Background.

The role of cardiovascular factors in predicting renal outcome has not been extensively elucidated. In this study, we report a prospective evaluation of the impact of left ventricular hypertrophy (LVH) on outcome in non-diabetic patients with chronic kidney disease (CKD).

Methods. We studied 144 patients (99 men; age 62 ± 14 years) with stage 3–4 CKD, with baseline assessment of LVH using echocardiography. LVH was defined as left ventricular mass index (LVMI) ≥ 116 g/m² in men or ≥ 90 g/m² in women. LVH progression was defined as an increase in LVMI of at least 15% over a 3-month period.

Results. LVH was present in 81–86% of patients after dialysis [3]. In contrast to the above findings, Farkouh et al. found that a single HD treatment produced no significant change in the cTnI level’s diagnostic classification [5]. We found that 94% of patients had stable cTnI levels without change in classification after dialysis with a high-flux membrane. Clinically, this is evidence that one does not need to be concerned with the timing of blood sampling in relation to HD when following TnI levels for a patient suspected of having an ACS.

Conclusion

In conclusion, in asymptomatic ESRD patients, most patients have a normal TnI level but many do have slight elevations in TnI using a new-generation assay. Levels remained stable over a 3-month period in most patients. Very few patients had elevations in the AMI range. HD treatment does not appear to affect the level. The significance of the low-level elevations seen in this study will remain unclear until further outcome studies are performed.

Conflict of interest statement. None declared.

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Is left ventricular hypertrophy a powerful predictor of progression to dialysis in chronic kidney disease?

Ernesto Paoletti¹, Diego Bellino¹, Anna Maria Gallina², Marco Amidone¹, Paolo Cassottana³ and Giuseppe Cannella¹

¹Divisione di Nefrologia, Dialisi e Trapianto, ²Dipartmento di Scienze della Salute dell’Università and ³Divisione di Cardiologia, Azienda Ospedaliera Universitaria San Martino, Genova, Italy

Correspondence and offprint requests to: Ernesto Paoletti; E-mail: ernesto.paoletti@hsanmartino.it

Abstract

Background. The role of cardiovascular factors in predicting renal outcome has not been extensively elucidated. Herein, we report a prospective evaluation of the impact of left ventricular hypertrophy (LVH) on outcome in non-diabetic patients with chronic kidney disease (CKD).

Methods. We studied 144 patients (99 men; age 62 ± 14 years) with stage 3–4 CKD, with baseline assessment of LVH...
of left ventricular mass index (LVMi) by echocardiography, estimated glomerular filtration rate (eGFR) by MDRD equation, 24-h blood pressure profile and 24-h proteinuria. Combined end point was progression to ESRD requiring dialysis, or death within 5 years.

**Results.** Forty-nine patients (34%) progressed to dialysis, 24 (17%) died, 57 (39%) were dialysis-free after 5 years and 14 were lost to follow-up. Multivariate Cox proportional hazards analysis showed that increased LVMi (HR 1.28, 95% CI 1.17–1.40 for each 10-g/m² increase, P < 0.0001) and reduced eGFR (5% risk increase for each 1-mL/min reduction, P = 0.027) were the significant predictors of the combined end point in stage 3 CKD patients, whereas LVMi proved to be the only significant predictor of the combined end point in patients with stage 4 CKD (HR 1.19, 95% CI 1.09–1.31, P < 0.0001). The same analysis showed that LVMi was the only significant predictor of progression to dialysis in stage 3 CKD patients (HR 1.42, 95% CI 1.23–1.64 for each 10-g/m² increase, P < 0.0001), while a 20% increase in the risk of progression to ESRD was observed for each 10-g/m² increase in LVMi (P < 0.0001), and a 10% increase for each 1-mL/min reduction in eGFR (P = 0.046) in patients with stage 4 CKD. When evaluating the predictive role of LVMi on outcome using AUC-ROC curves, the overall performance of the model including LVMi (AUC 0.877, 95% CI 0.8–0.954) was superior to the model including eGFR (AUC 0.737, 95% CI 0.656–0.817) for the end point of progression to dialysis (P = 0.026, Hanley test).

