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ORIGINAL ARTICLE

Parathyroidectomy is safe and improves symptoms in elderly patients with primary hyperparathyroidism (PHPT)

Michael J. Stechman*, Mary Weisters*, Fergus V. Gleeson†, Gregory P. Sadler* and Radu Mihai*

*Department of Endocrine Surgery, John Radcliffe Hospital, Oxford, UK and †Department of Radiology, Churchill Hospital, Oxford, UK

Summary

Objective Parathyroidectomy for primary hyperparathyroidism (PHPT) is curative in over 95% of cases. Although PHPT affects up to 2% of the elderly population, whose life expectancy may be a decade or more, such patients may be denied surgery because of perceived risk. This study investigates the outcomes of surgery for PHPT in the elderly.

Design and patients Consecutive patients with PHPT treated at a tertiary referral centre over 5 years.

Measurements A prospective database recorded clinical, biochemical and pathological information. Pasieka's parathyroid symptom scores were obtained pre-operatively and post-operatively, from a recent subgroup of 70 consecutive patients. Deaths during follow-up were identified using the NHS Strategic Tracing Service. Statistical analysis was performed with SPSS v12.0.

Results Between November 2002 and October 2007, 224 patients (17–89 years) underwent surgery for PHPT. In the subgroup comprising patients aged >75 years there was a significantly greater proportion of women (47/56 *vs.* 52/81, $P < 0{\cdot}05$). Pre-operative indices of these patients were similar to younger patients, as were proportions undergoing minimally invasive parathyroidectomy ($n = 134$) or bilateral neck exploration ($n = 90$). Patients >75 years had a longer hospital stay (1·6 *vs.* 0·8 days, $P = 0{\cdot}003$). Pasieka's symptom scores improved significantly at 3–6 months postoperatively in all age groups. During a minimum median follow-up of 22 months, there were seven patients with persistent/recurrent disease. Median 2-year survival of those aged 60–74 and those over 75 ranged from 85–90%.

Conclusion Parathyroidectomy is safe in the elderly and is associated with a significant improvement in symptoms. As survival after operation is similar to younger patients, surgery should be considered in all elderly patients with PHPT.

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Correspondence: Michael J. Stechman, Department of Endocrine Surgery, John Radcliffe Hospital, Headington, Oxford, OX3 9DU. Tel.: +441865 220924; Fax: +441865 220925; E-mail: mstechman@doctors.org.uk

Introduction

Primary hyperparathyroidism (PHPT) is a relatively common disorder affecting up to 0·3% postmenopausal women[1] and up to 2% of the elderly population.[2,3] Parathyroidectomy is expected to be curative in over 95% of cases of sporadic PHPT.[4] Traditionally, debate hinged upon whether or not surgical treatment should be offered to elderly patients because it was deemed too invasive or of unacceptable risk in light of their co-morbidities.

Consensus guidelines have set the threshold for treating all patients under the age of 50 years.[5,6] For the majority of older patients with mild hypercalcaemia and no signs of bone disease or renal impairment, PHPT is a slow, progressive disease. In a recently published prospective non-randomized study including 15-year follow-up of a cohort of 116 patients monitored at Columbia University,[7] a third of patients developed an indication for parathyroidectomy. More robust data is missing as no other study published to date has addressed progression of PHPT over such a long time scale. Randomized trials of parathyroidectomy *vs.* best medical treatment over 1–2 years follow-up found evidence for[8,9] and against[10] parathyroidectomy. The emphasis of all these studies was not on the age-specific management of PHPT. Nevertheless, several authors in the United States have suggested that elderly patients should undergo parathyroidectomy as majority of them tolerate surgery well and they derive significant benefit in terms of improvement in symptoms and better cardiovascular and skeletal health.[11–13]

The advent of scan-directed minimally invasive parathyroidectomy (MIP) has changed the perception of referring physicians and has lowered the threshold for referral.[14,15] This phenomenon is similar to that noted in vascular surgery with endovascular aortic aneurysm stenting,[16,17] and laparoscopic colorectal[18,19] and biliary surgery.[20] As a result, parathyroidectomy is becoming the first choice not only for patients presenting with severe biochemical abnormalities and symptoms, but also for those with minimal hypercalcaemia who may be labelled as 'asymptomatic'.[14,21]

