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Minimally Invasive Parathyroidectomy for Primary Hyperparathyroidism – Current Views, Issues and Controversies

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1. Introduction

Although primary hyperparathyroidism (pHPT) remains a relatively uncommon endocrine disease in Asian countries with an incidence ranging from 17 to 33 / 100,000 cases per year, it has been increasing over the last decade. (Bilezikian et al. 2000; Lo et al. 2004; Chen et al., 2010) In contrast, in the Western world, pHPT is a relatively more common disease with an estimated incidence of 42 to 190/100,000 cases per year. Surgical treatment or parathyroidectomy remains the only curative therapy for patients with pHPT. The goal of surgery is to normalize postoperative calcium levels by excising all hyperfunctioning parathyroid tissue. Traditionally, this has been achieved by way of bilateral neck exploration (BNE) which involves examination of all four parathyroid glands and excision of any enlarged glands. However, with improvement in preoperative localization techniques and the commercial availability of quick intraoperative parathyroid hormone assay (IOPTH), an increasing number of endocrine surgeons are now performing minimally invasive parathyroidectomy (MIP). In experienced hands, many studies have found that MIP is not only a less invasive procedure associated with shorter hospital stay and less pain but also can achieve similar long-term cure rate of up to 95-98% as BNE which many would still regard it as the gold standard procedure. With this in mind, the purpose of this review is to look at the current views, issues and controversies associated with the use of preoperative localization studies, IOPTH and various surgical techniques of MIP by a comprehensive MEDLINE search using several specific keywords. These keywords include “minimally invasive parathyroidectomy”, “focused parathyroidectomy”, “intraoperative parathyroid hormone” and “parathyroid adenoma”. Since the success of MIP depends partly on the accuracy of preoperative localization studies and IOPTH, it is imperative to assess them in an evidence-based method. The review would look specifically on the use of ^{99m}Tc Sestamibi (MIBI) and high-resolution ultrasound (USG) as both modalities are the most commonly employed and accurate imaging before MIP. The review would also look at the issues when there are concordant and discordant results between the MIBI and USG as well as examine the role of surgeon-performed USG (SPUS) in pHPT. Regarding the IOPTH, it remains controversial whether it should be routinely used in all cases of pHPT as some still question the cost-benefit and the “added value” of this particular operative adjunct.

Furthermore, there are still many unresolved issues regarding the most appropriate choice for IOPTH measurements and what criteria for defining biochemical cure. However, it is certain that the recent findings in IOPTH dynamics during MIP have helped us in better understanding of the disease itself. The previous concept of histology and gland size has now been challenged and is gradually being replaced by the concept of biochemical cure based on changes in IOPTH dynamics. Last and not the least, the review will look at various MIP techniques and evaluate which is most commonly used and performed and the reasons behind this.

2. Surgical indications and guidelines

The famous mnemonic "stones, bones, abdominal groans and psychiatric moans" concludes the symptoms of hyperparathyroidism or more specifically hypercalcemia. All patients suffering from the classical symptoms and signs of pHPT should undergo surgical treatment, as it is the only way for cure. On the other hand, the National Institute of Health (NIH) guidelines, as concluded at the third Workshop on the Management of asymptomatic pHPT, had a clear direction for the asymptomatic group of patients to choose between surgery and consideration of medical monitoring. In treating the asymptomatic patients, we are aiming at reversing the decreased bone density, reducing the risk of fractures, reducing frequency of kidney stones and improving the neuro-cognitive elements. The consensus also stressed on the identification of Vitamin D deficiency, as it often complicates the diagnosis of pHPT. Therefore the optimal reference range of PTH assay should be based on adequate Vitamin D repletion, as physiologically, PTH and Vitamin D are closely inter-related.

