Pasieka’s Parathyroid Symptoms Scores Correlate with SF-36 Scores in Patients Undergoing Surgery for Primary Hyperparathyroidism

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Abstract

Background Parathyroidectomy for primary hyperparathyroidism (PHPT) is expected to trigger an improvement in the quality of life. This has been demonstrated previously by using the SF-36 questionnaire, whose interpretation is difficult in routine clinical practice. As an alternative, the 13-item questionnaire developed by Pasieka et al. can be used to assess the severity of symptoms on a visual analogue from which a parathyroid assessment of symptoms score (PAS) can be calculated. The purpose of this study was to correlate results of these two assessment tools.

Methods Prospective case-series study recruiting consecutive unselected patients who underwent successful parathyroidectomy for PHPT. SF-36(v2) and Pasieka’s questionnaires were collected before parathyroidectomy and at 3, 6, and 12 months postoperatively.

Results Between November 2005 and December 2006, 101 patients were diagnosed with PHPT (30 men; aged 18–89 years). Preoperative PAS ranged 0–1040 and did not correlate with the severity of hypercalcemia (2.91 ± 0.25; range, 2.56–3.4 mmol/l). Scores from the SF-36 questionnaire were under the 50th percentile for the normal population in three domains (vitality, emotional role, and physical role). Minimally invasive parathyroidectomy was performed in 69 patients and bilateral cervical exploration in 32 patients. All were found to have a single parathyroid adenoma and were normocalcemic at 3–12 months after parathyroidectomy.

At follow-up, there was a significant reduction of PAS from 460 ± 257 preoperatively to 254 ± 234 at 3 months postoperatively (n = 72), to 245 ± 215 at 6 months (n = 50), and 249 ± 212 at 12 months (n = 63) (p < 0.05, Student’s t-test). There was a significant and persistent improvement in five domains of SF-36 questionnaire: bodily pain, general health, vitality, social functioning and mental health. Overall analysis of 244 assessments using both questionnaires demonstrated a negative correlation between increasing PAS and decreasing mental component scores and physical component scores of the SF-36 assessment (r² = 0.372 and 0.301, respectively).

Conclusions Pasieka’s parathyroid assessment of symptoms scores (PAS) correlate with SF-36 questionnaire scores. Because PAS allows easier and faster analysis, we advocate that Pasieka’s questionnaire should be integrated into the assessment of patients with PHPT as a reliable tool to identify symptomatic changes that correlate with improved quality of life.

Introduction

Patients with primary hyperparathyroidism (PHPT) assessed using the Medical Outcomes Study Short-Form Health Survey (SF-36) questionnaire are found to have a significant impairment in their quality of life (QoL) with the potential for significant improvement after parathyroidectomy. This was first demonstrated in a randomized trial that involved 53 patients with asymptomatic PHPT and mild hypercalcemia, in which those who underwent parathyroidectomy had a significant improvement in two domains of the SF-36 questionnaire (emotional role functioning and social functioning), whereas those on long-term follow-up had a significant worsening in five domains of the SF-36 questionnaire (social functioning, physical problem, emotional...
problem, energy, health perception) [1]. These findings were subsequently confirmed in a prospective cohort analysis of 43 patients with asymptomatic PHPT [2] and more recently in a prospective multicenter study, including 100 French patients [3] and a prospective randomised trial of 50 patients with mild asymptomatic PHPT [4]. In contrast, other authors failed to demonstrate a benefit of surgical intervention in patients with asymptomatic PHPT in comparison with long-term medical follow-up, although at baseline all patients had significantly lower QoL and more psychological symptoms compared with age- and sex-matched healthy subjects [5].

An important contribution to this field has been the development of a surgical outcome tool designed specifically for PHPT symptoms. This was first validated by Pasieka and coworkers in a cohort of 63 Canadian patients [6] and subsequently confirmed in a multicenter trial involving 203 patients from Canada, United States, and Australia [7]. Using a set of 13 questions, a parathyroid assessment of symptoms score (PAS) is derived from the self-assessed responses on a 100-mm visual analogue scale. It was found that a significant reduction in preoperative symptoms occurs within 10 days of parathyroidectomy [6], and this effect remains apparent during a 12-month follow-up [7]. This evaluation tool was further validated in a group of 71 Australian patients, of whom some 80% identified a significant decrease in symptoms 12 months after parathyroidectomy [8].

