JOURNAL OF THE
american geriatrics society

VOLUME XXIII SEPTEMBER 1975 NUMBER 9

Printed in U.S.A.

Management of Primary Hyperparathyroidism in the Elderly*

MELVIN A. BLOCK, MD**, ALFREDO XAVIER, MD† and BROCK E. BRUSH, MD‡

Department of General Surgery, Henry Ford Hospital, Detroit, Michigan

ABSTRACT: Of 166 surgical patients for whom the diagnosis of primary hyperparathyroidism was established over a 20-year period, about one-third were over 60 years of age. For an additional 9 patients, no operation was advised, usually because of other life-endangering disease and the presence of only a mild degree of hypercalcemia without complications. In recent years, nearly 50 per cent of the patients did not have renal calculi or osteitis fibrosa cystica; this was unrelated to age. Most of the patients with management problems were seen since 1965. Age alone was not a dominant factor in relation to serious complications from hypercalcemia, the presence of other critical disease increasing the risk of operation, or the development of major postoperative complications. The only death from primary hyperparathyroidism occurred in a 74-year-old patient who refused re-operation and died from an acute hypercalcemic crisis. A liberal, but selective, policy of surgical treatment is justified for primary hyperparathyroidism in the elderly. Patients for whom the diagnosis of primary hyperparathyroidism is established may be separated into three groups: those for whom early operation is indicated, those for whom operation should be delayed to permit recovery from other life-endangering acute disease, and those for whom operation is unjustified because of minimal uncomplicated hypercalcemia and other serious disease greatly limiting life expectancy. These categories encompass all age groups and are not restricted to the elderly. All patients require periodic re-evaluation.

*Presented at the 32nd Annual Meeting of the American Geriatrics Society, Eden Roc Hotel, Miami Beach, FL, April 16-18, 1975.
**Chief, Division V, Department of General Surgery.
Address for correspondence: Melvin A. Block, MD, Department of General Surgery, Henry Ford Hospital, 2799 Grand Boulevard, Detroit, MI 48202.
†Resident, Department of General Surgery.
‡Chief, Division I, Department of General Surgery.

The increased recognition of primary hyperparathyroidism during recent years includes the older age groups. In a significant number of these patients, renal lithiasis or osteitis fibrosa cystica, as complications of hypercalcemia, may not be evident. Furthermore, such patients may have other serious medical problems. Therefore, the question of the advisability of operation for primary hyperparathyroidism arises in a substantial number of elderly patients. Our experience has been evaluated in an effort to provide information which will permit currently the formulation of policies for operation on patients of advanced age with primary hyperparathyroidism.

MATERIAL

The diagnosis of primary hyperparathyroidism was established during the 20-year period, 1955 through 1974, for a total of 175 patients. Operation was not advised for 9 of these patients because of the high surgical risk in the presence of other serious medical diseases when there was only a mild degree of hypercalcemia. The records of the 175 patients were reviewed according to different age groups to assess several factors including the complications of hypercalcemia, risk factors for operation, postoperative complications, technical operative factors, the course of the disease, and associated thyroid disease.

RESULTS

Significant factors related to primary hyperparathyroidism for various age groups among the 166 patients, for whom operation had been advised, are shown in Table 1. There has been a progressive increase in the numbers of patients for whom this diagnosis has been made, particularly since 1970. Approximately one-third of the patients have been over 60 years of age in each decade. For the total of 166 patients, 61 per cent were over 50 years, 35 per cent over 60 years, and 7 per cent over 70 years of age. More than 70 per cent of patients were female, irrespective of age.

In about two-thirds of the patients treated before 1970, evidence of renal calculi or osteitis fibrosa cystica had developed (Table 2). Subsequently, only 48 per cent showed these complications of hypercalcemia. Of the total group of 53 patients over 60 years of age, 43 per cent did not have renal calculi or osteitis fibrosa cystica.

Twenty-five patients (15 per cent of 166 patients) showed serious complications from hypercalcemia before operation (Table 3). The majority of these problems occurred in patients treated since 1965. Only 10 of the 25 patients were over the age of 60, so age alone is not a major factor in the development of these complications.

