

Long term satisfaction of patients after surgery for primary hyperparathyroidism: Analysis of 71 patients

Primer hiperparatiroidizm cerrahisi sonrası hastaların uzun dönem memnuniyeti: 71 hastanın analizi

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SUMMARY

Objective: The aim of this study is to discuss the necessity of surgery by analysing the long term results and satisfaction of the symptomatic and asymptomatic patients who had parathyroidectomy for primary hyperparathyroidism.

Method: Patients who had parathyroidectomy because of primary parathyroid pathology or during thyroid surgery as concomitant parathyroid pathology between June 1999 and September 2010 were enrolled to the present, retrospective study. A total of seventy one patient were included to the study. The Pasioka Symptom Scoring System and SF-36 questionnaire are applied to the patients. The patients were divided into two groups as symptomatic and asymptomatic. The answers to the Pasioka Symptom Scoring System's last 5 questions examining general health, surgical satisfaction and quality of life were evaluated between symptomatic and asymptomatic patients.

Results: Number of the symptomatic patients were 38 (53.5%) whereas 33 patients (46.5%) were asymptomatic. Average length of follow up was 60 months. Among the operated 71 patients; 67 (94.4%) were cured, 4 (5.6%) had persistent hyperparathyroidism and 2 of these patients were operated again, the other two patients were out of follow up.

Conclusions: Asymptomatic patients with primary hyperparathyroidism may have masked neurocognitive and psychiatric complaints and these patients' quality of life can be improved with surgery.

Keywords: Hyperparathyroidism, primary, asymptomatic

ÖZET

Amaç: Çalışmanın amacı primer hiperparatiroidizm nedeniyle paratiroidektomi yapılmış semptomatik ve asemptomatik hastaların uzun dönem sonuçlarını ve memnuniyetlerini değerlendirerek cerrahinin gerekliliğini tartışmaktır.

Yöntem: Retrospektif çalışmamıza Haziran 1999 ile Eylül 2010 tarihleri arasında primer paratiroid patolojisi nedeniyle veya eşlik eden paratiroid patolojisi olup tiroid cerrahisi esnasında paratiroidektomi yapılan hastalar dahil edilmiştir. Toplam 71 hasta çalışmaya dahil edilmiştir ve hastalara The Pasioka Symptom Scoring System ve SF-36 anketleri uygulanmıştır. Hastalar semptomatik ve asemptomatik olmak üzere iki gruba ayrılmıştır. The Pasioka Symptom Scoring System anketinin son 5 sorusunun yanıtları asemptomatik ve semptomatik hastalar arasında genel sağlık durumu, cerrahi memnuniyet ve hayat kalitesini değerlendirmektedir.

Bulgular: Semptomatik hastaların sayısı 38 (%53.5) iken 33 (%46.5) hasta asemptomatik grupta idi. Ortalama takip süresi 60 aydı. 71 Hasta arasından 67 hastada (%94.4) kür sağlandı, 4 hastada (%5.6) persistan hiperparatiroidizm gelişti ve 2 hasta tekrar opere edildi; 2 hasta ise izlem dışı kaldı.

Sonuç: Asemptomatik primer hiperparatiroidizmlili hastalarda nörokognitif ve psikiyatrik yakınmalar maskelenebilir ve bu hastaların yaşam kaliteleri cerrahi ile iyileştirilebilir.

Anahtar sözcükler: Hiperparatiroidizm, Primer, Asemptomatik

INTRODUCTION

Hyperparathyroidism is the most common disease of the parathyroid glands and is a common disorder with 1/1000 incidence¹. Hyperparathyroidism can be primary, secondary and tertiary. Primary hyperparathyroidism is the most common type¹ which is caused by autonomic over excretion of parathormone (PTH) by one or more parathyroid glands². Secondary hyperparathyroidism is defined as increased PTH production caused by exogenous anomaly and related hyperplasia (98%) or adenomatous changes (2%). Symptoms of hyperparathyroidism are various but most patients suffer from loss of energy, depression, osteopenia, thinning hair, urolithiasis, headaches or heart palpitations. Nonetheless; some patients claim that they have no complaints. The management of these asymptomatic patients and the need for surgery is an issue of argument. The main purpose of this study is to analyse the long term results and patient satisfaction after parathyroidectomy in patients with primary hyperparathyroidism and to discuss the necessity for operation.

MATERIAL AND METHODS

This retrospective study was performed with the patients who had parathyroidectomy for primary hyperparathyroidism in Ankara Numune Education and Research Hospital 4. General Surgery Department between June 1999 and September 2010.

