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The Influence of Surgery on the Risk of Death in Patients with Primary Hyperparathyroidism

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The previous finding of an increased risk of premature death in a consecutive series of 896 patients operated on for primary hyperparathyroidism between 1953 and 1982 [1] raised the question of the role that surgery plays in relation to the risk of death. In the present study, undertaken to examine that issue, 3 factors—age, calendar year of surgery, and time passed after surgery—have been found to be significantly related to the risk of death ($p < 0.001$), each factor contributing independently. A correlation was found between a late calendar year of surgery and a low degree of hyperparathyroidism as evaluated by serum calcium and creatinine levels. There was an increased risk of premature death in all age groups. The risk was less among patients operated on in later years. The observed normalization of the increased risk of death with time after surgery also took place sooner in patients operated on in later years. Our finding of improved survival following surgical intervention contrasts favorably with the findings of others in studies of subjects with untreated mild hyperparathyroidism. We have also found that preoperative serum calcium levels affect the risk of death, and that there is an additional factor related to the calendar year of surgery affecting the risk of death. Circumstantial evidence indicates that the duration of hyperparathyroidism contributes to this factor. Our results also show that early surgery decreases the risk of premature death in mild cases of the disease.

In a previous study we found that patients with primary hyperparathyroidism had an increased risk of premature death, even if they underwent successful parathyroid surgery [1]. The findings may lead to hesitation about the benefits of surgery, especially in cases of mild disease. Surgical treatment has previously been questioned for such cases [2–9]. The 896 patients reported in our previous article were surgically treated over a period of 30 years, and comprised a heterogenous population. In the present study, we analyzed the importance of the epidemiological factors—age, calendar year of surgery, and time passed after surgery—for the risk of premature death in the same population as referred to above. Changes in the degree of hyperparathyroidism during the period were assessed by analyzing the preoperative serum calcium and creatinine values.

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The aim of this article is to illustrate the long-term prospects after surgery for a representative series of patients with primary hyperparathyroidism, using mortality for evaluation.

Material

Eight hundred ninety-six consecutive patients, 656 women and 240 men, were operated on for primary hyperparathyroidism at Sahlgren's hospital in the years 1953–1982. The diagnosis was microscopically verified in all cases. Their histories were reviewed and they were followed until the end of 1986. The mean age at surgery was 57.3 years (standard deviation [SD]: 12.2, range: 11–83 years). The age and sex distribution of the series is shown in Figure 1. The cure rate was 97%, and mortality within 1 month of operation was 0.9%. The mean follow-up time was 12.9 years (SD: 6.1, range: 4–33 years). At follow-up, 294 patients had died, which was more than expected when compared with a control group, based on Swedish population statistics and matched for sex, age, and calendar year ($p < 0.001$). This increased risk of premature death was similar for both sexes. Further details of the patients have been given in a previous article [1].

Methods

The laboratory data reported in our earlier study suggested that the patients operated on toward the end of the 30-year period, 1953–1982, had milder disease. Such a trend has been found in many series [1–5, 10]. In the present study, we used Pitman's test [11] to investigate the relationship between the preoperative serum calcium level and the creatinine level as well as the relationship between each of these 2 laboratory values and the calendar year of surgery. All p values given in this article are 2-sided.

To characterize the serum calcium level, 2 separate definitions were used. Peak serum calcium is the mean value of the 2 highest values analyzed per patient at our laboratory. Mean serum calcium is the mean value of all observations made at our laboratory per patient within the immediate preoperative period (<6 weeks). There were 1–13 observations made per patient within this period, the mean number being 4.85 (SD: 2.77). The

Fig. 1. Age and sex distribution of 896 consecutive cases operated on for primary hyperparathyroidism at Sahlgren's Hospital in the years 1953–1982.

