Brain-derived neurotrophic factor in heart failure

Heart failure is a deadly disease and is the focus of several ongoing biomarker studies. However, it is quite difficult to scientifically validate a specific biomarker because many biomarkers are neither disease specific nor tailored by therapeutic approach (1). Hence, although biomarkers are a subject of scientific papers, they rarely appear in clinical markets.

In a recent case–control study, Barman et al. (2) showed that peripheral brain-derived neurotrophic factor (BDNF) levels, in relation to New York Heart Association (NYHA) class, were lower in patients with heart failure with reduced ejection fraction (HFrEF) compared with age-and sex-matched healthy individuals. The authors determined that decreased serum BDNF levels were associated with death and rehospitalization in with HFrEF, suggesting that BDNF can be a useful prognostic biomarker.

BDNF, produced by many cell types, is associated with neuronal plasticity when secreted as a neurotrophin. The blood–brain barrier is an uninterrupted monolayer of specialized endothelial cells, which creates a functional barrier between the nervous system and circulating blood (3). This layer is composed of endothelial cells, astrocytes, which are considered responsible for producing BDNF in the brain, and pericytes (3, 4). However, BDNF is also known to be synthesized in megakaryocytes and stored in platelets; however, the function of BDNF in peripheral blood has not been completely elucidated (5). Additionally, BDNF can be produced by peripheral mononuclear cells, including eosinophils (6, 7). Of note, platelets, as the major storage site, can significantly influence BDNF levels in plasma (8).

Although peripheral BDNF is pathophysiologically linked with and a well-studied biomarker of major depression (9), decreased peripheral BDNF levels have been described in some neurodegenerative disorders (10). Thus, it is important to note that ethically and technically, it is almost impossible to measure central levels of BDNF. BDNF stored in platelets was shown to be released at the injury site and hence may play a role in tissue trauma or neuronal hyperreactivity, resulting in post-inflammatory pain (11). Notably, peripheral BDNF levels were also shown to be influenced by anti-depressant medication (12, 13). It is interesting to note that depression and platelet function are associated with each other via peripheral BDNF levels (14). This might be the peripheral manifestation of a central disease. On the other hand, considering the significant influence of platelets on BDNF levels, anti-platelet therapy might stand as a confounder of plasma levels to some extent. A previous study showed that clopidogrel but not aspirin reduced the release of BDNF from the stored granules, resulting in decreased plasma levels (15).

Along with the brief and interesting introductory notes, there are several limitations of the current observation. First, not only platelet levels but also the functional status of platelets, which are a major source of peripheral BDNF levels, were not thoroughly evaluated. Second, considering that depression is closely linked to peripheral BDNF levels and depression is a major comorbidity of HFrEF, depending on NYHA class, further studies are necessary to determine the role of BDNF in relation to the occurrence and degree of depression in patients with HFrEF.

Mehmet Birhan Yılmaz
Department of Cardiology, Faculty of Medicine, Dokuz Eylül University; İzmir-*Turkey*

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Address for correspondence: Dr. Mehmet Birhan Yılmaz, Dokuz Eylül Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, İzmir-*Türkiye*
Phone: +90 505 292 74 42 E-mail: cardioceptor@gmail.com
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