



Original research

The extent of improvement of health-related quality of life as assessed by the SF36 and Paseika scales after parathyroidectomy in patients with primary hyperparathyroidism – A systematic review and meta-analysis



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HIGHLIGHTS

- Parathyroidectomy for PHPT potentially improves function and quality of life.
- However, there is no quantitative evidence to support this for all studies.
- Provides evidence that parathyroidectomy improves the quality of life of PHPT patients.

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ABSTRACT

Background: Previous studies have shown that parathyroidectomy for primary hyperparathyroidism (PHPT) improve the function and quality of life of patients. The aim of this systematic review and meta-analysis is to determine the health-related quality of life outcomes among those having surgical management for PHPT. **Methods:** Several databases were searched (MEDLINE, EMBASE, PubMed, Current Contents) for studies in which health-related quality of life was measured by reliable and validated instruments (SF-36 and Paseika Questionnaire) before and after parathyroidectomy for patients with primary hyperparathyroidism (PHPT). For the SF-36, score differences greater than 5 points indicate clinically relevant changes. **Results:** There were six studies with quality of life data. The SF-36 data was derived from 238 patients, with a mean age of 59 years and 71% were females. The range of follow up after surgery was 6 months to one year. The pre- and post-parathyroidectomy SF-36 quality of life scale scores were vitality (44 vs. 60, $p < 0.001$), physical functioning (51 vs. 69, $p < 0.001$), bodily pain (50 vs. 65, $p < 0.001$), general health (54 vs. 64, $p < 0.001$), role physical (34 vs. 52, $p < 0.001$), role emotional (43 vs. 59, $p < 0.001$), role social (60 vs. 74, $p < 0.001$), and mental health (55 vs. 71, $p < 0.001$). The Paseika data was derived from 203 patients, with a mean age of 54 years and 67% were females. The pre- and post-parathyroidectomy Paseika scores were feeling tired (51 vs. 19, $p < 0.001$), feeling thirsty (29 vs. 12, $p < 0.001$), mood swings (33 vs. 12, $p < 0.001$), joint pains (32 vs. 14, $p < 0.001$), irritability (31 vs. 10, $p < 0.001$), feeling blue (31 vs. 14, $p < 0.001$), feeling weak (37 vs. 15, $p < 0.001$), itchy (17 vs. 7, $p < 0.001$), forgetful (27 vs. 16, $p < 0.001$), headache (18 vs. 5, $p < 0.001$), abdominal pain (19 vs. 8, $p < 0.001$), bone pain (38 vs. 17, $p < 0.001$), ability to move off chair (27 vs. 11, $p < 0.001$). **Conclusion:** Parathyroidectomy significantly improves the short to medium-term health-related quality of life of patients suffering from primary hyperparathyroidism.

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1. Introduction

Primary hyperparathyroidism (PHPT) is a condition in which one or more of the parathyroid glands becomes autonomous and hyperactive. A patient with this endocrine disorder typically

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demonstrates increased serum calcium levels and inappropriately elevated parathyroid hormone levels.

Primary hyperparathyroidism (PHPT) occurs in 0.2%–0.5% of the population and is the most common cause of hypercalcemia in outpatients and second to cancer in the inpatient population [1]. Classic presentations of PHPT are: bone pain, nephrolithiasis, psychiatric disorders and gastrointestinal symptoms. Currently, most patients are diagnosed from a routine blood test and they have few or no specific symptoms [2].

Parathyroidectomy remains the treatment of choice for patients with PHPT accompanying obvious symptoms and complications. Patients with “asymptomatic” PHPT are often referred to those who report only subjective symptoms such as fatigue, irritability and mood swings and they remain to be the majority of cases [3]. The National Institute of Health (NIH) has developed guidelines for the surgical management of asymptomatic PHPT, but it has not included the effects of these symptoms on quality of life as an indication and parameter for parathyroidectomy [1,4].

