CLINICAL STUDY

Persistent disease after surgery for primary hyperparathyroidism: the long-term outcome

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Abstract

Objective: Nineteen patients with persistent primary hyperparathyroidism were investigated to evaluate their clinical and laboratory status a long time after treatment was ended. The risk of persistent disease and need for extensive surgery for cure, i.e. more than two neck operations, or mediastinal exploration, was also evaluated.

Design: The medical records of 896 consecutive patients operated on for primary hyperparathyroidism were scrutinised at follow-up, a mean of 10.3 years after surgery. Data on state of health, medication, bone fractures and other diagnoses were collected by use of a questionnaire. There were 600 patients still alive, among whom 13 had persistent disease and they were compared with 509 patients who were cured and without any suspicion of recurrent disease, according to laboratory examination.

Results: Serum calcium and creatinine values had with few exceptions remained stable over the years. In five patients, serum calcium levels were within the normal range at follow-up. Still, all 19 patients were considered hyperparathyroid. They had substantial cardiovascular morbidity, and their state of health was not as good as that of the patients who were surgically cured. After one operation, 5.5% (95% confidence interval (CI) 4.0–7.2%) had persistent disease, and 2.1% after reoperation. Extensive surgery for cure was performed in 2% of the patients (95% CI 1.1–3.2%).

Conclusions: We found that the state of health was significantly better for patients with cured primary hyperparathyroidism than for patients with persistent disease, but serious deterioration of laboratory values was uncommon. The result of the present study supports surgical treatment.

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Introduction

Surgery is the effective treatment for primary hyperparathyroidism. However, several patients have been reported to get on rather well without surgery (1–6), although this could not have been predicted. At present the arguments for treatment of primary hyperparathyroidism appear weighty even in asymptomatic disease. The success rate of parathyroid surgery is high, but not 100%. The aim of this paper was to find out what happened in the long run to the few patients who were not cured in spite of surgery, and also how frequently extensive surgery was necessary for cure.

Patients and methods

The medical records of all patients operated on for primary hyperparathyroidism at Sahlgrenska Hospital in Göteborg in the years 1953–1982 were scrutinised ($n = 896$). Generally, bilateral neck exploration had

been performed, and hyperparathyroidism was histopathologically verified in all cases. In 1986–1987 a long-term follow-up was performed to determine mortality (7) and also the patients' laboratory data and medical status (8) after surgery for primary hyperparathyroidism. Because of different follow-up procedures three groups of patients were defined: group I was patients followed up at Sahlgrenska Hospital; group II was patients followed up outside Göteborg; and group III included the patients who were deceased. The 600 patients alive were contacted by letter containing an invitation to take part in a follow-up programme including a questionnaire, laboratory tests and blood pressure measurement. For the deceased, group III, medical records from the period after the operation at Sahlgrenska Hospital were searched for. Follow-up values of serum calcium concentration were obtained in 787 patients (88%), with a mean follow-up time of 10.03 years (s.d. 6.0) (8). The serum calcium and creatinine levels were determined in all patients, but for those living in Göteborg and examined at Sahlgrenska

Hospital, group I, ionised serum calcium and parathyroid hormone levels were also taken. Reference limits varied slightly between laboratories, but the upper reference limit of total serum calcium concentration did not. The reference limits of the laboratory of Sahlgrenska Hospital of total serum calcium were 2.20–2.60 mmol/l, of ionised serum calcium 1.18–1.31 mmol/l, of serum parathyroid hormone 10–65 ng/l (IRMA), or <9.6 pmol/l (RIA), and of serum creatinine <120 µmol/l for male and <110 µmol/l for female (8).

Cure after parathyroid surgery had been defined as serum calcium concentration <2.55 mmol/l during the first postoperative year (7). According to the medical records kept until the end of 1982 there were 27 patients out of 896 who with this definition were considered to have persistent disease (7). Two of these patients died postoperatively, one in 1962 within 24 h with cardiac arrest and acute haemorrhagic pancreatitis, the other in 1965 after 10 days with duodenal ulcer disease and acute uraemia, both with severe hypercalcaemia. The post-mortem examination of the latter revealed a myeloma in a lumbar vertebra to have caused her persistent hypercalcaemia instead of persistent hyperparathyroidism. Two additional patients were not found at scrutiny to have had true persistent disease. Four patients were surgically cured in 1983 and 1984. Nineteen patients were left with persistent disease: three patients had declined further surgery after their second unsuccessful operation. The remaining 16 patients were left without further surgery as they were considered to have only mild serum calcium elevations after their primary surgery, 2.44–2.70 mmol/l at discharge, and 12 of them had gained a substantial decrease. After the first postoperative year there was no regular routine for check-ups. Unfortunately serum calcium determinations taken at the out-patient department were differently documented and therefore in a few cases lost to the present follow-up. The situation at follow-up was evaluated for each patient, the mode of surgery, the serum calcium and creatinine levels, and the history after parathyroid surgery. The risk for the need for extensive surgery for cure was estimated, and also the risk of persistent disease after surgery for primary hyperparathyroidism, with and without reoperations considered, and 95% confidence intervals (CIs) were calculated exactly by use of the binomial distribution (9).

