrovascular accident, presentation as STEMI, or Killip IV classification was more common in the BMS group ($p < 0.05$). Demographics, characteristics, angiographic, and procedural data are shown in Table 1.

In-hospital adverse events

Compared with the BMS group, the DES group was associated with significantly lower in-hospital incidence of ventricular arrhythmia (2.6% vs. 5.8%, p = 0.001) and acute renal failure (0.6% vs. 2.3%, p = 0.007). The rates of the other in-hospital adverse events were identical between the groups, including all-cause mortality (1.1% vs. 1.7%, p = 0.289), cardiac mortality (0.9% vs. 1.3%, p = 0.780), nonfatal MI (1.1% vs. 0.6%, p = 0.227), unplanned PCI (0.5% vs. 0.3%, p = 0.694), and hemorrhagic or ischemic stroke (0% vs. 0.4%, p = 0.201).

One-year cardiovascular outcomes

The rates of all-cause mortality, nonfatal MI, TVR, and MACE at 1 year were 5.1% (119/2322), 3.6% (83/

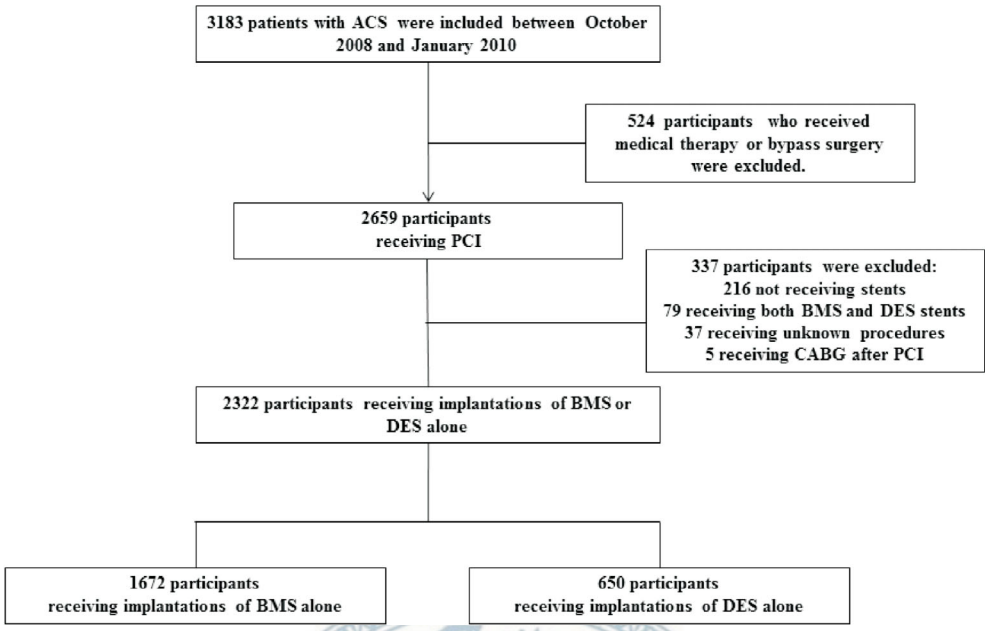

Figure 1. *The flow chart for patient selection. ACS, acute coronary syndrome; BMS, bare-metal stents; CABG,coronary bypass surgery; DES, drug-eluting stents; PCI, percutaneous coronary intervention.*

2322), 6.8% (157/2322), and 14.1% (327/2322), respectively. The DES group compared with the BMS group had significantly lower cumulative incidences of all-cause mortality (3.4% vs. 5.8%, p = 0.008) and TVR (5.2% vs. 7.4%, p = 0.035) at 1 year using Kaplan-Meier analysis, but similar incidences of cardiac mortality (1.4% vs. 2.2%, p = 0.198), nonfatal MI (3.1% vs. 3.8%, p = 0.421), and stroke (1.1% vs. 1.5%, p = 0.437) (Figure 2). Significant reductions were observed in cumulative incidences of 3 cardiovascular composites at 1 year in the DES group as compared with the BMS group, including MACE (10.2% vs. 15.6%, p < 0.001); the composite of all-cause mortality, nonfatal MI, and stroke (6.6% vs. 10.5%, p < 0.001); and the composite of all-cause mortality, nonfatal MI, TVR, and stroke (10.8% vs. 16.9%, p < 0.001) (Figure 3). In-hospital and 1-year adverse outcomes between groups are outlined in Table 2.

After adjusting for confounding factors including age, Killip class, diabetes mellitus, heart failure and ACS type, the BMS group referenced as the DES group appeared significantly higher 1-year risk of cardiovascular events: all-cause mortality (HR = 1.85, 95% CI = 1.08-3.18, p = 0.026), TVR (HR = 1.59, 95% CI = 1.03-2.44, p = 0.035), MACE (HR = 1.68, 95% CI = 1.23-2.29, p = 0.001), the composite of all-cause mortality, nonfatal MI, and stroke (HR = 1.61, 95% CI = 1.10-2.37, p = 0.015), and the composite of all-cause mortality, nonfatal MI, TVR, and stroke (HR = 1.66, 95% CI = 1.23-2.24, p = 0.001) (Table 3). Table 4 shows differences in cardiovascular outcome at 1 year between DES and BMS subgroups. DES subgroup was associated with significantly lower cardiovascular composite events in the patient population with STEMI, NSTEACS, Killip class I, thrombolysis in myocardial infarction (TIMI) blood flow 0/1, or TIMI 2/3 blood flow.

