



International Journal of Clinical Cardiology & Research

Review Article

Endogenous Endothelial Repair System in Heart Failure: Focus on Progenitor Endothelial Cell Dysfunction -

Alexander E. Berezin*

Private Clinic "Vita-Center", 3, Sedova str, Zaporozhye, Ukraine, Senior Consultant of Therapeutic Unit, Internal Medicine Department, State Medical University of Zaporozhye, Ukraine

***Address for Correspondence:** Alexander E. Berezin, Private Clinic "Vita-Center", 3, Sedova str, Zaporozhye, Ukraine, Senior Consultant of Therapeutic Unit, Internal Medicine Department, State Medical University of Zaporozhye, 26, Mayakovskiyav, Zaporozhye, Ukraine, Tel: +380612894585; E-mail: dr_berezin@mail.ru; aeberezin@gmail.com

Submitted: 26 August 2017; **Approved:** 31 August 2017; **Published:** 31 August 2017

Citation this article: Berezin AE. Endogenous Endothelial Repair System in Heart Failure: Focus on Progenitor Endothelial Cell Dysfunction. Int J Clin Cardiol Res. 2017;1(2): 057-059.

Copyright: © 2017 Berezin AE. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



ABSTRACT

Heart Failure (HF) a leading cause of premature death in patients with established Cardio Vascular (CV) disease. Although the global burden of HF is increasing, there is no evidence regarding promising results that improves long-term clinical outcomes especially for HF with preserved and mid-regional pump function. In this context, determination of the vulnerable populations at higher risk of HF development and progression is very promising. Endothelial Dysfunction (ED) plays a central role in the manifestation of HF regardless its phenotypes. There is a large body of evidence regarding that the Endothelial Progenitor Cells (EPCs) as a component of endogenous vascular repair system could be modified by several stimuli including epigenetic factors and thereby they are involved in the pathogenesis of ED. However, there is unclear whether EPC dysfunction is only whitened of HF or it could be a factor of HF manifestation in vulnerable population. The short communication is depicted the uncertain role of EPC dysfunction in pathogenesis of HF.

Keywords: Heart failure; Biomarkers; Endothelial Progenitor Cells; Prediction.

INTRODUCTION

Heart Failure (HF) remains a leading cause of mortality in patients with established Cardio Vascular (CV) disease [1,2]. There is a strong trend toward reducing death rate due to HF associated with steady increased frequencies of newly manifested HF in developed countries, although in developing countries the HF mortality rate appears to be exaggeratedly high [3]. Identification of the vulnerable populations at higher risk of HF development and progression has now based on the early diagnosis of CV disease (atherosclerosis, hypertension, coronary heart disease, peripheral artery disease, and vasculitis) and metabolic states including diabetes, abdominal obesity, thyroid dysfunction, as well as other CV risk factors which may pre-exist CV diseases and particularly HF [4]. The short communication is depicted the uncertain role of EPC dysfunction in pathogenesis of HF.

Endothelial dysfunction in HF

Endothelial Dysfunction (ED) is considered an integral state in the development of HF regardless its phenotypes [5] and even contributes in clinical outcomes across all stages of CV continuum [6]. There is a large body of evidence regarding that the exhausted reparative ability of vasculature in resulting in several factors including pre-existing co-morbidities, some severe diseases that had appeared prior HF manifestation (trauma, infections, inflammatory diseases), and traditional CV risk factors could be primary reasons for loss of endothelial cell integrity and shaping ED [7-9]. In this context, Endothelial Progenitor Cells (EPCs) that are mobbed from bone marrow precursors and peripheral tissue residences and involved in reparative processes through differentiation and turn-into mature endothelial cells are promising biomarkers of ED with possible predictive value [10,11].

Endothelial progenitor cell dysfunction: definition and role in HF

EPC dysfunction is determined as weak function and / or decreased circulating number of endothelial precursors [12]. Indeed, decreased number of circulating EPCs was found a strong predictor of CV death, CV outcomes and HF-related events in HF patients with reduced and preserved left ventricular ejection fraction independently etiology of the disease [12-14].

On the other hand, EPCs that circulate in the peripheral blood in patients at higher risk of HF and in individuals with established HF presented lowered survival ability and partially inconvenience to be differentiated to mature endothelial cells under influence of essential innate stimuli including transforming growth factor-beta, tumor necrosis factor-alpha (TNF- α) and other inflammatory

cytokines [15,16]. This phenomenon was previously described as EPC dysfunction and it was widely diagnosed in the patients with diabetes, abdominal obesity, hypertension and other CV risk factors [17]. Interesting, that all these factors promote oxidative stress and mitochondrial dysfunction in target cells including EPCs that is suitable for different pathophysiological stages of HF.

