Right Ventricular Dysfunction in Asymptomatic Diabetic Patients

WOJCIECH KOSMALA, MD[1]
PAOLO COLONNA, MD[2]
MONIKA PRZEWLOCKA-KOSMALA, MD[1]
WALENTYNA MAZUREK, MD, PHD[1]

Diabetes is thoroughly evidenced to increase the risk of development of heart failure even in the absence of frequently coexisting comorbidities such as coronary artery disease and hypertension.

Cardiac adverse effects influenced by diabetes have been demonstrated thus far for the left ventricle, particularly systolic and diastolic dysfunction identified at rest (1–9) and/or during exercise (10–11). To date, no information is available regarding the possible involvement of the right ventricle in the pathological process evoked by diabetes. In clinical practice, right ventricular dysfunction is relevant in a variety of disease states affecting both the course and prognosis (12–16), and therefore one may assume that right ventricular performance is also an important issue in diabetic patients.

The objective of the present study was to assess right ventricular systolic and diastolic function using conventional echocardiography and tissue Doppler imaging (TDI) in diabetic patients without coronary artery disease and with and without coexisting hypertension.

RESEARCH DESIGN AND METHODS

The study group encompassed 27 diabetic and normotensive patients (DMN group) and 36 patients with coexisting diabetes and hypertension (DMHT group) who were prospectively enrolled between October 2002 and May 2003. The control group included 33 healthy volunteers. Coronary artery disease was excluded according to negative dobutamine stress echocardiography, treadmill exercise electrocardiographic test, the absence of myocardial ischemia in 24-h electrocardiographic Holter monitoring, and, in 27 patients, normal coronary angiogram. Other exclusion criteria included valvular or congenital heart disease, decreased left ventricular ejection fraction <50%, endocrine and systemic diseases other than diabetes, absence of stable sinus rhythm, serum creatinine >2.5 mg/dl, conduction or rhythm disturbances, pulmonary diseases and pulmonary hypertension, and tricuspid insufficiency exceeding I°/IV°. All medications were stopped at least five half-lives before the study, except for insulin and oral hypoglycemic drugs. Clinical and demographic data on the participants are shown in Table 1.

Each subject participating in the study underwent echocardiographic examination using GE Vingmed System V equipment with a 2.5-MHz multifrequency transducer. The evaluation included measurements of left and right ventricular dimensions and wall thicknesses; left ventricular ejection fraction by modified Simpson's biplane method; tricuspid plane systolic excursion, reflecting the global right ventricular systolic function (17); left and right ventricular conventional Doppler parameters of diastolic function (peak early and peak late diastolic flow velocity and isovolumic relaxation time [IRT]); and TDI to assess right and left ventricular longitudinal myocardial function in the basal and mid-segments. TDI was performed in the apical views (four chamber, two chamber, and long axis). Color TDI was superimposed on two-dimensional images, with the depth of imaging and the sector angle adjusted to obtain a color Doppler frame scanning rate >140 Hz. Myocardial regional velocity curves (Fig. 1) were reconstituted from digitized images and analyzed offline. The following TDI variables were evaluated (18): peak systolic velocity (S_m), peak early diastolic velocity (E_m), peak late diastolic velocity (A_m), and regional IRT (IRT_m).

All tissue velocity curves were analyzed by one observer (W.K.) who was blinded to all of the patients' data, and the intraobserver variability estimated in 25 consecutive patients was 4.2–7.6% for different parameters.

Results are expressed as means ± SD and percentages. Student's two-tailed *t* test, χ^2, ANOVA, and Pearson rank correlation test were used where appropriate. *P* values of <0.05 were considered statistically significant.

RESULTS

No statistically significant differences were found among all groups regarding age, sex, heart rate, BMI, and plasma creatinine. The DMHT group exhibited significantly higher systolic and diastolic blood pressure, higher prevalence of left ventricular hypertrophy, and more prescriptions for antihypertensive (ACE inhibitors, β-blockers, Ca antagonists, and diuretics) and lipid-lowering (statins and fibrates) drugs. The DMHT and DMN groups did not demonstrate differences with respect to diabetes treatment, type and duration of diabetes, plasma glucose, HbA_{1c}, and prevalence of diabetes complications. All of the groups investigated did not differ in right ventricular systolic function as expressed by tricuspid plane systolic excursion and S_m in the basal and mid-segments of the right ventricle.

Deterioration of right ventricular diastolic function was shown in both diabetic groups, which was indicated by TDI parameters (significantly lower values of E_m and E_m-to-A_m ratio in the basal and mid-segments and longer IRT_m in the mid-segment) and by significantly longer right ventricular IRT estimated from conventional Doppler. No statistical differences in all evaluated indexes of right ventricu-

From the [1]Department of Cardiology, Medical University, Wroclaw, Poland; and the [2]Division of Cardiology, Azienda Policlinico, Bari, Italy.

