# **Parathyroid Surgery**

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# Abstract

Parathyroid surgery for hyperparathyroidism is a safe and effective strategy for durably reducing PTH hypersecretion and improving and/or reversing systemic consequences such as bone density loss and nephrocalcinosis. This overview provides a summary of currently available operative approaches for primary, secondary, and tertiary forms of hyperparathyroidism. Multidisciplinary communication is valuable at all phases of management. Surgeons should clearly communicate key details such as the method of parathyroid surgery and the extent of exploration (how many parathyroid glands were examined). The expertise of a surgeon, or specialized care for patients with parathyroid disease, is associated with improved outcomes. Parathyroid surgery remains the most effective method of treating hyperparathyroidism and can be accomplished with minimal morbidity. Long-term follow-up of patients who have been treated with parathyroidectomy is important to monitor for successful maintenance of normal calcium balance and resolution of sequelae of hyperparathyroidism.

#### Keywords

Parathyroidectomy • Cryopreservation • Autotransplantation • Intraoperative measurement of parathyroid hormone • Neck exploration

# The Evolution of Parathyroid Surgery

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M. Milas, MD The Thyroid Center, Department of Endocrine Surgery, Cleveland Clinic, 9500 Euclid Ave F20, Cleveland, OH 44195, USA Surgical management of parathyroid disease has evolved in response to several fundamentally new and important developments. Instead of being a rare endocrine disorder, primary hyperparathyroidism (PHPT) now accounts for the most common cause of hypercalcemia in the outpatient population, with estimated prevalence of 1 in 500 women and 1 in 2,000 men [1]. More patients are being diagnosed in earlier phases of PHPT in part incidentally because calcium has become a routine component of automated chemistry panels, and in part because practitioners are also recognizing the need to screen patients with osteoporosis, osteopenia, and kidney stones more comprehensively for underlying PHPT with panels that include calcium, intact parathyroid hormone (PHPT), and 25-hydroxyvitamin D levels. Technological innovations have also expanded the options available for parathyroid surgery. Once conducted predominantly via bilateral neck exploration, parathyroidectomy is now approached via a focused exploration to a radiologically identified abnormality [2]. Multiple methods of performing parathyroidectomy are available, and expertise in this surgery requires not only knowledge in evaluating parathyroid glands but also selection of operation appropriate for a specific patient's parathyroid diagnosis [3–5]. Several multidisciplinary publications have offered guidelines for the indications and timing of parathyroid surgery, in response to these epidemiologic and technologic shifts and to the challenge of what constitutes best treatment for apparently asymptomatic PHPT [6-8]. Despite these guidelines, patients with PHPT remain, as a group, under-referred and under-treated surgically [9]. This chapter catalogues the parathyroid operations in current surgical practice, while emphasizing those constant principles of management which are essential to surgical success.

## The Goals of Parathyroid Surgery

The operative goals for the treatment of proven PHPT include achievement of a durable normocalcemic state and normal PTH, avoidance of injury to the laryngeal nerves, completion of surgery with minimal postoperative morbidity and negligible mortality, and consideration of cosmetic scar appearance that is acceptable to the patient. The operative goals for the treatment of secondary or tertiary hyperparathyroidism (SHPT/THPT) are identical, although the longterm durability of normal PTH levels can be more challenging to achieve. Operating on a patient without a clear diagnosis of PHPT undermines the ability to achieve these goals, thus proper patient selection and confirmation of the diagnosis before surgery cannot be overemphasized.

# **Indications for Parathyroid Surgery**

In 2005, national professional associations of endocrine surgeons and endocrinologists jointly issued guidelines that operative management is clearly indicated for all patients with classic symptoms or complications of PHPT [7]. Less widespread has been the recognition that parathyroidectomy offers significant benefits to those with SHPT and THPT [10, 11]. Another challenge has been decision-making for those with apparently asymptomatic PHPT, not only in defining the timing of surgery (when to refer) but also, with some controversy, whether these patients require surgery. Experts organized by the National Institutes of Health in 2002 proposed parathyroidectomy for the following patients with PHPT: (1) those <50 years of age, (2) who cannot participate in appropriate follow-up, (3) with a serum calcium level >1.0 mg/dl above the normal range, (4) with urinary calcium >400 mg/24 h, (5) with a 30% decrease in renal function, or (6) with systemic complications of PHPT including nephrocalcinosis, osteoporosis (T-score lower than -2.5 SD at the lumbar spine, hip, or wrist), or a severe psychoneurologic disorder [12]. The development, timing, and progression of disease in patients with asymptomatic PHPT are difficult to predict. Long-term nonoperative management can be costly [13]. For these reasons, other experts have advised a more liberal approach to recommendations of parathyroidectomy beyond the NIH criteria, provided that surgery can be performed safely and with minimal risks for a disease that, in some patients, may be minimally problematic at the time of presentation [6, 8]. Thus, for example, parathyroidectomy may be appropriate to consider for patients with osteopenia (T-scores -1 to -2.5 SD) and mild neurocognitive symptoms. A recent multidisciplinary review advised, indeed, that surgery offers the best option for preventing or reversing complications of hyperparathyroidism and should

be considered in discussions about management options upon diagnosis [6].

