

Percutaneous Coronary Intervention

Comparison of Clinical Outcomes in Patients Undergoing Coronary Intervention with Drug-Eluting Stents or Bare-Metal Stents: A Nationwide Population Study

Shih-Hsien Sung,^{1,4,5,6} Tzu-Ching Chen,^{7,8} Hao-Min Cheng,^{2,3,4,5,6} Jia-Chun Lee,^{2,3}
Hui-Chu Lang⁷ and Chen-Huan Chen^{2,4,5,6}

Background: The aim of this propensity score-matched cohort study was to investigate the prognostic impacts of drug-eluting stents (DES) and bare-metal stents (BMS) in patients undergoing percutaneous coronary intervention (PCI).

Methods: We conducted a retrospective cohort study based on the National Health Insurance program. Patients who had undergone coronary stenting between Jan. 2007 and Dec. 2008 were recruited and monitored until the end of 2010. Subjects with either BMS or DES were matched 2:1 by propensity score, which adjusted for age, sex, stent number and Charlson comorbidity index (CCI). The Kaplan-Meier method and Cox regression models were used for prognostic analyses.

Results: Among a total of 966 patients with a mean age of 66 years, 644 subjects had BMS and 322 subjects had DES. The incidence of myocardial infarction (MI) and death were significantly lower in the DES group as compared with the BMS group for the three-year follow-up duration. With adjustments for age, sex, premium-based monthly salary, levels of hospital care, stent number, CCI, medications, and acute coronary syndrome presentation in the index hospitalization, use of DES rather than BMS was associated with reduced adverse coronary events (hazard ratio and 95% confidence interval: 0.55, 0.38-0.81 in the whole population, and 0.44, 0.26-0.73 in the subgroup patients with stable coronary artery disease).

Conclusions: Implantation of DES was related to better outcomes than for BMS, in terms of reducing MI and mortality after PCI. The survival benefit for patients with DES was even greater in patients with stable coronary artery disease.

Key Words: Bare-metal stent • Drug-eluting stent • Propensity score

Received: July 1, 2015 Accepted: June 8, 2016

¹Department of Medicine; ²Department of Medical Education; ³Laboratory of Evidence-Based Healthcare, Taipei Veterans General Hospital; ⁴Cardiovascular Research Center; ⁵Department of Medicine; ⁶Department of Public Health; ⁷Institute of Hospital and Health Care Administration, National Yang-Ming University; ⁸Department of Medical Research, Mackay Memorial Hospital, Taipei, Taiwan.

Corresponding author: Dr. Chen-Huan Chen, Department of Medical Education, Taipei Veterans General Hospital, No. 201, Sec. 2, Shih-Pai Road, Taipei, Taiwan. Tel: 866-2-2871-2121; ext. 2073; Fax: 886-2-2871-7431; E-mail: chench@vghtpe.gov.tw

* Hui-Chu Lang is a co-corresponding author.

INTRODUCTION

Coronary artery disease (CAD) has been a major public health and medical concern in both developed and developing countries and is the leading cause of death worldwide,¹ causing approximately 1 in 5 deaths in the United States.² In Taiwan, heart disease has been ranked among the top three leading causes of death since 2000. The mortality rate from heart disease per 100,000 population was 47.6 in 2000, increasing to 57.1

in 2005 and 67.7 in 2010.² The therapeutic strategies for symptomatic CAD involve percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). PCI with further coronary stenting can achieve significant outcome improvement on coronary blood flow reconstruction, and relief of symptoms for a majority of patients with CAD.

Compared to bare-metal stents (BMS), deployment of drug-eluting stents (DES) in the coronary arteries can not only immediately reconstruct the blood flow, but also prevent near-term in-stent restenosis by the slow release of the drugs. Widespread use of DES has been observed since it became available, because of its superiority over BMS in reducing target lesion revascularization (TLR) and target vessel revascularization (TVR).³⁻¹¹ Although deployment of DES is more expensive at the onset, considering its long-term therapeutic benefit, it is believed that DES may have an overall economic benefits.¹²⁻¹⁴ Even though DES rather than BMS may reduce adverse events mainly with TLR and TVR, patients with acute coronary syndrome receiving DES may have a higher risk of cardiac death than those receiving BMS.¹⁵ Moreover, in patients with stable CAD, DES may only improve short-term rather than long-term clinical outcomes.¹⁶

Since the National Health Insurance Bureau firstly partially reimbursed for DES in 2006 in Taiwan, there has been a huge growth in the utilization of DES.¹⁷ Initially, there was some concern that DES use was probably not cost-effective compared to BMS in patients with stable CAD.¹⁸ However, the results from a hospital-based study with limited follow-up period could lack generalizability.¹⁹ Moreover, the uneven baseline characteristics of the compared study populations might confound the results. Therefore, the purpose of this study was to compare the clinical outcomes after implantation of DES versus BMS in a real-world practice, using a propensity score matched cohort. We further examined not only clinical but also socioeconomic factors related to incident myocardial infarction (MI) or deaths in this study population.

