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**Long-term renal survival in malignant hypertension**

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**Abstract**

**Background.** Some studies have shown an improvement in the prognosis of patients with essential malignant hypertension (MHT), but data about long-term outcome and prognostic factors of these patients are scarce.

**Methods.** We performed a single-centre retrospective analysis of 197 patients with MHT, diagnosed in the period 1974–2007.

**Results.** Incidence of MHT remained stable along the different periods of the study. Renal damage at presentation was common (63% of patients) but renal function improved or remained stable after diagnosis in a majority of patients. The probability of renal survival was 84 and 72% after 5 and 10 years, respectively. Diagnosis during the first period (1974–85) of the study, previous chronic renal impairment, baseline renal function and proteinuria,
Malignant hypertension (MHT) is defined by very high blood pressures (BP) accompanied by bilateral haemorrhages or exudates, or both, with or without papilloedema in funduscopic examination. Although some studies reported a decrease in the incidence of MHT in recent decades [1], other investigations have not confirmed this trend [2–4]. Earlier clinical descriptions of MHT reported a dismal prognosis, with a very low patient survival [5–7]. The prognosis started to improve after 1970, with the development of modern antihypertensive drugs. Some series published in those years reported renal and patient survival of 50 and 75%, respectively, at 5 years [8]. The introduction of calcium channel blockers (CCB) and of drugs that block the renin–angiotensin system (RAS) after 1980 was followed by a further improvement of prognosis, with renal and patient survival of 81 and 90%, respectively, at 5 years [9–14].

Several clinical and analytical parameters at presentation have shown a significant prognostic influence. Among them, the degree of renal function and the value of proteinuria at presentation, Afro-American ethnicity and a secondary aetiology of MHT (in opposition to malignized essential hypertension) have confirmed this negative prognostic impact along several clinical studies [13,15,16]. Nevertheless, very few have investigated the influence of clinical and analytical variables throughout follow-up on the long-term outcome of MHT patients. This issue is particularly relevant considering that, nowadays, the majority of patients remain fortunately alive after the diagnosis and treatment of MHT; the identification of those factors that would influence the long-term outcome of renal function should be extremely important in order to avoid the need for chronic maintenance therapy.

The aims of the present retrospective study are to report the long-term outcome of renal function in a cohort of 197 patients with essential MHT in whom a long-term follow-up was performed and to identify those clinical and biochemical factors having an influence on the final results. In addition, we aimed to analyse possible differences and historical trends along the different periods of the study. The primary outcome was the improvement or stabilization of renal function after the diagnosis of MHT. Major secondary outcomes included the need for maintenance dialysis, cardiovascular events and all-cause mortality.

**Materials and methods**

This retrospective study was performed in a single centre, Hospital 12 de Octubre, Madrid, Spain. Hospital 12 de Octubre is a tertiary hospital attending a population that has oscillated between 650,000 and 900,000 persons since its foundation.

**Patients**

We performed a retrospective analysis of patients with essential MHT diagnosed in our hospital in the period September 1974–December 2007. The diagnosis of MHT was based on the detection of very high BP accompanied by a hypertensive retinopathy Grade III or IV.

We initially obtained a list of all of the patients who had been seen with a diagnosis of MHT at our hospital during the above referred period. The case records of all these patients were examined in order to assure that the diagnosis of MHT was correctly established, according to the diagnostic criteria referred above. Three hundred and twenty-nine patients met these criteria. All the cases (102 patients) in whom a diagnosis of secondary MHT was established were excluded from the study. Three patients died during the initial admission because of stroke (two patients) and uraemic complications (one patient). Twenty-seven patients did not perform any follow-up visit after hospital discharge, whereas regular follow-up after hospital discharge was available in the remaining 197. The date of hospital admission with the diagnosis of MHT was established as the baseline point for each patient. Mean follow-up was 93 ± 88 months.

Fifty-two patients (26%) were lost to follow-up after a mean follow-up of 60 ± 63 months. Their mean serum creatinine (Scr) and proteinuria in the last visit were 1.6 ± 1.2 mg/dL and 0.5 ± 1.2 g/24 h, respectively, without significant differences with respect to the remaining patients. Their data were censored at the last visit and included for the analysis.