Retrospective analysis showed that 86 patients were operated for primary hyperparathyroidism in our clinic. During the analysis we found that 11 patients were out of follow up and 4 patients refused to answer the questionnaire so they were excluded from the study. Preoperative, operative and postoperative information was gained from Ankara Numune Education and Research Hospital 4. General Surgery Department Thyroid and Parathyroid Diseases Patient Forms and hospital automation system.

Patients were classified as symptomatic and asymptomatic. The patients who had complaints of bone pain, easy tiring, unstable mood, depression, stomachache, fatigue, irritability, joint pain, forgetfulness, having difficulty in standing up or getting out of a car, headache, itching and thirstiness were included in the symptomatic group. Whereas the patients who had elevated calcium and PTH levels in the routine blood analysis were included in the asymptomatic group.

The Pasioka Symptom Scoring Questionnaire³, prepared for parathyroid diseases, and the SF-36 scoring questionnaire⁴ for life quality were applied.

These questionnaires were applied to 51 patients face to face, to 20 patients by phone calling.

Demographic properties, coexisting illnesses before the operation and during the intercourse, duration of complaints and coexisting thyroid pathology of the patients were questioned and recorded.

Duration of the complaints were noted as months. Patients' preoperative and postoperative total calcium, ionized calcium, PTH, vitamin D levels were specified numerically. Ultrasonography (USG) and scintigraphy findings were recorded. Pathology results were noted as adenoma or hyperplasia. If available; frozen was noted as "adenoma", "hyperplasia", "adenoma and hyperplasia separation can not be made", "parathyroid gland". Also adenoma localization in the USG, scintigraphy and operation was noted. Operative indications were processed to the database. 2009 NIH criteria were evaluated for each patient and recorded.

In postoperative follow up; patients were divided into three groups as cured, relapse or persistent disease.

Serum calcium and PTH levels were measured every 3 months in postoperative first six months and then they were controlled every six months.

Patients who had at least one Pasioka symptom according to the preoperative history were included to the symptomatic group. Patients who had no symptoms but diagnosed incidentally as primary hyperparathyroidism were included to the asymptomatic group.

The SF-36 questionnaire was applied to evaluate the patients' last health condition and to confirm the Pasioka illness questionnaire. SF-36 questionnaire applied to patients one by one and answers were compared between symptomatic and asymptomatic group for the purpose of the study.

Statistical Analysis: SPSS 16.0 programme was used for the statistical analysis. Preoperative and postoperative results were compared with Wilcoxon's test.

RESULTS

71 patients were enrolled to the study. Mean age was 58 (27-83); 56 patients (78.9%) were female whereas 16 patients (21.1) were male.

There were 38 patients (53.5%) in the symptomatic group and 33 patients (46.5%) in the asymptomatic group. Symptomatic patients' duration of the complaints was average 24 months; ranging from 2 months to 5 years. There was a concomitant

thyroid pathology in 15 patients in the asymptomatic group, and in 22 patients in the symptomatic group.

In the symptomatic group 7 patients had renal stones, 3 patients had subperiosteal resorption on the X-rays and 12 patients had hypertension as coexisting illnesses. In the asymptomatic group 2

patients had renal stones and 11 patients had hypertension as coexisting illnesses; none of these patients had subperiosteal resorption on the X-rays.

In the asymptomatic group, asymptomatic 32 patients had high calcium levels, 5 of had low GFR, 10 of had low T score and 15 of age were less than 50. (Table-1).

Table 1. Patients' operation indications (2009 NIH criterias)

Patients	Ca value >1 mg/dl of normal values	GFR ¹ < 60 ml/dk	T score ² < 2 or pathologic fracture	Refuse medical therapy	Patient age < 50
Symptomatic (n=38)	36	5	10	0	15
Asymptomatic (n=33)	32	4	6	0	12

(¹GFR: Glomerular filtration rate; ²T score: bone density test score)

Preoperative mean total calcium levels were average 11.65 mg/dl (10.4-15.3), ionized calcium levels were 5.65 (4.5-8.3) and PTH levels were 35.25 (5.1-208). In terms of preoperative total

calcium levels, ionized calcium levels and PTH levels there were no significant difference between symptomatic and asymptomatic groups (Table-2).