MATERIALS AND METHODS

Study design

We conducted a retrospective cohort study based

on the National Health Insurance Research Database (NHIRD) of Taiwan's National Health Insurance program. On March 1, 1995, Taiwan launched a single-payer National Health Insurance program. As of 2007, more than 22.60 million of Taiwan's 22.96 million population were enrolled in this program. The database of this program contains Registration Files and Original Claim Data for reimbursement. Large computerized de-identified databases derived from this system by the Bureau of National Health Insurance, Taiwan (BNHI) and maintained by the National Health Research Institutes, Taiwan, are provided to scientists in Taiwan for research purposes.²

Study population

This study extracted the database from the period of 2006 to 2010. Patients eligible for this study were treated with coronary stenting between January 1, 2007, and December 31, 2008. We used both procedure codes 36.06 (Insertion of coronary artery stent(s)) for stenting procedure) and material codes (see Appendix) to identify patients who received different types of stents during the intake period. The date of the first claim of stenting between January 2007 and December 2008 was defined as the index date. Only patients who did not receive stents during the one-year washout period before the index date were included.

A total of 1576 subjects were recruited. Patients who received both BMS and DES in the same procedure ($n = 32$) or had coronary stenting within the prior year were excluded ($n = 16$). Both groups were matched 2:1 by propensity score, which were adjusted for age, sex, stent number and Charlson comorbidity index (CCI). Additionally, the patients' premium-based monthly salaries were also recorded. We finally had 966 patients in this analysis, of whom 644 were in the BMS group and 322 were in the DES group (Figure 1).

Outcome measurement

The adverse coronary events regarding MI and death during the follow-up period were identified until the end of 2010. MI was defined using the ICD-9-CM code: 410, as the principle diagnosis of admission, and it was confirmed by those visits to the emergency department and utilization of intensive care. Death was further identified by the National Death Registry.

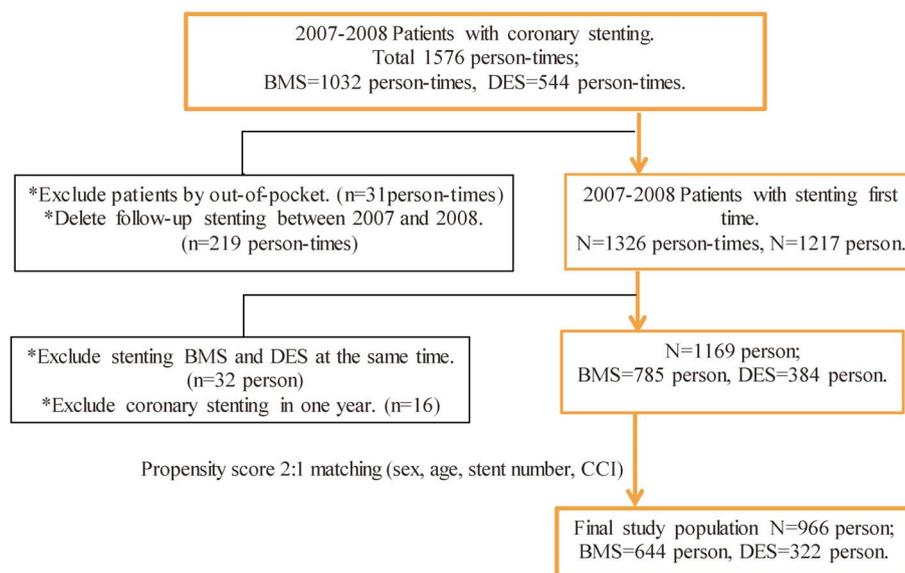


Figure 1. The flow chart of patient selection. BMS, bare-metal stents; DES, drug-eluting stents.

Statistical analysis

Continuous variables are presented as mean \pm standard deviation and were compared using the Student's T test. Categorical variables were presented as number and percentage, and were compared by the Cochran-Mantel-Haenszel Chi-Square test. The Kaplan-Meier method and the log-rank test were used for survival analyses. The Cox proportional hazards model was used for prognostic analyses of MI or death. In subgroup analysis of patients with stable CAD, patients who had acute coronary syndrome (ACS) upon index hospitalization were excluded. All statistical tests were conducted by using the SAS 9.3 (SAS Institute Inc., Cary, North Carolina, USA) and SPSS 18 (SPSS Inc., Chicago, Illinois, USA). A p value of < 0.05 was defined to be significant.