Some patients with indications for parathyroidectomy may not be medically fit for surgery or have other reasons to forego parathyroidectomy. Percutaneous ethanol ablation, bisphosphonates, and calcimimetic agents are available nonoperative treatment options. The calcimimetic agents reduce calcium and PTH levels while administered, are more frequently administered to patients with SHPT, but their long-term impact on improving systemic consequences of hyperparathyroidism is unclear [14]. Frequently monitoring laboratory values, avoiding dehydration and excess calcium intake, and periodic re-assessment for surgery are important components of nonoperative management.

# Fundamental Concepts of Parathyroid Exploration

Parathyroid surgery relies on the knowledge of normal anatomical distribution of parathyroid glands, supranumerary and ectopic variations, and embryologic details that might affect the interpretation of parathyroid findings. It is also important to recognize variations of normal morphology and the spectrum of diseased parathyroid morphology. Proficiency with delicate surgery around the head and neck, upper mediastinum, and occasionally deeper intrathoracic mediastinal territory is necessary [15].

Although most patients receive some kind of parathyroid imaging studies, these are principally meant for localization of suspected site or sites of parathyroid disease, and not for diagnosis. A "positive" imaging study does not confirm the diagnosis of hyperparathyroidism (thyroid nodules can be a source of false positives, for example). A "negative" imaging study does not exclude the diagnosis of hyperparathyroidism. Because the risk of ectopic mediastinal or ectopic cervical parathyroid abnormalities is quite rare, conducting comprehensive bilateral neck exploration is possible without imaging studies and is advisable when imaging studies are negative. Indeed, this strategy has had a decades-long successful track-record [15–19]. Preoperative imaging is valuable, however, as it facilitates focal explorations and expedient surgery, and can alert to more challenging scenarios of ectopic or multigland disease.

Treatment of single adenomas is simple excision of the abnormal gland. Multigland hyperplasia is ideally treated with subtotal parathyroidectomy and parathyroid cryopreservation. While abnormal parathyroid glands need to be removed to ensure cure of hyperparathyroidism, it is likewise important to safeguard the viability of normal parathyroids and avoid hypoparathyroidism. Normal parathyroid glands are approximately 5–6 mm in greatest dimension, weigh 15-35 mg, and can be inconspicuous with their orange-tan color embedded or flattened within a surrounding yellow fatty tissue envelope (Fig. 20.1). The appearance of parathyroids can be variable even when they are biochemically functioning normally. When diseased, parathyroid glands may display variable morphological changes in size, shape, texture, and firmness (Fig. 20.2). For example, the median size (and range) of an individual abnormal parathyroid gland size varies with disease type: 700 mg (200-10,000 mg) for single adenomas, 150 mg (75-200 mg) in primary hyperplasia, and 1,000 mg (200–10,000 mg) for secondary hyperplasia [15]. Abnormal parathyroids are generally fuller in all dimensions, have a darker brown or reddish-brown color, and do not compress easily or are significantly firm when gently probed. They may have an irregular and knobby shape, more prominent vascular pedicles, or a plexus of vasculature. Glands of patients with secondary and THPT may be sclerotic and light in color from this fibrosis. There is ongoing interest and some controversy in defining what truly constitutes an abnormal parathyroid, and whether this is a matter of purely morphological form, biochemical function, or a combination of both.

In general, the search for parathyroid glands along the usual anatomical distribution of superior ("upper") and inferior ("lower") parathyroids can be viewed as a "primary parathyroid survey" [15]. It takes into consideration exploring all the regions shown in Fig. 20.3 until the remaining



Fig. 20.1 Examples of normal parathyroid glands (arrows)

three parathyroids have been identified. It is useful to develop a systematic order of exploration and practice it routinely. A convenient strategy is to target exposure of the most abnormal parathyroid first, then the ipsilateral parathyroid, and finally explore the contralateral side. When all parathyroids have been identified, assessment about the disease process (single adenoma, double adenoma, or hyperplasia) can be made and a decision about which parathyroids to remove and in what order can be determined. A "secondary parathyroid survey" refers to exploration of cervical regions when parathyroid position is more unusual or ectopic, and when the above primary survey has not led to conclusive findings (Fig. 20.4) [15]. Important areas to examine are retroesophageal spaces, where parathyroid glands are most commonly missed because they have



**Fig. 20.2** Variable morphology of normal parathyroid glands (**a**), abnormal parathyroid glands (**b**), and parathyroid hyperplasia by illustrations (**c**) and in a surgical examples (**d**) of multigland disease (*left*) and single

adenoma (SA) (*right*). (**a**–**c**) Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2008–2011. All Rights Reserved



