Current Status of Percutaneous Coronary Intervention With Drug-Eluting Stents in Asia
Seung-Jung Park, MD, PhD; Young-Hak Kim, MD, PhD

In the last 3 decades, there has been a revolutionary change in the treatment of coronary artery disease. Through advances in equipment and technical skills, percutaneous coronary intervention (PCI) is being applied to increasingly more complex patients and lesions. In particular, coronary stenting has emerged as an effective strategy to prevent recurrence after PCI. However, restenosis in the stented segment remained a major issue in coronary stenting.1

The recent introduction of drug-eluting stents (DES) has dramatically reduced restenosis rates compared with bare metal stent (BMS) use. Large randomized clinical trials have confirmed the benefits of DES over BMS in terms of decreasing the incidence of in-stent restenosis and the need for repeat revascularization.2–4 As a result, there has been a very rapid worldwide shift in the treatment of coronary stenosis from BMS to DES, including in most Asian countries. However, concern remains over late-occurring stent thrombosis after DES implantation.5–7

The prevalence of coronary artery disease has increased considerably in Asian countries over the past several decades as a result of shifts toward a more “westernized” lifestyle. Accordingly, PCI with stents is a common procedure in Asia, with >300,000 cases performed each year.8,9 The present article describes the current status of DES use in Asian countries using both published and unpublished data. A few randomized studies have been performed in Asian countries, allowing the examination of pertinent registries to explore issues relating to DES in Asian countries. However, this review article cannot cover the disparities of patient demographics, practice pattern, and outcomes in all the different Asian countries because of a striking lack of published data. In addition, within the scope of the current review, the majority of data may reflect the performance of advanced centers in which PCI is practiced by experienced operators.

Use of DES in Asia
Although several types of DES are now available in Asian countries, 3 have been used the most: the sirolimus-eluting (SES; Cypher, Johnson & Johnson Cordis, Miami, Fla), paclitaxel-eluting (PES; Taxus, Boston Scientific, Natick, Mass), and zotarolimus-eluting (Medtronic Vascular, Inc, Santa Rosa, Calif) stents. These 3 DES slowly release potent antiproliferative drugs into the tissue from a nonresorbable polymer matrix completely covering the stent struts. The findings of large randomized clinical trials showing the restenosis reduction efficacy of these stents have led to their use in Asian countries.2,4,10 These DES typically cost about US $2000 to $3000 compared with about US $700 to $1000 for a BMS. Some other DES were made by homegrown medical companies in China and India with proprietary DES designs.

The penetration rate of DES use is diverse across countries, depending on the economic status, patient or physician preference, and availability of medical reimbursement and marketing. In developed countries such as Japan and Korea, DES make up almost 90% of coronary stents in PCI.11,12 In contrast, in less-developed countries, the penetration differs vastly between large cities and rural areas. Nevertheless, the use of DES is rapidly expanding.

Differences in Procedures and Outcomes Between Asia and Western Countries
With the limited inclusion criteria of large randomized trials used as a basis for DES approval, on-label indication for DES is restricted to simple coronary lesions. However, the emerging evidence of DES efficacy for complex patients and lesions indicates that off-label use is very popular worldwide in PCI treatment. Indeed, in Western countries, off-label use makes up >60% of DES applications.13,14 Although the nationwide performance of DES has not been measured, tertiary hospital reports indicate that off-label use in Asian countries is becoming similar to that in Western countries.11,12,15

The j-Cypher registry is a large DES registry in Japan.12 The study is a physician-directed registry monitored by an independent regulatory body. Beginning in April 2006, 41 cardiac centers in Japan have included 10,887 patients treated with DES in 22,770 PCI treatments. The penetration rate in early 2007 was 91%. The patient profiles were found to be similar or a bit more complex than those in Western studies in terms of lesions and clinical complexities, as shown in Table 1.14,16–19 The data of the j-Cypher registry showed that 43% of patients had a history of diabetes mellitus and 53% had undergone prior PCI, which indicates a higher risk of PCI than other Western DES registries. In addition, the patients had very extensive coronary atherosclerosis; the mean num-

