ORIGINAL ARTICLE

Minimally Invasive Video-assisted Parathyroidectomy Without Intraoperative Parathyroid Hormone Monitoring

Juan Pablo Rodrigo,a,b,∗ Andrés Coca Pelaz,a Patricia Martínez,a Rocío González Marquez,a Carlos Suáreza,b

a Servicio de Otorrinolaringología, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain
b Instituto Universitario de Oncología del Principado de Asturias, Universidad de Oviedo, Oviedo, Asturias, Spain

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KEYWORDS
Primary hyperparathyroidism; Surgery; Video-assisted; Intraoperative parathyroid hormone

Abstract
Introduction and objectives: Surgical treatment of primary hyperparathyroidism has evolved from the classical bilateral neck exploration to minimally invasive techniques due to recent advances in preoperative localisation methods. The additional value of intraoperative parathyroid hormone (PTH) monitoring is questioned. The aim of this study was to analyse the results of minimally invasive video-assisted parathyroidectomy (MIVAP) without intraoperative PTH monitoring.

Methods: The patients who underwent MIVAP without PTH monitoring for primary hyperparathyroidism between 2007 and 2013 were evaluated. In all cases the suspected enlarged gland was identified preoperatively by 99Tc-sestamibi scintigraphy, ultrasound or computed tomography. Results: 71 patients were studied (56 females and 15 males), with a mean age of 60 years. In 3 cases (4%) the technique was converted to open parathyroidectomy. Calcium and PTH levels were normalised after first surgery in 69 cases (97%), and after a second surgery in the remaining 2 cases (a second contralateral and a second intrathyroid adenoma). One patient developed a postoperative wound infection, 1 postoperative hypocalcaemia, and 4 transient vocal fold paralysis. No permanent vocal fold paralysis or other complications were observed. Conclusions: MIVAP is a safe, effective surgical technique to cure primary hyperparathyroidism. Intraoperative PTH monitoring may not be routinely necessary in patients treated with this technique.
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∗ Corresponding author.
E-mail address: juanpablo.rodrigo@sespa.princast.es (J.P. Rodrigo).

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**PALABRAS CLAVE**

Hiperparatiroidismo primario; Cirugía; Videoasistida; Hormona paratiroida intraoperatoria

**Paratiroidectomía minimamente invasiva videoasistida sin determinación intraoperatoria de hormona paratiroida**

**Resumen**

*Introducción y objetivos:* La cirugía del hiperparatiroidismo primario ha evolucionado desde la clásica exploración bilateral del cuello hacia las técnicas mínimamente invasivas gracias a la mejora en los métodos de localización preoperatoria. La necesidad de emplear la determinación intraoperatoria de hormona paratiroida (PTH) como adjunto a estas técnicas es debatida. El objetivo de este estudio es analizar los resultados de la paratiroidectomía mínimamente invasiva videoasistida (MIVAP) sin la determinación de PTH intraoperatoria.

*Métodos:* Se estudia a los pacientes intervenidos mediante MIVAP entre los años 2007 y 2013 por hiperparatiroidismo primario sin realizar determinación de PTH intraoperatoria. En todos los casos, había una localización preoperatoria del posible adenoma mediante gammagrafía con 99Tc-sestambí, ecografía o tomografía computarizada.

**Resultados:** Se incluyó en el estudio a 71 pacientes (56 mujeres y 15 varones) con una edad media de 60 años. Hubo que convertir la técnica a paratiroidectomía abierta en 3 casos (4%). Se consiguió la normalización de los niveles de calcio y PTH en la primera cirugía en 69 pacientes (97%) y en los 2 restantes (un segundo adenoma contralateral y otro segundo adenoma intratiroideo) en una segunda intervención. Un paciente presentó una infección de la herida quirúrgica, otro una hipocalcemia, y 4 una parálisis recurrencial transitoria. No hubo parálisis permanentes ni otras complicaciones.

**Conclusiones:** La MIVAP es una técnica eficaz y segura para el tratamiento quirúrgico del hiperparatiroidismo primario. La determinación de PTH intraoperatoria no parece ser necesaria de rutina en los pacientes operados mediante esta técnica.

