ORIGINAL ARTICLE

Surgical Outcome of Patients with Hyperparathyroidism in a Non-Specialist Surgical Ward

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Summary

Aim of the study was to audit patients who had undergone parathyroidectomy in University of Malaya Medical Centre (UMMC), and compare surgical outcomes with that in the literature. Data on demography, aetiology, surgical indications, pre-operative localization, surgery and complications was obtained retrospectively from medical records of patients undergoing parathyroidectomy between 1st October 2000 to 31st October 2005. Twelve patients were identified. Mean age was 50.6 years. Sixty seven percent were females. The ratio of Chinese, Malays and Indians was 7:4:1. Most surgeries were performed in the last two years (91.7%). Aetiology was mainly tertiary hyperparathyroidism (83%). All patients had pre-operative ultrasound localization. Half underwent total parathyroidectomy without autotransplantation. There were no re-do operations. Mean duration of surgery was 1.96 hours. All patients had abnormal calcium levels at some point following surgery, but 90% were normocalcaemic at last follow up. Other complications were recurrent laryngeal nerve injury (one) and wound infection (one). There were no peri-operative mortalities. The mean duration of hospital stay was 7.75 days (range 3-17 days). The median duration of follow-up was 11 months. The outcome of parathyroidectomy in UMMC is satisfactory with few major complications. Despite this, intensive effort is needed to further improve these results to match those obtained in specialist endocrine centres.

Key Words: Parathyroidectomy, Surgical outcome, Complications, Primary hyperparathyroidism, Secondary hyperparathyroidism, Tertiary hyperparathyroidism, Hypercalcaemia, Hypocalcaemia

Introduction

The first successful removal of a parathyroid adenoma for hyperparathyroidism was reported in 1925 in Vienna by Felix Mandl[1]. However, to this day, the anomalous number and location of these glands can still pose a major obstacle to successful surgery.

The evolution of endocrine surgery as a sub-speciality has consolidated experience and expertise in this area. Indications for surgery have been refined for the different forms of hyperparathyroidism[2-5]. Advances in imaging and surgical technique have also contributed to improved management of this complex condition. For instance, a combination of pre-operative localization of parathyroid glands with sestamibi isotope scintigraphy and intra-operative PTH monitoring has been shown to significantly reduce the extent of surgery and shorten hospital stay[6-8].

As a result of these advances, specialist endocrine centres report impressively low morbidity and mortality rates for parathyroidectomy, with success rates (as measured by need for further surgical intervention) of greater than 95%[9-10].

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Parathyroidectomies in University of Malaya Medical Centre (UMMC) are performed by general surgeons with an interest in endocrine surgery, rather than dedicated endocrine surgeons. As such, it could be predicted that success rates, mortality and morbidity would fall short of specialist centres. To determine whether this was true, an audit of patients who had undergone parathyroidectomy in UMMC was undertaken.

Materials and Methods

This was a retrospective study of all patients in UMMC who had undergone parathyroidectomy for hyperparathyroidism between 1st October 2000 to 31st October 2005. Patients were identified from operative record books and their medical records subsequently traced.

Demographic data, aetiology of hyperparathyroidism, surgical indications, pre-operative localization studies were recorded. Type, duration and extent of surgical intervention were also assessed. In addition, information on post-operative complications, duration of hospital stay and final histo-pathological diagnoses was included.

Results

Medical folders of only 12 out of 13 patients that were identified to have undergone parathyroidectomy within the five-year study period could be located. The highest number of parathyroid surgeries was recorded in 2005 (seven), followed by 2004 (four) and 2001 (one). Surprisingly, none were performed in 2000 and 2003.

Age ranged from 33 to 70 years old with a mean of 50.6 years. Sixty seven percent were females. The ratio of Chinese, Malays and Indians was 7:4:1. Only two patients had primary hyperparathyroidism. One of them had hypercalcaemia and a history of renal calculi and bone disease with marked reduced bone density; she was 69 years old. The other patient was hypercalcaemic only, and was 59 years old. The majority of patients (10, 83%) had tertiary hyperparathyroidism. The main surgical indications included hypercalcemia, elevated intact parathyroid hormone, biochemical evidence of increased bone turnover, enlarged glands on radiological imaging and failure of medical management. Unfortunately, the other complications of hyperparathyroidism were not well documented except for one patient who underwent a bone density test. All patients underwent pre-operative localization with ultrasound. Sestamibi isotope scintigraphy or other imaging modalities were not performed in any of the patients. Four patients had concurrent multi-nodular goitres and one had a thyroid cyst. Both patients with primary hyperparathyroidism had single-gland parathyroidectomy. Of the ten patients with tertiary hyperparathyroidism, six underwent total parathyroidectomy without auto-transplantation. Three underwent subtotal parathyroidectomy; the remaining patient had two-gland parathyroidectomy, as only two glands could be identified at surgery. Despite this, no further surgical re-intervention was required. Frozen section was obtained intra-operatively in 10 out of 12 cases. The figure would have been higher if not for equipment damage on two occasions. Duration of surgery spanned from one to three hours with a mean of 1.96 hours. One surgery did not have the duration documented.