2.1 Surgical indications for "asymptomatic" patients

According to the NIH guidelines, "asymptomatic" patients with the following features should undergo surgery:

1. Hypercalcemia with serum calcium $>1\text{mg/dl}$ above the upper limits of normal;
2. Peri or post menopausal women, and men age >50 with a bone density T-score of -2.5 or less at the lumbar spine, femoral neck, total hip or 33% radius; Premenopausal women and in men younger age <50 with the bone density Z-score of -2.5 or less; Any patient with the presence of a fragility fracture.
3. Age less than 50

Table 1 summarized the changes in surgery criteria in the last decade. In the 2008 consensus, hypercalciuria was taken out from the guidelines because it is not a specific risk factor for kidney stones in primary hyperparathyroidism. However, it remains an important part of the initial workup to rule out familial hypocalciuric hypercalcemia. There were also questions over the accuracy of glomerular filtration rate (GFR) estimation by creatinine clearance and whether a numeral cut-point was better than an age invariant standard. The new consensus was made, based on the fact that a GFR of less than 60ml/min represented renal insufficiency to the extent that would cause parathyroid hormone elevation. The criteria "fracture fragility" was added to the newest guidelines because apart from bone mineral density, primary hyperparathyroidism would also affect the bone size and structure which in turn influence the fracture proclivity. Patients with age less than 50 were included as part of the targeted group as these patients would have greater risk of complications over time.

Measurement	1990	2002	2008
Serum calcium (>upper limit of normal)	1-1.6 mg/dl	1.0 mg/dl	1.0 mg/dl
24 hour urine for calcium	>400mg/d	>400mg/d	Not indicated
Creatinine clearance (Calculated)	Reduced by 30%	Reduced by 30%	Reduced to <60ml/min
Bone Mineral Density	Z-score <-2.0 in forearm	T-score <-2.5 at any site	T-score <-2.5 at any site and/or previous fracture fragility
Age (yr)	<50	<50	<50

Table 1. Comparison of new and old guidelines for parathyroid surgery in asymptomatic primary hyperparathyroidism

However, guidelines for normocalcaemic hyperparathyroidism were yet to be established with more evidence coming up. Parathyroid surgery should be performed only by highly experienced surgeon, or otherwise failure and complication will be unacceptably high and not cost effective. (Bilezikian et al., 2009)

2.2 Are patients with pHPT truly asymptomatic?

There is increasing evidence that patients with pHPT are not truly asymptomatic and if this proves to be true than all patients with pHPT would theoretically benefit from surgery. As a surgeon, it is not uncommon to see that patients with mild evidence of depression and anxiety at preoperative visits often improve after a successful parathyroidectomy. One of the explanations for this is that it is believed that there is a strong link between serum calcium levels and cognitive function. (Roman et al., 2011) In a general population cohort study of more than 4000 individuals, Schram et al. found that high serum calcium levels were associated with faster decline in cognitive function, especially for people older than 75 years. This finding persisted even if people with abnormally high serum calcium levels were excluded. (Schram et al, 2007) Weber et al. evaluated 66 patients who underwent parathyroidectomy for pHPT pre-and postoperatively with 2 validated psychometric instruments and a health-related quality of life health survey (SF-12). They found that patients had significantly more depression and anxiety preoperatively than at 1 year postoperatively, whereas their physical functioning did not change. In this study, preoperative neuropsychological symptoms were related to the serum calcium levels. (Weber et al, 2007) Roman et al. studied 55 patients undergoing either parathyroidectomy for pHPT or thyroid resection for benign thyroid disease as controls and compared their neurocognitive test scores and psychological symptoms before and after surgery. They found that patients with pHPT reported more symptoms of depression and showed greater delays in spatial learning preoperatively than patients with thyroidectomy, but they improved significantly 1 month after surgery at a level equivalent to the controls. Interestingly, patients with greater change in PTH levels were more likely to improve in their learning efficiency after parathyroidectomy. (Roman et al., 2005) The same group also recently assessed the timing and magnitude of psychological and neurocognitive changes before and after parathyroidectomy and found significant improvements in psychological and neurocognitive measures at all postoperative visits. The most pronounced improvements were noted in depressive and anxiety symptoms, and visuospatial and verbal

memory. Examination of change scores revealed that postoperative reduction in PTH was associated with a decrease in state anxiety, which was also associated with improvement in visuospatial working memory. (Roman et al., 2011)