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2730
The number of lesions per patient was 1.4±0.8, and the mean stent length per patient was 41.2±27.4 mm. However, of interest, the clinical outcomes compared favorably with those of Western countries. Over the 1-year follow-up, the incidence of death, myocardial infarction, and target lesion revascularization was 3.7%, 1.4% and 7.2%, respectively. The composite of death, myocardial infarction, and target lesion revascularization occurred in 11.4% of patients. The incidence of definite or probable 1-year stent thrombosis according to the definition of the Academic Research Consortium was 0.6%. In contrast, recent large registries focusing on the long-term safety of DES showed that the incidence of stent thrombosis at 1 year ranged from 0.6% to 3.2% in Western countries. The Reduction of Atherothrombosis for Continued Health (REACH) registry has already reported a trend of lower cardiovascular event rates in Asia. Therefore, the possibility of differential outcomes of DES between Asian and Western countries is an interesting issue for further research.

### Efficacy in Complex Patient Subsets

Off-label use of DES has generally been associated with an increased risk of death, myocardial infarction, or repeat revascularization compared with on-label use. Although information about the safety and efficacy of off-label use of DES in Asia is limited, such indication is common in real-world practice. Table 2 shows the favorable midterm outcomes of DES treatment in complex patient and lesion subsets, which still need confirmation by further randomized clinical trials.

### Left Main Coronary Artery Stenosis

Although it is recommended that unprotected left main coronary artery stenosis be treated by surgical treatment, many institutions in Asian countries have adopted PCI as an alternative to bypass surgery. The safety and feasibility of DES for left main stenosis have been well demonstrated in several studies. Park et al reported that the incidence of repeat revascularization in Korea at 1 year was lowered by DES use (2% in 102 patients) compared with historical controls using BMS (17% in 121 patients; *P* < 0.001), with comparable rates of death and myocardial infarction. The efficacy of DES was particularly highlighted in the treatment of ostial or shaft left main lesions. A multinational registry from Korea and Europe showed that only 1 patient underwent target lesion revascularization after DES implantation in 147

### Table 1. Comparison of Baseline Clinical and Procedural Characteristics Across the Large Registries*

<table>
<thead>
<tr>
<th>Trial</th>
<th>j-CYPHER</th>
<th>DESCover</th>
<th>e-CYPHER</th>
<th>SCAAR</th>
<th>Cardiac Care Network of Ontario</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>Japan</td>
<td>US</td>
<td>Worldwide</td>
<td>Sweden</td>
<td>Canada</td>
</tr>
<tr>
<td>Patients, n</td>
<td>5115</td>
<td>5541</td>
<td>15 157</td>
<td>6033</td>
<td>5106</td>
</tr>
<tr>
<td>Age, y</td>
<td>68±10</td>
<td>64±12</td>
<td>62±11</td>
<td>65 (57–73)</td>
<td>62±12</td>
</tr>
<tr>
<td>Male, %</td>
<td>75</td>
<td>68</td>
<td>78</td>
<td>71</td>
<td>70</td>
</tr>
</tbody>
</table>

Clinical presentation, %

- Stable angina: 54, 15, 42, 30, NA
- Unstable angina/NSTEMI: 14, NA, 33, 53, NA
- STEMI: 7, NA, 13, 16, NA
- Silent ischemia/old MI: 24, 25, 13, 1, NA
- Off-label use, %†: 80, 54, NA, NA, NA
- Prior MI, %: 29, 27, 30, 37, 38
- Prior PCI, %: 53, 37, 29, 10, 6
- Prior CABG, %: 8, 19, 11, 10, 10
- Multivessel disease, %: 55, 42, 57, 53, NA
- Diabetes mellitus, %: 44, 31, 29, 24, 38
- Chronic kidney disease, %: 51, 6, NA, 1, NA
- History of heart failure, %: 13, 10, NA, 7, 5
- Peripheral vascular disease, %: 12, 9, 7, NA, 6
- History of stroke, %: 9, NA, 3, 6, 4

DES

- SES: 29.0±15.5, 19.3±7.0, NA, NA, NA
- SES/PES: 41.2±27.4, 27.3±16.1, NA, NA, NA
- Direct stenting, %: 24, 40, 34, NA, NA
- Use of intravascular ultrasound, %: 41, NA, NA, NA, NA

*Data are presented as mean±SD, median (interquartile range) in the SCAAR registry, or percentage.
†Off-label indication included off-label and untested use of DES based on the manufacturers’ instructions for use.