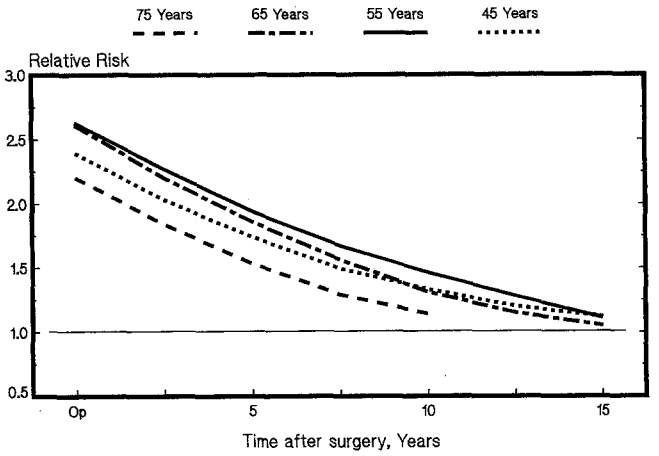

Fig. 2. The relative risk of death depending on time after operation for primary hyperparathyroidism. The relative risks show patients from 4 different age groups. Age at surgery is given. All were operated on in 1970.

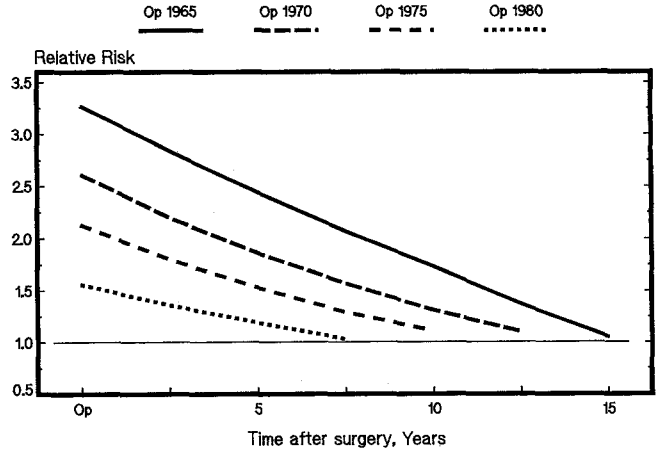

Fig. 3. The relative risk of death depending on time after surgery for primary hyperparathyroidism (pHPT) in 4 different years of operations. The relative risks show patients who were 65 years old at surgery.

correlation coefficient between the peak and the mean serum calcium levels was also calculated. The creatinine value sampled when the patient was in optimal condition as to fluid and electrolyte balance was used for the statistical analysis.

The relationship between the risk of death and the 3 factors, age (X), calendar year of surgery (Y), and time passed after surgery (Z), was tested separately with a survival test according to Mantel [12]. To investigate whether these factors contributed to the risk of death independent of one another, another survival test was used and one factor at a time was tested when the influence of the others had been eliminated [13]. In this test, a survival function is used. As the survival function is a function of time, there is a time parameter included. The time parameter may be defined in different ways, and the results may depend on the choice of time parameter: if there is an influence on the relationship tested by the time parameter itself, this influence is eliminated by using that very time parameter.

All 3 variables were found to influence the risk of death independently when time passed after surgery and age were used as time parameters. They are, therefore, suitable for use in forming a function for estimating the risk of death of a hyperparathyroid patient. The following logistic model was used [14]:

$$R = 1/[1 + \exp(-aX - bY - cZ - d)] \qquad \text{(eq. 1)}$$

in which R is the risk of death in a given year, X is the age of the patient in question that year, Y is the calendar year of surgery, and Z is the time period passed after surgery. a, b, c, and d are constants, estimated according to the maximum likelihood method on the basis of the mortality of the hyperparathyroid population [1]. Age and calendar year were given within 1-year intervals while the postoperative time period was given within 5-year intervals. Verification of hypotheses generated by the model (eq. 1) cannot be performed using significance tests on the basis of the same material used for the calculation of the values of the constants. If extreme values of X, Y, and Z are chosen, reliability is restricted. The risk is given as the number of deaths per 1,000 individuals per year.

For comparison, the incidence of death in the corresponding age groups of the Swedish population, matched for sex, was calculated for each calendar year. The death rates in the annual official reports published by the Swedish Central Bureau of Statistics were used for this calculation [15], as was data on the mean populations in Sweden during the corresponding years [16]. The age groups in the Swedish population used as control material contained 20,000–130,000 individuals during the period studied.

