Left Ventricular Mass in Patients With Type 2 Diabetes Is Independently Associated With Central but not Peripheral Pulse Pressure

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An increase in left ventricular mass (LVM) occurs in the presence of type 2 diabetes, apparently independent of hypertension (1), but the determinants of this process are unknown. Brachial blood pressure is not representative of that at the ascending aorta (2) because the pressure wave is amplified from central to peripheral arteries. Central blood pressure is probably more clinically important since local pulsatile pressure determines adverse arterial and myocardial remodeling (3,4). Thus, an inaccurate assessment of the contribution of arterial blood pressure to LVM may occur if only brachial blood pressure is taken into consideration. In this study we sought the contribution of central blood pressure (and other interactive factors known to affect wave reflection, e.g., glycemic control and total arterial compliance) to LVM in patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS

— The study population comprised 90 type 2 diabetic patients with normal ejection fractions (>50%), no history of coronary artery disease, and normal exercise stress echocardiograms. Patients underwent a standard echocardiographic assessment in which LVM was calculated by Devereux's formula (5) and indexed to height$^{2.7}$ (g/m$^{2.7}$; LVM index [LVMI]). Resting supine brachial blood pressures were recorded in duplicate by sphygmomanometry. Central (ascending aortic) blood pressure and total arterial compliance were recorded by simultaneous radial tonometry and echocardiographic pulsed-wave Doppler as previously described (6). Brachial artery reactivity and carotid intima media thickness were obtained by standard ultrasound methods as previously described (7).

RESULTS

— Patients were stratified into tertiles of LVMI (first tertile 22.6–40.4, second tertile 40.5–50.9, and third tertile 51.2–97.1 g/m$^{2.7}$) based on the LVMI range within the study population. As shown in Table 1, there was a trend ($P = 0.05$ for both) for a difference in age and triglycerides between the groups. Use of Ca^{2+} channel blockers was also more frequent among those with increased LVM ($P = 0.02$). With each LVMI tertile, there was a significant stepwise increase in brachial and central pulse pressure and in brachial and central systolic blood pressure ($P < 0.05$ for all). There were no differences between the LVMI tertiles in terms of heart rate, cardiac output, peripheral vascular resistance, or the parameters of vascular function and structure examined in this study, except for total arterial compliance, which reached borderline significance ($P = 0.04$).

LVMI was positively correlated with brachial pulse pressure ($r = 0.31$, $P = 0.003$), central pulse pressure ($r = 0.34$, $P = 0.001$), brachial systolic blood pressure ($r = 0.32$, $P = 0.002$), central systolic blood pressure ($r = 0.36$, $P = 0.001$), and antihypertensive medication ($r = 0.24$, $P = 0.03$). Negative associations were observed with pulse pressure amplification ($r = -0.24$, $P = 0.02$) and heart rate ($r = -0.26$, $P = 0.02$), but not with total arterial compliance ($r = -0.08$, $P = 0.43$), glycemic control ($r = -0.10$, $P = 0.37$), or any other biochemical variable ($P > 0.05$). A multiple regression model was constructed with LVMI as the dependent variable. The above univariate correlates, in addition to age and BMI, were entered as possible determinants of LVMI. Significant correlations were found for BMI ($P = 0.03$) and central ($P = 0.002$) but not peripheral ($P = 0.70$) pulse pressure (for the model $R = 0.32$, $P = 0.005$). Independent predictors of central pulse pressure were duration of type 2 diabetes ($P = 0.02$), BMI ($P = 0.002$), and antihypertensive medication ($P = 0.01$).

CONCLUSIONS

— The presence of type 2 diabetes has been reported to be an independent factor contributing to an increase in LVM (1); however, determinants of LVM in this patient group are incompletely understood. The novel finding in this current study was that central (ascending aortic) blood pressure predicted LVMI in patients with type 2 diabetes. This association was observed independently of brachial blood pressure and other known contributors to LVM such as glycemic control and total arterial compli-

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Abbreviations: LVM, left ventricular mass; LVMI, LVM index.

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

Table 1—*Clinical, echocardiographic, and hemodynamic data based on LVMI*

Variable	LVMI first tertile	LVMI second tertile	LVMI third tertile	*P* value
n	30	30	30	
Age (years)	62 ± 8	58 ± 6	59 ± 6	0.05
Height (cm)	168.2 ± 8.4	168.4 ± 11.1	167.6 ± 10.5	0.94
Type 2 diabetes duration (years)	11 ± 9	9 ± 9	14 ± 11	0.23
HbA_{1c} (%)	8.1 ± 1.9	7.7 ± 2.0	7.7 ± 1.3	0.50
HOMA-IR	9.0 ± 12.6	7.2 ± 4.0	11.9 ± 14.7	0.34
Triglycerides (mmol/l)	1.4 ± 0.8	2.0 ± 1.1	2.0 ± 1.2	0.05
LVMI ($g/m^{2.7}$)	33.3 ± 4.8	45.0 ± 3.1	62.6 ± 11.4	<0.001
LVM (g)	137 ± 31	186 ± 37	251 ± 47	<0.001
Ca^{2+} channel blocker use (%)	10	17	40	0.02
Mean arterial pressure (mmHg)	89 ± 11	94 ± 8	93 ± 10	0.12
Brachial blood pressure (mmHg)				
Systolic	119 ± 14	125 ± 11	129 ± 14	0.03
Diastolic	74 ± 10	79 ± 9	76 ± 11	0.08
Pulse pressure	45 ± 10	47 ± 10	53 ± 16	0.003
Central blood pressure (mmHg)				
Systolic	108 ± 13	116 ± 10	119 ± 13	0.005
Diastolic	75 ± 10	81 ± 9	77 ± 11	0.03
Pulse pressure	33 ± 9	36 ± 10	42 ± 15	<0.001
Augmentation pressure (mmHg)	5.8 ± 7.1	5.9 ± 4.0	8.3 ± 5.5	0.02
Amplification of pulse pressure (ratio)	1.39 ± 0.18	1.32 ± 0.15	1.28 ± 0.15	<0.001
Brachial artery reactivity (% change)				
Hyperemia	0.05 ± 0.03	0.05 ± 0.04	0.04 ± 0.05	0.14
Nitroglycerine	0.15 ± 0.09	0.15 ± 0.08	0.12 ± 0.06	0.10
Carotid intima media thickness (mm)	0.71 ± 0.14	0.68 ± 0.11	0.67 ± 0.09	0.45
Total arterial compliance (ml/mmHg)	1.15 ± 0.46	1.18 ± 0.53	1.13 ± 0.57	0.04