**Conclusions.** LVH proved to be the strongest predictor of the risk of progression to dialysis in non-diabetic CKD, especially among patients with less advanced renal dysfunction. Regardless of whether it is a simple marker or a pathogenetic factor, LVH encompasses all factors possibly affecting renal and general outcome in CKD patients.

**Keywords:** chronic kidney disease; dialysis; left ventricular hypertrophy; mortality; outcome

**Introduction**

Epidemiological studies have reported a high prevalence of chronic kidney disease (CKD) in the general population since the KDOQI clinical practice guidelines were extensively adopted to identify and classify renal disease [1–3]. Only a minority of CKD patients, however, progress to end-stage renal disease (ESRD) requiring dialysis treatment. The main reason for this may be either the high incidence of CV death in CKD patients before they reach ESRD [4] or the heterogeneity in the risk of progressive renal function worsening due to complex interactions among genetic, environmental and pathogenetic factors [5].

Among these factors, reduced glomerular filtration rate and high urinary albumin excretion were identified as the main predictors of CKD progression to ESRD [6,7]. Furthermore, a recent study showed that combining the two data greatly improved the chances of identifying patients at increased risk of ESRD [8]. However, most studies lack information on many other potentially important risk factors, and especially on cardiovascular ones [9,10].

Establishing reliable and early indexes for identifying patients at high risk of developing ESRD should be a priority in the current effort to establish both clinical practice guidelines and plans for medical and financial management of CKD [5,11].

Therefore, the aim of this study was to evaluate the power of left ventricular hypertrophy (LVH) as compared with traditional risk factors in predicting the combined end point of progression to ESRD requiring renal replacement therapy (RRT), or death in a population of non-diabetic, stage 3 and 4 CKD patients who had previously been evaluated by echocardiography and 24-h ambulatory blood pressure monitoring (ABPM) for left ventricular mass determination and blood pressure profile assessment.

**Materials and methods**

**Patients and study design**

Two hundred and forty-four patients from a cohort of 315 consecutive CKD patients who were referred to our renal unit for the first time were considered eligible for our previous study [12]. Exclusion criteria were diabetes in 35 patients, severe ischaemic heart disease or severe valvular disease in 23, inadequate acoustic window for echocardiographic examination in 5, malignancies in 2, and unwillingness to participate in the study in 6. All 244 patients had undergone both 24-h ABPM BP assessment and echocardiographic examination for left ventricular mass index (LVMi) measurement since the aim of our previous study was to assess the prevalence of LVH and its clinical correlate in a population of non-diabetic, CKD subjects [12].

From this historical cohort, we prospectively evaluated the 144 subjects with overt CKD (83 with stage 3 and 61 with stage 4 CKD) who had not yet reached ESRD at the time of the first observation. These patients underwent periodic clinical and biochemical profile evaluation which was scheduled on the basis of baseline CKD stage as well as on renal disease progression rate.

The present study was designed with two primary end points, i.e. the combined end point of progression to ESRD requiring RRT or death from all cause, and progression to ESRD requiring RRT, all occurring within 5 years.

The study protocol was drawn up according to the Declaration of Helsinki and in keeping with the recommendations issued by the ethical committee of our institution. Each patient gave informed consent.

**Measurements and definitions**

Descriptions of both the ABPM and the echocardiographic studies are reported elsewhere [12].

ABPM was performed using Space labs 90207 (SpaceLabs Inc., Redmond, WA, USA). We derived the average 24-h systolic blood pressure (SBP) and diastolic blood pressure (DBP), the awake SBP and DBP, and the asleep SBP and DBP from the ABPM data. Pulse pressure (PP) was calculated as SBP–DBP for each set of BP measurements, either office or ABPM. Dipping was defined as a ≥10% reduction in night-time ambulatory BP compared with daytime ambulatory BP, whereas reverse dipping was defined as no reduction, or even an increase in night-time ABPM BP compared with daytime values [13]. Arterial hypertension was defined as an average BP ≥130/80 mmHg according to the criteria issued by the NKF-Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in CKD [14]. On the basis of ABPM records, patients were classified as normotensives, dippers, non-dippers or reverse dippers.

