National Morbidity Study⁴ found that 60% of those on the practice list made contact with their general practitioner each year compared with the 50% in one year and 66% in three years found in this survey. This discrepancy may be due to the fact that not all contacts are recorded in the notes, as they would be in a special prospective study.

A similar explanation may account for the finding of a blood pressure recording in only 164 (24%) of the notes. Perhaps blood-pressure measurements are not always converted into actual recordings in the notes, and the fact that the blood pressure was raised in 74 (45%) of all patients with a recording suggests that normal blood pressures may not always be recorded. Blood-pressure measurements may also be recorded elsewhere than the practice notes, for example—if taken as part of an insurance or pre-employment medical examination or as part of a visit to an antenatal or family planning clinic. These categories were found in a population survey⁵ to account for over 20% of the most recent blood-pressure measurements in men and women respectively. Despite the fact that most women aged between 20 and 39 would be expected to have had a blood-pressure measurement as part of family-planning or antenatal care, there was a blood-pressure recording in the notes of only 35 (18%) of this group (table I). In the population survey⁵ 88% of women aged 17-39 reported having had a blood-pressure measurement, but when it had been performed in the course of family-planning or antenatal care the general practitioner had performed the measurement in only 12%. Apparently in this part of London family-planning and antenatal care are performed outside the general-practice setting.

We compared the figure of 24% of notes with a blood-pressure recording with another study from Scotland,^{6,7} in which a blood-pressure recording was found in 32-48% of the notes of patients aged 45-64 from three general practices. Another study in Scotland,⁸ showed the use of a sphygmomanometer in 9-15% of practice consultations.

That relatively few people have a blood-pressure recording in their general-practice notes may not be too important since it appears that most adults have had their blood pressure measured at some time.⁹ Of greater concern is the lack of action taken

when hypertension has been discovered. Whichever criteria are used for defining hypertension, many people in this sample, found by general practitioners to have raised blood pressure, have not received further attention for the condition. In the context of general practice Tudor Hart⁹ has adopted Pickering's criteria¹⁰ for hypertension (which are higher than others), and advises treatment in men at diastolic levels of 100 or 105 mm Hg according to age, with women starting 10 mm Hg higher.

As in the study of the management of hypertension in hospital,¹ we have found that people with raised blood-pressure levels have not received treatment, and some do not appear to have had a repeat measurement to see if the elevation has persisted. Furthermore, we were surprised to find that the commonest drugs selected for treatment were sedatives or tranquillisers, since these drugs have never been shown to be effective in the management of hypertension.

This work formed part of an MD thesis by RFH, accepted by London University.

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Diabetic cardiomyopathy: the preclinical phase

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Summary

Left ventricular function was assessed by measuring systolic time intervals in insulin-requiring diabetics with and without significant microangiopathy. The results were compared with those in normal controls. Significant microangiopathy was defined as proteinuria over 3 g/24 h or proliferative retinopathy. Left ventricular function was also assessed one and a half years later by echocardiography in four patients with microangiopathy. Patients with angina, previous myocardial infarction,

hypertension, and alcoholism were excluded. All had normal electrocardiograms and chest radiographs. Diabetics with microangiopathy had impaired left ventricular function, whereas those with uncomplicated diabetes had normal function. This finding supports the existence of a specific diabetic cardiomyopathy due to microangiopathy rather than the metabolic defect. The association of microangiopathy and impaired left ventricular function may explain the high immediate mortality and the high incidence of cardiogenic shock and congestive heart failure after myocardial infarction in diabetics.

Introduction

Recent clinical and epidemiological studies have suggested that diabetics might develop myocardial dysfunction in the absence of large coronary artery disease, hypertension, or valvular disease (diabetic cardiomyopathy). Rubler *et al*¹ reported four patients with diabetic glomerulosclerosis who presented with cardiomegaly and congestive failure of unknown cause. Hamby

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*et al*² noted a high incidence of diabetes among his series of patients with idiopathic cardiomyopathy. The Framingham study,³ analysing the role of diabetes in congestive heart failure, found that the incidence of congestive failure among diabetics was higher than among the non-diabetic cohorts. The excessive risk seemed to be independent of hypertension and large coronary artery disease. The conclusion was "that some form of cardiomyopathy was associated with diabetes as a result of small vessel disease or metabolic disorder."

If diabetic cardiomyopathy is a distinct condition it may pass through a preclinical phase when left-ventricular function is impaired, and this phase could be detected by using sensitive non-invasive methods. Systolic time measurements¹ and echocardiography⁵ were performed in insulin-requiring diabetics with and without significant microangiopathy to determine whether the cardiac dysfunction was a result of small vessel disease or the metabolic disorder.