**Data collection**

Demographic, clinical and analytical data were compiled from medical records. All the cardiovascular events (myocardial infarction, unstable angina, heart failure, atrial fibrillation and stroke) were recorded, independently of whether hospitalization was required or not.

Estimated glomerular filtration rate (eGFR) was calculated by the modification of diet in renal disease-4 formula (MDRD-4) equation.

For each patient, an average systolic blood pressure (SBP) and diastolic blood pressure (DBP) was determined for each 6-month block during follow-up; the averages of every 6-month period SBP and DBP are presented by the time-averaged SBP and DBP. Proteinuria during follow-up was measured by 24-h urine protein collection. Although protein/creatinine ratio could have been a more reliable marker of proteinuria than 24-h proteinuria, it was impossible to retrospectively obtain the data required to calculate this ratio in patients diagnosed before 1990. In a similar manner to SBP and DBP, the time-averaged proteinuria represents an average of the mean of every 6-month period’s proteinuria measurements.

Complete therapy was carefully recorded, both at admission and during follow-up. Oral antihypertensive drugs prescribed to every patient were grouped into the following classes: RAS blockers (angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers), CCB, beta blockers (BB) and diuretics. Patients were censored at the start of renal replacement therapy, death or lost to follow-up.

**Outcome**

The primary outcome of the study was the improvement or stabilization of renal function after the diagnosis of MHT. Major secondary outcomes included the need for maintenance dialysis, cardiovascular events and all-cause mortality.
Definitions

The improvement or stabilization of renal function was defined by a Scr that did not increase >0.3 mg/dL during follow-up in patients with a baseline Scr <1.5 mg/dL, >0.5 mg/dL in those with a baseline Scr 1.5–2.5 mg/dL and >0.7 mg/dL in patients with a baseline Scr >2.5 mg/dL. Patients were grouped according to the presence of improvement or stabilization of renal function during follow-up (Group 1) or renal function worsening (Group 2).

Renal impairment was defined by an eGFR lower than 60 mL/min/m². Microhaematuria was defined by the presence of at least five erythrocytes per high power field in urinary sediment examination and proteinuria by a urinary protein excretion higher than 0.3 g/24 h.

In order to analyse if the incidence, clinical presentation and prognosis of essential MHT had changed over time, the whole period of the study (September 1974–December 2007) was divided into three different periods: 1974–85, 1986–96 and 1997–2007.

Statistical analysis

Clinical characteristics at presentation and patient survival were analysed in the cohort of 227 patients diagnosed of essential MHT. Long-term outcome analyses were confined to the 197 patients in whom data about follow-up were available. Normally distributed variables are displayed as mean ± standard deviation or 95% confidence interval and compared using Student’s t-test, Fisher’s test, one-way analysis of variance or Pearson’s correlation coefficients. Categorical variables are expressed as percentage and compared with chi-square test. The probability of survival with improved or stable renal function after initial admission, as well as survival without chronic dialysis and patient survival, was calculated by means of Kaplan–Meier analysis and curves were compared with the use of the log-rank test. Cox proportional hazard model was performed to explore the influence of several variables on the occurrence of survival. Only variables being significant in univariate analysis were included by forward stepwise entry into the multivariate model.

A P-value of <0.05 was considered significant. Statistical analysis was performed with the SPSS software (version 15.0 for Windows).

Results

Presentation

The most relevant clinical characteristics at baseline are shown in Table 1. Almost all the patients were Caucasians (220 patients, 96.9%); 6 (2.6%) patients were Black and 1 (0.4%) was Oriental.

