

Endothelial progenitor cell and adhesion molecules determine the quality of the coronary collateral circulation/ Endothelial progenitor cells (CD34 + KDR +) and monocytes may provide the development of good coronary collaterals despite the vascular risk factors and extensive atherosclerosis

Endotelial progenitor hücreler ve adezyon molekülleri koroner kollateral dolaşımın kalitesini belirler/Endotelial progenitor hücreler (CD34 + KDR +) ve monositler vasküler risk faktörleri ve yaygın aterosklerozla rağmen iyi koroner kollateral gelişimini sağlayabilirler

Dear Editor,

We read with great interest the paper by Kocaman et al. (1) entitled "Endothelial progenitor cells (CD34+KDR+) and monocytes may provide the development of good coronary collaterals despite the vascular risk factors and extensive atherosclerosis." The authors evaluated simultaneously the effects of endothelial progenitor cells (EPC) and inflammatory cells on the presence and the extent of coronary artery disease (CAD) and the grade of coronary collateral growth in patients with clinical suspicion of CAD. They found that the patients with good collateral growth had significantly higher EPC in comparison to patients with poor collateral growth. They stated that the presence of EPC was associated with reduced risk for CAD and was an independent predictor for good collateral growth. They also found that CD34+KDR-, CD34+KDR+ and CD34-KDR+ cells, and a CD34-KDR- cell subpopulation were highest in number in good collateral group among all study population.

Coronary collaterals are the connections between portions of the same coronary artery and between different coronary arteries (2).

A strong, positive correlation was identified between coronary collateral flow and the number of circulating CD34+/CD133+ endothelial progenitor cells in patients with CAD. Moreover, endothelial-cell-marker expression was more common in EPCs isolated from patients with adequate collateral flow than in EPCs from patients with poor collateral flow (3).

In a recently published study performed by Tokgözoğlu et al. (4), they found that the number of EPCs were significantly greater in patients with good coronary collateral formation. Furthermore, circulating EPCs were higher among patients with normal coronary vessels compared to patients with CAD for CD133 (+)/34(+) and CD34(+)/KDR(+) cells. They demonstrated that EPC count was an independent predictor of coronary collateral formation after adjustment for other cardiovascular risk factors and extent of CAD. Finally, they concluded that increased circulating EPCs provided better collateral formation compared to those with lower EPC counts.

Güray et al. (5) investigated the levels of soluble endothelial adhesion molecules (CAMs) and vascular cell adhesion molecule (VCAM-1) intercellular adhesion molecule-1 (ICAM-1) and E-selectin were compared between patients with poor coronary collaterals and patients with well-developed collaterals in a study published in 2004. They created two groups according to the Rentrop collateral degree (Group A: grade 0 and 1; Group B: grade 2 and 3 collaterals). They found that the

levels of soluble VCAM-1, ICAM-1, and E-selectin were significantly higher in group A in comparison with group B. They concluded that poor collateral circulation is associated with increased levels of soluble CAMs in patients with obstructive coronary artery disease.

Presence of collaterals that feed the jeopardized myocardial area may limit the infarct size after coronary occlusion and may even provide a survival benefit. However, some patients develop good collateral circulation, whereas others do not. The inter-individual variations of endothelial cell marker expression and soluble adhesion molecules may explain why some patients develop adequate collateral circulation whereas others do not.

Consequently, as the endothelium and inflammatory cells play a crucial role in the development of collaterals after a sudden or slowly progressing stenosis of coronary arteries, endothelial progenitor cells and soluble adhesion molecules determine the formation and the quality of the collaterals.

