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# Clinical outcomes of drug-eluting stents versus bare-metal stents in patients with cardiogenic shock complicating acute myocardial infarction

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ABSTRACT

*Background:* To investigate the cardiovascular (CV) outcomes of drug-eluting stents (DESs) versus bare-metal stents (BMSs) in patients with acute myocardial infarction (AMI) complicated by cardiogenic shock (CS).
*Methods:* Data from the Taiwan National Health Insurance Research Database was analyzed between January 1, 2007 and December 31, 2011. A total of 3051 AMI patients in CS were selected as the study cohort. Their clinical outcomes were evaluated by comparing 1017 subjects who used DESs to 2034 matched subjects who used BMSs.
*Results:* The risk of the primary composite outcome (i.e., death, myocardial infarction, stroke, and coronary revascularization) was significantly lower in the DES group compared with the BMS group [56.1% vs. 66.2%, hazard ratio (HR), 0.74; 95% CI, 0.67–0.81] with a mean follow-up of 1.35 years. The patients who received DESs had a lower risk of coronary revascularization (HR, 0.78; 95% CI, 0.67–0.91) and death (HR, 0.70; 95% CI, 0.62–0.79) than those who used BMSs. However, the risks of myocardial infarction (HR, 0.89; 95% CI, 0.66–1.18), ischemic stroke (HR, 1.02; 95% CI, 0.67–1.53) and major bleeding (HR, 0.80; 95% CI, 0.56–1.14) were similar between the two groups.
*Conclusions:* Among patients with CS complicating AMI, DES implantation significantly reduced the risk of percutaneous coronary revascularization and death compared to BMS implantation.


## 1. Introduction

Cardiogenic shock (CS) is the most common cause of death among patients hospitalized for acute myocardial infarction (AMI), with an incidence of approximately 2.5%–8% [1]. Despite advances in medical treatment and revascularization techniques, including percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), CS remains associated with a high mortality ranging from 22% up to 88% [2–4].

Early revascularization therapy in CS has been shown to be superior to initial medical stabilization with a significant 12.8% absolute risk reduction for 6-month mortality and a 13.2% risk reduction for 6-year mortality according to the randomized SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock trial [5,6]. A recent study also reported improved in-hospital mortality among CS patients managed invasively when compared with those managed conservatively [7]. However, whether the use of the drug-eluting stent (DES) is more beneficial compared with the bare-metal stent (BMS) for patients with CS complicating AMI is unclear, with limited and inconsistent results being reported in different studies [8,9].

DES has been reported to be more efficacious than BMS in reducing mortality rates [10,11] or repeat revascularization rates [12–14] among AMI patients; however, these studies enrolled only a small proportion of patients with CS. Jaguszewski et al. [9] conducted a single center study which suggested a reduced all-cause mortality among CS patients treated with DESs compared with BMSs. On the other hand, Champion et al. [8] strongly suggested that DES should not be the treatment of choice in patients with CS because of a trend toward a higher mortality after DES implantation in this patient population. As a result, there is an ongoing debate concerning the cardiovascular (CV) benefits of DES vs. BMS treatment in this high risk group of patients.

Given the current controversy over the benefits of DESs compared with BMSs among CS patients, a nationwide cohort study was conducted

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to evaluate the efficacy and safety of DESs vs. BMSs with respect to CV outcomes including mortality, myocardial infarction, stroke, coronary revascularization, and major bleeding in patients with CS complicating AMI.

## 2. Methods

### 2.1. Data source

This nationwide population-based cohort study was conducted using the National Health Insurance Research Database (NHIRD) released by the Taiwan National Health Research Institute (NHRI). The data of NHIRD contain registration files and original claim data submitted by medical institutions that seek reimbursement through the NHI program. The NHIRD has been described in previous studies [15,16]. Briefly, the NHI program covers the medical needs of 99.9% of the population in Taiwan (about 23.20 million in 2012). All clinical diagnoses have been recorded according to the International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes. The accuracy of the diagnoses of major diseases in the claims database such as myocardial infarction, chronic kidney disease, or stroke has been validated [17–19]. The records and information of the patients were de-identified prior to analysis to ensure patient anonymity. This study was approved by the Ethics Institutional Review Board of Chang Gung Memorial Hospital.

