Use of endothelial progenitor cell capture stent (Genous Bio-Engineered R Stent) during primary percutaneous coronary intervention in acute myocardial infarction: Intermediate- to long-term clinical follow-up

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Aims We assessed the use of the endothelial progenitor cell (EPC) capture stent in primary percutaneous intervention in ST-elevation myocardial infarction (STEMI).

Methods and Results One hundred and twenty patients with acute STEMI without cardiogenic shock received 129 EPC capture stents. Procedural success was achieved in 95% of patients. Dual antiplatelet therapy was given for a month and statin therapy started immediately after the procedure. The study end points are major adverse cardiac events in hospital and at 30 days, 6 months, and 1 year. Hypertension was present in 47.5% and diabetes mellitus in 30% of the patients. The left anterior descending artery was the treated artery in 54% of the patients. Mean lesion length was 17.4 ± 7.15 mm with mean reference vessel diameter of 3.18 ± 0.6 mm. Platelet glycoprotein IIb/IIIa inhibitor was used in 14% of patients and 58% had thrombosis before stent implantation. Ninety-five percent of patients achieved Thrombolysis in Myocardial Infarction 3 flow with cumulative major adverse cardiac event rate at 1.6% in hospital, 4.2% at 30 days, 5.8% at 6 months, and 9.2% at 1 year. There was 1 patient each with acute and subacute stent thrombosis but no incidence of late stent thrombosis.

Conclusion Using EPC capture stent during primary percutaneous coronary intervention for STEMI is feasible and safe.

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A primary concern in primary percutaneous coronary intervention (PCI) in patients with ST-elevation myocardial infarction (STEMI) is the thrombogenic milieu which predisposes to no-reflow phenomenon and higher risk of stent thrombosis.¹ The endothelial progenitor cell (EPC) capture stent (Genous stent, OrbusNeich, Fort Lauderdale, FL) is a stent coated with murine monoclonal antihuman CD34 antibodies designed to attract circulating EPCs to rapidly establish a functional endothelial layer and promote healing. With the increase in the number of circulating EPCs in the first few hours of acute myocardial infarction (AMI), and further enhancement with initiation of statin therapy,²,³ EPC capture stent may be preferable over currently available stents for PCI in patients with STEMI.

The objective of this study was to evaluate the feasibility and safety of the use of EPC capture stent in primary percutaneous coronary intervention during STEMI.
inhibitors. The activated clotting time was kept between 200 and 250 seconds and >360 seconds in patients who did or did not receive GP IIb/IIIa inhibitors, respectively. Percutaneous coronary intervention was carried out in the standard fashion with thrombectomy device or balloon predilatation used according to the discretion of the operators. Patients were thereafter maintained on 100 mg of aspirin indefinitely unless otherwise contraindicated and on 75 mg of clopidogrel daily for a month. Immediate statin therapy in the form of simvastatin 20 mg was initiated soon after the procedure. This was titrated according to subsequent low-density lipoprotein cholesterol level. Patients who had any contraindication to dual antiplatelet therapy were excluded from the study.

Data collection
Clinical and demographic data were collected and included age, sex, smoking history, family history of premature coronary artery disease, and comorbidities such as diabetes mellitus, hypertension, and dyslipidemia.

Adjunct therapies were also taken into account and included the use of thrombolytic therapy, glycoprotein IIb/IIIa antagonist agents, and thrombosis or thrombectomy devices. Lesion characteristics with regard to lesion location, American College of Cardiology/American Heart Association lesion morphology classification, vessel size, lesion length, Thrombolysis in Myocardial Infarction (TIMI) flow score, and Thrombolysis in Myocardial Perfusion (TMP) score were recorded. Off-line quantitative coronary analysis was done by one of the investigators and reviewed by a second investigator.

Safety profiles with regard to no-reflow, acute, subacute, and late stent thrombosis were recorded. Patients were monitored for inhospital events. The 1-, 6-, and 12-month follow-up were carried out either by phone enquiry or clinic visits. Major adverse cardiac events (MACE) of death, myocardial infarction, and target vessel revascularization were accounted for and verified by hospital and census records. Independent adjudication of clinical events was carried out by external auditors.

Statistical analysis
Data were analyzed using the SPSS version 13.0 statistical software (SPSS, Inc, Chicago, IL). Discrete data are presented as frequencies and percentage, whereas continuous variables are presented as means and SDs.

