Brain-derived neurotrophic factor as biomarker

To the Editor,

The publication on "Prognostic significance of brain-derived neurotrophic factor (BDNF) levels in patients with heart failure and reduced left ventricular ejection fraction" is very interesting (1). Barman et al. (1) concluded that decreased serum BDNF levels were associated with death and rehospitalization in patients with HF, suggesting their usefulness as prognostic biomarkers. As commented in the editorial, concurrent medical disorders can alter the clinical significance of BDNF (2). Nevertheless, there are other concerning factors regarding the usefulness of BDNF as a biomarker. For example, in laboratory medicine, poor reproducibility of the BDNF assay is common, which limits its usefulness as a biomarker (3). In addition, the conditions of blood sample collection and processing can significantly affect the BDNF levels (4). As reported by Tsuchimine et al. (5), anticoagulant compounds as well as the storage time and temperature during blood sampling can affect the measurements of plasma BDNF levels.

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References

1. Barman HA, Şahin I, Atıcı A, Durmaz E, Yurtseven E, Ikitimur B, et al. Prognostic significance of brain-derived neurotrophic factor levels in patients with heart failure and reduced left ventricular ejection fraction. Anatol J Cardiol 2019; 22: 309-16.
2. Yılmaz MB. Brain-derived neurotrophic factor in heart failure. Anatol J Cardiol 2019; 22: 317-8.
3. Polacchini A, Metelli G, Francavilla R, Baj G, Florean M, Mascaretti LG, et al. A method for reproducible measurements of serum BDNF: comparison of the performance of six commercial assays. Sci Rep 2015; 5: 17989.
4. Pareja-Galeano H, Alis R, Sanchis-Gomar F, Cabo H, Cortell-Ballester J, Gomez-Cabrera MC, et al. Methodological considerations to determine the effect of exercise on brain-derived neurotrophic factor levels. Clin Biochem 2015; 48: 162-6.
5. Tsuchimine S, Sugawara N, Ishioka M, Yasui-Furukori N. Preanalysis storage conditions influence the measurement of brain-derived neurotrophic factor levels in peripheral blood. Neuropsychobiology 2014; 69: 83-8.

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DOI:10.14744/AnatolJCardiol.2020.84699

Author`s Reply

To the Editor,

We would like to thank the author(s) for their interest and valuable comments on our manuscript entitled "Prognostic significance of brain-derived neurotrophic factor (BDNF) levels in patients with heart failure and reduced left ventricular ejection fraction" (1). In the authors' letter to the editor, the authors mentioned that there are potential concerns regarding the usefulness of BDNF as a biomarker.

The main aim of our study (1) was to investigate the relationship between BDNF levels in patients with heart failure (HF) and reduced left ventricular ejection fraction (LVEF), considering death or rehospitalization due to HF. Several recent studies have shown the association of BDNF with cardiovascular diseases. The prognostic significance of BDNF has been demonstrated in patients with hypertension, HF, and coronary artery disease (CAD) (2, 3). Because antidepressant medications can affect BDNF levels, patients with a history of a psychiatric disorder, such as major depressive disorder, schizophrenic disorder, or organic brain disorders, were excluded from our study. Like other studies that investigated the relationship between BDNF and heart failure (3-5), we measured BDNF levels using ELISA. Since BDNF is released from many tissues, such as brain, heart, endothelial, and skeletal muscle (6), it is unknown which organ decreases BDNF levels in patientswith HF the most. It is believed that the mean serum BDNF levels are 100-fold higher than plasma levels because of platelet degranulation during the coagulation process (7). Because the majority of circulating BDNF is stored in platelets, it has been shown in the literature that the amount of BDNF in serum is similar to that in washed platelet lysates (8). Reliable biomarkers for diagnosis, treatment follow-up, and prognosis remain an unmet medical requirement. There is a consensus that BDNF can be an important measurable biomarker. However, future studies are needed to provide the basis for obtaining optimal BDNF measurements suitable for future clinical trials using human serum.