The most common complication noted was abnormalities in total serum calcium levels. Seven patients developed a diverse range of total serum calcium levels, both hyper and hypocalcaemia throughout their post-operative hospitalization. Six out of the seven patients had these levels optimized to the normal range before being discharged. Only three patients had normal total serum calcium throughout the post-operative period. One patient each was discharged despite being persistently hypercalcaemic and hypocalcaemic respectively. Six patients (50%) had their intact parathyroid hormone levels measured during their hospitalization. Two of these had undergone total parathyroidectomy with the remainder having had less than total parathyroidectomy.

Duration of hospital stay ranged from three to seventeen days with a mean of 7.75 days. The duration of follow-up ranged from 5 to 63 months, with a median period of 11 months. After being discharged, patients had their serum calcium and intact parathyroid hormone monitored at various intervals to detect long term complications of surgery. However, for clarity, only monthly results (if any, and based on the date of discharge) were assessed. Four patients developed hypocalcaemia with intermittent hypercalcaemia. Three patients had intermittent hypercalcaemia. One patient was initially hypocalcaemic. Two patients had normal calcium levels throughout their follow-up period.

Surprisingly, two patients had no record of calcium levels following discharge. Nine out of the other ten patients were normocalcaemic at their last follow-up. The remaining patient was hypercalcaemic. Records of intact parathyroid hormone levels after discharge were also found for only ten patients. Eight patients had normal levels at their last follow up. Two patients had levels above the normal range but did not require surgical re-intervention (both were normocalcaemic). The single hypercalcaemic patient at follow-up had histologically proven total (four-gland) parathyroidectomy and very low iPTH levels; the hypercalcaemia was likely due to over-supplementation.

Recurrent laryngeal nerve injury occurred in one patient, resulting in right vocal cord palsy. This patient had undergone a sub-total parathyroidectomy. Although there was no associated thyroid pathology, there was some difficulty in locating the right inferior parathyroid, which could explain the subsequent injury. Her voice has since returned to normal following medialization. Another patient developed wound infection five days post-operatively. There were no peri-operative mortalities. Final histological diagnosis revealed parathyroid hyperplasia in six patients while the other six had parathyroid adenomas. Of the six that had hyperplasia, four had four-gland hyperplasia, one had three-gland hyperplasia and the other, two-gland hyperplasia. Four patients had single-gland adenoma (including the patients with primary hyperparathyroidism). Two patients had two-gland adenomas.

Discussion

Parathyroidectomy is a fairly uncommon procedure in UMMC. This is partly a reflection of case-mix; unlike Western countries which have predominantly primary hyperparathyroidism, the majority of patients here have secondary or tertiary hyperparathyroidism, which can, to a large extent, be managed medically. In fact, for patients at high risk for surgical morbidity or mortality, conventional medical treatment may be eminently preferable. Nonetheless, there appears to be an increasing trend for performing parathyroidectomies.

Parathyroidectomies in UMMC were frequently done in patients with renal hyperparathyroidism, the majority of whom were diabetics. There was only one case each of adult polycystic kidneys and systemic lupus erythematosus (SLE). This is not entirely surprising as the incidence of diabetes mellitus, and subsequent nephropathy, is high among Malaysians[11,12]. However, we would have expected a larger proportion of Indians (there was only one Indian patient) if this were the only reason, as they have a higher prevalence of diabetes mellitus than Malays and Chinese.

Of the two patients with primary hyperparathyroidism, no mention was made in the medical notes of whether these were sporadic adenoma or linked to the more sinister multiple endocrine neoplasia (MEN). Perhaps, this could be blamed on poor medical documentation, but if indeed MEN has not been ruled out, then efforts need to be undertaken to do so as it is associated with poor prognosis. The decision to undertake surgical intervention for hyperparathyroidism is somewhat controversial at the present moment. There are currently many guidelines available at the surgeons' disposal and among them are the National Institutes of Health (NIH) Consensus Development Conference 1990 and the 2002 update. Nevertheless, many surgeons do not follow these recommendations as evidenced by a study in the United States[13]. However, both patients with primary hyperparathyroidism in UMMC did meet at least one of the NIH criteria. Surprisingly, none of the patients with tertiary hyperparathyroidism could be confirmed to properly fulfill either NIH or Tominaga criteria. Poor documentation rather than failure to fully assess surgical indications may be to blame for the seeming non-compliance to guidelines.

Surgical management of hyperparathyroidism has reached its present echelon primarily as a result of three major advances; namely sestamibi isotope scintigraphy for pre-operative localization, minimally invasive surgery and the development of rapid parathyroid hormone immunoassays. In UMMC, the pre-operative localization study of choice is neck ultrasound, although sestamibi scanning is available. Apart from being non-invasive and cheaper, ultrasound is accurate if executed by an experienced radiologist. Sestamibi isotope scintigraphy with computed tomography is successful in detecting single parathyroid adenomas in 95% of patients with primary hyperparathyroidism[14]. However, a recent study disclosed no significant difference in cure rate between patients who had pre-operative scintigraphy against those who did not[15]. Hence, it is not surprising that it is not utilized unless there is a failed operation that requires repeat neck exploration[16]. Fortunately, as far as this study is concerned, re-exploration has not been necessary. Surgeons in UMMC currently perform a

standard open neck exploration through a cervical incision under general anaesthesia. Each individual parathyroid gland is identified and removed when indicated. Biopsies of all normal-sized glands are taken to verify their true nature.

