SUMMARY - Objective: To assess echocardiographic evidence of cardiomyopathy and its association with microalbuminuria in type 2 normotensive non-proteinuric diabetic patients

Material and methods: Forty consecutive normotensive non-proteinuric type 2 diabetic patients were studied. Body mass index, blood pressure, urinary albumin excretion, ECG at rest and after exercise, left ventricular mass, and shortening fraction using two-dimensional and M-mode echocardiography were measured in every patient.

Results: Among the 40 patients studied, 17 (42.5%) presented with microalbuminuria, 16 (40.0%) with left ventricular hypertrophy, 22 (55.0%) with systolic dysfunction and 3 (7.5%) with ECG changes compatible with cardiac ischaemia. No significant difference existed between normoalbuminuric and microalbuminuric patients for age, known duration of diabetes, body mass index, systolic and diastolic blood pressure. Ventricular mass correlated to urinary albumin excretion rate (r = 0.34; p = 0.04) and shortening fraction to diastolic blood pressure (r = – 0.40; p = 0.01).

Conclusion: Left ventricular structure and function might be altered in African type 2 diabetic patients in the absence of hypertension, and microalbuminuria may be an early biochemical marker of these abnormalities.

Key-words: cardiovascular, diabetes mellitus, microalbuminuria, Africa.

RÉSUMÉ - Masse du ventricule gauche et fonction systolique chez des diabétiques africains : association avec la microalbuminurie.

BUTS : Étudier la masse et la fonction ventriculaires gauches au sein d’une population de diabétiques de type 2 Africains et leur relation avec l’excrétion urinaire d’albumine (EUA).

MATÉRIEL ET MÉTHODES : Ont été inclus dans cette étude préliminaire 40 patients camerounais, normotendus, non protéinuriques présentant un diabète de type 2 connu depuis au moins 1 an. L’indice de masse corporelle, la pression artérielle au repos, l’EUA, l’ECG au repos et à l’effort, la masse et la fraction de raccourcissement du ventricule gauche (échocardiographie M-mode et bi dimensionnelle) ont été évalués.

RÉSULTATS : Dix-sept (42,5 %) patients ont présenté une microalbuminurie, 16 (40,0 %) une hypertrophie ventriculaire gauche, 22 (55,0 %) une dysfonction systolique ventriculaire gauche et 3 (7,5 %) des anomalies ECG compatibles avec une ischémie. Il n’existait pas de différence significative entre les patients normo- et microalbuminuriques par rapport à l’âge, la durée du diabète, l’indice de masse corporelle et la pression artérielle. La masse ventriculaire gauche était corrélée à l’excrétion urinaire d’albumine (r = 0.34 ; p = 0.04) et la fraction de raccourcissement à la pression artérielle diastolique (r = – 0.40 ; p = 0.01).

CONCLUSION : Il existe chez certains diabétiques de type 2 Africains, une hypertrophie et une dysfonction systolique du ventricule gauche, même en l’absence d’hypertension artérielle. La microalbuminurie pourrait en être un marqueur biochimique précoce.

Mots-clés : cardiovasculaire, diabète, microalbuminurie, Afrique.

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Cardiovascular complications account for the highest mortality in diabetic patients, mainly due to coronary artery disease and congestive heart failure [1]. Diabetes is associated with high prevalence of hypertension, dyslipidaemia and microalbuminuria, all known independent cardiovascular risk factors [2]. Apart from being associated to increased cardiovascular morbidity, microalbuminuria is the hallmark of diabetic microvascular complications [3].

The prevalence of myocardial infarction is low in the Africans, however, congestive heart failure and stroke are the most important cause of cardiovascular death in adults [4]. Even in populations with low cardiovascular risk, diabetes is associated with increased prevalence of risk factors and incidence of cardiovascular death [5]. It is not clearly established whether congestive heart failure develops as a result of longstanding hypertension, unrecognised myocardial infarction or from a specific cardiomyopathy, or a combination of the above.

Hemodynamic and pathological studies demonstrate changes such as left ventricular dysfunction with filling abnormalities, myocardial hypertrophy, fibrosis, and microvascular alterations in diabetic heart usually asymptomatic unless congestive heart failure supervenes [6], and congestive heart failure is 2-5 times more prevalent in diabetic population [7].

This preliminary study was designed to look for echocardiographic evidence of cardiomyopathy in normotensive African diabetic patients and its association with microvascular complications.

### PATIENTS AND METHODS

#### Patients

This cross sectional study was undertaken in a referral hospital in the city of Yaoundé (Cameroon) over a six-month period. Forty consenting black African type 2 diabetic patients were consecutively enrolled after they had given their informed consent to participate. They were diagnosed on the basis of WHO 1985 criteria, all treated with oral hypoglycaemic drugs, and had been followed in our clinic for at least 12 months. No other medication was reported. Patients with hypertension (>140/90 mmHg), macroalbuminuria (>300 mg/24 h; dipstick method), urinary tract infection (microscopic examination of mid-stream urine sample), sickle cell disease (medical record), or pregnancy were excluded.