NSTEMI indicates non–ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; and MI, myocardial infarction.
patients with ostial or shaft stenosis. However, the overall outcomes of DES treatment varied according to the patient’s clinical or angiographic profile. For patients at high surgical risk in Taiwan, the incidence of mortality and repeat revascularization was 9% and 25%, respectively, over 2 years of follow-up. Recently, the Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization (MAIN-COMPARE) study analyzed data from 2240 patients with unprotected left main coronary artery disease treated at 12 medical centers in Korea. Of these, 318 were treated with BMS, 784 were treated with DES, and 1138 underwent coronary artery bypass graft (CABG) surgery. Using the propensity-score matching, patients treated with BMS or DES were nearly 11 or 6 times, respectively, as likely to need a repeat revascularization as those who underwent CABG. However, the rates of death and the combined rates of death, MI, and stroke were similar in the 2 groups receiving PCI or CABG. The ongoing Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease (PRECOMBAT) clinical study, a randomized multicenter clinical trial in Korea, will evaluate the usefulness of DES for unprotected left main coronary artery stenosis compared with CABG.

### Chronic Total Oclusions

Although the procedural success has been improved by advances in techniques and equipment, the high incidence of restenosis was a major limitation of PCI for chronic total occlusion. Several nonrandomized studies have suggested that DES significantly reduced the rate of restenosis and repeat revascularization. Nakamura et al compared the outcomes of 60 patients receiving SES with those of 120 patients receiving BMS to treat chronic total occlusion. Angiographic restenosis and reocclusion rates were 2% and 0% for SES and 32% (P=0.001) and 6% (P=0.001) for BMS, respectively. Similar results were observed by Jung et al, who evaluated the outcomes of 107 patients treated with SES and 29 patients treated with PES. The angiographic restenosis rate was 9.4% for SES and 28.6% for PES (P=0.02).

### Long Lesions

Long coronary lesions have been an important predictor of restenosis and target lesion revascularization. Current reports in Asia demonstrated a dramatic effect of DES in reducing restenosis compared with BMS. Kim et al performed a nonrandomized registry study comparing SES or PES with BMS for long coronary lesions. The 6-month angiographic restenosis rate was 9.3% in 223 lesions treated with SES (P<0.001 versus BMS), 21.3% in 194 lesions treated with SES and 29 patients treated with PES. The angiographic restenosis rate was 9.4% for SES and 28.6% for PES (P=0.02).

### Table 2. Studies Evaluating Outcomes of DES Treatment for Complex Lesion and Patients in Asian Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Inclusion</th>
<th>Patients, n</th>
<th>Type of DES</th>
<th>Design</th>
<th>Long-term outcomes</th>
<th>Patients, n</th>
<th>Type of DES</th>
<th>Design</th>
<th>Long-term outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korea</td>
<td>Unprotected left main stenosis</td>
<td>102</td>
<td>SES</td>
<td>Single-center registry</td>
<td>Follow-up duration*</td>
<td>11.7±3.4 mo</td>
<td>Death, %</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Japan</td>
<td>Chronic total occlusion</td>
<td>60</td>
<td>SES</td>
<td>Multicenter registry</td>
<td>1 y</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Korea</td>
<td>Long lesion</td>
<td>500</td>
<td>SES/PES</td>
<td>Multicenter randomized</td>
<td>9 mo</td>
<td>1 y</td>
<td>35.7±8.1</td>
<td>9 mo</td>
<td>25±8 mo</td>
</tr>
<tr>
<td>Japan</td>
<td>Bifurcation</td>
<td>99</td>
<td>SES with DCA</td>
<td>Multicenter registry</td>
<td>Death, %</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Korea</td>
<td>BMS restenosis</td>
<td>120</td>
<td>SES</td>
<td>Single-center registry</td>
<td>Cardiac death, %</td>
<td>0</td>
<td>0</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Korea</td>
<td>Diabetes mellitus</td>
<td>225</td>
<td>SES</td>
<td>Single-center registry</td>
<td>MI, %†</td>
<td>0</td>
<td>0</td>
<td>9.8</td>
<td>9.8</td>
</tr>
<tr>
<td>China</td>
<td>Multivessel disease</td>
<td>235</td>
<td>SES</td>
<td>Single-center registry</td>
<td>TLR, %</td>
<td>2</td>
<td>3</td>
<td>4.8</td>
<td>4.8</td>
</tr>
<tr>
<td>Korea</td>
<td>Acute ST-elevation MI</td>
<td>232</td>
<td>SES/PES</td>
<td>Multicenter randomized</td>
<td>Death/MI/TLR, %</td>
<td>NA</td>
<td>NA</td>
<td>14.0</td>
<td>14.0</td>
</tr>
</tbody>
</table>

