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Minimally invasive parathyroidectomy by unilateral neck dissection—experience in a regional hospital in Hong Kong

香港一所分區醫院以單側頸清除術進行微創甲狀旁腺切除

Objective. To compare the efficacy and safety of minimally invasive open parathyroidectomy with localised unilateral neck dissection to the conventional method of bilateral neck exploration and parathyroidectomy as a surgical treatment for primary hyperparathyroidism.

Patients and methods. Eleven patients diagnosed with primary hyperparathyroidism at Queen Elizabeth Hospital from 1 January 2002 to 31 December 2002 were treated surgically with minimally invasive open parathyroidectomy. Their results were compared to a retrospective series of 15 patients treated by conventional bilateral neck exploration and parathyroidectomy between 1 January 2001 and 31 December 2001. Demographic data; cure, recurrence, and complication rates; operating time; and hospital stay were analysed.

Results. The cure rate was 100% in both groups. There was no recurrence in either group. Minor complication rates were 9% and 20% in the minimally invasive open parathyroidectomy and the control groups, respectively. Mean operating time was 63 minutes in the minimally invasive open parathyroidectomy group, and 92 minutes in the control group. The mean postoperative hospital stay for the minimally invasive open parathyroidectomy group was 1.36 days. Three of these procedures were performed as day surgery. The mean hospital stay for the control group was 2.93 days. The operating time and hospital stay were significantly shorter in the minimally invasive open parathyroidectomy group.

Conclusion. Minimally invasive open parathyroidectomy is a viable alternative treatment method for primary hyperparathyroidism. It has comparable cure and recurrence rates to the conventional approach. It is safe, with a lower complication rate, and has the benefits of being a shorter procedure and allowing a shorter hospital stay. It can be performed as day surgery, further reducing hospital costs.

目的：本文針對治療原發性甲狀旁腺功能亢進的兩種手術，即以局部單側頸清除術進行微創甲狀旁腺切除，以及先施行雙側探查術而後切除甲狀旁腺的常規手術，比較兩者的功效與安全性。

患者及方法：伊利沙伯醫院分別在兩段期間為患上原發性甲狀旁腺功能亢進症的病人施行不同手術：在 2002 年 1 月 1 日至 12 月 31 日，11 位患上此病症的病人接受微創甲狀旁腺切除術；在 2001 年 1 月 1 日至 12 月 31 日，15 位患上同樣病症的病人接受了雙側探查術而後切除甲狀旁腺的常規手術。本文利用不同的病例資料比較兩種手術的結果，包括人口數據，治癒、復發、出現併發症的比率，手術所需時間，及留院時間。

結果：兩組患者的治癒率均為100%，並無出現復發。施行微創甲狀旁腺切除術一組，出現輕微併發症的比率為 9%，手術平均需時 63 分鐘，患者術後平均需要留院1.36天，其中有3宗為日間手術。至於對照組，出現輕微併發症的比率為20%，手術平均需時92分鐘，患者術後平均需要留院2.93天。由此可見，施行微創甲狀旁腺切除術，可以明顯縮短手術所需時間以及留院時間。

結論：微創甲狀旁腺切除術是原發性甲狀旁腺功能亢進的一種可行療法，從治癒和復發的比率來說，與傳統的常規手術效果相同。這種微創手術方法安全，出現併發症的機會輕微，同時手術程序相對較短，留院時間因而可以縮減，而且病人接受日間手術，可進一步降低醫院的成本。

Key words:
Parathyroid hormones;
Parathyroidectomy;
Surgical procedures, minimally invasive

關鍵詞：
甲狀旁腺激素；
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Introduction

Primary hyperparathyroidism is most commonly caused by a single parathyroid adenoma. Hyperplasia or double adenoma of the parathyroid glands accounts for only a small percentage of cases.[1-3] Bilateral cervical exploration with visualisation of all the parathyroid glands and excision of the abnormal gland or glands, has been the gold treatment standard for primary hyperparathyroidism. Even with preoperative localisation of the abnormal gland, bilateral exploration is still considered necessary because localisation is not 100% accurate[1-3]; a second or even third abnormal gland might not be identified by the localisation studies. Unilateral exploration risks missing cases of parathyroid hyperplasia or double adenoma in the absence of evidence that all other parathyroid glands apart from the one removed are normal or suppressed. Theoretically, this is demonstrated by a drop in parathyroid hormone (PTH) level soon after excision of the abnormal parathyroid gland. This drop in PTH level can be detected by rapid intra-operative PTH assay and is taken as the surgical endpoint.