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**Introduction**

Primary hyperparathyroidism results from excess production of parathyroid hormone (PTH) by one or more hyperfunctioning parathyroid glands. There are 3 pathological conditions which can cause hyperfunction of the glands: adenoma, hyperplasia or carcinoma. Adenoma is a benign tumour which is encapsulated with a normal gland remnant and is the most common cause (85%–95%) of primary hyperparathyroidism; although it usually only affects one gland (single adenoma), 2%–5% of patients can have more than one adenoma. Hyperplasia comprises enlarge-ment of the entire glandular parenchyma, which affects 4 glands; it is responsible for 5%–15% of sporadic cases, although it is the rule in patients with type 1 and 2 multiple endocrine neoplasms (MEN), and in familial hyperparathyroidism not associated with MEN. Carcinoma of the parathyroid glands is very rare, representing fewer than 2% of primary hyperparathyroidisms.

The incidence of hyperparathyroidism in Spain is approximately 10 cases per 100,000 inhabitants per year and most commonly affects women of an advanced age. The clinical presentation has evolved over the years and it is rare to find classical manifestations of the disease (renal lithiasis, bone pain, abdominal discomfort, lethargy, osteitis fibrosa cystica...). Patients tend to be diagnosed without symptoms during a study of hypercalcaemia found on biochemical testing, or with a few symptoms such as fatigue, muscular pain and depression. Diagnosis of primary hyperparathyroidism is biochemical and is made when there is hypercalcaemia with an increase in PTH levels and normal renal function. Hypophosphataemia, hypercalciuria and reduced 25-dihydroxvitamin D levels also usually present. However, it should be taken into account that it can present as normocalcaemic hyperparathyroidism or hypercalcaemia with PTH levels at the high end of normal.

Hyperparathyroidism is treated by surgical excision of the hyperfunctioning parathyroid tissue. It should be indicated for all symptomatic patients but it is debated in those who are asymptomatic. According to the consensus backed by the U.S. National Institutes of Health, surgery is indicated in asymptomatic patients who fulfil the following criteria: under 50 years of age; calcaemia exceeding normal levels by 1 mg/dl; reduced creatinine clearance of 30%, and low bone mass defined as a T score lower than −2.5 in any area (hip, wrist, spine). It would also be indicated for patients for whom follow-up is not possible.

With recent advances in abnormal gland location studies (computerised tomography [CT], ultrasound, technetium-99m sestambí imaging and single-photon emission computed tomography [SPECT]), and given that the great majority of cases are caused by a single adenoma, surgery has evolved from the traditional bilateral neck exploration with identification of the 4 glands to minimally invasive techniques directed at the affected gland. However, in cases where multiglandular disease (MEN, familial hyperparathyroidism) is suspected or there has been no preoperative location, bilateral exploration is still indicated. The curative effects of directed parathyroidectomy are similar to those of bilateral exploration, with the advantage of better cosmetic results, less...
post-operative pain, shorter operating time, and shorter hospitalisation (including as an outpatient).

Minimally invasive techniques can be performed conventionally (with a smaller incision and not searching for the 4 glands), endoscopically (through trocars and gas insufflation) or video-assisted. Minimally Invasive Video Assisted Parathyroidectomy (MIVAP) was described by Miccoli et al.\textsuperscript{5} and is performed through a 15 mm incision assisted by a 5 mm 30° endoscope that enables the surgical field to be magnified which helps in the location of the parathyroids and the recurrent nerve. It has the additional advantage over the endoscopic approach in that it does not require insufflation with carbon dioxide and allows the surgeon to feel. Cure rates above 95% have been described with this technique, similar to those of bilateral exploration of the neck.\textsuperscript{6,9}

In an attempt to improve cure rates and avoid reoperation, intraoperative PTH monitoring is usually recommended with minimally invasive techniques.\textsuperscript{2,10,11} However, this is not available in all centres and there are studies which indicate that the benefit gained if there has been preoperative location is marginal.\textsuperscript{12-14}

The objective of this work is to describe our results in the treatment of primary hyperparathyroidism using the MIVAP technique, without monitoring PTH intraoperatively.

