

# Decreased number and function of endothelial progenitor cells in patients with migraine

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偏頭痛患者的內皮前驅幹細胞數量較少功能減弱

# Abstract

**Objective:** Migraine carries an increased risk for cardiovascular and cerebrovascular diseases that cannot be explained by traditional cardiovascular risk factors. The circulating endothelial progenitor cell (EPC) number is a surrogate biologic marker of vascular function, and diminished EPC counts are associated with higher cardiovascular risk. We investigated whether abnormalities in EPC levels and functions are present in migraine patients.

**Methods:** Consecutive headache patients (n = 166) were enrolled, including those with tension-type headache (TTH; n = 74), migraine without aura (MO; n = 67), and migraine with aura (MA; n = 25). EPC colony-forming units in peripheral blood samples and migratory capacity to chemoattractants (stromal cell-derived factor 1 and vascular endothelial growth factor) and cellular senescence levels were assayed in risk factor-matched subjects (n = 6 per group).

**Results:** The TTH group had more cardiovascular risk factors, more headache days, and higher Framingham risk scores than the other two groups. Mean numbers of EPC colony-forming units were  $47.8 \pm 24.3$  in TTH,  $20.4 \pm 22.2$  in MO, and  $8.6 \pm 10.1$  in MA patients ( $p < 0.001$  in TTH vs MO;  $p = 0.001$  in MO vs MA). EPC colony counts of normal subjects (n = 37) were not significantly different from those with TTH. Multiple linear regression models identified only MO, MA, and the presence of migraine (MO + MA) as significant predictors of EPC levels. In addition, EPCs from migraine patients (MO and MA) showed reduced migratory capacity and increased cellular senescence compared with EPCs from TTH or normal subjects.

**Conclusion:** Circulating endothelial progenitor cell (EPC) numbers and functions are reduced in migraine patients, suggesting that EPCs can be an underlying link between migraine and cardiovascular risk.

**GLOSSARY:** ACE= angiotensin-converting enzyme; ATR= angiotensin receptor;  $\beta$ -gal=  $\beta$ -galactosidase; BMI= body mass index; CAD= coronary artery disease; CADASIL= cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; CFU= colony-forming unit; EBM= endothelial basal medium; EPC= endothelial progenitor cell; HDL= high-density lipoprotein; HPF= high-power field; IL= interleukin; KDR= kinase-insert domain receptor; LDL= low-density lipoprotein; MA= migraine with aura; MO= migraine without aura; PBS= phosphate-buffered saline; SA- $\beta$ -gal= senescence-associated  $\beta$ -galactosidase; SDF-1= stromal cell-derived factor 1; TNF= tumor necrosis factor; TTH= tension-type headache; VEGF= vascular endothelial growth factor.