Thus in minimally invasive open parathyroidectomy (MIOP), the abnormal gland is localised preoperatively and subsequently excised by unilateral focused dissection, with assays of PTH levels made at predefined stages of the surgical procedure. A significant decrease in PTH levels after excision of the abnormal gland is taken to mean there is no need to explore the other glands. Having all the potential benefits of a minimally invasive procedure, MIOP is now often used as an alternative approach in treating primary hyperparathyroidism. The objective of this study was to investigate how MIOP compares with conventional bilateral neck exploration and parathyroidectomy as a surgical treatment for primary hyperparathyroidism.

Patients and methods

Eleven patients with primary hyperparathyroidism underwent MIOP at Queen Elizabeth Hospital in 2002. Their results were compared to a historical cohort of 15 patients from 1 January 2001 to 31 December 2001 who underwent conventional bilateral cervical exploration and parathyroidectomy. Exclusion criteria included all patients with negative localisation, multiple uptakes on sestamibi scan, those who underwent redo-exploration for recurrent or persistent hyperparathyroidism, patients with a mediastinal parathyroid, and those with multiple endocrine neoplasia (MEN) syndrome. From 1 January 2002 to 31 December 2002, 13 consecutive patients were diagnosed with primary hyperparathyroidism and agreed to surgical treatment. Two subsequently diagnosed with MEN syndrome by endocrinologists were excluded from the study. The remaining 11 patients each had a single abnormal parathyroid gland positively identified by sestamibi scan, with or without additional ultrasonography, and all underwent MIOP.

Fig. Surgical photograph illustrating the 3-cm abbreviated Kocher incision

Anaesthesia

All the MIOP procedures were done under general anaesthesia. Propofol was avoided as it could interfere with the PTH assay.

The surgical approach

The side of the neck selected for the incision was guided by the localisation study. An abbreviated Kocher incision (lateral approach) was used. This involves a 2- to 3-cm paramedian skin crease incision on the anterior border of the lower third of the sternomastoid muscle (Fig). Using standard instruments, dissection was made to locate the abnormal parathyroid gland. Excessive manipulation was avoided and the recurrent laryngeal nerve was not routinely identified.

Rapid PTH assay is now possible using commercially available modified immunochemiluminometric assay kits. In this study, the Immulite Turbo intact PTH assay (Diagnostic Products Corporation, Los Angeles, US) was used. Blood samples were taken from a peripheral vein on incision (B1), on identification of the abnormal parathyroid gland but before ligation of its feeding vessel (B2), 10 minutes after the parathyroid delivery (P1), and 20 minutes post-delivery (P2). The time taken to identify the abnormal parathyroid gland (the time from B1 to B2) ranged from 8 to 27 minutes. The elapsed time from blood sampling to hormone value reporting ranged from 15 to 19 minutes. Frozen section was not used. The wound was closed after parathyroid delivery and the operating team then waited for the rapid PTH assay results. Whether the operation ended at this point or proceeded to bilateral neck exploration and parathyroidectomy depended on the PTH results. The assay results were considered positive and the endpoint of surgery reached if there was a 50% or more drop in PTH level in either of the P specimens compared with B1 or B2. If the assay was negative (a less than 50% drop in PTH), the procedure was converted to the conventional bilateral neck exploration and parathyroidectomy procedure. The operating time from incision to the time of anaesthesia reversion was recorded.