RESULTS

The baseline characteristics of the study population are shown in Table 1. Age, gender distribution, stent number, CCI, and the use of dual antiplatelet therapy (DAPT) were similar between the 2 groups, following propensity score matching. However, subjects in the DES group had a higher premium-based monthly salary, were more likely to be treated in medical centers, and took statins more frequently.

Acute myocardial infarction incidence rate

During the follow-up period, the incidence of MI was 7.8% in the first year in the BMS group, decreasing in the second year and the third year to 1.4% and 0.7%, respectively (Table 2). The annual incidences of MI in the DES group in the first three years were 2.2%, 2.6%, and 0.2%, respectively. There was a significantly lower MI incidence rate in the DES group than in the BMS group in the first follow-up year (2.2% vs. 7.8%, $p = 0.0003$); however, no significant difference was noted in the second and the third follow-up year. The cumulative incidence of MI was also significantly lower in the DES group than in the BMS group during the follow-up over three years (5.0% vs. 9.9%, $p = 0.009$). Referring to BMS, the crude hazard ratio of DES was 0.48 for MI (Table 2).

Mortality rate

In-hospital mortality was not different between the BMS group (1.6%) and the DES group (1.2%) during the index hospitalization (Table 2). However, the post-discharge mortality in the BMS group was 10.6% in the first, 5.1% in the second, and 2.2% in the third follow-up year. In contrast, in the DES group, the annual mortality was 5.7%, 5.3%, and 1.0%, respectively, during the 3 follow-up years. Comparing these figures with the BMS group, there was a significant reduction of total mortality in the DES group in the first follow-up year (5.7% vs. 10.6%, $p = 0.01$); the cumulative mortality was also sig-

Table 1. Baseline characteristics of the study population

Variable	BMS (n = 644)	DES (n = 322)	
	n (%)	n (%)	
Sex			1.0 ^a
Female	168 (26.1%)	84 (26.1%)	
Male	476 (73.9%)	238 (73.9%)	
Age			1.0 ^a
30-64	294 (45.7%)	147 (45.7%)	
≥ 65	350 (54.3%)	175 (54.3%)	
(Mean ± SD)	65.9 ± 12.3	65.8 ± 11.9	0.92 ^b
Premium-based monthly salary (\$NT)			< .0001 ^a
≤ 19,200	162 (25.1%)	60 (18.6%)	
19,201~21,900	225 (35.0%)	80 (24.8%)	
≥ 21,901	121 (18.8%)	97 (30.1%)	
Levels of hospital care			0.04 ^a
Medical center	335 (52.0%)	190 (59.0%)	
Non-medical center	309 (48.0%)	132 (41.0%)	
Disease severity			
Stent number			1.0 ^a
1	492 (76.4%)	246 (76.4%)	
2	128 (19.9%)	64 (19.9%)	
3	24 (3.7%)	12 (3.7%)	
CCI (points)			1.0 ^a
0-1	134 (20.8%)	67 (20.8%)	
2	94 (14.6%)	47 (14.6%)	
≥ 3	416 (64.6%)	208 (64.6%)	
Drug therapy			
DAPT	590 (91.61%)	303 (94.10%)	0.2 ^a
Statins	315 (48.91%)	183 (56.83%)	0.02 ^a

^a Cochran-Mantel-Haenszel Chi-Square test. ^b Cox Proportional Hazard Regression Model, based on different stent type. BMS, bare metal stent; CCI, Charlson comorbidity index; DAPT, dual antiplatelet therapy; DES, drug-eluting stent.

Table 2. Incidence of myocardial infarction (MI) and mortality between patients with bare-metal stent and drug-eluting stent in the three year follow-up period