Address correspondence and reprint requests to Wojciech Kosmala, Klinika Kardiologii AM, Pasteura 4, 50-367 Wroclaw, Poland. E-mail: kosmw@kard.am.wroc.pl.

Received for publication 30 July 2004 and accepted in revised form 9 August 2004.

Abbreviations: IRT, isovolumic relaxation time; TDI, tissue Doppler imaging.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

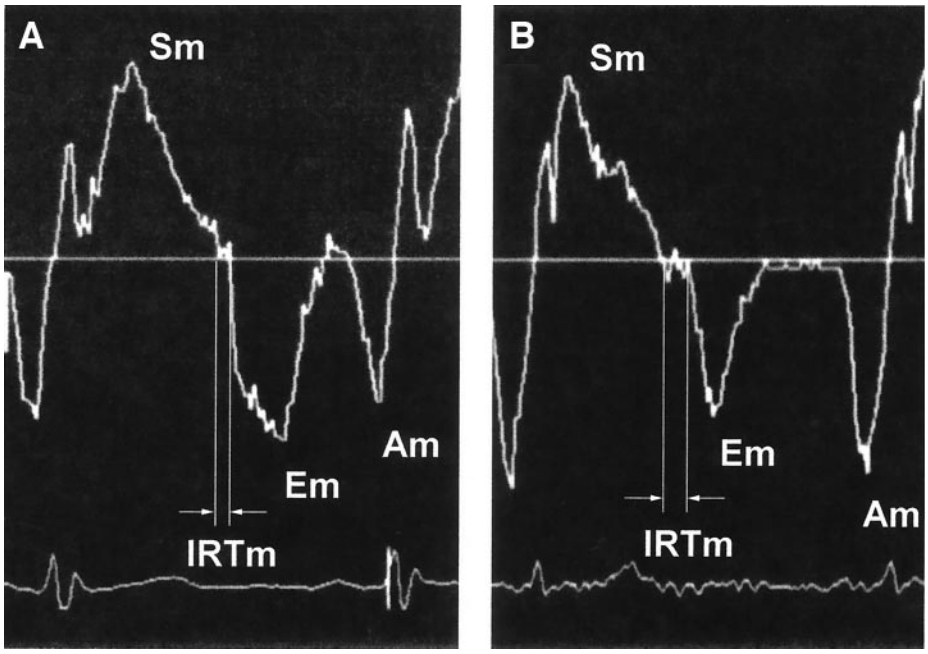

Figure 1—*Examples of right ventricular myocardial velocity curves in a healthy subject (A) and diabetic patient (B). Both E_m and E_m-to-A_m ratio are lower (9.0 vs. 11.1 cm/s and 0.88 vs. 1.09, respectively) and IRT_m longer (60 vs. 37 ms) in the patient with diabetes.*

Table 1—*Clinical and echocardiographic data in diabetic patients and control subjects*

