Diabetic cardiovascular autonomic neuropathy

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Diabetic Cardiovascular Autonomic Neuropathy (DCAN), the most studied form of Diabetic Autonomic Neuropathy, is a frequent and early complication of Diabetes, with a prevalence of around 20% in unselected patients[1].

The DCAN Subcommittee of Toronto Consensus Panel on Diabetic Neuropathy defines DCAN as an "impairment of cardiovascular autonomic control in patients with established diabetes after excluding other causes"[2].

Clinical correlates of DCAN are age, diabetes duration, glycaemic control, diabetic sensorimotor polyneuropathy and the microangiopathic diabetic complications; emerging ones are cardiovascular risk factors –such as blood pressure (BP)– and cardiovascular diseases[3]. Despite its prevalence, clinical and prognostic impact, DCAN is widely under-diagnosed[1].

The gold standard of diagnostic assessment of DCAN is cardiac autonomic reflex tests (CARTs). They are based on heart rate, blood pressure, and sudomotor responses and were discovered by Ewing et al. in the 1970s[5]. CARTs involve measuring autonomic responses through changes in heart rate (HR) variability and blood pressure (BP). Sympathetic function is assessed by BP response to postural changes, the Valsalva maneuver. Parasympathetic function is assessed by HR response to deep breathing, changes in posture (i.e., lying to standing), and the Valsalva maneuver[6,7]. In the autonomic reflex tests, the HR response to respiration is measured as the expiration to inspiration (E:I) ratio, which measures beat to beat sinus arrhythmia (R-R variation) during paced deep expiration and inspiration. Heart rate is measured via electrocardiogram with the patient in the supine position and breathing at 6 breaths per minute (bpm); a difference of >15 bpm is considered normal. Heart rate response to standing is known as the 30:15 ratio and usually consists of an initial increase and then decrease in HR[7,8]. In this test, the R-R interval is measured at 15 beats and 30 beats after standing, with the normal value > 1.03[6,7,9]. Heart rate response to Valsalva involves an initial increase in HR followed by an excessive decrease in HR, and the normal ratio of longest to shortest R-R interval is >1.2[7,8,10]. Sympathetic function is assessed by noting changes in systolic BP in the supine position and again after standing for 2 minutes, with normal being a fall of < 10 mm Hg[7,10].

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The Toronto Consensus recommends that diagnosis of DCAN be based on the use of CARTs, i.e., heart rate response to deep breathing, standing, Valsalva maneuver, and BP response to standing, and that more than one heart rate test and OH test are required. Moreover, the performance of CARTs should be standardized, the influence of confounding variables minimized, and age-related normal ranges of heart rate tests strictly required[11].

The DCAN Subcommittee of Toronto Consensus Panel on Diabetic Neuropathy recommends that patients with Type 2 Diabetes Mellitus (T2DM) be screened for DCAN at the time of diagnosis and those with Type 1 Diabetes Mellitus (T1DM) within 5 years of their diagnosis, especially in patients exhibiting multiple risk factors, such as poor glycemic control, smoking, hypertension, or dyslipidemia. The Panel also recommends that screening be part of a perioperative risk assessment in patients with coronary artery disease[5]. Similarly, guidelines from the American Diabetes Association (ADA) recommend that diabetic patients displaying common DCAN symptoms—such as lightheadedness, weakness, palpitations, and syncope that occurs on standing—undergo further assessment to rule out causes other than CAN, especially if they have microvascular and/or neuropathic complications or hypoglycemia unawareness[5,6].

The role of intensive diabetes therapy in delaying the development of DCAN in T1DM is confirmed, whereas only limited evidence exists for intensive multifactorial intervention in T2DM. On the other hand, symptomatic treatment of clinical correlates of DCAN like Orthostatic Hypotension is available and advisable[11].

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