This prospective study was setup to compare changes in the SF-36 questionnaire and Pasieka’s parathyroid symptoms scores in a cohort of consecutive unselected patients with PHPT.

Patients and methods

With the approval of the local research ethics committee, consecutive unselected patients with biochemical diagnosis of primary hyperparathyroidism were recruited in the study. Demographic, biochemical, radiological, operative, and histological details were recorded in a prospective database. Clinic letters were scrutinized to identify the number of symptoms reported by the patients. All patients underwent parathyroid imaging with Tc$^{99m}$-sestamibi scan and neck ultrasound. Those with concordant imaging were offered minimally invasive parathyroidectomy and those with negative or nonconcordant imaging underwent bilateral cervical exploration.

Quality of life assessment

Patients were assessed at the preoperative outpatient clinic visit, at the first follow-up outpatient visit (6–12 weeks postoperatively), and subsequently contacted by post at 6 and/or 12 months postoperatively.

Parathyroid assessment of symptoms score (PAS) was derived from the answers to the standardized questionnaire developed by Pasieka et al. [6]. The 13 items explored included: bone pain, feeling tired easily, mood swings, feeling “blue” or depressed, pain in the abdomen, feeling weak, feeling irritable, pain in the joints, being forgetful, difficulty getting out of a chair or car, headaches, itchy skin, and being thirsty. Each item was scored according to the response on a 100-mm visual analogue scale and PAS was calculated as the sum of all 13 answers, with a maximum PAS possible of 1300.

The SF-36(v2) questionnaire was made available to all patients at each assessment. The responses were analyzed using the commercially available SF Health Outcomes™ Scoring Software (QualityMetric Inc., Lincoln, USA).

Statistical analysis

Nonskewed data are presented as means ± standard deviation (range) and descriptive statistics using parametric comparisons (t-test) were calculated. Skewed data were analyzed by using nonparametric test (Mann–Whitney U-test) and presented as median values.

Results

Demographic and biochemical data

Between November 2005 and December 2006, a total of 101 patients with biochemical diagnosis of PHPT were recruited in the study (30 men; aged 18–89 (mean, 61 ± 17) years). Their preoperative plasma corrected calcium was 2.93 ± 0.24 mmol/l (range, 2.54–3.9 mmol/l, normal range 2.05–2.65 mmol/l) and PTH concentration was 23.7 ± 26.9 nmol/l (range, 5.7–193, normal range 0.2–7.5 nmol/l).

Minimally invasive parathyroidectomy was performed in 69 patients with concordant sestamibi and neck ultrasound scans. Thirty-two patients with negative or nonconcordant preoperative localization studies underwent bilateral cervical exploration. All patients were found to have a parathyroid adenoma, weighing 100–12,000 mg (mean 1,680 ± 3,187 mg, median 1,000 mg). During follow-up, all patients were normocalcemic at 3 months (n = 101) and 12 months (n = 78).

All patients were contacted by mail on three occasions after their operation. All but seven patients replied at least once. Their responses were grouped at 3 months (n = 74), 6 months (26 ± 6 weeks, n = 49), and 12 months (54 ± 13 weeks, n = 68) postoperatively.
Preoperative assessment

Pasieka’s parathyroid symptoms score (PAS) ranged from 0 to 1040 of a potential maximum score of 1300. Only 16 patients had scores lower than 200, a cutoff considered nonspecific according to historical controls [6]. There was no correlation between calcium levels and PAS (Fig. 1). Scores for patients with minimal raise in calcium (Ca²⁺ < 2.8 mmol/l) were similar to those in patients with more severe hypercalcemia (462 ± 255 vs. 459 ± 260; p = NS).

Preoperative clinic letters recorded in decreasing order of frequency the presence of lethargy (n = 62), polyuria/polydypsia (n = 44), neuropsychiatric symptoms (n = 40), aches and pains (n = 34), renal stones (n = 17), and gastrointestinal symptoms (n = 8). The number of symptoms recorded for individual patients did not correlate with their self-reported PAS (Fig. 2).

