

# The actual role of classic bilateral cervicotomic approach for primary hyperparathyroidism in the era of minimally invasive surgery



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## Introduction

Primary hyperparathyroidism is a common disease (1). Bilateral neck exploration has been the gold standard of surgical treatment for several decades (2) and has produced excellent results with cure rates above 98-99% (3, 4). However, in recent years this protocol has been challenged by an increasing number of authors claiming a unilateral, targeted approach as procedure of choice (5-8). Such targeted approach has become feasible by emerging preoperative localisation techniques such as  $^{99m}\text{Tc}$ -sestamibi scintigraphy (MIBI) first described by Coakley in 1989 (9).

Reliability has been remarkably enhanced by substruction techniques (10) or even more by a combination with SPECT (single photon emission computed tomography) (11). High resolution ultrasonography added further to enhanced preoperative identification of enlarged glands. A substantial progress was the development of quick parathyroid hormone (PTH) assay used to prove complete removal of all hyperfunctioning parathyroid tissue during operation (12). Specifically, the combination of reliable preoperative localisation with intraoperative proof of successful removal of all diseased tissue has in many ways turned around the strategies in surgical treatment of primary hyperparathyroidism (13).

This report and review intends to underscore the value of standard bilateral neck exploration in a substantial patient subgroup carrying particular features which may render a targeted approach difficult or inadvisable.

## Riassunto

**RUOLO ATTUALE DELLA CERVICOTOMIA BILATERALE TRADIZIONALE PER IPERPARATIROIDISMO PRIMARIO NELL'ERA DELLA CHIRURGIA MININVASIVA**

*I miglioramenti ottenuti dalle tecniche di localizzazione preoperatoria dell'adenoma paratiroideo e la disponibilità del dosaggio del qPTH intraoperatorio (che consente di dimostrare la completa rimozione del tessuto paratiroideo iperfunzionante) hanno favorito lo sviluppo di procedure operative meno invasive, che hanno parzialmente sostituito la classica tecnica di esplorazione bilaterale del collo. Con il presente studio sono stati esaminati 1099 interventi consecutivi di paratiroidectomia per iperparatiroidismo primario eseguiti in un arco di tempo pari a 16 anni: il tasso di guarigione dopo il primo intervento è stato del 97,1%. Dal 1999 al 2001, 200 pazienti sono stati sottoposti ad un'esplorazione bilaterale del collo, e 63 ad una esplorazione unilaterale (33 pazienti sono stati trattati con la paratiroidectomia mininvasiva videoassistita e 30 con paratiroidectomia mininvasiva aperta). Nei rimanenti 200 pazienti l'esplorazione paratiroidea mininvasiva unilaterale non era attuabile per la concomitante presenza di un gozzo (n=102), per la mancanza di localizzazione preoperatoria (n=30), per precedenti di chirurgia tiroidea (n=10), sospetto di malattia multighiandolare (n=10), o altre cause (n=8).*

*Sebbene l'esplorazione unilaterale consenta un'eccellente percentuale di guarigione nei pazienti anziani, essa non è consigliata nei casi in cui sussista una alta probabilità di coinvolgimento multighiandolare, in presenza di un gozzo o di adenoma paratiroideo di notevoli dimensioni, alti livelli di PTH, mancanza di localizzazione preoperatoria o della disponibilità del qPTH.*

**Parole chiave:** Cervicotomia bilaterale, iperparatiroidismo primario, chirurgia mininvasiva videoassistita, chirurgia mininvasiva radioguidata.

## Abstract

*Recent advances in preoperative localisation of parathyroid adenomas and intraoperative prove of complete removal of hyperfunctioning parathyroid tissue have fostered less invasive operative procedures which directly target the diseased gland. Such strategies have partially replaced the previous gold standard procedure of bilateral neck exploration. We herein report on our own series of 1099 consecutive operations for primary hyperparathyroidism performed in a 16 year period and provide information and arguments for pri-*

mary bilateral exploration in selected cases. 97.1% of patients were cured by the primary operation. From 1999 through 2001, 200 patients underwent bilateral neck exploration, whereas 63 unilateral operations were performed (33 patients were treated by minimally invasive video-assisted parathyroidectomy (MIVAP) and 30 by minimally invasive open parathyroidectomy (MIOP). In the remaining 200 patients minimally invasive unilateral parathyroid surgery was not feasible due to concomitant goiter (n=102), lack of preoperative localisation (n=30), previous thyroid surgery (n=10), suspected multiglandular disease (n=10), or other reasons (n=8). In 40 patients the decision for bilateral neck exploration was made despite feasibility of a unilateral approach.

Conclusion: Whereas unilateral exploration produced excellent cure rates in older patients, it is not recommended in patients with a high likelihood of multiglandular disease, presence of a large or multinodular goitre, high PTH levels, giant adenoma, unclear MIBI scans or an unreliable QPTH assay. Contrasting recent reports on a dramatic shift of technique towards minimally invasive procedures unilateral parathyroid surgery may not be preferably advisable in a majority of patients from countries with insufficient iodine supplementation.

