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Premature Death in Patients Operated on for Primary Hyperparathyroidism

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To investigate long-term survival after operation for primary hyperparathyroidism, a follow-up study was performed on 896 consecutive patients in whom this diagnosis had been clinically and microscopically verified. These patients were operated on in the years 1953–1982. Their mean age at operation was 57.3 years [standard deviation (SD) 13.1], overall cure rate was 97.0%, and postoperative mortality was 0.89%. Follow-up was 99.8% complete by the end of 1986. Mean follow-up time was 12.9 years (SD: 6.1). Two-hundred ninety-four patients were deceased, which was 118 more than in a control group ($p < 0.001$). The latter was based on Swedish population statistics, matched for age, sex, and calendar year. Each year, the control group was the same size as the hyperparathyroid population. The risk of premature death remained increased ($p < 0.001$) even after exclusion of poor-risk patients having their hyperparathyroidism diagnosed when being treated or followed because of other serious diseases. The main causes of premature death for the hyperparathyroid patients were cardiovascular and malignant diseases. Both occurred more often than in the control group ($p < 0.001$). The results demonstrate that primary hyperparathyroidism causes damage that is not reversed by surgery.

Two long-term follow-up studies suggested that patients operated on for primary hyperparathyroidism run an increased risk of death compared to age- and sex-matched controls [1, 2]. Both claimed that cardiovascular disease is the cause of premature death. Neither of the 2 studies revealed an increased risk of dying from malignant disease, although there are reports indicating an increased occurrence of malignant disease among patients with primary hyperparathyroidism [3–5].

Detailed knowledge of the prognosis of the hyperparathyroid patients after operation is essential in planning optimal treatment and design of follow-up. The above-mentioned studies have raised an important issue, which can only be investigated by studying large representative series of hyperparathyroid patients who have been thoroughly examined before surgery and at follow-up. With such a series that is based on uniform clinical and surgical strategies, we have studied the issue of mortality after operation for primary hyperparathyroidism.

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Previous studies have suggested that patients operated on for primary hyperparathyroidism run an increased risk of premature death. The aim of the present study is to find out whether this supposition can be verified.

Material and Methods

Patients

Eight-hundred ninety-six patients were included in this study: 656 women (73.2%) and 240 men (26.8%). They were identified by applying the criteria belov when scrutinizing the records of patients who had parathyroid surgery at Sahlgren's Hospital from 1953 to the end of 1982. Early in the 1960's, there was a detailed preoperative program drawn for these patients, which was used thereafter. It included a questionnaire concerning symptoms and history, laboratory tests, and x-rays of special interest to hyperparathyroidism. These data are now available in more than 95% of the cases with few exceptions. Laboratory tests were done on at least two samples and glomerular filtration rates were measured in most cases. As a rule, intravenous pyelogram was performed, but, in a few cases, only an abdominal stone survey[1] was done. All patients were taken care of within 1 unit in the clinic and by a limited number of surgeons. The microscopic specimens were all scrutinized by Dr. Göran Hansson at the Department of Pathology, Östra sjukhuset, Göteborg. Only cases with histologically verified hyperparathyroidism were included in this series. The histopathological examination showed the existence of an adenoma in 1 gland in 753 cases (84.0%), chief cell hyperplasia in 2 or more glands in 109 cases (12.2%), and water-clear cell hyperplasia in 32 cases (3.6%). There were 2 cases of parathyroid cancer (0.2%).

Six patients with serum creatinine values above 300 μmol/l and possibly combined causes of renal impairment were excluded as it was impossible to judge whether their hyperparathyroidism was primary or secondary. Four patients in the series had serum creatinine values above 300 μmol/l. In total, 112 patients with functional renal impairment were included in

[1] X-ray of kidneys, ureters, and urinary bladder. Contrast medium was not used.