Whether this increasing volume of surgical interventions covers all age groups is yet to be determined, but there is indirect evidence suggesting it is unlikely. Even though the disorder may be several times more common in patients older than 75 years than in

younger patients,[2] only 25% of parathyroidectomies are performed on elderly patients.[4]

Examination of current statistics on life expectancy in England suggests that the average 60-year old will live until 82–85 years and the average 75-year old until 86–87,[22] thus an elderly person with PHPT may experience symptoms for many years if left untreated. They are also at increased risk of further morbidity from complications of PHPT, such as bony fractures.[23] As the population ages, more and more patients will present with PHPT and previous assumptions on age and fitness for surgery will need to be re-examined,[12] particularly as newer, less invasive procedures gain popularity.[14,15]

To date, there have been no studies looking at mortality of elderly patients during follow-up after surgery, and at objective assessment of quality of life (QoL) in this group of patients in the UK. In light of this, there is a need for data on the current outcome of surgical treatment in terms of its feasibility, complications and effect upon QoL in the elderly.

The aim of this prospective comparative case series was to investigate these factors in patients over the age of 75 years treated for PHPT in a single teaching hospital during a 5-year period.

Patients and methods

We recorded clinical, biochemical, operative and pathological details of a cohort of consecutive patients referred to a tertiary referral centre from both general practice and hospital endocrinologists over a 5-year period. All patients with biochemical diagnosis of PHPT were considered for surgical intervention.

Patients with positive concordant Tc^{99m}-sestamibi and neck ultrasounds had a MIP without intra-operative PTH testing as described previously.[24] Bilateral neck exploration (BNE) was performed in all other patients.

Parathyroid assessment of symptoms scores (PAS) were obtained pre-operatively and at 3–6 months post-operatively, from 70 consecutive patients presenting in the last 30 months[25] to examine the effect of surgery upon QoL. The scores were derived from the answers to the standardized questionnaire developed by Pasieka *et al.* [26] The 13 items explored included: bone pain, fatigue, mood swings, feeling 'blue' or depressed, abdominal pain, feeling weak, increased irritability, joint pain, forgetfulness, difficulty getting out of a chair or car, headaches, itchy skin and increased thirst. 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.

Information on deaths during follow-up was obtained through the National Health Strategic Tracing Service (http://www.connectingforhealth.nhs.uk/systemsandservices/nsts). Information on post-operative morbidity was obtained retrospectively from the hospital notes of patients with delayed discharge.

Statistical analysis was performed using SPSS 12.0.1 (SPSS Inc., Chicago, IL, USA). Student's *t*-test and analysis of variance (ANOVA) were used for parametric variables, Chi-squared test was used for categorical values and the Wilcoxon signed ranks test was used for paired nonparametric data. Survival analysis was by the Kaplan–Meier method.

Results

Between January 2002 and November 2007, 224 patients (166 female, age 17–89 years) underwent surgery for PHPT. Seventy-three percent were referred from hospital endocrinologists and of the remainder, half were referred from general practitioners and half from consultants in other specialties.

Patients were divided into three groups on the basis of age: those less than 60 years old ($n = 81$), 60–74 years old ($n = 87$) and those 75 and above ($n = 56$). The median ages of patients in each group were 50 (range 17–59), 68 (range 60–74) and 79 years (range 75–89) respectively. There were significantly more women in the over-75 years group, but other pre-operative indices were similar between all groups (Table 1).

When pre-operative symptoms were analysed, a greater proportion of patients over the age of 75 presented with neuropsychiatric symptoms and fewer presented with kidney stones, but these differences did not reach statistical significance. The proportion of each age group presenting with other symptoms was similar between the three groups (Fig. 1).

Over the time studied, approximately two-thirds of patients from each group underwent scan-directed parathyroidectomy via a focused approach (Fig. 2). However, use of the technique increased from approximately 50% of patients in the first 2 years after its introduction, to more than 70% of patients in the last 12 months

Table 1. Biochemical, operative and post-operative characteristics of 224 patients divided into three groups on the basis of their age at the time of treatment

Age	17–59 years	60–74 years	>75 years	*P*-value†
N	81	87	56	–
Females/Males	52/29	67/20	47/9*	0·02
Pre-op Ca^{++} (mean ± SD) mmol/l	2·97 ± 0·28	2·96 ± 0·24	2·94 ± 0·24	0·79
Pre-op PTH (mean ± SD) pmol/l	21·3 ± 18·8	18·3 ± 15·5	18·1 ± 9·8	0·40
Mean length of operation in minutes (range)	50 (15–144)	46 (15–120)	42 (10–120)	0·18
Post-op Ca^{++} at last follow-up (mean ± SD) mmol/l	2·38 ± 0·13	2·41 ± 0·13	2·41 ± 0·16	0·18
Median follow-up in months (range)	24 (1–59)	26 (3–59)	22 (3–59)	–
Persistent disease (Plasma Ca^{++}>2·64)	3	0	4	0·33
Deaths during follow-up	1	6	4	0·6

* Significantly more women aged > 75 years;
† χ^2-test and ANOVA.