Lower

**Fig. 20.3** Expected distribution of superior (*upper*) and inferior (*lower*) parathyroid glands where abnormalities develop. Reprinted with permission, Cleveland Clinic

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sunken into the deep posterior space behind the tracheoesophageal groove, often lying on the anterior surface of the spine and below the main trunk of the inferior thyroid artery (Fig. 20.5) [20]. Other regions include the thymus, carotid and jugular sheath, and consideration of intrathyroidal parathyroid glands (which can be suspected from preoperative ultrasound). The secondary survey should *not* be performed just to locate a normal parathyroid, but a missing pathologic gland. In these cases, the thymus should be retracted out of the mediastinum as far as possible

without avulsion, carefully examined, palpated, and removed (Fig. 20.6). For clearly mediastinal parathyroid glands, surgery often entails collaboration with thoracic surgeons, as operative approaches are tailored to the anatomical location within the chest and can include thoracotomy, median sternotomy, and various thoracoscopic surgeries [21].

The detailed description of operative findings is more important than the actual technology or method involved with parathyroid surgery. Thus, the operative report should specify what



**Fig. 20.4** Distribution of parathyroid glands found at reexploration for persistent and recurrent disease, providing the basis for a "secondary survey" at the time of parathyroidectomy. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2008–2011. All Rights Reserved

**Fig. 20.5** The retroesophageal area is the most common source of missed parathyroid abnormalities. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2008–2011. All Rights Reserved

parathyroid site or sites were explored (the intent and the extent of surgery), whether any ectopic regions needed evaluation, and the diagnosis based on the findings. The incisional length, the anesthetic or perioperative care, or the use of qualifiers such as "minimally invasive surgery" do not sufficiently describe what pathology was investigated and ultimately found. Instructive, for example, would be procedure titles such as "one-gland parathyroid exploration endoscopically via midline incision," "two-gland parathyroid exploration via robotic trans-axillary approach," "four-gland parathyroid exploration via 3 cm midline incision," "one-gland parathyroid exploration via 5 cm lateral neck approach," and "with or without radioguidance or IOPTH" added as qualifiers.

# Surgical Options in Performing Parathyroidectomy

# **Bilateral Exploration**

This approach involves directed and systematic examination of all four parathyroid glands in their expected anatomical distributions. It can be considered comprehensive parathyroid examination, in contrast to the majority of other operations which are focused on identifying just one suspected abnormality [17–19]. Bilateral exploration can be performed in a minimally invasive way, with small incisions and gentle dissection. The relevance of bilateral or comprehensive parathyroid exploration is that some patients have



**Fig. 20.6** Cervical thymectomy (**a**) removes abnormal ectopic parathyroid glands, as shown in operative specimen of single adenoma (**b**) with typical brown appearance

surrounded by yellow thymic fat. (a) Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2008–2011. All Rights Reserved

significantly higher risk for multigland parathyroid disease (Table 20.1) and achieving normocalcemia is contingent on the evaluation of all parathyroid glands and the appropriate resection of those that are functionally and/or morphologically abnormal. Awareness of patterns of multigland disease, such as the asymmetric distribution of double adenomas to favor superior parathyroid glands is helpful. A recent survey of parathyroid surgeons, as well as published reports on large patient case series, have indicated that bilateral parathyroid exploration may be required in up to 30% of patients who are referred for surgery, and that a decision to convert from focal to bilateral exploration occurs intraoperatively in an additional 10% of patients [2]. **Table 20.1** Indications for bilateral exploration of parathyroid glands as the initial surgery for primary hyperparathyroidism

Absolute indications
Known or suspected multiple endocrine neoplasia syndromes
Intraoperative PTH fails to drop after resection of suspected single adenoma
Failure to find diseased gland at location indicated by imaging studies
Finding more than one abnormal parathyroid during intended focal or unilateral neck exploration
Negative imaging studies
Imaging studies suggesting multiple sites of disease
Co-existing thyroid cancer or bilateral goiter requiring total thyroidectomy
Advisable indications
Discordant parathyroid imaging studies
Unavailability of intraoperative PTH measurement
Inability to obtain preoperative imaging
Lithium-induced PHPT
Non-MEN familial hyperparathyroidism
Co-existing thyroid pathology that may require operative intervention
Surgeon preference or experience

### **Focal Exploration**

Focal exploration of one parathyroid site, guided by radiologic identification of suspected disease at that location, is the prevailing approach to modern parathyroid surgery [2, 22–25]. It is most often accompanied by intraoperative measurement of parathyroid hormone (IOPTH), although more recent reports are raising the possibility of conducting focal exploration without IOPTH [26]. The radiologic modalities useful for localization include Tc99-sestamibi scan, neck ultrasonography, fourdimensional computed tomography, and magnetic resonance imaging, while other types are reserved for use in challenging or re-operative parathyroid cases [27-32]. There are numerous methods of Tc99-sestamibi imaging and some can be more effective at localization of parathyroid disease [30]. It is important for a surgeon especially, and even nonsurgical specialists caring for patients with hyperparathyroidism, to know which method is used in their patients and become familiar with viewing and critically scrutinizing the images.