Results
A total of 129 EPC capture stents were implanted in 120 patients in this study. The mean age is 54 ± 11 years and 103 (86%) are males. The demographic characteristics of the study population are listed in Table I. Hypertension is present in 47.5%, diabetes mellitus in 30%, and dyslipidemia in 67.5% of patients. More than half of the patients are smokers (47.5% of whom were
current smokers, whereas 8.3% were previous smokers). Platelet glycoprotein IIb/IIIa inhibitor was used in 14.2% of patients and 58% received adjunctive thrombectomy treatment (55.8% with Nipro thromboaspiration catheter and 2.5% with the X-SIZER device, eV3 Inc., MN) before stent implantation (Table II).

The lesion characteristics of the study population are defined in Table III. Only the culprit lesion was treated during the primary intervention. The left anterior descending artery is the treated artery in 54.2% of patients with American College of Cardiology/American Heart Association type B lesions accounting for 77% of the cases. The mean lesion length was 17.4 ± 7.15 mm and mean reference vessel diameter was 3.18 ± 0.6 mm. The median diameter of stent implanted was 3.0 mm, with 95% and 93% of the patients achieving TIMI 3 and TMP 3 flow respectively at the end of the procedure (Tables IV and V).

There was one case of inhospital mortality from acute stroke. Another patient had acute closure due to an untreated proximal dissection accounting for the one inhospital myocardial infarction and revascularization. At 1 month, another patient had subacute stent thrombosis (SAT) 10 days after the index procedure with resultant myocardial infarction and subsequent target lesion revascularization. There were 2 patients who died, one from cardiac failure and another one from sudden cardiac arrest.

At 6 months, one patient died from heart failure whereas another had repeat target vessel revascularization. The latter patient presented with unstable angina and her angiogram showed in-stent restenosis. She was referred for coronary bypass surgery in view of the multivessel coronary artery disease.

At 12-month follow-up, 4 patients presented with anginal symptoms and were documented to have angiographic in-stent restenosis; one was referred for coronary bypass surgery, whereas 3 had repeat coronary angioplasty with stenting (Table VI).

### Discussion

The use of EPC capture stent in primary treatment in acute STEMI is safe and feasible with low rate of MACE at 4.2% at 30 days and 5.8% at 6 months. There were 2 (1.7%) patients with acute and SAT, and another with sudden cardiac death within 30 days, which could be classified as probable stent thrombosis by current definitions. There was no incidence of late stent thrombosis.

Percutaneous transluminal coronary angioplasty in AMI has been demonstrated to be superior to thrombolytic therapy with regard to the restoration of normal coronary blood flow. But concerns with regard to acute vessel closure and vessel restenosis remained, and this paved the way for stent implantation during AMI. Stent thrombosis and slow flow then became a concern in primary angioplasty. Drug-eluting stent (DES), although can effectively reduce the rate of vessel restenosis, is known to cause increased inflammation, enhanced platelet aggregation, and delayed healing which can potentially increase the risk of thrombotic complications, especially in a high-risk situation such as AMI.

Endothelial progenitor cell capture stent is coated with murine monoclonal antihuman CD34 antibodies. It is designed to attract circulating EPCs by the antibodies immobilized on the stent surface, forming a functional endothelial lining over the stent, and thus rapidly stabilizing the repair process and promoting healing. Recent research suggests that EPCs mobilized from bone marrow into peripheral blood contribute to endothelial cell regeneration and postnatal neovascularization. During AMI, there is mobilization and increased circulating EPCs which peaked at day 7. The functional role of these EPCs is unknown but is thought to be able to participate in neovascularization. The concept of increased circulating EPCs attracted to the surface of the

### Table IV. TIMI score of intervened vessels

<table>
<thead>
<tr>
<th>TIMI score</th>
<th>Preintervention</th>
<th>Postintervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>88 (73.3%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>1</td>
<td>7 (5.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>2</td>
<td>5 (4.2%)</td>
<td>6 (5.0%)</td>
</tr>
<tr>
<td>3</td>
<td>20 (16.7%)</td>
<td>114 (95.0%)</td>
</tr>
</tbody>
</table>

### Table V. TMP score of intervened vessels

<table>
<thead>
<tr>
<th>TMP score</th>
<th>Preintervention</th>
<th>Postintervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>97 (80.8%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>1</td>
<td>0 (0.0%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>2</td>
<td>2 (1.7%)</td>
<td>7 (5.8%)</td>
</tr>
<tr>
<td>3</td>
<td>21 (17.5%)</td>
<td>111 (92.5%)</td>
</tr>
</tbody>
</table>