DCA indicates debulking coronary atherectomy; MI, myocardial infarction; and TLR, target lesion revascularization.

- Follow-up duration: 3.4 mo to 11.7 mo
- Death: 0 to 0%
- Cardiac death: 0 to 0.8%
- MI: 0 to 0
- TLR: 2 to 5.8%
- Death/MI/TLR: NA to 4.9%
- Stent thrombosis: NA to 0.6%

*Long-term outcome was presented as the incidence of events for the follow-up period in mean±SD or at a fixed interval.

†MI was presented as nonfatal MI in which periprocedural cardiac enzyme elevation was not included. However, Kim et al included periprocedural creatine kinase-MB elevation.

‡Stent thrombosis was classified according to the Academic Research Consortium.

**Table notes:**
- **Follow-up duration:** 3.4 mo to 11.7 mo
- **Death:** 0 to 0%
- **Cardiac death:** 0 to 0.8%
- **MI:** 0 to 0
- **TLR:** 2 to 5.8%
- **Death/MI/TLR:** NA to 4.9%
- **Stent thrombosis:** NA to 0.6%

**Table references:**
- Nakamura et al
- Kim et al
- Jung et al
- Nakamura et al
- Yang et al
- Lee et al

**Table headings:**
- **Country:** Korea, Japan, Korea, Japan, Korea, Korea, China, Korea
- **Type of DES:** SES, SES, SES/PES, SES with DCA, SES, SES, SES/PES, SES/PES
- **Design:** Single-center registry, Multicenter registry, Multicenter randomized, Single-center registry, Single-center registry, Single-center registry, Multicenter randomized, Multicenter randomized

**Follow-up duration:** 3.4 mo to 11.7 mo

**Depths:**
- **Death:** 0 to 0%
- **Cardiac death:** 0 to 0.8%
- **MI:** 0 to 0
- **TLR:** 2 to 5.8%
- **Death/MI/TLR:** NA to 4.9%
- **Stent thrombosis:** NA to 0.6%
with angiographic restenosis even in the DES era. In multivariate analysis, long lesions and diabetes mellitus or small vessels were independent predictors of angiographic restenosis after DES placement.37,38

Bifurcation Lesion
A high incidence of restenosis in bifurcation coronary lesions remains problematic even with treatment with DES. The rates of restenosis and target lesion revascularization vary with bifurcation morphology or stenting technique. When the ostium of the side branch has no significant stenosis, single stent implantation crossing the side branch (single stenting technique) is preferred. Kim et al25 compared the single stenting technique with the complex stenting technique (stenting in both the main vessel and side branch) in 116 patients with left main bifurcation stenosis. The single stenting strategy was associated with lower rates of angiographic restenosis (5.3% versus 24.4%; P=0.024) and target lesion revascularization (0% versus 12.2%; P=0.005) than the complex stenting technique. Chen et al26 similarly showed that the angiographic restenosis rate was 17.4% for 62 patients who had true bifurcation lesions with side-branch ostial stenosis and were treated with complex bifurcation stenting. In addition, Tsuchikane et al27 tested the role of debulking atherectomy for bifurcation lesions before SES placement in a multicenter prospective registry. They performed debulking atherectomy at the main vessel and/or side branch and subsequent single stenting at the main vessel with SES. Until now, the angiographic restenosis rate has been 1.3% (1 of 76) at the main vessel and 2.6% (2 of 76) at the side branch. Therefore, further randomized studies assessing an optimal bifurcation stenting strategy and further clinical studies assessing usefulness of new bifurcated stents in Asia are required.