Many patients state dramatic improvements in their sense of well-being and thus better quality of life following surgical correction of the disease [5]. Several studies have shown this by quantitatively and qualitatively describing the outcomes before and after the surgical procedure. However, the sample sizes are small and they use different instruments to measure outcomes. This paper aims to provide a systematic review and a meta-analysis of the health-related quality of life outcomes among patients who underwent parathyroidectomy for PHPT.

1.1. Quality of life assessment tools

Paseika and co-workers has developed Pasiieka’s parathyroid assessment of symptoms scores (PAS), which is a disease-specific surgical outcome tool [3,5–7]. Although not designed as a quality of life instrument per se, it evaluates several domains specific to PHPT. This standardized questionnaire explores 13 items that includes: bone pain, feeling tired, mood swings, feeling blue, abdominal pain, feeling weak, irritability, joint pains, forgetfulness, difficulty getting out of chair or car, headaches, itchy skin, and feeling thirsty. PAS uses a 100 mm visual analogue scale and is calculated as the sum of all 13 answers, with maximum possible score of 1300 [5].

SF-36 Health Survey is a well-recognized and validated quality of life questionnaire that measures eight different areas. This multidimensional self-administered 36-item instrument allows reproducible data that evaluates: physical functioning, social functioning, bodily pain, general health perceptions, vitality, role limitations due to emotional problems (role-emotional), role limitations due to physical health problems (role-physical) and mental health. Number of questions for each domain varies from 2 to 10. Scores range from 0 (poor health status) to 100 (best health status) [8,9] SF-36 is a useful tool for assessing patient outcomes after operation for hyperparathyroidism [14].

Pasiieka’s parathyroid assessment of symptoms scores (PAS) correlate with SF-36 questionnaire scores [10]. Both tools are reliable to identify symptomatic changes in patients with PHPT.

2. Methods

2.1. Study protocol

We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. A systematic search of the databases MEDLINE, PubMed, EMBASE, and Current Contents from 1996 through to November 2014, to identify relevant articles. The search used the combination of keywords: (1) primary

hyperparathyroidism; (2) parathyroidectomy; (3) health-related quality of life; (4) Pasiieka; and (5) SF-36, which were searched as text word and as exploded medical subject headings where possible. The reference lists of relevant articles were also searched for appropriate studies. No language restrictions were used in either the search or study selection. A search for unpublished literature was not performed.

2.2. Study selection

We included studies that met the following inclusion criteria: (1) health-related quality of life measurement which uses either Pasiieka Health Questionnaire and or SF-36; (2) quantitative presentation of data; (3) pre- and post-operative comparison of scores. No restrictions were put on the study design, location, gender of patients, population size or language of publication. We excluded studies that did not meet the inclusion criteria.

2.3. Data extraction

The data extraction was performed using a standardized data extraction form, collecting information on the publication year, study design, number of cases, number of controls, total sample size, temporal direction, population type, country, continent, economic development, case control matching, mean age, number of adjusted variables, the risk estimates or data used to calculate the risk estimates, (confidence intervals) CIs or data used to calculate CIs, the scores of each parameter measured in both Pasiieka and SF-36. Quality of the studies was not assessed and authors were not contacted for missing data. Adjusted ratios were extracted in preference to non-adjusted ratios, however, where ratios were not provided, unadjusted (Odds Ratios) ORs and CIs were calculated. Where more than one adjusted ratio was reported, we chose the ratio with the highest number of adjusted variables. Where multiple risk estimates were available in the same study, for example due to the use of different comparator groups, they were included as separate risk estimates.