3. Preoperative parathyroid localization

Accurate preoperative localization plays a pivotal role in the success of MIP. Numerous imaging techniques such as technetium Tc99m sestamibi imaging (MIBI), high-resolution ultrasound (USG), magnetic resonance imaging (MRI), and computed tomography (CT) have been used to guide the surgeon and to assist with the preoperative planning. Among these imaging studies, MIBI and / or USG have been the two most commonly used preoperative imaging modalities because they are both readily available and relatively inexpensive. MRI and CT have also been advocated as second-line localization modalities as they do not appear to have better accuracy than MIBI or USG but they can localize inferiorly located or deeply seated parathyroid glands (e.g. mediastinal adenoma). When comparing the accuracy in detecting abnormal parathyroid glands between MIBI and USG, some have found that MIBI is more accurate than USG while other studies have found the opposite or similar accuracies. (Cheung et al., 2011) In our experience, MIBI has a higher overall sensitivity, accuracy and positive predicted value (PPV) in detecting abnormal parathyroid glands than USG (85%, 97% vs 94% vs. 57% vs 89%, 56%, respectively). (Lo et al., 2007) In fact, at our institution, we would rely more on the findings of the MIBI than USG. However, since USG could provide additional localization information in approximately 10-15% of patients with negative or equivocal MIBI, we have not abandoned the use of USG as a preoperative localizing tool. (Lo et al., 2007) In our clinical practice, all biochemically-confirmed pHPT patients would undergo MIBI and if the MIBI is negative or equivocal, an additional USG by our radiologists would be performed. However, we would still perform an intraoperative USG by ourselves just before the skin incision to guide the placement of the small skin incision. Our experiences with MIBI and USG have been consistent with those of other institutions. Quiros et al. reported their experience on 71 patients with pHPT who underwent both preoperative MIBI-SPECT and USG and found that if the MIBI was either negative or "ambiguous", preoperative USG could localize an additional 14% of enlarged parathyroid glands and so further facilitate MIP in these patients. (Quiros et al., 2004) Similarly, Adler et al. recently evaluated the added benefit of USG to MIBI in pHPT and reported that USG led to additional localization information in 14% of patients, although this benefit was less in patients with a clearly positive 1-gland MIBI scan. (Adler et al, 2011) Apart from MIBI and USG, 4D-CT has been shown to be a promising adjunct to other imaging studies. 4D-CT could provide exquisitely detailed, multiplanar images that accentuate the differences in the perfusion characteristics of hyperfunctioning parathyroid glands (i.e. rapid uptake and washout), compared with normal parathyroid glands and other structures of the neck. (Starker et al., 2011) In contrast to other axial imaging studies such as CT or MRI, the 4D-CT images could provide both anatomical information (which is vital for the surgeon) and functional information based on changes in perfusion in a single study. Starker et al. compared 4D-CT with MIBI and USG for parathyroid localization and found that 4D-CT had improved sensitivity (85.7%) over MIBI (40.4%) and USG (48.0%) in parathyroid localization. (Starker et al., 2011) Similarly, Cheung et al. recently reported the results of a meta-analysis of preoperative localization techniques which included MIBI, USG and 4D-CT in patients with pHPT. They found a total of 43 studies which met their inclusion

criteria and of these, 19 studies were on USG, 9 studies on MIBI-SPECT and 4 studies on 4D-CT studies. USG had pooled sensitivity and PPV of 76.1% and 93.2%, respectively whereas MIBI-SPECT had a pooled sensitivity and PPV of 78.9% and 90.7%, respectively. 4D-CT had the highest sensitivity and PPV of 89.4% and 93.5%, respectively. Therefore, the authors concluded that MIBI-SPECT and USG had similar localization ability but 4D-CT may have improved accuracy. (Cheung et al., 2011)