At follow-up the patients alive with persistent hyperparathyroidism were compared with the patients alive who were surgically cured and without any suspicion of recurrent disease as evaluated by their follow-up levels of serum calcium and parathyroid hormone. In the questionnaire it was asked whether the patient had been treated for bone fracture during the follow-up period, and if so, in what year, and which bone had been injured. It was asked about current medication, which was answered either by marking given

alternatives, or by writing the name of the drug, or both. There was also a section in which the patients were asked to evaluate their state of health by marking the suitable answers (a–e) to five simple questions: (a) I am in excellent health (yes/no); (b) I am concerned about some kind of disorder/worry/anxiety (no = 0, slightly = 1, moderately = 2, substantially = 3); (c) my condition/discomfort/illness affects my everyday life (no = 0, slightly = 1, moderately = 2, substantially = 3); (d) I need frequent medical care or am under investigation because of a serious situation (yes/no); and (e) I am in a nursing home permanently (yes/no). The filling in of the questionnaire was generally checked by the nurse who took the follow-up blood samples.

A two-tailed *t*-test was used for comparison of mean age between the two patient groups studied. Fisher's exact test was used for comparison of proportions in these two groups, and also for the 'yes/no' answers. A test for trend in contingency tables (10) was used when comparing the state of health in the two groups, as for the graded answers in b and c, described above. All *P* values given are two-tailed.

Results

Primarily, after one operation, persistent hypercalcaemia because of hyperparathyroidism occurred in 49 out of 896 patients, 5.47%, shown in Table 1. Thirty-two underwent further parathyroid surgery, and 29 out of 49 became surgically cured, 20 with multiple-gland disease, and nine with single-gland disease, the latter generally with an unusual site of the pathological gland, or a fifth gland. One patient had an adenoma inside the thyroid capsule. Another had instead the problem of diseased parathyroid tissue being implanted in the neck muscles, which proved to be very difficult to remove. Mediastinal exploration was performed in 13 patients, and in 12 of them the pathological parathyroid gland was found in the mediastinum. Extensive surgery, defined as more than two neck explorations, or mediastinal exploration, was performed in 18 patients. We found 5.5% risk of having persistent hyperparathyroidism after one operation, with 95% CI 4.0–7.2%. If reoperations were considered, 19 out of 896 patients

Table 1 The events of 49 patients who had persistent primary hyperparathyroidism after their primary neck operation.

	No. of patients
Died within 24 h	1
Left with persistent disease	16
Declined reoperation	3
Normocalcaemic after two operations	19
Normocalcaemic after three operations	7
Normocalcaemic after four operations	2
Normocalcaemic after five operations	1
Total	49

had persistent disease, and the risk was 2.1%, with 95% CI 1.2–3.3%. The risk of undergoing extensive surgery because of primary hyperparathyroidism at our clinic during this period was 2.0% with 95% CI 1.1–3.2%.

The 19 patients with persistent disease, four men and 15 women, were numbered according to year of surgery and are shown in Table 2. It shows their preoperative peak serum calcium level, which was the mean of the two highest values registered, their level at discharge after surgery, and the serum calcium level(s) thereafter. It also shows the mode of surgery performed, and who were operated on for hyperparathyroidism more than once.

Table 3 shows the follow-up data of the 19 patients with persistent disease, including a summary of their medical situation. Mean age at follow-up was 70.6 years (s.d. 7.97), and mean follow-up time for the deceased was 3.6 years, and for the 13 patients alive a mean 10.3 years, range 4.2–21.1 years. There were nine patients of group I, four with increased parathyroid hormone levels, and five with high hormone levels in relation to their serum calcium concentration, verifying hyperparathyroidism being the cause of hypercalcaemia. Such verification was available in only one of four patients of group II, and in one of six patients of group III. In spite of five patients having all follow-up serum calcium determinations within normal values, persistent hyperparathyroidism was still the probable diagnosis in these cases. They all had persistent hypercalcaemia after surgery, for which no other reason had been found. Fourteen patients had normal serum creatinine values at follow-up, two had values at the upper reference limit, and three had slight elevations (125–140 µmol/l). Thirteen patients had treatment for hypertension at surgery for hyperparathyroidism, and 17 had hypertension at follow-up. Cardiovascular disease, hypertension excepted, occurred in six patients at surgery and in 15 at follow-up.

