Left ventricular hypertrophy in hypertensive type 2 diabetic patients according to renal function

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Abstract

Aim. – Cardiovascular disease is the main cause of death in diabetic patients undergoing haemodialysis. Dialysis and hypertension increase left ventricular hypertrophy (LVH), a strong predictor of cardiovascular events. This study evaluated left ventricular structure and function in three groups of hypertensive type 2 diabetic patients with different renal function, and assessed the factors associated with LVH, in an Afro-Caribbean population.

Methods. – Left ventricular structure and function were measured by ultrasonography. Group 1 consisted of 150 patients with normal renal function, group 2 included 183 patients with renal dysfunction and the third group comprised 75 dialysis patients.

Results. – Left ventricular mass/height$^{2.7}$ increased from group 1 to groups 2 and 3 (49.00 g/m$^{2.7}$, 57.12 g/m$^{2.7}$ and 59.75 g/m$^{2.7}$, respectively; $P<0.0001$). The prevalences of LVH were 48.3% in group 1, 64.8% in group 2 and 70.3% in the dialysis patients ($P=0.001$). LVH was more concentric than eccentric in groups 2 and 3.

The factors significantly associated with LVH were obesity in groups 1 and 2, and an increase of 10 mmHg in pulse pressure in groups 2 and 3, according to multivariate logistic-regression analysis.

Conclusion. – Our study confirmed that, in a population of Afro-Caribbean hypertensive type 2 diabetic patients, renal failure was associated to an increased left ventricular mass/height$^{2.7}$. The data show that the variables associated with LVH differ according to renal profile. This finding will be of value in the treatment and follow-up of these patients.

Keywords: Echocardiography; Dialysis; Type 2 diabetes mellitus; Hypertension; Pulse pressure

Résumé

Hypertrophie ventriculaire gauche chez des patients hypertendus diabétiques de type 2 selon la fonction rénale.

But. – Les complications cardiovasculaires représentent la cause principale de décès des patients diabétiques en insuffisance rénale chronique terminale dialysés. La dialyse et l’hypertension artérielle favorisent l’hypertrophie ventriculaire gauche (HVG) qui est un puissant facteur prédictif d’événements cardiovasculaires. Ce travail a étudié la fonction ventriculaire gauche dans trois groupes de patients diabétiques hypertendus avec des fonctions rénales différentes. Les variables associées à l’HVG ont été mises en évidence dans cette population afro-caribéenne.

Méthodes. – L’étude ventriculaire gauche a été réalisée par ultrasonographie. Le groupe 1 était composé de 150 patients avec une fonction rénale normale, le groupe 2 a inclus 183 patients avec une dysfonction rénale et le groupe 3, 75 patients en dialyse.

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Keywords: Echocardiography; Dialysis; Type 2 diabetes mellitus; Hypertension; Pulse pressure
1. Introduction

Both diabetes mellitus and end-stage renal disease (ESRD) have been shown to be independently associated with a high cardiovascular risk, and cardiovascular diseases are the leading cause of death among diabetic patients undergoing haemodialysis. A major therapeutic challenge in this population, therefore, is to significantly reduce the impact of cardiovascular risk factors. In the French West Indies island of Guadeloupe, the prevalence of type 2 diabetes is as high as 10.1% of the general population, compared with only 3.6% in the population of continental France [1]. Diabetic nephropathy is the leading cause of ESRD, as shown by a survey estimating a 22% prevalence of diabetes in the population undergoing dialysis [2]; since then, it has increased to an estimated 33%. In Guadeloupe, around 400 patients are receiving renal replacement therapy. As cardiovascular events accounted for the majority of deaths and events in such patients [3], several cardiovascular parameters and indicators have been investigated. It was found that left ventricular hypertrophy (LVH) was a powerful and independent predictor of increased morbidity and mortality [4,5]. In addition, dyslipidaemia and hypertension are both strongly correlated with the left ventricular mass index [6,7].