The median preoperative scores of the SF-36(v2) questionnaire were lower than the 50% percentile in three domains: vitality (36.9 ± 23.7%), emotional role (12.9 ± 10.9%), and physical role (9.9 ± 10.4%) (Fig. 3). There was no significant difference in the scores of patients with calcium levels below or above 2.8 mmol/l. There was no correlation between calcium levels and the overall physical component scores and mental component scores derived from the SF-36 analysis (Fig. 3).

Postoperative improvement in symptoms and quality of life

Patients have completed a total of 191 follow-up assessments, with a median of two postoperative assessments per patient. Their last assessment was after a mean of 43 ± 21 (range, 8-94; median, 49) weeks postoperatively.

Compared with the preoperative symptoms scores, there was a significant decrease in PAS at 3 months after parathyroidectomy (460 ± 257 vs. 254 ± 234; n = 72, p < 0.01). Eighteen of 20 patients with mild hypercalcemia (Ca²⁺ < 2.8 mmol/l) had an improvement in PAS (from 430 ± 198 to 204 ± 169, p < 0.05). In patients with more severe hypercalcemia (Ca²⁺ > 2.8 mmol/l), an improvement in PAS was observed in 40 of 52 patients (from 495 ± 274 to 286 ± 258, p < 0.05). At 3 months, the percentage improvement in PAS was higher in patients with mild hypercalcemia (Ca²⁺ < 2.8 mmol/l) (62% ± 28% vs. 49% ± 26%, p = NS).

The improvement in PAS was persistent for patients reassessed at 6 months (445 ± 252 vs. 245 ± 215; n = 50, p < 0.05) and 12 months (434 ± 240 vs. 249 ± 212; n = 63, p < 0.05). At 1 year postoperatively, there were persistent significant improvements in the mean scores for 10 of the 13 parameters assessed by Pasieka’s questionnaire (Table 1). Changes in PAS were similar in patients undergoing minimally invasive parathyroidectomy or bilateral cervical exploration (Fig. 4).

A significant improvement in five components of the SF-36(v2) questionnaire was demonstrated at 3 months postoperatively: bodily pain, general health, vitality, social functioning, and mental health (p < 0.01, Mann–Whitney U-test; Fig. 5). This improvement was persistent at 6 months and 12 months (Fig. 5). At 12 months of follow-up, the physical component scores were improved by >10% in 20 of 58 patients and the mental component scores were improved by >10% in 31 of 58 patients.
Fig. 3  Preoperative SF-36 scores in a cohort of 101 patients with primary hyperparathyroidism. Preoperative median scores for patients with calcium levels below or above 2.8 mmol/l are plotted. The relationship between preoperative calcium levels and physical and mental component scores was analyzed in a group of 101 patients.

Table 1  Changes in individual parameters of the Pasieka’s parathyroid symptoms score at 12 months after parathyroidectomy in 101 patients with primary hyperparathyroidism

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preoperative scores</th>
<th>Scores at 12 months postoperatively</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeling tired</td>
<td>59.3 ± 30.2 (70)</td>
<td>29.9 ± 25.7 (30)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Feeling thirsty</td>
<td>36.5 ± 34.2 (30)</td>
<td>17.0 ± 23.8 (5)</td>
<td></td>
</tr>
<tr>
<td>Mood changes</td>
<td>36.8 ± 33.3 (25)</td>
<td>17.1 ± 19.6 (10)</td>
<td></td>
</tr>
<tr>
<td>Joint pains</td>
<td>43.3 ± 32.5 (50)</td>
<td>24.3 ± 27.1 (20)</td>
<td></td>
</tr>
<tr>
<td>Irritability</td>
<td>34.4 ± 30.6 (25)</td>
<td>17.7 ± 20.8 (10)</td>
<td></td>
</tr>
<tr>
<td>Feeling blue</td>
<td>39.9 ± 33.9 (35)</td>
<td>22.6 ± 26.7 (10)</td>
<td></td>
</tr>
<tr>
<td>Feeling weak</td>
<td>36.7 ± 31.0 (40)</td>
<td>22.4 ± 25.6 (10)</td>
<td></td>
</tr>
<tr>
<td>Itchy</td>
<td>23.8 ± 33.7 (0)</td>
<td>11.6 ± 18.1 (0)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Forgetful</td>
<td>32.4 ± 30.4 (30)</td>
<td>26.1 ± 29.1 (15)</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>14.2 ± 25.7 (0)</td>
<td>6.3 ± 11.8 (0)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>18.5 ± 31.1 (0)</td>
<td>10.9 ± 23.3 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>Bone pain</td>
<td>34.6 ± 31.7 (25)</td>
<td>27.6 ± 30.6 (20)</td>
<td></td>
</tr>
<tr>
<td>Ability to move off a chair</td>
<td>16.5 ± 24 (10)</td>
<td>16.1 ± 23.8 (0)</td>
<td></td>
</tr>
</tbody>
</table>