In-Stent Restenosis
Intracoronary radiation was the standard treatment for in-stent restenosis of BMS. However, recent reports showed that DES achieved superior outcomes over radiation therapy. Lee et al41 compared the angiographic and clinical outcomes of 120 patients receiving SES with those of a historical control of 240 patients receiving intracoronary beta-radiation for treatment of diffuse (≥10 mm in length) in-stent restenosis of BMS. They observed a significantly lower angiographic restenosis (5.3% versus 24.4%; P=0.001) and target lesion revascularization rate (0% versus 12.2%; P=0.005) than the beta-radiation therapy. Consequently, the rate of 3-year target lesion revascularization was 5.8% for SES and 15.4% for radiation patients (P=0.009). Therefore, all manufacturers have withdrawn their intracoronary radiation products from the marketplace. Studies evaluating an optimal irradiation technique for treatment of in-stent restenosis with DES are being performed. Although a small registry showed the safety and efficacy of repeat DES treatment for DES restenosis,42 further randomized studies are needed.

Diabetic Patients
Diabetes mellitus was a traditional risk factor of long-term recurrence or mortality in stent placement. However, because most registry studies had small study populations, the outcomes of DES treatment in diabetic patients were not consistent across the clinical studies. Yang et al43 compared clinical outcomes of 225 diabetic and 560 nondiabetic patients receiving DES and found that the angiographic restenosis rate (10.1% in diabetic versus 8.2% in nondiabetic patients; P=0.41) and target lesion revascularization rate (4.4% in diabetic versus 4.1% in nondiabetic patients; P=0.84) were comparable. In another study by Gaku et al,37 however, diabetes mellitus was an independent predictor of angiographic restenosis in 249 patients receiving SES. Large registries with extended follow-up will clarify the influence of diabetes mellitus on long-term mortality or repeat revascularization. In addition, large randomized studies will evaluate the usefulness of DES in diabetic patients with multivessel coronary artery disease compared with bypass surgery.

Multivessel Disease
Multivessel disease is a typical off-label indication of DES. However, several recent registries have shown that the recurrence rate of PCI for multivessel disease was comparable to that for bypass surgery with improved long-term patency of DES. Yang et al44 compared the clinical outcomes of 235 multivessel DES placements with those of a contemporaneous control of 231 surgery patients for multivessel stenosis. Over 2 years, the incidence of death, myocardial infarction, or cerebrovascular events was comparable between DES (3.2%, 2.3%, and 1.4%, respectively) and bypass surgery (2.3%, 0.9%, and 3.3%, respectively) patients. However, the repeat revascularization rate was lower in bypass surgery than in DES patients (2.8% versus 10.4%; P=0.001). This finding was contrast to the Arterial Revascularisation Therapies-II (ARTS-II) clinical trial comparing the outcomes of multivessel DES (607 patients) with those of a historical control of bypass surgery in the ARTS-I trial (605 patients).45 The 1-year composite incidence of death, myocardial infarction, stroke, or repeat revascularization was not statistically different between DES and surgery patients (10.4% versus 11.6%). Further randomized control studies, like the ongoing Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX), Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM), or Coronary Artery Revascularization in Diabetes (CARDia) trials conducted in Western countries, are required in Asia to assess the safety and efficacy of multivessel DES placements for the Asian population.

Acute Myocardial Infarction
Recent randomized studies in Western countries observed a clear benefit of DES in reducing angiographic restenosis and target lesion revascularization in patients with acute myocardial infarction.46,47 Registry studies in Asian countries also showed similar outcomes. Park et al48 observed that DES (221 patients), compared with a historical control of BMS (228 patients), had a reduced incidence of adverse cardiac events, including death, myocardial infarction, or target lesion revascularization (6.6% versus 14.0%; P=0.011), which was driven by a lower target lesion revascularization rate (4.8% versus 9.6%; P=0.028). This result was in
agreement with a randomized study in Korea comparing the safety and efficacy of SES and PES for 232 patients with acute ST-elevation myocardial infarction.\textsuperscript{49} The angiographic restenosis rate at 6 months was 4\% for SES and 16\% for PES (\textit{P}=0.04).

