Drug-Eluting Stents for Acute Myocardial Infarction*

H. Vernon Anderson, MD, FACC,†
Richard W. Smalling, MD, PhD, FACC,†
Timothy D. Henry, MD, FACC‡
Houston, Texas; and Minneapolis, Minnesota

With recent hysteria regarding late thrombosis of drug-eluting stents (DES) now apparently subsiding, it may be useful to pause, reflect for a moment, and consider some recent pertinent results regarding their wider use. These new results arise from the sphere of DES for percutaneous coronary intervention (PCI) in acute ST-segment elevation myocardial infarction (STEMI). Clinical trials of DES showed they reduce the rates of restenosis and target vessel revascularization compared with bare-metal stents (BMS) in elective PCI (1,2). This reduction appears to be especially potent for PCI of chronic occlusions (3), an important comparator. It was logical for clinicians to believe that DES would be superior to BMS in the STEMI setting too. But the needed randomized clinical trial data until now were lacking. Early reports of registry data had been unequivocally encouraging. Lemos et al. (4) in 2004 reported results on 186 consecutive STEMI patients treated with DES, compared with 183 STEMI patients treated with BMS.

Follow-up at 300 days revealed reduction in target vessel revascularization (TVR) (1.1% vs. 8.2%, p < 0.01) as well as reduction in major adverse cardiovascular events (MACE) (9.4% vs. 17%, p = 0.02) in favor of DES. Mortality though was not different (8.3% vs. 8.2%). Newell et al. (5) in 2006 reported results on 306 consecutive STEMI patients who received a DES (n = 156) or a BMS (n = 150). Follow-up at 6 months revealed significant reductions in mortality (1.9% vs. 10.1%, p = 0.003) and TVR (1.3% vs. 8.1%, p = 0.005) also in favor of DES. The stage was set.

In this issue of the Journal, Menichelli et al. (6) in Rome, Italy report the results of the SESAMI (Sirolimus-Eluting Stent Versus Bare-Metal Stent In Acute Myocardial Infarc-

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†From the †University of Texas Health Science Center and Memorial Hermann Heart and Vascular Institute, Houston, Texas; and ‡Minneapolis Heart Institute at Abbott Northwestern Hospital, Minneapolis, Minnesota.

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A total of 1,624 patients were randomized in these 3 noteworthy trials. Inclusion and exclusion criteria were somewhat different. The TYPHOON and PASSION trials excluded patients who received any fibrinolytic, whereas the SESAMI trial included them. Primarily because of this, the TYPHOON and PASSION trials excluded larger proportions of screened patients than the SESAMI trial did. Thus the TYPHOON trial excluded 65%, the PASSION trial 40%, and the SESAMI trial 24%. After fibrinolytics the major exclusions were for higher-risk features, such as cardiogenic shock, resuscitation with uncertain neurological status, and high-risk angiographic characteristics. The 3 trials therefore are based on lower-risk infarct patients. Understandably none of the trials were powered for the end point of death. Yet when combined data are examined, death occurred in 2.7% (22 of 811) of DES patients and 3.8% (31 of 813) of BMS patients (p = 0.264 by Fisher exact test) (Table 1). Now this is beginning to get interesting.

The 3 trials had different end points. The primary end point in the TYPHOON trial was TVF, which was a composite defined as TVR, recurrent infarction, or target-vessel-related death at 1 year. The primary end point in the PASSION trial was the first occurrence of a serious (i.e., major) adverse cardiac event (usually termed MACE) at 12 months, including death from cardiac causes, recurrent myocardial infarction requiring hospitalization, and ischemia-driven revascularization of a target lesion. Thus, the primary end point of TVF in the TYPHOON trial matches closely the primary end point of MACE in the PASSION trial. In addition to their primary end points, all 3 trials reported rates of TLR, and/or TVR, and/or TVF, and/or MACE. For convenience, in Table 1, the highest rates of either TLR or TVR, and the highest rates of TVF or MACE, are shown. The stent thrombosis rates in Table 1 are the highest reported at 1 year. The TYPHOON and PASSION trials used similar definitions of acute, subacute, and late thrombosis, whereas the SESAMI trial used a newer definition of definite/probable/possible. While one strength of these trials is the uniform 1-year follow-up, even longer-term results will be important, particularly in regards to stent thrombosis. For simplicity, the single statistical test applied to the categorical data in Table 1 was the Fisher exact test. Clearly, recurrence after PCI for STEMI, counted as TLR/TVR, or TVF/MACE, is significantly reduced by approximately 50% with DES compared with BMS.