Median ± standard deviation (median) for individual scores are detailed. Comparison was done using Student’s t-test.
Correlation between PAS and SF-36 responses

A total of 244 simultaneous questionnaires were administered at the time of diagnosis (n = 92), at 3 months follow-up (n = 62), at 6 months follow-up (n = 43), and at 12 months follow-up (n = 47). There was a linear correlation between PAS and the physical component scores (PCS = 48.7–0.021 × PAS, r² = 0.3025) and between PAS and the mental component scores (MCS = 44.4–0.025 × PAS, r² = 0.372) (Fig. 6).

Discussion

This study confirms for the first time in a UK population an improvement in symptoms and quality of life after successful parathyroidectomy. This was demonstrated using the self-reported severity of symptoms using a parathyroid-specific assessment questionnaire developed by Pasieka et al. and by comparing these results with the replies to the widely used SF-36 questionnaire.

Whether patients with mildly symptomatic PHPT benefit from surgical intervention or whether they should be enrolled in long-term follow-up programs continues to be debated by endocrine surgeons and endocrinologists [9]. Several studies organized in large surgical centers have shown that parathyroidectomy is followed by rapid improvement in quality of life (QoL) persisting for up to 1 year [1–3, 10, 11]. This topic has been reviewed recently [12]. In contrast, a randomized, controlled trial of 191 patients with very mild hypercalcemia (2.69 ± 0.08 mmol/l) found no difference in the SF-36 scores in those undergoing surgery or monitored for up to 2 years [5]. The controversy also is fueled by the criticism that individual studies using the SF-36 questionnaire have identified improvements in different components of the nine scores generated by this assessment tool. Furthermore, scoring of the SF-36 questionnaire can be rather cumbersome and relies on a comparison with the norm of an American population and might not be directly applicable to other countries. Thus, the use of the SF-36 questionnaire remains limited to enthusiasts assessing trial patients and has not been incorporated in routine clinical practice.

In an attempt to create an assessment tool specific for PHPT, some have used a 53-question survey based on the Health Outcomes Institute Health Status Questionnaire and found an improvement in patients’ perception of general health, muscle strength, energy level, and mood up to 24 months after parathyroidectomy [13]. Similarly, a recent publication has reported the use of a questionnaires investigating the presence and severity of 21 symptoms and associated conditions frequently observed in patients with PHPT, including appetite loss, weight loss, thirst, polyuria, headaches, itchy skin, muscular pain, amyotrophy, gout, nausea, abdominal pain, abdominal distension, constipation, ulcer, pancreatitis, mood swings, anxiety, forgetfulness, angina pectoris, and palpitation [3]. In this context, the 13-item parathyroid assessment of symptoms score described by Pasieka et al. [6] provides a more easily applicable method to quantify the severity of symptoms in patients with PHPT. This tool was used in several studies in North America and Australia [7, 8].