|                  | All patients (N = 227) | Follow-up patients (N = 197) | Group 1 (N = 149) | Group 2 (N = 48) | P-value*
|------------------|------------------------|-----------------------------|-------------------|-----------------|--------
| Age (years)      | 49.2 ± 13.4 (19–88)    | 49.1 ± 13.1 (19–88)         | 49.7 ± 12.9 (21–88) | 47.3 ± 13.6 (19–76) | 0.272   |
| Gender (M/F)     | 144/83                 | 125/72                      | 92/57             | 33/15           | 0.381   |
| Known hypertension (%) | 145 (63.9) | 126 (64)                  | 94 (63.1)        | 32 (66.7)       | 0.653   |
| Smokers (%)      | 77 (34.1)              | 71 (36)                     | 56 (37.6)        | 15 (31.3)       | 0.427   |
| Known chronic kidney disease (%) | 19 (8.4) | 16 (8.1)                  | 5 (3.4)          | 11 (23)         | 0.000   |
| SBP (mmHg)       | 207.8 ± 32.4 (175–280) | 206.1 ± 32.4 (170–280)      | 204.0 ± 32.8 (175–280) | 212.6 ± 30.6 (180–280) | 0.110   |
| DBP (mmHg)       | 125.3 ± 21.4 (115–190) | 124.2 ± 21.2 (110–190)      | 123.4 ± 21.4 (114–180) | 126.4 ± 20.6 (122–190) | 0.398   |
| BMI (kg/m²)      | 29.7 ± 6.6 (16.8–55.4) | 29.5 ± 6.1 (16.7–51.8)      | 29.8 ± 5.8 (17.3–51.8) | 26.4 ± 7.5 (16.7–42.8) | 0.092   |
| Scr (mg/dL)      | 2.49 ± 2.9 (0.6–24.9)  | 2.53 ± 3.0 (0.6–24.9)       | 1.61 ± 1.0 (0.6–6.37) | 5.39 ± 4.8 (0.9–24.9) | 0.000   |
| GFR (mL/min/m²)  | 49.4 ± 27.0 (2–144)    | 49.8 ± 27.3 (2–144)         | 57.3 ± 24.3 (7–144) | 26.4 ± 22.4 (2–99) | 0.000   |
| Proteinuria (g/day) | 0.83 ± 1.96 (0–9) | 0.8 ± 2.0 (0–9)           | 0.36 ± 0.6 (0–5)  | 2.27 ± 3.7 (0–9) | 0.002   |
| Microhaematuria (%) | 58 (25.6)           | 52 (26.5)                  | 24 (16%)         | 30 (62.5)       | 0.000   |

*P-value refers to differences between Groups 1 and 2.

Table 1. Clinical characteristics at baseline

Treatment

All the patients were treated rapidly and aggressively to decrease BP to values lower than 140/90 mmHg. Oral antihypertensive drugs were started immediately after admission, RAS blockers (72%), diuretics (49%), CCB (38%) and BB (33%) being the most commonly prescribed agents. Patients continued to receive these oral antihypertensive agents after hospital discharge and most of them needed more than one class of antihypertensive drugs to control BP; the mean number of antihypertensive drugs prescribed during follow-up was 2.9 ± 1.1, ranging from 0 to 6.

Renal involvement

Renal function impairment was detected at admission in 144 patients (63%). Among them, 125 (85%) had an acute worsening of renal function. Fifteen patients (6.6%) required haemodialysis treatment shortly after their admission because of severe renal impairment and uraemic symptoms. Of them, seven (46.7%) had previous chronic renal impairment. Only two patients (13%) partially recovered the sufficient renal function to abandon dialysis.

Long-term renal function outcome

Long-term outcome of renal function was analysed in 197 out of the 227 patients in whom follow-up was available. In 149 patients (75.6%) (Group 1), renal function showed an improvement or stabilization during follow-up, whereas it deteriorated in the remaining 48 (24.3%) (Group 2). As it is shown in Table 1, patients of Group 2 had a significantly worse renal function at baseline, higher proteinuria and a more common finding of microhaematuria than Group 1 patients.