Patients and methods

Insulin-requiring diabetics were selected from a diabetic clinic. Those with blood pressure over 150/90 mm Hg, angina, or previous myocardial infarction were excluded. None of the patients studied were on oral hypoglycaemic drugs, beta-blockers, or diuretics. None took significant amounts of alcohol. The diabetics were divided into two groups: those with significant microangiopathy, and those with no microangiopathy. These two groups were compared with normal age- and sex-matched controls. The 14 women with microangiopathy had either proliferative retinopathy or proteinuria over 3 g/24 h. The mean age and postprandial blood sugar concentration (calculated from three previous clinic visits) were comparable with those of 14 patients with uncomplicated diabetes (see table II). The 14 controls had a similar mean age to that of the diabetics.

Systolic time intervals—Left ventricular function was assessed by simultaneous recordings of the carotid pulse, phonocardiogram, and electrocardiogram on a four-channel recorder (Hewlett Packard) at a paper speed of 100 mm/s. The test was done in the postabsorptive phase, the patients not having had their morning dose of insulin. Total electromechanical systole (Q-S2 interval) was the duration from the

TABLE III—Results of echocardiography in four diabetics with microangiopathy compared with results in 20 normal controls

Case No	End diastolic diameter (cm)	End systolic diameter (cm)	End diastolic volume (ml)	End systolic volume (ml)	Fractional shortening (%)	Ejection fraction (%)
6	4.8	3.9	110.6	59.3	18.8	46
7	4.1	3.1	68.9	29.8	24.4	57
9	4.8	3.7	110.6	50.6	22.9	54
10	3.7	2.9	50.6	24.4	21.6	52
Mean ± SD					21.9 ± 2.4	52.3 ± 4.6
Control value					33.8 ± 4.0	62.5 ± 5.5
P value					0.001	0.01

Q wave to the first vibration of the second heart sound. Left ventricular ejection time (LVET) was measured from the beginning of the upstroke of the carotid pulse to the incisural notch. The pre-ejection period (PEP) was obtained by subtracting LVET from Q-S2. The increase in the (PEP:LVET) × 100 (normal 33.3 ± 4.1) is a sensitive index of left ventricular dysfunction.

Echocardiography became available one and a half years after the initial study was completed. Recordings were done on Polaroid film using the Echoline 20 A. Seven of the original 14 diabetics with microangiopathy were available for study but recordings from only four patients were accepted as being technically good. Left ventricular function was assessed as previously described.⁵ Left ventricular diastolic diameter (LVD) and left ventricular end systolic diameter (LVES) were measured. Fractional shortening (FS) was derived as follows:

$$FS = \frac{LVD - LVES}{LVD} \times 100.$$

Left ventricular diastolic volume (LDV) and end systolic volume (LESV) were derived by cubing LVD and LVES respectively. Ejection fraction:

$$EF = \frac{LDV - LESV}{LDV} \times 100.$$

The systolic time recordings and measurements were performed by a technician in our non-invasive cardiovascular diagnostic unit. She was not aware of the patient's category. The tests were repeated for confirmation but the values given are from the initial recordings. I performed the echocardiography and was aware of the patient category. Only technically excellent records were used for measurement. Echocardiography was performed mainly to confirm impaired left ventricular function.

Results

Table I gives the clinical details of the 14 patients with microangiopathy. None were in advanced renal failure as judged by their serum creatinine levels.

Table II shows that the diabetics with microangiopathy had impaired left ventricular function, while those with uncomplicated diabetes had normal function ($P < 0.001$). Mean age, sex, and recent control were comparable in the two groups of diabetics but those without microangiopathy had had diabetes for longer.

The results of echocardiography in the four diabetics with microangiopathy showed that left-ventricular function was significantly impaired when compared with that in 20 normal controls.

One patient with microangiopathy (case 11) died after bronchopneumonia one and a half years after the initial study. At necropsy her kidneys showed diffuse glomerulosclerosis (diabetic nephropathy). The heart weighed 450 g. The major coronary arteries were free of significant occlusive disease. Microscopy showed scattered small areas of fibrosis. Some of the intramural coronary arteries showed narrowing of the lumina due to focal deposition of mucopolysaccharide material in the subendothelial layers (microangiopathy) (see figure).

Discussion

This study supports the idea that there is a specific diabetic cardiomyopathy associated with substantial microangiopathy rather than the metabolic derangement. An abnormally raised PEP:LVET ratio is a sensitive index of impaired left ventricular function and correlates well with the ejection fraction derived

TABLE I—Clinical details of the 14 diabetics with microangiopathy

Case No	Age (years)	Duration of diabetes	Nephropathy (serum creatinine: mmol/l)*	Retinopathy†	PEP:LVET × 10 ²
1	47	5	++ (0.05)	+	42.0
2	61	10	++ (0.05)	+	50.0
3	24	8	++ (0.06)	+	48.1
4	65	8	++ (0.04)	++	50.0
5	50	8	++ (0.06)	+	43.0
6	37	15	+++ (0.15)	+	50.0
7	30	18	++ (0.06)	++	44.2
8	25	11	++ (0.05)	+	39.6
9	49	8	++ (0.09)	+	46.0
10	44	5	++ (0.09)	+	45.0
11	65	15	+++ (0.15)	++	42.0
12	59	19	++ (0.06)	++	46.0
13	65	15	++ (0.15)	++	41.5
14	33	8	+++ (0.11)	+	46.1

*Nephropathy: ++ = proteinuria <3 g/24 h; +++ = 3-5 g/24 h; ++++ = >5 g/24 h. Normal serum creatinine concentration 0.04-0.13 mmol/l.