### 2.2. Study group and cohort definition

All patients in the NHIRD who were admitted for AMI (ICD-9-CM code 410) were identified between January 1, 2007 and December 31, 2011. Only patients with CS who received coronary intervention were included in this study. CS was defined as: [1] the use of dopamine doses >880 mg; [2] the use of norepinephrine >88 mg; [3] the combined use of dopamine and norepinephrine; or [4] the use of an intra-aortic pump to stabilize hemodynamics. In the study of Intra-aortic Balloon Support for Myocardial Infarction with Cardiogenic Shock, [20] the median dosage of dopamine was approximately 4.1–4.2 μg/kg per minute and 0.3–0.4 μg/kg per minute of norepinephrine. The definition of catecholamine dosage in the current study was, therefore, approximately 5 μg/kg per minute for a 60 kg adult for 2 days (dopamine) and 0.5 μg/kg per minute for a 60 kg adult for 2 days (norepinephrine).

The index hospitalization was defined as the date when the patient was admitted for AMI. The follow-up period was defined as the time from the index hospitalization to the date of death, loss to follow-up, or until December 31, 2011, whichever occurred first. AMI patients were classified into a DES or BMS group according to the type of stent they received. Patients who used sirolimus, everolimus, zotarolimus, biolimus, tacrolimus, or paclitaxel stents were defined as the DES group while those who received BMS stents were defined as the BMS group.

Patients were excluded if they met any of the following criteria: [1] they received stent implantation before index admission; [2] they received more than one type of stent (i.e., both DES and BMS) during the coronary intervention; [3] no stent implantation was performed (Fig. 1).

### 2.3. Outcomes and covariate measurements

The primary outcome of major adverse CV events was a composite of myocardial infarction, coronary revascularization, stroke, and death during the follow-up period. Coronary revascularization was defined as percutaneous coronary revascularization or coronary artery bypass surgery. Stroke included ischemic, hemorrhagic or unspecified stroke. Death and causes of death were identified according to the registry data of the NHIRD. Secondary outcomes evaluated included heart failure on admission and major bleeding. The definition of major bleeding has been described previously and listed in the Appendix Table [21].

### 2.4. Propensity score matching

Propensity score matching (PSM) was conducted to minimize selection bias. The PSM matched each patient who received DESs with two patients who received BMSs according to propensity score using a nearest-neighbor matching algorithm. The propensity score was defined as the predicted probability, given the covariates, of being designated as the treated group (DESs) obtained from the logistic regression. We chose the following covariates to calculate the propensity score: patient's characteristics (such as age, sex, history of MI, stroke, or peripheral arterial disease); baseline comorbidities (such as diabetes, hypertension, dyslipidemia, coronary artery disease, heart failure, chronic kidney disease, dialysis, atrial fibrillation, gout, chronic obstructive pulmonary disease, or malignancy); angiographic and procedural characteristics [such as number of stented diseased vessels, number of stents implanted, aspiration catheter use, intra-aortic balloon pump (IABP) use, intubation or venoarterial extracorporeal membrane oxygenators (ECMO) use]; medications administered at discharge, as well as the indexed year and month (Table 1). The matching procedure was performed using SAS Version 9.3 (SAS Institute, Cary, NC).

### 2.5. Statistical analysis

The clinical characteristics between the study groups (DES and BMS groups) were compared using the chi-square test for categorical variables and the independent sample t-test for continuous variables. The risk of time to event for a primary or secondary outcome after the index hospitalization was compared between study groups using Cox proportional hazard model with adjustment based on the propensity score. The cumulative incidence of the primary composite outcome and its components for each study group was depicted and compared using the log-rank test. All data analyses were performed using SPSS 22 (IBM SPSS, Armonk, NY: IBM Corp).

## 3. Results

### 3.1. Patient characteristics

There were 9854 AMI patients with CS who received coronary intervention from January 2007 to December 2011. After relevant exclusion and propensity score matching, a total of 3051 patients with CS complicating AMI were identified for data analysis (Fig. 1).

The average age of the overall cohort was 68.6 years ($SD$ = 13.3 years) and the ages ranged from 22.7 to 101 years. The mean follow-up period was 1.35 years ($SD$ = 1.42 years) with a maximum of 5.0 years. Of these 3051 patients, 1017 (33.3%) received DES implantation and 2034 matched comparison patients (67.7%) received BMS implantation. Among those who received DESs, 119 (10.6%) received sirolimus-eluting stents, 183 (16.4%) received everolimus-eluting stents, 407 (36.4%) received zotarolimus-eluting stents, 66 (5.9%) received biolimus-eluting stents, 297 (26.5%) received paclitaxel-eluting stents and 47 patients (4.2%) received mixed type of DESs. No difference in the distribution of the baseline characteristics or comorbidities was noted between study groups after PSM matching (Table 1).

In total, 44.6% of the DES group and 44.8% of the BMS group received IABP, and 35.2% of the DES group and 33.8% of the BMS group were intubated. There were no significant differences in the use of medication at discharge which included aspirin, clopidogrel, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs), statin, proton-pump inhibitors (PPIs), and calcium channel blockers between the DES and BMS groups (Table 1).