The evolution of clinical parameters during follow-up is expressed in Table 2. Group 1 patients showed a better control of BP and had a mean proteinuria significantly lower than those in Group 2. The number of Group 1 patients treated with RAS blockers, CCB and BB was higher...
Table 3. Univariate and multivariate analyses of renal outcome (improvement or stabilization of renal function)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate OR (95% CI)</th>
<th>P-value</th>
<th>Multivariate OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Period of diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1974–85</td>
<td>3.21 (1.32, 7.81)</td>
<td>0.01</td>
<td>4.48 (0.81, 24.7)</td>
<td>0.085</td>
</tr>
<tr>
<td>1986–96</td>
<td>1.67 (0.69, 4.04)</td>
<td>0.253</td>
<td>1.41 (0.31, 6.42)</td>
<td>0.65</td>
</tr>
<tr>
<td>1997–2007</td>
<td>0.92 (0.77, 0.97)</td>
<td>0.047</td>
<td>0.95 (0.82, 1.12)</td>
<td>0.41</td>
</tr>
<tr>
<td>Previous chronic kidney disease</td>
<td>8.56 (2.80, 26.16)</td>
<td>0.000</td>
<td>2.98 (0.34, 25.85)</td>
<td>0.321</td>
</tr>
<tr>
<td>baseline Scr (mg/dL)</td>
<td>1.956 (1.53, 2.50)</td>
<td>0.000</td>
<td>1.023 (0.52, 2.00)</td>
<td>0.946</td>
</tr>
<tr>
<td>baseline GFR (mL/min/1.73 m²)</td>
<td>0.942 (0.924, 0.961)</td>
<td>0.000</td>
<td>0.977 (0.93, 1.02)</td>
<td>0.350</td>
</tr>
<tr>
<td>Baseline proteinuria (g/day)</td>
<td>3.414 (2.08, 5.60)</td>
<td>0.000</td>
<td>1.639 (0.82, 3.24)</td>
<td>0.156</td>
</tr>
<tr>
<td>Microhaematuria (%)</td>
<td>8.425 (3.96, 17.88)</td>
<td>0.000</td>
<td>1.854 (0.49, 6.90)</td>
<td>0.358</td>
</tr>
<tr>
<td>Follow-up SBP (mmHg)</td>
<td>1.033 (1.01, 1.05)</td>
<td>0.001</td>
<td>1.032 (0.97, 1.08)</td>
<td>0.235</td>
</tr>
<tr>
<td>Follow-up DBP (mmHg)</td>
<td>1.04 (1.01, 1.06)</td>
<td>0.007</td>
<td>0.938 (0.86, 1.02)</td>
<td>0.136</td>
</tr>
<tr>
<td>Follow-up proteinuria (g/day)</td>
<td>3.91 (2.29, 6.67)</td>
<td>0.001</td>
<td>2.722 (1.59, 4.64)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

- P-value refers to differences between Groups 1 and 2.

than in Group 2, but this difference did not reach statistical significance.

As shown in Table 3, the following factors were significantly associated with an increased risk of renal function worsening during follow-up by univariate analysis: diagnosis during the first period (1974–85); previous chronic kidney disease; baseline renal function (Scr and eGFR) and proteinuria; presence of microhaematuria; and SBP, DBP and proteinuria during follow-up. By multivariate analysis, only follow-up proteinuria (OR, 2.72; 95% CI, 1.59–4.64) maintained its significance as risk factor associated with such unfavourable prognosis. Univariate and multivariate analyses performed after the exclusion of those patients with known chronic kidney disease (n = 16) showed similar results: follow-up proteinuria (OR, 3.37; 95% CI, 1.78–6.38) was the only factor significantly associated with the risk of renal function worsening.

Patients were stratified according to the mean time-averaged proteinuria during follow-up in four groups: proteinuria <0.5 g/24 h (n = 151), 0.5–1 g/24 h (n = 10), 1–2 g/24 h (n = 17) and >2 g/24 h (n = 19). As shown in Figure 1, the probability of renal survival (estimated on the basis of an improvement or stabilization of Scr during follow-up) was significantly higher among those patients in whom proteinuria had been maintained below 0.5 g/24 h in comparison with patients with proteinuria higher than 0.5 g/24 h (P < 0.00001). Renal survival for patients with proteinuria <0.5 g/24 h was 100, 100, 95 and 85% after 1, 5, 10 and 20 years of follow-up, in comparison with 86, 50, 8 and 0% at the same periods of follow-up for patients with proteinuria >2 g/24 h.