**Stent Thrombosis and Antiplatelet Therapy**

Stent thrombosis after DES implantation, especially late stent thrombosis, has been a major concern since a number of studies showed a greater risk of such thrombosis with DES compared with BMS.\textsuperscript{5,6} Park et al\textsuperscript{7} in Korea reported that the incidence of late stent thrombosis, defined as definite or probable stent thrombosis occurring after 1 month after the procedure, was 0.6\% in 1911 patients who received DES in a real-world practice. Independent predictors of stent thrombosis were premature antiplatelet discontinuation, primary stenting for acute myocardial infarction, and total stent length, which were factors similar to the data of Western countries.\textsuperscript{5,50,51} However, it has not been made clear whether the increased occurrence of late DES stent thrombosis contributes to an increased risk of death or MI compared with BMS in Asian countries. In a registry report from Korea, the incidence of angiographically proven late stent thrombosis was similar for SES (0.33\% in 2447 patients) and BMS (0.17\% in 4104 patients) use.\textsuperscript{51} This finding is consistent with that of a registry report in China showing comparable risks of late stent thrombosis of 1.3\% for DES (626 patients) and 0.2\% for BMS (448 patients; \textit{P}=0.062) use.\textsuperscript{15} The incidence of angiographic late stent thrombosis in Japan ranged from 0\% to 0.6\% in single-center studies examining SES.\textsuperscript{12,52,53} On the basis of these results in Asia, late stent thrombosis appears to be very infrequent and occurs at similar rates for DES and BMS. However, because most such studies were performed in underpowered and single-center registries and had a follow-up of <2 years, further studies involving more patients and a longer follow-up are required to determine more precisely the association between DES and late stent thrombosis and how it compares with BMS use.

Although the labeling duration of dual antiplatelet therapy with aspirin and clopidogrel was 3 months for SES and 6 months for PES, current guidelines recommend treatment for at least 1 year in patients at low risk of bleeding, especially in off-label use.\textsuperscript{\textit{6}} Most hospitals in Asia follow this guideline of long-term dual antiplatelet therapy with aspirin and clopidogrel.\textsuperscript{15,51,54} However, in Japan, ticlopidine plus aspirin had been used before August 2007 because of off-label indication of clopidogrel after DES implantation. Thus, some DES patients may still be taking ticlopidine, and replacement with clopidogrel may be needed. Although a few registries showed comparable efficacy between ticlopidine and clopidogrel,\textsuperscript{12,37} the long-term benefits of ticlopidine are not well established. In addition, serious side effects of ticlopidine such as liver dysfunction or neutropenia are not uncommon.\textsuperscript{54}

Triple antiplatelet therapy with aspirin, clopidogrel, and cilostazol may have a role in patients at high risk of stent thrombosis. Although the efficacy has not been fully established in the DES era, triple combination therapy had a benefit in preventing subacute stent thrombosis at 30 days in patients treated with BMS.\textsuperscript{55} The incidence of subacute stent thrombosis was 0.1\% in 1415 patients with triple treatment and 0.5\% in 1597 patients with dual standard treatment (\textit{P}=0.024). Nevertheless, the incidence of overall adverse drug complications, including major bleeding, neutropenia, and thrombocytopenia, was comparable between triple (2.6\%) and dual (1.8\%, \textit{P}=0.14) antiplatelet therapies. In addition, the triple regimen may have a potential benefit of reducing intimal growth of DES in complex lesion subsets.\textsuperscript{56} The Drug-Eluting Stenting Followed by Cilostazol Treatment Reduces Late Restenosis in Patients With Long Native Coronary Lesions (DECLARE-Long) study demonstrated that the addition of 6 months of cilostazol achieved a significant reduction in in-stent late loss compared with dual antiplatelets (0.34±0.49 mm versus 0.51±0.49 mm, \textit{P}=0.031) after DES implantation for long coronary lesions.\textsuperscript{57} Therefore, the efficacy of triple antiplatelets compared with standard dual antiplatelets in preventing stent thrombosis and the recurrence of DES should be evaluated in a nonbiased, randomized, double-blind controlled trial.