The risk of operation was significantly increased for 36 patients (Table 4). In the majority of cases, the increased risk factors were related to arteriosclerosis or renal insufficiency. However, 18 or 50 per cent of these patients were under the age of 60. Thus, advanced age alone was not the dominant factor. During the second decade of the study, more patients (31 of 126, or 25 per cent) were operated upon with increased risk than in the first decade (5 of 40, or 12.5 per cent).

There was no mortality associated with the

TABLE 2
Incidence of Renal Lithiasis and Osteitis Fibrosa Cystica in Primary Hyperparathyroidism

Time Period	Frequency of Renal Lithiasis or Osteitis Fibrosa Cystica
1955–1959	62%
1960–1964	63%
1965–1969	67%
1970–1974	48%

TABLE 1
Significant Factors in Primary Hyperparathyroidism, Related to Age

Factor	1955–1964 Age Group (yrs.) <50	50–59	60–69	70–80	1965–1974 Age Group (yrs.) <50	50–59	60–69	70–80	Total No. of Patients
No. of patients in group	19	9	10	2	45	40	31	10	166
Renal stones, or osteitis fibrosa cystica	13	6	6		28	17	18	6	94
Serious complications of hypercalcemia	1		1		10	4	7	2	25
Increased operative risk	2	1	2		5	10	14	2	36
Operation delayed due to risk factor					4	4	2	2	12
Major postop. complication	1				1	2	1	2	7
Associated thyroid disease	3	4	6	2	6	16	8	3	48
Previous neck operation	3				6	1	5	2	17

TABLE 3
Serious Complications from Hypercalcemia, in Primary Hyperparathyroidism

Complications	No. of Patients
Chronic renal insufficiency; loss of a kidney	11
Gastrointestinal (nausea and vomiting, ulcer, pancreatitis)	5
Operations for renal lithiasis	4
Recurrent bone fractures	3
Severe bone deformities	1
Weakness; inability to work	1
Total	25 (15% of total patients

TABLE 4
Factors Significantly Increasing Operative Risk in Primary Hyperparathyroidism

Factor	No. of Patients
Arteriosclerotic heart disease (angina, previous myocardial infarct)	13
Chronic renal insufficiency (persistent blood urea nitrogen over 50 mg/100 ml)	7
Occlusive peripheral arterial disease	4
Previous stroke	3
Valvular heart disease	2
Cardiac arrythmias	2
Occlusion of aorta and renal artery	1
Abdominal aortic aneurysm	1
Hepatic cirrhosis	1
Severe hypertension	1
Severe pulmonary insufficiency	1
Total	36

operation for primary hyperparathyroidism. The one patient with carcinoma of the parathyroid died two months after operation from pneumonia with septicemia, metastases, and consequences of vascular calcification.

One death from recognized primary hyperparathyroidism occurred during the period of this study. Four normal-appearing parathyroid glands were found at operation, and confirmed by microscopic study of biopsy specimens. A fifth parathyroid gland could not be found. Hypercalcemia persisted but the patient refused further surgical treatment. She died two years later at the age of 74 in a hypercalcemic crisis with a serum calcium level of 19.2 mg per 100 ml. A parathyroid tumor involving a fifth parathyroid was found in the superior mediastinum at postmortem examination.

Major nonfatal complications occurred in 7 patients postoperatively. Only 2 of these patients were more than 60 years of age. In 3 patients, permanent postoperative hypoparathyroidism developed after subtotal parathyroidectomy for multiple parathyroid gland involvement. One patient, aged 52, who had experienced prior myocardial infarcts and a cerebrovascular accident, sustained another myocardial infarct postoperatively. A 76-year-old patient recovered completely from a cerebrovascular accident which developed postoperatively. Atrial fibrillation required treatment after operation in a 43-year-old patient who had sustained a previous myocardial infarction. Another patient had an acute psychosis postoperatively. Again, major complications after operation on the parathyroid glands were not particularly related to advanced age.