The sequence of operation is simple: a small incision is placed for optimal exposure of the underlying parathyroid gland, the abnormal gland is identified, IOPTH is measured before removing the gland and also 10 min afterwards, expecting that a drop of at least 50% in IOPTH value becomes the metric of disease cure and signals end of the operation.

## Limited

Limited parathyroid exploration refers to the examination of both parathyroids on one side of the neck, or some contralateral combination that evaluates more than one, but less than the full complement of glands. It is often an incidental rather than planned approach, although some surgeons prefer to assess both unilateral parathyroid glands, even when only one is expected to be diseased [2].

# Radioguided

The concept of radioguidance during surgery has been applied in two ways: the use of Tc-99 sestamibi injected before surgery to aid detection of an abnormal parathyroid in situ and the use, after similar injection, to judge the nature of parathyroid disease ex vivo after excising abnormal and biopsying normal parathyroid glands [33–38]. The radioactivity counts are obtained with a small hand-held, pencil-like probe and quantitatively displayed on a monitor. This approach has probably had most success in the latter, ex vivo application. The radioguided approach can also be helpful during surgery for ectopic mediastinal disease that requires sternotomy, here again performing better to confirm an abnormal parathyroid contained within the excised tissue. The strong background signals from adjacent thyroid tissue in the neck, or large vasculature and cardiac structures in the mediastinum, which both take up the radioisotope, limit its usefulness to pinpoint small areas of signal unique to the parathyroid in vivo.

# Technical Innovations in Surgical Approach

A number of surgical approaches have been developed that can accomplish bilateral, focal, or limited parathyroid operations with innovative means, whether technical or cosmetic in nature. These include operating via smaller neck incisions (2-3 cm) using endoscopic tools and highdefinition monitors that provide excellent visual display while allowing minimal dissection [23, 24]. The endoscopic and videoscopic equipment can function via incisions that are placed outside the neck region, such as in axillary folds and periareolar breast lines. Recently, robotic technology has emerged via a transaxillary approach, demonstrating feasibility but cautioning that its ultimate benefits and indications require further study [39].

# Special Circumstances in Parathyroid Surgery

The descriptions of the basic surgical techniques above are most applicable to first-time parathyroid operations, where the epidemiology of PHPT particularly is expected to reveal a single adenoma. Nuances in surgical care are present for patients who undergo re-operative parathyroid surgery or have confirmed multigland disease from a number of etiologies-sporadic PHPT, hereditary syndromes such as the multiple endocrine neoplasias (MEN) and familial hyperparathyroidism, and SHPT or THPT. An individualized treatment plan is critical for these patients, taking into account all of the relevant details of their medical histories, including prior operations, imaging findings, and possible risks of higher long-term recurrence rates, such as seen with MEN patients and SHPT.

### Subtotal Parathyroid Resections

When multiple abnormal parathyroid glands exist, surgical treatment has to balance the need to excise abnormal tissue with the need to have an adequate residual amount that maintains normal calcium and PTH balance. When two or three parathyroid glands are abnormal, the residual one or two normal glands are more than sufficient for this task. However, when all four parathyroid glands are abnormal, then the residual portion has to be crafted from one of the abnormal glands. This can be accomplished by leaving a small quantity of one parathyroid in situ, supplied by its own vascular pedicle, or by removing the entirety of parathyroids from their deep cervical location and autografting a small portion into another superficial site, where new vascular supply must be recruited [15]. A number of superficial locations have been used for this purpose, including the sternocleidomastoid muscle, the brachioradialis muscle of the nondominant forearm, and subcutaneous tissue pockets of the anterior chest wall. The definition of "small" is best judged by the operating surgeon. If there is availability to cryopreserve parathyroid tissue, more generous resection can be undertaken, leaving remnants that may be only  $5 \times 3 \times 2$  mm or about 25 mg in aggregate. If there is concern about viability or adequacy of parathyroid volume, or lack of cryopreservation, then the surgeon must estimate what "subtotal" degree of resection is best. In general, the aim is to leave remnants that might be equivalent to one normal parathyroid gland, significantly reducing the volume of abnormal glands which can be three- to tenfold hypertrophied.

The need for subtotal resections affects those patients with sporadic HPT, familial hyperparathyroidism and MEN, SHPT, and most patients with THPT. Cervical thymectomy is recommended for these patient groups, in order to remove small foci of ectopic parathyroid tissue in the thymus which are expected to be hyperplastic as well. The preferred surgery for those patients with primary sporadic hyperplasia or familial disease is subtotal parathyroidectomy that leaves a neck remnant in situ [40]. By contrast, patients with SHPT have benefited from total parathyroidectomy, leaving no residual parathyroid tissue, and near-total parathyroidectomy with extremely minimal amounts of tissue left in the neck or autotransplant sites [10, 11]. When there is concern to avoid any future re-operations in the neck, then autotransplantation into the brachioradialis muscle, especially in SHPT patients still undergoing dialysis, is convenient. Ideally, any of these operative interventions are accompanied by parathyroid cryopreservation.