Table 1. Characteristics of patients in the minimally invasive open parathyroidectomy (MIOP) and control groups*

Characteristic	MIOP group	Control group
Age (years)	41-86 (56.27)	22-78 (54.07)
Preoperative serum calcium (mmol/L)	2.59-2.91 (2.76)	2.53-3.34 (2.78)
Preoperative parathyroid hormone level (pmol/L)	9.90-25.30 (15.36)	6.60-142.0 (24.63)

* The results are not significantly different between the two groups (Student's *t* test, P>0.05), implying homogeneity; mean values are in brackets

Table 2. Outcome parameters for patients in the minimally invasive open parathyroidectomy (MIOP) and control groups*

Outcome parameter	MIOP group	Control group	P value (2-tailed)
Operating time (minutes)	44-154 (63.36)	55-160 (92.0)	0.030
No. of frozen sections	0-1 (0.01)	1-7 (2.20)	0.000
Postoperative stay (days)	0-7 (1.36)	2-5 (2.93)	0.014

* Mean values are in brackets

Postoperative monitoring and discharge

After the operation, serum calcium levels were monitored on day 0, day 1, day 7, and thereafter 3-monthly. The criteria for discharge include the patient being ambulatory, with a total serum calcium between 2.0 and 2.6 mmol/L and no symptoms of hypocalcaemia, and afebrile. The duration of postoperative hospital stay was noted.

Historical control group

For the control group, records of all the patients with primary hyperparathyroidism who underwent surgery in the period from 1 January 2001 to 31 December 2001 were reviewed. There were 15 patients and all were treated with conventional bilateral cervical exploration and parathyroidectomy. Data were analysed and compared with the prospective series of patients who had MIOP in 2002, as described.

Statistics

The data were analysed by independent sample Student's *t* test using the Statistical Package for the Social Sciences (Windows version 10.0; SPSS Inc., Chicago, US). A P value of less than 0.05 was considered significant.

Results

Eleven patients underwent MIOP in 2002 and 15 patients underwent conventional cervical exploration and parathyroidectomy in 2001. The age, and preoperative serum calcium and PTH levels were comparable for the two groups (Table 1). Patients in both groups underwent preoperative localisation by sestamibi scan, with or without additional ultrasonography evaluation. There was no re-exploration carried out in either group.

Cure rates were 100% in both groups. None of the patients had recurrence of hypercalcaemia over a mean follow-up period of 5.09 (range, 3-10) months in the MIOP group and 12 (3-23) months in the control group. There were no deaths in either group. In the MIOP group, there were no long-term complications or instances of symptomatic hypocalcaemia requiring replacement. However, one patient developed a postoperative fever of unknown origin, which subsided with conservative treatment. Among the historical control group, two patients had transient symptomatic hypocalcaemia requiring calcium replacement, and one had a wound haematoma that was managed conservatively. Two cases in the MIOP group required conversion to conventional bilateral exploration and parathyroidectomy (conversion rate, 2/11 [18%]). In one of these patients, the abnormal parathyroid gland could not be identified on minimal dissection. It was identified only after conversion to bilateral neck exploration and was located in the thoracic inlet, adhering to the back of the manubrium, making identification through the initial small incision difficult. In the other case, the abnormal gland was not apparent after conversion, necessitating a right hemithyroidectomy.

For the MIOP group, the mean operating time (including the two patients requiring conversion) was 63 (range, 44-154) minutes, compared with 92 (55-160) minutes in the control group. The mean postoperative hospital stay for the MIOP group was 1.36 days, whereas for the control group it was 2.93 days. Both the difference in operating time and hospital stay were shown to be statistically significant (P<0.05) [Table 2]. Within the MIOP group, three procedures were performed as day surgery, and six further cases were discharged on day 1. The remaining two patients, who were octogenarians living alone, required longer hospitalisation for social reasons. Frozen section was not used in the MIOP group. In contrast, frozen section was needed in the control group (a mean of 2.20 specimens per patient).

