



Letter to the Editor

Cardiac autonomic recovery in type 2 diabetes mellitus and coexistent hypertension: Cutoff values, dipping status, and medications



Dear Editor,

We read with great interest the recent article entitled 'Co-Existence of hypertension worsens post-exercise cardiac autonomic recovery in type 2 diabetes' by Verma et al¹ in your distinguished journal. In their well-designed article, the authors investigated the effect of coexistence of hypertension (HT) on cardiac autonomic functions assessed by heart rate recovery (HRR) and heart rate variability (HRV) in type 2 diabetes mellitus (T2DM).

We have three comments regarding this study. First, HRR at 1 minute (HRR1min) and 2 minutes (HRR2min) in this study was still within the normal limits (HRR1min: 27.3 bpm and HRR2min 42.8 bpm for patients with T2DM and HT). Although several variables influence HRR, suggested thresholds for abnormality are ≥ 12 bpm at 1 min for the upright position, ≥ 18 bpm at 1 min for the supine position, and ≥ 22 bpm at 2 min for the sitting position.² Although HRR indices were lower in patients with T2DM and HT, these values are not enough for diagnosis of cardiac autonomic dysfunction.

As a second comment, circadian blood pressure patterns of patients were not reported in the present study. Nocturnal dipping of arterial blood pressure is a part of the normal circadian pattern, and non-dipping is associated with severe end-organ damage and increased risk of cardiovascular events, especially in hypertensive patients.² Blunting of the nocturnal fall in blood pressure (BP) associates with lower HRR indices after graded maximal exercise in both normotensive and hypertensive groups, and this relationship is more prominent in the hypertensive group.³

As a final comment, use of statins was common in patients with T2DM and/or HT, and there was no use of statin in the healthy control group. It has been demonstrated that statins improve autonomic function, as reflected by an increase in HRV.⁴ Furthermore, statin treatment could significantly increase parasympathetic modulation of the heart rate.⁵

Conflict of interest

The authors declare that they have no conflict of interest to disclose.

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Author response

Exercise has profound and complex effects on cardiac autonomic modulation such that a shift in the balance from parasympathetic to sympathetic dominance during transition from rest to exercise and the recovery period after exercise increases the susceptibility of the heart to dysrhythmias. The main objective of the study¹ was to assess postexercise cardiac autonomic recovery in patients with coexisting T2DM and Hypertension (HTN) and not the diagnosis of cardiac autonomic neuropathy (CAN). The study acknowledges in the limitations that while impairments in recovery parameters are suggestive of CAN, the presence of CAN was not objectively assessed.

Regarding the first comment, the recovery profile as demonstrated by HRR1 and HRR2 was found to be indicative of cardiac autonomic dysfunction, in diabetes mellitus (DM) and HTN. Okutucu et al² present that the suggested thresholds for normal responses are likely to vary depending on the population studied. The review² presents a comprehensive account of HRR observed across different populations with the thresholds ranging from 6.5 to 30 bpm for the first minute. We used the cutoffs proposed by Sacre et al³ who confirmed the diagnostic performance of blunted HRR1 and HRR2 in cardiac dysautonomia with optimal cutoff being ≤ 28 bpm (sensitivity 93%) and ≤ 50 bpm (sensitivity 96%), respectively. Moreover, they examined patients with type 2 diabetes, making these thresholds more specific to our study population.

Second, blunted nocturnal BP response is indeed an important clinical manifestation of CAN; however, as emphasized, the purpose of the present study was mainly to examine recovery after maximal exercise and while well correlated with HRR, nocturnal BP does not reflect the recovery kinetics.

Finally, statins have been demonstrated to improve exercise tolerance⁴ and increase the heart's response to parasympathetic stimulation through their cholesterol-lowering effect via altered $G\alpha_{i2}$ expression.⁵ Additionally, while hydrophilic statins improve the vagal modulation of the heart rate, hydrophobic statins might reverse the effect of lipid-lowering on cholesterol biosynthesis and parasympathetic responsiveness.⁵ In the present study, the compromise of cardiac autonomic modulation was evident in the patient groups, despite the use of statins as compared with the healthy group with no reported use.¹ Although it would be interesting to further explore this interaction and confounding effects of other medications, it was beyond the scope of the present investigation.

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