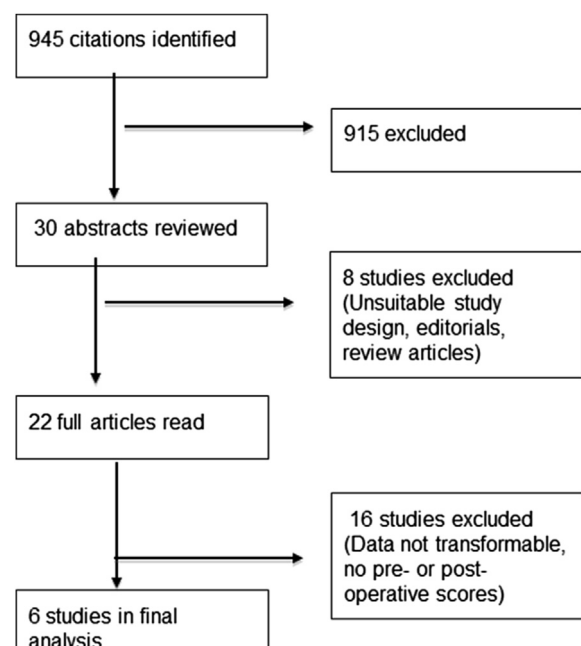


Fig. 1. Identification, inclusion and exclusion of studies in the meta-analysis.

2.4. Statistical analysis

Pooled odds ratios and 95% confidence intervals were calculated for the effect of parathyroidectomy for primary hyperparathyroidism using a random effects model. We tested heterogeneity with Cochran's Q statistic, with $P < 0.10$ indicating heterogeneity, and quantified the degree of heterogeneity using the I^2 statistic, which represents the percentage of the total variability across studies which is due to heterogeneity. I^2 values of 25, 50 and 75% corresponded to low, moderate and high degrees of heterogeneity respectively. We quantified publication bias using the Egger's regression model. All analyses were performed with Comprehensive Meta-analysis (version 2.0), Englewood, NJ, USA (2005).

3. Results

3.1. Literature search

From the 945 studies identified, 6 studies met the primary inclusion criteria (Fig. 1). Articles were excluded because they used different health-related quality of life indicators, no pre- and post-operative quantitative scores given or only qualitative descriptions were provided. There were 5 cohort studies and 1 case-series. Two studies used Paseika's parathyroid assessment of symptom scores (PAS) and 3 studies used SF-36 questionnaire scores. One study used both PAS and SF-36 questionnaire scores. All studies reported pre- and post-operative assessment scores. Total study population was 399 individuals. The lengths of post-surgical follow-up were about 6 months to 1 year.

3.2. Paseika scale

The Paseika data was derived from 203 patients, with a mean age of 54 years and 67% were females. The range of post surgical follow up was 6 months to 1 year. The pre- and post-parathyroidectomy Paseika scores were feeling tired (51 vs. 19, $p < 0.001$), feeling thirsty (29 vs. 12, $p < 0.001$), mood swings (12 vs. 33, $p < 0.001$), joint pains (32 vs. 14, $p < 0.001$), irritability (31 vs. 10, $p < 0.001$), feeling blue (31 vs. 14, $p < 0.001$), feeling weak (37 vs. 15, $p < 0.001$), itchy (17 vs. 7, $p < 0.001$), forgetful (27 vs. 16, $p < 0.001$), headache (18 vs. 5, $p < 0.001$), abdominal pain (19 vs. 8, $p < 0.001$), bone pain (38 vs. 17, $p < 0.001$), ability to move off chair (27 vs. 11, $p < 0.001$). Overall, the standard difference in Paseika scores showed a decrease in scores (improvement) across all areas (Fig. 2).

The improvements were most substantial for 'feeling tired', 'bone pain', and 'feeling weak'. There was variation among the scores and high heterogeneity was reported for most variables (Table 1), except abdominal pain.

3.3. Quality of life (SF-36)

The SF-36 data was derived from 238 patients, with a mean age of 59 years and 71% were females. The range of post-surgical follow up was 6 months to 1 year. The pre- and post-parathyroidectomy SF-36 quality of life scale scores were vitality (44 vs. 60, $p < 0.001$), physical functioning (51 vs. 69, $p < 0.001$), bodily pain (50 vs. 65, $p < 0.001$), general health (54 vs. 64, $p < 0.001$), role physical (34 vs. 52, $p < 0.001$), role emotional (43 vs. 59, $p < 0.001$), role social (60 vs. 74, $p < 0.001$), and mental health (55 vs. 71, $p < 0.001$). Overall, the standard difference in the SF-36 scores showed an increase in scores (improvement) across all areas (Fig. 3). The improvements were most substantial for 'bodily pain', 'mental health', and 'vitality'. There was variation among the scores and high heterogeneity was reported for most variables (Table 2).

