Arterial Blood Pressure, Serum Calcium and PTH in Elderly Men with Parathyroid Tumors and Primary Hyperparathyroidism*

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Abstract. In patients with parathyroid tumors and primary hyperparathyroidism (PHPT), the relationship between arterial blood pressure (BP) and both serum calcium and parathyroid hormone (PTH) is still unclear. The aim of this study was to investigate whether a correlation exists between BP and the main biochemical parameters in men with confirmed sporadic PHPT due to a solitary parathyroid adenoma. A series of 38 elderly (>64 years) men (median age 69 years, range 65-78 years) were enrolled in the study. Twenty-nine (76.3%) were asymptomatic, while 9 (23.7%) had renal diseases (i.e. renal stones, impaired renal function). The main preoperative biochemical parameters were the following: serum calcium=2.77±0.25 mmol/l, PTH=166.5±157.0 ng/l, alkaline phosphatase (ALP)=107.6±37.0 U/l, and creatinine=82.5±8.1 μmol/l. In each patient, the BP was recorded three times at 2-3 min intervals using an automatic device, and the mean values were recorded. All patients successfully underwent parathyroidectomy. As expected, there was a significant relationship between age and both systolic and diastolic BP (β=0.39, p=0.018; β=0.41, p=0.014, respectively). There was also a correlation between systolic and diastolic BP (β=0.39, p=0.01) and between serum calcium and PTH (β=0.51, p=0.008). A weak relationship (β=0.28, p=0.04) between serum calcium and creatinine was also found. However, no significant relationship between systolic or diastolic BP and serum calcium (β=0.012, p=0.94; β=0.065, p=0.71) or PTH (β=0.08, p=0.65; β=0.17, p=0.32), respectively, was observed. In conclusion, our study confirms that in men with parathyroid tumors and PHPT, the BP values are independent of both serum calcium and PTH levels.

Primary hyperparathyroidism (PHPT) is the commonest cause of hypercalcemia in adults (1). The hospitalization rate for PHPT was 8.0 per 100,000 in 1999 and its estimated prevalence is 1 per 1000 in the USA and 4 per 1000 in Sweden, respectively (2, 3). The peak incidence is observed among women aged from 50 to 60 years, who are twice as affected as men (3). Currently, most patients with PHPT are discovered because of asymptomatic hypercalcemia and thus they should be managed according to the Workshop guidelines reported in 2009 (4). Solitary parathyroid adenoma is the main cause of PHPT, accounting for at least 85% of cases (3, 5). All patients with hyperfunctioning parathyroid adenomas have an increased risk of cardiovascular diseases, which are directly related to serum calcium levels (6). However, the relationship between arterial blood pressure (BP) and both serum calcium and parathyroid hormone (PTH) is still unclear, especially in the elderly.

The aim of this study was to investigate whether a correlation exists between BP and the main biochemical parameters in men with parathyroid adenomas and PHPT.

Patients and Methods

A series of 38 consecutive elderly (>64 years) men (median age 69 years, range 65-78 years) with confirmed sporadic PHPT were enrolled in the study. Twenty-nine (76.3%) patients were asymptomatic, while 9 (23.7%) had renal diseases (i.e. renal stones, impaired renal function). Patients with a history of angina, stroke, myocardial infarction, diabetes mellitus, as well those under the age of 65 or who were treated for arterial hypertension, were excluded.
Written informed consent was obtained from all participants. All patients underwent successfully parathyroidectomy and the final pathology showed a parathyroid adenoma in all cases.

Blood samples were obtained from all the participants after overnight fasting and were assayed in duplicate. Serum intact PTH was measured through two-site chemiluminescent immunometric assay, using two goat monoclonal antibodies against human PTH, while both serum calcium and creatinine were measured spectrophotometrically, by standard laboratory methods (7). Arterial BP measurements were obtained using an automatic device. Three recordings were made the day before surgery, at 2- to 3-minute intervals, as previously reported (8). The reported data are expressed as mean±standard deviation (SD). To evaluate the linear relationship between pairs of variables, the standardized β coefficient calculation was used. Differences were considered significant at a $p$-value <0.05.

Results

The main preoperative biochemical and clinical parameters are reported in Table I. As expected, there was a significant relationship between age and both systolic and diastolic BP ($\beta=0.39$, $p=0.018$; $\beta=0.41$, $p=0.014$, respectively). There was also a significant correlation between systolic and diastolic BP ($\beta=0.39$, $p=0.01$) and between serum calcium and PTH ($\beta=0.51$, $p=0.008$). A weak relationship ($\beta=0.28$, $p=0.04$) between serum calcium and creatinine was also found. As reported in Table II, no significant ($p=NS$) relationship between systolic or diastolic BP and serum calcium or PTH was observed (Figure 1).