	BMS (n = 644)	DES (n = 322)	p
MI incidence N (%)			
1 st year	50 (7.8%)	7 (2.2%)	*0.0003 ^a
2 nd year	9 (1.4%)	8 (2.6%)	0.3 ^a
3 rd year	5 (0.7%)	1 (0.2%)	0.66 ^a
Cumulative MI incidence N (%)			*0.008 ^c
One year	50 (7.8%)	7 (2.2%)	
Two year	59 (9.2%)	15 (4.8%)	
Three year	64 (9.9%)	16 (5.0%)	
Risk of MI HR (95% CI)	1	0.48 (0.28-0.84)	*0.009 ^b
Mortality			
In hospital (%)	10 (1.6%)	4 (1.2%)	0.75 ^a
Follow-up after index hospitalization, n (%)			
1 st year	67 (10.6%)	18 (5.7%)	*0.01 ^a
2 nd year	33 (5.1%)	17 (5.3%)	1.0 ^a
3 rd year	8 (2.2%)	2 (1.0%)	0.49 ^a
Cumulative mortality, n (%)			*0.03 ^c
One year	77 (11.9%)	22 (6.9%)	
Two year	110 (17.0%)	39 (12.2%)	
Three year	118 (19.2%)	41 (13.2%)	
Risk of mortality HR (95% CI)	1	0.70 (0.50-0.97)	*0.04 ^b

^a Cochran-Mantel-Haenszel Chi-Square test. ^b Cox Proportional Hazard Regression Model, based on different stent type. ^c Log-rank test.

BMS, bare-metal stent; CI, confidence interval; DES, drug-eluting stent; HR, hazard ratio.

nificantly lower in the DES group than in the BMS group (13.2% vs. 19.2%, $p = 0.03$). By using Cox proportional regression analysis, DES was associated with lower mortality than BMS (hazard ratio and 95% confidence interval: 0.70, 0.50-0.97) (Table 2).

1) Risk of mortality

The multivariate Cox regression analysis showed that age, CCI, premium-based monthly salary, level of hospital care, and the uses of DAPT or statins rather than stent type were independently associated with mortality in the total study population (Table 3). Patients who were older had a higher CCI or lower premium-based monthly salary, were more likely to incur death. While patients have been treated in medical centers, taking DAPT or statins, they would have improved

survival. In contrast, for patients with stable CAD, DES was related to a significant reduction of all cause mortality, independent of age, gender, stent number, CCI, premium-based monthly salary, levels of hospital care, and use of DAPT or statins.

2) Risks of adverse coronary events

Regarding adverse coronary events, stent type was an independent predictor in the total study population and in the subpopulation with stable CAD, in addition to age, CCI, and use of DAPT (Table 4). Again, the lower the premium-based monthly salary, the higher risks for adverse coronary events were observed in total study population, but not in patients with stable CAD.

With adjustments for age, gender, premium-based monthly salary, levels of hospital care, numbers of stents,

Table 3. Cox proportional hazard regression model on mortality rate analysis in total study population and in subpopulation with stable coronary artery disease

	Model 1 (n = 966)		Model 2 (n = 625)	
	HR	p (95% CI)	HR	p (95% CI)
Stent type				
BMS	1		1	
DES	0.74	0.15 (0.48-1.12)	0.54	*0.04 (0.30-0.96)
Sex				
Female	1		1	
Male	0.93	0.73 (0.62-1.39)	1.29	0.40 (0.72-2.30)
Age	1.04	*< .0001 (1.02-1.06)	1.05	*< .0001 (1.03-1.08)
Stent number				
1	1		1	
2	1.48	0.06 (0.98-2.22)	0.86	0.65 (0.46-1.63)
3	0.97	0.95 (0.42-2.25)	0.21	0.12 (0.03-1.52)
CCI (points)				
0-1	1		1	
2	0.65	0.37(0.24-1.71)	0.61	0.47 (0.16-2.29)
≥ 3	2.56	*0.002 (1.43-4.59)	3.13	*0.002 (1.52-6.44)
Premium-based monthly salary (\$NT)				
≤ 19,200	1		1	
19,201~21,900	0.67	*0.04 (0.46-0.98)	0.83	0.51 (0.49-1.43)
≥ 21,901	0.35	*0.003 (0.18-0.70)	0.47	0.11 (0.18-1.20)
Level of hospital				
Medical center	1		1	
Non-medical center	1.33	*0.12 (0.93-.1.91)	1.42	0.16 (0.87-2.32)
Drug therapy				
DAPT	0.21	*< .0001 (0.13-0.31)	0.21	*< .0001 (0.12-0.37)
Statins	0.65	*0.03 (0.44-0.97)	0.72	0.24 (0.42-1.25)

Model 1: total study population. Model 2: subjects with stable coronary artery disease.

BMS, bare-metal stent; CI, confidence interval; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; HR, hazard ratio; Charlson comorbidity index.

