



Diabetic Cardiac Autonomic Neuropathy: When, Why and How?

Robert C. Welsh, MD, FRCPC, FACC

Anthony's Fatigue

- Anthony, 43, has a 20-year history of insulin-dependent diabetes mellitus.
- He presents with non-specific symptoms of fatigue on exertion, dizziness, post-prandial bloating and intermittent diarrhea.
- His lightheadedness is associated with changes in body positioning.
- Anthony's physical exam demonstrates orthostatic hypotension, with blood pressure decreasing from 145/90 mmHg to 96/70 mmHg when he goes from lying to standing, with no change in a resting relative tachycardia at 100 bpm.
- Anthony has associated diagnoses of hypertension, microalbuminuria and diabetic retinopathy.
- His current medical therapy includes insulin, a statin, an angiotensin-converting enzyme inhibitor and low-dose acetylsalicylic acid.

What is Anthony's diagnosis? For the answer, see page 24.



Q: What is the cause of autonomic dysfunction in diabetic patients?

Diabetes mellitus is one of the leading public health problems in the industrialized world and has a profound effect on the cardiovascular system. The current aging population, in association with decreased exercise and increasing body weight, has made diabetes mellitus one of the most prominent risk factors for vascular disease.

Autonomic neuropathy typically begins 10 years after the onset of diabetes mellitus and is slowly progressive. Hyperglycemia appears to be a direct risk factor for autonomic involvement in diabetes. The autonomic neuropathy associated with diabetes affects the gastrointestinal system, leading to bloating, diarrhea, vomiting and other complaints, as well as the heart, which is termed cardiac autonomic dysfunction.

Cardiac autonomic dysfunction is associated with increased angina threshold as a consequence of the autonomic, as well as sensory, neuropathies. The neuropathy may

involve the sympathetic nervous system and the parasympathetic nervous system, resulting in a fixed, rapid heart rate that does not respond to standard physiologic stimuli, such as the Valsalva manoeuvre or carotid sinus massage, or medications, such as beta-blockers. In two large-scale studies, more than one-third of patients with diabetes showed evidence of cardiac autonomic neuropathy, which has been associated with depressed left ventricular function.¹

Q: *How is cardiac autonomic dysfunction diagnosed?*

Cardiac autonomic dysfunction should be considered in patients presenting with symptoms of autonomic neuropathy affecting the gastrointestinal system, such as:

- diarrhea,
- nausea,
- vomiting,
- malnutrition or
- bowel incontinence.

The autonomic neuropathy can also lead to impotence and urinary incontinence.

The most common clinical scenario for cardiac autonomic dysfunction would be orthostatic hypotension and/or unexplained resting relative tachycardia (90 bpm to 110 bpm). Cardiac autonomic dysfunction may be diagnosed by

abnormalities in two or more of the following:

- a resting heart rate of 100 bpm or more after 15 minutes of rest,
- a lack of beat-to-beat variability on an electrocardiographic recording (less than 10 bpm),
- a ratio of the longest R-R interval to the shortest of 1.1 or less during the Valsalva manoeuvre,
- a ratio of the R-R interval of the 30th beat to the 15th beat after standing of one or less and/or
- a 30 mmHg or more fall in systolic blood pressure after one minute of standing.

Q: *How does cardiac neuropathy affect diabetic patient management?*

Diabetic patients with cardiac autonomic neuropathy can represent a challenge, both in the clinical diagnosis of cardiac disease as well as in the management. Patients suffering from diabetes with associated cardiac autonomic neuropathy are more likely to lack symptoms associated with significant ischemia and, as mentioned earlier, may also have associated congestive heart failure. The autonomic neuropathy can also be associated with an abnormal heart rate response to stimuli, making standard diagnostic tests, such as exercise tolerance testing, challenging.

With regards to the medical therapy of the diabetic patient with cardiac autonomic neuropathy, further challenges are encountered. First, the standard preventative therapy with anti-hypertensive agents may be associated with significant orthostatic hypotension. Heart rate reduction with calcium channel blockers or beta-blockers may not occur with residual resting

About the author...




Dr. Welsh is an Interventional Cardiologist, Director of the University of Alberta Cardiology Residency Training Program and Co-Director of the University of Alberta Chest Pain Program at the University of Alberta Hospital, Edmonton, Alberta.

tachycardia. In the presence of severe coronary artery disease, this resting tachycardia may be associated with provokable ischemia.

Furthermore, typical signs and symptoms of hypoglycemia may fail to appear because of damage to the sympathetic innervation of the adrenal gland, which causes a lack of epinephrine release.

Q: *Does the optimal treatment of diabetes decrease the risk of autonomic neuropathy?*

It is generally agreed that therapy directed at the control of excessive fatty acid mobilization and oxidation and protein catabolism is essential in diabetes mellitus.

The Diabetes Control and Complications Trial studied more than 1,440 patients with insulin-dependent diabetes mellitus for a mean of 6.5 years. Patients randomized to intensive control (tight control) were shown to have a reduction in the incidence and progression of retinopathy, microalbuminuria and clinical neuropathy, compared to those receiving more conventional therapy.² In terms of cardiovascular disease and peripheral vascular disease, the tight control group had a 41% reduction that was not statistically significant, but was consistent with the main results. Therefore, tight control remains the goal for the treatment of diabetes mellitus to reduce lifelong complications. 

References

1. Zola B, Kahn JK, Juni JE, et al: Abnormal cardiac function in diabetic patients with autonomic neuropathy in the absence of ischemic heart disease. *J Clin Endocrinol Metab* 1986; 63(1):208-14.
2. Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group: Effect of intensive therapy on the microvascular complications of Type 1 diabetes mellitus. *JAMA* 2002; 287(19):2563-9.

More on Anthony

Anthony's physical exam, in conjunction with his gastrointestinal complaints, led to a presumptive diagnosis of autonomic neuropathy. Anthony's non-specific symptoms of fatigue, provoked by exertion, were investigated through a standard exercise treadmill test. During that test, Anthony completed four minutes and 32 seconds on the Bruce protocol before developing symptoms of fatigue. His peak heart rate was 120 bpm, with the ECG demonstrating ST depression diffusely throughout the precordial leads.

Anthony was diagnosed with exercise-induced ischemia. Beta-blockers were added to his current therapy, and he was referred to a cardiologist for further investigation.