Pharmacological therapy

Some medication prescriptions were obviously different between the groups. In-hospital use of any heparin (94.2% vs. 91.2%, p = 0.010) and glycoprotein IIb/IIIa inhibitor (22.2% vs. 11.7%, p < 0.001) were more common in the BMS group. For example, the prescription rates of DAPT with aspirin plus clopidogrel (78.8% vs. 57.6%, p < 0.001), beta-blockers (65.5% vs. 59.1%, p = 0.007), and statins (67.6% vs. 62.1%, p = 0.018) were significantly higher in the DES group than those in the BMS group at 6 months. Prescriptions of DAPT with aspirin plus clopidogrel dramatically declined in both groups particularly in the BMS group (91.7% in hospital, 57.6% at 6 months, and 22.3% at 1 year), despite at least 1-year DAPT recommended in patients with ACS.[26-30] Medication prescription rates during the 1-year follow-up are illustrated in Figure 4.

Table 1. Baseline characteristics between BMS and DES groups

	BMS (n = 1672)	DES (n = 650)	p value*
Patient number, n (%)	1672 (72.01)	650 (27.99)	< 0.001
Age (years), mean ± SD	62.44 ± 13.46	62.03 ± 13.27	0.517
Male, n/N (%)	1341/1672 (80.20)	524/650 (80.62)	0.823
Body mass index, (kg/m^2), mean ± SD	25.42 ± 3.81	25.64 ± 3.87	0.229
History of, n/N (%)			
Diabetes mellitus	575/1658 (34.68)	199/648 (30.71)	0.070
Dyslipidemia	604/1647 (36.67)	293/649 (45.15)	< 0.001
Hypertension	1009/1646 (61.30)	408/648 (62.96)	0.461
Cigarette smoker	797/1651 (48.27)	239/637 (37.52)	< 0.001
Family history of CVD	267/1262 (21.16)	142/495 (28.69)	< 0.001
Known coronary artery disease	314/1672 (18.78)	162/650 (24.92)	0.001
MI	123/308 (39.94)	63/159 (39.62)	0.948
Percutaneous coronary intervention	218/312 (69.87)	126/161 (78.26)	0.052
Coronary artery bypass surgery	30/308 (9.74)	16/160 (10.00)	0.929
Congestive heart failure	60/1672 (3.59)	29/650 (4.46)	0.325
Atrial fibrillation	37/1671 (2.21)	20/650 (3.08)	0.228
Cerebrovascular accident	148/1672 (8.85)	37/650 (5.69)	0.012
Blood pressure, heart rate at ED, (mean ± SD)			
Systolic blood pressure	138.13 ± 32.66	140.62 ± 31.74	0.100
Diastolic blood pressure	81.27 ± 20.76	83.18 ± 20.27	0.047
Heart rate	80.06 ± 21.92	81.30 ± 20.34	0.216
Types of ACS, n/N (%)			< 0.001
ST elevation MI	1080/1672 (64.59)	308/650 (47.38)	
Non-ST elevation MI	458/1672 (27.39)	240/650 (36.92)	
Unstable angina	134/1672 (8.01)	102/650 (15.69)	
Killip classification, n/N (%)			< 0.001
I	846/1420 (59.58)	357/524 (68.13)	
II	278/1420 (19.58)	82/524 (15.65)	
III	130/1420 (9.15)	52/524 (9.92)	
IV	166/1420 (11.69)	33/524 (6.30)	
Median time to CAG (hours)	2.65	17.22	< 0.001
Culprit coronary artery, n/N (%)			
Left main	31/1672 (1.85)	24/650 (3.69)	0.009
Left anterior descending artery	811/1672 (48.50)	360/650 (55.38)	0.003
Left circumflex artery	311/1672 (18.60)	133/650 (20.46)	0.306
Right coronary artery	650/1672 (38.88)	185/650 (28.46)	< 0.001
TIMI artery flow, n/N (%)			0.006
TIMI 0/1	932/1511 (61.68)	310/572 (54.20)	
TIMI 2	318/1511 (21.05)	136/572 (23.78)	
TIMI 3	261/1511 (17.27)	126/572 (22.03)	
Peak cardiac enzymes, (mean ± SD)			
Creatine kinase	1061.57 ± 1775.32	1051.81 ± 2019.49	0.914
Creatine kinase-myocardial band	67.78 ± 110.96	55.12 ± 88.55	0.014
Troponin I or T	14.85 ± 45.25	12.94 ± 38.89	0.368
Echocardiography, n/N (%)			0.154
Normal	861/1365 (63.08)	328/487 (67.35)	
Mild LV systolic dysfunction	317/1365 (23.22)	109/487 (22.38)	
Moderate LV systolic dysfunction	137/1365 (10.04)	40/487 (8.21)	
Severe LV systolic dysfunction	50/1365 (3.66)	10/487 (2.05)	
Estimated ejection fraction (if done)	54.28 ± 12.31	55.25 ± 12.55	0.145
Percutaneous coronary intervention			
Done within 48 hours, n/N (%)	1352/1662 (81.35)	456/639 (71.36)	< 0.001
Median time to intervention, (hours)	2.90	17.22	< 0.001
Number of lesions treated, (mean ± SD)	1.36 ± 0.69	1.47 ± 0.78	0.001

*, comparison between BMS and DES groups by chi-square test for categorical variables and by ANOVA test for continuous variables; ACS, acute coronary syndrome; BMS, bare-metal stent; CAG, coronary arterogram; CVD, cardiovascular disease; DES, drug-eluting stent; ED, emergency department; LV, left ventricle; MI, myocardial infarction; SD, standard deviation; TIMI, thrombolysis in myocardial infarction. Mild, moderate, or severe LV systolic dysfunction indicates estimated LV ejection fraction of 41-50%, 20-40%, or < 20%, respectively.