Table 4. Cox proportional hazard regression model of adverse coronary events in total study population and in subpopulation with stable coronary artery disease

	Model 1 (N = 966)		Model 2 (N = 625)	
	HR	p (95% CI)	HR	p (95% CI)
Stent type				
BMS	1		1	
DES	0.53	*0.001 (0.36-0.78)	0.42	*0.001 (0.25-0.71)
Sex				
Female	1		1	
Male	0.95	0.76 (0.66-1.35)	1.40	0.20 (0.83-2.35)
Age	1.03	*0.0003 (1.01-1.04)	1.04	*0.0009 (1.02-1.06)
Stent number				
1	1		1	
2	1.17	0.40 (0.81-1.70)	0.72	0.26 (0.40-1.28)
3	0.88	0.72 (0.43-1.81)	0.31	0.11 (0.08-1.29)
CCI (points)				
0-1	1		1	
2	1.11	0.79 (0.50-2.53)	1.01	0.99 (0.34-2.97)
≥ 3	3.82	*< .0001 (2.19-6.65)	4.36	*< .0001 (2.21-8.58)
Premium-based monthly salary (\$NT)				
≤ 19,200	1		1	
19,201~21,900	0.75	0.10 (0.54-1.05)	0.88	0.61 (0.55-1.42)
≥ 21,901	0.56	*0.02 (0.34-0.93)	0.58	0.15 (0.27-1.23)
Level of Hospital				
Medical center	1		1	
Non-medical center	1.05	0.78 (0.77-1.43)	1.31	0.22 (0.85-2.01)
Drug therapy				
DAPT	0.25	*< .0001 (0.17-0.37)	0.24	*< .0001 (0.14-0.41)
Statins	0.82	0.22 (0.59-1.13)	0.87	0.55 (0.55-1.38)

§-2 Log Likelihood $p < .0001$.

Model 1: total study population. Model 2: subjects with stable coronary artery disease.

BMS, bare-metal stent; CI, confidence interval; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; HR, hazard ratio; Charlson comorbidity index.

CCI, and ACS presentation in index hospitalization, patients with DES were associated with better clinical outcomes, including fewer adverse coronary events (log-rank, $p = 0.001$, Figure 2) and less mortality (log-rank, $p = 0.03$, Figure 3).

DISCUSSION

In this propensity score-matched cohort study, we clearly demonstrated that DES was associated with lower risks for adverse coronary events in patients undergoing PCI during a post-procedure 3-year follow-up duration. The benefits were even greater in patients with stable CAD when DES was related to reduced mor-

tality. In addition to known risk factors, including age and comorbidities, the individual economical situation, indexed by premium-based monthly salary, was also related to clinical outcomes. However, such associations were attenuated in patients with stable CAD.

Drug-eluting stent versus bare-metal stent in clinical outcomes

Although it has been demonstrated that DES rather than BMS is effective in reducing intimal hyperplasia and consequent TLR and TVR, there remains a debate on the survival benefits of PCI vs DES in the long run.^{20,21} The randomized control trials usually showed no significant differences in the long-term rates of death or MI after PCI with DES or BMS for either off-label or on-label

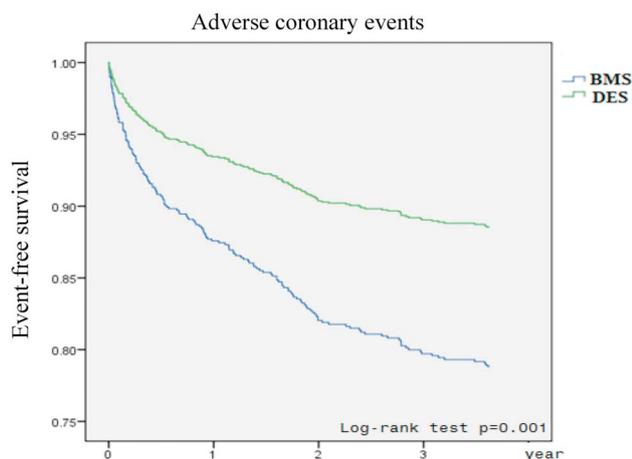


Figure 2. Event-free survival analysis of adverse coronary events for patients with bare-metal stent (BMS) or drug-eluting stent (DES) after accounting for age, sex, premium-based monthly salary, levels of hospital care, Charlson comorbidity index, and whether or not acute coronary syndrome at index admission.