### Parathyroid Autotransplantation

This process of autotransplantation or autografting involves mincing parathyroid tissue into 2–3 mm fragments that are then inserted between muscle fibers or subcutaneous tissue pockets. They eventually become vascularized and function equally well to sense and regulate calcium balance from these new locations. This process is feasible using normal parathyroid tissue or benign hyperplastic tissue derived from multigland disease or single adenomas. Obviously, autografting too much tissue derived from a hyperplastic source is prone to regrowth and recurrent hyperparathyroidism that may require re-excision. Parathyroid autotransplantation is also the process by which patients who become severely hypocalcemic after parathyroid surgery can be rescued, provided they had autologous parathyroid tissue cryostored from the original surgery.

# **Parathyroid Cryopreservation**

This process involves mincing excess parathyroid tissue obtained at the time of parathyroidectomy (Fig. 20.7) into 2–3 mm fragments which are then processed with serum and other protective substances for long-term storage at  $-80^{\circ}$ F [15, 41]. They can be unthawed, prepared in a sterile fashion, and re-implanted into muscle or subcutaneous tissue. Viability tapers off with longer time in cryostorage, with decreasing chance of succesful grafting when using tissue stored for more than 2–3 years [42].



**Fig. 20.7** Patients undergoing subtotal parathyroidectomy (**a**) benefit from parathyroid cryopreservation preparation (**b**) which may be needed for concomitant or later

autotranplantation (c). (a) Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2008–2011. All Rights Reserved





Fig.20.7 (continued)

# **Parathyroid Re-operation**

Because of scarring from prior operations that increases surgical risks and the potential to cause hypocalcemia from repeat surgery, parathyroid reoperations aim to explore only the focus of recurrent or missed parathyroid disease, rather than comprehensive bilateral dissection. Re-operations should not be embarked on without radiologic localization, and even the criteria for relying on imaging are stricter than at initial surgery: at least two imaging studies have to agree on the same site when a single parathyroid abnormality is anticipated or the same pattern of expected disease, if it is multigland in nature. The potential for parathyroid autotranplantation and need for parathyroid cryopreservation is higher with re-operative surgery. A thoughtful, methodical, and detailed strategy is essential for treatment of patients with recurrent or persistent hyperparathyroidism [43–45].

# **Parathyroid Carcinoma**

This has an incidence of less than 1% of all parathyroid operations and is not a multigland phenomenon. The surgery requires not just excision of the malignant parathyroid but also ipsilateral thyroid lobectomy and central neck dissection. It is not unusual for parathyroid cancer to invade the recurrent laryngeal nerve and have higher potential for postoperative hoarseness. In these cases, the decision to explore the contralateral parathyroids may be tempered by the need to avoid additional complications.

# Concomitant Thyroid Surgery for Thyroid Disease

As many as 40% of patients with hyperparathyroidism may have co-existing thyroid disease, ranging from nonoperative conditions such as hypothyroidism and thyroiditis to nodular goiters (Fig. 20.8). This may become apparent preoperatively during examination or imaging, or intraoperatively. Use of neck ultrasound during parathyroid diagnostic evaluation allows identification of thyroid disease ahead of surgery and can identify more precisely those patients who may require partial or total thyroidectomy during the course of parathyroid surgery. A 4% incidence of previously undiagnosed thyroid cancer can be expected among patients undergoing parathyroid surgery [46–48].

# Perioperative Care

A thorough discussion of realistic benefits from parathyroid surgery and potential risks should precede any parathyroid operation. The overall risks associated with parathyroid surgery are small, and the aggregate of transient and permanent complications ought to be less than 5% [49, 50]. Infections occur exceptionally rarely with parathyroidectomy. Neck hematomas requiring operative evacuation and permanent hoarseness from recurrent laryngeal nerve injury should likewise be minimal (0.5–1%). There must be



**Fig. 20.8** Example of concomitant thyroid pathology in the form of a hyperplastic nodule (Thy) requiring thyroid lobectomy at the time of excision of large single parathyroid adenoma (SA). Both were evident on thyroid ultrasound

delicate tissue handling to avoid damage to normal parathyroids or disruption of abnormal glands. The actual tissue of these structures should never be grasped itself; rather, forceps and instruments should handle the surrounding fatty tissue, filmy adventitia, or vessels. Transient hypocalcemia can readily be treated with calcium and vitamin D supplements when there is a known sufficient quantity of residual parathyroid tissue. Long-term hypocalcemia becomes a greater risk (thought still rare at <1%) with subtotal or near-total excision of multigland parathyroid hyperplasia. The need to re-implant cryopreserved parathyroid tissue usually becomes evident within 6 months of surgery if the cervical remnants become nonfunctional. The potential for missed ectopic or supranumerary parathyroids and persistent or recurrent hyperparathyroidism (1-2%) should be discussed with patients before surgery to properly inform expectations of surgery.

