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The epidemiology of left ventricular hypertrophy in type 2 diabetes mellitus

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Abstract *Aims/hypothesis:* Patients with type 2 diabetes mellitus are at greater cardiovascular risk than the general population. Although it is widely acknowledged that diabetes is a risk factor for coronary artery disease, the increased prevalence of potentially lethal left ventricular abnormalities in this population is less well appreciated. *Methods:* We carried out an echocardiographic study of 500 subjects with type 2 diabetes mellitus to assess the prevalence of left ventricular hypertrophy (LVH) and left ventricular systolic dysfunction (LVSD). We also assessed whether abnormalities in diastolic filling parameters were present. *Results:* Of the 371 patients in whom left ventricular mass could be successfully assessed, 264 had LVH (71%). Left ventricular systolic dysfunction was much less common, being present in 16/385 patients (4.2%). Long axis contraction was abnormal in 29/429 patients (6.8%). Diastolic filling abnormalities were present in 178/435 (41%) of patients who could be classified using the selected criteria. *Conclusions:* We conclude that left ventricular abnormalities are common in type 2 diabetic patients. As medical therapy is available for both LVH and LVSD and has been demonstrated to reduce cardiovascular death, these left ventricular abnormalities could be ideal targets for screening, followed by selective therapeutic intervention.

Keywords Diabetes mellitus · Diastolic abnormalities · Left ventricular hypertrophy · Left ventricular systolic dysfunction · Long axis contraction

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Abbreviations ASE: American Society of Echocardiography · AV: atrioventricular · AVPD: atrioventricular plane displacement · ECG LVH: electrocardiographic left ventricular hypertrophy · HOPE: Heart Outcomes Prevention Evaluation · LIVE: Left Ventricular Hypertrophy Indapamide Versus Enalapril · LVH: left ventricular hypertrophy · LVMI: left ventricular mass index · LVSD: left ventricular systolic dysfunction · RWT: relative wall thickness

Introduction

The prevalence of diabetes mellitus is increasing, with projections suggesting that, worldwide, the number of adults with diagnosed type 2 diabetes will more than double to 300 million in 2025 [1]. This is of major public health importance since patients with type 2 diabetes are at increased risk of developing and dying from cardiovascular disease, which accounts for up to 70% of deaths in this population [2]. The epidemiology and characteristics of coronary artery disease in type 2 diabetes are well described in the literature [3–7]. The focus in reducing cardiovascular deaths in diabetes tends almost exclusively to be on reducing fresh coronary events. However, abnormalities in the left ventricular structure and function could be equally important contributors to cardiac death in diabetes [8]. Despite this, the prevalence and spectrum of left ventricular abnormalities have not been comprehensively described in a large sample of type 2 diabetic subjects.

It is well established that various left ventricular abnormalities strongly promote cardiac death, in particular left ventricular hypertrophy (LVH) [9–13] and left ventricular systolic dysfunction (LVSD) [14, 15]. Impaired long axis contraction of the left ventricle may also be associated with increased mortality [16]. Furthermore, the presence of left ventricular diastolic filling abnormalities has been demonstrated to place an individual at increased cardiovascular risk [17, 18] and is associated with impaired exercise tolerance [19]. We sought to determine the prevalence of these potentially modifiable left ventricular abnormalities,

namely LVH, LVSD, left ventricular long axis contraction and diastolic filling abnormalities, in a cohort of 500 type 2 diabetic subjects.

Methods

Study population

Five hundred volunteers with type 2 diabetes mellitus were randomly recruited from the Diabetes Centre, Ninewells Hospital, Dundee, between April 2002 and October 2003. The only inclusion criterion to be fulfilled was the presence of type 2 diabetes mellitus, defined according to World Health Organization guidelines [20] and ascertained from the Diabetes Centre patient casenotes. The only exclusion criteria were frailty and the inability to give written, informed consent to the study. All subjects who volunteered for the study attended the hospital on one further occasion, during which routine history, examination, ECG and transthoracic echocardiography were performed. Ethical approval was obtained from the Tayside Committee of Medical Research Ethics and all participating subjects gave written, informed consent.