Key words: Bilateral cervicotomy, primary hyperparathyroidism, videoassisted mininvasive surgery, radio-guided mininvasive surgery.

procedures included a horizontal incision of the platysma and a later dissection of the paratracheal space. Strap muscles were divided in the median line when using MIVAP, whereas they were simply retracted in the lateral approach.

Systematic localisation studies were performed from July 1999 on. This included MIBI scanning performed a dual-phase technique with subtraction (15). Ultrasound was performed by a number of experienced endocrinologists using a probe with a range from 8-13 MHz. Intraoperative PTH was routinely measured by a two-site immunochemiluminometric method with the Quick-Intra-Operative intact PTH (QPTH) assay (Nichols Institute Diagnostics, San Juan Capistrano, CA, USA) on venous blood after induction of anaesthesia before skin incision and 10 minutes after removal of an enlarged gland from 1999 on. A reduction of PTH levels of above 50% of baseline values was defined as a marker of adequate abnormal gland excision (16). All patients underwent pre- and postoperative laryngeal exploration by an otolaryngologist. In all patients cure was ascertained by postoperative measurements of serum calcium levels.

Sequencing of the RET proto-oncogene was performed in cases with a positive family history of hyperparathyroidism or syndrome-associated endocrine tumours or presence other diagnostic clues for a hereditary or multiglandular disease.

## Patients and methods

This is a single centre experience on 1099 consecutive patients operated for primary hyperparathyroidism between April 1986 and November 2002. All operations were carried out by a small group of experienced endocrine surgeons. From 1986 through 1999 primary bilateral neck exploration was performed as a standard procedure. This included a 4.0 to 6.0 cm horizontal Kocher incision 2 cm above the suprasternal notch followed by horizontal incision of the platysma and midline separation of the strap muscles. Following the identification of the thyroid capsule the paratracheal space was dissected and all four parathyroid gland were routinely identified. Ectopic glands were searched for only when no parathyroid adenoma was found in orthotopic position. Upper pole vessels were deliberately divided when necessary. The recurrent laryngeal nerve was routinely identified.

From July 1999, minimally invasive procedures were also applied. We either used minimal-invasive video-assisted parathyroidectomy (MIVAP) (14) or a minimal open lateral approach. MIVAP was carried out through a 1.5 to 2.0 cm horizontal incision 1 to 2 cm above the suprasternal notch, with or without insufflation of carbon dioxide using a 5 mm camera providing a 30° angle optic with 10 fold magnification and additional conventional retractors. The minimal open lateral approach was performed by a 2.0-3.0 cm incision at the front rim of the inferior third of the sternocleidomastoid muscle. Both

## Results

Cure was achieved in 1068 patients (97.1%) of all 1099 patients (Table I). These results did not change significantly by introduction of localisation studies, intraoperative QPTH measurement or use of minimally invasive techniques.

Bilateral neck exploration persisted to be the most frequent procedure after introduction of minimally invasive procedures in 1999. Table II shows the rationale for choosing a bilateral rather than unilateral of minimally invasive approach in those patients operated upon after 1999. Minimally invasive procedures were associated with problems in 5 patients (7.9%). In one patient there was persistence of hyperparathyroidism despite adequate drop in intraoperative QPTH levels.

This was due to multi-glandular disease. In one case the drop of PTH level as indicated by the QPTH assay was faulty, equally leading to persistence of hyperparathyroidism requiring a second operation. In one case the preoperative localisation by MIBI scanning and ultrasound was wrong; this required a larger incision during the operation.

There were two recurrent nerve palsies, whereof one was transient.

In one of these patients the adenoma was not found despite conversion of the operation to an open procedure and extensive bilateral exploration.

Table I – CURE RATES AND COMPLICATIONS BEFORE AND AFTER INTRODUCTION OF MINIMALLY INVASIVE TECHNIQUES

<i>Interval</i>	<i>localisation study</i>	<i>QPTH</i>	<i>MIP</i>	<i>number</i>	<i>cure (n/%)</i>	<i>pers. Hypo-calcemia</i>	<i>pers. RLN palsy</i>
1986-1999	No	No	No	836	811/836 97.0%	5/836 0.6%	15/836 1.7%
1999-2002	Yes	Yes	-	263	257/263 97.7%	2/263 0.7%	2/263 0.7%
1999-2002	Yes	Yes	n	200	197/200 98.5%	2/200 1.0%	1/200 1.5
1999-2002	Yes	Yes	y	63	60/63 95.2%	0	1/63 1.5%
Overall	-	-	-	1099	97.1%	0.6%	1.5%

Table II – INDICATIONS FOR SELECTION OF BILATERAL NECK EXPLORATION AS OPERATIVE PROCEDURE IN 200 PATIENTS OPERATED AFTER 1999

<i>Indication</i>	<i>number</i>	<i>% of all</i>
Concomitant goitre	102	51%
Failure of pre-operative localisation	30	15%
Previous thyroid surgery	10	5%
Preoperative suspicion of multiglandular disease	10	5%
No specific indication	40	20%
Other	8	4%
Total	200	100%

