EC MICROBIOLOGY
Review Article

Thyroidectomy Indications and Complications

Masoud Ahmad Alghamdi[1]*, Mohammed Ibrahim Aljikhlib[2], Areej Hamed Alsofiani[3], Fahad Rudayni Alharbi[4], Khalid Ahmed S Alghamdi[5], Mebsam Hassan Ali Alzayer[6], Khairat Hassan Ageel AL-Ameer[7], Yousef Mohammed Ajaj[8], Najd Abdulrahmman Alsukhayri[3], Yousef Ali Alghamdi[9], Reaah Ibrahim Ali Assiry[7] and Khadra Ali Saeed Al Saab[7]

[1]Consultant of General Surgery, King Fahad General Hospital-Jeddah, Saudi Arabia

[2]Ibn Sina National College for Medical Studies, Saudi Arabia

[3]Taif University, Taif, Saudi Arabia

[4]King Fahad Specialist Hospital-Burydah, Buraydah, Saudi Arabia

[5]Albaha University, Saudi Arabia

[6]Khafji General Hospital, Saudi Arabia

[7]King Khalid University, Saudi Arabia

[8]King Abdulaziz University, Saudi Arabia

[9]Saudi Red Crescent Authority-Jeddah, Saudi Arabia

***Corresponding Author**: Masoud Ahmad Alghamdi, Consultant of General Surgery, King Fahad General Hospital-Jeddah, Saudi Arabia.

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Abstract

Introduction: The thyroid gland has been described for a long time but was first named by this name by the Romans because they noticed that it was "shield-shaped". Moreover, thyroid masses were described in the medical literature since the twelfth century, as in the year 1170, the physician Robert Frugardi described the examination of a goiter. Surgery of the thyroid was undertaken a long time before that thyroid gland diseases' pathophysiology was well understood. Surgical operations were usually fraught with adverse events, including major bleeding, surgical infections, and trauma to peripheral structures, all of which were linked to high morbidity and mortality rates that could reach forty percent.

Aim of Work: In this review, we will discuss thyroidectomy.

Methodology: We did a systematic search for thyroidectomy using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

Conclusions: The surgical techniques of thyroidectomy, as well as surgical technologies, remained to improve. Recently, several new instruments (for example, the introduction of harmonic technology) and advanced approaches like video-assisted thyroidectomy and robot-assisted thyroidectomy have improved. This review discusses the preoperative evaluation, intraoperative considerations, surgical technique(s), and postoperative concerns for patients undergoing thyroidectomy.

Keywords: *Thyroidectomy; Indications; Complications; Endocrine Disorders*

Introduction

The thyroid gland has been described for a long time but was first named by this name by the Romans because they noticed that it was "shield-shaped". Moreover, thyroid masses were described in the medical literature since the twelfth century, as in the year 1170, the physician Robert Frugardi described the examination of a goiter. Surgery of the thyroid was undertaken a long time before that thyroid gland diseases' pathophysiology was well understood. Surgical operations were usually fraught with adverse events, including major bleeding, surgical infections, and trauma to peripheral structures, all of which were linked to high morbidity and mortality rates that could reach forty percent.

Even until the nineteenth century, surgery of the thyroid was considered to be a barbaric act, as described by the physician Samuel Gross as "horrid butchery," and prohibited by the French medical society because of its relatively high mortality rates. As technology advanced and with the emerging of aseptic techniques, mortality rates linked to these surgical operations significantly declined [1]. During the 1850s, surgical operations on the thyroid were done through oblique, longitudinal, or vertical neck incisions. Jules Boeckel was the first to introduce the collar incision in thyroid surgeries in the year 1880, and this surgical approach was later popularized by Theodore Kocher. Theodor Kocher, whose reported mortality for thyroidectomies dropped to one percent, was later awarded the Nobel Prize in the year 1909 for his contributions to the field of thyroid surgeries during the late nineteenth century [2,3].

The surgical techniques of thyroidectomy, as well as surgical technologies, remained to improve. Recently, several new instruments (for example, the introduction of harmonic technology) and advanced approaches like video-assisted thyroidectomy and robot-assisted thyroidectomy have improved. This review discusses the preoperative evaluation, intraoperative considerations, surgical technique(s) and postoperative concerns for patients undergoing thyroidectomy.

Methodology

We did a systematic search for thyroidectomy using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: thyroidectomy, indications, complications, endocrine disorders.