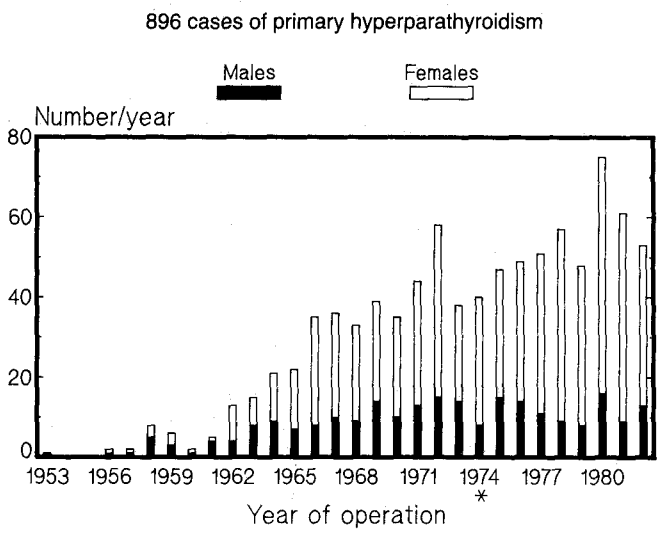

Fig. 1. Number of patients operated on for primary hyperparathyroidism each year from 1953 to 1982 at Sahlgren's Hospital with men and women listed separately. *Median year for surgery in the series.

the series. Functional renal impairment was defined as creatinine values exceeding 115 μmol/l for women and 125 μmol/l for men when the patient had an optimally restored fluid and electrolyte balance. The latter patients were considered to be cases of primary hyperparathyroidism because no other cause was found for the renal impairment (n = 84) or they had either hypercalcemia or verified renal stone disease before they developed renal impairment, which was the case in 28 of the 112 patients who had renal, prostate, or urinary bladder disease diagnosed in addition to hyperparathyroidism. The frequency of renal stone disease among the patients with normal renal function was 51%, and it was 65% among the 112 patients with raised serum creatinine values. This difference was significant (Fisher's exact 2-tailed test, $p < 0.01$). There was no difference in the rate of renal stone disease in patients with raised serum creatinine values and hyperparathyroidism only (n = 84) compared to patients with unrelated urinary tract disease in addition to hyperparathyroidism (n = 28).

Four-hundred thirty-nine patients were inhabitants of Göteborg, while 409 came from other parts of the western region and 48 from other regions of Sweden. Reoperative surgery was performed in 64 cases, of which 29 had been referred to Göteborg because of persistent hyperparathyroidism. Thus, the frequency of reoperations after primary operation at Sahlgren's Hospital was 4.0%. The median year for surgery in the series was 1974. Forty-four percent of the patients operated on up to 1974 were citizens of Göteborg compared to 56% of patients treated after 1974. Figure 1 shows the number of patients operated on annually and also demonstrates the sex distribution. The annual number of cases increased up to the mid-1970's and, since then, 50–60 patients have been operated on each year.

Surgical Strategy

Operation has been advised in cases with verified hypercalcemia after causes other than hyperparathyroidism have been excluded; however, old (>75 years) or fragile patients with asymptomatic disease and only slight hypercalcemia (<2.75 mmol/l) have not been offered surgery. Sixty-four percent of the patients were operated on within 1 year of the first serum calcium concentration above 2.60 mmol/l and 79% within 2 years.

At operation, 4 parathyroid glands were identified, if possible. When only 1 gland was enlarged, it was excised, in most cases together with a biopsy from a normal-looking gland. When 2 or 3 glands were enlarged, a biopsy was also taken from the remaining gland(s) as a rule. When all 4 glands were enlarged, subtotal parathyroidectomy was performed in most cases. In recent years, however, the routine method for treatment of parathyroid hyperplasia has been total parathyroidectomy and autotransplantation of part of the diseased parathyroid tissue into the abdominal subcutaneous fat [6]. During one period, autotransplantation of diseased parathyroid tissue into muscle tissue was also performed [7]. Facilities for examination of frozen sections were always available but were not used in every case.

Methods at Follow-Up and Statistics

The 896 patients were identified by their national registration numbers and searched for through the population register, which contains information on all citizens in Sweden and is updated monthly. In this way, the patients still alive and those deceased during the last 3 years were easily traced. The others were searched for at the Swedish Central Bureau of Statistics (SCB) [8], which also provided information about the time, place, and cause of death. Data concerning patients who had died in recent years were obtained from local authorities. Data concerning patients who had emigrated were obtained from foreign national registries.

