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Cardiovascular Disease Risk in HIV Infection and Endothelial Progenitor Cells

Costiniuk et al [1] recently claimed that the increased cardiovascular disease risk (CVDR) seen in human immunodeficiency virus (HIV) infection cannot be attributed to reduced endothelial progenitor cells (EPCs), because in their study they only found a trend toward lower EPC levels in HIV-infected individuals compared with healthy controls. In contrast, 2 previous studies had indicated that HIV-infected young individuals with low CVDR had lower EPC levels than uninfected controls with similar age and classical CVDR factors [2, 3].

Under normal conditions, the integrity of the endothelium depends on a balance between endothelial vascular injury and repair, which involves the recruitment of EPCs in the bloodstream [4]. EPCs protect from atherosclerosis as a result of their vascular repair capacity [5]. EPCs are a heterogeneous group of cells that can be characterized by the expression of different proteins, such as CD45, CD133, CD34, CD31, and VEGFR-2 (or KDR) [6]. There is no consensus on the phenotypic characterization of these cells, which may be a source of discrepancy among studies. Whereas the study by Costiniuk et al [1] defined EPCs as CD45dimCD34+KDR+ cells, we additionally tested for CD31 and CD133 to better characterize EPC subsets [3]. During differentiation from immature to mature EPCs, CD133 expression is lost [7]. Thus, true EPCs are defined as CD45\textsuperscript{dim}CD34+KDR+CD31+CD133+, whereas late EPCs are CD45\textsuperscript{dim}CD34+KDR+CD31+CD133+. Performing the analyses in our study population [3] using the EPC definition criteria employed by Costiniuk et al [1], we also did not find differences in total EPC levels when comparing HIV-infected individuals and controls. However, when expression of CD31 and CD133 was additionally taken into account, 67% of CD45\textsuperscript{dim}CD34+KDR+ cells were CD31+CD133+ (late EPCs), whereas only 15% were CD31+CD133+ (true EPCs) in HIV-infected individuals. These figures were 57% and 32%, respectively, in healthy controls. Thus, although late EPCs contributed the most to total EPCs (Figure 1), true EPC levels were significantly lower in HIV-infected than in uninfected controls ($P = .012$), supporting the interpretation that the protective effect of EPCs on the development of atherosclerosis is impaired in HIV infection.

Altogether, these results suggest that the phenotypic characterization of EPCs requires considering the expression of CD45, CD34 and KDR, along with CD31 and CD133. Otherwise, true EPCs will not be distinguished from late EPCs, which represent the majority of the total EPC population.

Notes

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Figure 1. Different contribution of endothelial progenitor cell (EPC) subsets according to human immunodeficiency virus (HIV) status. Abbreviation: PBMCs, peripheral blood mononuclear cells.
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