Parathyroid surgery can be performed with local/regional anesthesia or a general anesthetic [2, 51]. Postoperative management as an inpatient hospitalization, outpatient visit or overnight observation is contingent on many factors, including the patient's type of parathyroid disease and overall health, the operation that was performed and surgeon's preference in management, and regional hospital and insurance requirements [2]. The incisional discomfort from parathyroid surgery is usually minimal and treated by over-thecounter analgesics. Recuperation with full return to normal activities and work occurs typically in a week. Long-term management relies on diligent monitoring of calcium and PTH levels to observe durable cure of hyperparathyroidism. A full biochemical panel that includes calcium, PTH, and vitamin D levels should be checked at 2 weeks after surgery during the first postoperative visit, then at 6 months and then annually for the remainder of the patient's lifetime. Transient SHPT from vitamin D deficiency in an otherwise cured patient can be seen in up to 20-30% of patients in the first year after surgery and requires reassurance (of both patient and referring physicians), treatment, and monitoring [52]. It is important to ensure that the patient receives adequate calcium and vitamin D supplementation after surgery. Minimal daily calcium carbonate or citrate supplementation is 500-600 mg taken 2-3 times daily. Depending on the degree of vitamin D deficiency, some patients may require overthe-counter supplements of 800-2,000 IU daily of vitamin D3 cholecalciferol, while others need a prescription-level strength such as 50,000 IU ergocalciferol weekly (for 25-hydroxyvitamin D <20 ng/ml) and very rarely 0.25 or 0.5  $\mu$ g daily of calcitriol (for 1,25-dihydroxyvitamin D

deficiency or significant hypocalcemic symptoms). These patients should be re-evaluated with blood tests at 3 months after surgery to determine the need for ongoing vitamin D supplementation. Durable cure after comprehensive parathyroidectomy means 95–98% success rate, with 2–5% of patients at risk to develop recurrent hyperparathyroidism.

# Conclusion

Parathyroid surgery for hyperparathyroidism is a safe and effective strategy for durably reducing PTH hypersecretion and improving and/or reversing systemic consequences such as bone density loss and nephrocalcinosis. This overview provided a summary of currently available operative approaches for primary, secondary, and tertiary forms of hyperparathyroidism. Multidisciplinary communication is important at all phases of management, and is valuable postoperatively to know what type and extent of parathyroid surgery was performed. The expertise of a surgeon or specialized care for patients with parathyroid disease is associated with improved outcomes [50]. Parathyroid surgery remains the most effective method of treating hyperparathyroidism and can be accomplished with minimal morbidity. Long-term follow-up of patients who have been treated with parathyroidectomy is essential to monitor for successful maintenance of normal calcium balance and resolution of sequelae of hyperparathyroidism.

### References

- Mazzaglia PJ, Berber E, Kovach A, Milas M, Siperstein A. The changing presentation of hyperparathyroidism over three decades. Arch Surg. 2008;143: 260–6.
- Greene A, Mitchell J, Davis R, Barbosa G, Tsinberg M, Berber E, et al. National trends in parathyroid surgery from 1997–2007: a decade of change. J Am Coll Surg. 2009;209:332–43.
- Phitayakorn R, McHenry CR. Parathyroidectomy: overview of the anatomic basis and surgical strategies for parathyroid operations. Clin Rev Bone Miner Metabol. 2007;5(2):89–102.