Operation was delayed for 12 patients because of the more urgent need to treat other disease, or permit recovery from a recent significant arterial occlusion (Table 5). One patient died of a myocardial infarction while under treatment for arteriosclerotic heart disease. Only 4 of these patients were over 60 years of age. All were treated after 1965.

No operation was advised for primary hyperparathyroidism in 9 patients — all seen after 1965. Two of these patients are being followed during recovery from other acute disease and probably will be advised to undergo operation later. Other severe medical problems and the lack of evidence for serious effects from the hypercalcemia led to the decision not to proceed with the operation. Renal calculi were present in only 1 patient. Five of this group were over 70 years of age, the youngest being 52. Two died from other disease within one year after the diagnosis of primary hyperparathyroidism.

Associated thyroid disease was present in 48, or 29 per cent, of the 166 surgical patients (Table 6). Of the 48 patients with associated thyroid disease, 19 were more than 60 years old. Of the 4 patients with thyroid carcinoma, 2 were over 60 years old.

TABLE 5
Operation Delayed for Primary Hyperparathyroidism

Reason for Delay		No. of Patients
Urgent need to treat other condition:		6
Zollinger-Ellison syndrome	3	
Obstruction of biliary tract (stone)	1	
Carotid endarterectomy	1	
Pulmonary insufficiency	1	
To permit recovery from:		6
Cardiac failure	3	
Recent stroke	2	
Advanced pregnancy	1	
Total		12

TABLE 6
Thyroid Disease Associated with Primary Hyperparathyroidism

Thyroid Disease		No. of Patients
Benign nodules		26
Chronic lymphocytic thyroiditis		13
Carcinoma of thyroid		4
Autonomous functioning nodule		1
Operation primarily for thyroid disease:		4
hyperthyroidism	2	
benign nodules	2	
Total		48 (29% of 166 pts.)

Four of the patients were operated on primarily for thyroid disease; the parathyroid tumors and primary hyperparathyroidism were an incidental finding.

Technical difficulties at operation were increased by previous operations on the anterior neck in 17 patients. For 10 patients, re-operation for hyperparathyroidism was required. Previous operations for thyroid disease had been performed on an additional 6 patients. A stab wound to the anterior neck had necessitated operation in 1 case. The majority of patients in this category were seen after 1965. Six were over 60 years of age.

Two patients died within three years from causes apparently unrelated to the parathyroid operation. Neither was over 60 years of age. One died at the age of 42 from a cerebrovascular accident one year postoperatively. The other, aged 49, died at home suddenly without obvious cause, one year postoperatively.

A POLICY FOR SURGICAL THERAPY

Our experience to date is considered to justify a selective, but liberal, policy for operation on elderly patients with primary hyperparathyroidism. The risk of operation is low, even when the presence of cardiovascular or other disease increases it. The factors increasing risk are not restricted to the elderly. Life-endangering complications of hypercalcemia may occur at any age. Our success rate in correcting hypercalcemia by a single operation for primary hyperparathyroidism during this period of time has been approximately 97 per cent (1). This is similar to the Mayo Clinic experience (2).

The absence of renal lithiasis or osteitis fibrosa cystica is not a contraindication to operation for primary hyperparathyroidism in the elderly. These complications of hypercalcemia can arise with additional time. A hypercalcemic crisis can occur in the absence of renal or bone changes due to primary hyperparathyroidism, as evidenced by our patient who died at the age of 74 with acute hypercalcemia. Apparently there are a number of nonspecific effects of hypercalcemia on the cardiovascular, musculoskeletal, gastrointestinal, and nervous systems. At least some patients achieve a sensation of improved well-being after the correction of hypercalcemia, even though they were considered to be asymptomatic preoperatively. An added dividend is the occasional detection and correction at operation of significant thyroid disease (3).