The objective of the present study was to evaluate left ventricular structure and function in three groups of hypertensive type 2 diabetic patients: group 1 had normal renal function; group 2 had impaired renal function; and group 3 were patients undergoing haemodialysis. Another goal was to assess the factors associated with LVH in each patient group in an Afro-Caribbean diabetic hypertensive population.

2. Subjects and methods

2.1. Study population

This cross-sectional study was conducted in type 2 diabetic patients followed-up in Guadeloupe, all of whom also had hypertension. Group 1 consisted of 150 such patients, with normal renal function, who had been referred by the diabetology unit during the period from January 2003 to December 2007. Some had been referred for cardiovascular symptoms (angina pectoris or dyspnoea). Others were at a high cardiovascular risk, defined as men aged over 45 years, and women aged over 55 years, with a history of diabetes of >5 years’ duration and one additional risk factor: smoking; obesity, defined as body mass index (BMI) >30 kg/m²; or dyslipidaemia, defined as HDL cholesterol <0.35 g/L or LDL cholesterol >1.30 g/L, or triglycerides >2 g/L.

Group 2 included 183 hypertensive type 2 diabetic patients, with renal failure or proteinuria, who had been referred by the nephrology units. Group 3 included 75 hypertensive type 2 diabetic patients undergoing haemodialysis.

2.2. Data collection

Demographic information such as age, gender, weight, height, diabetes duration and familial history of cardiovascular disease was recorded for all patients. Each patient’s history of cardiovascular disease, such as ischaemic heart disease, stroke, heart failure and peripheral artery disease, was also assessed. In addition, BMI (weight/height²) and body surface area (Dubois and Dubois formula) were calculated.

Obesity was defined as a BMI ≥30 kg/m². Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg, or a history of hypertension including the current use of antihypertensive medication.

2.3. Blood pressure measurement

Blood pressure (BP) was measured after cardiac ultrasound examination in the sitting position by a single investigator, using an automated recorder (Welch Allyn) and a suitably sized cuff. The average SBP and DBP measurements were calculated from three readings of each, while pulse pressure (PP) was calculated as SBP–DBP.

2.4. Assessment of renal function

Creatinine clearance (creat Cl) was calculated using the Cockcroft–Gault and the modification of diet in renal disease (MDRD) formulas. Calculation with the Cockcroft–Gault formula was creat Cl (mL/min) = [(140 – age (years) × weight (kg)/creatinine (μmol/L)) × k], in which k = 1.23 for men and 1.04 for women. The calculation with the MDRD was creat Cl (mL/min) = 186 × serum creat−1.154 × (age)−0.203 × 0.742 if female) × (1.21 if African-American).

Renal failure was defined as creat Cl <60 mL/min. Proteinuria was calculated as urinary albuminuria >200 mg/L in the
first morning urine sample. Microalbuminuria was defined as an albuminuria between 20 mg/L and 200 mg/L in the first morning urine sample.

2.5. Echocardiography

Echocardiography was performed by a single expert cardiologist, using a Philips HDI 5000 sonogram system equipped with a P4-2 phased-array probe. The dimensions of the interventricular wall thickness (IVST) and left ventricular posterior wall thickness (PWT) were measured at end-diastole. The left ventricular internal diameter was measured at end-diastole (LVIDd) and end-systole (LVIDs). End-diastolic measurement criteria included the Penn convention [8]. Left ventricular mass (LVM) was calculated as LVM = (1.04 × (IVST + LVIDd + PWT)^3 − LVIDd^3) − 13.6 [8]. This value was then adjusted for height^{2.7} to give the left ventricular mass/height^{2.7} (LVM/H^{2.7}). Cutoff values for LVH were taken as LVM/H^{2.7} >50 g/m^{2.7} in men and >47 g/m^{2.7} in women [9]. Relative wall thickness was defined as (IVST + PWT)/LVIDd [10], which allowed the type of LVH to be determined. Left ventricular fractional shortening (LVFS) was calculated as [(LVIDd−LVIDs)/LVIDd] × 100.