#### Methods

Age, sex, history of diabetes was recorded for each patient. Weight (to 0.1 kg in light clothing), height (to 0.5 cm), waist and hip circumferences (to 1 cm) were measured, and body mass index (weight/height$^2$ in kg/m$^2$) and the waist-to-hip ratio were calculated. Blood pressure was measured by the same observer [ES] between 8-10 AM using a mercury sphygmomanometer with a suitable sized cuff (1st and 5th Korotkoff used, patients sitting, after a 5-min rest), and the mean of three measurements was recorded. Fundoscopy was performed by a consultant ophthalmologist after dilatation for the diagnosis of diabetic retinopathy classified as non proliferative, pre-proliferative and severe (proliferative and/or maculopathy) stages.

Complete overnight urine samples (8PM – 8AM) were collected, the volume recorded, and microalbuminuria detected using Micral II Test immunological dipstick method (Boehringer Mannheim, Germany). Urinary albumin excretion rate was expressed in mg/24hour with the cut-off used for microalbuminuria at 30 mg/24 hour.

Exercise tests were performed on a bicycle ergometer, with simultaneous recording of a 12-lead ECG and blood pressure, starting at a workload of 25 W and increasing by 25 W every 3 minutes until theoretical individual maximum heart rate, or symptoms or ECG abnormalities occurred.

M-mode and two-dimensional echocardiography were done using an ADR-4000SLC ultrasound machine with a 3 MHz transducer. Left ventricular mass indexed to the body surface area was calculated using the Devereux formula [8]. Cut-off for the diagnosis of left ventricular hypertrophy were >134 g/m$^2$ in men and >110 g/m$^2$ in women. Shortening fraction (SF) was calculated as SF = (LVEDD-LVESD)/LVEDD × 100%; where LVESD = end systolic left ventricular internal dimension, LVEDD = end diastolic left ventricular internal dimension. Left ventricular systolic dysfunction was considered for a shortening fraction <28% [9].

#### Statistical analysis

Results are expressed as frequency and mean (standard deviation). Differences in each normally distributed variable were analysed using an unpaired t-test. Spearman correlation was performed to analyse relationship between variables. The Chi$^2$ test with continuity correction was used where appropriate. Urinary albumin excretion was skewed and had to be log transformed before analysis. Significant level was set at p < 0.05.

#### RESULTS

The patients were aged 39 to 66 years, with known duration of diabetes ranging from 1-14 years, mean BMI of 26.6 (4.7) kg/m$^2$, and blood pressure ranging from 108-140/62-90 mmHg (Systolic/diastolic), and diabetic retinopathy in 30% of the subjects. The characteristics of the patients are shown in Table I.
Microalbuminuria was diagnosed in 17/40 (42.5%) patients. No significant difference was observed between patients with and without microalbuminuria with regard to age, duration of diabetes, body mass index and blood pressure. However microalbuminuria was associated with diabetes retinopathy ($p = 0.01$) (Table II), and urinary albumin excretion correlated with diastolic blood pressure ($r = 0.34$, $p = 0.04$), but not with systolic blood pressure. ECG changes compatible with ischaemia were found in 3 patients (1 normoalbuminuric and 2 microalbuminuric).

Left ventricular hypertrophy was diagnosed in 16/40 (40.0%) patients. There was no association between left ventricular mass and age, known duration of diabetes, and BMI, but WHR tended to be higher in women with hypertrophy (Table II). There was a significant correlation between left ventricular mass and urinary albumin excretion rate ($r = 0.34$; $p = 0.04$), but not with blood pressure. Retinopathy was associated with left ventricular hypertrophy ($p < 0.05$).

Twenty-two patients (55.0%) had a shortening fraction $< 28\%$ (left ventricular systolic dysfunction). Diastolic blood pressure was significantly higher in the patients with ventricular dysfunction, and shortening fraction was negatively correlated with diastolic blood pressure ($r = -0.40$; $p = 0.01$) but not with systolic blood pressure. There was no association between left ventricular systolic dysfunction and duration of diabetes, obesity, retinopathy, microalbuminuria and left ventricular hypertrophy. The subgroups of patients with normal and abnormal shortening fraction were otherwise similar, though WHR tended to be higher in women with systolic dysfunction (Table II).

### DISCUSSION

This preliminary study in an African diabetic population, shows that heart muscle disease complicates diabetes independently of hypertension. This disease is characterised either by left ventricular hypertrophy or left ventricular dysfunction or both. Half of the patients or more had at least one feature of the disease. These results are confirmatory of the existence of a specific cardiomyopathy in diabetic patients [10].

