Surgical methods in primary hyperparathyroidism

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Introduction

Surgical treatment of primary hyperparathyroidism (PHPT) was first performed in 1925 by Felix Mandel in Vienna. Since then neck exploration and parathyroidectomy has become the treatment of choice with a very high cure rate (95-99%) and a low morbidity (1-3%)[1]. As most patients (85%) with PHPT have a single adenoma, bilateral exploration is not mandatory, but lack of reliable preoperative localization of the enlarged gland has up to recently necessitated such an approach in most cases. Improvement in localization procedures, rapid intraoperative PTH assays, and developments in surgical techniques and instruments have lead to development of minimal invasive focused procedures now accounting for up to two thirds of all surgical parathyroid procedures[2].

Surgical procedures

Bilateral neck exploration (BNE)

In the traditional BNE the neck is explored through a low collar incision of 4-6 cm. The neck fascia is divided between the strap muscles and the thyroid lobes are exposed. All four parathyroid glands are visualized, and in case an adenoma is found the enlarged gland is excised, and the pathology is confirmed by frozen section. In hyperplasia usually 3 or 3½ glands are excised leaving a remnant of 50-100 mg in situ.

BNE is the procedure of choice in case of negative preoperative localization or suspicion of hyperplasia (family history, MEN).

Cervical thymectomy (MEN 1 og 2a)

Minimal invasive parathyroidectomy (MIP)

The development of rapid intraoperative PTH assays has in conjunction with better localization procedures been key factors for the development of MIP. The most commonly used procedures are unilateral exploration, focused operation and minimal invasive video assisted parathyroidectomy (MIVAP) [3;4].

Unilateral exploration

By this technique on one side is explored in the same way described above, but after localizing an adenoma and a normal gland the operation is finished without exploring the other side. It is easy to continue on the contralateral side if an adenoma was not found in the first explored side.

This procedure is convenient in cases where preoperative localization has been inclusive, but with some indication of a lesion on one side.

Focused operation

In the focused procedure a small incision is placed over the preoperatively localized adenoma, which is excised after minimal dissection and without full exposure of the thyroid lobe and search for normal parathyroid glands. I case the adenoma is an enlarged upper gland, the incision of 1.5 cm is usually placed at the anterior border of the sternocleidomastoid muscle. The plane of the dissection is medial to the vascular

sheet, and the area behind the thyroid gland is approached from lateral. This gives good access to all upper glands and lower glands located at the posterolateral border of the thyroid. Adenomas coming from the lower glands and located caudal to the thyroid lobe (in the thyroid-thymic ligament) are preferable reached from a small (1.5 cm) transverse incision in the midline. As in BNE, the cervical fascia is opened in the midline. Usually the adenoma is easily localized and excised.

The focused operation demands preoperative localization, preferably as concordant localization with both sestamibi-scintigraphy and ultrasonography[5].

Most often, MIP is performed in general anesthesia (GA), but the procedures can be performed in local/cercical anesthesia, especially if GA is associated with increased risk, the operations mig

Minimal invasive video assisted parathyroidectomy (MIVAP)

Completely endoscopic procedures was introduced by Gagner in 1996[6], but have not been generally accepted. Contrary to this, in Europe the so-called video-assisted technique has gained some footing in leading centers.

In the video-assisted procedure with central approach developed by Miccoli[7], a small (15 mm) horizontal incision is placed in the midline and the cervical fascia is opened between the strap muscles. Via a 10 mm trochart the space around the thyroid gland is opened by shortly applying an increased pressure of 12 mmHg. Hereafter, dissection is performed with small instruments and a five mm endoscope (Fig. 1). Both sides can be explored. The procedure is very efficient for adenomas in the lower glands, but it also possible to reach an adenoma located in one of the upper parathyroids.

By the Henry technique[8], a lateral approach is used (Fig. 2). The first incision is placed at the medial border of the sternocleidomastoid muscle, and the space medial to the cervical vessels is opened to the thyroid. A 10 mm trochart with an endoscope is placed. Further two 2-3-mm trocharts are placed along the muscle-border above and below the endoscope. A pressure of 8 mm Hg is applied. After mobilization of the adenoma the trocharts are removed and the ligation of vessels is done directly. The procedure is suitable for adenomas in the upper parathyroids and adenomas placed on the lover pole of the thyroid gland.