3.1 Patients with negative preoperative localization studies

Patients with negative imaging represent an important subset of patients with pHPT because of increased frequency of multiglandular disease (38% vs 15% in patients with positive localization study). (Chan, R. K. et al., 2008) Because of the higher incidence of multiglandular disease, surgery needs to be conducted with a level of suspicion that multiglandular disease exists to ensure that all diseased glands are resected during the operation. In our experience, those with scan-negative and USG-negative results had significantly smaller sized parathyroid adenomas even if they only suffered from single gland disease.(Lo et al., 2007). The incidence of both MIBI- and USG-negative patients ranged between 12 - 18%. (Lo et al., 2007) One study compared the parathyroid histology between those with negative MIBI and with positive MIBI.(Mihai et al., 2006) They found that those with negative MIBI had a higher incidence of chief cells than those with positive MIBI, who had a higher incidence of oxyphilic cells. (Mihai et al., 2006)

4. Surgical management

While surgical intervention remains the only curative therapy for patients with hyperparathyroidism, conventional BNE with resection of enlarged parathyroid gland was the gold standard for treatment of pHPT. With the emerging preoperative and intraoperative localization technique as discussed in previous sections, focused-approach or MIP is coming to the throne.

4.1 Definition of cure

The general accepted definition of cure in publication is to achieve normocalcemia for at least 6 months postoperatively. Operative failure or persistent disease is defined as presence of hypercalcemia within 6 months of parathyroidectomy. Recurrent disease can be defined as recurrence of hypercalcemia after 6 months postoperative.

4.2 Surgical options

4.2.1 Conventional BNE

BNE is the traditional surgical approach for management of pHPT. In general it gives a successful rate of greater than 95% and with complication rate of less than 4%. It involved a classic transverse incision at skin crease of about 5cm. All 4 parathyroid glands were identified and examined. All the morphologically abnormal glands were removed. IOPTH can be used as an adjunct for confirmation of cure. In case the IOPTH was negative, extra dissection may be needed to identify ectopic glands. A delayed second stage operation with relocalization by imaging can be considered if ectopic glands could not be found intraoperatively. (Augustine et al., 2011)

4.2.2 MIP

MIP has now become the standard approach for surgical management of pHPT. It is the approach of choice for patients diagnosed with pHPT caused by a solitary parathyroid adenoma, and it is fast becoming an alternative approach in parathyroid reoperations. It comes in various forms and under various names; these include total endoscopic approach, video-assisted approach, radio-guided approach and mini-incision approach. In principle, however, they are similar, as they involve surgical excision of one single abnormal parathyroid gland (ie, adenoma) without disturbing the other three parathyroid glands. Therefore, a better collective name for them should be the focused approach.

Although the extracervical approaches have been described for both unilateral and BNE, they have not been adopted widely. (Ikeda et al. 2000; Lang 2010) Among the endocrine surgeons, the most popular approach remains the open mini-incision approach with no video assistance. The mini-incision approach in MIP is technically similar to the one in MIT. Essentially a 2 cm incision is made at the medial border of SCM. The site of incision is marked after performing a bedside USG in the operating theater. The incision site is placed close to the localized parathyroid adenoma such that minimal tissue dissection is required. Like the mini-incision approach in MIT, a subplatysmal space is developed, and the plane between SCM and strap is opened up. Once the common carotid artery is identified, it is important to dissect all the way down to the prevertebral fascia medial to the artery such that the thyroid lobe and parathyroid glands can be retracted medially. At this point, the parathyroid adenoma usually is identified and carefully excised in whole.

