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# Reversible Hypertension in Primary Hyperparathyroidism – Pre- and Posteroperative Blood Pressure in 75 Cases

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**Summary.** In 75 operatively proved cases of primary hyperparathyroidism (PH) mean systolic and diastolic blood pressure (BP) values were significantly higher pre- than postoperatively. There were 27 patients (36%) who showed hypertension before operation (systolic BP $\geqq$ 150 mm Hg, mean 169 $\pm$ 20 mm Hg). In 20 of these the hypertension was reversible after successful treatment of PH, in seven cases elevated values persisted. The mean age of patients with persisting hypertension was significantly higher than the group with normalization of BP after operation ($P < 0.01$). As far as clinical presentation of PH was concerned it were those cases with hypercalcaemic syndrome and with accidentally discovered hypercalcaemia who most often showed hypertension. In cases with recurrent urolithiasis and with osteitis fibrosa as leading symptoms there was no significant increase of hypertension as compared to the whole group. Because of the relatively high incidence of hypertension in PH this possibility should be taken into consideration in each diagnostic clarification of hypertensive patients.

**Key words:** Primary hyperparathyroidism – Blood pressure – Reversible hypertension

## Introduction

A highly significant correlation between serum calcium level and both systolic and diastolic blood pressure (BP) was demonstrated in a recently published study on 9,321 male subjects [15]. In more recent pathophysiological considerations concerning the development of hypertension, calcium plays an important role [3, 8, 18, 19]. In addition, the effect of calcium antagonists on the treatment of hypertension indicates possible relationships between calcium and BP [21, 27]. In contrast to this, results of epidemiologic and animal studies have suggested an inverse relationship between calcium intake and BP [20]. In a randomized clinical trial a calcium-supplemented group showed a significant decrease in diastolic BP [2]. Oral magnesium supplementation also was able to lower BP [9]. In primary hyperparathyroidism (PH) hypertension is a well-known symptom [12–14, 25] but little is known about incidence, reversibility and pathogenesis.

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## Patients and Methods

In 75 cases of PH, BP values were analysed from the preoperative hypercalcaemic stage and the postoperative normocalcaemic stage. In all cases the diagnosis was proved by the histological finding of parathyroid adenoma or hyperplasia and by the typical postoperative fall in serum calcium. Patients on antihypertensive drugs or with retention of urea and creatinine were excluded from the study. The mean age of the 52 women was 55 years (SD: $\pm$12), mean preoperative serum calcium 3.19 mmol/l (range: 2.65–5.50, SD: $\pm$0.53). The mean age of the 23 men was 48 years (SD: $\pm$15), average preoperative serum calcium 3.20 mmol/l (range: 2.63–4.25, SD: $\pm$0.43). BP was measured with the method of Riva-Rocci at different days three times preoperatively and three times postoperatively. During these measurements the patients had no bed-rest. They were either in the preoperative diagnostic phase or a few days before release from hospital. A mean value was calculated from each of the three determinations.

Serum calcium was calculated from three different preoperative determinations which were performed by atomabsorption spectrophotometry. Parathyroid hormone was measured by a radioimmunoassay against the aminoterminal end of the molecule [5].

## Results

The mean values and stadard deviations of the systolic and diastolic BP are shown in Table 1 for

all 75 cases. There is a highly significant decrease in systolic and diastolic BP after operative correction of PH that is about the same for both sexes. The distribution of the individually determined BP levels can be seen in Figs. 1a and b. While for systolic BP (Fig. 1a) a considerable number of cases show values of 150 mm Hg and higher (up to 230 mm Hg) preoperatively, this broad spectrum narrows postoperatively to the left, i.e. to lower values. Only seven of the 75 cases have a BP of 150 mm Hg or more. In Fig. 1b a corresponding postoperative shift of values to the left can be recognized for the diastolic BP after operative correction of hyperparathyroidism. Preoperatively 48 patients (64%) are normotensive and 27 (36%) are hypertensive (systolic BP $\geqq 150$ mm Hg). The mean serum calcium for the normotensive group is $3.21 \pm 0.46$ mmol/l and for the hypertensive group $3.39 \pm 0.58$ mmol/l (p ns). For the hypertensive cases the systolic BP decreases from 169 mm Hg preoperatively to 135 mm Hg postoperatively, i.e. 34 mm Hg on average. The diastolic BP decreases on average by 13 mm Hg, from 96 preoperatively to 83 postoperatively (Fig. 2). Taken together, the 48 normotensive cases also show a significant decrease of BP. The seven cases with persisting hypertension after