**Material and Methods**

The clinical history was checked of the patients who were operated for primary hyperparathyroidism by MIVAP in our hospital, between January 2007 and June 2003. All the patients had been diagnosed with primary hyperparathyroidism by their endocrinologists and had been referred for surgery because they met the established indications: symptomatic hyperparathyroidism or asymptomatic complying with the conditions of the NIH\textsuperscript{4} consensus. Patients were considered candidates for MIVAP when the affected gland had been located by one of the available imaging tests: CT, ultrasound, 99Tc sestamibi scan or SPECT-CT. In addition, the patients had to fulfill the following conditions: no previous surgery of the thyroid or parathyroid glands, the largest diameter of the adenoma being less than 4 cm, no goitre, no suspicion of hyperplasia (MEN, familial hyperparathyroidism).

71 patients who met these conditions were included in the study; 56 (79%) were female and 15 (21%) male, with a mean age of 60 (range from 23 to 86). The preoperative calcaemia levels of these patients were between 9.8 and 15.56 mg/dl, with a mean of 11.61 mg/dl and a median of 11.5 mg/dl. And PTH levels were in a range between 55 and 2236 pg/ml, with a mean of 273 and a median of 147 pg/ml.

The 99Tc sestamibi gammagrapy scan was the most frequently used location study, in 57 patients, locating a possible adenoma in 49 cases (86%). A CT scan was performed on 45 patients, locating a possible adenoma in 41 (91%). Ultrasound was performed on 36 patients, which located a possible adenoma in 26 cases (72%). More than one location test was performed on 47 patients, on 10 patients only a gammagrapy scan was performed, on 11 only a CT scan and on 3 only ultrasound.

The surgical technique used was MIVAP, described by Miccoli et al.\textsuperscript{15} Briefly, a horizontal incision of about 15 mm was made in the cervical midline halfway between the cricoids and the sternal notch (Fig. 1A). After dissection through the midline to reach the thyroid, we continued towards the side where the adenoma was located through the plane between the adenoma and the prelaryngeal muscles, creating a work space between the vascular axis and the thyroid using separatars. On reaching the posterior face of the thyroid the adenoma was located (Fig. 1B), and was dissected and removed following bipolar cautersiation of its vascular pedicle, having identified the lower thyroid artery and the recurrent nerve (Fig. 1C). The other parathyroid gland ipsilateral to the adenoma was located to check that its appearance was normal. The wound was closed with an intradermal suture (Fig. 1D). No drain was left in any of the cases.

The patients underwent checks by the Endocrinology Department after one month, 3 months and 6 months, and then annually, to confirm that the hyperparathyroidism had been cured.

**Results**

Out of the 71 patients for whom surgery using the MIVAP technique was indicated (Table 1), it was possible to operate on 68 patients using this technique. It had to be converted to open surgery in 3 patients, 2 because the adenoma was not found and it was decided to perform a bilateral exploration, and in the third case the adenoma was very attached to the adjacent structures as it was partially infarcted. In the 2 cases where the adenoma had not been found initially, it was not located by open exploration either, and therefore, since the gammagraphic scan had indicated a suspected intrathyroid location, a hemithyroidectomy was performed in the end, the intrathyroid location was confirmed and the patients were cured. The adenoma was located in the

| Table 1  Summary of Patient Characteristics and Results of Treatment. |
|-------------------|------------|----------|
| Characteristic     | Number of cases (%) |
| Gender             |            |          |
| Female             | 56 (79)    |          |
| Male               | 15 (21)    |          |
| Location of the adenoma |          |          |
| Upper right        | 7 (10)     |          |
| Lower right        | 28 (39)    |          |
| Upper left         | 16 (22.5)  |          |
| Lower left         | 16 (22.5)  |          |
| Double adenoma     | 2 (3)      |          |
| Intrathyroid       | 2 (3)      |          |
| Conversion to open surgery |          |          |
| No                 | 68 (96)    |          |
| Yes                | 3 (4)      |          |
| Cure               |            |          |
| First surgery      | 69 (97)    |          |
| Second surgery     | 2 (3)      |          |
| Surgical complications |          |          |
| Recurrent transient paralysis | 4 (5.6)   |          |
| Infection          | 1 (1.4)    |          |
remaining 68 patients and it was removed without intraoperative complications. The location of the adenoma was upper right in 7 cases, lower right in 28 cases, upper left in 16 cases and lower left in 16 cases. 2 right-sided adenomas were found in one of the patients, which were removed and contralateral exploration using the same MIVAP technique found that the two parathyroids appeared normal. The mean duration of surgery was 72 min (median 60 min, and range between 30 and 150 min).