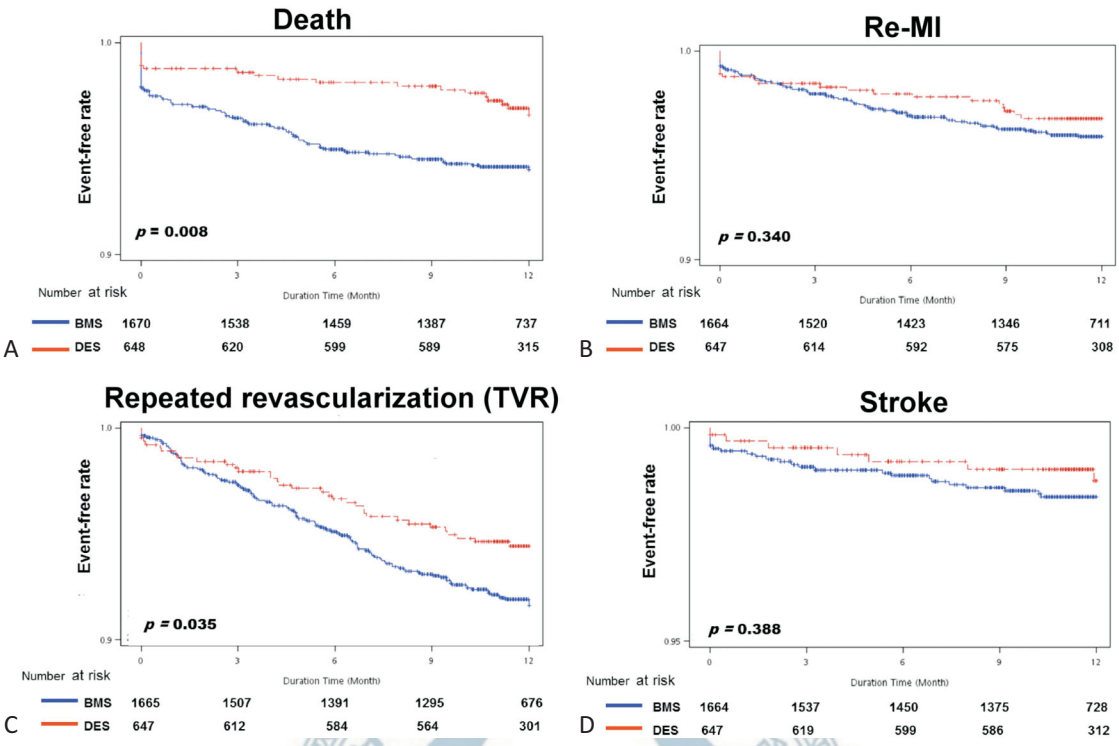

Figure 2. *The Kaplan-Meier plots show the cumulative 1-year incidence of all-cause mortality (A), nonfatal myocardial infarction (B), repeat target-vessel revascularization (C), and nonfatal stroke (D) in the patients receiving BMS or DES. BMS, bare-metal stent; DES, drug-eluting stents; MI, myocardial infarction.*