Echocardiography was performed on each subject within 1 week either prior to or following ABPM using a two-dimensional guided M-mode echocardiograph according to the American Society of Echocardiography (ASE) recommendations [15]. Left ventricular mass (LVMi) was calculated according to the formula, LVMi = 0.80 × 1.04 × [(IVSd + PWDd + 0.6) × BSA] – 13.8, where IVSd and PWDd are the left ventricular interventricular septum and posterior wall thickness measured in the parasternal long-axis view with the M-mode echocardiograph.
lysed separately for stage 3 CKD patients and for those with stage 4 CKD.

Both univariate and multivariate models were ana-
sion to ESRD requiring dialysis or death, and for death-censored risk of

progressions of categorical variables.

Analyses were performed using the statistical package SPSS 13.0 (SPSS,

Statistical analyses

A value of P < 0.05 was considered statistically significant.

A value of P < 0.05 was considered statistically significant.

Normality of distribution was assessed by the Kolmogorov–Smirnov

test. The significance of association between each clinical and demo-

graphic variable (age, duration of either arterial hypertension or chronic

kidney disease and the time at the first observation, number of antihyper-
tensive medications, serum creatinine, Hgb, total cholesterol, triglycer-

ides, serum albumin, iPTH, daily urinary protein excretion, and each

set of ABPM-derived BP values) was determined by calculating Spear-

man’s correlation coefficient (r). Comparisons between groups were made

by the unpaired t-test for continuous variables. Fisher’s exact test or the

chi-square test, when appropriate, was used for between-group compar-
sions of categorical variables.

Cox proportional hazards analyses were performed to assess the hazard

ratio (HR) and 95% CI for the risk of the combined end point of progres-

sion of this period. Subjects who were alive at end point had

found between the 130 patients who were followed up for

5 years and the 14 who were lost to follow-up. At baseline,

24-h PP was directly associated with age (r = 0.56; P < 0.0001), 24-h proteinuria (r = 0.19; P = 0.026) and

LVMi (r = 0.18; P = 0.022), whereas both 24-h proteinuria and LVMi were inversely associated with eGFR (P = 0.039 and P = 0.045, respectively). Furthermore, a signifi-

cant inverse association was found between LVMi and FS (P = 0.004).

Table 1 shows a comparison analysis of demographic and

clinical data between the 73 subjects who reached the com-

bined end point within the 5-year observation period and the

57 subjects who were still alive and dialysis-free at the end of

this period. Subjects who were alive at end point had

higher eGFR and lower baseline LVMi than patients who

either had started dialysis or had died in the meantime (both

P < 0.0001, unpaired t-test). Moreover, a higher proportion

of subjects reaching the end point of dialysis or death had

Comparison between groups was made by unpaired t-test for continuous variables. Fisher’s exact test or the chi-square test, when appropriate, was used for between-group comparison of categorical variables.

Table 1. Baseline demographic and clinical parameters of the study population

<table>
<thead>
<tr>
<th>Age, years (range)</th>
<th>Gender, M/F (%)</th>
<th>Diagnosis of renal disease, GN/TI/HPT/APKD/other (%)</th>
<th>eGFR, mL/min</th>
<th>Stage CKD, 3/4 (%)</th>
<th>Hgb, g/dL</th>
<th>Serum albumin, g/dL</th>
<th>Total cholesterol, mg/dL</th>
<th>Triglycerides, mg/dL</th>
<th>Uric acid, mg/dL</th>
<th>iPTH, pg/mL</th>
<th>24-h SBP, mmHg</th>
<th>24-h DBP, mmHg</th>
<th>24-h PP, mmHg</th>
<th>Dippers/non-dippers/reverse dippers (%)</th>
<th>Patients on RAAS blockers/other antihypertensives/statins (%)</th>
<th>24-h urinary protein excretion rate, g/day</th>
<th>LVMi, g/m² BSA</th>
<th>FS, %</th>
<th>LV geometry, normal/concentric LVMi/ eccentric LVMi/systolic dysfunction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>62 (17–76)</td>
<td>99 (69)/45 (31)</td>
<td>54 (37)/11 (8)/62 (43)/9 (6)/8 (6)</td>
<td>32.9 ± 12.3</td>
<td>83 (58)/61 (42)</td>
<td>11.9 ± 1.8</td>
<td>3.9 ± 0.7</td>
<td>229 ± 59</td>
<td>206 ± 150</td>
<td>7.0 ± 2.3</td>
<td>82 ± 64</td>
<td>139 ± 16</td>
<td>81 ± 9</td>
<td>58 ± 14</td>
<td>11 (8)/88 (61)/45 (31)</td>
<td>46 (32)/101 (70)/68 (47)</td>
<td>1.1 ± 1.78</td>
<td>145 ± 41</td>
<td>37.9 ± 8.4</td>
<td>52 (36)/37 (26)/38 (26)/17 (12)</td>
</tr>
</tbody>
</table>