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References

1. Barman HA, Şahin I, Atıcı A, Durmaz E, Yurtseven E, Ikitimur B, et al. Prognostic significance of brain-derived neurotrophic factor levels in patients with heart failure and reduced left ventricular ejection fraction. Anatol J Cardiol 2019; 22: 309-16. [CrossRef]
2. Manni L, Nikolova V, Vyagova D, Chaldakov GN, Aloe L. Reduced plasma levels of NGF and BDNF in patients with acute coronary syndromes. Int J Cardiol 2005; 102: 169-71. [CrossRef]
3. Takashio S, Sugiyama S, Yamamuro M, Takahama H, Hayashi T, Sugano Y, et al. Significance of low plasma levels of brain-derived neurotrophic factor in patients with heart failure. Am J Cardiol 2015; 116: 243-9. [CrossRef]
4. Fukushima A, Kinugawa S, Homma T, Masaki Y, Furihata T, Yokota T, et al. Serum brain-derived neurotropic factor level predicts adverse clinical outcomes in patients with heart failure. J Card Fail 2015; 21: 300-6. [CrossRef]
5. Kadowaki S, Shishido T, Honda Y, Narumi T, Otaki Y, Kinoshita D, et al. Additive clinical value of serum brain-derived neurotrophic factor for prediction of chronic heart failure outcome. Heart Vessels 2016; 31: 535-44. [CrossRef]
6. Yamamoto H, Gurney ME. Human platelets contain brain-derived neurotrophic factor. J Neurosci 1990; 10: 3469-78. [CrossRef]
7. Radka SF, Holst PA, Fritsche M, Altar CA. Presence of brain-derived neurotrophic factor in brain and human and rat but not mouse serum detected by a sensitive and specific immunoassay. Brain Res 1996;709:122–301. [CrossRef]
8. Fujimura H, Altar CA, Chen R, Nakamura T, Nakahashi T, Kambayashi J, et al. Brain-derived neurotrophic factor is stored in human platelets and released by agonist stimulation. Thromb Haemost 2002; 87: 728–34. [CrossRef]

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A new marker for ventricular tachyarrhythmias in patients with post-infarction left ventricular aneurysm: Big endothelin-1

To the Editor,

We read with interest the article entitled "Big endothelin-1 as a clinical marker for ventricular tachyarrhythmias in patients with post-infarction left ventricular aneurysm" by Ning et al. (1). In this study, the authors demonstrated that big endothelin-1 (B-ET-1) may be an independent predictor of ventricular tachyarrhythmias (VT) in patients who develop left ventricular aneurysm (LVA) following acute myocardial infarction (AMI). Although the research was well conducted, we have some concerns that should be clarified.

Several previous studies have shown that B-ET-1 levels are remarkably elevated in patients with coronary artery disease and AMI (2-4). In particular, one experimental study revealed that plasma levels of ET-1 sharply rise following AMI, reaching a peak value at 6 h and returning toward the normal range by 24 h (4). However, the authors of the present study have not mentioned the time at which plasma levels of B-ET-1 were measured.

Moreover, the authors mention that informed consent was obtained from the study participants prior to enrolment in the study. However, they acknowledge that the major limitation of the study was the observational retrospective study design. We considered that the data was prospectively collected but retrospectively analyzed. We believe that this issue regarding the methodological design should be explained in detail.

In previous reports, LVA is commonly located in the anterior wall, whereas inferoposterior or posterolateral aneurysms are less common (5). In this article, the investigators have not provided any information regarding the location of LVA. Moreover, we speculated whether there is a significant difference in the VT burden and plasma levels of B-ET-1 depending on the location of LVA.

In the present research, the authors stated that all arrhythmia-related information, including that from patients who underwent placement of an implantable cardioverter defibrillator (ICD), was collected and reviewed. Hence, it would be valuable to know whether there is a difference between plasma levels of B-ET-1 in patients who had multiple ICD shocks due to multiple recurrent VT attacks and in those without ICD shock.

Overall, although some clinical information was missing in the article, the findings of the present study may be valuable in terms of providing new insights into biomarker-guided targeted therapies for VT.

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References

1. Ning X, Yang Z, Ye X, Si Y, Wang F, Zhang X, et al. Big endothelin-1 as a clinical marker for ventricular tachyarrhythmias in patients with post-infarction left ventricular aneurysm. Anatol J Cardiol 2019; 22: 256-61.
2. Wang Y, Zhang Y, Zhu CG, Guo YL, Huang QJ, Wu NQ, et al. Big endothelin-1 level is a useful marker for predicting the presence of isolated coronary artery ectasia. Biomarkers 2017; 22: 331-6.
3. Qing P, Li XL, Zhang Y, Li YL, Xu RX, Guo YL, et al. Association of Big Endothelin-1 with Coronary Artery Calcification. PLoS One 2015; 10: e0142458.