By the end of 1986, the 896 patients were traced as follows: 294 patients were deceased, 592 patients were living in Sweden, 8 patients were living abroad, and 2 patients could not be located. One of the latter was a man of Yugoslavian origin, born in 1933 who was operated on in 1965. The other was a woman born in 1939 and operated on in 1972, who emigrated to the United States of America in 1974. Both had single adenomas. It has been assumed, in the statistical calculations, that they are still alive.

The starting date for calculating follow-up time is the date hyperparathyroidism was cured. In cases of persistent disease, the date of the last operation performed was used instead. All dates were given in years and months.

The primary causes of death given in this report were based on the death certificates, which were formulated in accordance with the International Classification of Deaths (ICD) [9]. This classification is also used by the Swedish Central Bureau of statistics [8, 10]. One modification was made: when the primary cause of death noted in the SCB registry was hyperparathyroidism, and the direct cause was renal disease with uremia, the cause given in our report was instead death from renal disease. There were 5 such cases in the series.

The correlation between age at operation and calendar year was tested with Pitman's test.

The control material was the Swedish population. The annual official reports published by the SCB [8] give the total number

of deaths as well as the number of deaths from different causes for age groups spanning 5 years for each sex [10]. Information on the size of the corresponding mean populations is also given [11]. From these data, a control group was formed. Each calendar year it had the same size as the hyperparathyroid population and the same sex and age distribution. The number of deaths of the control group was the sum of all deaths during the 33-year-long period, when the numbers of deaths had first been calculated each year—for each age group, for men and women separately (see appendix). Forming the control group in this way eliminates the risk of possible influences from changes in death rates that might have taken place in the Swedish population in the years 1953–1986. It also guarantees that the control group does not turn into a badly matched group as time passes, as could be the risk when matching is done with fixed individuals over a long period of time.

Comparison of the number of deaths in the hyperparathyroid group and the control group in the corresponding period was made with a 2-tailed test based on the Poisson distribution: $p < 0.05$ was considered to be significant.

In any consecutive series of hyperparathyroid patients, there are a number of cases that have been diagnosed because another illness brought the patient to the hospital. If this illness in itself is serious, there is a risk of adding extra mortality to the hyperparathyroid population. In order to eliminate this possible bias, the situation at diagnosis of hyperparathyroidism was analyzed. A selected series was formed from which a patient was excluded if hyperparathyroidism had been detected during medical care for an acute illness or chronic disease, that in itself could carry an increased risk of death. These included myocardial infarction, episodes of heart failure, arrythmias, stroke, diabetes, malignant tumors, and multiple endocrine neoplasia syndromes. Also, patients with hypertension of more than 2 years' duration prior to the first documentation of an elevated serum calcium concentration were excluded. In this way, the 725 patients of the selected series had their hyperparathyroidism detected either because of symptoms of hyperparathyroidism itself, e.g., renal stone disease, or by chance, i.e., medical care, because of some harmless condition irrelevant to hyperparathyroidism, but which resulted in the measurement of serum calcium levels as part of the routine evaluation. The statistical procedure described above was repeated with this selected series.

Results

Age and Laboratory Data at Surgery

Mean age at operation of the 896 patients was 57.3 years (SD: 13.1). For women it was 58.8 years (SD: 12.2, range: 17–83) and for men, 53.4 years (SD: 14.5, range: 11–83). During the whole period there was a trend towards a rising number of women while the number of men was fairly constant (Fig. 1). There was a gradual increase in age at operation during the period ($p < 0.001$). Mean age in the beginning of the period, from 1953 to 1965 (n = 97), was 52.7 years (SD: 10.9) while at the end, from 1980 to 1982 (n = 189), it was 60.7 years (SD: 12.7). The increase in mean age at operation concerned both sexes, but it was more obvious for women ($p < 0.05$ for men and $p < 0.001$ for women). The relationship between age at operation and year of operation was consistent with a linear regression function, as the correlation coefficient was only marginally increased with a second order function. During the period, the mean age for women increased by 1 year per 5 years, and for men by 1 year per 6.7 years (Fig. 2).