| GN, glomerulonephritis; TI, chronic tubulointerstitial nephropathy; HPT, hypertensive nephropathy; APKD, polycystic kidney disease; eGFR, estimated
| glomerular filtration rate; CKD, chronic kidney disease; Hgb, haemoglobin; iPTH, intact parathyroid hormone; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; LVMi, left ventricular mass index; BSA, body surface area; LVMi, left ventricular hypertrophy; FS, left
| ventricular fractional shortening; L VH, left ventricular hypertrophy. |
stage 4 CKD and greater prevalence of LVH as well as a more unfavourable LV geometric pattern such as eccentric LVH or systolic dysfunction compared with surviving dialysis-free subjects (all P < 0.0001, Fisher’s exact test or chi-square test). In contrast, no significant differences were observed in the two groups regarding age, gender, and the prevalence of arterial hypertension, dipping habit, albuminuria, serum albumin and anaemia. Lastly, higher LVMi (167 ± 41 g/m²) and greater prevalence of stage 4 CKD (65%) were the only significant differences we observed in the 49 patients who reached ESRD and who started dialysis as compared with the 57 subjects who were still alive, dialysis-free after the 5-year observation period (both P < 0.0001; unpaired t-test and Fisher’s exact test, respectively).

Risk of progression to dialysis or death (combined end point)

Univariate Cox regression analysis showed a 27% increase in the risk of the combined end point for each 10-g/m² increase in baseline LVMi and a 6% increase for each 1-mL reduction in baseline eGFR for patients with stage 3 CKD (Table 3), and an 18% increase for each 10-g/m² increase in baseline LVMi and a 9% increase for each 1-mL reduction in eGFR in patients with stage 4 CKD (Table 4). Multivariate analysis showed that LVMi (HR 1.28; 95% CI 1.17–1.4; P < 0.0001) and, to a lesser extent, eGFR (HR 0.95; 95% CI 0.90–0.99; P = 0.027) were significant predictors of the risk of combined end point in stage 3 CKD patients (data adjusted for age, pulse pressure and proteinuria) (Table 3), whereas LVMi (HR 1.194; 95% CI 1.09–1.31; P < 0.0001) was significant in stage 4 CKD patients (data adjusted for age, pulse pressure and proteinuria) (Table 4).
CI \(1.09 - 1.31\) proved to be the only significant predictor of the combined end point in patients with stage 4 CKD (data adjusted for age, pulse pressure, eGFR and proteinuria) (Table 4). Figure 1 shows Kaplan–Meier curves for combined end point-free survival in the 144 stage 3–4 CKD patients subdivided according to the presence or absence of LVH at baseline (Figure 1).

When evaluating the role of the various baseline LV geometric patterns in predicting the combined end point-

![Graph 1](https://example.com/fig1.png)

**Fig. 1.** Kaplan–Meier analysis of combined end point-free survival in patients with LVH and in those with normal LV Mi at baseline (log-rank \(P < 0.001\)).

### Table 5. Cox proportional hazard analysis of progression to dialysis in 83 stage 3 CKD patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariate analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, 1-year increase</td>
<td>1.005 (0.971–1.041)</td>
<td>0.77</td>
</tr>
<tr>
<td>Proteinuria, 1-g/24 h increase</td>
<td>1.063 (0.75–1.507)</td>
<td>0.73</td>
</tr>
<tr>
<td>24-h PP, 1-mmHg increase</td>
<td>1.025 (0.935–1.063)</td>
<td>0.22</td>
</tr>
<tr>
<td>eGFR, 1-mL/min increase</td>
<td>0.961 (0.905–1.02)</td>
<td>0.19</td>
</tr>
<tr>
<td>LV Mi, 10-g/m² increase</td>
<td>1.285 (1.147–1.438)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Multivariate analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, 1-year increase</td>
<td>1.027 (0.989–1.067)</td>
<td>0.16</td>
</tr>
<tr>
<td>Proteinuria, 1-g/24 h increase</td>
<td>1.292 (0.848–1.969)</td>
<td>0.23</td>
</tr>
<tr>
<td>24-h PP, 1-mmHg increase</td>
<td>1.061 (0.966–1.167)</td>
<td>0.22</td>
</tr>
<tr>
<td>eGFR, 1-mL/min increase</td>
<td>0.96 (0.90–1.02)</td>
<td>0.26</td>
</tr>
<tr>
<td>LV Mi, 10-g/m² increase</td>
<td>1.42 (1.23–1.64)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