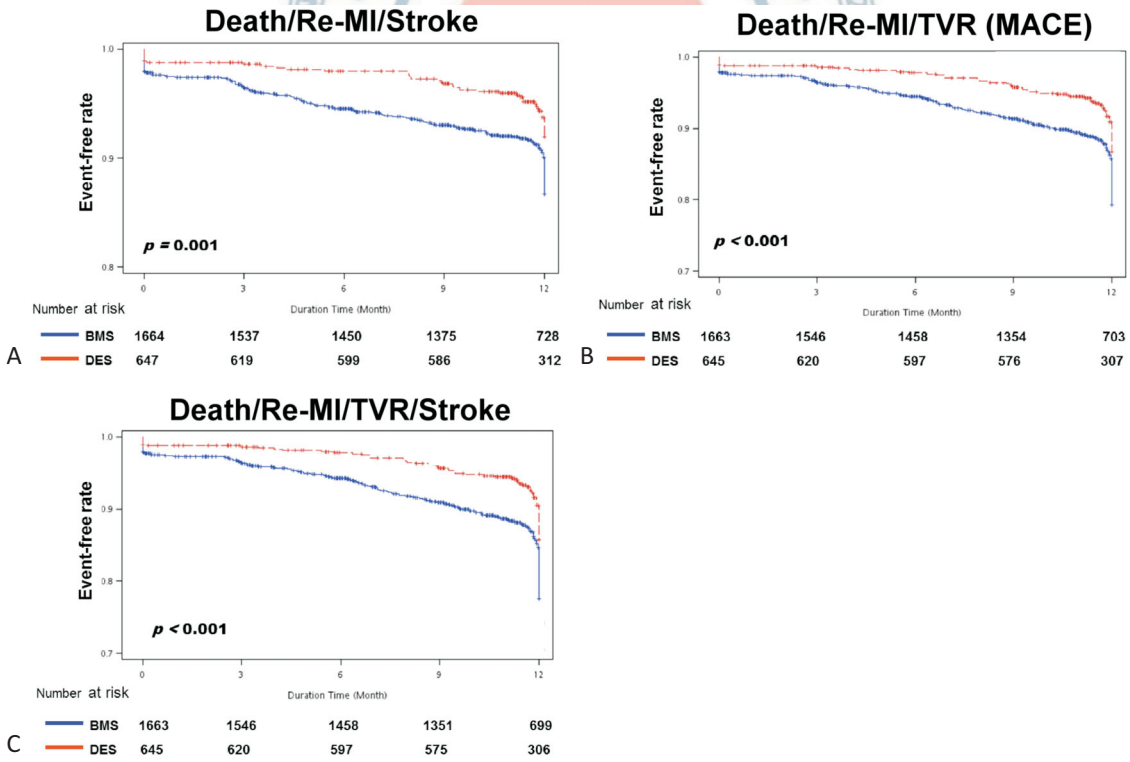

Figure 3. *The Kaplan-Meier plots show the cumulative 1-year incidence of major adverse cardiac events (all-cause mortality, nonfatal MI and TVR) (A), composite of all-cause mortality, nonfatal MI, and stroke (B), and composite of all-cause mortality, TVR, nonfatal MI, and stroke (C) in the patients receiving BMS or DES. BMS, bare-metal stent; DES, drug-eluting stents; MACE, major adverse cardiac events; MI, myocardial infarction; TVR, target vessel revascularization.*

Table 2. In-hospital and 1-year adverse outcomes between BMS and DES groups

	BMS	DES	p value*
In-hospital outcomes, n/N (%)			
All-cause mortality	28/1672 (1.67)	7/650 (1.08)	0.289
Cardiac mortality	22/1671 (1.32)	6/650 (0.92)	0.436
Nonfatal MI	10/1672 (0.60)	7/650 (1.08)	0.277
Unplanned TVR	5/1672 (0.30)	3/650 (0.46)	0.694
Hemorrhagic or ischemic stroke	7/1672 (0.42)	0/650 (0.00)	0.201
TIMI bleeding	33/1672 (1.97)	7/650 (1.08)	0.136
Cardiogenic shock	72/1672 (4.31)	23/650 (3.54)	0.402
Ventricular arrhythmia	97/1672 (5.80)	17/650 (2.62)	0.001
Atrial fibrillation	40/1672 (2.39)	15/650 (2.31)	0.904
Acute renal failure	38/1672 (2.27)	4/650 (0.62)	0.007
1-year outcomes, n/N, (%)			
All-cause mortality	97/1672 (5.80)	22/650 (3.38)	0.018
Cardiac mortality	37/1671 (2.21)	9/650 (1.38)	0.196
Nonfatal MI	63/1672 (3.77)	20/650 (3.08)	0.421
TVR	123/1672 (7.36)	34/650 (5.23)	0.067
Hemorrhagic or ischemic stroke	25/1672 (1.50)	7/650 (1.08)	0.437
MACE	261/1672 (15.61)	66/650 (10.15)	< 0.001
Mortality/nonfatal MI/stroke	176/1672 (10.53)	43/650 (6.62)	0.004
Mortality/nonfatal MI/TVR/stroke	282/1672 (16.87)	70/650 (10.77)	< 0.001

*, comparison between BMS and DES groups by chi-square test for categorical variables and by ANOVA test for continuous variables. BMS, bare-metal stent; DES, drug-eluting stents; MACE, major adverse cardiac event(s); MI, myocardial infarction; TIMI, thrombolysis in myocardial infarction; TVR, target vessel revascularization.

Table 3. Cox regression analysis shows estimated risk of 1-year outcomes of the BMS group referenced as the DES group

	Unadjusted HR (95% CI)	p value*	Adjusted HR (95% CI)[#]	p value*
All-cause mortality	1.906 (1.18-3.09)	0.009	1.850 (1.08-3.18)	0.026
Cardiac mortality	1.582 (0.76-3.29)	0.212	1.414 (0.62-3.24)	0.413
Nonfatal MI	1.277 (0.77-2.11)	0.341	1.199 (0.68-2.13)	0.534
Hemorrhagic or ischemic stroke	1.443 (0.62-3.34)	0.391	1.082 (0.42-2.82)	0.872
TVR	1.500 (1.03-2.19)	0.036	1.586 (1.03-2.44)	0.035
MACE	1.683 (1.28-2.21)	< 0.001	1.679 (1.23-2.29)	0.001
mortality/nonfatal MI/stroke	1.737 (1.24-2.44)	0.002	1.612 (1.10-2.37)	0.015
mortality/nonfatal MI/TVR/stroke	1.718 (1.32-2.24)	< 0.001	1.660 (1.23-2.24)	0.001

*, risk estimation of 1-year cardiovascular outcomes in the BMS group referenced as the DES group using Cox regression analysis for variables; [#], Cox regression analysis adjusted for the confounding factors including age, Killip class, diabetes mellitus, heart failure and ACS type. ACS, acute coronary syndrome; BMS, bare-metal stent; DES, drug-eluting stents; CI, confidence interval; HR, hazard ratio referenced as the DES group; MACE, major adverse cardiac event(s); MI, myocardial infarction; TVR, target vessel revascularization.