**Table 1.** Mean values, standard deviations and results of paired *t*-test for the preoperative and postoperative systolic and diastolic BP in 75 patients with primary hyperparathyroidism

| Blood pressure (mm Hg) | *n* | Preop. mean (±SD) | Postop. mean (±SD) | Paired *t* | *t*-Test *p*< |
|---|---|---|---|---|---|
| Systolic | 75 | 145 (23) | 128 (14) | 7.62 | 0.0005 |
| Diastolic | 75 | 89 (10) | 81 (8) | 6.40 | 0.0005 |

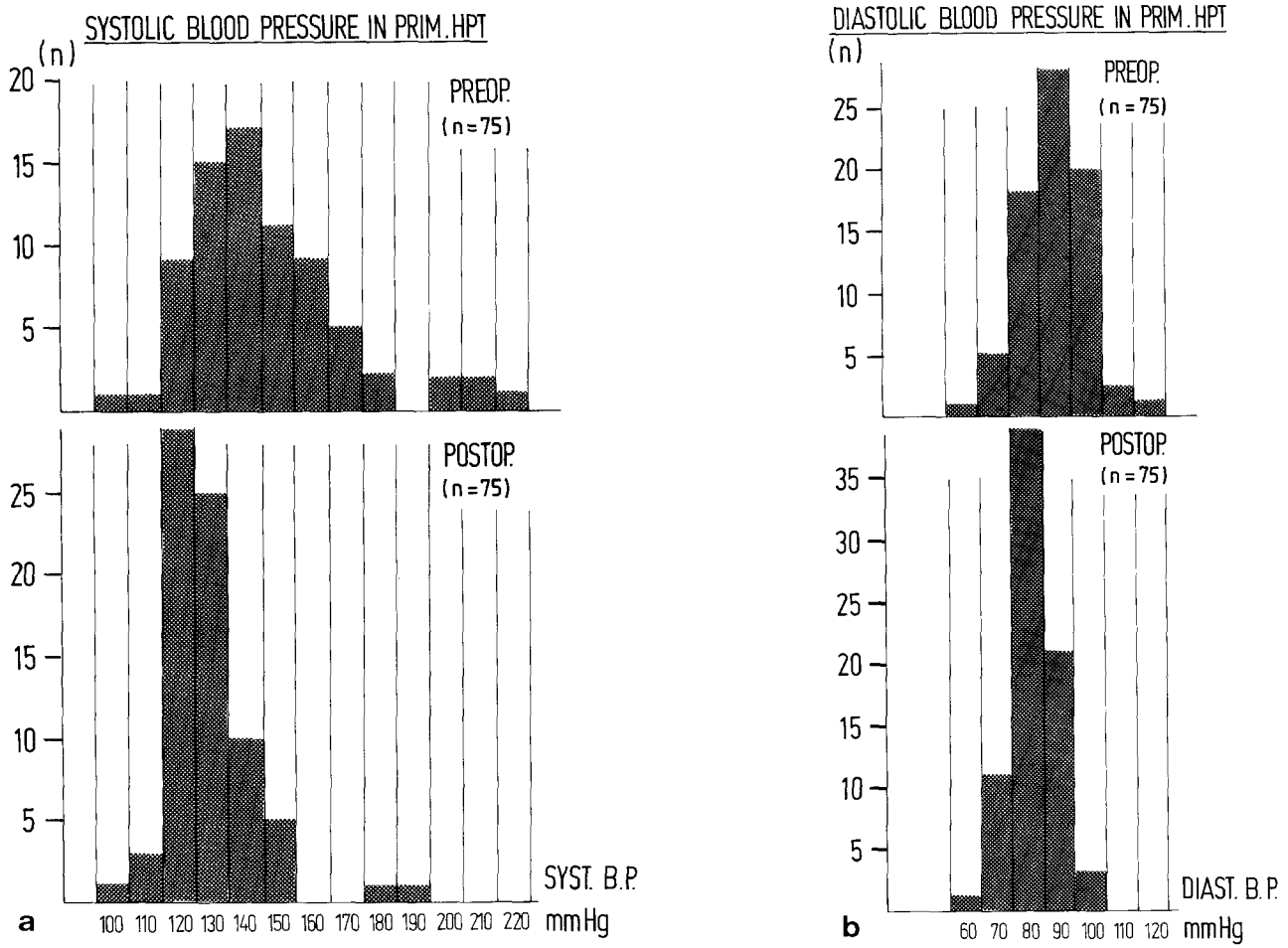


**Fig. 1a, b.** Patterns of incidence of individual systolic (**a**) and diastolic (**b**) blood pressure values in 75 patients with primary hyperparathyroidism. Postoperatively there is no narrowing and shifting to the left of the spectrum of the systolic and diastolic values

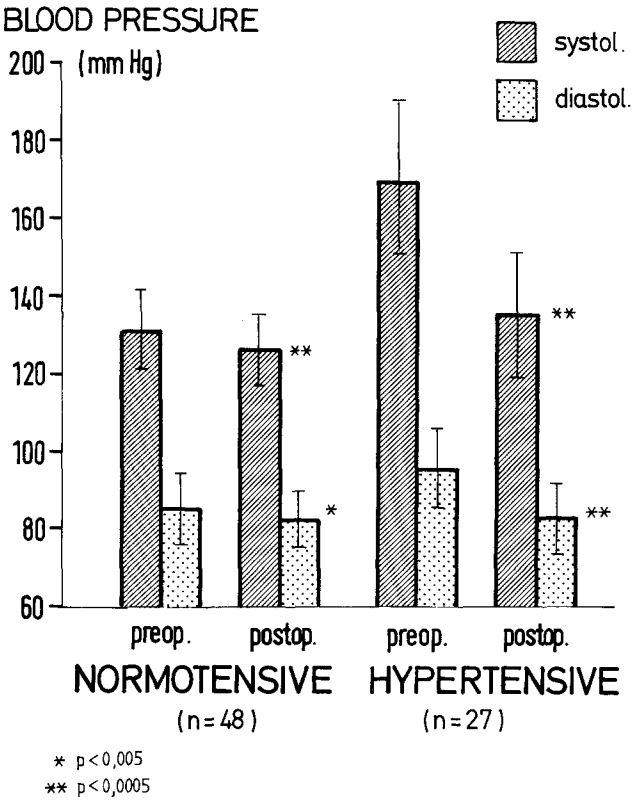


**Fig. 2.** Mean values and standard deviations for the preoperative and postoperative systolic and diastolic BP after allocation of patients to a normo- and hypertensive group (borderline: systolic BP $\geqq$ 150 mm Hg)

operation (mean age 68.5 years) are significantly older than the 20 cases with normalization of BP (mean age 58.7 years, $P<0.01$). Of the normalized cases, which could be controlled several times during the first postoperative year, 16 remained normotensive without further treatment.

In order to find out a possible relationship between serum calcium and BP, the preoperative serum calcium levels and corresponding BP values were correlated. A statistically significant correlation could not be found for the females, the males or the whole group. Equally there was no correlation between parathyroid hormone levels and BP, while parathyroid hormone and calcium show a close correlation. Furthermore there was no correlation between preoperative systolic BP and age of patients.