The anatomopathological diagnosis was adenoma in all cases (double in one case, as mentioned), the adenoma was atypical (with mitosis) in 2 cases. The largest diameter of the adenomas varied between 0.5 and 4 cm (median of 1.5 cm) and the weight between 0.8 and 10.3 g (median of 0.84 g).

A biochemical cure (normalisation of calcium and PTH levels after 6 months) was achieved in 69 of the 71 patients (97%) after surgery. The hyperparathyroidism persisted in 2 patients. After location using SPECT-CT which indicated the presence of remaining hyperfunctioning parathyroid tissue, further surgery was performed using the conventional technique of bilateral exploration of the neck in the 2 cases resulting in a cure for both. Another adenoma was located in one of the cases contralateral to the one which had been removed initially, the two remaining glands were normal in appearance. In the other case, the 3 remaining glands appeared normal, which was confirmed by biopsy; according to the findings of SPECT-CT, which showed uptake in right-sided hemithyroid, a right-sided hemithyroidectomy was performed finding an intrathyroid parathyroid adenoma, which would correspond with a supernumerary gland. There were no cases of recurrence of the hyperparathyroidism, with a mean follow-up of 40 months (range between 7 and 80 months).

In terms of postoperative complications, 4 (5.6%) patients presented transient recurrent paralysis, which resolved in less than 3 months in all cases. There were no cases of permanent paralysis. One patient presented a wound infection and 2 decompensated heart failure. There were no haemorrhages or other complications related to the surgery. One patient presented a clinical picture of severe postoperative hypocalcaemia (hungry bone syndrome), which required intravenous calcium for 2 weeks.

If we exclude the 2 patients with decompensated heart failure, the mean postoperative hospital stay was 1.65 days (median of 1), with a range between 1 and 7 days.

Discussion

The treatment for hyperparathyroidism is the surgical removal of all the hyperfunctioning parathyroid tissue. Given the good results of surgery and its low morbidity, all patients should be offered surgical treatment, including asymptomatic patients who do not meet the NIH consensus criteria. Moreover, surgery is both effective and cost-effective compared to medical treatment if life expectancy is greater than 5 years.
Surgery for primary hyperparathyroidism has evolved in recent years from traditional bilateral exploration of the neck finding the 4 parathyroid glands and then removing the enlarged glands, to minimally invasive surgery. This evolution is due to the fact that the majority of cases are caused by a single adenoma and because improved preoperative location techniques enable surgery directed at the gland affected by the adenoma, with similar results to those of conventional surgery\(^3\)\(^-\)\(^9\) and involving less discomfort for the patient.

The minimally invasive techniques include directed, radio-guided, endoscopic and video-assisted parathyroidectomy. In directed parathyroidectomy,\(^3\) only the enlarged gland which has been identified beforehand is removed, without locating the others, through a smaller incision than the conventional (3–4 cm). In radio-guided parathyroidectomy,\(^1\) the patients are injected with 99Tc- sestamibi 2h before surgery, and subsequently a gamma probe is used to locate the enlarged gland; this is performed through an incision of about 2–4 cm, as in directed surgery. After removing the affected gland, its radioactivity is compared with that of the surgical bed, which enables the removal of all of the hyperfunctioning tissue to be confirmed. Radio-guided parathyroidectomy is particularly useful in the case of ectopic or reoperated glands. However, radio-guided parathyroidectomy has not been adopted as a standard technique due to problems with logistics and equipment: as it offers little benefit in primary cases compared to preoperative location.\(^2\) Endoscopic parathyroidectomy is performed through 4.5 mm trocars which can be placed centrally or laterally, or even transaxillary, according to described variations, insufflating carbon dioxide to achieve a working space.\(^1\) Although good curative and cosmetic results have been described, this technique has a greater learning curve, it is more difficult to see the recurrent nerve, and it has been associated with possible complications, such as tachycardia, hypercapnia, respiratory acidosis, subcutaneous emphysema and gas embolism; therefore it is not widely used. By contrast, the MIVAP described by Miccoli et al.\(^5\) does not require insufflation, requires few specific instruments, has a short learning curve, allows bilateral exploration of the neck through the same incision and can be easily converted to conventional technique when necessary. However, many surgeons consider that it offers few advantages compared to conventional directed parathyroidectomy, apart from a smaller incision,\(^3\) and it is not widely used either.