Electrocardiography

A resting 12-lead ECG was recorded for each subject at 10 mm/mV and 25 mm/s with the subject lying supine. ECG left ventricular hypertrophy (ECG LVH) was defined as the presence of either the Sokolow–Lyon criterion or the Cornell voltage product criterion, as used for entry into the Losartan Intervention for Endpoint Reduction in Hypertension study.

Echocardiography

Transthoracic echocardiography was performed by one trained operator (A. Dawson) using a Hewlett-Packard (Andover, MA, USA) Sonos 2500 Phased Array Imaging System with a 2.5 MHz transducer. The scan was performed with the patient lying in the left lateral position at approximately 45°.

Left ventricular hypertrophy assessment

Two-dimensional directed M-mode measurements were made from the parasternal long-axis view just below the tips of the mitral valve. All measurements were made according to the American Society of Echocardiography (ASE) recommendations at end-diastole, taken as the onset of the QRS complex. The leading edge method was used to measure interventricular septal wall thickness, left ventricular internal diameter and left ventricular posterior wall thickness. Measurements were made over at least three separate cardiac cycles and the average taken. Left ventricular mass was calculated according to the formula of Devereux et al. [21] and indexed to height$^{2.7}$ to give a left ventricular mass index (LVMI). Left ventricular hypertrophy was defined as an LVMI greater than 47 g/m$^{2.7}$ in women and greater than 50 g/m$^{2.7}$ in men. Left ventricular mass was also indexed to body surface area and LVH defined as LVMI greater than 110 g/m^2 in women and greater than 134 g/m^2 in men. LVMI was not calculated in cases in which either poor image quality or inadequate image alignment prevented accurate M-mode measurements from being made.

Left ventricular geometry was classified as normal, concentric remodelling, eccentric left ventricular hypertrophy or concentric left ventricular hypertrophy, based on left ventricular mass and relative wall thickness. Relative wall thickness (RWT) was defined as ([2PWTd]/LVIDd) (PWT is posterior wall thickness, LVID is left ventricular internal diameter) and a value <0.45 was defined as normal. Normal left ventricular geometry was defined as normal left ventricular mass and normal RWT, concentric remodelling defined as normal left ventricular mass and increased RWT, eccentric LVH defined as increased left ventricular mass and normal RWT, and concentric LVH defined as increased left ventricular mass and increased RWT.

Left ventricular systolic function assessment

Quantitative assessment of left ventricular systolic function was made using the modified biplane Simpson's method to calculate a left ventricular ejection fraction [22]. Three measurements from successive cardiac cycles were made in the two-chamber and four-chamber views. Left ventricular systolic dysfunction was defined as a left ventricular ejection fraction less than 45%.

Assessment of diastolic parameters

Doppler echocardiographic recordings were performed by pulsed-wave Doppler with the sample volume at the tips of the mitral valve leaflets in the apical four-chamber view, in accordance with ASE guidelines. At least three measurements from three consecutive cardiac cycles were made for each parameter. Transmitral recordings were used to measure the peak velocity of early rapid filling (E wave) and peak velocity of atrial filling (A wave), from which the E/A ratio was calculated. E-wave deceleration time was measured as the time interval between the peak of the E-wave and the point at which its descending segment, or its extrapolation, crossed the zero-velocity baseline. Isovolumic relaxation time was the time between aortic valve closure and the onset of diastolic flow. This was assessed in accordance with ASE guidelines by placing a pulsed-wave sample volume between the aortic and mitral valves in the apical five-chamber view, enabling mitral valve inflow and aortic valve outflow signals to be obtained simultaneously.

Age-related threshold values used for defining abnormal E/A ratio, E-wave deceleration time and isovolumic relaxation time were those proposed by the European Study Group on Diastolic Heart Failure [23].

Assessment of long axis contraction

The method of left atrioventricular plane displacement (AVPD) was used to assess long axis contraction of the left ventricle [16]. In the four-chamber view, the 2D-guided M-mode cursor was placed at the lateral region of the atrioventricular plane at the mitral annulus, perpendicular to the direction of movement of the left ventricle, producing an M-mode recording of the atrioventricular (AV) plane displacement. The vertical distance between the point of the AV plane most distant from the apex and the point closest to the apex was measured in the M-mode. This procedure was repeated at the septal region of the AV plane in the four-chamber view, and the inferior and anterior regions of the AV plane in the two-chamber view. At least three measurements were made from each region, giving 12 measurements from which the mean left AVPD was calculated. A mean value of less than 10 mm was taken as an abnormal AVPD.