- Terris DJ, Stack Jr BC, Gourin CG. Contemporary parathyroidectomy: exploiting technology. Am J Otolaryngol. 2007;28(6):408–14.
- Lew JI, Solorzano CC. Surgical management of primary hyperparathyroidism: state of the art. Surg Clin North Am. 2009;89(5):1205–25. Review.
- Udelsman R, Pasieka JL, Sturgeon C, et al. Surgery for asymptomatic primary hyperparathyroidism: proceedings of the third international workshop. J Clin Endocrinol Metab. 2009;94(2):366–72.
- AACE/AAES Task Force on Primary Hyperparathyroidism. The American Association of Clinical Endocrinologists and the American Association of Endocrine surgeons position statement on the diagnosis and management of primary hyperparathyroidism. Endocr Pract. 2005;11(1):49–54.
- Bilezikian JP, Khan AA, Potts Jr JT. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the third international workshop. third international workshop on the management of asymptomatic primary hyperthyroidism. J Clin Endocrinol Metab. 2009;94(2):335–9.
- Wu B, Haigh PI, Hwang R, et al. Underutilization of parathyroidectomy in elderly patients with primary hyperparathyroidism. J Clin Endocrinol Metab. 2010;95(9):4324–30.
- Pitt SC, Sippel RS, Chen H. Secondary and tertiary hyperparathyroidism, state of the art surgical management. Surg Clin North Am. 2009;89(5):1227–39.
- Milas M, Weber CJ. Near-total parathyroidectomy is beneficial for patients with secondary and tertiary hyperparathyroidism. Surgery. 2004;136(6):1252–60.
- Bilezikian JP, Potts Jr JT, Fuleihan G-H, et al. Summary statement from a workshop on asymptomatic primary hyperparathyroidism: a perspective for the 21st century. J Bone Miner Res. 2002;17 Suppl 2: N2–11.
- Zanocco K, Angelos P, Sturgeon C. Cost-Effectiveness analysis of parathyroidectomy for asymptomatic primary hyperparathyroidism. Surgery. 2006;140(6): 874–81. discussion 881–2.
- Wüthrich RP, Martin D, Bilezikian JP. The role of calcimimetics in the treatment of hyperparathyroidism. Eur J Clin Invest. 2007;37(12):915–22.
- Ritter H, Milas M. Parathyroidectomy: bilateral neck exploration. In: Terris D, editor. Operative techniques in otolaryngology. St. Louis, MO: Elsevier; 2009. p. 44–53.
- Ruda JM, Hollenbeak CS, Stack Jr BC. A systematic review of the diagnosis and treatment of primary hyperparathyroidism from 1995 to 2003. Otolaryngol Head Neck Surg. 2005;132(3):359–72.
- Siperstein A, Berber E, Wagner K, Alghoul M, Stephen A, Milas M. Prospective evaluation of sestamibi, ultrasound, and rapid PTH to predict the success of limited exploration for sporadic primary hyperparathyroidism. Surgery. 2004;136:872–80.
- Siperstein A, Berber E, Barbosa G, Tsinberg M, Greene A, Mitchell J, et al. Predicting success of limited exploration for 10 hyperparathyroidism using ultra-

sound, sestamibi scan, and intraoperative PTH: analysis of 1,055 cases. Ann Surg. 2008;248(3):420–8.

- Moalem J, Guerrero M, Kebebew E. Bilateral neck exploration in primary hyperparathyroidism—when is it selected and how is it performed? World J Surg. 2009;33(11):2282–91.
- Perrier ND, Edeiken B, Nunez R, Gayed I, Jimenez C, Busaidy N, et al. A novel nomenclature to classify parathyroid adenomas. World J Surg. 2009;33(3): 412–6.
- Iacobone M, Mondi I, Viel G, Citton M, Tropea S, Frego M, et al. The results of surgery for mediastinal parathyroid tumors: a comparative study of 63 patients. Langenbecks Arch Surg. 2010;395(7):947–53.
- Miccoli P. Parathyroid surgery: we only need a minimal surgical approach. J Endocrinol Invest. 2005; 28(6):570–3.
- Seybt MW, Terris DJ. Minimally invasive thyroid and parathyroid surgery: where are we now and where are we going? Otolaryngol Clin North Am. 2010; 43(2):375–80.
- 24. Miccoli P, Berti P, Materazzi G, Ambrosini CE, Fregoli L, Donatini G. Endoscopic bilateral neck exploration versus quick intraoperative parathormone assay (qPTHa) during endoscopic parathyroidectomy: a prospective randomized trial. Surg Endosc. 2008; 22(2):398–400.
- 25. Lew JI, Irvin 3rd GL. Focused parathyroidectomy guided by intra-operative parathormone monitoring does not miss multiglandular disease in patients with sporadic primary hyperparathyroidism: a 10-year outcome. Surgery. 2009;146(6):1021–7.
- 26. Sugino K, Ito K, Nagahama M, Kitagawa W, Shibuya H, Ohkuwa K, et al. Minimally invasive surgery for primary hyperparathyroidism with or without intraoperative parathyroid hormone monitoring. Endocr J. 2010;57(11):953–8.
- Milas M, Stephen A, Berber E, Wagner K, Miskulin J, Siperstein A. Ultrasound for the endocrine surgeon: a valuable clinical tool to enhance diagnostic and therapeutic outcomes. Surgery. 2005;138:1193–201.
- Solorzano CC, Lee TM, Ramirez MC, Carneiro DM, Irvin GL. Surgeon-performed ultrasound improves localization of abnormal parathyroid glands. Am Surg. 2005;71(7):557–62. discussion 562–3.
- Gurney TA, Orloff LA. Otolaryngologist—head and neck surgeon—performed ultrasonography for parathyroid adenoma localization. Laryngoscope. 2008; 118(2):243–6.
- Sharma J, Mazzaglia P, Milas M, Berber E, Schuster D, Halkar R, et al. Radionuclide Imaging for hyperparathyrodism: which is the best <sup>99</sup>Tc-sestamibi modality? Surgery. 2006;140:856–65.
- Rodgers SE, Hunter GJ, Hamberg LM, Schellingerhout D, Doherty DB, Ayers GD, et al. Improved preoperative planning for directed parathyroidectomy with 4-dimensional computed tomography. Surgery. 2006; 140(6):932–40. discussion 940–1.
- Yen TW, Wang TS, Doffek KM, Krzywda EA, Wilson SD. Reoperative parathyroidectomy: an algorithm for

imaging and monitoring of intraoperative parathyroid hormone levels that results in a successful focused approach. Surgery. 2008;144(4):611–9. discussion 619–21.