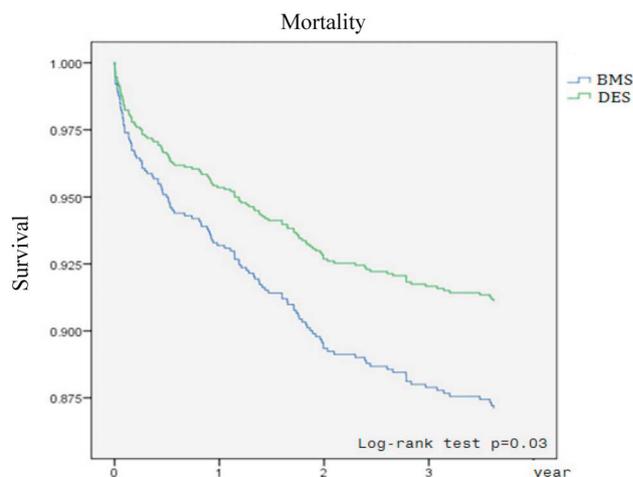


Figure 3. Survival analysis for patients with bare-metal stent (BMS) or drug-eluting stent (DES) after accounting for age, sex, premium-based monthly salary, levels of hospital care, Charlson comorbidity index, and whether or not acute coronary syndrome at index admission.

indications.²² However, the results from real-world practice may differ since the standardized population is usually absent. In a meta-analysis of the comparisons between DES and BMS, DES indeed manifested advantages over BMS on reducing mortality and myocardial infarction.²²

In the present study, there was no significant difference in mortality rate between DES (1.2%) and BMS (1.6%) during index hospitalization, which indicated a similar procedural successful rate and quality of acute management between groups. Furthermore, we conducted a propensity score matching cohort study to minimize the selection bias from unobservable confounders to strengthen the study results. The present study clearly demonstrated a clinical benefit to diminish adverse coronary events by using DES rather than BMS in a national-representative population-based study, consistent with published observational studies.²²

Moreover, the present study also proposed a survival benefit using DES rather than BMS, because the DES group had a significantly lower cumulative mortality rate (13.2%) than the BMS group (19.2%) during a 3-year follow-up duration. The results consisted of published data regarding the elderly, in small vessel disease, and in chronic total occlusive disease.^{23,24} We further demonstrated the majority of advantages appeared in the first years after PCI. The results might suggest the possibility of late catch-up phenomenon, and late or very late stent thrombosis in patients with DES,^{25,26} even

though no increased hazards associated with DES in the second and third follow-up year were observed in the homogenous Chinese population.

Patients with stable coronary artery disease

There has been a long-term debate regarding the validity of PCI in patients with stable CAD, while the COURAGE trial illustrated comparable clinical outcomes between patients who underwent optimal medical therapy with and without PCI.²⁷ However, the post hoc analyses showed that the use of DES for patients with stable CAD was superior to BMS for 1 year, with decreasing benefits noted over continued follow-up.¹⁶ In a network meta-analysis, Caruba et al. suggested similar rates of death and myocardial infarction in stable CAD subjects treated with either DES or BMS.²⁸ But in the present study, we also showed similar results as the COURAGE trial that patients could benefit from DES, compared to BMS, particularly in the first year after PCI. The results may support the findings that DES was associated with late or very late stent thrombosis, resulting in late loss of clinical benefits.²⁶ However, there was ongoing disagreement regarding whether the clinical benefit in the first year was related to DES per se or the extended use of DAPT, as per guideline recommendation.²⁹ Data in the CREDO study suggested a prolonged DAPT for at least 1 year, even for patients with stable CAD who underwent PCI with BMS.³⁰ Following the recommendations from

guidelines for stable CAD, only patients with DES but not BMS were strongly recommended to undergo at least 1 year DAPT.²⁹ Giving a potential confounder of DAPT duration, observational studies but not randomized control trials may propose clinical benefits of DES comparing to BMS. The reimbursement of DAPT for Taiwanese patients with stable CAD who underwent PCI with either DES or BMS was limited to 3 months before 2012. Since the out-of-pocket expenses for DAPT were not taken down in NHIRD, we were not able to evaluate the interaction between the duration of DAPT and DES/BMS.

In addition, in multivariate Cox regression analysis, DES provided greater survival benefits in patients with stable CAD rather than in the total study population. However, DES indeed was independently associated with lower risks for adverse coronary event in both the total and in the subpopulation with stable CAD, supporting the clinical applications of DES for patients with either acute coronary syndrome or stable CAD.

Factors affecting mortality rate and myocardial infarction incidence

Apart from the significant findings of stent type in mortality and MI, age, comorbidities, indexed by CCI, and premium-based monthly salary were also independent predictors of adverse coronary events in the total study population. While premium-based monthly salary was referencing individual salary, it could serve as an index of individual economic status. No doubt patients with better economic status would typically experience better clinical outcomes. The present study showed the economic status was an independently prognostic indicator in total study population rather than in patients with stable CAD. This may indicate that the out-of-pocket pay is higher in patients with acute coronary syndrome than stable CAD. Beyond the stent type, the prognostic value of premium-based monthly salary was dismal in patients with stable CAD, encouraging the government to rethink the cost effectiveness of total reimbursement of DES. Since newer generation DESs were more effective at reducing repeated revascularization, stent thrombosis, MI in clinical trials, the advantages of DES over BMS might be greater nowadays.