**Chronic dialysis**

Of the 48 patients with progressive renal function worsening (Group 2), 40 (83.3%) finally needed maintenance dialysis. By multivariate analysis, only Scr at baseline (OR, 1.66; 95% CI, 1.05–2.62) and follow-up proteinuria (OR, 3.36; 95% CI, 1.75–6.45) showed a significant association with the risk of chronic dialysis. Renal survival without chronic dialysis for the whole group of patients was 90, 84, 77 and 68% after 1, 5, 10 and 20 years of follow-up, respectively.

**Cardiovascular events and mortality**

Forty-six cardiovascular events appeared during follow-up in 33 patients: 24 cerebrovascular events, 11 acute coronary syndromes, 5 episodes of heart failure and 6 severe peripheral arterial disturbances. Smoking and SBP at pre-
sentation were the only factors that significantly predicted the risk of cardiovascular events, both in univariate and multivariate analyses (OR, 2.73; 95% CI, 1.24–6.02 for smoking and OR, 1.01; 95% CI, 1.00–1.02 for SBP).

Of the 227 patients with essential MHT, 9 (3.9%) died, 3 of them during the initial admission (stroke in 2, uraemic complications in 1) and 6 during follow-up. By Kaplan–Meier analysis, patient survival for the whole cohort of patients with essential MHT was 97, 96, 96 and 91% after 1, 5, 10 and 20 years of follow-up, respectively.

Incidence of MHT and changes over time

The incidence of new patients with essential MHT remained stable during the different periods of the study. Mean incidence was 0.80 cases per 100 000 persons per year in the period 1974–85, 0.85 in the period 1986–96 and 0.94 in the period 1997–2007.

As shown in Table 4, BP values, the number of patients treated with diuretics and the number of patients who started chronic dialysis were significantly higher among those diagnosed in the first period of the study. On the contrary, the number of patients treated with RAS blockers and CCB and the number of those who improved or stabilized their renal function were significantly higher among those diagnosed in the second and third periods.

Discussion

Although some studies have reported a decreasing incidence of MHT in the last decades [1], others have not confirmed this tendency [2–4]. Our study agrees with the latter, showing a stable incidence of MHT throughout the duration of the study (1974–2007).

Earlier reports depicted a very poor renal prognosis for MHT patients, with an important proportion of surviving patients needing chronic dialysis or transplantation. Our study confirms that renal involvement is a major component of essential MHT, with a majority (63%) of patients presenting with an acute derangement of renal function. However, renal prognosis of our patients exhibits a clearly