Table 2. Calcium and parathormone levels before surgery

		Mean value	p
Total Ca (mg/dl)	Symptomatic	11.7995	0.059
	Asymptomatic	11.4788	
Ionise Ca (mg/dl)	Symptomatic	5.6721	0.412
	Asymptomatic	5.6415	
PTH (pmol/l)	Symptomatic	35.6842	0.734
	Asymptomatic	34.7531	

All patients had USG but scintigraphy was done to 58 patients. USG couldn't view the parathyroid adenoma in 27 of the 71 patients whereas scintigraphy couldn't view the adenoma in 22

patients. The adenoma determining rate was calculated as %61 for USG and %62 for scintigraphy. Localisation of the adenomas are given in table 3.

Table 3. Distribution of Parathyroid adenomas which were defined by USG, scintigraphy or peroperative.

	USG(%)	Scintigraphy(%)	Peroperative (%)
Right superior	0(%)	3 (4.2)	3 (4.2)
Right inferior	17 (23.9)	16(22.5)	30(42.3)
Left superior	5 (7)	1(1.4)	7(9.9)
Left inferior	22 (31)	16(22.5)	31 (43.7)
Couldn't view	27 (38)	22(31)	0 (%)

Solitary adenoma was seen in all patients except two who had two adenomas. Frozen section was reported as adenoma in 62 (%87.3) of the 71 patients'; whereas in 8 patients (%11.3) distinction between adenoma and hyperplasia failed with frozen.

Postoperative total calcium values were between 4.3 mg/dl and 10.6 mg/dl (average 9.11 mg/dl), ionized calcium values were between 4 mg/dl and 5.9 mg/dl (average 4.56 mg/dl), PTH values were between 1.1 pmol/l and 13.9 pmol/l (average 4.85 pmol/l) and vitamin D values were between 5.5 ng/ml and 35 ng/ml (average 16.47 ng/ml).

Mean follow up of the patients was 60 (± 31.2) months. Persistent hyperparathyroidism occurred in 4 patients, and continued after reoperation in 2 patients.

Based on the answers to the Pasioka questionnaire; asymptomatic patients had significant

improvement in preoperative and postoperative easy tiring, unstable mood, depression, stomachache, fatigue, nervousness, headache scores. But there was no significant difference in the bone pain, joint pain, forgetfulness, having difficulty in standing up or getting out of a car, itching and thirstiness scores (Table 4). Also significant improvement was detected in the symptomatic group in preoperative and postoperative bone pain, easy tiring, unstable mood, depression, stomachache, fatigue, nervousness, joint pain, having difficulty in standing up or getting out of a car, headache scores. But there was no significant difference in the forgetfulness, itching and thirstiness scores (Table 5). Surgical satisfaction was significantly higher in the symptomatic group.

Table 4. Average score for the Pasioka Symptom Scoring System of the asymptomatic patients

Pasioka Symptoms	Average score		P
	preoperative	postoperative	
Pain in the bones	14.5(± 5.6)	14.8 (± 6.6)	0.655
Feeling tired easily	27.2(± 11.2)	19.3 (± 9.9)	0.004
Mood swings	33.0(± 15.1)	15.1 (± 10.0)	0.001
Feeling depressed	40.6(± 13.2)	14.8 (± 9.0)	0.001
Pain in the abdomen	19.6(± 8.8)	16.6 (± 6.4)	0.029
Feeling weak	34.3(± 16.1)	22.1 (± 14.7)	0.006
Feeling irritable	30.0(± 13.9)	14.5 (± 6.1)	0.001
Pain in the joints	19.0(± 9.1)	17.5 (± 7.5)	0.222
forgetfulness	21.5(± 9.7)	20.9 (± 9.7)	0.317
Difficulty getting out of a chair or car	21.2(± 9.2)	21.8 (± 9.1)	0.564
headache	30.9(± 11.8)	19.3 (± 10.2)	0.002
Itchy skin	10.9(± 2.9)	11.8 (± 5.8)	0.317
Being thirsty	14.8(± 10.6)	13.3 (± 6.9)	0.317

Table 5. Average score for the Pasioka Symptom Scoring System of the symptomatic patients