For abbreviations, see Table 1.

### Table 6. Cox proportional hazard analysis of progression to dialysis in 61 stage 4 CKD patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariate analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, 1-year increase</td>
<td>1.007 (0.973–1.013)</td>
<td>0.48</td>
</tr>
<tr>
<td>Proteinuria, 1-g/24 h increase</td>
<td>0.925 (0.77–1.113)</td>
<td>0.41</td>
</tr>
<tr>
<td>24-h PP, 1-mmHg increase</td>
<td>1.003 (0.973–1.021)</td>
<td>0.78</td>
</tr>
<tr>
<td>eGFR, 1-mL/min increase</td>
<td>0.867 (0.783–0.962)</td>
<td>0.006</td>
</tr>
<tr>
<td>LV Mi, 10-g/m² increase</td>
<td>1.194 (1.093–1.304)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Multivariate analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, 1-year increase</td>
<td>1.02 (0.948–1.052)</td>
<td>0.23</td>
</tr>
<tr>
<td>Proteinuria, 1-g/24 h increase</td>
<td>1.07 (0.835–1.37)</td>
<td>0.6</td>
</tr>
<tr>
<td>24-h PP, 1-mmHg increase</td>
<td>1.009 (0.954–1.03)</td>
<td>0.66</td>
</tr>
<tr>
<td>eGFR, 1-mL/min increase</td>
<td>0.902 (0.812–1.008)</td>
<td>0.046</td>
</tr>
<tr>
<td>LV Mi, 10-g/m² increase</td>
<td>1.196 (1.073–1.33)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

For abbreviations, see Table 1.

![Graph 2](https://example.com/fig2.png)

**Fig. 2.** Kaplan–Meier analysis of dialysis-free survival in patients with LVH and in those with normal LV Mi at baseline (log-rank \(P < 0.001\)).

![Graph 3](https://example.com/fig3.png)

**Fig. 3.** The AUC-ROC curves for combined end point (A) and the end point of progression to dialysis (B) as predicted by a model including LV Mi alone, eGFR alone or both. Clinical predictors in both models included age, 24-h proteinuria and 24-h pulse pressure.
Risk of progression to dialysis

Univariate Cox proportional hazards analysis showed that each 10-g/m² increase in baseline LVMi was associated with a 28% increase in the risk of progression to ESRD requiring dialysis within the 5-year follow-up period in patients with stage 3 CKD (Table 5), whereas a 19% increase in the HR for each 10-g/m² increase in baseline LVMi and a 13% increase for each 1-mL reduction in eGFR were observed in patients with stage 4 CKD (Table 6). Multivariate analysis proved that increased LVMi was the only significant predictor of the risk of progression to dialysis in patients with stage 3 CKD (data adjusted for age, eGFR, pulse pressure and 24-h urinary protein excretion rate) (Table 5), whereas a 20% increase in the risk for each 10-g/m² increase in baseline LVMi and a 10% increase for each 1-mL reduction in eGFR were observed in patients with stage 4 CKD (data adjusted for age, pulse pressure and proteinuria) (Table 6).

Figure 2 shows Kaplan–Meier curves for dialysis-free survival in the 144 CKD patients with and without LVH at baseline (Figure 2).