Study limitations

This study encountered some limitations regarding se-

lection bias, information bias, and the inherent deficiency of the NHIRD. Since the therapeutic guidelines, reimbursement policy, and out-of-pocket payment might vary each year, we only enrolled subjects who did not have coronary morbidities and underwent their first coronary intervention in the first year of DES partially reimbursed. In addition, we conducted a propensity-score matching cohort to minimize the influence of unobserved variables, giving a relative small case number a trade-off. Because of the limited sample size, we are not able to adjust the individual morbidity but a CCI. The statistical power was sufficient to demonstrate the advantages of DES. Since the economic burden for each patient was not measurable, the selection bias could not be totally ruled out by using propensity score matching in this study. Moreover, the reimbursement of DAPT in Taiwan ran for only 3 months for stable CAD, and 9 months for ACS, regardless of who is using DES or BMS. Since data related to out-of-pocket payment for extended DAPT were not available in NHIRD, we were not able to manage the important confounder, as well as the other inherent deficiency of CAD severity, drug compliance, patient care quality, and family support. Neither we could evaluate the effectiveness of DES on target lesion and target vessel revascularization. Lastly, the premium-based monthly salary in this study may not reflect the actual household income.

CONCLUSIONS

In the propensity-matched cohort study of Taiwan beneficiaries with CAD, the implantation of DES during the coronary intervention was related to better outcomes than BMS, in terms of reducing MI and mortality after PCI. The survival benefits of DES were even greater for patients with stable CAD compared to BMS. Further studies are needed to confirm the generalizability of the present results.

REFERENCES

1. Finegold JA, Asaria P, Francis DP. Mortality from ischaemic heart disease by country, region, and age: statistics from World Health Organisation and United Nations. *Int J Cardiol* 2013;168:934-45.
2. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics--2009 update: a report from the American Heart

- Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2009;119:e21-181.
3. Babapulle MN, Joseph L, Bélisle P, et al. A hierarchical Bayesian meta-analysis of randomised clinical trials of drug-eluting stents. *Lancet* 2004;364:583-91.
 4. James SK, Stenestrand U, Lindback J, et al. Long-term safety and efficacy of drug-eluting versus bare-metal stents in Sweden. *N Engl J Med* 2009;360:1933-45.
 5. Kastrati A, Dibra A, Spaulding C, et al. Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute myocardial infarction. *Eur Heart J* 2007;28:2706-13.
 6. Morice MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med* 2002;346:1773-80.
 7. Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;349:1315-23.
 8. Schofer J, Schlüter M, Gershlick AH, et al. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). *Lancet* 2003;362:1093-9.
 9. Spaulding C, Daemen J, Boersma E, et al. A pooled analysis of data comparing sirolimus-eluting stents with bare-metal stents. *N Engl J Med* 2007;356:989-97.
 10. Stettler C, Wandel S, Allemann S, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. *Lancet* 2007;370:937-48.
 11. Stone GW, Ellis SG, Cox DA, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med* 2004;350:221-31.
 12. Bakhai A, Stone GW, Mahoney E, et al. Cost effectiveness of paclitaxel-eluting stents for patients undergoing percutaneous coronary revascularization: results from the TAXUS-IV Trial. *J Am Coll Cardiol* 2006;48:253-61.
 13. Eisenstein EL, Wijns W, Fajadet J, et al. Long-term clinical and economic analysis of the Endeavor drug-eluting stent versus the Driver bare-metal stent: 4-year results from the ENDEAVOR II trial (Randomized Controlled Trial to Evaluate the Safety and Efficacy of the Medtronic AVE ABT-578 Eluting Driver Coronary Stent in De Novo Native Coronary Artery Lesions). *JACC Cardiovasc Interv* 2009;2:1178-87.
 14. Willich S, Müller-Riemenschneider F, McBride D, et al. Health economic evaluation of the use of drug-eluting stents. *Herz* 2013;38:57-64.
 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. Horst B, Rihal CS, Holmes DR Jr, et al. Comparison of drug-eluting and bare-metal stents for stable coronary artery disease. *JACC Cardiovasc Interv* 2009;2:321-8.
 17. Yu T, Wang YC. PCV6 Comparative effectiveness of different drug-eluting coronary stents - a systematic review of Taiwan studies. *Value in Health* 2012;15:A630.
 18. Hung CS, Cheng CL, Chao CL, et al. Cost-effectiveness of drug-eluting stents in patients with stable coronary artery disease. *J Formos Med Assoc* 2011;110:109-114.
 19. Hwang S, Chen K, Yin W, et al. Cost-effectiveness analyses of drug-eluting versus bare-metal stents. *J Intern Med Taiwan* 2010; 21:258-69.
 20. Stone GW, Ellis SG, Cox DA, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med* 2004;350:221-31.
 21. Kastrati A, Mehilli J, Pache J, et al. Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. *N Engl J Med* 2007;356:1030-9.
 22. 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.
 23. Douglas PS, Brennan JM, Anstrom KJ, et al. Clinical effectiveness of coronary stents in elderly persons: results from 262,700 medicare patients in the American College of Cardiology-National Cardiovascular Data Registry. *J Am Coll Cardiol* 2009;53:1629.
 24. Patel MR, Marso SP, Dai D, et al. Comparative effectiveness of drug-eluting versus bare-metal stents in elderly patients undergoing revascularization of chronic total coronary occlusions: results from the National Cardiovascular Data Registry, 2005-2008. *JACC Cardiovasc Interv* 2012;5:1054-61.
 25. Nordmann AJ, Briel M, Bucher HC. Mortality in randomized controlled trials comparing drug-eluting vs. bare metal stents in coronary artery disease: a meta-analysis. *Eur Heart J* 2006; 27:2784-814.
 26. Lagerqvist B, James SK, Stenestrand U, et al. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. *N Engl J Med* 2007;356:1009-19.
 27. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med* 2007;356:1503-16.
 28. Caruba T, Katsahian S, Schramm C, et al. Treatment for stable coronary artery disease: a network meta-analysis of cost-effectiveness studies. *PLoS One* 2014;9:e98371.
 29. 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) a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2009;54:2205-41.
 30. Steinhilbl SR, Berger PB, Mann JT 3rd, et al. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. *JAMA* 2002;288: 2411-20.

