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Letter by Asosingh et al Regarding Article, “Circulating Endothelial Progenitor Cells in Patients With Eisenmenger Syndrome and Idiopathic Pulmonary Arterial Hypertension”

To the Editor:

Diller and colleagues¹ report a decrease in circulating progenitor cells and a trend of increased colony-forming units endothelial-like cells in idiopathic arterial hypertension compared with healthy controls. This is an interesting article in light of other reports, including 1 by our group, which report that circulating CD34⁺/CD133⁺ and colony-forming units endothelial-like cells are increased in idiopathic pulmonary arterial hypertension.^{2,3} Given this disparity, clarification of technical aspects related to the way in which the circulating progenitor cells were enumerated by Diller et al¹ would help in understanding the differences in the data. The authors report that mononuclear cells were separated and isolated by Ficoll separation and by centrifugation with Vacutainer (Becton Dickinson, San Jose, Calif) cell preparation tubes in the Diller study. However, it is not clear if the use of these different isolation steps yield similar numbers of (rare) precursor cells. In addition, the fluorescence-activated cell-sorting analysis was based on 100 000 lymphomonocytic events, which means that some of the fluorescence-activated cell-sorting analyses with low numbers of progenitors (0.01%) are based solely on 10 positive events. It is conceivable that accuracy and reproducibility of this isolation approach, as well as data, may be compromised with such low numbers of positive events. Moreover, information about signal-to-noise ratio, critical in the analysis of rare events, is also missing. Furthermore, the authors corrected the percentage of precursor cells for the number of lymphomonocytic cells in the same subject, making it difficult to compare findings across studies of progenitors, because there may be interindividual variations in the total lymphomonocytic counts that would alter the results relative to quantification of rare circulating cells. For a generalized interpretation of the data, it would be helpful to know what the differences were in the lymphomonocytic counts and the actual percentage of progenitor cells present in blood without the nonstandard correction for lymphomonocytic cells. Finally, the quantification of circulating CD34⁺/CD133⁺ cells does not usually include the subclassification by CD45 positivity,⁴ because these cells are nearly all angiogenic hematopoietic cells and by definition all CD45⁺.⁴ Thus, presentation of the total population of CD34⁺/CD133⁺ cells in blood would be helpful in allowing comparison to other published studies.

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Disclosures

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