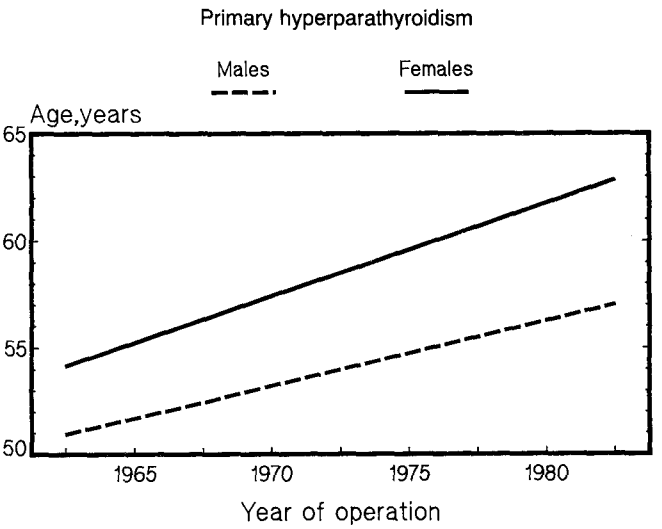

Fig. 2. Mean age at operation for primary hyperparathyroidism increased linearly from the 1960's to the 1980's for both men and women.

The serum calcium concentration registered for each patient was the mean value of the 2 highest values (peak values) observed in the immediate preoperative period. The mean peak serum calcium concentration was 3.03 (SD: 0.50) in the beginning of the period and 2.81 mmol/l (SD: 0.27) at the end. The mean serum creatinine levels also decreased during the period, from 117 (SD: 43) in the beginning to 91 μmol/l (SD: 56) at the end. The mean laboratory values given here are calculated for the periods 1953–1965 and 1980–1982.

Immediate Postoperative Results

The overall cure rate was 97% (869 patients), the results of the reoperations also considered. Cure was defined as a stable serum calcium concentration <2.55 mmol/l during the first postoperative year. Thirty-eight patients (4.2%) were supplemented with vitamin D for at least 2 years after the operation. When dividing the patients into equal groups of past and recent cases, there were 29 (6.5%) of 448 in the former group and 9 (2.0%) of 448 in the latter who needed replacement therapy to maintain normal serum calcium levels. Twenty-one of the hypoparathyroid patients had multiple gland disease, 16 were reoperative cases, and 11 were subjected to total thyroidectomy (Fig. 3).

Eight patients (0.89%) died within 1 month of operation (Table 1). Since September, 1974, one (0.22%) patient of 448 has died postoperatively.

Results of Follow-Up

The mean follow up-time was 12.9 years (SD: 6.1, range: 4–33) for the whole series, 12.3 years (SD: 5.8) for women, and 14.5 years (SD: 6.5) for men. Follow-up was 99.8% complete.

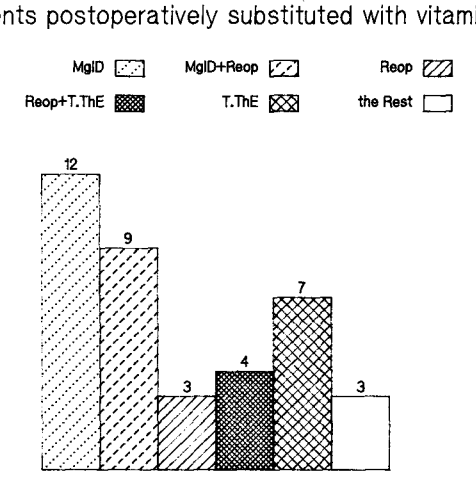

Fig. 3. Most of the patients that needed replacement therapy were shown to be included in 1 or 2 of 3 categories: multiple gland disease, n = 21 (MglD), reoperative cases, n = 16 (Reop), and patients who were subjected to total thyroidectomy, n = 11 (T.ThE).

Table 1. Postoperative mortality within 1 month after operation for primary hyperparathyroidism: 8 (0.89%) of 896 cases.