APPENDIX

ICD-9-CM coding algorithms for Charlson comorbidities	533.4-533.7, 534.4-534.7 Mild liver disease 571.2, 571.5, 571.6, 571.4-571.49 Diabetes 250-250.3, 250.7
0 No complications	2 Diabetes with end organ damage, 250.4-250.6 Hemiplegia 344.1, 342-342.9 Moderate or severe renal disease 582-582.9, 583-583.7, 585, 586, 588-588.9
1 Myocardial infarction 410-410.9, 412 Congestive heart failure 428-428.9 Peripheral vascular disease 443.9, 441, 441.9, 785.4, V43.4, Procedure 38.48 Cerebrovascular disease 430-437, 438 Dementia 290-290.9 Chronic pulmonary disease 490-496, 500-505, 506.4 Connective tissue disease 710.0, 710.1, 710.4, 714-714.2, 714.81, 725 Ulcer disease 531-534.9, 531.4-531.7, 532.4-532.7,	3 Malignancy, including leukemia and lymphoma 140-172.9, 174-195.8, 200-208.9 Moderate or severe liver disease 572.2-572.8, 456.0-456.21
	6 Metastatic solid tumor 196-199.1 AIDS 042-044.9
Codes of coronary artery stents	
Stent	Material code
BMS	CBP01206FNJD, CBP01210FNJD, CBP012535SHC, CBP012540SHC, CBP0135040SB, CBP0138938SB, CBP0150200BB, CBP0150201BB, CBP0150281BB, CBP0150282BB, CBP0174935SB, CBP0182926AB, CBP01CSUNATM, CBP01DRVNXM4, CBP01GENXXBU, CBP01MV829GU, CBP01R1521RB, CBP01S103NAC, CBP01S108NAC, CBP01S115NAC, CBP01S563NAC, CBP01S585NAC, CBP01S6275VE, CBP01S660DVE, CBP01S670DVE, CBP01S7353VE, CBP01S914NAC, CBP01S915NAC, CBP01S983NAC, CBP01SY250R5, CBP01TC250R5, CBP01TSUNATM, CBP01V7841GU, CBP01VFP01CK, CBP01ZETANGU, CBP01S796NAC, CBP01GAZ22BS, CBP01S563NAB, CBP01S983NAB, CBP01V1S1NAB, CBP01V7844AB, CBP01ZETANAB
DES	CBP06ELUT1M4, CBP06ELUT1SB, CBP06ELUT2CD, CBP06ELUT2SB, CBP06ELUT1AB, CBP06ELUT1BB, CBP06ELUT2AB, CBP06ELUT2M4, CBP06ELUT1RB