The role of LVMi and eGFR in predicting outcome

AUC-ROC curves showed that a model, which included both LVMi and eGFR, was highly predictive of both the combined end point (AUC 0.854, 95% CI 0.772–0.935) and the progression to dialysis (AUC 0.884, 95% CI 0.814–0.955) (Figure 3). Moreover, a comparison of the AUC-ROC curves by the Hanley test showed that the model including both LVMi and eGFR was more predictive than models including either LVMi or eGFR alone in predicting both the combined end point (P = 0.004 vs LVMi alone and P = 0.001 vs eGFR alone) and the progression to dialysis (P < 0.001 vs LVMi and P = 0.019 vs eGFR). Lastly, the model including LVMi provided significantly higher sensitivity and specificity than the model with eGFR in predicting progression to dialysis (P = 0.026).

Discussion

Prospective analysis of our historical cohort of non-diabetic CKD patients [12] showed that baseline LVH was the strongest predictor of a composite end point consisting of either ESRD requiring dialysis, or death.

LVH has indeed been independently associated with adverse outcome in the general population and in renal patients as well [20–22]. The most relevant and novel finding of our study, however, is that LVH also proved to be the most significant predictor of ESRD requiring RRT, despite the inclusion of eGFR values in the Cox proportional hazards model, as well as the only predictor of the progression to dialysis in patients with less advanced CKD.

Although we do not present a definite explanation for this finding, we do hypothesize that LVH could be a marker of the risk of renal disease progression towards the end stage because the same pathogenetic factors that are involved in kidney damage are also responsible for the increase in both LV wall thickness and internal dimension.

In our cohort, baseline LVH was in fact significantly associated with elevated PP and older age, whereas no associations were shown with eGFR, the degree of anaemia, dyslipidaemia, iPTH or serum albumin [12].

However, the prevalence of arterial hypertension in our cohort was similar in patients reaching ESRD and in dialysis-free survivors. Moreover, 24-h BP values did not significantly predict the risk of developing ESRD and dialysis, thus ruling out the possibility that inadequate BP control may have played a major role in both cardiac hypertrophy and CKD progression in our patients. Furthermore, cardiac and renal involvement could be the effect of endothelial dysfunction inducing generalized vascular damage in CKD patients, which is consistent with findings from the cohort enrolled in the LIFE Study which demonstrated a significant association of LVH with urinary albumin excretion [23]. Accordingly, a significant association was indeed found in our sample between increased PP, an indirect expression of vascular stiffness, and both LVMi and proteinuria. Recent reports that are consistent with this pathogenetic hypothesis have shown that NT-proBNP and proANP, which are recognized markers of cardiac function impairment, proved to be strong predictors of CKD progression to ESRD in non-diabetic patients [24,25].

LVH might also exert a direct pathogenetic effect on the progression of CKD to ESRD. Reports exist showing that LVH may be associated with subclinical worsening of systolic LV function [26–28]. Moreover, mild impairment in systolic LV function reportedly predicts the risk of adverse CV outcome in dialysis patients [29]. Interestingly, in our cohort, a significant, inverse relationship was shown between LVMi and left ventricular fractional shortening. Moreover, consistent with previous reports in dialysed patients [18], our patients with LV systolic dysfunction showed worse outcome. We observed a direct association between increased PP and LVH, thus confirming the role of arterial stiffness and the consequent increase in velocity of backward reflected waves to the LV in the pathogenesis of cardiac hypertrophy [30]. We cannot rule out that a mild reduction in renal perfusion induced by slightly impaired LV systolic function associated with pathological, highly pulsatile perfusion in the kidney microvasculature as an effect of reduced elasticity of conduit arteries [31] may have played a role in promoting a progressive, further reduction in renal function of patients with pre-existing CKD.

Another finding of this study is that increased urinary protein excretion rate did not prove to be a significant predictor of the risk of progression to dialysis in our cohort. We speculate that this might be the consequence of the stronger pathogenetic role played by LVH which possibly masked the effect of proteinuria in predicting adverse renal outcome.

Lastly, no predictive role for anaemia was found in our sample. This is consistent with an interventional study that showed neither regression of LVH nor slowing of renal disease progression in CKD patients in whom complete anaemia correction was achieved by epoetin therapy [32].