The 13 patients alive at follow-up are shown in Table 4, with their own evaluation of their state of health, and also their history of bone fractures and cardiovascular disease. Four of the 13 patients alive with persistent disease had had fractures during the follow-up period (30.8%), and 74 patients of the 509 with cured hyperparathyroidism (14.5%), although this difference was not significant. There appeared to be a trend towards a higher rate of anxiety among the patients with persistent disease ($P = 0.076$), and the degree of discomfort and illness was significantly worse for the patients with persistent disease ($P < 0.01$), as was the occurrence of cardiovascular disease and/or hypertension ($P < 0.05$). Mean age of the 13 patients was higher, 70.3 years (s.d. 9.5), as compared with that of the cured patients, 65.7 years (s.d. 11.8), although this difference was not significant ($P = 0.164$). Mean follow-up time was 10.3 years (s.d.

5.4) for the former, and 11.3 years (s.d. 5.5) for the latter, and mean preoperative peak serum calcium level was 2.83 mmol/l (s.d. 0.14) and 2.88 mmol/l (s.d. 0.30) respectively.

Discussion

At long-term follow-up of 19 patients with persistent hyperparathyroidism, hypercalcaemia had with few exceptions kept stable and the serum calcium level was in most cases only marginally elevated. Only 16 out of 36 total serum calcium determinations performed at follow-up were elevated, and only two patients had both of the taken values increased. Besides these two, only three patients had one value above 2.75 mmol/l. There was no substantial progression of renal impairment, as evaluated by the serum creatinine values. But we could also observe that the health descriptions of these patients were not at all satisfying. They had substantial cardiovascular morbidity, as was previously shown to be part of the hyperparathyroid condition (11).

Six out of 19 patients with persistent disease died 2.2–11.8 years after surgery for primary hyperparathyroidism at the mean age of 74.8 years (s.d. 6.76). They all had cardiovascular illness and/or hypertension, which was also their main cause of death with one possible exception: patient no. 1 who fell because of a cerebral haemorrhage and got a skull fracture and epidural bleeding as well. They also appeared to suffer from symptoms considered to be related to hyperparathyroidism.

It was reported that untreated or persistent hyperparathyroidism is a rather stable condition without progressive increase of serum calcium levels (2–6), and compatible with long survival and lack of demonstrable deleterious effects on kidney and bone (4). This was just partly in agreement with our findings; long survival is a matter of definition. Our patients were too few for strict evaluation of survival, but 5 years below average length of life might not be 'long survival'. Furthermore, there appeared to be a negative effect on bone among the patients with persistent disease, their bone fracture frequency being doubled, but this difference was not significant. We found instead a significantly greater share of patients with persistent disease to have hypertension and/or cardiovascular disease. The conclusions in previous reports were divergent between recommending surgical treatment and conservative follow-up (1–6). It seems as if the lack of change in serum calcium and creatinine values over time was generally the main argument not to recommend surgery in this debate (2–4, 12). These laboratory tests are easily measured but give only limited clinical information. A tendency towards high cardiovascular morbidity occurring in hyperparathyroidism was noted by Palmér *et al.* (12), and towards illness of various kinds by Corlew

Table 2 Serum calcium levels (Ca/s) (mmol/l) of 19 patients before and after surgery for primary hyperparathyroidism, serum calcium decrease after surgery, and values taken thereafter, and at follow-up. The number of excised (exc) parathyroid glands (Pth), and number of parathyroid gland biopsies (b) out of the number macroscopically identified parathyroid glands are shown. *Opx2* means operated on twice; *Impl* means excision of implanted parathyroid tissue; *Thyr-x* = thyroidectomy; *H-thyr-x* = hemithyroidectomy; *Ad* = parathyroid adenoma; *Hpl* = Parathyroid hyperplasia. Group I was patients followed up in Göteborg, and group II outside Göteborg. Group III were patients deceased at follow-up.