2.6. Statistical analysis

A descriptive analysis of the demographic characteristics of the three patient groups was performed. Mean values and standard deviation (S.D.) were calculated for continuous parameters, and frequencies were used for the categorical variables. The chi-square test and Student’s t test were used to compare ratios and mean values between patient groups. P values <0.05 were considered to be statistically significant.

Multivariate logistic-regression analysis was used in each group to estimate the odds ratios (OR) and their 95% confidence intervals (95% CI) to assess the association between LVH and the explanatory covariates, such as female, age >60 years, obesity, 5-year diabetes duration, 10 mmHg increase in PP and previous cardiovascular disease.

All analyses were performed using the SPSS v15.0 statistical software package (SPSS, Chicago, IL).

3. Results

3.1. Demographic characteristics of the study patients

The demographic characteristics of the three patient groups are presented in Table 1. As expected, serum creatinine and albuminuria increased from group 1 to group 3, while creatinine clearance decreased. Mean creatinine was 74.73 µmol/L for group 1, 144.74 µmol/L for group 2 and 697.52 µmol/L for group 3 (P<0.0001). Taking the three groups altogether, 60% of the patients were female. Also, patients in group 2 were older (67 years) than those in groups 1 and 3 (63 years; P<0.0001). The average diabetes duration increased from group 1 to group 3.
Antihypertensive treatments used by the Guadeloupe hypertensive type 2 diabetic patients according to renal function.

<table>
<thead>
<tr>
<th>Antihypertensive drugs</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>150</td>
<td>22.7</td>
<td>182</td>
<td>28.6</td>
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<tr>
<td>Calcium-channel blockers</td>
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<td>45.3</td>
<td>181</td>
<td>61.9</td>
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<td>Diuretics</td>
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<td>40.7</td>
<td>182</td>
<td>41.8</td>
</tr>
<tr>
<td>ACEI or ARAII</td>
<td>150</td>
<td>7.3</td>
<td>182</td>
<td>15.4</td>
</tr>
<tr>
<td>Central agents</td>
<td>150</td>
<td>7.3</td>
<td>182</td>
<td>15.4</td>
</tr>
</tbody>
</table>

ACEI: angiotensin-converting enzyme inhibitors; ARAII: angiotensin II receptor antagonists.

3, with 11.26 years for group 1, 14.31 for group 2 and 17.11 years for group 3 (P < 0.0001). A similar finding was found for previous cardiovascular disease, with the highest values seen in group 3, those undergoing haemodialysis (9.3% for group 1, 18.6% for group 2 and 43.1% for group 3; P < 0.0001). Mean BMI was higher in non-haemodialysis patients (groups 1 and 2). Prevalence of obesity decreased from group 1 to group 3, with the lowest value seen in the dialysis group (43%, 41% and 19% for groups 1, 2 and 3, respectively; P = 0.001). No significant difference was found between groups in terms of dyslipidaemia or smoking.

SBP was higher in patients in group 2 (147.48 mmHg) than in groups 1 (140.35 mmHg) and 3 (138.92 mmHg) (P < 0.01). DBP was similar across the three groups, while PP was higher in group 2 (66.67 mmHg) compared with group 1 (59.55 mmHg; P < 0.001). As for antihypertensive treatment, calcium-channel blockers were more often prescribed in group 3 (45% in group 1, 62% in group 2 and 71% in group 3; P < 0.0001), while angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists were used by around 80% of those in groups 1 and 2, but by only 51% of patients in group 3 (P < 0.0001; Table 2).