	DMN group	DMHT group	Control group	DMN vs. control	DMHT vs. control	DMN vs. DMHT
n	27	36	33	—	—	—
Age (years)	58.5 ± 11.3	56.6 ± 9.9	58.2 ± 7.9	NS	NS	NS
Male sex	14 (52)	21 (58)	17 (51)	NS	NS	NS
Duration of diabetes (years)	10.1 ± 7.3	9.3 ± 5.9	—	—	—	NS
Type of diabetes (type 1/type 2)	3/24	4/32	—	—	—	NS
Systolic blood pressure (mmHg)	128.2 ± 12.3	163.5 ± 16.2	125.7 ± 11.1	NS	0.001	0.001
Diastolic blood pressure (mmHg)	76.5 ± 5.9	95.0 ± 8.3	74.3 ± 7.1	NS	0.001	0.001
BMI (kg/m^2)	26.6 ± 4.6	28.3 ± 3.3	26.5 ± 3.9	NS	NS	NS
Fasting plasma glucose (mmol/l)	8.0 ± 2.4	8.3 ± 2.2	4.7 ± 0.47	0.001	0.001	NS
HbA_{1c} (%)	7.5 ± 1.9	7.7 ± 1.8	—	—	—	NS
Diabetic retinopathy	9 (33)	13 (36)	—	—	—	NS
Microalbuminuria/proteinuria	6 (22)	9 (25)	—	—	—	NS
Insulin	11 (41)	16 (44)	0 (0)	—	—	NS
Sulfonylureas	14 (52)	20 (56)	0 (0)	—	—	NS
Metformin	6 (22)	10 (28)	0 (0)	—	—	NS
Left ventricular ejection fraction (%)	66.2 ± 6.4	67.1 ± 7.6	66.2 ± 9.2	NS	NS	NS
Right ventricular end-diastolic dimension (mm)	20.8 ± 2.9	21.3 ± 2.7	20.9 ± 3.0	NS	NS	NS
Right ventricular free wall thickness (mm)	3.8 ± 0.8	4.0 ± 1.0	3.7 ± 0.7	NS	NS	NS
TPSE (mm)	19.7 ± 3.1	20.1 ± 3.2	19.8 ± 2.7	NS	NS	NS
Right ventricular E-to-A ratio	1.17 ± 0.25	1.14 ± 0.17	1.19 ± 0.18	NS	NS	NS
Right ventricular IRT (ms)	54.3 ± 17.3	54.1 ± 19.2	43.2 ± 15.5	0.03	0.02	NS
Right ventricular basal segment S_m (cm/s)	11.8 ± 0.91	12.3 ± 2.34	12.2 ± 1.63	NS	NS	NS
Right ventricular basal segment E_m (cm/s)	9.1 ± 1.91	8.8 ± 1.84	10.5 ± 1.95	0.007	0.003	NS
Right ventricular basal segment E_m-to-A_m ratio	0.80 ± 0.20	0.79 ± 0.17	0.91 ± 0.22	0.05	0.02	NS
Right ventricular basal segment IRT_m (ms)	40.6 ± 12.8	41.7 ± 14.6	37.7 ± 12.9	NS	NS	NS
Right ventricular mid-segment S_m (cm/s)	9.5 ± 1.5	9.6 ± 2.0	9.7 ± 1.73	NS	NS	NS
Right ventricular mid-segment E_m (cm/s)	7.8 ± 1.49	7.7 ± 1.60	8.9 ± 1.84	0.01	0.007	NS
Right ventricular mid-segment E_m-to-A_m ratio	0.87 ± 0.20	0.88 ± 0.18	0.97 ± 0.19	0.04	0.04	NS
Right ventricular mid-segment IRT_m (ms)	50.8 ± 14.4	50.2 ± 12.3	42.3 ± 9.6	0.009	0.006	NS

Data are *n* (%) or means ± SD. E-to-A ratio, peak early–to–peak late diastolic velocity ratio; TPSE, tricuspid plane systolic excursion.

lar diastolic function were noted between diabetic patients with and without hypertension. Left ventricular systolic and diastolic dysfunction was predominantly revealed in the studied diabetic population by TDI parameters, which has been previously described (19).

No significant correlations were found between estimated echocardiographic parameters and indexes of diabetic control (plasma glucose and HbA_{1c}) as well as duration of diabetes.

CONCLUSIONS — The main clinical findings of our study are that in diabetic patients without clinically evident heart disease, *1*) not only left ventricular but also right ventricular function is impaired and 2) the deterioration of right ventricular performance implicates diastolic abnormalities but not systolic ones.

No additive effect of concomitant hypertension in terms of further enhancement of right ventricular dysfunction was shown. Impairment in right ventricular diastolic function was evidenced mainly by TDI-derived indexes (decreased E_m and E_m-to-A_m ratio in both the basal and mid-segments and prolonged IRT_m in the mid-segment of the right ventricular free wall) and by only one conventional Doppler parameter, right ventricular IRT. Thus, TDI seems to prevail over other echocardiographic approaches in the evaluation of right ventricular myocardial abnormalities in diabetic patients, appearing to be more sensitive and more independent from various confounders, such as preload or respiratory variations. In our study, we found significant prolongation of IRT_m in only the mid-segment, which usually refers to the trabecular portion of the right ventricle, whereas in the basal segment, which belongs to the right ventricular inflow component, the differences were statistically negligible. Whether this diversity could be related to regional inhomogeneity of the right ventricle in diabetic subjects requires further investigation. The subclinical right ventricular diastolic abnormalities in diabetic patients should be considered when planning pharmacotherapy to prevent the development of symptomatic right ventricular dysfunction. Furthermore, right ventricular diastolic indexes may eventually prove prognostically important in diabetes, but this requires long-term follow-up.