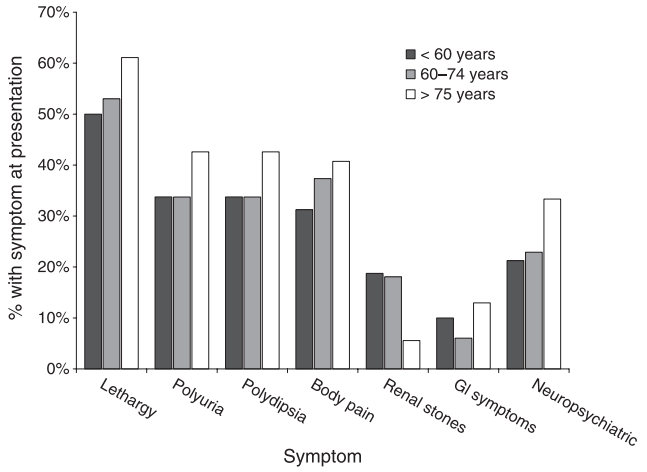

Fig. 1 Proportion of patients from each group presenting with each of the classical primary hyperparathyroidism (PHPT) symptoms. Clinic letters were scrutinized to assess the number of symptoms reported by individual patients. There was no statistical difference for the incidence of each symptom between the three age-groups (Chi-squared test, two degrees of freedom).

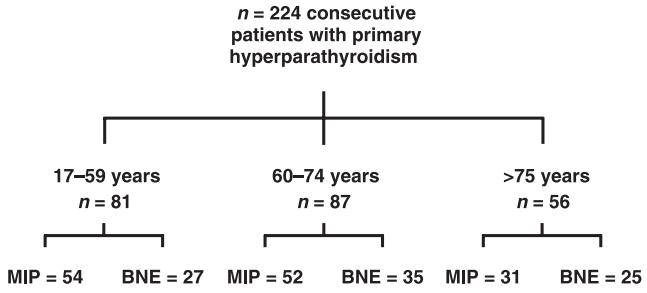

Fig. 2 Operative approach in 224 consecutive patients undergoing parathyroidectomy for sporadic PHPT. Age group did not affect the likelihood of pre-operative localisation by ^{99m}TcSestamibi and ultrasound (P = ns Chi-squared test with two degrees of freedom). (MIP – minimally invasive/focused parathyroidectomy, BNE – bilateral neck exploration).

studied. Surgery was curative in 96·8% of patients and pathological findings, such as the incidence of double adenoma, did not vary according to age. At follow-up, there were seven patients with persistent/recurrent PHPT, three in the youngest age group and four in the oldest age group (Table 1).

Mean length of hospital stay was similar for those aged up to 60 and those aged 60–74 (0·77 days (range 0–5) and 0·8 days (0–7) respectively). Those aged 75 and above stayed significantly longer in hospital (mean 1·6, range 0–15 days, $P < 0{\cdot}001$, ANOVA) because of a smaller number of patients undergoing day-case surgery. The proportion of elderly patients undergoing day-case surgery increased dramatically from less than 10% over the first 2 years after introduction of MIP, to 45% by the end of the study period when the technique was well-established. Accordingly, average length of stay of those aged over 75 years decreased from a mean of 3 days to 1·33 days over that time and for the last 2 years 70–80% of such patients have been successfully discharged within 24 h of surgery. In contrast, the overall rate of day-case parathyroidectomy increased from 20% at the beginning of the study to 70% by the end. As would be expected, those under 60 were most likely to be discharged on the day of surgery and the day-case rate in these patients increased from 20% to 80% over the 5-year period.