Statistics

Values are quoted as means and 95% confidence intervals. A minimum of three measurements was used to calculate the mean for each parameter. Comparisons of continuous variables between groups were performed with the independent samples *t*-test. Comparisons between categorical variables were performed using the chi-square test. Standard multiple regression analysis was performed to establish which variables were independently related to left ventricular mass. All statistical analyses were performed using SPSS for Windows version 11.0. A value of $p<0.05$ was considered to be statistically significant.

Results

Patient characteristics of the 500 subjects studied are listed in Table 1.

Table 1 Patient characteristics (mean±SD) of the 500 diabetic subjects studied

Variable	Mean (SD)
Males (%)	61.6
Age (years)	63.8 (10.59)
BMI (kg/m^2)	29.79 (5.11)
Duration of diabetes (years)	5.96 (5.47)
Systolic blood pressure (mm Hg)	141.49 (18.8)
Diastolic blood pressure (mm Hg)	78.60 (10.5)
HbA_1C (%)	7.45 (1.26)
Creatinine	90.5 (19.9)
Total cholesterol (mmol/l)	4.94 (1.04)
HDL-cholesterol (mmol/l)	1.28 (0.37)
Current smokers (%)	17
History of hypertension (%)	61.0
History of ischaemic heart disease or stroke (%)	16.2
LVH on ECG (%)	9.2
LVMI (g/m$^{2.7}$)	
Males	60.70 (17.17)
Females	57.57 (15.77)
Left ventricular ejection fraction (%)	61.50 (8.84)
Treated with	
Insulin	17%
Metformin	52%
Sulphonylurea	36%
Statin	41%
ACEI/ARB	35%/8%
Ca^{2+} antagonist	31%
Diuretic	26%

ACEI/ARB, ACE inhibitor/angiotensin receptor blocker

Left ventricular hypertrophy

A left ventricular mass index was obtainable in 371/500 subjects (74%); those in whom left ventricular mass could not be assessed only differed significantly from those in whom an adequate echocardiographic image could be obtained in age (66.3 [95% CI 64.5–68.1] vs 63.0 [95% CI 61.9–64.1] years, respectively, $p=0.002$). The proportion of subjects with LVH was 43% (159/371) when left ventricular mass was indexed to body surface area and 71% (264/371) when left ventricular mass was indexed to height$^{2.7}$. Tables 2 and 3 show the characteristics of patients with and without left ventricular hypertrophy. Multivariate analysis was performed to include all possible determinants of left ventricular mass index: sex, age, BMI, duration of diabetes, smoking status, systolic BP, diastolic BP, creatinine and HbA_1c. This model explained only 18.4% of the variation in LVMI, and the factors independently related to LVMI were BMI (standardised $\beta=0.401$, $p<0.001$), age (standardised $\beta=0.209$, $p=0.001$) and sex (standardised $\beta=0.170$, $p<0.004$). Patients with LVH were significantly more likely to be prescribed calcium channel antagonists (51 vs 22%, $p=0.028$), diuretics (37 vs 16%, $p=0.026$) and oral nitrates (13 vs 4%, $p=0.025$) than patients without LVH. The distribution of left ventricular geometry in the studied population ($n=371$) is shown in Figs. 1 and 2: the majority of LVH was eccentric rather than concentric, regardless of whether left ventricular mass was indexed to body surface area or to height$^{2.7}$. The results were almost identical if a cut-off value for RWT of 0.43 (as used in other studies) was used instead of 0.45 (results not shown).