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<tbody>
<tr>
<td>Incidence (new patients/100 000 persons per year)</td>
<td>0.80</td>
<td>0.85</td>
<td>0.94</td>
<td>0.725</td>
</tr>
<tr>
<td>Age at presentation (years)</td>
<td>46.3 ± 12.7 (19–81)</td>
<td>50 ± 13.2 (21–88)</td>
<td>51.1 ± 14 (22–82)</td>
<td>0.083</td>
</tr>
<tr>
<td>Patients &gt;65 years (%)</td>
<td>4 (5.8)</td>
<td>10 (11.5)</td>
<td>16 (22.5)</td>
<td>0.012*</td>
</tr>
<tr>
<td>SBP at presentation (mmHg)</td>
<td>216.5 ± 35.2 (150–280)</td>
<td>200.6 ± 30.4 (150–280)</td>
<td>208.2 ± 30.2 (160–280)</td>
<td>0.009*</td>
</tr>
<tr>
<td>DBP at presentation (mmHg)</td>
<td>131.8 ± 17.4 (100–160)</td>
<td>121.3 ± 21.5 (84–190)</td>
<td>123.7 ± 23.5 (79–180)</td>
<td>0.007*</td>
</tr>
<tr>
<td>Scr at presentation (mg/dL)</td>
<td>2.97 ± 3.1 (0.6–14.9)</td>
<td>2.46 ± 3.1 (0.7–24.9)</td>
<td>2.07 ± 2.2 (0.6–14)</td>
<td>0.189</td>
</tr>
<tr>
<td>SBP during follow-up (mmHg)</td>
<td>154.8 ± 23.1 (119.4–220)</td>
<td>146.6 ± 15.1 (120–191.7)</td>
<td>146.1 ± 20.7 (110–203.3)</td>
<td>0.032*</td>
</tr>
<tr>
<td>DBP during follow-up (mmHg)</td>
<td>97.9 ± 13.6 (70–150)</td>
<td>88.9 ± 9.9 (72.5–129.7)</td>
<td>85.9 ± 12 (69–120)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Proteinuria during follow-up (g/day)</td>
<td>0.90 ± 1.8 (0–7.7)</td>
<td>0.65 ± 1.3 (0–6.27)</td>
<td>0.35 ± 0.7 (0–3.4)</td>
<td>0.129</td>
</tr>
<tr>
<td>RAS blockers (%)</td>
<td>11 (18.9)</td>
<td>59 (74.6)</td>
<td>52 (86.6)</td>
<td>0.000*</td>
</tr>
<tr>
<td>BB (%)</td>
<td>20 (34.5)</td>
<td>22 (27.8)</td>
<td>20 (33.3)</td>
<td>0.663</td>
</tr>
<tr>
<td>CCB (%)</td>
<td>2 (3.4)</td>
<td>34 (43)</td>
<td>35 (58.3)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Diuretics (%)</td>
<td>37 (63.8)</td>
<td>22 (27.8)</td>
<td>31 (51.7)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Patients who improved or stabilized renal function (%)</td>
<td>37 (63)</td>
<td>61 (77%)</td>
<td>51 (85%)</td>
<td>0.025*</td>
</tr>
<tr>
<td>Dialysis (%)</td>
<td>19 (32.8)</td>
<td>14 (17.7)</td>
<td>7 (11.7)</td>
<td>0.013*</td>
</tr>
<tr>
<td>Cardiovascular events (%)</td>
<td>10 (17.2)</td>
<td>12 (15.2)</td>
<td>8 (13.3)</td>
<td>0.840</td>
</tr>
<tr>
<td>Death (%)</td>
<td>3 (5.2)</td>
<td>2 (2.5)</td>
<td>2 (3.3)</td>
<td>0.707</td>
</tr>
</tbody>
</table>

*P < 0.05, significant difference between the first period (1974–85) and second and third periods.

Fig. 1. Renal survival (improvement or stabilization of renal function) according to mean proteinuria during follow-up (log-rank test, P < 0.00001). Solid line, all patients. Filled squares, patients with proteinuria <0.5 g/24 h. Filled diamonds, patients with proteinuria between 0.5 and 1 g/24 h. Filled triangles, patients with proteinuria between 1 and 2 g/24 h. Multiplication symbol, patients with proteinuria >2 g/24 h.
favourable change in comparison with classic series. Renal function improved or remained stable after diagnosis in the majority of our patients and the probability of renal survival for the whole cohort (estimated on the basis of an improvement or stabilization of Scr during follow-up) was 84 and 72% after 5 and 10 years of follow-up, respectively. Furthermore, a tendency to better results regarding renal prognosis was observed along the last periods of our study.

With regard to long-term renal survival of MHT patients, previous studies underlined the prognostic value of renal impairment at presentation as well as the beneficial influence of a tight control of BP during follow-up [13,15,16]. Our study also confirms that the severity of renal failure at presentation and a worse BP control during follow-up are detrimental prognostic factors for renal survival. However, a new parameter, not analysed in previous studies, emerged in ours as the most important prognostic factor for renal survival: mean proteinuria during follow-up. In fact, multivariate analysis showed that mean proteinuria during follow-up was the only significant prognostic parameter for the improvement or stabilization of renal function after initial diagnosis.

The crucial role of follow-up proteinuria among our patients agrees with the important prognostic influence that residual proteinuria has been shown to play in several chronic renal diseases [17,18] and it is particularly interesting with regard to the choice of antihypertensive agents [19]. Many experimental and clinical studies have demonstrated that RAS blockers share a specific anti-proteinuric effect and that the beneficial effect that these agents have shown in diabetic and non-diabetic nephropathies [17,19,20] are mainly related to a reduction in proteinuria. Our data strongly suggest that the treatment of MHT patients should be based on RAS blockers, in order to provide a reassuring low amount of proteinuria during follow-up in addition to a strict control of BP. The involvement of RAS exacerbation in the pathogenesis of MHT [21] would increase the indication of these agents in MHT patients. On the other hand, it is tempting to speculate that the improvement in the long-term prognosis of MHT could be related to the availability of RAS blockers in recent decades. Whereas only a few patients in the first study period (1974–85) were treated with RAS blockers, the majority of patients received these agents in the second (1986–96) and third (1997–2007) periods in which renal prognosis significantly improved.