As PH can present clinically with different syndromes the question appeared to be whether hypertension is in any way correlated to these different clinical appearances of PH. In Table 2 the 75 cases are grouped according to the indications, i.e. to the symptoms that led to hospitalisation and diagnosis. The most frequent clinical presentations of

**Table 2.** Incidence of hypertension in different groups of patients according to the leading symptoms of primary hyperparathyroidism

| Leading symptoms | *n* | Normotensive | Hypertensive |
|---|---|---|---|
| Urolithiasis | 45 | 35 | 10 |
| Skeletal symptoms | 10 | 7 | 3 |
| Hypercalcaemia (accid. finding) | 9 | 3 | 6 |
| Hypercalcaemic syndrome | 8 | 3 | 5 |
| Peptic ulcers | 2 | — | 2 |
| Pancreatitis | 1 | — | 1 |
| | 75 | 48 | 27 |

PH, the renal syndrome and the skeletal syndrome, do not show a significant accumulation of hypertensive cases in comparison to the general incidence of 36%. In the asymptomatic cases however, in whom the hypercalcaemia was discovered accidentally, and in the life-threatening cases of acute hypercalcaemic syndrome there was a relatively high incidence of hypertension. Altogether 11 of 17 cases had an elevated BP.

## Discussion

The clinical picture of PH appears in various combinations of renal, skeletal, gastrointestinal, vegetative and neurologic-psychiatric symptoms [17, 22]. The hypercalcaemia dependent QT-shortening in the surface ECG and disturbances in cardiac rhythm are well-known symptoms as concerns the cardiovascular system [23], while only little attention has been paid to the arterial hypertension which is also a very common symptom in this disease. The incidence of hypertension in PH varies between 10% and 70% in a review of the literature [7]. From the data of the nine groups mentioned a mean incidence of 38% of hypertension can be calculated in a total number of 1,056 examined patients. This agrees well with the incidence of 36% found in our series.

Reversibility of hypertension was 74% (20 of 27 cases) in our patients. In an earlier study by Hellström et al. [13] hypertension was reversible in only 20% of cases and in some patients hypertension even developed after operation. This may be due to the fact that some of these patients had already suffered irreversible damage to the kidneys, while we excluded such patients in our study. Paloyan et al. [21] report on six patients who had already been treated for "essential hypertension" with diuretics for several years. In each case PH was found as etiology. After operative correction

patients did much better subjectively, but the elevated BP persisted in each case. Hypertension had obviously existed for too long a period. A correlation between serum calcium level and BP was described by different authors [3, 7] and a direct effect of calcium on the smooth muscle cells of the arteries was discussed. In the present series of 75 patients a significant correlation between the serum calcium level and BP could not be demonstrated. In two other studies [7, 8] it was also reported that there was no correlation between both parameters, ruling against the hypothesis that hypercalcaemia per se is the dominant cause of hypertension in hyperparathyroidism. A review of the data in this and related studies leads to the conclusion that the hypertension of hyperparathyroidism is heterogeneous in origin. The data of two studies suggest an effect of parathyroid hormone on plasma renin activity [6, 26].

Concerning the possible influence of the clinical presentation of PH on the incidence of hypertension, Hellström et al. [13] reported that cases with bone disease more often had a high BP than cases with recurrent kidney stones. However, in cases of already impaired renal function there was a correlation between kidney damage and degree of hypertension. In cases of urolithiasis without impaired renal function (Table 2) we found hypertension somewhat less frequently than expected. However in patients with mainly skeletal symptoms there was no increased incidence of high BP. There was only a relatively high incidence in those patients in whom hypercalcaemia was detected by chance or who developed malignant hypercalcaemia. There are obviously cases in which hypertension was up to then the only symptom, but hypertension had not induced a search for PH. Among 900 cases of hypertension, Rosenthal and Roy [24] found seven cases of hypercalcaemia due to PH. This is an incidence of PH of 1:130 in hypertension which is much more than the overall morbidity of this disease and confirms the existence of patients with PH who are asymptomatic except for hypertension over a long period of time.

From our results and from the quoted literature it has been proved necessary that determinations of parathyroid hormone or at least serum calcium should be included in the diagnostic procedure of hypertension.

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