Of course, some limitations must be acknowledged in our study.
First of all, sample size is small, and 10 patients were missed and lost to follow-up. Secondly, there is great heterogeneity in patients’ age and higher prevalence of men, two factors which may affect LVH in CKD. Furthermore, we have no data concerning the behaviour of LVMI during the observation period, and we did not evaluate the potential role of changes in some predictors and the effect of intervention on such factors during follow-up in counteracting role of changes in some predictors and the effect of intervention which may affect L VH in CKD. Furthermore, we importantly in less advanced renal disease patients for whom progression of their renal disease. This could be especially about the CV outcome of CKD patients but also about the CV outcome of CKD patients as compared with well-known risk factors of progression to ESRD and death, namely eGFR, proteinuria and arterial hypertension. This is indeed the first long-term observation in CKD patients to point out the pivotal role of LVH in predicting not only the risk of death but also of ESRD requiring dialysis. On the basis of our findings, it is conceivable that LVH agglomerates and encompasses all the potential mechanisms involved in inducing either ESRD or death in patients with overt CKD. Accordingly, systematic assessment of morphology and function of the LV should be considered a key tool in order to obtain prognostic information not only about the CV outcome of CKD patients but also about the progression of their renal disease. This could be especially important in less advanced renal disease patients for whom intervention might still be effective in slowing down progression to the end stage.

Conflict of interest statement. None declared.

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Salivary testosterone for the diagnosis of androgen deficiency in end-stage renal disease

Estela M.L. Cardoso1,2, Liliana N. Contereras1,2, Elida G. Tumilasci3, Alicia Elbert4, Elvira C. Aguirre5, Daniel R. Aquilano6 and Alejandro L. Arregger1

1Endocrine Research Department, Instituto de Investigaciones Médicas A. Lanari, School of Medicine, University of Buenos Aires, Buenos Aires, Argentina, 2CONICET, Buenos Aires, Argentina, 3Laboratory of Salivary Glands, School of Medicine, University of Buenos Aires, Buenos Aires, Argentina, 4CEREA Dialysis Unit, Buenos Aires, Argentina, 5Department of Nephrology, Instituto de Investigaciones Médicas A. Lanari, School of Medicine, University of Buenos Aires, Buenos Aires, Argentina and 6IABE, La Plata, Argentina

Correspondence and offprint requests to: Estela M.L. Cardoso; Email: endoexp2000@yahoo.com

Abstract

Background. Hypogonadism is frequent in patients with end-stage renal disease (ESRD). Salivary testosterone (Sal-T) is a non-invasive tool to screen androgen deficiency in adult male with normal renal function. However, available data on its utility in ESRD are not conclusive.

Objectives. The objectives of the study were: (i) to compare free testosterone fractions in saliva (SAL-T) and serum (Free-T); (ii) to establish the correlation of Sal-T with circulating total (TT) and bioavailable testosterone (Bio-T); (iii) to detect androgen deficiency through Sal-T; (iv) to determine the correlation of Sal-T with clinical parameters.

Methods. The study included: 60 adult ESRD men on haemodialysis (20–60 years old) with decreased libido referred from two dialysis centres; 112 eugonadic and 40 hypogonadic adult men with normal renal function as controls. Simultaneous morning saliva and serum samples were obtained for testosterone measurements by liquid RIA (SAL-T; TT). Free-T and Bio-T were calculated by the Vermeulen equation.

Results. Sal-T (0.338 ± 0.177 nM) and Free-T (0.338 ± 0.165 nM) did not differ (P > 0.900) in ESRD as well as in control (0.337 ± 0.182 and 0.337 ± 0.172 nM, respectively; P > 0.900). Sal-T levels correlated positively (P < 0.0001) with Free-T (r = 0.95), TT (r = 0.80) and Bio-T (r = 0.76) in ESRD. Sal-T negatively correlated with age and years on dialytic therapy. Sal-T showed 100% sensitivity and specificity to differentiate patients with androgen deficiency (22%) from those with normal androgen levels (78%). Hypogonadism was hypergonadotropic in 69% cases and hypogonadotropic in 31%.

Conclusions. These data demonstrate the value of morning Sal-T testing as a non-invasive approach to screen androgen status in ESRD patients.

Keywords: end-stage renal disease; haemodialysis; male androgen deficiency; salivary testosterone; serum testosterone

Introduction

A number of metabolic and endocrine disorders linked to chronic uremic syndrome remain a challenge in spite of the progresses in renal disease therapy [1,2]. As reported, two-thirds of men on haemodialysis (HD) have serum testosterone in the hypogonadal range [3,4]. This deficiency