EPC dysfunction as a central player in HF risk development

Although number and functionality of EPCs have validated to be strong predictors of HF risk development and advance, it had been remained unclear whether EPC dysfunction is only whitened of HF or it could be a factor of HF manifestation in vulnerable population. However, recent clinical trials have not confirmed ability of EPC collected from the patients with established HF having recovered function after treatment including cardiac rehabilitation programs, while a number of circulating EPCs may recover completely in some cases [18-20]. It has been suggested that the altered immune pattern of EPCs, which could be determined prior HF, is central player in worsening vascular / endothelial repair and contributes in ED [21]. Probably EPC functionality could be regulated by some epigenetic factors influencing on ability of precursors to differentiate into mature cells including endothelial cells. Moreover, it has noted that there is possibility to change of endothelial cell immune phenotype to cardiac cell phenotype in animal model [22]. Whether similar effects trigger structure and functional abnormality in cell precursors that involve in the pathogenesis of HF is not well established, although accumulation of reactive oxygen species leading to the swelling and fragmentation of mitochondria of EPCs has now described as factor of decreased repair ability of precursors [23]. Indeed, enhancement of oxidative stress and mitochondrial dysfunction of EPCs may negatively effect of number and function of one's (mobbing, proliferation, regeneration, apoptosis, differentiation, cell-cell interaction, survival) through intracellular signaling pathways (Akt/nitric oxide, PI3K/nitric oxide), which may operate in signal-regulated kinase and the inflammatory genes expression, such as interleukin-6 and TNF- α , and synthesis of specific mi RNAs (-126, -128, -130) [24,25]. Finally, epigenetically modified EPCs are not able to maintain the homeostasis of vasculature and trigger inadequate endothelial responses that realize ED and micro vascular inflammation. Probably, this model may be taken into consideration for creating novel molecular biomarkers of HF and target for personal treatment of the disease.

CONCLUSIONS

Evidence emerging from both animal and clinical studies has shown that EPC dysfunction may be crucial for pathogenesis of HF and however it is not excluded that worsening endogenous vascular repair system including EPCs could play a pivotal role in the



manifestation and progress of HF regardless etiology of the disease. Biomarker strategy based on determination of EPC dysfunction in patients at higher risk of HF development and in individuals with established HF maybe promising for HF diagnosis and stratification in future, while this conception requires more investigations for understanding.