Discussion

The first parathyroidectomy for primary hyperparathyroidism was performed by Felix Mandl in Vienna in 1925.[2] The gold standard treatment for primary hyperparathyroidism is bilateral cervical exploration with visualisation of all four parathyroid glands and excision of the abnormal one. The long-term cure rate exceeds 95% and the complication rate is between 1% and 2%.[1-3] Previously, the surgeon performing the procedure faced two unknowns prior to the operation—the number and the position of the abnormal parathyroid glands. Thus, the side of the neck chosen for the initial incision and exploration was largely a matter of conjecture; there was a need to explore both sides

of the neck to ensure that no abnormal parathyroid glands were overlooked. Nowadays effective localisation studies are available, notably sestamibi scans, and because of this the operative procedure has changed. Today the surgeon can begin his operation on the side of the neck that has an abnormal parathyroid gland, identified by localisation studies.

Bilateral exploration is carried out despite localisation studies in order to ensure the remainder of the glands are normal. Nevertheless, bilateral exploration appears unnecessary in most cases, as 85% to 90% of cases of primary hyperparathyroidism are due to a single adenoma, only around 10% to hyperplasia, and less than 5% to a double adenoma.[1-3] In most circumstances, excision of the adenoma results in a cure. Therefore, MIOP using a unilateral focused neck dissection appears a logical approach providing an endpoint indicator is available. Sestamibi scan, which is 90% sensitive and specific,[1,2] can indicate where the surgeon should commence the procedure but not where to end the procedure. Parathyroid hormone has a very short half life of 2 to 5 minutes in vivo.[1,2,4,5] Removal of all hyperfunctioning parathyroid tissue should therefore result in a significant drop in blood levels of PTH within minutes. Predicated on this theory, intra-operative PTH assay can be used as an endpoint indicator in parathyroidectomy. Based on experience from different centres, removal of all hyperfunctioning parathyroid tissue is assured if PTH levels drop by more than 50% of their original value.[1,2,4-10] A 50% drop in PTH level is therefore taken as an endpoint for MIOP.

This study has shown that MIOP is technically feasible. The incision is smaller and only one side is explored, minimising operating time and surgical trauma. As in all minimally invasive procedures, conversion to the conventional procedure may be required for various reasons. In this study, the two conversions were caused by failure to identify the abnormal parathyroid on focused dissection and were not due to problems with PTH level interpretation. Hopefully, with better experience with the technique, and better case selection according to sestamibi scan findings, conversion for technical reasons may be avoided. Preferably, the operating surgeon should examine the sestamibi scan film rather than the scan report alone, in order to identify the position of the abnormal parathyroid gland.

In this study, MIOP was comparable to conventional bilateral neck exploration in terms of cure and recurrence. The complication rate was lower in the MIOP group, with none of the patients having significant hypocalcaemia. In addition, the operating time was shorter by more than 30%. This implies a saving of operating theatre time, and the potential to accommodate more cases and shorten the waiting list for surgery. The hospital stay was also significantly shorter, with a more than 50% reduction from 2.93 days to 1.36 days. In fact, for younger ambulatory patients with reasonable family support, MIOP can be performed as day surgery. Shorter hospital stays, shorter operating time, the option of day surgery, and the fact that frozen section is no longer necessary translate into a significant reduction in resource requirements. The cost of the rapid assay PTH kits is around HK$3000 per set and each set can be used for five cases. Therefore, rapid PTH assay costs about HK$600 for each patient. This cost is readily offset by the other cost savings.

However, the results of this study should be interpreted with some caution since it was not a randomised controlled trial. Although the demographic data and disease parameters were shown to be statistically comparable between the two groups, it would be ideal if the case and control limbs were created by randomisation. The small number of cases requiring surgical treatment for primary hyperthyroidism (less than 20 per year in our institution), make randomisation difficult. Now that the MIOP has been found to be technically feasible and apparently safe and effective, larger scale randomised controlled trials might be carried out to confirm the findings of this study.

Conclusion

Minimally invasive open parathyroidectomy by localised unilateral neck dissection and parathyroidectomy, complemented by the use of rapid intra-operative PTH assay, is an effective alternative treatment method for primary hyperparathyroidism. It is safe, with a lower complication rate and comparable cure and recurrence rates to conventional bilateral neck exploration and parathyroidectomy. It has the benefits of shorter procedure time, shorter hospital stays, and the possibility of ambulatory surgery, therefore saving resources. Larger scale randomised controlled trials are now needed to confirm the results of this preliminary study.

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