Our study has several limitations, derived from its retrospective design. We cannot rule out the influence of confounding, non-identified factors on the long-term outcome of our cohort. Almost all the patients were Caucasians and, therefore, our results might not be applicable to patients with MHT from other races. On the other hand, the main strength of our study relies on the systematic follow-up of our patients and the disposal of their renal parameters throughout evolution.

Conclusion

In conclusion, patient and renal survival in MHT have improved in recent years and mean proteinuria during follow-up emerges as a very important prognostic factor for long-term renal outcomes. Taking into account that RAS activation is a key pathogenic mechanism in MHT and that RAS blockers have specific anti-proteinuric properties, treatment of MHT patients should be mainly based on this type of agents, with the addition of other antihypertensive agents, if required, to maintain a strict control of BP during follow-up.

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Conflict of interest statement. None declared.

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Sympathetic activity in chronic kidney disease patients is related to left ventricular mass despite antihypertensive treatment

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Abstract

Background. Chronic kidney disease (CKD) patients often have sympathetic hyperactivity, which contributes to the pathogenesis of hypertension and cardiovascular organ damage. Angiotensin-converting enzyme (ACE) inhibitors (ACEi) and angiotensin II receptor blockers (ARB) reduce sympathetic hyperactivity. Ideally, treatment should eliminate the relation between sympathetic activity and organ damage. The aim of the present study is firstly to compare left ventricular mass (LVM) of CKD patients using chronic ACEi or an ARB with LVM of controls. Secondly, we determine whether previously found muscle sympathetic nerve activity (MSNA) and arterial blood pressure during follow-up are predictive for the presence of increased LVM.

Methods. We restudied 20 CKD patients and 30 healthy volunteers matched for age. Sympathetic nerve activity was quantified by the microneurography (MSNA). Arterial blood pressure was the mean of office blood pressure measurements. LVM was quantified by magnetic resonance imaging (MRI) without contrast.

Results. The period between MSNA and MRI measurements was 9 ± 3 years. All patients were treated according to guidelines with an ACEi or an ARB. In CKD patients, mean systolic and diastolic arterial pressure were 129 ± 10 and 84 ± 5 mmHg, respectively, during follow-up. In patients, as compared to controls, LVM was 93 ± 16 versus 76 ± 18 g, LVM index 30 ± 5 versus 24 ± 4 g/m² and mean wall thickness 11 ± 2 versus 9.0 ± 1 mm (all P < 0.01). Moreover, MSNA was related to LVM (r = 0.65, P < 0.002), LVM index (r = 0.46, P < 0.03) and LV mean wall thickness (r = 0.84, P < 0.001).

Conclusions. In conclusion, the present study demonstrates that measures of LVM in CKD patients are greater than in healthy controls, despite a well-controlled blood pressure in the patients. Moreover, there is a positive relationship between these measures of LVM and MSNA, assessed years before, despite a standard antihypertensive treatment. These results support the notion that additional sympatholytic therapy could be beneficial.

Keywords: antihypertensive treatment; cardiovascular damage; chronic kidney disease; left ventricular mass; muscle sympathetic nerve activity

Introduction

Chronic kidney disease (CKD) is often accompanied by sympathetic hyperactivity [1–6]. Sympathetic nerve activity is related to left ventricular mass (LVM) and poor clinical outcome in patients with hypertension and in patients with chronic heart failure [2,7–11]. This effect is at least partially independent of its effect on blood pressure. Reduction of sympathetic hyperactivity may improve prognosis.

Zoccali and co-workers were the first to show that, also in end-stage renal disease (ESRD), sympathetic activity is related to clinical outcome [11]. In another study, they reported in a cohort of dialysis patients that plasma noradrenaline levels were related to the risk of having increased LVM [12]. Campese and co-workers showed in experimental settings that kidney injury is central in the