seems to be associated with adverse outcome in manifest CAD when measured with a commercially available assay. This information, in a large epidemiological study, may help to better understand the complex pathophysiological role of adiponectin in health and disease.

References


Vascular endothelial growth factor protein levels and gene expression in peripheral monocytes after stenting: a randomized comparative study of sirolimus-eluting and bare-metal stents

With great interest, we read the article by Kochiadakis et al.1 dealing with the relationship between monocyte vascular endothelial growth factor (VEGF) gene expression, VEGF serum level, and in-stent late luminal loss following stenting in stable coronary artery disease (CAD) patients. The authors demonstrate that the VEGF serum level 1 month after stenting was significantly lower in patients who received a sirolimus-eluting stent (SES) compared with those who received a bare-metal stent (BMS). Furthermore, monocyte VEGF gene expression 1 month after stenting positively correlated with in-stent late luminal loss after 6 months. This is an important study as it (i) highlights clearly detectable systemic effects of SES and (ii) underscores the usefulness of circulating monocytes as diagnostic tools.2

Kochiadakis et al. suggest that the lower VEGF level in the SES group can be attributed to the decreased VEGF gene expression of their circulating monocytes probably resulting in reduced VEGF protein production. Monocytes are certainly attractive indicators for drug-influenced gene regulation because of their easy accessibility. However, although serving as bioreactors and reservoirs for (paracrine) cytokines and chemokines during tissue repair and remodelling, monocytes/macrophages may not be regarded as important contributors to the VEGF concentration in human blood.Indeed, thrombocytes were shown to be the major source of VEGF in serum samples following its release during the in vitro clotting process.3 Elevated VEGF levels indicate local inflammation and are closely related to the presence of atherosclerotic risk factors.4 In contrast, the reduced VEGF serum level as well as the reduced VEGF monocyte level following SES implantation may rather reflect a systemic effect of ramapycin on cellular VEGF production.

Sirolimus-eluting stent-related reduction in VEGF serum levels may not only be beneficial, as proposed by Kochiadakis et al.1 Previously, it was shown that VEGF inhibition is associated with enhanced endothelial dysfunction and apoptosis.5 Likewise, the use of the VEGF inhibitor bevacizumab (Avastin®6) is potentially associated with increased cardiovascular complications.3 Therefore, decreased VEGF levels following SES implantation may reflect a reduced stimulus for endothelial regeneration and may therefore be causally linked with the elevated risk for SES-related late stent thrombosis.6

A recent study highlighted the positive correlation between maximal circulating monocyte count after coronary stenting with in-stent neointimal volume after 6 month follow-up.7 Although this publication is cited by Kochiadakis et al. as an argument that monocytes contribute to neointima formation, the authors did not provide monocyte count data themselves. It would be interesting to see whether the absolute monocyte count did differ in the two study groups following stent implantation. Instead, the authors suggest that the higher monocyte VEGF gene expression in the BMS group reflects monocyte activation after stent implantation, leading to inflammatory reactions which trigger pathophysiological mechanisms and ultimately restenosis. Further investigation of functional aspects of monocytes such as adhesion or chemotaxis may be a clue to get a clearer picture of the link between monocyte activation and potential consequences for neointima formation following coronary stenting.

References
VEGF expression by SES could affect and
Although not proven, the inhibition of
and may be related to stent thrombosis.
reduced stimulus for endothelial regeneration
following SES implantation may reflect a
further inferences. Further research efforts
could focus on that direction.
We do not dispute that it would be interest-
ing to look at the monocyte counts. On the
other hand, the aim of our study was to
investigate the link between angiogenic
factors and restenosis as these are reflected
through VEGF gene expression in monocytes
and not the number of monocytes, since this
is already known from previous reports to be
correlated with late luminal loss. Besides, mono-
cyte activation and their VEGF gene expression
do not depend on the absolute number of
monocytes. Nonetheless, we concur that
future studies should focus on the functional
aspects of monocytes, such as adhesion or che-
mataxis, in order to obtain a clearer picture of
the pathophysiology of neointima formation
following coronary stenting.

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Corrigenda
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On page D24, in Figure 18, the placement of
fluorine groups and stereochemistry in the
chemical structure of AZD6140 were incor-
rectly shown. The correct figure is reprinted
below.

Corrigendum to: ‘Natural history and
familial characteristics of isolated left
ventricular non-compaction’ [Eur Heart J
Juan Gimeno Blanes, Deirdre Ward, Elias
Sevdaulis, Efi Papa, Anatoli Kiotsekoglou,
Maria T. Tome, Denis Pellerin, William J.
McKenna, and Perry M. Elliott
Regrettably, on page 187, in the list of author
names, the name of Dr Kiotsekoglou was
incorrectly quoted as ‘Kiotsekolgou’.

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Letters to the Editor