Patient no.	Sex; group	Year of surgery	Parathyroid and thyroid surgery performed	Parathyroid diagnosis	Ca/s preop	Ca/s postop	Change (mol)	Change (%)	Ca/s 1st to 3rd year	Ca/s 4th to 6th year	Ca/s 7th to 12th year	Ca/s 13th to 20th year
1	M III	1962	3 exc/ 3 Pth; <i>opx 2</i> ;	1 Hpl + 1Ad	2.75	2.53	0.22	8.0	—	2.60–2.65	—	—
2	M III	1963	1 exc (original report lost)	Ad	2.85	2.45	0.40	14.0	2.50	2.75–2.90	2.55–2.65	—
3	F I	1967	1 exc/ 3 Pth; <i>Thyr-x</i>	1 Hpl Pth	2.60	2.45	0.15	5.8	2.60	2.75	2.34–2.42	2.50–2.70
4	F III	1968	1 exc + 1b/ 4 Pth; <i>H-thyr-x</i>	Ad	3.58	2.80	0.78	21.8	2.65	2.65–2.80	—	—
5	F II	1968	2 exc/ 3 Pth; <i>opx 2</i> ; <i>Thyr-x</i>	Ad	2.85	2.60	0.25	8.8	—	2.62	—	2.76–2.90
6	M I	1969	2 exc/ 4 Pth	Ad	2.75	2.55	0.20	7.3	—	2.60	2.70	2.55–2.60
7	F III	1971	3½ exc/4 Pth; <i>opx 2</i> ; <i>H-thyr-x</i>	3 Hpl Pth	2.75	2.55	0.20	7.3	2.45–2.65	—	2.55	—
8	F III	1973	1 exc + 2b/ 4 Pth;	Ad	3.10	2.55	0.55	17.7	2.50–2.70	—	—	—
9	F III	1973	1 exc/ 3 Pth	Ad	2.90	2.60	0.30	10.3	2.65	—	—	—
10	F I	1974	2 exc + 1b/ 3 Pth	3 Hpl Pth	3.10	2.80	0.30	9.7	—	2.80	2.60–2.80	2.80
11	F I	1975	2 exc + 1b/ 4 Pth	2 Hpl Pth	2.68	2.45	0.23	8.6	2.65	—	2.39–2.45	—
12	M II	1976	2 exc + 1b/ 4 Pth;	2 Hpl Pth	2.99	2.47	0.52	17.4	2.53–2.81	—	2.60–2.70	—
13	F I	1978	2 exc/4 Pth;	Ad	2.92	2.63	0.29	9.9	—	—	2.60–2.70	—
14	F I	1979	1 exc + 3b/ 4 Pth; <i>Impl</i> ; <i>Thyr-x</i>	Ad + <i>Impl</i>	2.95	2.44	0.51	17.1	2.60	—	2.80–3.10	—
15	F II	1979	1 exc + 1b/ 4 Pth;	1 Hpl Pth	2.76	2.44	0.32	11.6	2.66	2.82	2.20	—
16	F II	1981	1 exc/4 Pth	Ad	2.70	2.40	0.30	11.1	2.62	2.40–2.60	—	—
17	F I	1982	1 exc/ 2 Pth	Ad	2.90	2.50	0.40	13.8	2.70–2.80	2.60–2.90	—	—
18	F I	1982	1 exc/ 4 Pth	Ad	2.80	2.60	0.20	7.1	2.60	2.40–2.80	—	—
19	F I	1982	1 exc/ 4 Pth	Ad	2.80	2.40	0.40	14.3	2.70	2.55–2.64	—	—

Table 3 Result of follow-up of 19 consecutive patients left with persistent disease after surgery for primary hyperparathyroidism (HPT). Pathological values are marked (*). SglD = single-gland disease; MglD = multiple-gland disease. Patients of group I were followed up in Göteborg, those of group II outside Göteborg. The patients of group III were deceased (†) at follow-up in 1986, and for those their last serum calcium (Ca/s) registration found is given. Hypercalcaemia was graded: +++/++ = substantial; + = mild/moderate; m = marginal; and no = normocalcaemia. Ht = hypertension; CVD = cardiovascular disease; PTH/s = serum parathyroid hormone; iPTH = intact parathyroid hormone; Pers = persistent. Blood pressure, given in brackets, was measured at follow-up (mm Hg).