The basic data on all 896 patients in the series were used in the logistic model, and contributed to the results, although only a few representative diagrams were chosen for illustration. Extreme parameter values were avoided. High age, in itself, carries an increased mortality and, for this reason, we analyzed and demonstrated the results of 4 different age groups. In these groups, the patients and their controls were 45, 55, 65, and 75 years old at the time of operation. They were chosen as representative according to the age distribution of the series (Fig. 1). In Figures 2–4 the increase in the risk of death is illustrated in terms of the relative risk, i.e., the ratio between the risk found for the patients and the risk found for their matched controls. In Figures 5 and 6, the absolute risks are given instead.

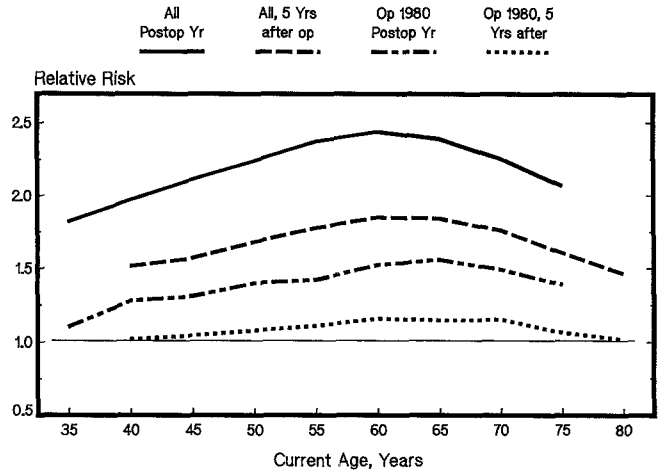

Fig. 4. The relative risk of death depending on age, during the postoperative year and 5 years after surgery for primary hyperparathyroidism (pHPT). The 2 upper curves are for all 896 patients in the series, and the 2 lower curves show the corresponding relative risks of the patients who were operated on in 1980.

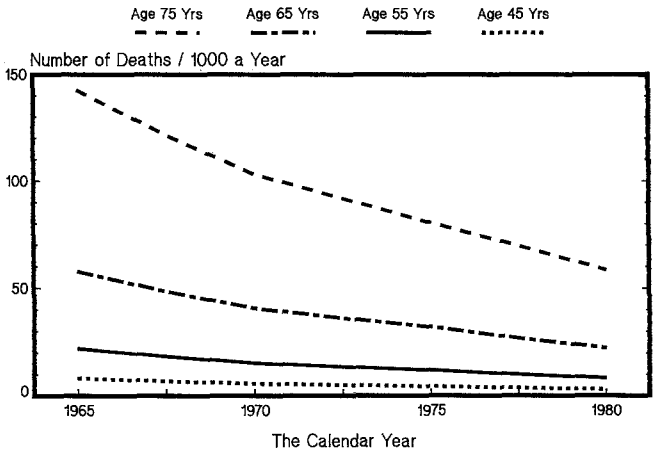

Fig. 5. The risk of death during the first postoperative year depending on the calendar year of operation for primary hyperparathyroidism. The risk is shown for patient groups of 4 different ages at surgery. All risks were high as compared with the controls.

Results

There was a relationship between the risk of death and age at surgery ($p < 0.001$), calendar year of surgery ($p < 0.001$), and time passed after surgery ($p < 0.001$). When predicting the risk of death, all 3 factors were found to contribute, independent of one another. The maximum likelihood method was used for estimation of the values of the constants of the risk function described above (eq. 1). All results concerning the estimation of the risk of death of different individuals at different points in time in relation to their surgery, are based on the following estimated values for the constants in the risk function described above (eq. 1): a = 0.1, b = −0.123, c = −0.341, and d = −8.926.

Preoperative Serum Calcium and Creatinine Levels

During the period 1953–1982, there was a decrease in preoperative serum calcium levels ($p < 0.001$) as well as in serum creatinine levels ($p < 0.001$).

In Table 1, the mean serum calcium levels are given for 4 periods of time. The first period spans 12 years, in order to include a meaningful number of patients. The following periods span 6 years each. The gradual decrease and the difference in level between peak and mean serum calcium levels, as defined above, can be seen in the table. The correlation coefficient between peak and mean serum calcium levels was 0.93.