DISCUSSION

The present report is based upon the analysis of the database of a nationwide and multicenter ACS registry in Taiwan. The study investigated cardiovascular outcomes of 2322 participants with ACS implanted with either BMS or DES. The major findings are: (1) The cumulative 1-year incidences of all-cause mortality, TVR, and composite cardiovascular events are significantly lower in the DES group as compared to those in the BMS group in a real-world setting; (2) After adjusting for the confounders, the BMS group referenced as the DES group significantly enhances the estimated 1-year risks of all-cause mortality by 84%, TVR by 54%, and MACE by

Table 4. Differences in cardiovascular composite events at 1 year between the BMS and DES subgroups

Subgroups, n/N (%)	Composite events, n/N (%)	p value*
STEMI (N = 1388)		0.005
BMS 1080/1388 (77.81)	174/1080 (16.11)	
DES 308/1388 (22.19)	30/308 (9.74)	
NSTEMI/UA (N = 934)		0.008
BMS 592/934 (63.38),	108/592 (18.24)	
DES 342/934 (36.62)	40/342 (11.70)	
Killip I (N = 1203)		0.001
BMS 846/1203 (70.32)	123/846 (14.54)	
DES 357/1203 (29.68)	28/357 (7.84)	
Killip II-IV (N = 741)		0.691
BMS 574/741 (77.46)	111/574 (19.34)	
DES 167/741 (22.54)	30/167 (17.96)	
TIMI 0/1 (N = 1242)		0.034
BMS 932/1242 (75.04)	162/932 (17.38)	
DES 310/1242 (24.96)	38/310 (12.26)	
TIMI 2/3 (N = 841)		0.013
BMS 579/841 (68.85)	95/579 (16.41)	
DES 262/841 (31.15)	26/262 (9.92)	

*, comparison between BMS and DES groups by ANOVA test; Cardiovascular composite indicates events of death, myocardial infarction, repeat revascularization, or stroke. BMS, bare-metal stent; DES, drug-eluting stent; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction; UA, unstable angina.

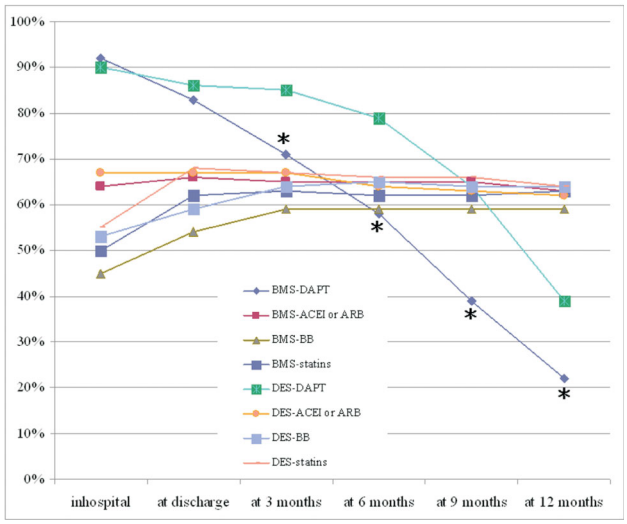

Figure 4. *The photo shows the prescription rates of medications during 1-year follow-up. Prescription rates of DAPT with aspirin and clopidogrel were significantly low in the BMS group compared with the DES group at 3, 6, 9, and 12 months. *, p < 0.001 in comparisons of prescription rates of DAPT between the BMS and DES groups during 1-year follow-up; ACEI or ARB, angiotensin converting enzyme inhibitors or angiotensin receptor blockers. ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocke; BB, beta-blockers; BMS, bare-metal stent; DES, drug-eluting stents; DAPT, dual antiplatelet therapy.*

64% in the ACS series; (3) DAPT is under-prescribed and under-persisted for the ACS participants undergoing coronary stentings in real practice.

Even though an abundance of evidence supports the use of DES in ACS patients, rare data comparing DES and BMS are available in a Taiwanese population.[25] The report has reinforced that the use of first-, second-, or newly-generated DES is beneficial in Taiwanese patients with ACS in a real-world setting. In the series, a majority (89.8%) of the participants were presented as acute MI (AMI). Numerous RCTs have identified that use of DES over BMS significantly reduces rates of repeat revascularization and/or MACE in AMI patients, with identical mortality, re-MI, and stroke.[4-12] The large-scale RCT, Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction, enrolling 3006 AMI patients showed that placement of first-generation PES (n = 2257) rather than BMS (n = 749) reduced 1-year and 3-year rates of ischemia-driven TLR with identical rates of other adverse ischemic events despite uneven DAPT after 6-month follow-ups between groups.[4,5] The other modest RCTs in size (270-745 participants) showed comparable results during the mid-term (8 months to 1 year) and long-term (3-4 years) periods.[6-12] Compared with BMS group, the "legacy" phenomenon of DES group indicating that the clinical benefit, at least with regard to lower repeat revascularization, has been sustained in the following years (2-5 years). This phenomenon is observed in some large RCTs[4-8,10-12,15-16,19] although the release of coated drugs was completed within months after implantation of DES. By contrast, the "catch-up" phenomenon of the DES group indicates that the clinical benefit is attenuated or abolished in the following years.[8,10,13,19,22] The mechanism resulting in the inconsistent phenomena is unknown. The conflicting results were also shown in the "Paclitaxel-Eluting Versus Conventional Stent in Myocardial Infarction with ST-Segment Elevation" (PASSION) trial and "Drug Elution and Distal Protection in Acute Myocardial Infarction" (DEDICATION) trials.[13-16] Both stent groups had similar rates of cardiac mortality, TLR, and MACE (mortality, MI, and TLR) at 1 year and at 5 years in the PASSION trial.[13,14]