Sixteen patients over 75 years stayed in the hospital for more than one night – the commonest complication observed was post-operative confusion (4 patients) which was self-limiting. One patient required re-exploration of the neck for a haematoma immediately post-operatively, one patient sustained a non-ST elevation myocardial infarct 3 days post-op and one patient's stay was prolonged because of re-anticoagulation for a prosthetic mitral valve. All other delayed discharges were for purely social reasons ($n = 9$). Lastly, there was one readmission one week after surgery for an infective exacerbation of chronic obstructive pulmonary disease.

Specific complications were minimal; one patient sustained a proven recurrent laryngeal nerve palsy which improved over 6–12 months such that no further intervention was required (rate of injury 0·45%). All patients received calcium supplements to be taken in the event of hypocalcaemic symptoms. With this policy, there were no delayed discharges because of low serum calcium. Lastly, there was no in-hospital mortality.

Patients from all three groups experienced a significant improvement in symptoms, with lower median Pasieka PAS scores at 3–6 months compared with pre-operative values (Fig. 3). An improvement in symptoms was reported by 28 of 30 (93·3%) patients under 60 years old, 20 of 25 (80%) patients 60–74 years old and 13/15 (86·7%) of those aged >75 years.

During a median follow-up period of 22 months (range 3–46 months), a greater proportion of the deaths occurred in those over the age of 60, but this difference did not reach statistical significance (Fig. 4).

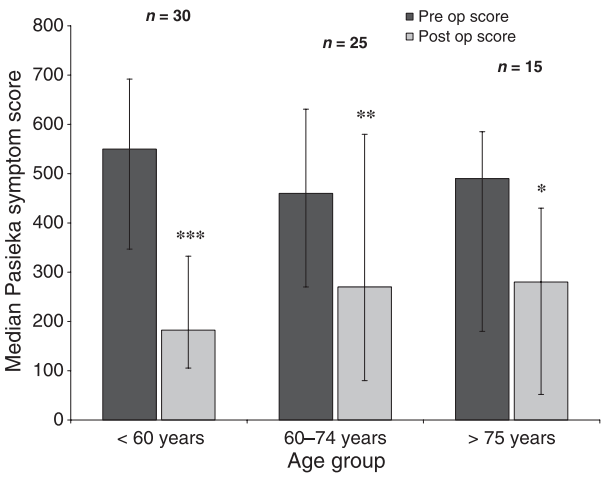

Fig. 3 Comparison of pre-operative and post-operative (at 3–6 months) median Pasieka's parathyroid symptom score by age group. Median pre- and post-operative symptom scores were not significantly different between age groups, inter-quartile ranges are shown. All age groups experienced significant improvement in their symptoms after surgery (***$P = 0{\cdot}000$, **$P = 0{\cdot}001$, *$P = 0{\cdot}003$, Wilcoxon signed-rank test).

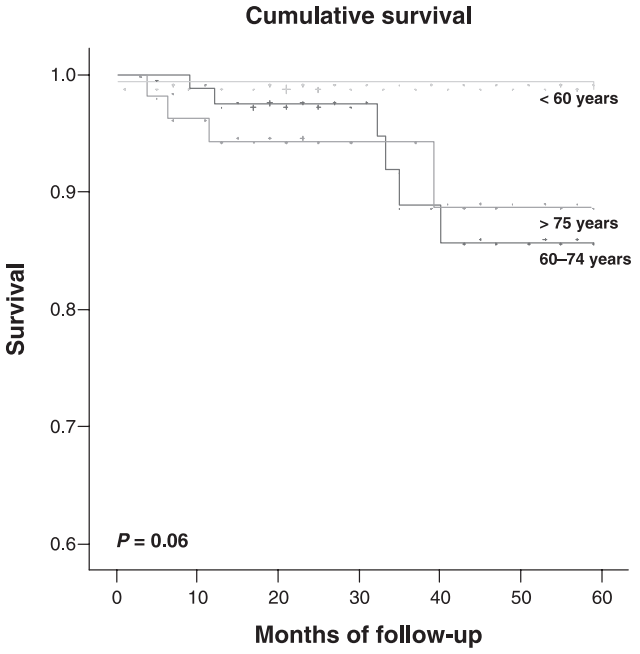

Fig. 4 Cumulative survival based upon age group. Although there were proportionally more deaths during follow-up in the older groups this was not statistically significant ($P = 0{\cdot}06$ for both) and those over 75 had a similar survival to those aged 60–74.