3.2. Echocardiography measurements

Echocardiography findings are shown in Table 3. The mean values of most parameters, including interventricular thickness (IVST), posterior wall thickness (PWT), relative wall thickness (RWT), LVM and left ventricular mass/height².7 (LVM/H².7), increased from group 1 to group 3, with the highest values seen in those undergoing haemodialysis. LVM/H².7 values were 49.00 g/m².7 for group 1, 57.12 g/m².7 for group 2 and 59.75 g/m².7 for group 3.
59.75 g/m^2.7 for group 3 (P < 0.0001). Prevalence of LVH was 70.3% in the dialysis patients, 64.8% in group 2 and 48.3% in group 1 (P = 0.001). LVH was generally more concentric than eccentric in groups 2 and 3 (Fig. 1).

### 3.3. Regression analysis of risk factors for LVH

Table 4 shows the adjusted OR for developing LVH. The adjusted variables were gender, age >60 years, diabetes duration >5 years, a 10 mmHg increment in PP and a history of cardiovascular disease.

The variables associated with LVH were: obesity, in group 1 (OR: 1.09 [0.83–1.44]; P < 0.0001); and obesity (OR: 3.47 [1.64–7.32]; P = 0.001) and PP (OR: 1.64 [1.28–2.10]; P < 0.0001) in group 2. In patients undergoing haemodialysis (group 3), obesity was not associated with LVH, and the OR for PP was 1.42 [1.06–1.91] (P = 0.02).

### 4. Discussion

To our knowledge, this is the first study carried out in an Afro-Caribbean population of hypertensive type 2 diabetic patients to demonstrate that left ventricular hypertrophy is increased in haemodialysis patients and that the factors associated with LVH differ according to renal status.

Black patients are more likely to have both diabetes and hypertension, the leading causes of renal failure. In addition, it has been demonstrated that these patients have a greater risk of end-stage renal disease than do white patients, regardless of diabetic and hypertensive status [11]. Several studies of patients undergoing haemodialysis have demonstrated that the presence of LVH is a strong and independent risk factor for cardiovascular death [7,12]. Moreover, in African-Americans, LVH contributes more to the risk of cardiovascular mortality than it does in white Americans [13]. For this reason, LVH should be routinely monitored in such a population to allow for adjustments in therapeutic interventions aimed at reducing mortality and cardiovascular morbidity.

Volume and pressure overload can exacerbate LVH in end-stage renal disease patients treated by haemodialysis, and a cumulative effect of concentric hypertrophy due to hypertension and arteriosclerosis, and eccentric hypertrophy, due to other factors such as anaemia, fluid overload and arteriovenous fistulae, have also been observed [14]. Our echocardiography findings, including an increased LV wall thickness and mass, are concordant with those found by London et al. [15] in their population undergoing haemodialysis. Kawada et al. [16] also showed that haemodialysis was independently associated with increased LV wall thickness and LV mass index.

The findings were similar in our hypertensive type 2 diabetic population undergoing haemodialysis, with values of LV mass/height^2.7 and percentages of LVH that increased from group 1 (with normal renal function) to group 2 (with renal failure) and group 3 (undergoing haemodialysis).

However, while there was a discrepancy in antihypertensive treatments across our patient groups, this cannot explain the observed differences in LVH. Calcium-channel blockers were more often prescribed in the end-stage renal disease group,
whereas our non-dialysis patients were more often treated with ACE inhibitors and angiotensin II receptor antagonists. Nevertheless, all of these medications are considered to be similarly effective for reducing LV mass [17].

However, blood pressure control appears to be more difficult to achieve in black populations compared with Caucasians. Riehle et al. [18], in a population of 19,864 patients, found that diabetic hypertensive African-American were less likely than white Americans to reach BP levels <130/80 mmHg, despite taking more antihypertensive medication prescriptions, and more ACE inhibitors and angiotensin II receptor antagonists, than Cauasian Americans.

Sheats et al. [19], in a population of 7795 hypertensive adults, demonstrated that BP was less controlled in African-Americans than in Caucasians despite similar treatment intensity, although black Americans more frequently received diuretics and calcium-channel blockers than did white Americans.