Indications

Currently, the major indications for doing thyroidectomy include: the presence of a gross extrathyroidal extension on the ipsilateral side of the gland, the presence of a gross residual disease reaching the recurrent laryngeal nerve, esophagus, or the tracheal wall, the presence of a huge vascular or capsular invasion, or the presence of a grade III malignancy or and aggressive Hürthle cell carcinoma.

Clearly, the rationale behind these main indications is to facilitate patients to receive radioactive iodine, that might be of real benefit in the long-term follow-up. However, in cases with grade III thyroid malignancy or aggressive Hürthle cell carcinoma, the role of radioactive iodine is still not well-understood. The decisions on completion thyroid surgery are generally complex and depend on the experience and judgement of each surgeon, the current institutional philosophies, and the presence of concerns raised by endocrinologists [4].

Despite that the debates about completion of thyroid surgery has been a debatable topic over the last fifty years, the recent guidelines that were published by the ATA look to tend more towards performing hemi-thyroidectomy and avoid performing complete thyroidectomy in most cases in the low-risk group [5]. This surely has been reflected in the eighth edition of the staging system, demonstrating higher incidence of hemi-thyroidectomy in the US and downstaging of thyroid malignancies [6].

Hypocalcemia

Hypocalcemia is usually defined as the presence of total serum calcium level that is less than two mM/L (eight mg/dL) or the presence of an ionized calcium level that is less than 1.1 mM/L (0.275 mg/dL). The occurrence of post-thyroidectomy hypocalcemia ranges between two percent to eighty-three percent according to the definition that is used by different authors. Some authors only include the presence of symptomatic hypocalcemia whereas other authors include asymptomatic hypocalcemia that is present along with transient hypoparathyroidism [7,8]. The occurrence of a long-term or irreversible hypocalcemia in reported series with more than one hundred cases is less than three percent. Using a threshold of total calcium level of two mM/L (eight mg/dL), Duclos., *et al.* concluded that there was a twenty-five percent incidence of developing post-operative hypoparathyroidism and a two percent incidence of developing irreversible hypo-parathyroidism. Post-operative hypo-parathyroidism originates from the presence of impaired secretion of the parathyroid hormone (PTH), which often results in the development of hypocalcemia that is linked to hyperphosphatemia. The normal post-operative response to surgical stress including hemodilution and anti-diuretic hormone secretion also decreases total serum calcium concentrations [9,10].

About fifty percent of total serum calcium is present in an ionized form, forty percent is albumin-bound and the remaining ten percent is compound to phosphate or citrate. It is thus advisable to perform what is known to ‘‘correct’’ the measurement of total calcium levels using this formula:

Corrected calcium’’ (mg/dL) = Total calcium/0.8 (4-albumin level (gm/dL))

The PTH concentrations is usually low and sometimes become undetectable. But PTH levels should be always understood in the context of renal function, vitamin D3 concentrations and magnesium concentrations [11]. Numerous studies have assessed the risk of development post-thyroidectomy hypoparathyroidism. The post-operative PTH concentration is a relatively good predictor of hypocalcemia than the use of only calcium concentrations [12]. therefore, Wand., *et al.* concluded that the use of calcium or Vitamin D supplementations was not necessary if the post-operative PTH concentrations were higher 5 pg/ml [13]. In a published meta-analysis of 4 Australian studies, Grodski., *et al.* demonstrated that an undetectable PTH concentrations at 4 hours following the surgical operation was associated with the later development of hypocalcemia with a sensitivity and specificity of 48.5% and 96.7%, respectively [14]. On the other hand, the sensitivity and specificity are generally based on the threshold level that is chosen. Measuring the relative decline of PTH benefits the predictive value. In another meta-analysis of 9 studies, Noordzij., *et al.* concluded that a PTH decline of more than sixty-five percent from basal PTH concentrations at six hours post-operatively was predictive of hypocalcemia with a sensitivity of 96.4% and a specificity of 91.4%. These findings have been confirmed in several other studies, most importantly by the recent study published by Lecerf., *et al*. The risk of post-operative hypocalcemia, either temporary or permanent, is affected by several factors: the venous drainage of the upper parathyroid glands that runs entirely by way of the thyroid circulation; the parathyroid glands that might lie beneath the thyroid capsule in patients who have large goiters [15]. This could sometimes result in temporary hypocalcemia in about fifty percent of patients, despite that the risk of developing irreversible hypocalcemia is usually less than two percent; the presence of an extremely large goiter, Grave’s disease, or a thyroid malignancy that requires extensive nodal dissection usually results in the removal of the lower parathyroid glands; repeat cervical exploration and adhesions might cause more trauma at the operative site with risk of devacularizing the parathyroid glands ; younger age and female gender.