In this study we have used the MIVAP technique as described by Miccoli et al.,\(^5\) having obtained results in terms of curing the hyperparathyroidism (97%) similar to those described in literature for any contrasted technique: almost all studies describe cure rates above 95% in the first operation.\(^3\)\(^,\)\(^5\)\(^,\)\(^8\)\(^-\)\(^9\)\(^,\)\(^14\)\(^-\)\(^17\)\(^,\)\(^18\) The few cases which are not cured are due to previously undetected multiglandular disease or ectopically located parathyroids (e.g. intrathyroidal). This high cure rate with directed techniques has also been attributed to intraoperative determination of PTH levels.\(^3\)\(^,\)\(^10\) Given the short half-life of PTH (3.5–5 min), determining this after removing the enlarged parathyroids helps to ensure that all the hyperfunctioning parathyroid tissue has been removed, without the need to identify the 4 glands. PTH is determined when surgery starts and 10 min after removing the enlarged glands; according to the criteria defined by Irvin et al.,\(^1\) a 50% decrease of pre-excisional levels indicates removal of all of the hyperfunctioning tissue, and the operation can be brought to an end. Using this criterion, 97% reliability has been described in identifying cured cases.\(^3\) For this reason, many authors recommend that directed techniques should be accompanied by intraoperative monitoring of PTH levels.\(^3\)\(^,\)\(^10\)\(^,\)\(^11\) However, additional time is required for PTH monitoring (estimated at around at least 30 min). It involves a cost and might not be available in all centres, therefore other authors have suggested that the benefit it offers is not significant and they do not support its routine use.\(^12\)\(^-\)\(^14\) We do not use intraoperative monitoring of PTH routinely either and we have obtained curative results similar to those described by authors who do use it, which supports its not providing additional benefit when the patient fulfils the requirements for MIVAP. Therefore, it would not be a cost-effective intervention, as it prolongs surgery unnecessarily for the great majority of patients in addition to the cost of the test. This does not mean that it might not be useful under other circumstances, such as suspected multiglandular disease, no preoperative location or reoperation; which are the occasions when we do use it.

It has been indicated that MIVAP is not associated with a greater risk of complications than the conventional technique or directed parathyroidectomy,\(^2\) as it provides good visualisation of the cervical structures and allows the surgeon to feel. In our series, we had no postoperative complications worthy of note, except a cervical infection, but 4 (5.6%) patients presented transient recurrent paralysis. This figure appears high compared to open procedures and could be due to greater traction on the recurrent nerve in MIVAP when the adenoma is touching it, as there is less room available for manoeuvre. Nonetheless, none of the patients presented permanent paralysis, in line with other studies which describe recurrent paralysis in less than 1% of cases.\(^1\)\(^,\)\(^14\)\(^,\)\(^15\)

The advantages attributed to MIVAP include less pain and faster patient recovery due to less operative trauma. This enables early discharge, with the consequent reduction in cost. In our experience, the great majority of the patients were discharged on the first post-operative day and when discharge was delayed, this was due to reasons which were not connected to the operation, but to the patients’ associated diseases. Therefore, it is a procedure which, in patients who are candidates because of their general condition, can be undertaken on an outpatient basis. Another additional benefit is cosmetic, as it leaves a small scar (approximately 1.5 cm) which cannot be seen in most patients.

In conclusion, MIVAP is a safe and effective technique in the treatment of primary hyperparathyroidism, with the benefit of less surgical trauma and better cosmetic result. When MIVAP is correctly indicated, the use of intraoperative PTH monitoring does not appear to be necessary to achieve good curative outcomes.

**Conflict of Interests**

The authors have no conflict of interests to declare.
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