Pasioka Symptoms	Average score		p
	Preoperative	postoperative	
Pain in the bones	72.8(±15.4)	18.1 (± 9.2)	0.001
Feeling tired easily	42.6(±21.6)	18.1 (± 9.8)	0.001
Mood swings	24.4(±16.5)	16.0 (± 10.7)	0.003
Feeling depressed	27.1(±14.5)	17.8 (± 9.0)	0.001
Pain in the abdomen	38.4(±18.5)	15.7 (± 6.8)	0.001
Feeling weak	61.8(±18.8)	20.7 (± 11.7)	0.001
Feeling irritable	25.2(±19.2)	19.4 (± 12.0)	0.016
Pain in the joints	70.7(±13.4)	18.9 (± 10.6)	0.001
forgetfulness	22.1(±13.3)	20.2 (± 8.5)	0.461
Difficulty getting out of a chair or car	22.3(±11.9)	15.7 (± 7.2)	0.003
headache	51.0(±21.5)	19.4 (± 10.8)	0.001
Itchy skin	11.3(± 8.1)	10.2 (± 1.6)	0.317
Being thirsty	16.3(±12.6)	14.2 (± 8.5)	0.246

There wasn't any significant difference between the answers of the symptomatic and asymptomatic groups to the questions of the SF-36 questionnaire which are examining the present physical function, pain, general health, energy, social function, mood and mind health.

DISCUSSION

In the current study, we aimed to determine if a new indication for parathyroid surgery could be added for asymptomatic patients with primary hyperparathyroidism. Based on the literature; half of the patients who are diagnosed as PHPT (primary hyperparathyroidism) are asymptomatic⁶ and the need for surgery in these patients is discussible. It is known that as the disease progresses; asymptomatic patients will become symptomatic so we tried to investigate if it would be right to perform surgery in these asymptomatic patients before they get symptomatic.

Most of the patients diagnosed as hyperparathyroidism in western countries are asymptomatic whereas in least developed countries there are many patients diagnosed by pathologic bone fractures, recurrent renal stones, nephrolithiasis or renal failure due to delayed diagnosis⁷. As the number of patients increased diagnosed in the asymptomatic phase; it has been the subject of debate if these patients had surgical treatment indication.

Flint et al in a study that analyses the time passed from the beginning of the symptoms to diagnosis and treatment found that time was between 8 days and 10 years; average 2 years⁸. Similarly in our

study the time from beginning of the symptoms to diagnosis was average 24 months.

Rubin and Bilezikian, in their study on 57 asymptomatic PHPT patients who were followed for 15 years showed that over time 37% of patients needed surgery⁹. In a similar study of Purnell and Scholz, 23% of patients required surgery because of the elevated levels of calcium and occurring complications. There is no parameter to predict the patients who will need surgery. These authors preferred surgery rather than follow up in the patients who don't mind surgery because it is impossible to predict who will have complications, it will be very difficult to deal with the complications and patients can escape from the follow up¹⁰. Most sources define asymptomatic patients as patients who don't have any classical bone – joint complaints and associated laboratory changes but have neurocognitive and psychiatric complaints like unstable mood, fatigue, anxiety and sleeping disorders. Possible reason for this condition is the decreased cerebral blood flow shown in untreated adenoma patients with SPECT¹¹. In this study it has been shown that the cerebral blood flow recovered in 13 of 14 patients after 12 months from surgery. Also hypertension and left ventricular function improved and cardiac irritability decreased. Life quality of the patients improved and neuropsychiatric symptoms decreased. Therefore the authors suggest to take these neuropsychiatric symptoms into operative indications.

In the reviews published after 2009 NIH meeting; it is stated that surgery is a cheap and cost effective treatment modality in experienced hands for all patients regardless to be symptomatic or

asymptomatic¹². Many clinicians indicate that NIH criteria are more to medical follow up in asymptomatic patients. Most endocrine surgeons emphasize that also these subjective complaints are important for deciding on surgery¹³. It has been reported that surgery could be offered even to PHPT patients who are not candidates of operation according to 2009 NIH criteria. Because surgery is far more cheaper than medical follow up and calcimimetic therapy¹⁴.

In addition, the decrease in the risk of cardiovascular disease in asymptomatic patients and improvement in bone mineral density after parathyroidectomy; has been demonstrated in studies. Our study showed that even asymptomatic patients had unrecognized minimal bone joint pain, motion system problems and neuropsychiatric symptoms. But after surgery these asymptomatic patients' answers were close to each other both in Pasiëka and SF-36 questionnaires and there was no significant difference.

In conclusion, we stated that asymptomatic patients usually have masked neurocognitive and psychiatric symptoms and those symptoms were improved with surgery. Additionally even if the patients are completely asymptomatic; bone density is improved after parathyroidectomy and so chance of experiencing a morbidity is decreased. Because of these reasons we believe that the decision for surgery in asymptomatic patients can be made more easily.

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