MIP is an operation associated with low morbidity and high success rates (greater than 95%), but the operating surgeon should be meticulous, familiar with the anatomy, and experienced. Unlike the traditional open method where all four parathyroid glands are identified, MIP requires accurate preoperative localization of the abnormal parathyroid gland before it can be attempted. This is because in MIP, the operating surgeon would not have the benefit of examining the other three parathyroid glands; therefore, there is a possibility of missing underlying multiglandular disease such as double adenomas or four-gland hyperplasia. In the author's center, over 70% of patients with newly diagnosed pHPT will be eligible for MIP because of a positive preoperative localization by MIBI or USG. (Lo et al. 2007) To further improve the surgical success of MIP and to minimize the possibility of persistent or recurrent HPT after MIP, some have advocated the routine use of various surgical adjuncts such as radioguided probes or a quick IOPTH at the time of operation, but to date, their routine use remains questionable because of the marginal benefit and the high cost-to-benefit ratio. Nevertheless, MIP with or without the use of adjuncts, when performed in experienced hands has an equivalent success rate of greater than 95%, as the conventional four-gland exploration, and has all the benefits one expects from minimally invasive surgery.

Similar to other minimally invasive procedures, MIP, when compared to conventional BNE, has obvious advantages as it decreases surgical morbidity in terms of cosmesis, pain, risk of recurrent laryngeal nerve injury, postoperative hypocalcaemia, etc. It can also reduce the cost, as well as the operative time and hospital stay. It is, in fact, currently an ambulatory surgery in many centres. Base on the fact that majority ~90% of patients with pHPT are having single hyperfunctioning adenoma, preoperative localization imaging

can often narrow down the pathology to the specific quadrant. A smaller, e.g. 2cm, incision is made over the suspected location of the adenoma. The authors adopted the lateral approach with dissection through the plane between the sternocleidomastoid muscle and the strap muscles. Dissection continued medial to the carotid artery to identify the prelocalised enlarged adenoma behind the thyroid gland. IOPTH can give extra confidence to the surgeon and to confirm cure of the disease. As we shall see later, there are increasing evidence that perhaps IOPTH may not be necessary, base on the fact that there is a high specificity of preoperative localization technique, especially in concordant MIBI and SUS. Udelsman et al. published data demonstrating the superior cure rate of MIP of 99.4% as compared to standard BNE of 97.1%.(Udelsman et al 2011). Suliburk et al also published the successful rate of MIP was as high as 98% even without IOPTH , depending on case selection.[6] The article also suggested that occult double adenoma was the major reason for failure. Among the 70% of the patients with double adenoma, the IOPTH has actually dropped by more than 50% after the first adenoma was removed. It is suggestive that the second adenoma remained dormant, or its function is suppressed until after the first adenoma is excised. Repeated MIBI scan after first operation can usually localize the second adenoma. On the other hand, in cases with hyperplasia or multiglandular disease (false positive MIBI), IOPTH may be useful. (Suliburk et al., 2011) [table 1] showed the published article on the outcome of MIP (Starker et al., 2011).

4.2.3 Endoscopic/video-assisted parathyroidectomy

Similar to MIP, endoscopic or video-assisted parathyroidectomy required accurate preoperative localization. Endoscopic instruments often provide better visualization of anatomic structures because of better lighting and magnification. An extra advantage of endoscope is that it can also facilitate mediastinal exploration from a transcervical approach.

5. IOPTH

Despite the fact that IOPTH has been commercially available for over 20 years, the issue of whether to routinely use it in MIP still remains unresolved. The arguments against its use mainly relates to the extra cost of the assay, the extra time required for the result to come back (i.e. extra theatre time), the inability in detecting multiglandular disease on some occasions and the limited added value in some select cases.(Stalberg et al., 2006; Suliburk, J. W. et al., 2011) Some groups without using IOPTH achieved similar cure rate as those with IOPTH. (Cho et al., 2011; Suliburk et al., 2011) As a result, some groups have advocated the use of IOPTH more selectively or in some situations such as in cases of discordant or equivocal localization studies. Kebebew et al. formulated a scoring system for this and suggested that patients with a score of 3 or more do not require IOPTH whereas a score of less than 3 would benefit from IOPTH. (Kebebew et al., 2006) Although these arguments may be true, most surgeons including us still prefer using IOPTH routinely in MIP. Some would argue that it is the “feel-good” factor which is important when performing this sort of a limited, focused approach parathyroidectomy because the surgeon do not have the benefit of looking at the other parathyroid glands and furthermore, the surgeon would be able to tell the patients and their relatives confidently that the IOPTH did drop after excision of the parathyroid gland.