The mean serum creatinine levels for the corresponding periods of time are presented in Table 2. The creatinine levels were related to the serum calcium levels ($p < 0.001$), although the relation was weak, the correlation coefficients being 0.23 and 0.20 for the 2 serum calcium values used. A high correlation coefficient was not, however, expected, as all patients in the series had high serum calcium levels, giving a relatively short range for the variable of serum calcium concentration. Furthermore, serious renal damage results in lower serum calcium levels. Table 3 illustrates how the proportion of patients with substantial disease, as evaluated using the serum calcium and creatinine values, decreased during the period; however, the absolute numbers of such patients have been remarkably constant although the number of patients diagnosed and operated on for the disease has increased markedly in recent years.

The Risk of Death Depending on Time after Operation

The change of the relative risk of death with time after operation for a patient operated on in 1970 is shown for the 4 age groups in Figure 2. It shows that the hyperparathyroid patients have an increased risk of death for up to 10–15 years after their operations, and then the risk approaches the level of the controls. This indicates a normalization of the increased risk of death with time after surgery.

The Risk of Death Depending on the Calendar Year of Surgery

Figure 5 shows the risk of death during the first postoperative year for persons who were operated on during the period from 1965 to 1980. The risk gradually decreased over the period, and was about twice as high in 1965 as in 1980.

The Change in the Risk of Death Depending on Time Passed after Operation for Different Calendar Years of Operation

Figure 3 shows changes in the relative risk of death after surgery for a patient 65 years of age at surgery if operated on in 1965, 1970, 1975, or 1980. The trend toward a more rapid normalization of the risk of death is clearly visible. This normalization occurred after approximately 5 years if the patient was operated on in 1980, but not until after 9 years if operated on in 1975, and after 12–14 years if the operation was in 1970 or 1965. Thus, the normalization took place sooner with a late calendar year of operation.