Table 2 Patient characteristics classified according to presence or absence of left ventricular hypertrophy (n=371) indexed to body surface area

Variable	LVH mean (95% CI) (n=159)	No LVH mean (95% CI) (n=212)	p value
Males (%)	58	60	0.749
Age (years)	65.3 (63.6–66.9)	61.3 (59.8–62.7)	<0.001
BMI (kg/m^2)	30.1 (29.3–30.9)	29.8 (29.1–30.5)	0.588
Duration of diabetes (years)	6.3 (5.5–7.1)	5.9 (5.1–6.7)	0.463
Systolic BP (mmHg)	144 (140–147)	141 (138–143)	0.157
Diastolic BP (mmHg)	78 (76–79)	79 (78–81)	0.169
Percentage with BP <130/80 mm Hg	21	27	0.306
History of hypertension (%)	67	59	0.161
History of ischaemic heart disease or stroke (%)	27	17	0.287
History of breathlessness (%)	28	13	0.001
HbA_1C (%)	7.39 (7.19–7.60)	7.48 (7.3–7.67)	0.512
Creatinine (μmol/l)	92.8 (89.2–96.3)	88.8 (85.8–91.8)	0.091
Total cholesterol (mmol/l)	4.76 (4.60–4.93)	5.00 (4.85–5.16)	0.037
HDL-cholesterol (mmol/l)	1.27 (1.20–1.35)	1.31 (1.26–1.37)	0.366
Current smokers (%)	11	17	0.138
LVH on ECG (%)	13.2	6.6	0.047
LVMI (g/m^2)			
Males	161.6 (156.9–166.3)	107.1 (104.2–110.1)	<0.001
Females	133.1 (128.0–138.2)	90.3 (87.6–92.9)	<0.001
Left ventricular ejection fraction (%)	60.2 (58.5–61.9)	63.5 (62.4–64.5)	0.002
Interventricular septum diameter (cm)	1.19 (1.15–1.22)	0.99 (0.97–1.02)	<0.001
Left ventricular diameter (cm)	5.20 (5.11–5.29)	4.71 (4.64–4.79)	<0.001
Posterior wall diameter (cm)	1.11 (1.06–1.16)	0.95 (0.93–0.97)	<0.001
Abnormal diastolic function (%)	54	65	0.031
Left atrial diameter (cm)	4.24 (4.14–4.33)	3.89 (3.81–3.98)	<0.001
AVPD (mm)	12.7 (12.3–13.1)	13.3 (13.0–13.6)	0.011

Left ventricular systolic dysfunction

An ejection fraction was obtainable in 385/500 subjects (77%); those in whom the ejection fraction could not be assessed differed from those in whom it could be assessed only in BMI (32.4 [95% CI 31.4–33.4] and 28.9 [95% CI 28.4–29.4] kg/m^2 respectively, p<0.001) and in sex (43% male vs 67% female, p<0.001). The prevalence of left ventricular systolic dysfunction was 4% (16/385). Table 4 shows the characteristics of subjects with and without LVSD. Multivariate analysis was performed including sex, age, BMI, duration of diabetes, smoking status, systolic BP, diastolic BP, creatinine and HbA_1c. This model explained 11.8% of the variation in ejection fraction. The factors independently related to ejection fraction were sex (standardised β=–0.248, p<0.001), BMI (standardised β=–0.132, p=0.027), age (standardised β=–0.141, p=0.033) and systolic blood pressure (standardised β=–0.152, p=0.029).

Left ventricular diastolic abnormalities

The prevalence of abnormal diastolic function was 40.9% in the 435 subjects that could be classified in this way (Electronic Supplementary Material [ESM], Table 1). There were no significant differences in baseline characteristics between those in whom an assessment of diastolic function could or could not be made. Left ventricular mass index was significantly higher in males with diastolic abnormalities but not in females. Multivariate analysis was not performed.

Left ventricular long axis contraction

AVPD was obtained in 429/500 patients (85.8%). Patients in whom AVPD could not be assessed were more likely to be female and had higher BMI than those in whom AVPD could be assessed. The prevalence of AVPD <10 mm was only 6.8% (29/429). As expected, those with an AVPD <10 mm were significantly older, with lower left ventricular ejection fractions and more diastolic abnormalities (ESM, Table 2). Multivariate analysis was performed,

Table 3 Patient characteristics classified according to presence or absence of left ventricular hypertrophy (n=371) indexed to height$^{2.7}$ only