First Author, Journal, year	Study design	Patient No.	Preoperative localization method	Success rate	Intraoperative Adjuncts	Criteria
Untch et al; J Am Coll Surg; Apr 2011	Retrospective, 2001-2010	516	MIBI +/- USG	99.00%	IOPTH	50% reduction + normal
Suliburk et al; ANZ J Surg; Feb 2010	Retrospective, 1998-2008	1020	MIBI + USG	97.80%	No IOPTH	n/a
Hwang et al; Ann Surg; Jun 2010	Prospective, 2006-2009	280	MIBI-SPECT + USG	97.90%	IOPTH in USG +ve/MIBI -ve	Miami criterion (50% reduction)
Lew et al; Surgery; Dec 2009	Retrospective, 1993-1998	173	MIBI	98.00%	IOPTH +/- BIJVS	Miami criterion (50% reduction)
Lew et al; Arch Surg; Jul 2009	Retrospective, 1993-2009	845	MIBI +/- USG	97.10%	IOPTH	Miami criterion (50% reduction)
Gill et al; Otolaryngol Head Neck Surg; Feb 2011	Retrospective 2005-2009	83	MIBI	97.00%	IOPTH	Miami criterion (50% reduction)
Udelsman et al; Ann Surg; Mar 2011	Retrospective 1998-2009	1037	MIBI / USG	99.40%	IOPTH	Miami criterion (50% reduction)
Quillo et al; Am Surg; Apr 2011	Retrospective, 1999-2007	198	MIBI	100% (MIBI neg excluded)	Radioguided	Norman 20% rule
Adil et al; Otolaryngol Head Neck Surg; Mar 2009	Retrospective, 1997-2007	368	MIBI	100% (MIBI neg excluded)	Radioguided	Norman 20% rule
Fouquet et al; Langenbecks Arch Surg; Aug 2010	Retrospective 2001-2008	387	MIBI + USG	98.00%	Total endoscopic lateral parathyroidectomy, IOPTH	Miami criterion (50% reduction)
Politz et al; Endocr Pract; Nov 2006	Retrospective, 2001-2004	118	MIBI	98% (MIBI neg excluded)	Radioguided	n/a
Pang et al; Br J Surg; Mar 2007	Retrospective, 2000-2005	500	MIBI +/- USG	97.40%	No IOPTH	n/a
Mihai et al; Br J Surg; Jan 2007	Retrospective, 2001-2006	298 (150 MIP, 148 BNE)	MIBI + USG	97.30%	No IOPTH	n/a
Cohen et al; Surgery; Oct 2005	Retrospective 1999-2004	139	MIBI-SPECT +/- USG	98.60%	IOPTH	Miami criterion (50% reduction)

Table 2. Summary of recent studies on MIP, respective preoperative localization and intraoperative adjuncts.