In certain patients the risk of exploration of the parathyroid glands for primary hyperparathyroidism is considered excessive and unwarranted. Life expectancy should be more than several years, to justify an elective procedure on the parathyroid glands. Severe cardiovascular disease in a patient with mild hypercalcemia and undetectable complications therefrom, makes the risk of operation greater than the risk of the hypercalcemia. In such patients, life expectancy is limited primarily by disease other than primary hyperparathyroidism. However, the level of serum calcium should be determined periodically in such patients. Although serum calcium concentration usually does not increase abruptly in primary hyperparathyroidism, this factor varies greatly and occasionally there is a rapid increase. In elderly patients, a history of eradication of a previous malignant lesion does not contraindicate exploration of the parathyroid glands for primary hyperparathyroidism. However, a search should be made for the presence of malignancy in elderly patients. Inoperable or uncontrollable cancer usually contraindicates exploration of the parathyroid glands even if the cancer and the hypercalcemia appear unrelated.

Exploration of the parathyroid glands should be delayed in certain patients with primary hyperparathyroidism. Stabilization following a myocardial infarction or a cerebrovascular accident usually requires six to twelve months before elective exploration of the parathyroid glands can be performed (4). Other disorders such as acute cholecystitis, common bile-duct obstruction, abdominal aortic aneurysm or occlusive peripheral arterial disease may require surgical correction before exploration of the parathyroids. Excessively high levels of serum calcium may be prevented in such patients by dietary or medical measures during the period of delay. Keen judg-

ment may be required in deciding which operation to perform for a given patient.

Each patient with primary hyperparathyroidism should be evaluated individually for operation on the basis of the immediate and anticipated health status as well as on the severity of the hypercalcemia and its complications. These factors are more important than age alone. Careful monitoring during and after operation is needed for high-risk patients.

An additional group of patients will require periodic re-evaluations if the diagnosis remains questionable because of borderline test values and the absence of complications of hypercalcemia. These patients also belong to all age groups.

DISCUSSION

The selection of patients for operation for primary hyperparathyroidism on the basis of the foregoing factors rather than on age per se, is supported by the Mayo Clinic experience with 147 patients bearing a provisional diagnosis of "biochemical" hyperparathyroidism (5, 6). About half of these patients were more than 60 years of age. At the end of five years, 20 per cent of the group required parathyroid surgery. Furthermore, a careful medical follow-up was found to be expensive and difficult. Long term medical treatment to control hypercalcemia appeared to be associated with a serious hazard to renal function. No criterion has been identified to indicate those patients likely to have difficulties from hypercalcemia in the future.

Considerable speculation concerns the reason for the greatly increased recognition of primary hyperparathyroidism in recent years. Many of these patients have mild hypercalcemia. All age groups are involved and some have other serious disease. Whether all of the increase in the diagnosis of this disease can be attributed to the general use of multichannel biochemical screening is uncertain. In this study, we evaluated the use of diuretic drugs but were unable to establish any significant role for this factor. It appears that senile osteoporosis is related to primary hyperparathyroidism in some patients (7). Abnormalities in intestinal absorption may be an important etiologic factor for hyperparathyroidism (8).

Certain clinical abnormalities observed in patients with primary hyperparathyroidism are questionably related to hypercalcemia. Thus, one of our patients with cardiac arrythmias, including A-V block, sinus arrest and bouts of atrial fibrillation at the age of 71 years, has been free of arrythmias after correction of hypercalcemia (9). In elderly patients it may be difficult to relate mental confusion to hypercalcemia when other more likely etiologic factors are present. Whether hypercalcemia increases the risk of operation for other life-endangering problems is difficult to determine but is likely in certain situations. Another age-related factor requires consideration for patients with primary hyperparathyroidism, i.e., if a corrective operation is not carried out, other serious disease may develop which increases the risk of operation later.

At operation the surgeon must not only perform the technical procedure of identification of the parathyroid glands, but must be a diagnostician in assessing gross abnormalities of these glands (1). From our experience we have concluded that the pathologist cannot be expected, at the time of operation, to indicate more than whether the removed specimen is parathyroid tissue. Sometimes the pathologist even has considerable difficulty in deciding, on the basis of usual techniques for permanent sections, whether the parathyroid tissue is abnormal. The surgeon should also examine the thyroid gland at the time of operation to determine whether a thyroid procedure is necessary.

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