4. Discussion

In 2009, the National Institute of Health (NIH) released a revised guideline of surgical indication for parathyroidectomy: serum calcium more than 1 mg/dl, GFR less than 60 ml/min (1.73 m^2), reduction in bone density, age less than 50 years, or overt classic symptoms. Hypercalciuria, in the absence of renal stones or nephrolithiasis, is no longer regarded as an indication for parathyroid surgery [4] (Table 3).

There is good evidence that surgery alleviates not only the

Table 1 Description of studies used in this meta-analysis.

Author	Country	Year	Method	Sample size
SF-36 as health-related quality-of-life outcome measures				
Caillard et al.	France	2007	Prospective multi-centre study	100
Sheldon et al.	USA	2002	Prospective cohort	72
Ramakant et al.	India	2011	Prospective	42
Eong et al.	UK	2007	Prospective cohort	24
Paseika's parathyroid assessment of symptoms scores (PAS)				
Mihai et al.	UK	2008	Prospective case-series	101
Greutelaers et al.	Australia	2004	Prospective	60
Ramakant et al.	India	2011	Prospective	42

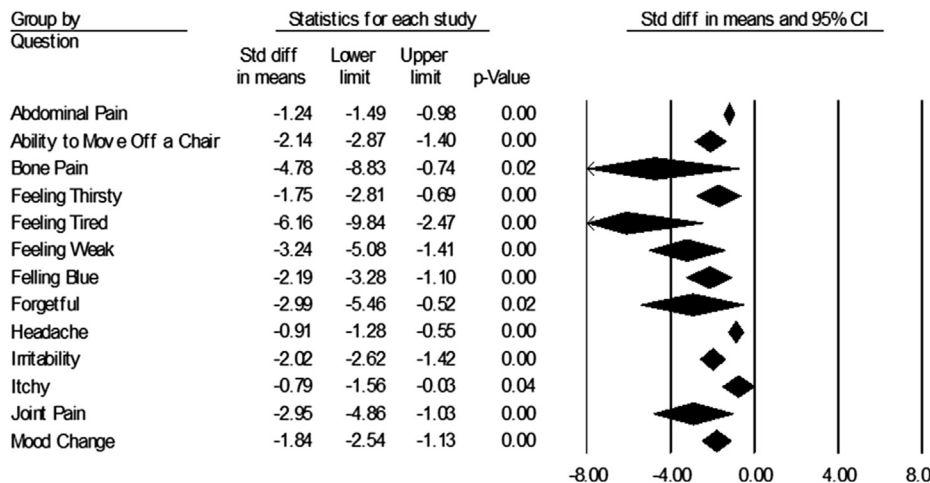


Fig. 2. Overall standard difference in mean scores for individual questions on the Paseika scale.

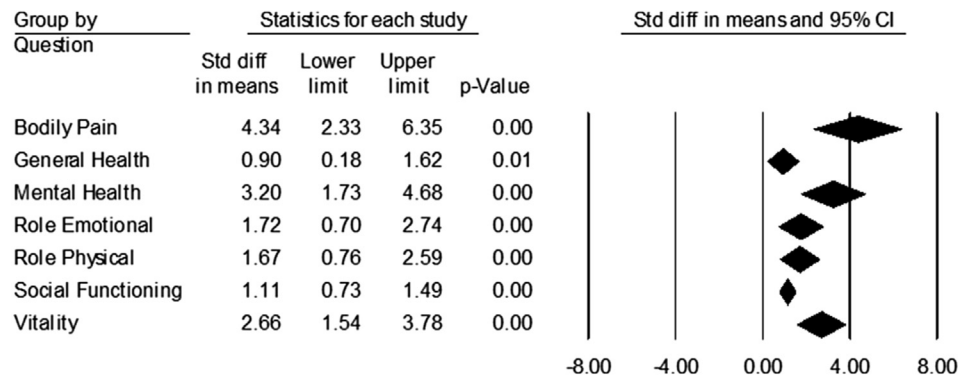


Fig. 3. Overall standard difference in mean scores for individual questions on the SF-36 scale.