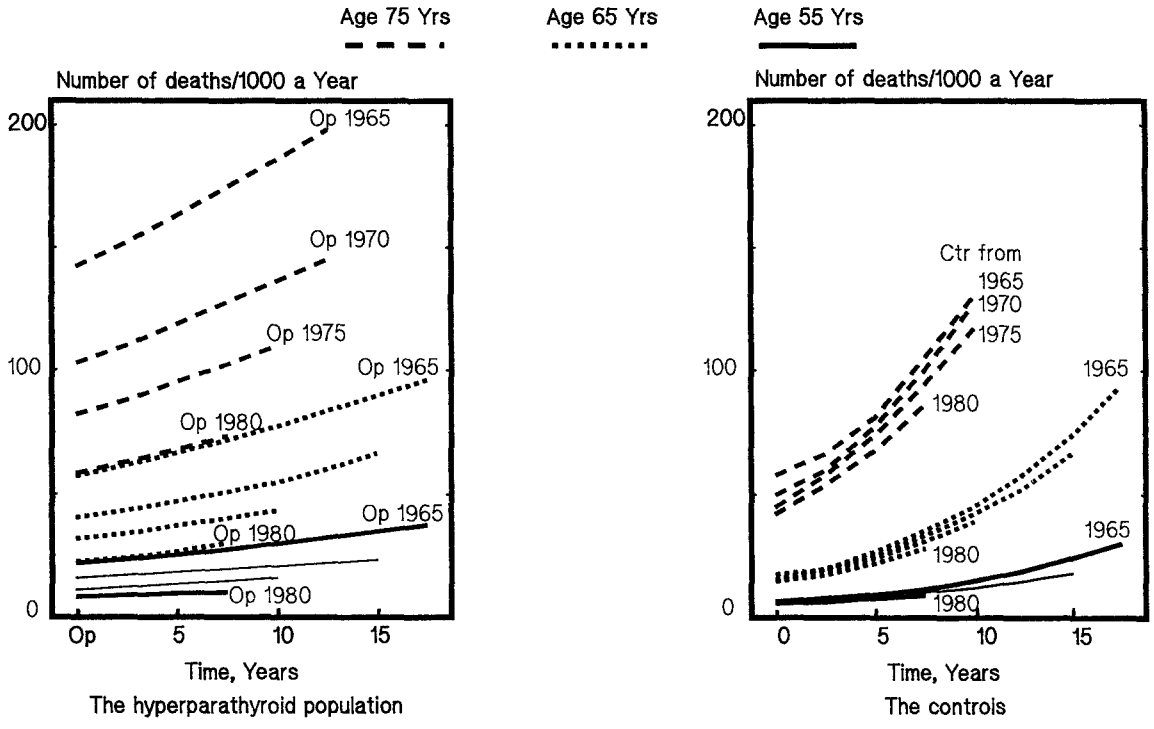

Fig. 6. The change in the risk of death depending on time, in a hyperparathyroid population operated on between 1965 and 1980, and in the Swedish population used as control material, matched for sex and age, during the same period. The risks in 3 different age groups are shown with separate line types. Ages at surgery of the patients and corresponding ages of the controls are given. The lines are marked with year of surgery for patients, and with corresponding years for contemporary controls.

Table 1. Preoperative peak and mean serum calcium levels.[a]

Period	n	Peak calcium (standard deviation) mmol/l	Mean calcium (standard deviation) mmol/l
1953–1964	75	3.04 (.54)	2.90 (.51)
1965–1970	200	2.99 (.38)	2.86 (.33)
1971–1976	276	2.93 (.33)	2.83 (.39)
1977–1982	345	2.86 (.30)	2.77 (.25)
All	896	2.92 (.36)	2.82 (.32)

[a]Reference range: 2.20–2.60 mmol/l.

Table 2. Preoperative mean serum creatinine levels.[a]

	Serum creatinine					
	Females			Males		
Period	n	μmol/l	(Standard deviation)	n	μmol/l	(Standard deviation)
1953–1964	38	111	(41)	37	135	(42)
1965–1970	142	95	(32)	58	108	(35)
1971–1976	197	93	(35)	79	114	(66)
1977–1982	279	84	(43)	66	104	(45)
All	656	91	(39)	240	113	(52)

[a]Reference range: females 50–115, males 60–125 μmol/l.

The General Trends with Regard to the Risk of Death during the Period

Figure 6 shows changes in the risk of death with time after operation for 3 age groups of hyperparathyroid patients with 4 different calendar years of operation: 1965, 1970, 1975, and 1980. It also shows changes in the risk of death of the matched groups in the Swedish population. There was a small trend toward a decrease in the risk of death in the Swedish population during the period, while the improvement in the surgically-treated hyperparathyroid population was conspicuous by comparison.

Table 3. Numbers and percentages of patients with peak serum calcium level ≥2.95 mmol/l and with elevated serum creatinine levels.

	All Patients		Females		Males	
	Peak calcium ≥2.95 mmol/l		Creatinine >115 μmol/l		Creatinine >125 μmol/l	
Period	n	(%)	n	(%)	n	(%)
1953–1964	39/75	(52)	11/38	(29)	17/37	(46)
1965–1970	80/200	(40)	16/142	(11)	5/58	(9)
1971–1976	98/276	(36)	22/197	(11)	12/79	(15)
1977–1982	81/345	(23)	18/279	(6)	11/66	(17)
All	298/896	(33)	67/656	(10)	45/240	(19)

The Risk of Death Depending on Age

Figure 4 shows the relative risk of death in the first postoperative year for all ages and also 5 years after operation. The risks shown are based on the whole series. The relative risks for patients operated on in 1980 are shown separately in the same figure. The relative risk of death was substantial in all age groups, but the highest relative risk of death was found in patients 55–70 years of age. This peak in the relative risk of

death was less pronounced as time passed after operation, but could consistently be found in this age group. The risk of death was also influenced by the calendar year of operation but was still found in the same age group.

In 1965, the relative risk during the first postoperative year was 2.8–3.4 for patients 45–70 years of age. In 1980, it was 1.3–1.6 for patients of this age. For a patient who was 35 years of age at surgery, the relative risk decreased from 2.6 in 1965 to 1.6 in 1975 to an almost normal risk of 1.1 in 1980.