No.	Year	Age (yr)	Sex	Cause of death	No. of days postoperatively
1	1963	54	F	Myeloma	10
2	1965	65	F	Hypercalcemic crises with pancreatitis	1
3	1966	53	F	Myocardial infarction	4
4	1966	68	F	Cardiosclerosis, heart failure	30
5	1967	83	F	Bronchopneumonia	26
6	1972	75	F	Myocardial infarction	21
7	1974	77	F	Cardiosclerosis, heart failure	18
8	1981	51	M	Cardiosclerosis	26

The total number of deaths at follow-up was 294 and the causes of death are given in Table 2. The numbers of deaths in the hyperparathyroid group and the equally-sized control group are given in Table 3, which also shows the p values. Comparison between the numbers of deaths in the 2 groups showed an increased premature mortality among the hyperparathyroid patients ($p < 0.001$). The ratio between the numbers of deaths from all causes in the 2 groups was 1.67, and there was no significant difference between men and women. This increased risk was shown to be due mainly to cardiovascular disease and malignant neoplasms.

Of the 156 patients who died from cardiovascular disease, 50 died from myocardial infarction, 44 from stroke, 53 from heart failure, and 9 from generalized atherosclerosis.

Among the 72 patients who died from malignant disorders, 24 different tumor locations were observed. Only for adenocarcinoma of the pancreas, including the papilla of Vater region, was there a significantly increased number of cases ($p < 0.05$). Patients with multiple endocrine neoplasia were not included among these malignancies.

Twenty-five patients died from renal diseases: 10 of them were classified as chronic nephritis, nephrosclerosis, or just

Table 2. The causes of death in 294 of 896 patients operated on for primary hyperparathyroidism.

	Women	Men	Total n (%)
Cardiovascular disease	101	56	157 (53.4)
Malignant disease	45	27	72 (24.5)
Renal disease (urinary infections included)	19	6	25 (8.5)
Infectious disease	8	2	10 (3.4)
Trauma	4	4	8 (2.7)
Gastrointestinal bleeding, peptic ulcer	4	2	6 (2.0)
Multiple endocrine neoplasia tumor	2	2	4 (1.4)
Primary hyperparathyroidism (crises)	2	–	2 (0.7)
Miscellaneous	7	3	10 (3.4)
All	192	102	294

Table 3. Comparison between the death rates of patients treated for primary hyperparathyroidism (pHPT) and controls.

	Women	Men	Total
Cause of death	pHPT/controls	pHPT/controls	pHPT/controls
Cardiovascular	101/64.4[a]	56/30.1[a]	157/94.6[a]
Malignant	45/31.9[b]	27/13.1[c]	72/45.0[a]
All	192/120.6[a]	102/55.1[a]	294/175.7[a]

[a] $p < 0.001$.
[b] $p < 0.05$.
[c] $p < 0.01$.

Table 4. Mean postoperative survival and mean age at death from cardiovascular, malignant and renal diseases and all causes for the deceased patients previously treated for primary hyperparathyroidism.

	Mean postoperative survival		Mean age at death	
	Years (SD).		Years (SD).	
Cause of death	Women	Men	Women	Men
Cardiovascular	7.5 (6.1)	7.5 (6.4)	75.3 (9.1)	69.5 (10.4)
Malignant	6.4 (4.5)	7.1 (4.7)	67.1 (11.9)	69.8 (8.5)
Renal	7.0 (4.3)	7.3 (5.0)	72.4 (6.8)	67.5 (7.8)
All	6.8 (5.3)	7.4 (5.9)	72.6 (10.7)	68.8 (10.9)

renal disease, 7 as chronic infections with acute exacerbation, 1 as acute cystopyelitis, and 7 as cases of uremia. The records of these patients revealed that 21 patients were uremic before death. Only 4 of the 25 who died from renal disease were operated on after 1974.

Mean age at death and mean number of years from operation to death for men and women are given in Table 4.