Patient no.	Sex; group	Year of surgery	Type of HPT	Total Ca/s at follow-up (mmol/l)	Ionised Ca/s (mmol/l)	Serum creatinine (μmol/l)	PTH/s RIA (pmol/l)	iPTH/s IRMA (ng/l)	Age (years)	Follow-up (years)	HPT status at follow-up	The patient's own health description, and a summary	Ht and CVD—year of diagnosis
1	M III	1962	MglD	2.63*	—	120	—	—	69	4.6	Pers? Ca: +	† 1972: skull fracture, intracranial haemorrhage; backache	Ht – 1962
2	M III	1963	SglD	2.60/2.65*	—	140*	—	—	73	9.1	Pers? Ca: +	† 1975: myocardial infarction; depression; leg fractures 1971+1972	Ht – 1963; CVD – 1973
3	F I	1967	SglD	2.50/2.70*	1.29	70	6.8	46	74	20.1	Pers* Ca: +	OK, minor malfunction, anxiety at times	Ht – 1986; CVD – 1970
4	F III	1968	SglD	2.65*	—	80	—	—	68	4.0	Pers? Ca: +	†1974: Breast cancer with metastases; body-pain; fracture of humerus 1971	Ht – 1965; CVD – 1961
5	F II	1968	SglD	2.90*/2.76*	—	74	175*	—	75	17.3	Pers* Ca: +++	Unwilling to communicate-lived isolated in a cottage; anxiety	Ht – yes; CVD – yes
6	M I	1969	SglD	2.60/2.55	1.28	104	11.4*	72*	75	18.1	Pers* Ca: m/no	Unwell, general bodypain; backache; anxiety; vertebral fracture 1985	Ht – for long time
7	F III	1971	MglD	2.55	—	110	—	—	77	8.0	Pers? Ca: m/no	† 1983; CVD; bodypain; anxiety; loss of initiative; considered odd	Ht – 1972; CVD – 1967
8	F III	1973	SglD	2.50/2.70*	—	100	—	—	71	0.2	Pers? Ca: +	†1976; CVD; senile dementia; chronic cystitis	Ht – 1962; CVD – 1962
9	F III	1973	SglD	2.65*	—	125*	Increased	—	68	1.0	Pers* Ca: +	†1975: cerebrovascular lesion; gout; Op. malignant tumour of the colon 1974	Ht – 1973; CVD – yes
10	F I	1974	MglD	2.80*/2.60	1.38*	90	16.3*	120*	82	12.8	Pers* Ca: ++	In a nursing home since 1982; anxiety; senile dementia; hip fracture 1984	Ht – 1974; CVD – yes
11	F I	1975	MglD	2.45/2.39	1.25	79	—	80*	66	11.8	Pers* Ca: no	Unwell, anxiety; cardiac angina; bleeding ulcer 1984 and 1986	CVD – 1974
12	M II	1976	MglD	2.60/2.60/2.70*	—	71	—	—	68	10.2	Pers? Ca: +	OK, minor malfunction; no medication; cerebrovascular lesion 1985	Ht – (160/100); CVD – yes
13	F I	1978	SglD	2.60/2.60	1.36*	74	8.7	53	74	9.1	Pers* Ca: +	OK, cardiac angina; hip fractures 1979+1985	Ht – 1977; CVD – yes
14	F I	1979	SglD	3.10*/2.90*	1.57*	132*	37.0*	337*	77	7.8	Pers* Ca: +++	Unwell, dementia; multiple cerebral infarctions; diabetes 1982	Ht – 1978; CVD – 1980
15	F II	1979	SglD	2.20	—	71	—	—	72	7.0	Ca: no?/ false?	Fine, but minor malfunction, diabetes 1982; cerebrovascular lesion in 1983	Ht – 1973; CVD – yes
16	F II	1981	SglD	2.60/2.40/2.40	—	50	—	—	51	4.7	Pers? Ca: m/no	Fine, medication for hypotension; dysuria; lower extremity fracture 1986	—
17	F I	1982	SglD	2.60/2.80*/2.90*	—	86	8.0	50	79	5.1	Pers* Ca: ++	OK, but dysuria, dizziness; in need of care; slightly senile, no medication	Ht – (170/90)
18	F I	1982	SglD	2.80*/2.40	1.29	73	—	42	60	4.2	Pers* Ca: ++	OK, anxiety at times	Ht – 1974
19	F I	1982	SglD	2.64*/2.55	1.32*	81	7.7	41	54	5.2	Pers* Ca: +	Unwell, anxiety, depression; cardiac angina	Ht – 1979; CVD – 1984

Table 4 Comparison of state of health of the patients still alive at long-term follow-up after surgery for primary hyperparathyroidism (pHPT) according to a questionnaire; 13 patients with persistent disease vs 509 patients who were surgically cured. Blood pressure measurements were also performed. Two-sided *P* values are given.