The results of the DEDICATION trial were borderline higher rates of cardiac mortality in the DES group at 1 year (p = 0.09) and significantly at 3 years (p = 0.013),[15,16] despite the non-significant difference in all-cause mortality and significant reductions in TLR and MACE. Previous research depicted that the use of SES versus BMS benefited Japanese patients with ACS in terms of lowering TVR/TLR and MACE.[33] The present study provides more convincing data to support the use of DES for the Taiwanese population with ACS in terms of improving 1-year cardiovascular outcome.

Some registries apart from the RCTs have reported the consistent results showing lower mortality in DES group compared with BMS group.[17-20,23,24] Large-scale registry studies comparing BMS and DES use in patients with NSTEACS or ACS FS are sparse, and moreover reveal conflicting results.[31-33] A cohort study reported by Li et al. collecting non-Asian patients with NSTEACS implanted with DES (PES or SES, n = 1493) or BMS (n = 366) showed no differences in TLR (5.1% vs. 4.0%, p = 0.4), TVR (8.0% vs. 7.2%, p = 0.6), and MACE (11.2% vs. 12.0%, p = 0.6) at 1 year.[28] The results reported by Mauri et al. demonstrated that in Massachusetts for patients with NSTEMI, the DES group had significantly lower rates of risk-adjusted mortality (12.8% vs. 15.6%, p = 0.04), recurrent MI (10.3% vs. 13.3%, p = 0.02), and TVR (9.8% vs. 15.2%, p < 0.001) at 2 years.[17] A study from New York's PCI registry including propensity-matching 4776 pairs of patients with NSTEMI revealed that the DES (PES or SES) group had a long-term benefit in terms of significantly lower mortality (14.5% vs. 16.6%, p < 0.001) and repeat revascularization (11.0% vs. 13.1%, p = 0.009) at a median follow-up period of 3.68 years.[29] A nonrandomized study reported by Ogita et al. recruiting 245 consecutive ACS patients undergoing BMS (n = 117) or SES (n = 128) implantations exhibited a "catch-up" phenomenon in the SES group with significant reductions in TVR (3.1% vs. 9.4%, p = 0.04) and MACE (3.9% vs. 12.0%, p = 0.03) at 8 months, but had similar event rates at 3 years.[31] The present study clearly showed the use of DES in the series was associated with lower 1-year mortality, TVR, and MACE in a real-world setting. However, we cannot conclude that implantations of DES totally contribute to the 1-year cardiovascular benefit, even though the possible confounders have been adjusted. As shown in Table 4, use of DES over BMS benefits subgroups with STEMI, NSTEACS, Killip I, TIMI 1/0 blood flow, or TIMI 2/3 blood flow, but not with Killip II/IV, in terms of reducing cardiovascular composite events.

In-hospital adverse event rates were similar between groups except for ventricular arrhythmia and acute renal failure being more common in the BMS group. No difference in in-hospital cardiovascular events between groups was observed. It seems reasonable because the in-hospital duration was too short to yield outcome differences. The BMS group included more patients with STEMI requiring primary PCI who were more likely to develop ventricular arrhythmia and receive emergent PCI. The mechanism of frequent acute renal failure needs further investigation. Remarkably, at least 12-month DAPT in the management of ACS is recommended as class I indication for preventing cardiovascular events irrespective of implantation of stent types.[26-30] It is very crucial to consider the barriers to limit DAPT because earlier discontinuation of DAPT may increase cardiovascular events.[34-36] Unsatisfactory prescription rates may be caused by the limited medical budge. Implantation of DES coupled with sufficiently longer DAPT may partially account for outcome benefit and legacy phenomenon.[1,34-39]

Limitations

Limitations of this study should be emphasized here: (1) the propensity for use of BMS and DES, the heterogeneity in clinical and angiographic characteristics, PCI-related variables, and uneven duration of DAPT had made the evaluation of risk or benefit more difficult. Even using a statistical adjusting model, the possibility of unmeasured confounders cannot be completely excluded, especially when marginally significant; (2) impacts of lesion characteristics (vessel size, lesion length, and thrombus burden), use of heparin or/and glycoprotein IIb/IIIa inhibitor, final angiographic results, and stent properties on outcomes were not investigated in the study. The factors may potentially affect outcome; (3) there was no mandatory angiographic follow-up in the study. Ischemia-driven endpoints may be underreported despite a real practice; (4) rare stent thrombosis was not evaluated in the registry. The concern might be tempered by the significant decrease in mortality and similar MI rate in the DES group; (5) one-year

period of follow-up for cardiovascular outcomes may be inadequate.