Nevertheless, the basis for using IOPTH in MIP is that after the removal of the hyperfunctioning or hypersecreting parathyroid adenoma or tissue, the serum PTH would drop and return to its normal range after a certain length of time provided that the remaining unexcised parathyroid glands are normal or not hyperfunctioning. Since the half-life of PTH is only 2-3 minutes in the presence of normal renal function, the recommendation is that one would anticipate a 50% drop from the pre-excision IOPTH level in 10 minutes after excision of the abnormal parathyroid gland. The earliest method for monitoring IOPTH was described by Irvin et al. in 1991 and the recommendation for a 50% decline from preexcision IOPTH level was established in 1993. (Irvin et al., 1991, 1993) This is now known as the “Miami criterion”. In this criterion, a successful parathyroid operation is defined as a 50% or more decline from the highest preincision or preexcision IOPTH obtained 10 minutes after excision of the hyperfunctioning parathyroid gland. Therefore, as a surgeon who is using IOPTH, we have shifted the operation end-point from the conventional concept of “abnormal” parathyroid glands based on size and histology in the era of BNE exploration to the current concept of “hyperfunctioning” parathyroid glands with MIP and IOPTH monitoring. However, this shifting in concept still remains somewhat controversial. For example, we recently analyzed 161 consecutive patients who underwent parathyroidectomy (with the majority being MIP) for pHPT at our institution and found that approximately 40% of patients remained to have elevated PTH despite all had normocalcemia (i.e. eucalcemic PTH elevation) at 6-month and had > 50% decline in IOPTH at the time of operation. (Lang et al, 2011) This finding appeared to be consistent to other studies. (Oltmann et al., 2011) Siperstein et al. showed that preoperative localizing studies and IOPTH failed to identify multiglandular disease in at least 16% of pHPT patients if routine BNE was employed in all patients. (Siperstein et al., 2008) This issue certainly raises concerns on whether by performing MIP and following the IOPTH criterion may lead to higher recurrences in the future. However, in many of the large (>1000 cases) series of image-guided MIP with IOPTH, it is reassuring to find that the long-term cure rate does not appear to be inferior to conventional BNE. (Udelsman et al 2011; Suliburk, J. W. et al, 2011)

The other issue relates to which is the best criterion for IOPTH in terms of highest sensitivity, and accuracy. There have been several studies comparing strategies for IOPTH testing. (Chiu et al., 2006; Carneiro et al., 2003; Barczynski et al., 2009) Barczynski et al. studied 260 patients with presumed solitary parathyroid adenomas based on concordant localization studies. The Miami criterion had the highest accuracy (97%) compared to the Halle (PTH level low normal at 15 minutes), Rome (>50% decline to normal at 20 minutes and / or < 7.5ng/L lower than the 10-minute value), and Vienna (≥50% decline at 10-minutes) criteria. However, in this series, only 3.5% of patients had multiglandular disease and that is comparably low when it is believed that in the era of MIP, the incidence of multiglandular disease would be in the region of 10%. Since multiglandular disease remains one of the biggest downfalls or weaknesses of IOPTH, some groups have advocated to use a more stringent criterion. The Mayo clinic recently reported their experience of 1882 patients. In their series, the incidence of multiglandular disease was 22.0% and they defined a successful exploration as 1 50% or more decline in IOPTH level from baseline and a normal or near-normal IOPTH level at 10 minutes postexcision. They compared this criterion (or the Mayo criterion) with the Miami criterion and found that the Miami criterion would have missed 22.4% of patients with multiglandular disease. They concluded that relying on a 50%

decrease alone potentially increases the rate of operative failure in patients with multiglandular disease.(Richards et al., 2011) Therefore, it would appear that which is the best IOPTH criterion or strategy depends on the incidence of multiglandular disease at your own institution. In our experience, we believe the Miami criterion is the most convenient criterion, given the fact that we encounter very few multiglandular disease in our locality.(Lang et al, 2010, 2011)

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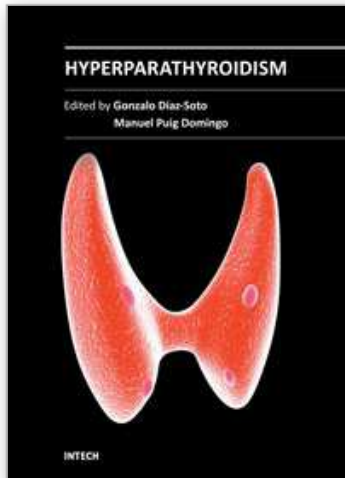
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This book is the result of the collaboration between worldwide authorities of different specialities in hyperparathyroidism. It aims to provide a general but deep view of primary/secondary and tertiary hyperparathyroidism, from a physiological basis to hyperparathyroidism in hemodialyzed patients, as well as new treatment approaches, techniques and surgical scenarios. We hope that the medical and paramedical researchers will find this book helpful and stimulating. We look forward to sharing knowledge of hyperparathyroidism with a wider audience.

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