The increased risk of premature death remained in the selected series from which the 171 patients who had their hyperparathyroidism discovered during treatment or follow-up of another serious disease were excluded. One-hundred eighty-nine of 725 patients were then deceased and, in the corresponding equally-sized control group, the number of deaths was 132.5 ($p < 0.001$). Mean follow-up time of these 725 patients was 13.3 years (SD: 6.2) and the ratio between observed and expected

number of deaths was 1.43. One-hundred twelve of these 725 hyperparathyroid patients died from cardiovascular disease compared to 67.5 in the control group ($p < 0.001$), and 50 died from malignant disease versus 32.8 in the control group ($p < 0.01$).

Discussion

Long-term survival studies after surgery for primary hyperparathyroidism have previously been reported from Helsinki and Uppsala [1, 2]. The patients in both studies were operated on in the years 1956–1979. The former series was composed of 334 patients and the latter of 441. Mean follow-up time was 5 and 7.7 years, respectively. In the Helsinki study, 34 deaths meant an increased mortality when compared with controls ($p < 0.05$). In the Uppsala study, there were 100 deaths and significantly increased mortality was found only for women 4–12 years after surgery for primary hyperparathyroidism.

The present study definitely confirms what the previous studies suggest, i.e., that there is an increased risk of premature death in patients who have been surgically treated for primary hyperparathyroidism.

Our series is composed of patients with sex, age, and histopathological distributions similar to other large series of patients with primary hyperparathyroidism [12–18]. It also shows the well-recognized trend in recent years toward a greater proportion of patients with mild or absent symptoms [13–18] and a greater number of women.

The trend toward a higher age at operation is interesting and has been noted before [18], but, to our knowledge, is proved statistically for the first time in the present study. With the increasing use of multichannel analyses, the detection of hypercalcemia occurs more often—especially among the elderly. Before, serum calcium concentration was mostly measured among patients with renal stone disease or gastric ulcers who were younger than the average patients in medical care units.

The mean observation time of 12.9 years, a cure rate of 97%, and a postoperative mortality of less than 1%, together with a considerable size make our series suitable for the study of long-term survival after surgery. We used exact criteria for the cohort. Only morphologically-verified hyperparathyroidism was accepted. We have also been careful to exclude secondary cases, since secondary hyperparathyroidism carries a greater risk of death. Consequently, our series is representative, large, and well-defined, and our results should be relevant to patients with primary hyperparathyroidism in general.

The choice of a control material made up of a population of 8 million and our matching procedure ensure exact figures on mortality for the control group. The death certificate data used have been demonstrated to be valid for epidemiological use, especially regarding cancer forms and cardiovascular diseases [19].

Concerning the 2 main causes of death, cardiovascular and malignant disease, our results are clear-cut in both the total series of 896 cases and the selected series of 725 cases. The introduction of the selected series served the purpose of avoiding a possible selection bias that could arise by including patients who, at the time of diagnosis, were treated or followed for other serious diseases.

The results of the Helsinki [1] and Uppsala [2] studies suggested an increased mortality from cardiovascular disease; however, the former study had a low number of deaths, and the latter had less convincing statistical power ($p < 0.06$). In the present series, we demonstrated that there is an increased mortality ($p < 0.001$) from cardiovascular disease in patients operated on for primary hyperparathyroidism. The higher mean age at death from cardiovascular disease for women compared to men with primary hyperparathyroidism seems to parallel the well-known higher age at onset of cardiovascular disease in women compared to men. As cardiovascular death predominates, it influences the mean age at death from all causes in both populations. One possible explanation for the increased cardiovascular mortality is hypertension, linked to primary hyperparathyroidism in an as yet obscure way [20, 21]. Other conditions associated with hyperparathyroidism—such as altered lipid metabolism [22]—could be implicated. A direct effect of hyperparathyroidism or hypercalcemia on vascular smooth muscle and the myocardium could exist as well [23]. Some of the increased cardiovascular mortality can be secondary to renal impairment caused by hyperparathyroidism of long duration. Several other observations also indicate the existence of an interaction between primary hyperparathyroidism or hypercalcemia and the circulatory system [24–27].