	Persistent disease		Cured pHPT		<i>P</i>
	<i>n</i>	%	<i>n</i>	%	
Total number	13	—	509	—	—
History of bone fracture	4	30.8%	74	14.5%	0.2282
I am in excellent health	2	15.4%	161	31.6%	>0.30
I am in excellent health and without medication	0	0%	84	16.5%	0.199
No hypertension and without cardiovascular medication	1	7.8%	200	39.3%	0.0309
I am troubled by some kind of disorder, worry or anxiety	10	77.0%	290	57.0%	0.0759
Not at all	3	—	219	—	—
Slightly	1	—	71	—	—
Moderately	7	—	165	—	—
Substantially	2	—	54	—	—
My condition, discomfort or illness affects my everyday life	13	100%	404	79.0%	0.0057
Not at all	0	—	105	—	—
Slightly	1	—	157	—	—
Moderately	7	—	144	—	—
Substantially	5	—	103	—	—
I am in frequent need of medical care, and/or have a serious situation	0	0%	18	3.5%	>0.30
In nursing home	2	15.4%	6	2.1%	0.0295

et al. (5). Mean follow-up time was greater than 10 years in three of these studies (1, 6, 12), and 8.2 years in one (5). In the remaining it was 3.5–5.6 years (2–4), which might not suffice for forming an opinion. It is well known that signs and symptoms in primary hyperparathyroidism are rarely obvious, that the serum calcium level alone does not fully reflect the degree of disease, and that marginally or moderately increased serum calcium levels may occur even in substantial hyperparathyroidism (5, 13–15). In a few of the follow-up studies mentioned above it was briefly reported that the patients were well (2–4). Mean age in these reports were only 50.8, 59.8 and 54.8 years respectively, which might explain this observation. But Van't Hoff *et al.* (3) also observed, in 22 hyperparathyroid patients who were not advised operation, that ten patients, mostly elderly, suffered from cardiovascular disease, which was not at that time considered related to their hyperparathyroidism, but was the grounds not to recommend surgery.

In the present patient series, 2.1% of the patients were left with persistent hyperparathyroidism, as compared with 1.3% reported by Bruining *et al.* in 1981 (16), and 3.7% by Lundgren *et al.* in 1992 (17). To the best of our knowledge, no long-term follow-up with detailed comparison of the clinical status of patients with persistent hyperparathyroidism and patients with cured disease has been performed previously, which may depend just on the fact that the numbers of patients with persistent disease are generally small. The answers in the questionnaires of the present study were equally collected and interpreted for all 522 patients studied in this perspective, making comparison of the subgroups reliable irrelevant of their size. We found that the state of health was described

as significantly better by the patients with cured hyperparathyroidism as compared with the ones with persistent disease. The finding of congruity between the results of the eight tests performed makes significance by chance unlikely; the difference was significant in three tests, a strong trend in one, and insignificant in four tests. The cured patients had marginally longer follow-up time and also slightly higher mean preoperative serum calcium levels, which factors therefore could not have produced these test results. Nor could the difference in age between the two groups explain the present findings, as it was statistically insignificant. An insignificant relationship would not be expected to indirectly produce a highly significant difference between other possibly related variables.

The risk of needing extensive surgery was 2.0% in our patient series. If a higher cure rate had been aimed at, the number of patients needing extensive surgery would probably have been higher. Mediastinal explorations will, however, always be necessary from time to time, and in our patient series it had to be done in at least 12 patients, or in 1.4% of them, the conclusion of which is that not more than about 98% of the patients with primary hyperparathyroidism could be expected to be cured by neck surgery alone. Van Heerden *et al.* (18) reported in 1991 a corresponding success rate after primary neck exploration of 98.2% in a consecutive series of 379 patients.

In summary, in our patient series, 18 patients, or 2.0%, needed extensive surgery for cure of their primary hyperparathyroidism. Another 19 patients, or 2.1%, were left with persistent disease. Their serum calcium and creatinine levels had with few exceptions remained stable at long-term follow-up, but these patients had generally cardiovascular morbidity. The

state of health of 13 of these patients who were still alive at follow-up was unsatisfactory in comparison with that of the patients who had been successfully surgically treated for primary hyperparathyroidism. Therefore the result of this study supports surgical treatment of primary hyperparathyroidism. It demonstrated, in contrast to previous reports on the subject, that persistent primary hyperparathyroidism ought not to be evaluated on the basis of laboratory data alone.

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