Discussion

The benefits of surgery are indisputable in patients with symptomatic hypercalcemia. In such patients, metabolic normalization and amelioration of symptoms are noted soon after operation. Objective benefits of surgery in mild and asymptomatic cases have been reported in only a few studies [17–21]. Still, many authors find surgical treatment in these cases justified on "theoretical grounds" [2, 3, 5, 22–24]. In a previous study, we found that patients operated on for primary hyperparathyroidism ran an increased risk of premature death [1]. To answer the question of whether surgery results in a reduction of the risk of premature death for patients with primary hyperparathyroidism, treated and untreated patients must be compared. A large, long-term study would then have to be performed in which asymptomatic patients would be randomized to surgery or nonsurgery groups. Such a study can only be performed with great difficulty for practical reasons, and would be dubious for ethical reasons. Thus, analyses of available data are performed instead.

In the present study, we analyzed data from a large representative series of hyperparathyroid patients (n = 896) with an almost complete (99.8%) and long follow-up (mean follow-up time: 12.9 years) [1]. With access to all data from this large series, the use of the generally accepted mathematical model (eq. 1) [14], and the fact that the relationships between the 3 variables used and the risk of death were highly significant, a reliable estimation of the risk of death was obtained. The model used is well suited to illustrate facts of a highly complex nature and it gives us the opportunity to understand realities and trends that would otherwise be concealed within vast amounts of data. In this way, useful information was obtained that could not be derived from the significance values only. All our results were consistent, and they gave a good picture of the effects of primary hyperparathyroidism after surgery.

The increased risk of premature death was found to apply to all age groups. The finding of an age-dependent maximum relative risk in the age interval 55–70 years might be a consequence of lower relative risks for the young and the aged, explained in separate ways. The young patients probably withstand better the deleterious effects of hyperparathyroidism and may have a better restorative capacity. In the aged, on the other hand, there are many other competing risk factors making the risk factors associated with hyperparathyroidism less important.

We found that patients operated on during the first part of the 30-year period of the series had much worse prognoses as to survival than those operated on toward the end of the period. Epidemiological factors outside the hyperparathyroid population do not explain the better prognosis of the patients in the recent years, as only marginal improvements of the risk of death occurred in the Swedish population during the same period. Both the mean serum calcium and the mean creatinine levels at diagnosis were higher in the early years of the period studied ($p < 0.001$). This implies that the patients operated on in these years generally had more pronounced disease which could explain their worse prognosis. Clinical parameters such as type and degree of symptoms could also be helpful in evaluation of the stage of the disease, but they are not easily measured in a uniform way nor easily distinguished as exclusive signs of hyperparathyroidism.

The duration of hyperparathyroidism is an unknown parameter in the majority of cases. A progressive increase in the serum calcium level is seldom found in untreated hyperparathyroid patients, even when they are observed for long periods of time [2, 7, 25, 26]. This means that the duration of the disease for patients with similar serum calcium levels can vary within wide limits. Knowing that primary hyperparathyroidism was considered a rare disease early in the period studied and serum calcium samples were not taken routinely, we can logically conclude that the duration of the disease of the patients at that time must have been much longer before diagnosis and surgery than today, when serum calcium sampling is frequently done [1–5, 10]. This nonmeasurable, yet natural relationship between duration and the calendar year of surgery indicates that the better survival in recent years could also be explained by the fact that the more recently operated patients generally had shorter durations of the disease. Probably the duration of hyperparathyroidism and the degree of hypercalcemia give rise to the damage resulting in premature death. In that case, the calendar year of operation and the serum calcium level should influence the risk of death independent of one another, which we found to be true. This was determined using the survival test mentioned above [13], and the relationship between calendar year of surgery and risk of death was tested by elimination of the influence of the serum calcium level with age as the time parameter ($p < 0.05$). The relationship between the preoperative serum calcium levels and the risk of death were correspondingly tested when the influence of the calendar year of surgery was eliminated using the same time parameter ($p < 0.05$ for mean serum calcium level and $p < 0.01$ for peak serum calcium level).