There was an angiographic substudy in the TYPHOON trial, with 210 patients (approximately 30%) receiving follow-up angigrams at 8 months. And of course, the primary end point in the SESAMI trial was angiographic, with 50% receiving angiograms at 1 year. Restenosis as a binary outcome event was reduced by about one-half (≤10% vs. ≥20%) based on angiographic data from these 2 studies. Since it is possible for some skeptics to criticize the low rates of angiography, the restenosis data do not have to be considered the strongest data contained in these studies, although in our opinion these data are quite good. The clinical outcome data therefore become paramount.

### Table 1

<table>
<thead>
<tr>
<th>Trial</th>
<th>Death</th>
<th>Re-MI</th>
<th>Stent Thrombosis</th>
<th>TLR/TVR</th>
<th>MACE/TVF</th>
<th>Restenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>TYPHOON (7)</td>
<td>DES: 7/355</td>
<td>15/355</td>
<td>18/355</td>
<td>33/355</td>
<td>26/355</td>
<td>44/355</td>
</tr>
<tr>
<td></td>
<td>BMS: 5/357</td>
<td>12/357</td>
<td>20/357</td>
<td>32/357</td>
<td>19/357</td>
<td>20/357</td>
</tr>
<tr>
<td>PASSION (8)</td>
<td>DES: 12/302</td>
<td>21/302</td>
<td>23/302</td>
<td>45/302</td>
<td>36/302</td>
<td>56/302</td>
</tr>
<tr>
<td></td>
<td>BMS: 6/303</td>
<td>10/303</td>
<td>16/303</td>
<td>26/303</td>
<td>16/303</td>
<td>26/303</td>
</tr>
<tr>
<td>SESAMI (6)</td>
<td>DES: 3/154</td>
<td>7/154</td>
<td>10/154</td>
<td>20/154</td>
<td>14/154</td>
<td>24/154</td>
</tr>
<tr>
<td>Total</td>
<td>DES: 22/811 (2.7%)</td>
<td>41/811 (5.1%)</td>
<td>53/811 (6.6%)</td>
<td>106/811 (13.2%)</td>
<td>66/811 (8.1%)</td>
<td>119/811 (14.6%)</td>
</tr>
<tr>
<td></td>
<td>BMS: 31/813 (3.8%)</td>
<td>55/813 (6.8%)</td>
<td>66/813 (8.1%)</td>
<td>121/813 (14.9%)</td>
<td>72/813 (9.0%)</td>
<td>134/813 (16.5%)</td>
</tr>
<tr>
<td>p</td>
<td>DES: 0.84</td>
<td>0.0002</td>
<td>0.88</td>
<td>0.0004</td>
<td>0.88</td>
<td>0.0004</td>
</tr>
<tr>
<td></td>
<td>BMS: 0.84</td>
<td>0.0002</td>
<td>0.88</td>
<td>0.0004</td>
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<td>0.0004</td>
</tr>
</tbody>
</table>
The issue of late (“really late”) stent thrombosis beyond 1 year is not addressed in these 3 trials. Recently accumulated data appear to indicate that premature discontinuation of dual antiplatelet therapy with aspirin and a thienopyridine plays a significant role in this odd, low-frequency late event. Whether stent thrombosis beyond a year after PCI for STEMI is greater, the same, or less with DES versus BMS remains an open question. The data examined here show that out to 1 year the stent thrombosis rates appear to be low and equivalent for DES and BMS.

In conclusion, based on available data, the routine implantation of DES is beneficial and can be recommended for patients undergoing PCI for STEMI.

Reprint requests and correspondence: Dr. H. Vernon Anderson, Cardiology Division, University of Texas Health Science Center, 6431 Fannin, Suite 1246, Houston, Texas 77030. E-mail: h.v.anderson@uth.tmc.edu.

REFERENCES


