Left Bundle Branch Block in Type 2 Diabetes Mellitus: A Sign of Advanced Cardiovascular Involvement

Eliscer Guzman, M.D., F.A.C.C., *Narpinder Singh, M.D., †Ijaz A. Khan, M.D., F.A.C.C., F.A.C.P., ‡ Andreas P. Niarchos, M.D., *Cherian Verghese, M.D., *Cesare Saponieri, M.D., †Harinder K. Singh, M.D., †Ramesh M. Gowda, M.D., †Balendu C. Vasavada, M.D., F.A.C.C.†, and Ronny A. Cohen, M.D., F.A.C.C.*

From the *Division of Cardiology, Woodhull Medical Center, Brooklyn, New York; †Division of Cardiology, Long Island College Hospital, Brooklyn, New York; and ‡Division of Cardiology, University of Maryland School of Medicine, Baltimore, Maryland

Objective: To evaluate left bundle branch block (LBBB) as an indicator of advanced cardiovascular involvement in diabetic (DM) patients by examining left ventricular systolic function and proteinuria.

Methods: Data of 26 diabetic patients with left bundle branch block (DM with LBBB) were compared with data of 31 diabetic patients without left bundle branch block (DM without LBBB) and 18 nondiabetic patients with left bundle branch block (non-DM with LBBB). The inclusion criteria were age >45 years, and diabetes mellitus type 2 of >5 years.

Results: Mean ages of patients in DM with LBBB, DM without LBBB, and non-DM with LBBB groups were 67 ± 8 , 68 ± 10 , and 65 ± 10 years, respectively ($P = \text{NS}$). Females were 65%, 61%, and 61%, respectively ($P = \text{NS}$). Left ventricular ejection fraction in DM with LBBB was significantly lower than in DM without LBBB and non-DM with LBBB ($30 \pm 10\%$ vs $49 \pm 12\%$ and $47 \pm 8\%$, $P < 0.01$). Left ventricular end-diastolic volume was significantly higher in DM with LBBB than in DM without LBBB and non-DM with LBBB (188.6 ± 16.4 mL vs 147.5 ± 22.3 mL and 165.3 ± 15.2 mL, $P < 0.03$). Similarly, left ventricular end-systolic volume was significantly higher in DM with LBBB than in DM without LBBB and non-DM with LBBB (135.4 ± 14.7 mL vs 83.7 ± 9.5 mL and 96.6 ± 18.4 mL, $P < 0.02$). No statistically significant difference was seen in left atrial size. Proteinuria in DM with LBBB (79.4 ± 18.9 mg/dL) was significantly higher than in DM without LBBB (35.6 ± 8.5 mg/dL, $P < 0.05$) and non-DM with LBBB (12 ± 3.5 mg/dL, $P < 0.05$); however, there was no significant difference in Hb A1c levels in DM with LBBB and DM without LBBB (9.01% vs 7.81% , $P = \text{NS}$).

Conclusions: Left bundle branch block in diabetic patients indicates advanced cardiovascular involvement manifesting with more severe left ventricular systolic dysfunction and proteinuria compared to both diabetic patients without left bundle branch block and nondiabetic patients with left bundle branch block.

A.N.E. 2004;9(4):362-365

diabetes mellitus; left bundle branch block; diabetic cardiomyopathy; proteinuria; diabetic microangiopathy; cardiovascular diabetology

Diabetes mellitus (DM) is a major risk factor for cardiovascular disease including microangiopathy and accelerated atherosclerosis with more severe, extensive, and diffuse lesions compared to those in nondiabetic patients.¹⁻³ Similarly, diabetic cardiomyopathy is a well-recognized complication of diabetes mellitus and occurs in the absence of ischemic, vascular, and hypertensive disease.⁴⁻⁶ The

left bundle branch block (LBBB) has been identified as an important feature in idiopathic dilated cardiomyopathy, and has also been reported in diabetic cardiomyopathy.⁷ The objective of this study was to evaluate left bundle branch block as an indicator of advanced cardiovascular involvement in diabetic patients by examining left ventricular systolic function and proteinuria.

METHODS

Data of 26 diabetic patients with left bundle branch block (DM with LBBB) were compared with data of 31 diabetic patients without left bundle branch block (DM without LBBB) and 18 nondiabetic patients with left bundle branch block (non-DM with LBBB). Diabetic patients (both with and without LBBB) were selected from the cardiology clinic of Woodhull Medical Center in a consecutive fashion for the study in a period of 3 years. The inclusion criteria were age >45 years, and diabetes mellitus type 2 of >5 years. Matched controls were selected who were nondiabetic but had left bundle branch block (non-DM with LBBB). Age, sex, race, ethanol use, hypertension, and coronary artery disease were matched among three groups. Hypertension was defined if patients had a history of hypertension or if they were on antihypertensive medications. Coronary artery disease was defined as if patients had a history of myocardial infarction, had angina pectoris with a positive stress test, or had coronary angiography done which had shown a decrease in lumen diameter of >50% in one or more of the major epicardial coronary arteries or their primary branches. Echocardiography was done as part of the protocol. The echocardiographic left ventricular ejection fraction and left ventricular end-systolic and end-diastolic volumes were recorded and compared among groups. Laboratory data for hemoglobin A1c (Hb A1c) and urine protein was recorded for all patients.

The continuous variables were expressed as mean and analyzed by Student's *t*-test. The categorical variables were expressed as a percentage and analyzed by chi-square statistics or Fisher's exact test as appropriate. A 2-tailed *P* value of 0.05 or less was considered significant. All the statistical analyses were performed using computer software, SPSS 7.0 (SPSS Inc., Chicago, IL).

RESULTS

The mean ages of patients in DM with LBBB, DM without LBBB, and non-DM with LBBB groups were 67 ± 8 , 68 ± 10 , and 65 ± 10 years, respectively (*P* = NS). Females were 65%, 61%, and 61%, respectively, in DM with LBBB, DM without LBBB, and non-DM with LBBB groups (*P* = NS). Left ventricular ejection fraction in DM with LBBB patients was significantly lower than in DM without LBBB

and non-DM with LBBB patients ($30 \pm 10\%$ vs $49 \pm 12\%$ and $47 \pm 8\%$, *P* < 0.01). Left ventricular end-diastolic volume was significantly higher in DM with LBBB patients than in DM without LBBB and non-DM with LBBB patients (188.6 ± 16.4 mL vs 147.5 ± 22.3 mL and 165.3 ± 15.2 mL, *P* < 0.03). Similarly, left ventricular end-systolic volume was significantly higher in DM with LBBB patients than in DM without LBBB and non-DM with LBBB patients (135.4 ± 14.7 mL vs 83.7 ± 9.5 mL and 96.6 ± 18.4 mL, *P* < 0.02). No statistically significant difference was seen in left atrial size (4.0 ± 0.2 cm in DM with LBBB vs 4.3 ± 0.5 cm in DM without LBBB vs 3.8 ± 0.4 cm in non-DM with LBBB, *P* = NS). Proteinuria in DM with LBBB patients (79.4 ± 18.9 mg/dL) was significantly higher than in DM without LBBB (35.6 ± 8.5 mg/dL, *P* < 0.05) and non-DM with LBBB patients (12 ± 3.5 mg/dL, *P* < 0.05); however, there was no significant difference in Hb A1c levels in DM with LBBB and DM without LBBB patients (9.01% vs 7.81%, *P* = NS) (Table 1).

DISCUSSION

This study demonstrated that the presence of left bundle branch block in diabetic patients is associated with advanced cardiovascular disease with more severe left ventricular dysfunction and proteinuria. Incidence and prevalence of diabetes mellitus has increased significantly due to aging of population, increasing obesity, and decrease in physical activity.^{1,8} This is exclusively due to increase in type 2 diabetes mellitus, which represents more than 90% of the all cases of diabetes mellitus. Diabetic patients have a considerable risk for cardiovascular disease and up to 80% of deaths within this group of patients are from cardiovascular disease.⁹ Macro- and microvascular disease like myocardial infarction, stroke, peripheral vascular disease, and microangiopathy accounts for the majority of morbidity and mortality associated with type 2 diabetes mellitus.^{10,11} Diabetes remains an independent predictor of congestive heart failure and of mortality among patients with congestive heart failure.^{12,13}

Left bundle branch block is commonly associated with dilated cardiomyopathy. We studied left bundle branch block and left ventricular size and function in diabetic patients by selecting diabetic patients with left bundle branch block and comparing their echocardiographic findings with

Table 1. Data of Diabetic Patients with Left Bundle Branch Block versus Diabetic Patients without Left Bundle Branch Block and Nondiabetic Patients with left Bundle Branch Block

Characteristics	DM with LBBB (n = 26)	DM without LBBB (n = 31)	Non-DM with LBBB (n = 18)	P value*
Age (years)	67 ± 8	68 ± 10	65 ± 10	NS
Females	17 (65%)	19 (61%)	11 (61%)	NS
LV ejection fraction	30 ± 10%	49 ± 12%	47 ± 8%	< 0.01
LV end-diastolic volume mL	188.6 ± 16.4	147.5 ± 22.3	165.3 ± 15.2	< 0.03
LV end-systolic volume, mL	135.4 ± 14.7	83.7 ± 9.5	96.6 ± 18.4	< 0.02
Left atrial size, cm	4.0 ± 0.2	4.3 ± 0.5	3.8 ± 0.4	NS
Urine proteins, mg/dL	79.4 ± 18.9	35.6 ± 8.5	12 ± 3.5	< 0.05
Glycemic control, Hb A1c	9.01%	7.81%	N/A	NS

*P value of comparison between DM with LBBB versus DM without LBBB and non-DM with LBBB.

DM = Diabetes mellitus; Hb = Hemoglobin; LBBB = Left bundle branch block; LV = Left ventricular; N/A = Not applicable; NS = Nonsignificant.

diabetic patients without left bundle branch block and nondiabetic patients with left bundle branch block. Interestingly, we found that patients with both left bundle branch block and diabetes mellitus had more severe left ventricular dysfunction compared to diabetic patients without left bundle branch block and nondiabetic patients with left bundle branch block; all groups were matched for comorbid conditions, age, race, and sex. Similarly, patients with both left bundle branch block and diabetes mellitus had larger left ventricular volumes compared to diabetic patients without left bundle branch block and nondiabetic patients with left bundle branch block. These patients were also found to have a higher level of proteinuria, even though no significant difference was found in serum level of Hb A1c.

Many studies of left bundle branch block, particularly in earlier literature, have concluded that left bundle branch block is associated with advanced cardiac disease and poor prognosis.^{14–17} Significant left ventricular systolic and diastolic function is known to develop due to abnormal sequence of left ventricular activation, and the concept of biventricular pacing in persistent recurrent heart failure is based on correcting this abnormal sequence of activation of left ventricular by simultaneously activating both the septum and the lateral wall. Left bundle branch block in idiopathic dilated cardiomyopathy may reflect the diffuse disease of left ventricle or it may be secondary to involvement of left bundle in initial myocarditis. Left bundle branch block in diabetes mellitus associated with severe left ventricular dysfunction may reflect the diffuse involvement of left ventricle in diabetes

mellitus. Our study also showed that patients with left bundle branch block were more likely to have higher amounts of protein in urine. The presence of proteinuria is a manifestation of the development of renal microangiopathy, which is a sign of generalized vascular microangiopathy; vascular microangiopathy is the mechanism proposed for the development of diabetic cardiomyopathy.^{18–20}

CONCLUSION

Left bundle branch block in diabetic patients indicates advanced cardiovascular involvement manifesting with more severe left ventricular systolic dysfunction and proteinuria compared to both diabetic patients without left bundle branch block and nondiabetic patients with left bundle branch block. Therefore, diabetic patients with left bundle branch block should be evaluated for left ventricular systolic dysfunction and proteinuria in order to institute appropriate preventive measures.

REFERENCES

1. Eschwege E, Simon D, Balkau B. The growing burden of diabetes mellitus in world population. *Int Diabetes Fed Bull* 1997;42:14–19.
2. Raman M, Nesto RW. Heart disease in diabetes mellitus. *Endocrinol Metab Clin North Am* 1996;25:425–438.
3. Shehadeh A, Regan TJ. Cardiac consequences of diabetes mellitus. *Clin Cardiol* 1995;18:301–305.
4. Regan TJ, Ahmed S, Haider B, et al. Diabetic cardiomyopathy: experimental and clinical observations. *N J Med* 1994;91:776–778.
5. Rodrigues B, McNeill JH. The diabetic heart: Metabolic causes for the development of a cardiomyopathy. *Cardiovasc Res* 1992;26:913–922.
6. Schannwell CM, Schneppenheim M, Perings S, et al. Left

- ventricular diastolic dysfunction as an early manifestation of diabetic cardiomyopathy. *Cardiology* 2002;98:33-39.
7. D'Angelo RJ, Sitsmahalakshmi K, Biddichandani M. Left bundle branch block and diabetes mellitus. *N Y State J Med* 1977;77:911-912.
8. Boyle JP, Honecutt AA, Narayan KM. Projection of diabetes burden through 2050: Impact of changing demography and disease prevalence in the US. *Diabetes Care* 2001;24:1936-1940.
9. Harris MI, Hadden WC, Kowler WC, et al. Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in US population aged 20-74 years. *Diabetes* 1987;36:523-534.
10. American Diabetic Association. Role of cardiovascular risk factor in prevention and treatment of macrovascular disease in diabetics. *Diabetic Care* 1989;12:573-579.
11. Kannel WB, McGee DL. Diabetes and cardiovascular disease: The Framingham study. *JAMA* 1979;241:2035-2038.
12. Dries DL, Sweitzer NK, Drazner MH, et al. Prognostic impact of diabetes mellitus in patients with heart failure according to etiology of left ventricular systolic dysfunction. *J Am Coll Cardiol* 2001;38:421-428.
13. Bauters C, Lamblin N, Mc Fadden EP, et al. Influence of diabetes mellitus on heart failure risk and outcome. *Cardiovasc Diabetol* 2003;2(1):1.
14. Johnson RP, Messer AL, Shreenivas MD. Prognosis in bundle branch block. *Am Heart J* 1951;41:225-238.
15. Smith S, Hayes WL. The prognosis of complete left bundle branch block. *Am Heart J* 1965;70:157-159.
16. Rotman M, Triebwasser JH. A clinical and follow-up study of right and left bundle branch block. *Circulation* 1975;51:477-484.
17. Hamby RI, Weissman RH, Prakash MN, et al. Left bundle branch block: A predictor of poor left ventricular function in coronary artery disease. *Am Heart J* 1983;106:471-477.
18. Rubler S, Dlugash J, Yuceoglu YZ, et al. New type of cardiomyopathy associated with diabetic glomerulosclerosis. *Am J Cardiol* 1972;30:595-602.
19. Jensen T. Albuminuria: A marker of renal and generalized vascular disease in insulin-dependent diabetes mellitus. *Dan Med Bull* 1991;38:134-44.
20. Jensen T, Deckert T. Diabetic retinopathy, nephropathy and neuropathy: generalized vascular damage in insulin-dependent diabetic patients. *Horm Metab Res Suppl* 1992;26:68-70.