International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Confluence of Genetic, Cardiac Autonomic Neuropathy in Diabetic Heart Disease: Unravelling the Path to Accelerated Cardiovascular Disease

Dr Aayushi Lal[1], Dr N. K. Gupta[2]

[1]Postgraduate Resident, Department of General Medicine, Pacific Institute of Medical Sciences, Udaipur

[2]Professor, Department of General Medicine, Pacific Institute of Medical Sciences, Udaipur

Abstract: ***A variety of adverse genetic and environmental factors exert a direct effect on the cardiovascular system in individuals with Diabetes Mellitus. These elements constitute an adverse milieu that results in a process of accelerated obstructive small and large vessel disease as well as non ischemic cardiomyopathy; autonomic dysregulation can also contribute to cardiovascular disease. With concomitant hypertension, the development and acceleration of atherosclerosis can be even more pronounced.***

Keywords: Type 2 Diabetes, Cardiac Autonomic Neuropathy, Heart Disease, Diabetic Heart Disease, Ischemic Heart Disease

Diabetic Heart Disease

While many factors contribute to ischemic heart disease, poor glycemic control in the hypertensive patient is associated with increased episodes of ST - segment depression as well as an increased left ventricular (LV) mass index [1]. In diabetes there is an increased incidence of congestive heart failure even without overt coronary artery or valvular heart disease, particularly in women [2].

Pathologically, diabetic cardiomyopathy is characterized by cellular hypertrophy and myocytolytic necrosis with replacement fibrosis [3–4] . The diabetic heart commonly has a great amount of microscopic fibrosis, with distribution of interstitial connective tissue throughout the myocardium [5]. When hypertension is superimposed on diabetes, irreversible myocardial damage ensues [6]. This is characterized by micro - vascular stenosis, with resistant focal areas of myocyte necrosis and replacement fibrosis [7]. With progressive myocardial loss, ventricular dilation ensues, with a clinical presentation as a dilated cardiomyopathy. Clinically, in early stages of diabetes, particularly in type 1 DM, ventricular relaxation may be delayed but with preserved ejection fraction. This is characterized by a decreased E/A wave ratio on echocardiogram.

Early in the disease process, systolic time intervals, especially pre ejection period /LV ejection time are frequently abnormal, reflecting decreased Contractility and /Or a reduction in diastolic volume, possibly due to diminished LV compliance [8].

Systolic function is frequently abnormal with concomitant hypertension but is less commonly affected in the normotensive patient [9]. Moreover, patients with diabetic autonomic neuropathy are more likely to have abnormal filling dynamics [10]. Young patients with type 1 DM and chronic complications demonstrate an increased frequency of diastolic dysfunction as shown with Doppler echocardiography where the ratio of early (E wave) to late (A wave) ventricular filling is reduced indicating a decrease in ventricular compliance [11]. Patients with diabetes and hypertension have a thicker interventricular septum [12] when compared with nondiabetic hypertensive patients.

In summary, diabetic cardiomyopathy represents the end result of a pathologic process that may involve large vessel atherosclerosis with occlusions producing relatively large areas of myocardial loss as well as small vessel vasospastic disease producing focal tissue loss. Both process result in fibrosis scarring, relative hypertrophy of remaining myocytes and ultimate ventricular dilation. Early on diastolic dysfunction with normal ejection fraction is common, while late stages with a reduced ejection fraction provide the usual picture of systolic dysfunction added to the features of diastolic dysfunction.

Cardiac Autonomic Neuropathy

The neuropathy associated with diabetes mellitus is a generalized disorder. Initially, it involves vagal nerves and later sympathetic pathways are affected. The evolving autonomic neuropathy alters the phasic changes that normally occur in the heart rate, termed heart rate variability (HRV). These heart rate fluctuations can be evaluated quantitatively with high frequency (HF) 24h multichannel digital ECG recorders and provide an evaluation of autonomic dysfunction [13].

Oscillations or changes in heart rate are regulated by autonomic control.

Using spectral analysis, three main frequency bands can be discerned; very low frequency (VLF: 0.033 to 0.04 Hz), low frequency (LF: 0.04 to 0.15 Hz) and high frequency (0.15 to 0.4 Hz.). The HF range reflects parasympathetic or vagal stimulation, whereas the VLF range is thought to reflect sympathetic stimulation. A change in HRV characterized by decrease in the HF rate and an increase in the VLF rate is an early manifestation of diabetic autonomic dysfunction. In the course of diabetes, however a low VLF /HF ratio represents clear development of an autonomic neuropathy and constitutes a poor prognostic sign [14].