Discussion

Patients with PHPT and parathyroid adenomas have an increased cardiovascular morbidity and in those who did not undergo surgery an increased incidence of acute myocardial infarction has been reported (9). The intima-media thickness (IMT) measurement of the common carotid artery is recognized as being useful in predicting the likelihood of cardiovascular events, since it is related to the extent and severity of atherosclerosis (10, 11). In a previous study we found an inverse relationship between IMT and serum PTH ($R=-0.56$, $p<0.01$), but no correlation ($p=NS$) between IMT and serum calcium ($R=-0.14$) or serum phosphate (12).

Experimentally, PTH infusion increases blood pressure in healthy individuals (13). PTH could be involved in the pathophysiology of essential hypertension and it is a significant predictor of delta systolic blood pressure in men, but not in women (14, 15). A positive association between serum PTH levels and arterial BP has long been observed (16-19) and recently re-evaluated (20). Several mechanisms have been hypothesized to explain the relationship between hypertension and elevation of serum PTH, such as increased activity of the sympathetic and the renin-aldosterone system, or increased secretion of aldosterone and cortisol from the adrenal cortex, endothelial dysfunctions, or a direct effect on vascular smooth muscle cells (21-24). Snijder et al. in their population-based study found that that PTH was a potentially modifiable determinant of BP in the general elderly population. Its possible population-specific determinants, such as sodium intake, calcium intake and vitamin D status, were considered as therapeutic tools to reduce arterial BP in the elderly (25).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Range</th>
<th>Reference intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca (mmol/l)</td>
<td>2.77</td>
<td>0.25</td>
<td>2.68</td>
<td>2.68-3.81</td>
<td>2.10-2.5</td>
</tr>
<tr>
<td>PTH (ng/l)</td>
<td>166.5</td>
<td>157.0</td>
<td>122</td>
<td>61-762</td>
<td>10-55</td>
</tr>
<tr>
<td>ALP (U/l)</td>
<td>107.6</td>
<td>37.0</td>
<td>103</td>
<td>28-190</td>
<td>56-128</td>
</tr>
<tr>
<td>Creatinine (μmol/l)</td>
<td>82.5</td>
<td>8.1</td>
<td>82</td>
<td>62-102</td>
<td>62-115</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>149.4</td>
<td>15.8</td>
<td>150</td>
<td>120-180</td>
<td>&lt;150</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>88.7</td>
<td>8.5</td>
<td>90</td>
<td>80-110</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>

Ca, Total serum calcium; PTH, parathyroid hormone; ALP, total alkaline phosphatase; BP, blood pressure; SD, standard deviation.

Table II. Results of multivariate analysis for systolic and diastolic blood pressure (BP).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>β</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.39</td>
<td>0.018</td>
</tr>
<tr>
<td>ALP</td>
<td>-0.45</td>
<td>0.006</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.012</td>
<td>0.94</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.16</td>
<td>0.35</td>
</tr>
<tr>
<td>PTH</td>
<td>0.08</td>
<td>0.65</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.41</td>
<td>0.014</td>
</tr>
<tr>
<td>ALP</td>
<td>-0.12</td>
<td>0.48</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.065</td>
<td>0.71</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.10</td>
<td>0.57</td>
</tr>
<tr>
<td>PTH</td>
<td>0.17</td>
<td>0.32</td>
</tr>
</tbody>
</table>

ALP, Alkaline phosphatase; PTH, parathyroid hormone.
Recently, Feldstein et al. (26) showed that serum total calcium was significantly related to night-time systolic BP (r=0.620, \( p<0.02 \)) and diastolic BP (r=0.758, \( p<0.002 \)). However, in a large group of patients with PHPT, the preoperative systolic BP was significantly related to serum calcium only when the influence of age was not considered, suggesting that there is no simple cause-and-effect relationship accounting for hypertension in PHPT (27). In our previous population-based study of 194 patients with PHPT, the multivariate analysis confirmed that none of the independent biochemical parameters considered (i.e. serum calcium, PTH, creatinine) significantly correlated with BP, which was mainly related to age and body mass index (8). In a small group of patients with PHPT and pre-operative hypertension, during follow-up none of the patients (aged 49±12 years) became normotensive, while 32% of those who were normotensive preoperatively developed clinical hypertension (28). In a more recent study, parathyroidectomy reduced BP in hypertensive patients with PHPT and this reduction was independent of treatment with antihypertensive medications (29). Patients with both PHPT and hypertension may show increased BP after parathyroidectomy, while those without a history of hypertension showed unchanged or slightly reduced BP values (30). However, in this study, serum concentrations of PTH and calcium were not significantly related to any of the BP variables measured.

In conclusion, our preliminary study confirms that in elderly men with hyperfunctioning parathyroid adenomas, arterial BP values are parameters independent of both serum calcium and PTH levels.

References


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