CONCLUSIONS

The report shows that the DES group implanted with DES benefitted Taiwanese patients with ACS in terms of lower 1-year all-cause mortality, TVR, and cardiovascular composite events without increased adverse events as compared with the BMS group. The study suggests that use of DES in patients with ACS is preferred to use of BMS with a consideration of cardiovascular benefit in a real-world setting.

CONFLICT OF INTEREST

Chi-Cheng Lai (none), Hon-Kan Yip (none), Tsung-Hsien Lin (none), Chiung-Jen Wu (none), Wen-Ter Lai (none), Chun-Peng Liu (none), Shu-Chen Chang (none), Guang-Yuan Mar (none).

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REFERENCES

1. Kawaguchi R, Kimura T, Morimoto T, et al. Safety and efficacy of sirolimus-eluting stent implantation in patients with acute coronary syndrome in the real world. *Am J Cardiol* 2010;106: 1550-60.
2. Kukreja N, Onuma Y, Garcia-Garcia HM, et al. The risk of stent thrombosis in patients with acute coronary syndromes treated with bare-metal and drug-eluting stents. *JACC Cardiovasc Interv* 2009;2:534-41.
3. Hirsch A, Verouden NJ, Koch KT, et al. Comparison of long-term mortality after percutaneous coronary intervention in patients treated for acute ST-elevation myocardial infarction versus those with unstable and stable angina pectoris. *Am J Cardiol* 2009; 104:333-7.
4. Stone GW, Witzenbichler B, Guagliumi G, et al. Heparin plus a glycoprotein IIb/IIIa inhibitor versus bivalirudin monotherapy and paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction (HORIZONS-AMI): final 3-year results from a multicentre, randomised controlled trial. *Lancet* 2011;377: 2193-204.
5. Stone GW, Lansky AJ, Pocock SJ, et al. Paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction. *N Engl J Med* 2009;360:1946-59.
6. Valgimigli M, Campo G, Percoco G, et al. Comparison of angioplasty with infusion of tirofiban or abciximab and with implantation of sirolimus-eluting or uncoated stents for acute myocardial infarction: the MULTISTRATEGY randomized trial. *JAMA* 2008; 299:1788-99.
7. Spaulding C, Teiger E, Commeau P, et al. Four-year follow-up of TYPHOON (trial to assess the use of the CYPHer sirolimus-eluting coronary stent in acute myocardial infarction treated with BalIOON angioplasty). *JACC Cardiovasc Interv* 2011;4:14-23.
8. Atary JZ, van der Hoeven BL, Liem SS, et al. Three-year outcome of sirolimus-eluting versus bare-metal stents for the treatment of ST-segment elevation myocardial infarction (from the MISSION Intervention Study). *Am J Cardiol* 2010;106:4-12.
9. van der Hoeven BL, Liem SS, Jukema JW, et al. Sirolimus-eluting stents versus bare-metal stents in patients with ST-segment elevation myocardial infarction: 9-month angiographic and intravascular ultrasound results and 12-month clinical outcome results from the MISSION Intervention Study. *J Am Coll Cardiol* 2008;51:618-26.
10. Violini R, Musto C, De Felice F, et al. Maintenance of long-term clinical benefit with sirolimus-eluting stents in patients with ST-segment elevation myocardial infarction 3-year results of the SESAMI (sirolimus-eluting stent versus bare-metal stent in acute myocardial infarction) trial. *J Am Coll Cardiol* 2010;55:810-4.
11. Menichelli M, Parma A, Pucci E, et al. Randomized trial of sirolimus-eluting stent versus bare-metal stent in acute myocardial infarction (SESAMI). *J Am Coll Cardiol* 2007;49:1924-30.
12. Di Lorenzo E, De Luca G, Sauro R, et al. The PASEO (paclitaxel or sirolimus-eluting stent versus bare metal stent in primary angioplasty) randomized trial. *JACC Cardiovasc Interv* 2009;2:515-23.
13. Vink MA, Dirksen MT, Suttorp MJ, et al. 5-year follow-up after primary percutaneous coronary intervention with a paclitaxel-eluting stent versus a bare-metal stent in acute ST-segment elevation myocardial infarction: a follow-up study of the PASSION (paclitaxel-eluting versus conventional stent in myocardial infarction with ST-segment elevation) trial. *JACC Cardiovasc Interv* 2011;4:24-9.
14. Dirksen MT, Vink MA, Suttorp MJ, et al. Two year follow-up after primary PCI with a paclitaxel-eluting stent versus a bare-metal