### Table VI. Cumulative events inhospital, 1 month, 6 months, and 1 year

<table>
<thead>
<tr>
<th></th>
<th>Inhospital, n (%)</th>
<th>1 mo, n (%)</th>
<th>6 mo, n (%)</th>
<th>1 y, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>120 (100%)</td>
<td>120 (100%)</td>
<td>120 (100%)</td>
<td>40 (33%)</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>1 (0.8%)</td>
<td>2 (1.7%)</td>
<td>2 (1.7%)</td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td>MACE</td>
<td>2 (1.7%)</td>
<td>5 (4.2%)</td>
<td>7 (5.8%)</td>
<td>11 (9.2%)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (0.8%)</td>
<td>3 (2.4%)</td>
<td>4 (3.3%)</td>
<td>4 (3.3%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1 (0.8%)</td>
<td>2 (1.5%)</td>
<td>3 (2.5%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>Revascularization (TLR/TVR)</td>
<td>1 (0.8%)</td>
<td>2 (1.7%)</td>
<td>3 (2.5%)</td>
<td>7 (5.8%)</td>
</tr>
</tbody>
</table>

TLR, Target lesions revascularization; TVR, target vessel revascularization.
broken atherosclerotic plaque to promote healing forms the basis of this study.

First-in-man study of the EPC capture stent demonstrated the safety and feasibility of this device for the treatment of de novo coronary artery disease. Our study represents the largest study number to date on the use of this stent for the treatment of patients. The low rate of MACE events (5.8% at 6 months) corroborated with the early observation that the stent may be safely deployed in patients even in a high-risk thrombotic milieu such as AMI. Interim analysis of the ongoing e-Healing registry of 1286 “real-world” patients showed an overall MACE rate of 1.6%, 0.14% acute stent thrombosis, and 0.4% SAT at 1-month follow-up. At 6 months, the MACE was 6.7%, SAT 0.56%, and late stent thrombosis 0.28%. Patients with AMI in the registry study had a MACE rate of 1.45%, but the number of patients was small. Our study results of MACE rates of 5.8% and 9.2% at 6 and 12 months, respectively, were encouraging, given that this is a high-risk subset of patients.

Patients who were treated with EPC capture stent in our study were prescribed an immediate dose of simvastatin 20 mg upon completion of the procedure. This might be subsequently titrated to reach the appropriate low-density lipoprotein cholesterol target. Statins have been shown to promote the survival, migration, and differentiation of adult bone marrow–derived EPC, and enhance EPC recruitment to sites of neovascularization.12

One of the most important observations in this study is the lack of late thrombosis in patients who received the EPC capture stent. This is of particular importance given the concern with increased rate of late stent thrombosis with DES. The safety profile, even in this high-risk patient group, appears comparable to that of DES.13 The need for repeat intervention was low at 2.5% at 6 months in our study. This is highly acceptable compared to published primary PCI results with bare metal stents.

The study is limited by the fact that it is a small registry study evaluating patients who received EPC capture stent in a prospective manner. It includes only clinical follow-up and lacks angiographic information to evaluate the late loss of this novel stent.

We conclude that the use of EPC capture stent in the setting of AMI is feasible and safe with no incidence of late stent thrombosis and an acceptable rate of repeat revascularization. A head-to-head randomized comparative study with a bare metal stent will be useful to determine its true efficacy.

References

Appendix A: Definition of terms
Acute stent thrombosis Occurrence of stent thrombosis within 24 hours after stent implantation
In-stent: The segment of the vessel covered by the stent
In-segment The segment of the vessel covered by the stent and includes 5 mm before and after the stented segment
Late stent thrombosis: Occurrence of stent thrombosis at least 30 days after stent implantation
Major adverse cardiac event: Cardiac death, nonfatal myocardial infarction and clinically driven target lesion revascularization
Minimal luminal diameter: The smallest diameter determined by quantitative coronary analysis
Myocardial infarction: Elevation of cardiac enzymes 3 times the upper limit of normal
Procedural success: Achieving residual stenosis of less than 10% with restoration of TIMI 3 flow upon termination of the procedure
Reference vessel diameter: The average diameter of the vessel determined by the average of the diameter of the vessel proximal and distal to the lesion
Subacute stent thrombosis: The occurrence of stent thrombosis more than 24 hours but less than 30 days after stent implantation
Target lesion: The index lesion treated
Target vessel: The vessel in which the treated lesion is located