The increased mortality from malignant disease in this study was not an unexpected finding since an increased incidence of malignant tumors has been reported in patients with primary hyperparathyroidism [3–5]. The absence of proof of an increased mortality from malignant disease in previous studies [1, 2] is not necessarily in disagreement with our results. The previous findings might be explained by the fact that these series were smaller and had shorter periods of observation and, therefore, contained relatively few deaths.

In the present series, the spread between different tumor sites indicates the connection between primary hyperparathyroidism and malignant disorders to be general rather than specific in character. One possible mechanism would be increased mitotic activity induced by hypercalcemia [28, 29]. The increased number of adenocarcinomas of the pancreas is interesting but awaits verification.

The present study indicates that irreversible changes come out of hyperparathyroidism in many cases. Premature aging would well be an explanation for the premature death from both cardiovascular and malignant disease. The finding that women with primary hyperparathyroidism have their menopause more than 4 years earlier than controls speaks in that direction [30].

A comment on the risk of death from renal disease should be given when primary hyperparathyroidism is discussed. In our series, it is the third cause of death. In this hyperparathyroid population, the official statistics listed only 7 patients to have died as a result of uremia. According to the SCB, uremia is regarded as an incomplete and unspecified cause of death and is used as a complement or in the absence of something more specific. When looking in the records, however, it was clear that uremia was the main cause of death in 21 of the 25 patients who died from renal disease. The diagnosis of uremia was either hidden behind different renal diagnoses or was graded as the second or third contributory cause of death. It is not compulsory to report more than the primary cause of death on the death certificate. As a consequence, the official statistics cannot

give useful information on this very point, and a control group concerning death from uremia cannot be confidently formed.

In this study, we calculated the relative risk of death in the total series of hyperparathyroid patients and also in the selected series from which patients were excluded if their hyperparathyroidism was detected when they were treated or followed for other serious diseases. In the total series, the ratio between observed and expected numbers of death was 1.67, and, in the selected series, 1.43. The rules of exclusion used, forming the selected series, ensures that poor-risk patients were not overrepresented. Ninety-two percent of the exclusions were made because of cardiovascular or malignant disorders. Also, in the selected series we found a firm relationship between hyperparathyroidism and premature death from both of these conditions. This demonstrates that both cardiovascular disease and malignant disease are associated with primary hyperparathyroidism. Therefore, the patients who at the time of diagnosis had known cardiovascular or malignant diseases should be included when analyzing the risk of premature death of the patients with primary hyperparathyroidism. This opinion is endorsed by the fact that many of the patients who were excluded from the total series when creating the selected series had substantially elevated serum calcium levels of probably long duration. This means that the increased risk of death of the total series reflects the true risk of death of primary hyperparathyroidism better than does that of the selected series.

To evaluate the degree of the increased risk of premature death for a hyperparathyroid patient who is operated on, one should see Table 4. Provided that the increased risk is constant in the series, which is an idealization, the confidence interval can be calculated with a test based on Poisson distribution. The 95% confidence limits of the ratio are 1.49–1.87. According to reasons presented above, this interval represents the appropriate increase of the risk of death of a consecutive series of patients operated on for primary hyperparathyroidism.

The conclusions from this study are that there is a risk of premature death for patients treated for primary hyperparathyroidism and that there are 2 main disorders causing death—cardiovascular, and malignant disease. These diseases have not previously been proved to be associated with primary hyperparathyroidism. The type of connection is still unknown, but the conclusion must be to accept its presence. As a consequence of our results, more attention should be given to cardiovascular and malignant diseases in the follow-up of patients with hyperparathyroidism. This might decrease the risk of premature death in these patients.