As for LV diastolic diameters, this was found to be similar across our three study groups, whereas it was increased in the dialysis groups in the London et al. and Kawada et al. studies [13,14].

This may be explained by the fact that our study population exclusively comprised hypertensive type 2 diabetic patients. Previous studies have shown that LV fractional shortening is often preserved in dialysis patients [16,20,21], and we obtained similar findings in our diabetic hypertensive population. LVH was also more eccentric in our hypertensive type 2 diabetics with normal renal function, which is in accord with the de Simone findings, which compared 475 hypertensive patients with 164 normotensive adults [9].

In our group 2 with renal dysfunction and group 3 with end-renal stage disease undergoing haemodialysis, concentric hypertrophy was more frequently found than eccentric hypertrophy, as has been reported elsewhere [7].

The parameters associated with LVH were not similar across our three groups. It was associated with obesity in our hypertensive type 2 diabetic patients with normal renal function and in those with impaired renal function, but not undergoing haemodialysis. BMI is the most potent risk factor of LVH in both male and female hypertensive patients, and in populations including normotensive and hypertensive subjects [9]. The risk of having LVH is twofold higher in obese hypertensive men than in those of normal weight, and threefold in women who are both obese and hypertensive [9].

In contrast, however, a recent work by Eguchi et al. [22] showed that type 2 diabetes was independently associated with an increased LV mass, and no interaction was observed between LVH and BMI. Yet, Kawada et al. [16] found that the significant risk factors for the LV mass index were BMI, age, haemodialysis and hypertension. In the present study, LVH was not associated with obesity in the group undergoing haemodialysis. This could be explained by the lower BMI in this group compared with the two other groups. In fact, a lower BMI is usually found in patients undergoing haemodialysis [15,16].

An increase of 10 mmHg of pulse pressure was associated with LVH in our patients with impaired renal function and in those undergoing haemodialysis. Tosawa et al. [23] demonstrated that, at any mean arterial pressure level, patients undergoing haemodialysis had higher PP values than those in the control groups with normal renal function. PP was demonstrated to increase cardiovascular risk in diabetics and patients undergoing haemodialysis [24]. In a study conducted in 2005 in 80 type 2 diabetic dialysis patients in Guadeloupe, PP allowed identification of patients with significant preexisting cardiovascular disease, with an area under the ROC curve of 0.71 [25].

One limitation of our present study is the number of patients in the group undergoing haemodialysis, which was smaller than in the two other groups. However, the sample size of our hypertensive type 2 diabetic patients is in accordance with the dialysis population of Guadeloupe (400 patients).

The cross-sectional design of our study is another limitation. On the other hand, one strength of our study is that it is a comparative study based on the highly reproducible and rigorous methodology of echocardiography. In addition, it is the first such study to be carried out in hypertensive type 2 diabetic patients in the French West Indies. Our results show that, to reduce LVH in hypertensive diabetic patients, obesity and pulse pressure are the parameters that need to be particularly followed, as these are the risk factors for LVH in such a population. Losing weight should be recommended in patients with either normal or impaired renal function (but no haemodialysis). For this reason, ACE inhibitors or angiotensin II receptor antagonists and calcium-channel blockers, which have demonstrated effects on LVH and on reducing aortic pulse wave velocity, should be prescribed as the first-line treatment in this patient population.

In conclusion, our study confirms that, in a population of Afro-Caribbean hypertensive type 2 diabetic patients, renal failure is associated with an increased LV mass/height ratio, with the highest values found in those undergoing haemodialysis. In addition, it appears that the factors associated with LVH differ according to the renal-function profile. These factors are: obesity in patients with normal kidney function; obesity and an increase of pulse pressure in those with kidney dysfunction; and an increase of pulse pressure in those undergoing haemodialysis. These findings need to be taken into account in the follow-up of such patients, and all attempts should be made to reduce these factors in these patients as well.

5. Conflict of interests

The authors declare no conflict of interests with this study.

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References