## Discussion

Minimally invasive parathyroid surgery has become feasible by substantial improvement of the preoperative localisation techniques and the intraoperative demonstration of complete resection of hyperfunctioning parathyroid glands. Evidently, a smaller scar may be considered "better" than a larger one by the patient himself. Minimally invasive procedures may be performed under local or regional anaesthesia in the form of a superficial cervical block (7, 17, 18). An additional advantage may be seen in lower costs, shorter hospital stays, and quicker recovery time (8, 19, 20), particularly when operations are performed in an ambulatory setting (6). The single surgeon experience of Udelsman (20) is characteristic of the dramatic shift of surgical treatment of primary HPT during the last five years due to the encouraging results of minimally invasive procedures. This series on 656 patients reports a 50% reduction in operating time, a seven-fold reduction in the length of hospital stay and a mean cost saving of more than 2000 \$ whilst maintaining a success rate of 98% for either technique, bilateral neck exploration or minimal procedure with comparable complication rates. Closer reading reveals that these data are based on a careful preoperative patient selection: no

Table III – RELATIVE AND ABSOLUTE CONTRAINDICATIONS TO MINIMALLY INVASIVE SURGERY OF THE PARATHYROID

<i>Condition</i>	<i>Argument</i>
Age <30 years	high incidence (>50%) of multiglandular disease
Multiglandular disease	need for removal of up to 4 glands, need for thymectomy
Sizable goitre	difficult identification of the parathyroid (relative)
Need for thyroidectomy	not safely done by minimally invasive techniques on a routine basis
Very high PTH level	suspicion of parathyroid cancer
Unclear MIBI scan	site of operation unclear
Giant adenoma	risk of spilling and seeding
Unreliable QPTH assay	no intraoperative control of success (relative)

patient needed simultaneous thyroid surgery or had reported concomitant thyroid pathology. A positive MIBI scan was present in 96% of patients subjected to a minimal procedure. Otherwise, a standard procedure was done. This selection procedure proved successful since single adenoma was the underlying pathology in 92% of minimal procedures, whereas 18% of patients treated by standard procedures had double adenoma or hyperplasia. These data must not be transferred to other less selected patient groups. Results of both, MIBI scanning and ultrasound deteriorate when large or multinodular goitres are present (21-24). Under such conditions, sensitivity and specificity may be well below 80%, even when procedures are combined. Study results may even be too optimistic, since different thyroid lesions present as pitfalls recognised only by the specialist and experienced examiner. As a consequence, the formerly autonomously performing surgeon becomes dependent on an independent expert, whose quality may be hard to control. When patients appear with scans and ultrasounds made outside the

hospital setting, it may be very hard to judge in how far findings are reliable. Redoing the examination in such situations may well eat up the cost saving originally intended.

One main question is that of the real benefit of a unilateral versus a bilateral exploration. As yet, there is only one randomized, prospective, controlled trial (25). In this study, histology and cure rate did not differ between the approaches. Patients in the bilateral group consumed more calcium post-operatively, and had a higher incidence of severe symptomatic hypocalcemia in the immediate post-operative period. The cost for these two procedures did not differ. This observation reduces the benefit to a rather transient and ephemere outcome combined with an aspect of cosmesis. In this regard, there is hence no need to rush to novel techniques since the trade-off is questionable in view of considerable learning curves.

The other crux of the issue is the difficulty to rule out multiglandular disease. There is a number of hereditary conditions associated with multiglandular hyperparathyroidism (26). The most frequent ones are multiple endocrine neoplasia type I, type II, the hyperparathyroidism jaw tumor syndrome associating fibro-osseous jaw tumours and various renal lesions, and familial isolated hyperparathyroidism, presenting as an autosomal dominant primary HPT without associated diseases. Whereas MIBI scan yields excellent results with sensitivity approaching 85-99% in patients with single adenomas (16), it is less valuable or even fails in multiglandular disease (27). In this respect the plea of Proye against unilateral exploration, which is based on the unexpected presence of multiglandular disease in seemingly sporadic primary HPT remains at least in part unsettled (28).

Another reason for caution is the fact of only short post-operative follow-up times in order to evaluate the true success rates. Operative failure may be evident only many years after initial surgery (29). It is well known, however, that very high cure rates above 98% are achieved on long-term follow-up after bilateral neck exploration (3, 30, 31). A recent study indicates, that an adequate drop of QPTH level during the initial operation is a good marker for long-term operative success (32). More data are needed, to prove the long-term efficacy of the targeted approach. Minimally invasive, targeted parathyroid surgery is a good procedure for the older patient with moderately elevated PTH level in whom multiglandular disease is unlikely, clear-cut preoperative localisation by ultrasound and MIBI scanning is present and when an experienced surgeon and a quick PTH assay are at hand. Our data show, that targeted parathyroid surgery may be unfeasible or inadvisable in a large proportion of patients in areas with insufficient iodine supplementation and a subsequent high incidence of goitre (>50%), a condition deteriorating the diagnostic work-up and the operative procedure. Due to

its excellent results and the independence from diagnostic tools primary bilateral cervical exploration remains a first rank procedure for every unselected patient with primary hyperparathyroidism.

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