REFERENCES

- Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. Authors/Task Force Members. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016; 37: 2129-200. <https://goo.gl/cgimwr>
- Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Colvin MM, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation*. 2017; 136: 137-161. <https://goo.gl/xjVfHG>
- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, et al. American Heart Association Statistics Committee; Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. *Circulation*. 2016; 133: 38-360. <https://goo.gl/ZZwDkV>
- van den Berg MJ, Bhatt DL, Kappelle LJ, de Borst GJ, Cramer MJ, van der Graaf Y, et al. SMART study group; REACH Registry investigators. Identification of vascular patients at very high risk for recurrent cardiovascular events: validation of the current ACC/AHA very high risk criteria. *Eur Heart J*. 2017. [Epub ahead of print]. <https://goo.gl/zRRPPn>
- Pouleur AC. Which biomarkers do clinicians need for diagnosis and management of heart failure with reduced ejection fraction? *Clin Chim Acta*. 2015; 443: 9-16. <https://goo.gl/q489vh>
- Berezin AE. Prognostication in different heart failure phenotypes: the role of circulating biomarkers. *Journal of Circulating Biomarkers*. 2016; 5: 01. <https://goo.gl/JUyAsv>
- Berezin AE, Kremzer AA. Analysis of various subsets of circulating mononuclear cells in asymptomatic coronary artery disease. *J Clin Med*. 2013; 2: 32-44. <https://goo.gl/J2AmS3>
- Berezin AE, Kremzer AA. Relationship between circulating endothelial progenitor cells and insulin resistance in non-diabetic patients with ischemic chronic heart failure. *Diabetes Metab Syndr*. 2014; 8: 138-44. <https://goo.gl/TERSDP>
- Chow SL, Maisel AS, Anand I, Bozkurt B, de Boer RA, Felker GM, Fonarow GC, et al. American Heart Association Clinical Pharmacology Committee of the Council on Clinical Cardiology; Council on Basic Cardiovascular Sciences; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; Council on Epidemiology and Prevention; Council on Functional Genomics and Translational Biology; and Council on Quality of Care and Outcomes Research. Role of Biomarkers for the Prevention, Assessment, and Management of Heart Failure: A Scientific Statement From the American Heart Association. *Circulation*. 2017; 135: 1054-1091. <https://goo.gl/65xztM>
- Wettersten N, Maisel AS. Biomarkers for Heart Failure: An Update for Practitioners of Internal Medicine. *Am J Med*. 2016; 129: 560-7. <https://goo.gl/m893Xt>
- Koller L, Hohensinner P, Sulzgruber P, Blum S, Maurer G, Wojta J, et al. Prognostic relevance of circulating endothelial progenitor cells in patients with chronic heart failure. *Thromb Haemost*. 2016; 116: 309-16. <https://goo.gl/puqSSz>
- Berezin A. Biomarkers for cardiovascular risk in diabetic patients. *Heart*. 2016; 102: 1939-1941. <https://goo.gl/yJgDMV>
- Berezin A, Kremzer A, Martovitskaya Y, Samura T, Berezina T. The novel biomarker risk prediction score in patients with chronic heart failure. *Clin Hypertens*. 2016; 22: 3. <https://goo.gl/EeF11g>
- Berezin AE, Kremzer AA, Samura TA, Martovitskaya YV. Apoptotic microparticles to progenitor mononuclear cells ratio in heart failure: relevance of clinical status and outcomes. *JCvD*. 2014; 2: 50-57. <https://goo.gl/ZQyiQc>
- Berezin AE. Impaired Phenotype of Endothelial Cell-Derived Micro Particles: The Missed Link in Heart Failure Development? *Biomarkers J*. 2016; 2: 14-19. <https://goo.gl/eHyL7D>
- Berezin AE, Kremzer AA, Berezina TA, Martovitskaya YV. Pattern of circulating microparticles in chronic heart failure patients with metabolic syndrome: relevance to neurohumoral and inflammatory activation. *BBA Clin*. 2015; 4: 69-75. <https://goo.gl/Jao9we>
- Berezin A. Endothelial progenitor cells dysfunction and impaired tissue repair: the missed link in diabetes mellitus development. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*. 2017; 11: 215-220.
- Billebeau G, Vodovar N, Sadoune M, Launay JM, Beauvais F, Cohen-Solal A. Effects of a cardiac rehabilitation program on plasma cardiac biomarkers in patients with chronic heart failure. *Eur J Prev Cardiol*. 2017; 24: 1127-1135. <https://goo.gl/883bi9>
- Berezin AE. Biological markers of cardiovascular diseases. Part 4. Diagnostic and prognostic value of biological markers at risk stratification among patients with heart failure. LAMBERT Academic Publishing GmbH. Moscow, 2015. <https://goo.gl/jmEeXo>
- Berezin A. Endothelial Derived Micro Particles: Biomarkers for Heart Failure Diagnosis and Management. *J Clin Trial Cardiol*. 2015; 2: 1-3. <https://goo.gl/KiqwtR>
- Berezin AE. Impaired pattern of endothelial derived microparticles in heart failure patients. *J Mol Genet Med* 2015; 9: 1. <https://goo.gl/N6MX7v>
- Nesti L, Natali A. Metformin effects on the heart and the cardiovascular system: A review of experimental and clinical data. *Nutr Metab Cardiovasc Dis*. 2017; 27: 657-669. <https://goo.gl/mz7v2e>
- Münzel T, Camici GG, Maack C, Bonetti NR, Fuster V, Kovacic JC. Impact of Oxidative Stress on the Heart and Vasculature: Part 2 of a 3-Part Series. *J Am Coll Cardiol*. 2017; 70: 212-229. <https://goo.gl/ivkdrG>
- Berezin A. Epigenetics in heart failure phenotypes. *BBA Clin*. 2016; 6: 31-7. <https://goo.gl/HQnRQE>
- Gevaert AB, Lemmens K, Vrints CJ, Van Craenenbroeck EM. Targeting Endothelial Function to Treat Heart Failure with Preserved Ejection Fraction: The Promise of Exercise Training. *Oxid Med Cell Longev*. 2017; 2017: 4865756. <https://goo.gl/oV5ez4>