

OBSERVATIONS

Cardiovascular Biomarkers, Cardiac Dysfunction, and Outcomes in Patients With Type 2 Diabetes: A Prospective, Multicenter Study

Although diabetes is a major risk factor for ischemic heart disease or heart failure (HF), and despite the fact that echocardiography has revealed a high prevalence of left ventricular (LV) diastolic and systolic dysfunctions and

hypertrophy (1–3), routine screening for cardiovascular disease using echocardiography in asymptomatic patients with type 2 diabetes is not recommended by current guidelines (4). The availability of laboratory markers of cardiovascular risk would substantially contribute to the early and simple screening of patients at increased risk of HF, allowing them to be better targeted with appropriate pharmacological therapies (5). As part of the LV Dysfunction in Diabetes (DYDA) study, we assessed the relations between different laboratory markers, including centrally assayed glycated hemoglobin (HbA_{1c}), N-terminal probrain natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein (hsCRP), and urine albumin/creatinine ratio (UACR), with clinical conditions and 2-year outcomes in 960 outpatients who were older than 45 years, had type 2 diabetes diagnosed based on World Health Organization criteria, were

free of symptoms or signs of cardiac disease, and were enrolled in 37 Italian diabetes care units (2,3).

Patients (61 ± 8 years old) were overweight (34.7% had a BMI ≥30 kg/m²), with a median diabetes duration of 7 years (range 4–13) and visceral adiposity (waist circumference 99 ± 11 cm). Of these patients, 58.9% had a history of treated hypertension; diabetic retinopathy was present in 12.6%, and renal dysfunction (estimated glomerular filtration rate <60 mL/min/1.73 m²) was present in 8.5%. Biomarker concentrations were within the normal range in almost half of the patients (median values: NT-proBNP 36 ng/L, hsCRP 1.7 mg/mL, UACR 7.8 mg/g).

Patients with elevated LV mass at baseline and a history of treated hypertension had significantly higher levels of NT-proBNP, hsCRP, and UACR but not HbA_{1c} (Table 1). Combined systolic and diastolic LV dysfunction was associated to higher

Table 1—Levels of biomarkers by history of hypertension and LV structural and functional characteristics as assessed by ECG and echocardiography at baseline

Variable	Category	NT-proBNP (ng/L)	hsCRP (mg/L)	UACR (mg/g)	HbA _{1c} , % (mmol/mol)
History of treated hypertension	Yes (n = 565)	42 (19–79)	2.0 (0.8–4.2)	8.9 (3.2–29.2)	6.7 (6.0–7.0) (50 [42–53])
	No (n = 395)	29 (15–57)	1.4 (0.7–2.9)	6.3 (1.5–17.3)	6.7 (6.0–7.0) (50 [42–53])
	<i>P</i>	<0.0001	<0.0001	0.002	0.97
LV hypertrophy on ECG	Yes (n = 37)	70 (31–94)	2.1 (1.0–3.3)	25.3 (4.5–39.3)	6.8 (6.0–8.1) (51 [42–65])
	No (n = 841)	35 (16–67)	1.7 (0.7–3.9)	7.4 (2.4–20.9)	6.7 (6.0–7.6) (50 [42–60])
	<i>P</i>	0.002	0.38	0.019	0.46
LV mass	<51 g/m ^{2.7} (n = 589)	33 (16–63)	2.2 (1.0–5.2)	7.9 (3.2–19.8)	6.8 (6.0–7.6) (51 [42–60])
	≥51 g/m ^{2.7} (n = 159)	50 (20–97)	1.5 (0.7–3.6)	10.3 (4.7–33.3)	6.7 (6.1–7.7) (50 [43–61])
	<i>P</i>	0.0001	0.0005	0.01	0.99
LV ejection fraction	>50% (n = 688)	35 (16–65)	1.7 (0.7–3.8)	8.3 (3.2–23.8)	6.7 (6.0–7.6) (50 [42–60])
	≤50% (n = 21)	75 (44–107)	2.1 (1.0–4.9)	11.7 (3.3–50.8)	6.8 (6.0–7.7) (51 [42–61])
	<i>P</i>	0.002	0.47	0.30	0.98
MFS	≤15% (n = 243)	39 (17–69)	1.8 (0.9–4.5)	11.8 (4.3–32.3)	6.8 (6.1–7.8) (51 [43–62])
	>15% (n = 466)	35 (16–67)	1.6 (0.7–3.3)	7.2 (2.4–19.0)	6.7 (6.0–7.5) (50 [42–58])
	<i>P</i>	0.32	0.054	0.0003	0.07
LV dysfunction*	Isolated LV systolic dysfunction (n = 151)	38 (14–63)	1.7 (0.9–4.7)	11.7 (4.5–32.3)	6.7 (6.1–7.9) (50 [43–63])
	Isolated LV diastolic dysfunction (n = 148)	33 (15–64)	1.5 (0.7–3.3)	7.5 (1.4–17.7)	7.0 (6.3–7.7) (53 [45–61])
	Combined LV dysfunction (n = 87)	42 (22–84)	1.8 (0.8–4.4)	12.1 (3.5–29.8)	6.8 (6.1–7.6) (51 [43–60])
	No LV dysfunction (n = 301)	36 (17–69)	1.7 (0.7–3.4)	6.6 (3.0–19.0)	6.5 (5.8–7.4) (48 [40–57])
	<i>P</i>	0.39	0.35	0.005	0.008

Biomarker concentrations shown as median (Q1–Q3). *LV systolic dysfunction was defined as LV ejection fraction ≤50% or midwall fractional shortening (MFS) ≤15%. LV diastolic dysfunction was identified by any condition that differed from normal LV diastolic function, defined as an E/A ratio (Doppler transmitral flow) between 0.75 and 1.5 and E wave deceleration time >140 ms.