stent for acute ST-elevation myocardial infarction (the PASSION trial): a follow-up study. *EuroIntervention* 2008;4:64-70.
15. Kaltoft A, Kelbaek H, Thuesen L, et al. Long-term outcome after drug-eluting versus bare-metal stent implantation in patients with ST-segment elevation myocardial infarction: 3-year follow-up of the randomized DEDICATION (drug elution and distal protection in acute myocardial infarction) trial. *J Am Coll Cardiol* 2010;56:641-5.
16. Kelbaek H, Thuesen L, Helqvist S, et al. Drug-eluting versus bare metal stents in patients with ST-segment-elevation myocardial infarction: eight-month follow-up in the drug elution and distal protection in acute myocardial Infarction (DEDICATION) trial. *Circulation* 2008;118:1155-62.
17. Mauri L, Silbaugh TS, Garg P, et al. Drug-eluting or bare-metal stents for acute myocardial infarction. *N Engl J Med* 2008;359: 1330-42.
18. Kaltoft A, Jensen LO, Maeng M, et al. 2-year clinical outcomes after implantation of sirolimus-eluting, paclitaxel-eluting, and bare-metal coronary stents: results from the WDHR (Western Denmark Heart Registry). *J Am Coll Cardiol* 2009;53:658-64.
19. Brodie BR, Stuckey T, Downey W, et al. Outcomes with drug-eluting stents versus bare metal stents in acute ST-elevation myocardial infarction: results from the Strategic Transcatheter Evaluation of New Therapies (STENT) Group. *Catheter Cardiovasc Interv* 2008;72:893-900.
20. Hannan EL, Racz M, Walford G, et al. Drug-eluting versus bare-metal stents in the treatment of patients with ST-segment elevation myocardial infarction. *JACC Cardiovasc Interv* 2008;1: 129-35.
21. Patel MR, Pfisterer ME, Betriu A, et al. Comparison of six-month outcomes for primary percutaneous revascularization for acute myocardial infarction with drug-eluting versus bare metal stents (from the APEX-AMI study). *Am J Cardiol* 2009;103:181-6.
22. Daemen J, Tanimoto S, García-García HM, et al. Comparison of three-year clinical outcome of sirolimus- and paclitaxel-eluting stents versus bare metal stents in patients with ST-segment elevation myocardial infarction (from the RESEARCH and T-SEARCH Registries). *Am J Cardiol* 2007;99:1027-32.
23. Kirtane AJ, Gupta A, Iyengar S, et al. Safety and efficacy of drug-eluting and bare metal stents: comprehensive meta-analysis of randomized trials and observational studies. *Circulation* 2009; 119:3198-206.
24. Brar SS, Leon MB, Stone GW, et al. Use of drug-eluting stents in acute myocardial infarction: a systematic review and meta-analysis. *J Am Coll Cardiol* 2009;53:1677-89.
25. Shyu KG, Wu CJ, Mar GY, et al. Clinical characteristics, management and in-hospital outcomes of patients with acute coronary syndrome – observations from the Taiwan ACS Full Spectrum Registry. *Acta Cardiol Sin* 2011;27:135-44.
26. Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA Focused Update of the Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 Guideline): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Developed in Collaboration with the American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2011;57;1920-59.
27. Hamm CW, Bassand JP, Agewall S, et al. ESC guidelines for the management of patients with acute coronary syndromes presenting without persistent ST-segment elevation. *Eur Heart J* 2011;32:2999-3054.
28. Kushner FG, Hand M, Smith SC Jr, et al. 2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update). *J Am Coll Cardiol* 2009;54:2205-41.
29. Van de Werf F, Bax J, Betriu A, et al. Management of acute myocardial infarction presenting with persistent ST-segment elevation. *Eur Heart J* 2008;29:2909-45.
30. Wijns W, Kolh P, Danchin N, et al. Guidelines on myocardial revascularization. *Eur Heart J* 2010;31:2501-55.
31. Li Y, Torguson R, Syed AI, et al. Effect of drug eluting stents on frequency of repeat revascularization in patients with unstable angina pectoris or non-ST-elevation myocardial infarction. *Am J Cardiol* 2009;104:1654-9.
32. Hannan EL, Samadashvili Z, Walford G, et al. Comparison of outcomes for patients receiving drug-eluting versus bare metal stents for non-ST-segment elevation myocardial infarction. *Am J Cardiol* 2011;107:1311-8.
33. Ogita M, Nakamura T, Fujiwara N, et al. Long-term clinical follow-up after sirolimus-eluting stent versus bare metal stent implantation in patients with acute coronary syndrome. *J Interv Cardiol* 2009;22:216-21.
34. Ho PM, Fihn SD, Wang L, et al. Clopidogrel and long-term outcomes after stent implantation for acute coronary syndrome. *Am Heart J* 2007;154:846-51.
35. Banerjee S, Varghese C, Samuel J, et al. Comparison of the impact of short (< 1 year) and long-term (> or = 1 year) clopidogrel use following percutaneous coronary intervention on mortality. *Am J Cardiol* 2008;102:1159-62.
36. Pfisterer M, Brunner-La Rocca HP, Buser PT, et al. Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents: an observational study of drug-eluting versus bare-metal stents. *J Am Coll Cardiol* 2006;48:2584-91.
37. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001;345:494-502.
38. Peters RJ, Mehta SR, Fox KA, et al. Effects of aspirin dose when used alone or in combination with clopidogrel in patients with acute coronary syndromes: observations from the clopidogrel in unstable angina to prevent recurrent events (CURE) study. *Circulation* 2003;7;108:1682-7.
39. Fox KA, Mehta SR, Peters R, et al. Benefits and risks of the com-

bination of clopidogrel and aspirin in patients undergoing surgical revascularization for non-ST-elevation acute coronary syndrome: the clopidogrel in unstable angina to prevent recurrent ischemic events (CURE) trial. *Circulation* 2004;110: 1202-8.

APPENDIX

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