

Letters to the Editor

Endothelial Dysfunction After Drug-Eluting Stent Was Never Predicted in Preclinical Studies

The recent report by Togni et al. (1) presents the results of a study that evaluated the coronary vasomotor response after sirolimus-eluting stent (SES) implantation. The investigators concluded that implantation of SES is associated with endothelial dysfunction in proximal and distal regions of treated coronary segment, whereas in the control group, bare-metal stents did not affect physiologic response to exercise.

Although clinical relevance of this finding is unknown, the underlying mechanism may be delayed vascular healing due to toxic effects of the sirolimus and paclitaxel to endothelial cells (EC). Indeed, studies in our laboratory (2) demonstrated that both drugs are toxic for EC in vitro and slowed their growth kinetics. Moreover, these drugs also negatively affected attachment characteristics of EC; because EC are anchored-dependent cell types without proper attachment, they regenerate very slowly (3).

However, preclinical studies with SES, poclitaxel-eluting stent (PES), and other drug-eluting stent (DES) demonstrated normal vascular healing at 1 month, and endothelial dysfunction was completely missed. This is mostly due to 1) difference in growth characteristics of human and animal EC, and 2) lack of study of endothelial dysfunction in animal models.

We agree with the researchers that endothelial dysfunction and incomplete vascular healing may influence persistent restenosis and late thrombosis and contribute to overall results of DES implantation.

Therefore, we suggest functional studies should be mandatory for contemporary DES preclinical programs.

We also completely agree with the editorial comments of Serry and Penny (4), who postulated that future studies needed to clarify the clinical relevance of these observations.

In conclusion, we want to congratulate Togni et al. (1) on a very interesting study, and we believe that further preclinical and clinical data will finally shed light on the role of endothelium after percutaneous coronary intervention.

*Nicholas Kipshidze, MD, PhD
Martin B. Leon, MD

*Lenox Hill Heart and Vascular Institute and
Cardiovascular Research Foundation
130 East 77th Street
9th Floor
New York, New York 10021
E-mail: NKipshidze@lenoxhill.net

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Life-Threatening Coronary Artery Spasm Following Sirolimus-Eluting Stent Deployment

We were interested to read the report by Togni et al. (1), with its accompanying editorial (2), on paradoxical coronary vasoconstriction associated with sirolimus-eluting stents (SESs). We would like to report a case of life-threatening coronary artery spasm following drug-eluting stent deployment. A 55-year-old man was recently treated in our department after presenting with recurrent ischemic symptoms. He first presented with angina in August 2003, when a proximal stenosis of the right coronary artery was treated with a paclitaxel-eluting stent (Conor Medsystems, Menlo Park, California) as part of a clinical trial. He developed further exertional angina in May 2004, when angiography revealed restenosis of the right coronary artery stent. This was treated by cutting balloon dilation followed by intracoronary brachytherapy with a 60-mm beta-emitting source (BetaCath, Novoste, Norcross, Georgia).

In November 2004 he presented with unstable angina when coronary angiography confirmed recurrent restenosis at the proximal and distal edges of the original stent. This was treated by the direct deployment of SESs (Cypher Select, Cordis Europa NV, Amersfoort, the Netherlands), overlapping the existing stent proximally and distally. Four hours after stent deployment, the patient developed chest discomfort associated with ventricular fibrillation. After successful defibrillation, he returned immediately to the catheterization laboratory, where repeat angiography showed the right coronary artery to be patent (Fig. 1). Within minutes of this diagnostic image, however, the patient developed further chest pain associated with ST-segment elevation in the inferior leads. Prompt repeat angiography at this stage confirmed occlusive spasm

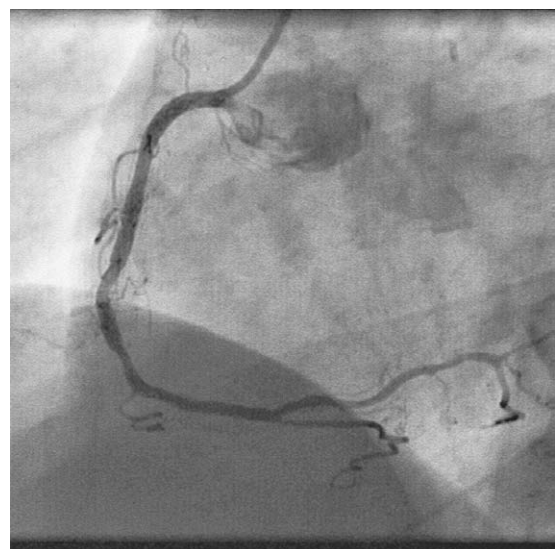


Figure 1. Angiographic appearances following cypher select stent deployment.