HRV with respiration and standing is decreased in diabetic patients, especially in those with evidence of peripheral or autonomic neuropathy [14]. Defects in parasympathetic innervation, expressed as an increased resting heart rate and a decrease respiratory variation in heart rate, are more frequent and occur relatively early in DM [15]. Defects in sympathetic innervation, expressed as a decrease in rise of the heart rate during standing, are less frequent and tend to occur later in the disease. A prospective study of patients with DM and without autonomic neuropathy has revealed a markedly diminished rate of survival in those with neuropathy, with a substantial incidence of sudden death. This may relate to an increased tendency to develop ventricular arrhythmias in diabetic patients. Further in diabetic patients with autonomic neuropathy, there is high incidence of QT prolongation at rest and especially after exercise possibly reflecting autonomic imbalance [16].

Simple bedside test in detecting autonomic neuropathy. A patient can be considered to have cardiac autonomic neuropathy if 2 or more of the following findings are present;

An excessive fall in blood pressure with standing. The fall in systolic blood pressure after 1 minute of standing is determined by cuff sphyngomanometry and is abnormal if it is > 30 mmHg [17].

1) An increased resting heart rate. This is determined after the patient is supine for 15 min, rate > 100 beats per minute is considered abnormal.
2) An abnormal heart rate response to standing. During ECG monitoring, the ratio of the R - R interval at the 30th beat after standing to the R - R interval at the 15th beat is determined abnormal if the ratio is < 1.00.
3) Decreased beat to beat HRV. This is determined by the difference between the minimum and maximum heart rate, as taken from ECG obtained during periods of inspiration and expiration with the patient breathing 6 times per minute A variability of < 10 beats per minute is considered abnormal.
4) An abnormal Valsalvamaneuver. Determined by having the patient blow into a manometer and maintaining 40mmHg for 15 s. Using ECG, ratio of the longest R - R interval after the maneuver to the shortest R - R interval during the maneuver is calculated. The ratio is abnormal if it is <1.10. Decreased sensitivity to ischemic pain in diabetic patients may also produce unrecognizedischemia with myocardial damage. As noted above, the diagnosis of an autonomic neuropathy in diabetic patients carries adverse prognosis [17].

References

[1] Melina D, Colivicchi F, Melina G,. Prevalance of silent ST - segment depression during long term electrocardiographic monitoring in asymptomatic diabetic patients with essential hypertension. Minerva Med 1993; 84; 301 - 305.
[2] Kannel WB, Castelli WP. Role of diabetes in congestive heart failure The Framingham study. Am J cardiol 1974; 34; 29 - 34.
[3] Yoarom R, Stammler G, Rose AG, Human coronary microvessels in diabetes and ischemia. Morphometric study of autopsy material. J Pathol 1992; 166; 265 - 270.
[4] van Hoeven KH, Factor SM. A comparison of the pathological spectrum of hypertensive diabetic, and hypertensive diabetic heart disease. Circulation 1990; 82; 848 - 855.
[5] Laws A, Reaven GM. Evidence for an independent relationship between insulin resistance and fasting plasma HDL - cholesterol, triglycerides and insulin concentrations. J Intern Med 1992; 231; 25 - 30.
[6] Frolich ED, Apstein C, et al. The heart in hypertension. N Engl. J Med 1992; 327; 998 - 1008.
[7] Gibbons GH, Dzau VJ. The emerging concept of vascular remodeling N Engl J Med 1994; 330; 1431 - 1438.
[8] Seneviratne BI. Diabetic cardiomyopathy; The preclinical phase. Br Med J 1977; 1; 1444 - 1446.
[9] ShapiroLM, Howat AP. Left ventricular function in diabetes mellitus; I. Methodology and prevalence and spectrum of abnormalities. Br Heart J 1981: 45; 122 - 128.
[10] Kahn JK, Zola B. Radionuclide assessment of left ventricular diastolic filling in diabetes mellitus with and without cardiac autonomic neuropathy. J Am Coll Cadiol 1986; 7; 1303 - 1309.
[11] Zarich SW, Arbuckle BE Cohen LR. Diastolic abnormalities in young asymptomatic diabetic patients assessed by pulsed Doppler echocardiography. J Am Coll Cardiol 1988; 12; 114 - 120.
[12] Venco A, Grandi A. Echocardiographic features of hypertensive diabetic heart muscle disease. Cardiology 1987;; 74; 28 - 34.
[13] Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standards of measurement, Physiological interpretation, and clinical use. Circulation 1996; 93; 1043 - 1065.
[14] Lloyd - Mostyn RH, Watkins, PJ. Defective innervation of heart in diabetic autonomic neuropathy. Br Med J 1975: 3; 15 - 17.
[15] Oikawa N, Umetsu M, et al. Quantitative evaluation of diabetic autonomic neuropathy by using heart rate variations; Relationship between cardiac parasympathetic or sympathetic damage and clinical conditions. Tohuku J Exp Med 1986; 148; 125 - 133.
[16] Kahn JK, Sisson JC. QT interval prolongation and sudden cardiac death in diabetic autonomic neuropathy. J ClinEndocrinalMetab 1987; 64; 751 - 754.
[17] Ewing DJ, Marty CN, Young RJ. The value of cardiovascular autonomic tests; 10 years experience in diabetes. Diabetes Care 1985; 8; 491 - 498.