The observed mortality rate for those over 75 years (4 deaths in 56 patients over 22 months) was equivalent to 39 deaths per 1000 of population per year. This value was lower than the expected mortality rate for females of a similar age, which ranged from 45·7 deaths per 1000 of population per year for those aged 75–84, to 143·8 deaths per 1000 per year in those over the age of 85 years.[22]

Discussion

This is the first study in the United Kingdom to examine the outcome of parathyroidectomy in elderly patients and to specifically collect QoL data. It shows that parathyroidectomy was safe, feasible and beneficial in the group of patients over the age of 75 that were referred for surgery in a high-volume centre. The data also give further weight to the opinion that the elderly with PHPT should be offered surgical treatment.

We acknowledge that this prospective case series with no controls is open to bias in that one can never know the size of the denominator of elderly patients with diagnosed PHPT that are not referred for surgery. As such this represents a weakness of this study as physicians and endocrinologists may refer only those they feel are fit for surgery, a factor that affects several previous studies[11–13,27] and has caused a notable delay in treatment in some elderly patients.[12] Ideally, the benefits of surgery in the elderly would be best assessed by means of a prospective randomized controlled trial recruiting patients from the total pool of those affected. However, the more that improved outcomes in surgical treatment for PHPT in the elderly are reported, the more able endocrinologists will feel to set up such a study or to consider surgery in this subset of patients.

During the study period, about two-thirds of patients underwent scan-directed MIP, and currently more than 70% of patients are treated by this route. This proportion is twice that observed in the national audit organized by the *British Association of Endocrine and Thyroid Surgeons*.[4] As expected, MIP is associated with a significantly shorter operating time and a higher proportion of patients being treated as a day case,[28] particularly those aged below 60 and to a lesser extent those aged 60–75.

Although the rate of day-case surgery increased in those aged 75 and over during the 5-year period, same-day discharge was still <50% by the end of the study, the remainder having an average of 2·2 days in-hospital stay. A combination of social as well as medical factors was found to influence the timing of discharge, although we now try and encourage a default position of ambulatory/day-case surgery for all patients undergoing surgery for PHPT, regardless of whether it is by focused or BNE approach.

In this series, <4% of patients had persistent disease as judged by serum calcium level greater than 2·62 mmol/l with a persistently raised PTH at a median follow-up of 22 months (range 1–59 months). This observation suggests that there is minimal compromise in cure rate via this approach, an important factor when considering surgical treatment for a symptomatic but 'benign' condition in potentially frail patients. This success rate has been achieved without using intra-operative PTH monitoring, which in our view adds little to the success rate of the operation but adds significant costs related to equipment, consumables, theatre time and manpower.[24]

We observed a significant improvement in symptom scores across all age groups in the sample of patients for whom data were obtained. Previous studies using this assessment tool demonstrated much lower pre-operative symptom scores in Canadian patients with PHPT,[29,30] suggesting that our cohort of patients was more symptomatic at presentation. Pasieka's PHPT symptom scores correlate well with the SF-36 QoL questionnaire,[25] the latter having been well validated in the UK population, and so it is likely that the Pasieka's score is valid in our cohort. Previous studies in the elderly have reported improvement in PHPT symptoms in the elderly using either visual analogue score for each symptom or the SF-36 questionnaire,[12,13] and this study represents further objective evidence that regardless of age, the majority of patients undergoing surgery experience an improvement in their symptoms.

Longer-term survival in this cohort of patients was good (approximately 85–90% at a median of 22 months) and the mortality rate during follow-up was in keeping with population-based data. This, along with improvements in symptoms during follow-up, suggests that parathyroidectomy will offer significant benefits to a high proportion of elderly patients undergoing surgery. It also supports the previous pleas for prompt referral of such patients,[12] and contradicts the assertion that age is a contraindication to parathyroid surgery.

Over the next 10–20 years, the United Nations Populations Division predicts that the percentage of the total population over 80 years of age will rise by a half to approximately 7%.[31] On that basis, the number of elderly patients requiring treatment for PHPT will increase in a similar fashion, representing a major challenge in the future to endocrinologists and endocrine surgeons alike.

In summary, the results of this study suggest that parathyroidectomy is safe in those over the age of 75 years and is associated with a significant improvement in symptoms. They also show that surgery can be carried out with minimal morbidity, as a day case or as a 23-h admission in the majority of patients. As long-term survival after operation is similar to younger patients, surgery should be considered in all elderly patients with primary hyperparathyroidism.

Competing interests/financial disclosure

Nothing to declare.

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