Genetics and Susceptibility of Coronary Collateral Formation

To the Editor:

In their excellent special review article on coronary collaterals, Koerselman et al.¹ outline the angiogenic cascade and discuss why coronary collaterals are important and why this individual potential to develop collaterals should be considered an additional indicator of cardiac vulnerability.

However, the authors do not emphasize the importance of the genetic predisposition of the individual patient to develop collaterals or to respond to different triggers. Schultz et al.,² in a study published in Circulation, found that patients with no collaterals had a significantly lower hypoxic induction of vascular endothelial growth factor (VEGF) than patients with collaterals. They concluded that the ability to respond to progressive coronary artery stenosis is strongly associated with the ability to induce VEGF in response to hypoxia. The observed interindividual heterogeneity in this response may be due to environmental, epigenetic, or yet-unknown genetic causes.

Hochberg et al.³ correlated the haptoglobin (Hp) phenotype with the presence or absence of coronary collaterals by angiography in 82 consecutive diabetic patients and 138 consecutive nondiabetic patients undergoing catheterization. They found that diabetic patients with the Hp phenotype 2-1 were more likely to have collaterals than diabetic patients with the Hp phenotype 2-2 (P=0.007). There was no correlation between Hp phenotypes and the presence of collaterals in nondiabetic patients. Hp phenotype thus appears to be associated with the development of the coronary collateral circulation in diabetic patients with coronary artery disease. Indeed, using the Strong Heart Study serum bank, Levy et al.⁴ reported that after multivariate analyses controlling for conventional risk factors, haptoglobin phenotype was a highly statistically significant, independent predictor for cardiovascular disease in patients with diabetes (odds ratios 5.0 [2-2 versus 1-1] and 2.3 [2-2 versus 2-1, P=0.002).

Koerselman et al.¹ are absolutely correct when stating, “The potential of individuals to develop coronary collateral circulation is often neglected but is of potential major importance in myocardial vulnerability. Well-developed coronary collaterals may help protect the myocardium from infarction during episodes of ischemia...” More research should be focused on genetic determinants of this important process. Identifying the genes and factors that render a patient less susceptible to coronary collateral formation may help in the treatment and management of those suffering from coronary artery disease or for prevention of further events in individuals with advanced coronary atherosclerosis.

Ariel Roguin, MD, PhD
Division of Cardiology
The Johns Hopkins Hospital
Baltimore, Md
aroquin1@jhmi.edu

Response

We agree with the comment made by Drs Roguin and Resar regarding our special review article on coronary collaterals.¹ The review addresses the yet-unresolved mystery of the coronary collateral circulation and its potential major role in myocardial vulnerability. We were restricted by the number of words, but also by our wish to keep it concise and readable. Consequently, we have only laterally referred to the complex but potentially very important subject of the genetics of angiogenesis and coronary collaterals by mentioning the promising field of therapeutic angiogenesis and gene therapy in cardiovascular disease.

Indeed, knowledge of clinical and genetic determinants of coronary collateral circulation may provide a better understanding of the pathogenesis of collaterals and may contribute to specific therapeutic measures. The finding that the haptoglobin phenotype appears to be associated with the development of coronary collaterals in diabetic patients with coronary artery disease² will stimulate further research for a possible association between other polymorphisms and collateral circulation. In this respect, candidate genes related to monocyte chemoattractant protein-1, vascular endothelial growth factor, hypoxia-inducing factor 1-α, and genes that are involved in inflammatory processes are of particular interest.

Jeroen Koerselman, MD
Yolanda van der Graaf, MD, PhD
Peter P.T. de Jaegere, MD, PhD
Diederick E. Grobbee, MD, PhD
Julius Center for Health Sciences and Primary Care and Department of Cardiology
Heart Lung Center Utrecht
University Medical Center Utrecht
Utrecht, the Netherlands
d.e.grobbee@jc.azu.nl

Genetics and Susceptibility of Coronary Collateral Formation
Ariel Roguin and Jon R. Resar

Circulation. 2003;108:e149
doi: 10.1161/01.CIR.0000101951.57939.7E
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 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/108/21/e149

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/