References

1. Ahmed SS, Jaferi GA, Narang RM, Regan TJ: Preclinical abnormality of left ventricular function in diabetes mellitus. *Am Heart J* 89:153–158, 1975
2. Regan TJ, Lyons MM, Ahmed SS, Levinson GE, Oldewurtel HA, Ahmad MR, Haider B: Evidence for cardiomyopathy in familial diabetes mellitus. *J Clin Invest* 60: 884–899, 1977
3. Paillole C, Dahan M, Paycha F, Solal AC, Passa P, Gourgon R: Prevalence and significance of left ventricular filling abnormalities determined by Doppler echocardiography in young type I (insulin dependent) diabetic patients. *Am J Cardiol* 64:1010–1016, 1989
4. Fraser GE, Luke R, Thompson S, Smith H, Carter S, Sharpe N: Comparison of echocardiographic variables between type I diabetes and normal controls. *Am J Cardiol* 75:141–145, 1995
5. Devereux RB, Roman MJ, Paranicas M, O'Grady MJ, Lee ET, Welty TK, Fabitz RR, Robbins D, Rhoades ER, Howard BV: Impact of diabetes on cardiac structure and function: the Strong Heart Study. *Circulation* 101:2271–2276, 2000
6. Poirier P, Bogaty P, Garneau C, Marois L, Dumesnil JG: Diastolic dysfunction in normotensive men with well-controlled type 2 diabetes: importance of maneuvers in echocardiographic screening for preclinical diabetic cardiomyopathy. *Diabetes Care* 24:5–10, 2001
7. Fang ZJ, Yuda S, Anderson V, Short L, Case C, Marwick TH: Echocardiographic detection of early diabetic myocardial disease. *J Am Coll Cardiol* 41:603–610, 2003
8. Vinereanu D, Nicolaides E, Tweddel AC, Madler CF, Holst B, Boden LE, Cinteza M, Rees AE, Fraser AG: Subclinical left ventricular dysfunction in asymptomatic patients with type II diabetes mellitus, related to serum lipids and glycated haemoglobin. *Clin Sci (Lond)* 105:591–599, 2003
9. Diamant M, Lamb HJ, Groeneveld Y, Endert EL, Smit JWA, Bax JJ, Romijn JA, de Roos A, Radder JK: Diastolic dysfunction is associated with altered myocardial metabolism in asymptomatic normotensive patients with well-controlled type 2 diabetes mellitus. *J Am Coll Cardiol* 42: 328–335, 2003
10. Mustonen JN, Uusitupa MIJ, Laakso M, Vanninen E, Lansimies E, Kuikka JT, Pyorala K: Left ventricular systolic function in middle-aged patients with diabetes mellitus. *Am J Cardiol* 73:1202–1208, 1994
11. Vered A, Battler A, Segal P, Liberman D, Yerushalmi Y, Berezin M, Neufeld HN: Exercise-induced left ventricular dysfunction in young men with asymptomatic diabetes mellitus (diabetic cardiomyopathy). *Am J Cardiol* 54:633–637, 1984
12. Cicala S, Galderisi M, Caso P, Petrocelli A, D'Errico A, de Divitiis O, Calabro R: Right ventricular diastolic dysfunction in arterial systemic hypertension: analysis by pulsed tissue Doppler. *Eur J Echocardiography* 3:135–142, 2002
13. Efthimiadis GK, Parharidid GE, Karvounis HI, Gemitzis KD, Styliadis IH, Louridas GE: Doppler echocardiographic evaluation of right ventricular diastolic function in hypertrophic cardiomyopathy. *Eur J Echocardiography* 3:143–148, 2002
14. Ghio S, Gavazzi A, Campana C, Inserra C, Klersy C, Sebastiani R, Arbustini E, Recusani F, Tavazzi L: Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. *J Am Coll Cardiol* 37:183–188, 2001
15. Sakata K, Yoshino H, Kurihara H, Iwamori K, Houshaku H, Yanagisawa A, Ishikawa K: Prognostic significance of persistent right ventricular dysfunction as assessed by radionuclide angiography in patients with inferior wall acute myocardial infarction. *Am J Cardiol* 85:939–944, 2000
16. Weidemann F, Eyskens B, Mertens L, Di Salvo G, Strotmann J, Buyse G, Claus P, D'hooge J, Bijnens B, Gewillig M, Sutherland GR: Quantification of regional right and left ventricular function by ultrasonic strain rate and strain indexes in Friedreich's ataxia. *Am J Cardiol* 9:622–626, 2003
17. Ueti OM, Camargo EE, Ueti A, de Lima-Filho EC, Nogueira EA: Assessment of right ventricular function with Doppler echocardiographic indices derived from tricuspid annular motion: comparison with radionuclide angiography. *Heart* 88: 244–248, 2002
18. Lind B, Nowak J, Dorph J, van der Linden J, Brodin LA: Analysis of temporal requirements for myocardial tissue velocity imaging. *Eur J Echocardiography* 3:214–219, 2002
19. Kosmala W, Kucharski W, Przewlocka-Kosmala M, Mazurek W: Comparison of left ventricular function by tissue Doppler imaging in patients with diabetes mellitus without systemic hypertension versus diabetes mellitus with systemic hypertension. *Am J Cardiol* 94:395–399, 2004