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References

1. Kocaman SA, Yalçın MR, Yağcı M, Şahinarslan A, Türkoğlu S, Arslan U, et al. Endothelial progenitor cells (CD34+KDR+) and monocytes may provide the development of good coronary collaterals despite the vascular risk factors and extensive atherosclerosis. *Anadolu Kardiyol Derg* 2011; 11: 290-9.
2. Tatlı E, Büyüklü M. Is coronary revascularization necessary for patients with well-developed coronary collaterals and coronary artery disease? *Int J Cardiol* 2008; 125: 103.
3. Lambiase PD, Edwards RJ, Anthopoulos P, Rahman S, Meng YG, Bucknall CA, et al. Circulating humoral factors and endothelial progenitor cells in patients with differing coronary collateral support. *Circulation* 2004; 109: 2986-92.
4. Tokgözoğlu L, Yorgun H, Gürses KM, Canpolat U, Ateş AH, Tülümen E, et al. The association between circulating endothelial progenitor cells and coronary collateral formation. *Atherosclerosis* 2011; 219: 851-4.
5. Güray U, Erbay AR, Güray Y, Yılmaz MB, Boyacı AA, Şaşmaz H, et al. Poor coronary collateral circulation is associated with higher concentrations of soluble adhesion molecules in patients with single-vessel disease. *Coron Artery Dis* 2004; 15: 413-7.

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Author's Reply

Dear Editor,

We thank the authors for their supportive comments on our article related to circulating CD34+KDR+ cells (1) in their letter entitled as 'Endothelial progenitor cell and adhesion molecules determine the quality of the coronary collateral circulation'. They also pointed that CD34+/CD133+ endothelial progenitor cells have a strong, positive correlation

with coronary collateral flow (2), together with more dense endothelial-cell-marker expression. In addition, they also argue that an interesting study in which was investigated the levels of soluble endothelial adhesion molecules (CAMs) and vascular cell adhesion molecule (VCAM-1) intercellular adhesion molecule-1 (ICAM-1) and E-selectin, and found that poor collateral circulation is associated with increased levels of soluble CAMs in patients with obstructive coronary artery disease (3). In conclusion, they said that the inter-individual variations of endothelial cell marker expression and soluble adhesion molecules might explain why some patients develop adequate collateral circulation whereas others do not, as well as the functional endothelium, inflammatory cells, specifically monocytes, and endothelial progenitor cells.

In our opinion, four points are very important in collateral development. First point is first response of jeopardized tissue to ischemia, second point is target tissue and cells for ischemic signals in collateral development, third point is the active and increased functional cells, and last point is the homing capability to ischemic tissue of functional effector cells. All of points can be disturbed by various risk factors, possibly with impairment of sufficient and required microenvironments at cellular level, or may be insufficient for good collateral growth in patients with defective genetically background.

The growth factors and cytokines such as VEGF and EPO (4), which are secreted in response to hypoxia, may stimulate the resident and remote cells to induce angio- and arteriogenesis with paracrine endocrine mechanisms. Lastly, some chemokines like CXCL1 are associated with the presence and extent of spontaneously visible coronary artery collaterals (5). The other important prerequisite for collateral vessel growth is endothelial function. Endothelial nitric oxide synthase activity was found to be related to the angiogenic capability in animal models (6) and clinical settings (7). Resident and bone marrow-derived progenitors and some monocyte subtypes (8, 9) were determined as effector cells for collaterals. They serve as bioreactors and reservoirs of various cytokines and chemokines, which stimulate arteriolar growth in a paracrine fashion. As a prerequisite, the functional integrity of the monocyte and EPCs are crucial for this process. A chemotactic deficit should hamper the monocyte and EPCs to reach sites of vascular remodeling and, thereby, its active participation in collateral growth.

The homing capability to ischemic tissue of functional effector cells is related to damaged endothelium as well as trans-migrant cell functions. This stage may possibly affected by microenvironment, such as oxidant status, signal transmission, and may be an anti-oxidant concentration in plasma, bilirubin (10).

The deleterious effects of vascular risk factors on factors necessary for collateral growth, including pro-angiogenic growth factors, endothelial function, the redox state of the coronary circulation, intra and intercellular signaling, monocytes and bone marrow-derived progenitors cells may impair collateral development by altered microenvironment of the coronary circulation.