Appendix

The control material was the whole Swedish population. Thus, the detailed official statistics on population and death rates are applicable [10, 11]. A control group was formed which was identical to the hyperparathyroid population throughout the period according to sex and age. The number of deaths in the control group was calculated as follows:

$$x_{y_g} = z_m \cdot \frac{D_m}{P_m} + z_f \cdot \frac{D_f}{P_f};$$

x: number of deaths in control group in 1 year (y) in 1 age group spanning 5 years (g);
y: current year and varies with number of years after operation; when starting with 1953, it varies from 0 to 33 (0 = 1953, 1 = 1954 . . . 33 = 1986) and when starting with 1982, it varies from 0 to 4 (0 = 1982, 1 = 1983 . . . 4 = 1986);
g: age groups 1–18—no. 1 = 11–15 years, no. 2 = 16–20 years . . . no. 18 = 96–100 years.
m: male;
f: female;
z: number of patients in 1 year (y) in 1 age group (g);
D: number of deaths in Swedish population in 1 year (y) in 1 age group (g);
P: mean Swedish population in 1 year (y) in 1 age group (g).

$X_y = x_{y_{(g=1-18)}}$ = number of deaths in control group in 1 year (y) in all age groups;

$X_Y = X_{(y=0-33)}$ = number of deaths in *whole* control group during follow-up period.

The number of deaths so obtained, X_Y, is the calculated observed number of deaths of the control group perfectly matched concerning age, sex, and period, and would be the death rate of the patients if they had not had primary hyperparathyroidism, i.e., the expected number of deaths of the patient series.

Résumé

Pour évaluer la survie à long terme après opération pour hyperparathyroïdie primaire, le devenir de 896 patients chez lesquels ce diagnostic avait été clinquement posé et vérifié histologiquement a été analysé. Ces patients ont été opérés entre 1953 et 1982. L'âge moyen au moment de l'intervention était de â 57.3 ans (ET: 13.1), le taux global de cure était de 97.0%, la mortalité post-opératoire était de 0.89%. Le suivi était complet à 99.8% à la fin de l'année 1986. Le suivi moyen était de 12.9 ans (ET: 6.1). Deux cent quatre vingt quatorze patients sont morts, 118 de plus que dans le groupe contrôle ($p < 0.001$), basé sur les statistiques suédoises d'une population composée de sujets comparables du point de vue âge, sexe, et année de mort. Le groupe de contrôle était de la même taille pour chaque année que pour la population hyperparathyroïde. Le risque de mort précoce chez les patients hyperparathyroïdes était augmenté ($p < 0.001$) même après exclusion des patients à haut risque dont l'hyperparathyroïdie avait été diagnostiquée pendant le traitement d'une autre maladie grave. Les principales causes de mort précoce chez le patient hyperparathyroïdien étaient soit une maladie cardiovasculaire, soit une maladie maligne. Les deux étaient plus fréquentes que dans le groupe de contrôle ($p < 0.001$). Ces résultats démontrent que l'hyperparathyroïdie est responsable de lésions qui ne sont pas réversibles après cure de l'hyperparathyroïdie.

Resumen

Con el fin de investigar la sobrevida a largo plazo después del tratamiento quirúrgico del hiperparatiroidismo primario, se realizó un estudio de seguimiento en 896 pacientes consecutivos

en los cuales se comprobó el diagnóstico por la clínica y por métodos microscópicos. Estos pacientes fueron operados en el período 1953–1982. Le edad promedio en el momento de la operación fue 57.3 años (DE: 13.1), la tasa global de curación 97.0%, y la mortalidad postoperatoria 0.89%. El seguimiento fue completo en el 99.8% de los casos hasta el final de 1986. El promedio de tiempo de seguimiento fue de 12.9 años (DE: 6.1); 294 pacientes murieron, cifra que fue 118 personas, mayor que en el grupo control ($p < 0.001$), el cual se basó en estadísticas suecas para una población similar en cuanto a edad, sexo, y años calendario.

El grupo control fue cada año del mismo volumen que el de la población hiperparatiroidea. El riesgo de muerte prematura se mantuvo aumentado ($p < 0.001$) aun después de excluir los pacientes de alto riesgo en los cuales se diagnosticó el hiperparatiroidismo mientras estaban bajo tratamiento por otras enfermedades serias. Las causas de muerte prematura principal en los pacientes hiperparatiroideos fueron las enfermedades cardiovasculares y las neoplasias malignas; ambas se presentaron con mayor frecuencia que en el grupo control ($p < 0.001$). Los resultados demuestran que el hiperparatiroidismo primario causa lesiones que no revierten con la cirugía.

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