As stated above, we showed that no general improvements for the total population during the period studied could explain the decreased risk of death in the hyperparathyroid population. Yet general improvements in medical treatment could influence the risk of death in a patient population like ours. To test this possibility, we divided our patients into 2 groups, those with substantial disease (serum calcium $\geq$2.95 mmol/l) and those with milder disease (serum calcium <2.95 mmol/l). We used the same survival test as above [13] and, eliminating the influence of the serum calcium levels, the relation between year of surgery and risk of death was tested separately in the 2 groups. In our opinion, the patients with substantial disease are the ones who would have more associated diseases and, consequently, be the beneficiaries of general improvements in medical treatment; however, the serious cases did not show any significant decrease in their risk of death with later calendar years of operation, whereas the mild or moderate cases did ($p < 0.05$). This would indicate that mild cases do benefit from the screen-

ing procedures leading to early detection and treatment, i.e., they benefited from a shorter duration of hyperparathyroidism.

The size of the core group of patients with substantial disease in the series, as reflected by the laboratory parameters, did not seem to change during the period. Frequent serum calcium sampling in a population leading to early treatment should, theoretically, have led to a notable reduction of the number of patients with substantial disease. The absence of such a reduction can be explained by the fact that the numbers given in the early years are probably far below the true numbers, i.e., serious cases may have also escaped diagnosis in the early years to a large extent. In that case, the numbers given for recent years may be correct and reflect a true and good effect of early treatment, which means that prevention of development of some severe cases of hypercalcemia was obtained. It is reasonable to assume that many early patients escaped diagnosis, despite the fact that their condition may have been serious. Death from cardiovascular disease is the most common cause of death in both hyperparathyroid patients and the general population [1]. It has never been an issue to determine whether hyperparathyroidism was involved, irrespective of how carefully the primary cause of death was determined. As serum calcium estimates were only rarely made, we cannot at all determine the true prevalence of the disease at that early time, and there is nothing indicating a true increase in the prevalence. The increase can just as well be explained simply in terms of greater recognition of primary hyperparathyroidism, for both mild and serious cases.

The finding of a shift from an increased risk of death toward a normal risk of death as time passed after surgery indicates a positive effect of surgery on survival. This normalization occurred sooner for patients with later calendar years at operation. The dilution of our series with mild cases that occurred in recent years must have contributed to the decrease in the risk of death. But we found not only a decrease in the risk of death but a normalization only a few years after surgery of all patients operated on in later years of the period. In another study on 172 hypercalcemic subjects considered to be cases of mild primary hyperparathyroidism, who were not treated and followed for 14 years between 1969 and 1983 [27], the overall survival of the untreated mildly hypercalcemic individuals was lower than that of the matched normocalcemic controls, and the trend toward a reduction of survival rates became obvious within 5 years from presentation. This means that a duration of more than 5 years of mild hypercalcemia is a clear risk factor for premature death. Consequently, a population with untreated and mild primary hyperparathyroidism cannot be expected to have a normal survival expectancy after 5 years of follow-up which, in fact, our treated cases from recent years had. This normalization can only be explained as an effect of surgical intervention. Thus, these facts together lend further support to the benefits of surgery at all stages, including mild disease.

Logically, high mortality in a population reflects high morbidity. The risk of death can, therefore, be used as a rough measure of morbidity. Thus, a decrease of the relative risk of death after surgery indicates that the patients who survive are often restored to health and generally recover well. Surgery also makes follow-up of untreated hypercalcemia unnecessary and, with time, there is also a cost benefit [10]. It has been claimed that primary hyperparathyroidism in the aged is a common and often mild disease without serious effects and that, therefore, surgery would not be recommended in such cases [7–9, 27, 28]. We, however, found noteworthy relative risks of death of 2.1 (all) and 1.4 (1980) for patients who were 75 years of age at surgery. Their risk of death clearly decreased after surgery. Hyperparathyroidism in the elderly is common, but in the absence of other distinctive features, there is no reason that it should be handled differently than in younger patients [29–31]. The elderly run an increased risk of complications, but the risks of parathyroid surgery are few [5, 29–31] and a careful individual risk evaluation with consideration of life expectancy should always be made [29].