We observed a high prevalence rate of microalbuminuria and left ventricular hypertrophy which may reflect the importance of cardiovascular risk in this population, both factors being proved to be independent cardiovascular risk factors [11]. Congestive heart failure might therefore appear in African patients as the end point of cardiomyopathy and account for the excess cardiovascular mortality attributed to diabetes. Indeed, in the background population, unlike the Caucasians whom cardiovascular morbi-mortality is mostly attributable to coronary artery disease, a low prevalence and incidence of coronary artery disease is reported in Sub Saharan Africa, though the picture is changing with epidemiological transition [12].

Whether left ventricular hypertrophy and dysfunction found in diabetic patients are attributable to diabetes per se or other pathological process has been questioned. Unfortunately, most studies failed to avoid

### TABLE I. Clinical characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>Age (year)</td>
<td>52.0 (8.4)</td>
<td>51.4 (7.8)</td>
</tr>
<tr>
<td>Known duration of diabetes (year)</td>
<td>4.8 (4.0)</td>
<td>4.6 (3.8)</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>28.6 (5.0)</td>
<td>25.2 (3.8)*</td>
</tr>
<tr>
<td>Waist/Hip ratio</td>
<td>0.90 (0.07)</td>
<td>0.95 (0.06)*</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>126 (11)</td>
<td>128 (12)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>78 (7)</td>
<td>77 (7)</td>
</tr>
<tr>
<td>Retinopathy (%)</td>
<td>31.6</td>
<td>28.6</td>
</tr>
<tr>
<td>Urinary albumin excretion (mg/24 h)$\equiv$</td>
<td>29.6 (5-132)</td>
<td>28.3 (5-180)</td>
</tr>
<tr>
<td>Left ventricular mass/BSA (g/m²)</td>
<td>120.5 (36.5)</td>
<td>139.5 (32.2)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>47.8 (10.8)</td>
<td>53.6 (9.0)</td>
</tr>
</tbody>
</table>

Results expressed as mean (standard deviation) unless otherwise specified.

$\equiv$ (range).

* $p < 0.05$. 

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the bias of hypertension and/or obesity. A recent study however evidenced in a population comparable to our patients, left ventricular diastolic dysfunction without systolic dysfunction in up to 60% of 46 normotensive type 2 diabetic men [13].

The present study was designed specifically to study normotensive patients and it demonstrates the presence of hypertrophy and systolic dysfunction in normotensive Type 2 diabetic patients. Furthermore, left ventricular mass was indexed to the body surface area to avoid the influence of obesity. However, this preliminary study did not include a non diabetic population.

Though this study was conducted in normotensive patients, it appeared clearly that features of diabetic cardiomyopathy were associated with increasing blood pressure levels. Increasing blood pressure could either be an etiologic factor or simply part of the hemodynamic features of diabetic cardiomyopathy as reported in experimental studies. Increased heart size may reflect the increase in circulating blood volume and systolic dysfunction could be secondary to increased peripheral resistance, as some studies have shown increasing peripheral resistance in diabetic patients. This could therefore be attributable to early changes preceding established hypertension [14].

Early nephropathy as defined by the presence of microalbuminuria was diagnosed in one half of this population with a relatively short mean known duration of diabetes (5 years), and was associated with retinopathy and left ventricular hypertrophy. Diabetes is usually diagnosed late in Africans and as previously reported in another African population, long-term poor glycaemic control may be the major cause of high prevalence rate of complications. Glycaemic control was not assessed in this study, but other investigators report similar or higher prevalence rates of diabetes complications in population with comparable duration of diabetes and with a poor glycaemic control [15].

### CONCLUSION

Our study has demonstrated the evidence of left ventricular hypertrophy and asymptomatic systolic dysfunction in diabetic patients of African origin with a relatively short duration of diabetes, and in the absence of hypertension. This study is also confirmatory of the association of microalbuminuria with left ventricular hypertrophy. Pathophysiological studies as well as earlier stages Doppler studies in wider groups are required.

<table>
<thead>
<tr>
<th>Table II. Characteristics of patients with and without microalbuminuria, left ventricular hypertrophy and systolic dysfunction.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EUA &lt; 30mg/24 h</strong></td>
</tr>
<tr>
<td>N</td>
</tr>
<tr>
<td>Age (year)</td>
</tr>
<tr>
<td>Duration of diabetes (year)</td>
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<td>BMI (kg/m2)</td>
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<td>Waist-to-hip ratio</td>
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<td>Urinary albumin excretion (mg/24 h)</td>
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<td>Left ventricular mass/BSA</td>
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<tr>
<td>Ejection fraction (%)</td>
</tr>
</tbody>
</table>

Results expressed as mean (standard deviation) unless otherwise specified.

–: without left ventricular hypertrophy; LVH +: with left ventricular hypertrophy.

LVSD –: without left ventricular systolic dysfunction; LVSD +: with left ventricular systolic dysfunction.

* p < 0.05.

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REFERENCES