Both techniques are performed in general anesthesia. As the open focused procedures, they depend on proper preoperative localization.

Comparative studies

Several retrospective studies have documented high cure rates (95-98%) after MIP[9-11]. Recently, two prospective studies comparing conventional parathyroid exploration with minimally invasive techniques have been published[12;13]. They demonstrate no differences in cure or complication rates between the surgical approaches.

The open minimally invasive parathyroidectomy has been compared with the video-assisted technique in one multicentre randomized trial[14]. The main findings were that open parathyroidectomy was faster than the video-assisted technique, but otherwise the outcomes were the same.

Surgery for familial hyperparathyroidism (MEN1, FHPT, MEN2A)

Hyperparathyroidism is the most common manifestation of MEN 1 (>90%), and usually it is the first clinical event. In these cases it is a polyclonal hyperplasia, although the glandular enlargement might be uneven distributed, and therefore wrongly regarded as mono-glandular disease[15]. The surgical treatment should be either subtotal parathyroidectomy with a remnant of 50-60 mg in the neck marked with a clip, or total parathyroidectomy combined with autotransplantation of 50-60 mg in the forearm or thigh (se description below). Both types of operation should be combined with cervical thymectomy in order to minimize the risk of recurrence from supernumerary parathyroids[16]. The recurrence rate is high after both procedures, and rates up to 20% should be expected after proper surgical procedures[17;18].

Parathyroid pathology and the recurrence risk in familiar hyperparathyroidism (FHPT) is similar to what is known form MEN 1. Also, the surgical approach follows the strategy described above[19].

In MEN 2A hyperparathyroidism is very seldom the primary manifestation, and parathyroidectomy is hardly ever performed as an independent procedure. On the other hand do these patients need neck operation for treatment or prevention of medullary thyroid cancer (MTC), and 10- 25% will develop hyperparathyroidism[20]. In these operations, the approach to the parathyroids is controversial if hyperparathyroidism is not present. Some recommend leaving the parathyroids in situ, while others perform a total parathyroidectomy with autotransplantation[21]. In the most recent review, it is concluded that hyperparathyroideim in MEN2 should be treated as non-familial HPT, and that prophylactic parathyroidectomy is not indicated in connection with thyroid surgery[20].

Surgery for persistent or recurrent primary hyperparathyroidism

Persistent hyperparathyroidism is defined as hypercalcemia occuring immediately postoperatively or within 6 months of the initial neck exploration. Recurrent disease appears later than six months after the primary operation. Five to ten percent of patients operated in specialized centers will need another operation[22]. Redo surgery is a challenging task. A large proportion represents incomplete resection of parathyroid tissue in patients with hyperplasia, but in a few cases it is a missed adenoma at the initial operation that is the background. Very often what you look for is relatively tiny parathyroid glands located in a previous operation field. Therefore, imaging studies are mandatory before surgery is decided, and concordant functional (MIBI, FDG-PET, 11C metionine PET) and anatomic imaging studies (ultrasonography, MR, CT) should be sought, and during surgery IOPTH should be applied[2;22]. Also, it is obligatory to have access to the initial operative rapport. Most missed glands are found at their proper localization. Ectopic upper glands are found behind the pharynx, above the superior thyroid pole, strictly within the thyroid lobe, or most often in the posterior mediastinum. Ectopic lower glands might be found within the carotid sheath and in the anterior mediastinum within or in relation to the thymus. Recurrence due to supernumerary parathyroids most often are found in close contact with the thymus[22].

After the primary operation there is a window for re-exploration within the first 3-4 days (if so preferably after proper localization by sestamibi scan), but thereafter a second procedure should be postponed at least for 3-4 months in order to minimize the increased risk of complications caused by the initial fibrosis and scarring after operation[22]. As reoperation very seldom is indicated without proper preoperative localization, some kind of focused operation is preferred. In case the localized enlarged gland it is at posterior cervical or posterior mediastinal site, a posterolateral approach is used. In these cases, the dissection is

performed medial to the carotid sheet. In case an adenoma is localized interiorly at the lower thyroid pole or along the thyroidthymic axis, a midline approach is used, but the pretracheal muscles are divided below the thyroid exposing the thyreothymic ligament[22].