Variable	LVH mean (95% CI) (n=264)	No LVH mean (95% CI) (n=107)	p value
Males (%)	58	64	0.244
Age (years)	63.9 (62.6–65.2)	60.7 (58.6–62.8)	0.008
BMI (kg/m^2)	30.6 (29.9–31.2)	28.3 (27.4–29.3)	<0.001
Duration of diabetes (years)	6.3 (5.6–7.0)	5.5 (4.5–6.5)	0.214
Systolic BP (mm Hg)	143 (140–145)	140 (136–144)	0.220
Diastolic BP (mm Hg)	78 (77–79)	80 (78–82)	0.080
Percentage with BP <130/80 mm Hg	24	26	0.680
History of hypertension (%)	66.3	53.3	0.024
History of ischaemic heart disease or stroke (%)	18	8	0.025
History of breathlessness (%)	22	12	0.029
HbA_1C (%)	7.5 (7.3–7.6)	7.4 (7.2–7.7)	0.762
Creatinine	91.6 (88.7–94.5)	88.0 (84.5–91.4)	0.157
Total cholesterol (mmol/l)	4.87 (4.74–5.00)	4.97 (4.75–5.20)	0.401
HDL-cholesterol (mmol/l)	1.28 (1.23–1.33)	1.33 (1.24–1.42)	0.423
Current smokers (%)	14.5	15.0	0.873
LVH on ECG (%)	11	6	0.120
LVMI (g/m$^{2.7}$)			
Males	68.8 (66.5–71.1)	42.6 (41.3–43.9)	<0.001
Females	63.3 (60.7–65.9)	40.8 (39.0–42.6)	<0.001
Left ventricular ejection fraction (%)	61.3 (60.0–62.5)	63.9 (62.6–65.2)	0.005
Abnormal diastolic function (%)	41.7	34.0	0.218
Interventricular septum diameter (cm)	1.13 (1.11–1.16)	0.94 (0.91–0.97)	<0.001
Left ventricular diameter (cm)	5.04 (4.97–5.12)	4.62 (4.52–4.73)	<0.001
Posterior wall diameter (cm)	1.07 (1.04–1.10)	0.89 (0.86–0.92)	<0.001
Left atrial diameter (cm)	4.14 (4.07–4.22)	3.78 (3.65–3.92)	<0.001
AVPD (mm)	12.9 (12.5–13.2)	13.5 (13.1–13.9)	0.019

including sex, age, BMI, duration of diabetes, smoking status, systolic BP, diastolic BP, creatinine and HbA_1c. This model explained 28.7% of the variation in AVPD and the factors independently related to AVPD were sex (standardised β=0.478, p<0.001) and BMI (standardised β=0.286, p<0.001).

Cardiac rhythm

Four hundred and eighty-four of 500 (96.8%) patients were in sinus rhythm; 2.8% of patients (14/500) were in atrial fibrillation. One patient (0.2%) had paced rhythm and one patient had second-degree heart block (0.2%).

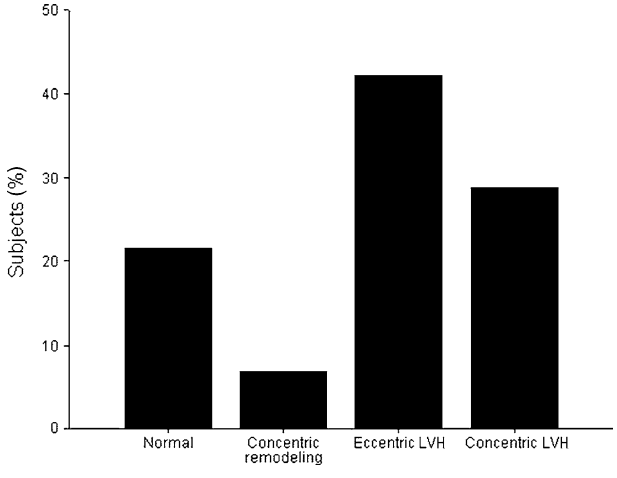

Fig. 1 Left ventricular geometry in the studied population (n=371)

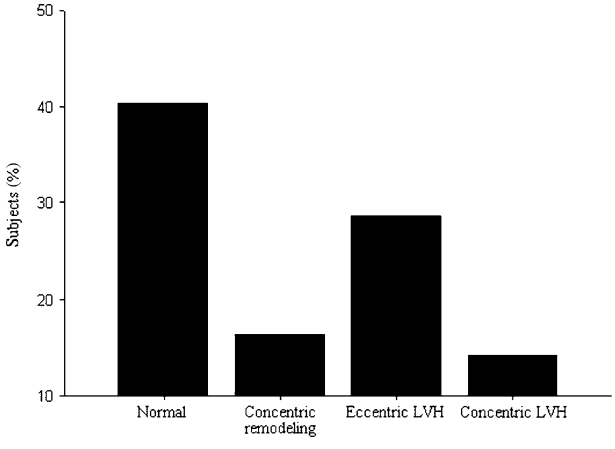

Fig. 2 Left ventricular geometry in the studied population, using left ventricular mass indexed to body surface area (n=371)