Depending on the aetiology, signs and symptoms and the results of the pre-operative localization studies, various degrees of parathyroidectomy can be contemplated. In primary hyperparathyroidism, only the abnormal gland(s) are removed. There is still some uncertainty about the optimum form of surgery in the management of renal hyperparathyroidism. Total or sub-total parathyroidectomy have been advocated. The arguments against sub-total parathyroidectomy have included the supposed higher risks of re-operative surgery in the neck should persistent or recurrent hyperparathyroidism occur. This fear does not seem to be borne out by more recent studies[17-19]. However, it has been suggested that total parathyroidectomy with autotransplantation offers better outcomes compared to subtotal parathyroidectomy, with less post-operative hypoparathyroidism and increased bone healing[20].

Total parathyroidectomy can be done with or without auto-transplantation. Controversy lies in the latter two techniques. Autotransplantation carries the risk of persistent or recurrent hyperparathyroidism, requiring repeated surgeries to remove hyperfunctioning tissue. This is in contrast to permanent hypoparathyroidism without autotransplantation.

Religious follow-up is needed to gauge the side effects of either technique. Chances are a supposed total parathyroidectomy could just turn out be a subtotal parathyroidectomy due to the presence of ectopic and supernumerary parathyroid glands. In addition, not all auto-transplanted tissue will survive, thus should recurrent hyperparathyroidism occur, there would be uncertainty as to the true source of parathyroid hormone, leading to an increased number of hospital visits for investigation and intervention.

It must be recognized that for many patients in developing countries such as Malaysia, the time and expense involved in rigorous follow-up, in addition to the complications of hypoparathyroidism constitute a significant financial and social burden, and must be considered when deciding on form of surgery. Sub-total parathyroidectomy may be preferable to avoid hypoparathyroidism but surgeons must be skilled enough to re-explore the neck safely should recurrent hyperparathyroidism occur. When total parathyroidectomy is performed, it may be preferable not to autotransplant and so avoid diagnostic difficulties should recurrent hyperparathyroidism occur. Hence, all total parathyroidectomies (six) in UMMC were performed without autotransplantation.

Intra-operative intact parathyroid hormone assays can further facilitate localization and confirmation of excision of all hyperfunctioning tissue, with a success rate of 94%[8]. However, this is not performed in UMMC as the low volume of patients means it is not cost-effective. The same holds true for intra-operative ultrasound.

The risk of complications in any surgery is present even in the safest and most ideal environment. When a parathyroid operation is unsuccessful, it may be attributed to one or more factors; inexperience of the operating surgeon, enlargement of more than one parathyroid gland, supernumerary and ectopic parathyroid glands or simply, an erroneous diagnosis. However, complication rates in established centres should be low[10].

Although all the patients in UMMC had at some point recorded serum calcium abnormalities, this was due to inadequate optimization of calcium supplementation rather than inadequate surgery. Even the patient who was hypercalcaemic at last follow up actually had a very low intact parathyroid hormone level. Duration of hospital stay was directly related to the severity of complications that arose post-operatively. Patients with good total serum calcium control were discharged within three to four days.

What was disheartening was the inconsistency of blood test monitoring during the follow-up period. The interval between tests was not uniform, nor was it explainable by the previous levels. Some patients had never had it measured at all; perhaps they were defaulters or were seeking treatment elsewhere. Even if a formal protocol were strictly adhered to by doctors, it would not improve matters if patients themselves default follow-up for various financial and social reasons.

The emergence of minimally invasive parathyroidectomy (MIP) has challenged the traditional approach of bilateral neck exploration for patients with hyperparathyroidism. MIP involves high-quality sestamibi scintigraphy to localize enlarged parathyroid

glands, limited exploration after surgeon-administered cervical block anesthesia, rapid intra-operative parathyroid hormone assay to confirm the adequacy of resection, and discharge within 1 to 3 hours of surgery[21], with high cure rates (100%), no long-term complications and 40% lower costs.

While promising, MIP works best for primary hyperparathyroidism; since most of the cases in UMMC are tertiary, the cost of equipment and skill acquisition for MIP may not be commensurate with patient load, although it would certainly improve the management of the few patients who are suitable. We acknowledge the limitations of this study. The sample population is small. With poor documentation, it is uncertain as to whether this is indeed a true representation of hyperparathyroidism management in UMMC.

Further effort (e.g. digital and computerized documentation, coordination of patient information etc.) needs to be undertaken in order to allow organized book-keeping and improved patient management.

Conclusion

The outcome of parathyroidectomy in UMMC is adequate with few major complications. Despite this, intensive effort is needed to further improve these results to match those obtained in specialist endocrine centres.

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