Table 2

Heterogeneity scores and levels of significance for the Paiseika scale.

PAS variable	I ²	p-Value
Abdominal pain	0.00	0.62
Ability to move off a chair	75.97	0.02
Bone pain	97.29	0.00
Feeling thirsty	90.95	0.00
Feeling tired	94.68	0.00
Feeling weak	92.97	0.00
Feeling blue	88.75	0.00
Forgetful	97.42	0.00
Headache	55.13	0.11
Irritability	65.61	0.05
Itchy	90.04	0.00
Joint pain	94.44	0.00
Mood change	77.86	0.01

Table 3

Heterogeneity scores and levels of significance for the SF-36 scale.

SF-36 Variable	I ²	p-Value
Role physical	93.00	0.00
Bodily pain	89.60	0.00
General health	91.80	0.00
Vitality	91.98	0.00
Social functioning	89.87	0.00
Role emotional	57.01	0.07
Mental health	87.78	0.00

classic manifestations but also the non-specific symptoms of patients with PHPT and hence, translates into a better quality of life [9,13–15,17–21]. The decision to operate should not be limited to severity of biochemical abnormalities [10]. All 6 studies included in this meta-analysis reported significant improvement in health-related quality of life following parathyroidectomy [3,8,10–12,16].

In the French study, all 8 domains of the SF-36 score were significantly improved and persisted for at least 1 year post-operatively [8]. Two similar studies conducted in the United Kingdom also showed marked improvement post-parathyroidectomy [10,12]. A positive change in their quality of life was also proven by using both PAS and SF-36 in a group of Indian patients with advanced PHPT [16].

Another study using SF-36 showed 'asymptomatic' patients who were preoperatively impaired, made improvements in mental health and energy/fatigue levels after the surgery. This group together with those who presented with classic symptoms showed significant improvement of quality of life with durable effect at 1 year [11].

Quality of life is improved in both short and medium term

following parathyroidectomy. We suggest that these validated quality of life assessment tools such as PAS and SF-36 be routinely incorporated in post-operative follow-up assessments. We also suggest impaired quality of life be included as one of the surgical indications for parathyroidectomy.

The majority of previous studies have been prospective cohorts and case-series, with small patient numbers and short to medium term follow up. Therefore whether the improvements of quality of life is durable in long term and can be applicable to subgroups of patients with primary hyperparathyroidism is unable to be determined by the current data. Larger scale longitudinal studies including multi-centre studies with long term follow up should be conducted to answer the durability and generalisability of the improvements of quality of life after parathyroidectomy in primary hyperparathyroidism.

5. Conclusions

This meta-analysis confirms that parathyroidectomy significantly improves the short to medium term health-related quality of life of patients with primary hyperparathyroidism. Hence, we strongly suggest that quality of life should be part of the assessment and considered as one of the criteria in selecting suitable patients with PHPT for parathyroidectomy.

Ethical approval

None required.

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Author contribution

Study design: Senarath Edirimanne, Guy D. Eslick.

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Conflict of interest

None.

Disclosure statement

The authors have nothing to disclose.