Collateral growth is a multistage process and different factors can harm the integrity of arteriogenesis. Known cells and cytokines may be a little part of arteriogenesis as well as unknown cells and cytokines/chemokines. Heterogeneity in collateral formation despite similar degrees of coronary obstruction can be related to different effects of inflammatory cells, the capability of homing factors in ischemic tissue and levels of both cytokine and chemokines related with ischemic tissue and functional cells on the development of collaterals. Besides, the above four points may contain the candidates for new important cells, cytokines and maybe receptors.

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References

1. Kocaman SA, Yalçın MR, Yağcı M, Şahinarslan A, Türkoğlu S, Arslan U, et al. Endothelial progenitor cells (CD34+KDR+) and monocytes may provide the development of good coronary collaterals despite the vascular risk factors and extensive atherosclerosis. *Anadolu Kardiyol Derg* 2011; 11: 290-9.
2. Tokgözoğlu L, Yorgun H, Gürses KM, Canpolat U, Ateş AH, Tülümen E, et al. The association between circulating endothelial progenitor cells and coronary collateral formation. *Atherosclerosis* 2011; 219: 851-4. [CrossRef]
3. Güray U, Erbay AR, Güray Y, Yılmaz MB, Boyacı AA, Şaşmaz H, et al. Poor coronary collateral circulation is associated with higher concentrations of soluble adhesion molecules in patients with single-vessel disease. *Coron Artery Dis* 2004; 15: 413-7. [CrossRef]
4. Şahinarslan A, Yalçın R, Kocaman SA, Erçin U, Tanalp AC, Topal S, et al. The relationship of serum erythropoietin level with coronary collateral grade. *Can J Cardiol* 2011; 27: 589-95. [CrossRef]
5. Keeley EC, Moorman JR, Liu L, Gimble LW, Lipson LC, Ragosta M, et al. Plasma chemokine levels are associated with the presence and extent of angiographic coronary collaterals in chronic ischemic heart disease. *PLoS One* 2011; 6: e21174. [CrossRef]
6. Amano K, Matsubara H, Iba O, Okigaki M, Fujiyama S, Imada T, et al. Enhancement of ischemia-induced angiogenesis by eNOS overexpression. *Hypertension* 2003; 41:156-62. [CrossRef]
7. Kocaman SA. Asymmetric dimethylarginine, NO and collateral growth. *Anadolu Kardiyol Derg* 2009; 9: 417-20.
8. Kocaman SA, Arslan U, Tavil Y, Okuyan H, Abacı A, Çengel A. Increased circulating monocyte count is related to good collateral development in coronary artery disease. *Atherosclerosis* 2008; 197: 753-6. [CrossRef]
9. Arslan U, Kocaoğlu İ, Falay MY, Balcı M, Duyuler S, Korkmaz A. The association between different monocyte subsets and coronary collateral development. *Coron Artery Dis* 2012; 23: 16-21. [CrossRef]
10. Erdoğan T, Çiçek Y, Kocaman SA, Canga A, Çetin M, Durakoğlugil E, et al. Increased serum bilirubin level is related to good collateral development in patients with chronic total coronary occlusion. *Intern Med* 2012; 51: 249-55. [CrossRef]

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Echocardiographic measurement of epicardial fat thickness: In search for a consensus/Correlation of echocardiographic epicardial fat thickness with severity of coronary artery disease-an observational study

Epikardiyal yağ kalınlığının ekokardiyografik ölçümü: Bir konsensus arayışında/Koroner arter hastalığının şiddeti ile ekokardiyografik epikardiyal yağ kalınlığının ilişkisi-gözlemsel bir çalışma

Dear Editor,

We read with great interest the article published by Shemirani et al. (1) in *The Anatolian Journal of Cardiology*, which showed a significant association between epicardial fat thickness (EFT) and coronary