In reoperative surgery the risk of postoperative hypoparathyroidism is increased in case pathologic tissue is found and removed. Therefore, judicious use of parathyroid autotransplantation is recommended[23]. Also cryopreservation of parathyroid tissue should be considered[22].

Autotransplantation and cryopreservation of parathyroid tissue

Autotranplantation of parathyroid tissue is very efficient, and viable and functioning tissue is seen in 80-90% of cases. After removal of the parathyroid gland, it is preserved in cold saline solution until the other part of the operation is finished. Usually about 60 mg is used for autotransplantation. It is sliced into 1 x 2-3 mm fragments and implanted into muscle tissue. In case the procedure is performed in conjunction with total parathyroidectomy in patients with parathyroid hyperplasia, easily accessible muscles in the forearm (m. brachioradialis) or thigh (vastus lateralis m. quadriceps femoris) are used. The localization of the implant is marked with clips or non-absorbable suture. If it is a normal gland that is unintended extirpated then implantation in the ipsilateral sternocleidomastoid muscle is performed.

In conjunction with autotransplantation, cryopreservation of parathyroid tissue is a valuable adjunct, especially in reoperation[22]. Transplantation of cryopreserved tissue is possible with success rates of 40-60% for up to 22 months after preservation[24]. The tissue is prepared as described above. The small fragments of glandular tissue is transferred to cold sterile RPMI medium supplemented with 10% autologous serum and 10% dimethylsulfoxide (DMSO), slowly frozen to minus 80°C, and stored in liquid nitrogen[23]. If needed for autotransplantation, the tissue fragments are thawed and transplanted in a similar manner as already described into muscle.

Anesthesia

Most often, parathyroid surgery is performed in general anesthesia (GA), but the procedures can be performed in local/cercical anesthesia (LA)[25-28], especially if GA is associated with increased risk[29]. In selected patients, the cure rate, morbidity, or length of stay has shown not to differ from operation in GA, and LA seem to be associated with lower post-operative pain, nausea, and vomiting[27;28].

MIP by the open methods are the preferred procedures to perform in LA, and preoperative localization is demanded, if possible as concordant localization with both sestamibi-scintigraphy and ultrasonography. The placement of the incision has to be marked by ultrasound pre-operatively.

LA is performed by infiltration of local anaesthetics around the incision line and along the sternocleidomastoid muscle anteriorly and posteriorly. This blocks the great auricular nerve, the anterior cervical nerve, and the supraclavicular nerve[26]. Sedation is added to this technique.

Adjuncts to parathyroid surgery

Ultrasonography

Ultrasonographic localization of parathyroid adenomas is almost mandatory in case focused operation (open or video-assisted) is performed. In these cases it is very informative to perform an ultrasound examination in the operation theater before the operation is started but after positioning of the patient on the

operation table. In difficult cases, especially redo-surgery, intraoperative ultrasonographic examination might be helpful. Therefore, ultrasonography should be available at the operation room when parathyroid surgery is performed.

Intraoperative PTH (IOPTH) monitoring

Intraoperative PTH measurement is today an option that always should be available in parathyroid surgery. Because of the short biologic halftime for parathyroid hormone in the circulation, PTH measurement performed 10 minutes after removal of a single adenoma will show a decrease in S-PTH of 50% or more (Miami Criteria). The use of IOPTH is recommended for patients undergoing 'targeted' parathyroidectomy on the basis of a single preoperative localization study and in redo-surgery[2]. On the other hand, when preoperative localisation with MIBI and ultrasonography is concordant for single-gland disease, the use of IOPTH is of little added value[2].

Frozen section

Frozen section should be an option in every parathyroid surgical procedure. In the positional statement of the European Society of Endocrine Surgeons (ESES) meeting in on modern techniques in pHPT surgery in Lund 2009[2], it was concluded that frozen section is recommended when the surgeon is in doubt about whether a nodule is parathyroid tissue. There was found no evidence to support the use of routine frozen section.

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