Reviewer's report

Title: Genetic Association Analysis of Coronary Collateral Circulation in Patients with Coronary Artery Disease Using 22 Single Nucleotide Polymorphisms Corresponding to 10 Genes Involved in Postischemic Neovascularization: Results of a 5-Year Prospective Study

Version: 2 Date: 3 January 2015
Reviewer: Stephan Schirmer

Reviewer's report:

Duran et al. report on a genetic association study in 677 patients with differing degrees of collateralization and their association with 22 SNPs of 10 genes known to be involved in collateral artery growth.

The manuscript is of importance to the field because of the quest for a better understanding of inter-individual differences in coronary collateralization and the search for therapeutic strategies if collateral arteries are grown insufficiently. There are, however, several limitations:

- The term "5-year prospective study" should be removed from the title, as the study is NOT a five year prospective study. Instead, patients have been gathered over a 5 year period. There is, however, no 5-year follow-up as suggested by this title.

- The most important limitation of assessing collateralization only by a modified Rentrop method needs to be more clearly stated. The original Rentrop method contained injection of contrast medium into the feeding collateral artery during occlusion of the recipient artery. This has not been performed in the current work. Furthermore, work of the last 20 years has repeatedly demonstrated that intracoronary physiological pressure or flow measurements to calculated collateral flow index are superior to an angiographic (Rentrop) technique.

- Also stating the difference between the two in the introduction section, the authors confuse important regulators of angiogenesis and arteriogenesis in their study. HIF1alpha and VEGF are of less importance in collateral artery growth. Thus, lack of their expression and differing collateralization is not surprising. Factors known to be involved in arteriogenesis as evident from clinical investigations such as interferon-beta were, on the other hand, not studies.

Minor comment:

- Language editing of the manuscript is necessary
- Reference 63 seems to come from an abstract not a full article.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being
published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests