Left ventricular diastolic dysfunction in type 2 diabetes mellitus patient without cardiovascular disease: the association with microalbuminuria

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Abstrak

Pada 28 kasus diabetes melitus (DM) tipe 2 tanpa kelainan kardiovaskular yang diperiksa di Bagian Metabolik Endokrin, Fakultas Kedokteran Universitas Indonesia/Rumah Sakit Umum Pusat Nasional Dr Cipto Mangunkusumo, Jakarta, mulai Oktober 2001 sampai Desember 2001, dilakukan pemeriksaan ekokardiografi untuk melihat fungsi diastolik ventrikel kiri dan dilakukan pemeriksaan urin mikroalbuminuria. Disfungsi diastolik ditemukan pada 73,7 % pasien DM tipe 2 tanpa mikroalbuminuria dan 66,7% pada DM tipe 2 dengan mikroalbuminuria. Tidak terdapat hubungan bermakna kejadian disfungsi diastolik pada kelompok DM tipe 2 dengan mikroalbuminuria maupun DM tipe 2 tanpa mikroalbuminuria. ***(Med J Indones 2005; 14: 169-72)***

Abstract

Twenty-eight cases of type 2 diabetes mellitus (DM) without any cardiovascular disease were recruited from the Department of Metabolic-Endocrine, Faculty of Medicine, University of Indonesia / Dr. Cipto Mangunkusumo General Hospital, Jakarta. Recruitment of the study began in October 2001 and was completed by December 2001. Participants were examined for echocardiography and microalbuminuria urinary examination. Diastolic dysfunction was found in 73.7% of type 2 diabetic patients without microalbuminuria and 66.7% in type 2 diabetic patients with microalbuminuria. Neither type 2 diabetic groups with nor without microalbuminuria indicated any significant association to the occurrence of diastolic dysfunction. ***(Med J Indones 2005; 14: 169-72)***

Keywords: *microalbuminuria, diastolic dysfunction, type 2 diabetes mellitus*

An experimental, clinical, epidemiological and pathological studies demonstrated that diabetes mellitus patients have structural and functional alteration of heart, which were independent against hypertension and coronary artery disease, which support diabetic cardiomyopathy.[1]

Left ventricular diastolic dysfunction may represent the early stage of diabetic cardiomyopathy.[2] This emphasized about the importance of early diagnosis of diastolic ventricular function in diabetic patients.

Poirier et al[3] have reported that the prevalence of diastolic dysfunction in type 2 diabetes mellitus male-patients with well-controlled blood glucose level was 60%. Nugroho et al[4] reported the occurrence of diastolic dysfunction in type 2 diabetes mellitus patients without any cardiovascular disease in Dr. Cipto Mangunkusumo Hospital was 73.3%.

The epidemiological evidence have indicated that albuminuria may predict cardiovascular morbidity and mortality in individuals with type 2 diabetes mellitus independent of conventional cardiovascular risk factors.[5-8] Although the mechanism of the association of albuminuria with cardiac events is not clear, it is possible that the vascular damages that lead to renal dysfunction may also be present in the vasculature of the heart, and consequently contribute to cardiac dysfunction.[9-10]

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Liu et al[11] reported the association of albuminuria with systolic and diastolic left ventricular dysfunction in type 2 diabetes mellitus in American Indian population with high prevalence of obesity and hypertension, hence they were specified ethnic-group.

The association of microalbuminuria with left ventricular diastolic dysfunction in Indonesia has not been reported. Differ from the study of Liu et al,[11] this study was a cross sectional study, which observed the association between microalbuminuria and left ventricular diastolic dysfunction in type 2 diabetes mellitus patients. Patients with any cardiovascular diseases such as hypertension, arrhythmia, coronary artery disease, valvular heart disease, left ventricular hypertrophy, and congestive heart failure were excluded from this study. Likewise the parameter of diastolic function assessment was not only based on mitral valve (MV) parameter but also pulmonary venous recording (PV) in order to distinguish the normal and the pseudo-normal diastolic dysfunction.

METHODS

This was a cross-sectional study at Metabolic Endocrine and Cardiology Clinic, Dr. Cipto Mangunkusumo Hospital. The study began in October 2001 and was completed by December 2001. The diagnosis of type 2 Diabetes Mellitus was established base on WHO criteria / National Consensus on Management of Diabetes Mellitus 1998.[12]

Clinical history, physical examination, ECG and Treadmill exercise test had been done in order to exclude other coronary or heart disease. Albuminuria was measured by collecting urine specimen in the morning using the technique of nephelometry. Microalbuminuria was defined as a ratio of albumin / creatinine > 30 and < 300 mg albumin / g creatinine. Macroalbuminuria was defined as a ratio of urinary albumin / creatinine >300 mg/g.

The echocardiography examination was conducted by using the instrument of Apogee CX 200. The examination was conducted on left lateral decubitus position by using mechanical transducer of 2.5-3 MHZ. All recordings and measurements were obtained by the same observer according too the recommendations of the American Society of Echocardiography.[13] The measurement of transmitral blood flow velocity and Doppler pulse sample volume were put on the middle of mitral annulus. In addition, transmitral Doppler flow pattern : peak E velocity in centimeters per second (peak early transmitral filling velocity during early diastole), peak A velocity in centimeters per second (peak transmitral atrial filling velocity during late diastole). Then, the E/A ratio and deceleration time in milliseconds (time elapsed between peak E velocity and the point where the extrapolation of the deceleration slope of the E velocity crosses the zero baseline)[14] were calculated. Pulmonary venous flow recordings were obtained from the four chamber view directed at the right upper pulmonary vein where sample volume was obtained 1-2 cm into the pulmonary vein. The following measurements were carried out : peak S wave velocity in centimeters per second (peak systolic pulmonary venous inflow velocity during ventricular systole), peak D velocity in centimeters per second (peak diastolic pulmonary venous inflow velocity during early phase of atrial diastole), and peak A wave velocity in centimeters persecond (peak reversed systolic wave during atrial contraction).

Statistical analysis

Data analysis was by SPSS Software. Data was expressed as mean $\pm$ SD. The diastolic dysfunction of both groups, the microalbuminuria and non-micro-albuminuria, were compared by chi square test.

RESULT

Clinical Characteristics

Table 1. General Characteristic

	No Albuminuria (n = 19)	Microalbuminuria (n = 9)	P
Age (yrs)	52.21± 6.56	51.11 ± 6.92	0.824
Duration of DM (yrs)	7.84 ± 4.92	7.11 ± 3.02	0.633
Body Mass Index (BMI)	25.02 ± 3.51	24.83 ± 2.36	0.887
Systolic blood pressure (mmHg)	119.47 ± 8.48	123.33 ± 8.66	0.25
Diastolic blood pressure (mmHg)	77.89 ± 4.19	77.78 ± 4.41	0.945
HbA1c	8.88 ± 1.88	7.61 ± 1.05	0.041

Type 2 diabetes mellitus patients with microalbuminuria and no-microalbuminuria had no significant difference for age, sex, disease duration, pulse rate, diastolic blood pressure and body mass index. Micro-albuminuria groups had higher mean score on the

systolic blood pressure than the non-albuminuria groups, but this difference was not statistically significant. HbA1C level was lower in microalbuminuria groups than the no-microalbuminuria group.

Table 2. Left Ventricular Diastolic Filling

	Type 2 Diabetes Mellitus Without microalbuminuria (n = 19)	Type 2 Diabetes Mellitus with microalbuminuria (n = 9)	P
E velocity (cm/s)	70.89 ± 13.92	76.78 ± 8.76	0.258
A velocity (cm/s)	80.53 ± 18.02	82.44 ± 10.49	0.771
Ratio E/A	0.92 ± 0.28	0.95 ± 0.21	0.46
Deceleration time (DT)	202.63 ± 47.82	225.56 ± 49.02	0.25
Isovolumic relaxation time (IVRT)	123.16 ± 18.87	117.78 ± 16.41	0.599
MV a wave	103.16 ± 15.29	104.44 ± 17.40	0.844
Diastolic dys-function (%)	73.7	66.7	1.00
PV systolic (PV S)	46.0 ± 14.5	48.78 ± 6.46	0.49
PV diastolic (PV D)	34.47 ± 12.19	35.44 ± 7.33	0.828
PV S/D	1.40 ± 0.38	1.46 ± 0.14	0.531
PV a duration	95.79 ± 21.16	90.0 ± 10.0	0.482
PV velocity	21.95 ± 4.10	22.33 ± 3.61	0.603

Mitral E velocity and mitral A velocity in micro-albuminuria and no-microalbuminuria had no statistical difference. Likewise, mitral isovolumetric relaxation time and mitral A wave duration were not different for both of groups. There was no significant difference for diastolic dysfunction for both of group.

DISCUSSION

The study of diastolic function in type 2 Diabetes Mellitus patients of Indonesian was reported by Nugroho et al.[4] The study found a high prevalence of diastolic dysfunction i.e. 73.3%. This data was similar to overseas study, which had been reported by Poirier et al[3], i.e. 60%.

The association between albuminuria and left ventricular systolic and diastolic dysfunction in type 2 diabetes mellitus patients was first reported by Liu et al.[11] They found that albuminuria was independently associated with systolic and diastolic dysfunction in type 2 diabetes mellitus. This may explain part of the association between albuminuria and enhancement of cardiovascular disease in diabetes mellitus patients.

This study was the first study in Indonesia, which reported the association between microalbuminuria and left ventricular diastolic dysfunction. Apart from Liu et al study,[11] in this study, patients with hyper-tension and coronary heart disease (CHD) were excluded.

In the study of Liu et al[12], there was a greater proportion of hypertension patients in albuminuria group compared to the non-albuminuria group. Likewise, there was significant greater proportion of CHD patient in macroalbuminuria group compared to the non-albuminuria group. Hence, by diastolic dysfunction in albuminuria group, it might be affected by hypertension, which probably act as confounder. Excluding the CHD patient also did statistical analysis study.

Microalbuminuria has been proposed to represent a marker of a generalized vascular dysfunction,[15] Some studies indicated microalbuminuria is associated with cardiovascular disease in diabetic and non diabetic patients.[16,17] The study of Liu et al[11] revealed an association of microalbuminuria with cardiomyopathy in type 2 diabetes mellitus.

In this study there was no significant association between microalbuminuria and diastolic dysfunction. May be microalbuminuria has minor role on cardiomyopathy, which has become the basic of diastolic dysfunction in diabetes mellitus other than coronary artery disease and hypertension with left ventricular hypertrophy. Other factor that may explain difference of the study of Liu et al,[11] was a relative-small sample number. Other cause was exclusion of hypertension patients who could affect diastolic function from the study.

CONCLUSION

There was no significant difference on diastolic dysfunction in type 2 diabetes mellitus patients with microalbuminuria compared to the non-microalbuminuria patients. We need larger sample number with prospective (cohort) design in order to observe the causative correlation of microalbuminuria and diastolic dysfunction.

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