Table 4 Patient characteristics classified according to presence or absence of left ventricular systolic dysfunction (n=385)

Variable	Ejection fraction <45% Mean (95% CI) (n=16)	Ejection fraction >45% Mean (95% CI) (n=369)	p value
Males (%)	81	67	0.284
Age (years)	67.2 (62.2–72.2)	64.2 (63.0–65.3)	0.265
BMI (kg/m^2)	28.7 (26.9–30.4)	29.0 (28.4–29.5)	0.823
Duration of diabetes (years)	4.4 (2.4–6.3)	6.1 (5.6–6.7)	0.224
Systolic BP (mm Hg)	136 (124–149)	142 (140–144)	0.339
Diastolic BP (mm Hg)	80 (74–87)	78 (77–80)	0.516
HbA_1C (%)	7.2 (6.7–7.6)	7.4 (7.3–7.6)	0.415
Creatinine	109.5 (92.6–126.3)	90.1 (88.0–92.2)	<0.001
Total cholesterol (mmol/l)	4.97 (4.34–5.59)	4.88 (4.77–5.00)	0.763
HDL-cholesterol (mmol/l)	1.30 (1.06–1.54)	1.29 (1.24–1.33)	0.922
Current smokers (%)	19	18	1.000
History of hypertension (%)	43.8	59.4	0.299
History of ischaemic heart disease or stroke (%)	50	15	0.001
History of breathlessness (%)	31	17	0.170
ECG LVH (%)	31	8	0.011
LVMI (g/m$^{2.7}$)			
Males	74.04 (64.9–83.2)	60.0 (57.5–62.5)	0.018
Females	57.2 (34.9–79.6)	57.1 (54.2–59.9)	0.987
Left ventricular ejection fraction (%)	38.6 (35.0–42.3)	62.5 (61.8–63.3)	<0.001
Interventricular septum diameter (cm)	1.03 (0.87–1.19)	1.07 (1.05–1.10)	0.471
Left ventricular diameter (cm)	5.64 (5.21–6.08)	4.91 (4.84–4.98)	<0.001
Posterior wall diameter (cm)	1.05 (0.88–1.22)	1.03 (1.00–1.06)	0.745
Left atrial diameter (cm)	3.99 (3.51–4.46)	4.14 (3.97–4.31)	0.754
Abnormal diastolic function (%)	75	39	0.017
AVPD (mm)	10.4 (9.33–11.4)	13.0 (12.8–13.2)	<0.001

Discussion

The two main left ventricular abnormalities assessed in our population of type 2 diabetic subjects were LVH and LVSD. Our primary finding is that there is a very high prevalence of LVH in subjects with type 2 diabetes (43–71%) and a somewhat lower prevalence of LVSD (4%). Our other main findings are that 41% of type 2 diabetic subjects had abnormalities in the diastolic parameters tested and 6.8% had abnormal left ventricular long axis contraction.

Left ventricular hypertrophy is an independent predictor of cardiovascular death that is currently rather ignored. This is despite the fact that in one head-to-head study, LVH was a bigger risk factor for death (relative risk 2.4) than left ventricular systolic dysfunction (relative risk 2.0) or multivessel coronary artery disease (relative risk 1.6) [24]. In addition, the cardiovascular risk associated with LVH can be reduced by LVH regression [25] and risk returns to normal if full LVH regression is achieved [26, 27]. For these reasons, detection of LVH and targeted intervention to normalise or reduce left ventricular mass could be a promising way of reducing cardiovascular mortality in patients with diabetes. The first step towards achieving this is to assess the prevalence of unsuspected LVH in routine diabetic patients, and this has not been addressed by any other large study. Early studies showed that diabetes is indeed associated with increased left ventricular mass [28], but there is no previous large study of its prevalence in a group of routine diabetic clinic patients. We therefore assessed the epidemiology of left ventricular abnormalities in type 2 diabetic patients to see whether therapeutic opportunities to reduce the high death rates in diabetics could be identified by routine echocardiography of all diabetic patients.

