Angiotensin-Converting Enzyme Tissue Activity in the Diffuse In-Stent Restenotic Plaque

Flavio Ribichini, MD; Francesco Pugno, MD; Valeria Ferrero, MD; Gianni Bussolati, MD, FRCPath; Germano Melissano, MD; Roberto Chiesa, MD; Carlo Di Mario, MD; Antonio Colombo, MD

We present the 6-month anatomic, histological, and immunohistochemical (IHC) images of a diffuse and aggressive type of in-stent restenosis of a popliteal artery of a patient homozygous for the D (deletion) allele of the ACE gene (Figures 1, 2, and 3).

A detailed description of the histological changes of the arterial wall with time after coronary stenting in humans was published recently.1 These findings have confirmed that the ultrasound-detected “neointima” observed >1 month after implantation is composed primarily of smooth muscle cells (SMCs) and a proteoglycan-rich matrix. In the first weeks after stenting, the metallic struts associate with inflammatory cells, local thrombus formation, and “dedifferentiated” α-actin-negative spindle-shaped cells. Later, multinucleated giant cells and α-actin-positive spindle-shaped cells are observed in a more differentiated fibrocellular lesion.1,2 ACE increases up to 100-fold during the transformation of monocytes to macrophages, and most of the dedifferentiated SMCs (α-actin-negative cells) stain for ACE.3 However, ACE activity is thought to be limited only to the first 2 months of the reparative process that follows postballoon injury.

Our samples reproduce the histological findings reported in 2 previous studies,1,2 but in contrast to the results of Ohishi et al3 obtained from postballon restenotic samples, IHC staining for ACE was seen even 6 months after stent implantation. In fact, the spindle-shaped cells observed in the most external part of the restenotic plaque (close to the wire) stained for ACE in our sample (Figure 3A).

The data presented suggest that the transition of the stent-induced inflammatory process, rich in ACE-positive cells, into a fibrocellular lesion composed of differentiated SMCs is not a time-determined sequence. Rather, it might be an ongoing process, evolving from peripheral areas (close to the wire) to central areas and ultimately leading to progressive lumen occlusion in patients with enhanced ACE activity. This is consistent with clinical studies that advocate a role of ACE in restenosis of coronary stents.4

References
Figure 1. Macroscopic view of a section of artery showing diffuse tissue growth within stent wires.

Figure 2. Hematoxylin-eosin microscopy of the arterial wall after removal of the metallic struts of the stent. Right, Muscularis of media of arterial wall. Around wire is a “wire cuffing” composed of inflammatory and spindle-shaped cells. Left, Core of restenotic plaque shows spindle-shaped cells and neovessels.
Figure 3. Amplification of wire cuffing tissue. IHC for ACE (Biomedicals Ag) and for α-actin (Dako) shows that (A) spindle-shaped cells in contact with metallic wires stain for ACE, and (B) spindle-shaped cells of plaque core, but not those close to stent wires, stain intensively for α-actin.
Angiotensin-Converting Enzyme Tissue Activity in the Diffuse In-Stent Restenotic Plaque
Flavio Ribichini, Francesco Pugno, Valeria Ferrero, Gianni Bussolati, Germano Melissano, Roberto Chiesa, Carlo Di Mario and Antonio Colombo

Circulation. 2000;101:e33-e35
doi: 10.1161/01.CIR.101.2.e33
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2000 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/101/2/e33

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/