

Letter to the Editor in Response to “Cardiac Autonomic Neuropathy in Diabetes Mellitus”

Lovely Chhabra, MD^a; Amandeep Goyal, MD^b; Yogeesh Prabahakar, BS^a; Nauman Khalid, MD^c

^aHEARTLAND REGIONAL MEDICAL CENTER, MARION, ILLINOIS; ^bMARIETTA MEMORIAL HOSPITAL, MARIETTA, OHIO;

^cWASHINGTON HOSPITAL CENTER, WASHINGTON, DC

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To the Editor:

Agashe et al. presented an excellent review on diabetes mellitus (DM)-induced cardiovascular autonomic neuropathy (CAN) and its associated clinical morbidity and mortality.¹ The authors succinctly described multiple clinical manifestations and comorbidities of CAN, such as orthostasis, resting tachycardia, exercise intolerance, increased risk of ischemic heart disease, silent myocardial infarction, and intraoperative cardiovascular morbidity and mortality.^{1,2} However, DM-induced CAN has recently been recognized as having a protective effect against stress-induced cardiomyopathy.

Takotsubo cardiomyopathy (TC), also known as stress-induced cardiomyopathy, is a syndrome characterized by transient regional systolic dysfunction of the left ventricle that occurs in the absence of angiographic evidence of significant obstructive coronary artery disease.³ An increased catecholamine surge leading to exaggerated cardiac sympathetic stimulation has long been thought to be the most plausible mechanism of TC pathogenesis. Exaggerated sympathetic stimulation from markedly elevated plasma catecholamine levels (both epinephrine and norepinephrine) can lead to catecholamine-mediated myocardial stunning or direct catecholamine myocardial toxicity.³⁻⁵ In a recent large meta-analysis of 959 papers comprising a total of 33,894 patients with TC, the prevalence rates of DM were significantly lower in TC than in similar age-matched populations.⁵ Recent data suggests that DM may be protective against the development of TC due to associated neuropathic changes in splanchnic autonomic sympathetic nerves or in adrenal chromaffin cells that are innervated by these autonomic nerves, thereby resulting in hyposecretion of epinephrine by the adrenals.

One may thus speculate that diabetic patients with more severe disease or prolonged disease duration may be comparatively more immune towards the development of TC.^{3,4} However, almost certainly, the interplay of factors such as DM, the physical and emotional magnitude of the

stressful stimulus, and the presence and severity of associated comorbid conditions would collaboratively play a role in the pathogenesis of TC.

Further prospective studies are needed to strengthen our understanding of the pathophysiological basis of TC and to further explore the relationship between diabetic CAN and TC. Since TC is not a benign illness as was thought previously, the potential role of autonomic denervation as one of the therapeutic measures may be explored in future studies to decrease and/or prevent recurrences of TC in high-risk patients.

REFERENCES

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RESPONSE FROM THE GUEST EDITORS:

We thank Dr. Chhabra and colleagues for their interesting additional information about diabetes mellitus-induced cardiovascular autonomic neuropathy and its potential protective role against Takotsubo cardiomyopathy.

Archana Sadhu, MD; Steven Petak, MD, JD
Houston Methodist Hospital, Houston, Texas