This study recruited 101 patients with PHPT who underwent successful parathyroidectomy. The PAS symptoms scores and SF-36–derived parameters were similar in those with calcium levels below or above 2.8 mmol/l. In addition, the postoperative improvements were not correlated with the severity of hypercalcemia. These data reinforce the fact that parathyroidectomy should not be restricted to patients with severe hypercalcemia. In view of the growing evidence for benefits of parathyroidectomy in patients with mild/asymptomatic PHPT [9], the decision to operate should not be limited by the severity of biochemical abnormalities. Our liberal decision to offer surgical treatment to all patients is in line with the view held by many that the selection of PHPT patients for parathyroidectomy based on the NIH criteria [14] is too restrictive. Several studies demonstrated that the incidence of preoperative nonspecific somatic and neuropsychiatric symptoms is equivalent in those who meet or do not meet the NIH criteria and their postoperative improvement in symptoms is equal [3, 4, 15].

Only nine patients in our study group were octogenarians, therefore, no subgroup analysis was done based on age. Anecdotal evidence suggests that old patients experience significant improvement in their lifestyle after parathyroidectomy, because many might consider that PHPT symptoms are “normal” during aging. In a retrospective study of 54 patients with PHPT who were aged 80 years or older, the group in San Francisco has demonstrated...
significant improvement of fatigue, weight loss, nocturia, bone pain, constipation, and major depression [16]. Similar data were reported in a group of 50 patients, octo- and nonagenarians from Madison, Wisconsin, of whom more than 60% reported improved physical functioning, social functioning, mental health, and reduction of bodily pain [17]. Based on this data, we consider that there should be no age limit for considering parathyroidectomy in elderly patients with acceptable life expectancy.

In our group of patients the postoperative improvement in QoL was similar in those who had a focused unilateral neck exploration (minimally invasive parathyroidectomy, MIP) or a bilateral neck exploration. Similar findings were reported in a multicenter trial in France [3]. In contrast, a study of 202 Australian patients found that those who underwent MIP had significantly better vitality and emotional role limitation scores than those having a bilateral neck exploration, possibly related to the patients’ perceptions of having had a “less invasive” surgical procedure [18]. These different findings are difficult to explain if one assumes that patients from different centers have similar expectations of symptomatic postoperative improvement irrespective of whether they are suitable for a scan-directed MIP. Our patients were recruited after confirming the biochemical diagnosis of PHPT and were offered an operation before knowing the scan results and the type of operation to be undertaken.
Analysis of data in this series has identified a good correlation between changes in Pasieka’s parathyroid symptoms score (PAS) and SF-36 scores for physical and mental components. However, there are differences between these two assessment tools. The Pasieka questionnaire is a disease-specific tool developed for primary hyperparathyroidism (PHPT), and hence, it seems to be able to demonstrate changes of higher amplitude. One the other hand, the SF-36 questionnaire offers a generic assessment that might not be sensitive enough for PHPT, and hence, postoperative improvements might be identified only for some of its components. As a last difference between these two questionnaires, the Pasieka’s score can be easily calculated as the sum of 13 numbers, whereas the SF-36 necessitates coding of the answers according to a standardized scale and the use of a special software to interpret these data. Because PAS allows easier and faster analysis, it is more likely to be adopted into routine clinical practice.

There are some limitations of this study. First, there was no randomization; parathyroid surgery was offered to all patients with secure biochemical diagnosis of PHPT. Second, we have not tested these assessments tools in a control group of patients undergoing neck surgery for other indications; hence, we have not assessed how specific and sensitive these questionnaires are for PHPT. We considered that some of these issues have been addressed in previous studies and preferred to use each patient as his own control by comparing the preoperative answers with those at 3–12 months postoperatively. Third, not all 101 patients replied to all follow-up questionnaires—a limitation inherent to all postal surveys. Because some of the patients enrolled in this study do not leave in the vicinity of the hospital, many were discharged to their referring physician for long-term biochemical follow-up and failed to reply to some of the three postoperative questionnaires.

**Conclusions**

Successful parathyroidectomy is followed by a decrease in severity of symptoms and an improvement in quality of life that is persistent 12 months postoperatively. We advocate that Pasieka’s questionnaire should be integrated into the assessment of patients with PHPT as a reliable tool to identify symptomatic changes that correlate with improved quality of life.

**References**


![Fig. 6](image-url)