LVH has, until now, been ignored because of two common misconceptions. The first is that LVH only occurs in severe hypertension. Considerable evidence exists to refute this. In our study, prevailing systolic or diastolic BP did not predict LVH in type 2 diabetics, although there was a slight excess of a history of hypertension (8–13%) in those with LVH as opposed to those without, but this was significant for one of the left ventricular mass parameters only. In Framingham, LVH occurred in 28% of women over 60 years with a systolic BP of 125–139 mm Hg [29].

Furthermore, evidence now suggests that BP explains only 25% of the variability in left ventricular mass [30]. Obesity and insulin resistance have been implicated in the pathogenesis of non-hypertensive LVH. Obesity has been demonstrated to be an independent predictor of left ventricular chamber size, left ventricular wall thickness and left ventricular mass [31, 32]. Insulin has been demonstrated to have trophic effects on cardiomyocytes in cell culture and may act as a growth factor, promoting the development of LVH [33]. It has also been suggested that, rather than acting on the heart directly, insulin may influence cardiac structure by stimulating the sympathetic nervous system [34].

The second misconception regarding LVH is that ACE inhibitors are a cure for LVH. This is not the case, as illustrated by both the Left Ventricular Hypertrophy Indapamide Versus Enalapril (LIVE) study [35], in which diuretics were better at reducing left ventricular mass than ACE inhibitors, and also by the Heart Outcomes Prevention Evaluation (HOPE) study [36]. In the LIVE study, treatment with indapamide for 48 weeks significantly reduced left ventricular mass index in hypertensive patients with LVH, whereas enalapril did not. This result could not be accounted for by differences in BP reduction as the magnitude of BP reduction was equivalent for the two treatments. The HOPE study demonstrated the benefits of ramipril in preventing or regressing ECG LVH in patients at high cardiac risk, nearly 40% of whom had diabetes mellitus. There was a relative reduction of approximately 40% in cardiovascular death in those patients in whom ECG LVH was prevented or regressed, compared with those in whom ECG LVH developed or progressed (3.4 vs 5.7%, p=0.001) [37]. The effect of ramipril on LVH was independent of the effect of ramipril on BP reduction. Although this risk reduction seems impressive, LVH itself increases mortality by 150–680% [12] and ACE inhibitors therefore reduce the risk of LVH but do not fully abolish it.

Left ventricular mass is a graded risk factor [38] and it can be argued that dichotomising LVH into being either present or absent is somewhat artificial and dependent upon the cut-off points used for its classification. Furthermore, there is debate as to whether left ventricular mass should be indexed to body surface area or to height. Previous work has demonstrated that the prevalence of LVH in obese populations is underestimated by indexing left ventricular mass to body surface area [39]. For this reason, we indexed left ventricular mass to both height$^{2.7}$ and body surface area, and found a difference of 28% in LVH prevalence between the two. Both methods have been prognostically validated: in one comparison between them, the risk ratio for a future cardiovascular event was considerably higher (4.06 CI 2.0–8.2) for the height$^{2.7}$ parameter than for the body surface area parameter (2.76 CI 1.4–5.5) [40]. However, there is a larger body of evidence linking the body surface area parameter to prognosis and it is still widely used. Inevitably there will be debate over which method of assessing LVH is better, but the key point is that the prevalence of LVH in type 2 diabetes is worryingly high (43 or 71%) whichever indexing method is used.

The majority of patients in our study with LVH had eccentric left ventricular geometry. Studies have suggested that concentric LVH may be associated with a higher risk of stroke, cardiac death and all-cause mortality than eccentric LVH, although this is controversial [41–43]. There was a relatively poor correlation between structural LVH and functional diastolic abnormalities in our study, with only around one-half of patients with diastolic abnormalities also having LVH, and vice versa. Previous work has established that diastolic abnormalities occur early in the course of diabetic cardiomyopathy and prevalence estimates of between 30 and 61% have been reported for asymptomatic left ventricular diastolic dysfunction [19, 44, 45]. Our results are supported by those of the Strong Heart Study, in which diastolic abnormalities in diabetic patients were found to be independent of left ventricular mass and left ventricular systolic function [46]. The mechanisms contributing to the pathogenesis of diastolic dysfunction in some diabetic patients, but not others, are not fully established, although some pointers do exist. Firstly, diastolic dysfunction has been shown to be associated with aortic stiffness in patients with diabetes mellitus with no coronary artery disease [47]. Secondly, altered diastolic function in type 2 diabetes is associated with reduced myocardial metabolism, assessed using magnetic resonance imaging [48]. It is possible that the degree of hyperglycaemia may also play a role, as a higher fasting glucose and glycated haemoglobin are associated with abnormal left ventricular relaxation in diabetic patients [46].