More common use of intravascular ultrasound during DES placement might contribute to the outcomes of DES in Asian countries. As shown in Table 1, 40\% of patients in the j-Cypher registry received intravascular ultrasound-guided PCI. In high-risk procedures like unprotected left main coronary stenting, intravascular ultrasound has been used in \(~80\%\) of patients.\textsuperscript{24} However, in Western countries, it is applied to selected procedures. In a multicenter Taxus in Real-life Usage Evaluation (TRUE) registry evaluating the real-world outcomes of PES in European countries, intravascular ultrasound was used in 9.7\% of patients.\textsuperscript{58} Although the clinical influence of intravascular ultrasound in DES placement is not clear, it is expected that avoidance of underexpansion, incomplete lesion coverage, or nonapposition of DES by intravascular ultrasound–guided stenting may decrease the risk of stent thrombosis.\textsuperscript{59,60}

**Special Issues in Asia**

Some Asian countries allow the use of DES not approved by the US Food and Drug Administration (FDA) or the European-CE because of their cheap price. However, there are few data regarding procedural or long-term safety and efficacy for these non–FDA/CE-approved devices.\textsuperscript{61,62} Medical practitioners in those countries believe that the local regulatory bodies should permit such DES use in patients who cannot afford internationally approved DES.\textsuperscript{63} In a nationwide survey in India, 66\% of cardiologists responded that non–FDA/CE-approved DES should be permitted for general use, although 28\% of cardiologists believed that these DES were inferior.\textsuperscript{63} New stent designs, innovations in drug delivery, and newer drugs are very important to overcome limitations and to improve the outcomes of current DES. However, of note, the acceptance of new devices should be based on nonbiased and carefully executed preclinical and clinical study.

In most Asian countries, the attractiveness of DES use for hospitals tends to be driven by the differences between the reimbursement and the cost of each episode of care. In South Korea and the Philippines, reimbursement of national medical savings plays a crucial role. However, in other developed
countries like Taiwan, Singapore, and Japan, there are more available options of reimbursement for DES use. Therefore, it is not certain whether DES are clearly cost-effective in the unrestricted, off-label use in the Asian healthcare system. A Western study suggested that the universal use of DES in all lesions is considered less cost-effective.63 Therefore, the cost-to-benefit ratio must be evaluated for optimal use in clinical practice for each country.

In addition, a careful review in each country is required to determine the differential prognosis and cost-effectiveness of DES compared with CABG. As the introduction of DES determine the differential prognosis and cost-effectiveness of cost-to-benefit ratio must be evaluated for optimal use in disease.

widespread DES use will improve outcomes and save costs None.

countries.

required to better clarify issues regarding DES use in Asian countries. However, it is important to consider that the rapid and widespread adoption of DES in Asian countries may be driven in part by nonrandomized registry findings, aggressive marketing by device companies, and the unbridled expectations of doctors and patients. Therefore, care is needed when DES are used in patients who have untested, complex characteristics or who are not able to adhere to long-term dual antiplatelet therapy. In addition, more data from randomized or nonrandomized trials are required to better clarify issues regarding DES use in Asian countries.

Conclusions
Rising incomes and population, combined with the increasing incidence of coronary artery disease, hypertension, obesity, and metabolic syndromes and the preference for nonsurgical treatment of coronary stenoses, are likely to boost the use of PCI in Asian countries. Accordingly, the percutaneous approach with DES is becoming the primary care option for patients with coronary artery stenosis. The limited data available to date suggest a high degree of success with DES use in many Asian countries. However, it is important to consider that the rapid and widespread adoption of DES in Asian countries may be driven in part by nonrandomized registry findings, aggressive marketing by device companies, and the unbridled expectations of doctors and patients. Therefore, care is needed when DES are used in patients who have untested, complex characteristics or who are not able to adhere to long-term dual antiplatelet therapy. In addition, more data from randomized or nonrandomized trials are required to better clarify issues regarding DES use in Asian countries.

Disclosures
None.

References


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