- Norman J, Politz D. 5,000 parathyroid operations without frozen section or PTH assays: measuring individual parathyroid gland hormone production in real time. Ann Surg Oncol. 2009;16(3):656–66.
- Norman J, Politz D. Measuring individual parathyroid gland hormone production in real-time during radioguided parathyroidectomy. Experience in over 8,000 operations. Minerva Endocrinol. 2008;33(3):147–57.
- Wineland A, Siegel E, Stack Jr BC. Reexamining normative radiation data for radioguided parathyroid surgery. Arch Otolaryngol Head Neck Surg. 2008; 134(11):1209–13.
- Chen H. Radioguided parathyroid surgery. Adv Surg. 2004;38:377–92.
- Olson J, Repplinger D, Bianco J, Chen H. Ex vivo radioactive counts and decay rates of tissues resected during radioguided parathyroidectomy. J Surg Res. 2006;136(2):187–91.
- Chen H, Sippel RS, Schaefer S. The effectiveness of radioguided parathyroidectomy in patients with negative technetium tc 99 m-sestamibi scans. Arch Surg. 2009;144(7):643–8.
- 39. Landry CS, Grubbs EG, Morris GS, Turner NS, Holsinger FC, Lee JE, et al. Robot assisted transaxillary surgery (RATS) for the removal of thyroid and parathyroid glands. Surgery. 2011;149(4):549–55.
- Melck AL, Carty SE, Seethala RR, Armstrong MJ, Stang MT, Ogilvie JB, et al. Recurrent hyperparathyroidism and forearm parathyromatosis after total parathyroidectomy. Surgery. 2010;148(4):867–73. discussion 873–5.
- 41. Cohen MS, Dilley WG, Wells Jr SA, Moley JF, Doherty GM, Sicard GA, et al. Long-term functionality of cryopreserved parathyroid autografts: a 13-year prospective analysis. Surgery. 2005;138(6):1033–40. discussion 1040–1.
- 42. Guerrero MA, Evans DB, Lee JE, Bao R, Bereket A, Gantela S, et al. Viability of cryopreserved parathyroid tissue: when is continued storage versus disposal indicated? World J Surg. 2008;32(5):836–9.

- 43. Richards ML, Thompson GB, Farley DR, Grant CS. Reoperative parathyroidectomy in 228 patients during the era of minimal-access surgery and intraoperative parathyroid hormone monitoring. Am J Surg. 2008; 196(6):937–42. discussion 942–3.
- Henry JF. Reoperation for primary hyperparathyroidism: tips and tricks. Langenbecks Arch Surg. 2010;395(2):103–9.
- Bonjer HJ, Bruining HA. Technique of parathyroidectomy. In: Clerk O, Duh Q, Kebebew E, editors. Textbook of endocrine surgery. 2nd ed. Philadelphia: W.B. Saunders; 2005. p. 439–48.
- 46. Gul K, Ozdemir D, Korukluoglu B, Ersoy PE, Aydin R, Ugras SN, et al. Evaluation of preoperative and postoperative thyroid pathologies in patients operated for primary hyperparathyroidism. Endocr Pract. 2009;24:1–18.
- 47. Morita SY, Somervell H, Umbricht CB, Dackiw AP, Zeiger MA. Evaluation for concomitant thyroid nodules and primary hyperparathyroidism in patients undergoing parathyroidectomy or thyroidectomy. Surgery. 2008;144(6):862–6. discussion 866–8.
- 48. Milas M, Alghoul M, Berber E, Stephen A, Mensah A, Siperstein A, et al. Impact of office neck ultrasonography on reducing unnecessary thyroid surgery in patients undergoing parathyroidectomy. Thyroid. 2005;15:1055–9.
- Lew JI, Rivera M, Irvin 3rd GL, Solorzano CC. Operative failure in the era of focused parathyroidectomy: a contemporary series of 845 patients. Arch Surg. 2010;145(7):628–33.
- Mitchell J, Milas M, Barbosa G, Sutton J, Berber E, Siperstein A. Avoidable reoperations for thyroid and parathyroid surgery: effect of hospital volume. Surgery. 2008;144(6):899–906. discussion 906–7.
- 51. Miccoli P, Barellini L, Monchik JM, Rago R, Berti PF. Randomized clinical trial comparing regional and general anesthesia in minimally invasive video-assisted parathyroidectomy. Br J Surg. 2005;92(7):814–8.
- Carty SE, Roberts MM, Virji MA, Haywood L, Yim JH. Elevated serum parathormone level after "concise parathyroidectomy" for primary sporadic hyperparathyroidism. Surgery. 2002;132(6):1086–92. discussion 1092–3.