The mean systolic BP of patients in our cohort did not meet the target for diabetic patients of 130 mm Hg. However, according to the results of the European Action on Secondary Prevention by Intervention to Reduce Events study [49], this is a fairly typical scenario with cardiac risk factor control remaining suboptimal in most patients in the real world. Perhaps being aware that a patient had LVH (or increased left ventricular mass) would motivate the prescribing physician to intensify cardiac risk factor control in these patients. This is given credence by a recent study demonstrating that doctors do optimise risk factor control in patients at high risk when risk scores are available during the consultation [50]. It is perhaps surprising that, in our study, only 35% of patients were receiving an ACE inhibitor at the time of the study visit, particularly when 61% of our patients had known hypertension. Part of this may be that LVH had not been identified in most of the patients prior to this study. In addition, most evidence suggests that the choice of drug used to lower BP is less important than the actual BP lowering achieved. Such a view was endorsed even for diabetes by the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial study, which was designed to determine whether a calcium channel antagonist (amlodipine), an ACE inhibitor (lisinopril) or an alpha blocker (doxazosin) would prevent the primary outcome of fatal CHD or non-fatal myocardial infarction significantly more than diuretic therapy [51]. Perhaps unexpectedly, there was no significant difference in the primary outcome between the four groups. In terms of secondary outcomes, chlorthalidone

was superior to lisinopril in preventing stroke, heart failure, angina and coronary revascularisation. Another reason for the low use of ACE inhibitors in our study may be that many of our patients had been established on alternative antihypertensives long before our study started and prior to the suggestion that ACE inhibitors might be preferable in diabetes to reduce microalbuminuria.

One limitation of our study is the fact that 24% of the patients screened did not have adequate echocardiographic images to allow M-mode measurements of left ventricular dimensions to be made. This is an inevitable limitation of all echocardiographic studies and imaging failure rates of 2–40% have been reported [11, 26, 52–54]. As expected, the two main contributors to inadequate echo images in our study were increasing age and high BMI. If anything, it is likely that such patients would be at greater risk of having LVH, and our figures may therefore underestimate the prevalence of LVH in the diabetic population. A further limitation of our study is that we did not seek to formally exclude silent myocardial ischaemia in our subjects, and it is therefore possible that some may have had significant obstructive coronary artery disease that was not yet clinically apparent and which may have contributed to the prevalence of left ventricular abnormalities. Our study also had no control group, in that we did not compare the prevalence of LVH in patients with and without diabetes and it could be suggested that our high prevalence of LVH may be due to hypertension. However, one study of patients with and without hypertension found the prevalence of LVH to be 27% in hypertensives (defined as BP>160/95) and 6% in normotensives [55]. The prevalence of LVH in our diabetic population was much higher than this, even allowing for the fact that 61% had a history of hypertension.

Type 2 diabetes is a major cause of cardiovascular morbidity and mortality and its prevalence is rising rapidly. Our study provides important information by demonstrating that there is a high prevalence of left ventricular abnormalities in this group. It is possible that routine screening for these abnormalities followed by targeted intervention may help reduce cardiovascular morbidity and mortality. Future work should be aimed at assessing the cost-effectiveness of screening diabetic patients for LVH and then optimising their treatment. As diabetic patients have higher cardiovascular death rates than non-diabetic patients, it may be more cost-effective to target LVH in the former, rather than in the latter. A recent hypothetical analysis of the cost-effectiveness of identifying LVH, performed by Witham et al., suggested that this may indeed be a very cost-effective strategy to reduce cardiovascular events in high-risk normotensive patients, such as diabetics [56].

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