References

- [1] M. Eilberger, W.K. Cheah, et al., The NIH criteria for parathyroidectomy in asymptomatic primary hyperparathyroidism, *Ann. Surg.* 239 (4) (2004 April) 528–535.
- [2] J. Bollerslev, S. Jansson, et al., Medical observation, compared with parathyroidectomy, for asymptomatic primary hyperparathyroidism: a prospective, randomized trial, *J. Clin. Endocrinol. Metabol.* 92 (5) (2007) 1687–1692.
- [3] B. Greutelaers, K. Kullen, et al., Pasioka Illness Questionnaire: its value in primary hyperparathyroidism, *ANZ J. Surg.* 74 (2004) 112–115.
- [4] J.P. Bilezikian, Aliya Khan, et al., Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the third international workshop, *J. Clin. Endocrinol. Metabol.* 94 (2) (2009) 335–339.
- [5] P. Gopinath, G. Sadler, et al., Persistent symptomatic improvement in the majority of patients undergoing parathyroidectomy for primary hyperparathyroidism, *Langenbecks Arch. Surg.* 395 (2010) 941–946.
- [6] J.L. Pasioka, L.L. Parsons, Prospective surgical outcome study of relief of symptoms following surgery in patients with primary hyperparathyroidism, *World J. Surg.* 22 (1998) 513–518.
- [7] J.L. Pasioka, L.L. Parsons, et al., Patient-based surgical outcome tool demonstrating alleviation of symptoms following parathyroidectomy in patients with primary hyperparathyroidism, *World J. Surg.* 26 (2002) 942–949.
- [8] C. Caillard, F. Sebag, et al., Prospective evaluation of quality of life (SF-36v2) and nonspecific symptoms before and after cure of primary hyperparathyroidism (1-year follow-up), *J. Surg.* 141 (2007) 153–160.
- [9] G. Talpos, H. Bone, et al., Randomized trial of parathyroidectomy in mild asymptomatic primary hyperparathyroidism: patient description and effects on the SF-36 Health Survey, *Surgery* 128 (2000) 1013–1021.
- [10] R. Mihai, G. Sadler, et al., Pasioka's parathyroid symptoms scores correlate with SF-36 scores in patients undergoing surgery for primary hyperparathyroidism, *World J. Surg.* 32 (2008) 807–814.
- [11] D.G. Sheldon, F. Lee, et al., Surgical treatment of hyperparathyroidism improves health-related quality of life, *Arch. Surg.* 137 (2002) 1022–1028.
- [12] K. Leong, R. Sam, et al., Health-related quality of life improvement following surgical treatment of primary hyperparathyroidism in a United Kingdom population, *Surgery* (2009) 5–8.
- [13] R. Burney, K. Jones, et al., Health status improvement after surgical correction of primary hyperparathyroidism in patients with high and low preoperative calcium levels, *Surgery* 125 (1999) 608–614.
- [14] R. Burney, K. Jones, et al., Assessment of patient outcomes after operation for primary hyperparathyroidism, *Surgery* 120 (1996) 1013–1019.
- [15] R. Quiros, M. Alef, et al., Health-related quality of life in hyperparathyroidism measurably improves after parathyroidectomy, *Surgery* 134 (2003) 675–683.
- [16] P. Ramakant, R. Verma, et al., Salutary effect of parathyroidectomy on neuropsychiatric symptoms in patients with primary hyperparathyroidism: evaluation using PAS and SF-36v2 scoring systems, *J. Postgrad. Med.* 57 (2) (2011) 96–101.
- [17] L. Coker, K. Rorie, et al., Primary hyperparathyroidism, cognition and health-related quality of life, *Ann. Surg.* 242 (5) (2005) 642–650.
- [18] L. Perez-Ruiz, Lasheras-Alonso, et al., The effects of successful parathyroidectomy on clinical and biological manifestations of primary hyperparathyroidism, *Acta Chir. Belg.* 106 (2006) 532–536.
- [19] J. Adler, R. Sippel, et al., The influence of surgical approach on quality of life after parathyroid surgery, *Ann. Surg. Oncol.* 15 (6) (2008) 1559–1565.
- [20] N. Perrier, D. Balachandran, et al., Prospective, randomized, controlled trial of parathyroidectomy versus observation in patients with "Asymptomatic" primary hyperparathyroidism, *Surgery* 146 (2009) 1116–1122.
- [21] G. Prager, A. Kalaschek, et al., Parathyroidectomy improves concentration and retentiveness in patients with primary hyperparathyroidism, *Surgery* 132 (2002) 930–936.