†Retinopathy: + = background; ++ = proliferative.

Conversion: SI to traditional units—Creatinine: 1 mmol/l ≈ 0.0113 mg 100 ml.

TABLE II—Index of left ventricular function in the three groups

	Diabetes		Controls
	with microangiopathy	without microangiopathy	
No	14	14	14
Mean age (years)	46.7	44.3	45.6
Mean duration of diabetes (years)	10.9	15	
Mean postprandial blood sugar (mmol/l)	10.3 ± 0.6	9.9 ± 0.5	
(PEP:LVET) × 100	45.3 ± 3.3	31.8 ± 3.1	32.9 ± 3.2
P value	<0.001		NS

Case 11. Section of myocardium showing perivascular fibrosis and small intramural coronary artery with focal protuberances due to subendothelial proliferation and accumulation of mucopolysaccharide material. (Periodic-acid Schiff $\times 100$.)

from invasive methods.⁶ Yet ejection fraction and resting systolic time intervals are not usually altered in chronic coronary heart disease even in the presence of angina unless there has been prior documented infarction.⁷ The strict selection of patients free of angina and previous myocardial infarction and with normal electrocardiograms and chest radiographs would exclude coronary heart disease as a cause of the increase in PEP:LVET in the diabetics with microangiopathy. Moreover, if coronary artery disease did influence the ratio one would expect intermediate changes in the diabetics without microangiopathy.

The association of renal disease with cardiomyopathy warrants comment as all our patients with significant microangiopathy had some degree of proteinuria, with three excreting over 5 g protein in 24 hours. Acute cardiac decompensation has been described in acute nephritis even in the absence of hypertension.⁸ None of the patients in the present study were in overt renal failure and none had oedema. Moreover, three had only mild proteinuria and yet had strongly increased PEP:LVET ratios. It therefore seems unlikely that the renal disease had any influence on their left ventricular function.

None of the patients were on drugs such as sulphonylureas (inotropic agents), beta-blockers (cardiac depressants), or diuretics (which reduce preload), or taking alcohol (depressant), which might have influenced the PEP:LVET ratio. Echocardiography also confirmed the impairment of left ventricular function, although the numbers were too small to warrant further discussion. It seems logical to conclude that the basis of the impaired left ventricular function was diffuse microangiopathy as illustrated at necropsy in case 11.

The concept of diabetic microangiopathy in the myocardium is not new. Ledet⁹ found concentric rings of periodic-acid Schiff-positive material in the smallest intramural coronary arteries of diabetics in a necropsy series. Pearce *et al*¹⁰ showed small-vessel disease by ventricular septal biopsy in living patients with congestive failure and diabetes. Hamby *et al*¹² in their series of 73 patients with primary myocardial disease found that 16 were diabetics. Their coronary angiograms were normal. Three of these came to necropsy and all had small-vessel disease. Rubler *et al*¹ reported four patients who presented with congestive failure of unknown cause with associated glomerulosclerosis and found small-vessel disease in one. Although these

studies postulated that myocardial disease was secondary to microangiopathy none could exclude the direct effects of the abnormal myocardial metabolism. The present study incriminates diffuse small-vessel disease as the main underlying cause of the cardiomyopathy.

The association of significant microangiopathy with impaired left ventricular function may have important clinical implications. It may explain the overall high immediate mortality and the high incidence of cardiogenic shock and congestive heart failure after myocardial infarction in diabetics.¹¹ The mortality rose to 70%, in patients with retinopathy who were also on oral hypoglycaemic drugs.¹² Female diabetics have a particularly high mortality and it is interesting that all our patients with impaired left ventricular function were women. (There were men with microangiopathy and impaired left ventricular function but they were excluded for reasons such as heavy alcohol intake, coronary heart disease, etc. The female dominance seems to be real.) Possibly only patients with significant microangiopathy are at special risk after myocardial infarction and uncomplicated diabetics may have an overall mortality comparable to that of non-diabetics, as observed in recent reports.¹³⁻¹⁵ Verska and Walker,¹⁶ analysing 35 diabetics after aortocoronary bypass, found good vein-graft flows and doubted the presence of microvascular disease in the myocardium of diabetics. There were no data on the presence or absence of microangiopathy elsewhere and presumably these were uncomplicated diabetics. The presence of substantial microangiopathy may preclude aortocoronary bypass surgery in diabetics. Finally, although left ventricular function is subclinically impaired in most diabetics with significant microangiopathy it is perhaps the exceptional few who would eventually develop overt cardiac failure in the absence of hypertension or coronary heart disease. Hypertension¹⁷ and coronary heart disease are both common in diabetics and these two major risk factors would increase the risk of congestive cardiac failure, thereby explaining the high overall incidence of congestive cardiac failure in diabetics, as observed in the Framingham study.³

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