

## Afferent signaling impairment from baroreceptors cannot fully explain decrease in heart rate variability in Marfan syndrome patients: an author's reply

We are grateful for the interest to our paper reporting low heart rate variability (HRV) in Marfan syndrome (MS) patients with FBN1 mutations [1]. The author of the letter [2] raised the question whether low HRV is related to FBN1 mutation or impaired baroreflex due to aorta and large vessels damage in MS [3]. We fully agree with the author's statement that the lesions of aorta and carotid arteries like dilation, dissection, and aneurysm may cause impairment of afferent signaling of baroreflex circuits resulting in reduction of HRV. However, there are several reasons why we think that this is not the only explanation for HRV decrease in MS.

Impairment of afferent signaling from baroreceptors, although important, is not the only possible reason for suppressed heart rate oscillations [3]. As it was mentioned in our study, we did not observe substantial differences in HRV parameters of MS patients with FBN1 mutations after surgery compared to those who did not undergo the Bentall surgery. Therefore, the separate analysis of HRV between subgroups with and without serious aortic damage was not performed [1]. Besides, we did not observe significant signs of baroreceptor feedback failure such as blood pressure instability, left ventricle hypertrophy, or orthostatic hypotension in our patients [4]. The data obtained from the HRV records during orthostatic testing further confirms the absence of clinically significant orthostatic intolerance in studied patients [1]. It is known that the major location of baroreceptors is the carotid bulb. However, in MS, damage to carotid arteries occurs relatively less frequently compared to lesions in the aorta [5]. Thus, we can expect only a partial loss of afferent baroreceptor signaling in MS and it is really difficult to determine these changes quantitatively.

The other reasons of HRV decrease in MS patients with FBN1 mutations have been extensively discussed [1]. As it was hypothesized previously, the HRV suppression may occur in energy deficient states of the cardiac pacemaker cells [6], and a number of conditions characterized by excessive

inflammation, oxidative stress, insulin resistance and other factors. Even mild changes and early stages of diseases may exert suppression of HRV far before the first clinically significant manifestation [7]. The most important possible clinical implications of low HRV in MS patients include increased risk of heart rhythm disorders and ventricular dysrhythmias in particular [8], which may be the cause of sudden death, independent of aortic aneurysms.

Thus, the question whether the decreased HRV is related to affected baroreceptor signaling or metabolic derangements caused by the FBN1 mutation in MS patients cannot be considered solved and further studies providing more accurate results are needed. Most likely both mechanisms to some extent take place in these patients. Nevertheless, the importance of HRV determination in MS for evaluation of ventricular dysarrhythmias should not be underestimated.

**Conflict of interest:** None declared

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