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Commentary

Cardiovascular Consequences and Circulating Stem Cells

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DESCRIPTION

During development, as well as in adult health and illness, the cardiovascular and haematopoietic systems have basic interrelationships. Although Haematopoietic Stem Cells (HSCs) arise from a specialized haemogenic endothelium in the embryo, the long-term viability of haemangioblasts is debatable. Rather, bone marrow-derived HSCs and downstream haematopoietic stem/progenitors make up the great bulk of circulating stem cells (CSCs) (HSPCs). Endothelial Progenitor Cells (EPCs), a subset of these cells, have endothelial specification and vascular tropism. In general, the numbers of HSCs, HSPCs, and EPCs are thought to be indicators of the organism's endogenous regeneration ability, particularly in the cardiovascular system. CSC research has centred on their physiologic significance in tissue/organ homoeostasis, their potential application in cell treatments, and their usage as clinical biomarkers throughout the last two decades. We present basic information on CSC biology and explore the clinical consequences of altering CSC levels in individuals with cardiovascular risk factors or existing cardiovascular disease. The growing body of evidence in the literature demonstrating the strong link between low CSC levels and poor cardiovascular outcomes in various patient groups is of special relevance. CSC levels must be evaluated in the context of the larger connection between hematopoiesis and cardiovascular function, including the involvement of clonal hematopoiesis and inflammatory myelopoiesis, in addition to their ability to assist in cardiovascular repair.

Circulating stem cells in peripheral arterial disease and heart failure

With increasing severity of atherosclerosis obliterans and carotid atherosclerosis, a considerable progressive decline of CSCs and EPCs was reported in diabetic individuals, who are particularly at risk for PAD. Compared to people with just CAD, peripheral blood levels of $CD34^+$ HSPCs and $CD34^+VEGFR2^+$EPCs were reported to be lower in patients with both CAD and PAD, data that were corroborated by additional research. When compared to individuals without CAD, those with low $CD34^+$ and $CD34^+VEGFR2^+$ counts had a 65 percent higher chance of developing PAD and CAD, demonstrating that a reduction in EPC populations, in particular, is linked to more widespread multi-site atherosclerosis.

In smaller communities, there have been inconsistent findings on the association between CSC numbers and the occurrence of HF or its severity. In a study involving over 1500 patients, those with HF had significantly lower circulating levels of $CD34^+CXCR4^+$ CSCs than those without HF, and their levels were linked to the severity of HF as measured by New York Heart Association functional class, presence of diastolic dysfunction, left atrial size, pulmonary hypertension, and levels of Brain-Derived Natriuretic Peptide (BNP). The lowest levels of $CD34^+CXCR4^+$ CSC counts were seen in patients with non-ischemic cardiomyopathy, perhaps due to a lack of CSC mobilisation in response to ischaemic events. Patients with intact or lowered ejection fraction had similar levels of CSC reduction.

Circulating stem cells and outcomes in patients with cardiovascular disease

The prognostic importance of CSC counts among patients with cardiovascular risk factors, CAD, or other cardiovascular disorders has been explored by a number of researchers. A recent meta-analysis summarises these findings. Despite the heterogeneity in the assays used, studies have consistently found that CSC depletion is related with poor outcomes in individuals with existing CAD or those at high risk for CVD. Low $CD34^+$ and $CD34^+CD133^+$CSCs were independently related with a two- to three-fold greater mortality risk over a 22-month follow-up in one of the biggest investigations to date, which included over 900 patients having coronary angiography for suspected or confirmed CAD. Low $CD34^+$, $CD34^+CD133^+$, and $CD34^+CXCR4^+$ CSCs, but not $CD34^+VEGFR2^+$ EPCs, exhibited equivalent predictive value for recurrent AMI or mortality in individuals with an acute coronary syndrome. The amount of $CD34^+CD133^+VEGFR2^+$EPCs mobilized following ischemic damage or infarction appears to be related to tissue recovery, such as left ventricular function recovery and mortality after AMI, or neurological function improvement after stroke.

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