Data are means ± SD unless otherwise indicated. Clinical variables were analyzed by ANOVA. Echocardiographic and hemodynamic data were analyzed by ANCOVA with age, serum triglycerides, and Ca^{2+} channel blocker use as the covariates. HOMA-IR, homeostasis model assessment of insulin resistance.

ance. We also observed central pulse pressure to be independently associated with duration of type 2 diabetes rather than any biochemical index of diabetes control or insulin resistance. Our findings extend previous work in nondiabetic populations whereby the structure of the left ventricle and large central arteries (i.e., carotid) were found to be determined by the shape of the arterial pressure waveform (and, therefore, pulse pressure) at the central site in question, rather than at peripheral sites such as the brachial artery, where blood pressure is traditionally measured (3,4).

Although central pressure independently predicted LVM in this current study, it was not a powerful association, with our regression model only accounting for ~10% of the variability in LVM. It should be noted that our study sample comprised mainly older people, meaning that our findings may not be relevant to younger patients. Also, we cannot discount the possibility that dissimilar antihypertensive medication regimens may have differentially affected vascular and myocardial function and therefore potentially confounded our results. However, the use of antihypertensive medication was included as a predictor variable in multiple regression analysis for determinants of LVMI and was found to be nonsignificant.

Several studies have shown central pressure and indexes of ventricular loading to be significantly elevated in populations with increased cardiovascular risk, despite having the same brachial blood pressure as control subjects (8,9). Others have shown central blood pressure to correlate with known predictors of mortality (4,10) and to predict mortality in high-risk patients (11) independently of brachial blood pressure. Central pressure is subject to alteration by individual physiological factors (i.e., pattern of ventricular ejection, distance to reflectance sites, pulse transit time, and intensity of wave reflection) (2) and medication (12), at least partially independent of peripheral pressure. This evidence, together with our own findings, argues for more widespread use of central pressure monitoring in patients with type 2 diabetes, especially for clinical research purposes.

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References

1. Devereux RB, Roman MJ, Paranicas M, O'Grady MJ, Lee ET, Welty TK, Fabsitz RR, Robbins D, Rhoades ER, Howard BV: Impact of diabetes on cardiac structure and function: the Strong Heart Study. *Circulation* 101:2271–2276, 2000
2. Nichols WW, O'Rourke MF: *McDonald's Blood Flow in Arteries: Theoretical, Experimental and Clinical Principles*. London, Edward Arnold, 1998
3. Saba PS, Roman MJ, Pini R, Spitzer M, Ganau A, Devereux RB: Relation of arterial pressure waveform to left ventricular

and carotid anatomy in normotensive subjects. *J Am Coll Cardiol* 22:1873–1880, 1993
4. Boutouyrie P, Bussy C, Lacolley P, Girerd X, Laloux B, Laurent S: Association between local pulse pressure, mean blood pressure, and large-artery remodelling. *Circulation* 100:1387–1393, 1999
5. Devereux RB, Reichek N: Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. *Circulation* 55:613–618, 1977
6. Carlier S, Marwick TH, Segers P, Verdonck P, Van Camp G, Cosyns B, Thomas JD: Non-invasive evaluation of left ventricular power output by simultaneous recordings of applanation tonometry and echocardiographic Doppler signals. *Comput Cardiol* 24:223–226, 1997
7. Haluska BA, Fathi R, Jeffriess L, Leano R, Carlier SG, Marwick TH: Noninvasive tests for arterial structure, function, and compliance: do they identify risk or diagnose disease? *J Am Soc Echocardiogr* 17: 195–202, 2004
8. Wilkinson IB, MacCallum H, Rooijmans DF, Murray GD, Cockcroft JR, McKnight JA, Webb DJ: Increased augmentation index and systolic stress in type 1 diabetes mellitus. *QJM* 93:441–448, 2000
9. Wilkinson IB, Prasad K, Hall IR, Thomas A, MacCallum H, Webb DJ, Frenneaux MP, Cockcroft JR: Increased central pulse pressure and augmentation index in subjects with hypercholesterolemia. *J Am Coll Cardiol* 39:1005–1011, 2002
10. Marchais SJ, Guerin AP, Pannier BM, Levy BI, Safar ME, London GM: Wave reflections and cardiac hypertrophy in chronic uremia: influence of body size. *Hypertension* 22:876–883, 1993
11. Safar ME, Blacher J, Pannier B, Guerin AP, Marchais SJ, Guyonvarc'h PM, London GM: Central pulse pressure and mortality in end-stage renal disease. *Hypertension* 39:735–738, 2002
12. Vlachopoulos C, Hirata K, O'Rourke MF: Pressure-altering agents affect central aortic pressures more than is apparent from upper limb measurements in hypertensive patients: the role of arterial wave reflections. *Hypertension* 38:1456–1460, 2001