To summarize, the improvement in survival of the hyperparathyroid population obtained in recent years can neither be explained in terms of general socioeconomic improvements, nor only by the dilution of our series with mild cases during the period. Rather, it is explained by the change in treatment during the 30-year-long period. The change is not in the surgery itself, but in the fact that it is performed at earlier stages of hyperparathyroidism than was previously the case. The clinical benefits of surgery were shown in a postoperative normalization of the risk of death that could not have been expected if the patients had remained untreated. Furthermore, we found that a low level of preoperative hypercalcemia in addition to a more recent year of surgery decreased the risk of death. A more recent calendar year of operation was also associated with less risk of death per se, independent of the serum calcium level. We interpret this additional decrease of the risk of death in cases that underwent surgery in more recent years to be related to the shorter duration of hyperparathyroidism at diagnosis, which is the result of the widespread use of routine serum calcium analyses. Our findings strengthen the basic theory that the longer the duration, and the more evident the metabolic abnormality of primary hyperparathyroidism, the greater the risk of irreversible impairment of tissue and organs, which lead to premature death. Our findings indicate that early surgery should be performed to shorten the duration, to prevent further serum calcium increases and, consequently, decrease the risk of premature death. Once the diagnosis of primary hyperparathyroidism is clear, surgery is indicated. Exceptions should not be made for the aged, beyond the natural considerations of the risks of surgery and an evaluation of life expectancy.

Résumé

Il a été démontré dans une étude antérieure portant sur 896 patients vus de façon consécutive et opérés pour hyperparathyroïdie primitive entre 1953 et 1982 [1] que le risque postopératoire de mort précoce était augmenté. Ceci pose la question de savoir quel rôle joue la chirurgie dans ce risque. Le but de cette étude a été d'examiner ce rôle. On a mis en évidence 3 facteurs indépendants, correlés de façon significative avec le risque de mort ($p < 0.001$): âge, année de l'acte chirurgical, et intervalle écoulé depuis l'acte chirurgical. L'année tardive de l'acte chirurgical et le degré d'hyperparathyroïdie, évalué par la calcémie et la créatininémie, étaient correlés entre eux. Le risque de mort précoce était augmenté chez tous les patients, quel que soit leur âge. Ce risque était toutefois moindre chez les patients opérés pendant ces dernières années. Le risque de mort en rapport avec la durée de l'intervalle écoulé depuis

l'acte chirurgical s'est normalisé d'autant plus vite que le malade a été opéré plus tard dans la période d'étude. La survie postchirurgicale dans cette étude, contraste avec les résultats des sujets ayant une hyperpathyroïdie modérée non traitée. Nous avons trouvé également que la calcémie préopératoire était correlée avec le risque de mort et que l'année de l'acte chirurgical était sans doute en rapport avec la durée même de l'hyperparathyroïdie. Nos résultats démontrent que la chirurgie pratiquée au début dans l'hyperparathyroïdie modérée diminue le risque de mort précoce.

Resumen

El hallazgo, previamente informado, de muerte precoz en una serie consecutiva de 896 pacientes operados por hiperparatiroidismo primario entre 1953 y 1982 [1], planteó el interrogante sobre el papael de la cirugía en relación con el riesgo de muerte. En el presente estudio, emprendido con el propósito de examinar este fenómeno, se encontraron 3 factores significativamente relacionados con el riesgo de muerte ($p < 0.001$) cada uno con una contribución independiente: edad, año calendario de la cirugía, y tiempo transcurrido después de la cirugía. Se encontró correlación entre un año calendario tardio de la cirugía y un bajo grado de hiperparatiroidismo, según evaluación por los niveles séricos de calcio de creatinina. Se presentó un riesgo aumentado de muerte precoz en todos los grupos de edad. El riesgo fue menor en los pacientes operados en los últimos años. La normalización del riesgo aumontado de muerte con el lapso postoperatorio también se observó en los pacientes operados en los últimos años. Nuestros hallazgos de mejor supervivencia después de la intervención quirúrgica contrastan favorablemente con los hallazgos en otros estudios sobre pacientes con hiperparatiroidismo leve no tratado. También encontramos que los niveles preoperatorios de calcio sérico afectan el riesgo de enfermedad, y que existe un factor adicional relacionado con el año calendario de la cirugía; evidencia circunstancial indica que la duración del hiperparatiroidismo contribuye a este factor. Nuestros resultados muestran que la cirugía temprana disminuye el riesgo de muerte precoz también en los casos de hiperparatiroidismo leve.

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