Intra-operative measures that decreases rates of developing hypocalcemia include a systematic search for parathyroid glands along with the visualization and sparing of two or more of them and the application of careful protection of their blood supply by applying meticulous dissection and sparing the peri-glandular fat. These measures aid in avoiding the development of low-grade chronic hypocalcemia, that could have long-term negative effects on the metabolism of bones [16]. The development of subclinical hypoparathyroidism is usually underestimated [17]. If glandular infarction happens because of venous occlusion, complete devascularization, or other difficulties which are related to the underlying thyroid disease, some authors suggest a systematic policy of morcellization of at least one parathyroid gland with the implantation into the sternocleidomastoid or the forearm muscles. This protocol is associated with decreases in the occurrence of irreversible hypoparathyroidism.

During the peri-operative period, the administration of oral supplementation with calcium (two gm/day) plus vitamin D (cholecalciferol) should be started one week before the surgery and is continued for two weeks after surgery; this decreases the occurrence and the severity of post-operative hypocalcemia and improves the quality of life of the patient.in addition, pre-operative detection of the presence of vitamin D deficiency (25-OH-VitD3 that is below a threshold level of twenty ng/ml) must be routinely performed. Vitamin D3 concentrations must be always measured at the initial consultation and supplements should be administrated if needed. Prescription of 100,000 IU of oral cholecalciferol is the most common formulation. A second Vitamin D3 level must be measured 2 months following surgical operation. It is best to detect the presence of a Vitamin D deficiency at the first consultation.

There is no general agreement regarding the treatment of hypoparathyroidism. Detection usually depends on the measurement of calcium and PTH concentrations. This must ideally be done 6 hours after the surgery. Treatment depends on a combined therapy of both calcium and Vitamin D (usually in the form of calcitriol). It's not necessary to institute treatment for relative hypocalcemia when the patient does not have symptoms (calcium level 2 - 2.2 mM/L; 8 - 8.8 mg/dL), as this could stimulate hypertrophy of remaining parathyroid glands. However, it is essential to keep in mind that hypocalcemia starts at about forty-eight hours following surgery; the patient should be completely informed of the possible risks and symptoms of hypoparathyroidism and arrangements must be prepared for continuous outpatient measurement of calcium and phosphate.

If the patient develops any symptoms like paresthesias, or neuromuscular excitability, treatment will consist of administration of calcium and vitamin D every day. Generally, we start with administrating 500 - 1000 mg of calcium carbonate. Calcium citrate could be used when there is an underlying achlorhydria (like the case with PPI medications), as calcium carbonate needs an acidic medium for proper GI absorption. Vitamin D is usually administered as calcitriol at an initial dose of 0.5 - 1g two times a day. Doses must be altered according to every week measurement of calcium and phosphate concentrations until biological equilibrium is reached. Magnesium deficiency, that could cause resistance to PTH, should be diagnosed and managed (1.5g of magnesium/day). The first daily dose of calcium must occur at several hours' interval from the replacement dose of thyroid hormone, as calcium salts reduce the bioavailability of levothyroxine.

A patient who manifests with acute severe symptomatic hypocalcemia (with calcium levels that are less than 1.75 mM/L, < 7 mg/dL), or with the development of tetany, muscular fasciculations, carpopedal spasm, or positive Chvostek sign with associated risks of cardiac decompensation or laryngospasm must be managed immediately with IV calcium gluconate (one or two ampules of ten percent solution) for one to two days plus oral supplements of calcium (three gm) and 2 to 3g of dehydrocholecalciferol plus 1 - 2 gm of magnesium when hypomagnesemia is present. Calcium gluconate could be administered as an initial one-ampoule intravenous bolus followed by infusion of one to three mg of calcium gluconate in 500 ml of D5W over twelve hours.

Recurrent laryngeal nerve injury

The occurrence of recurrent laryngeal nerve injury, both unilateral or bilateral, at thyroidectomy is extremely low but still not zero. Incidence rates vary based on several factors including the interval of follow-up post-surgery with a mean incidence at one year of 2.3% versus 9.8% in the immediate post-operative period; the modality of diagnosis, with incidence ranging from less than two percent to six percent based on whether indirect mirror laryngoscopy or the more preferred fiberoptic laryngoscopy is routinely performed post-operatively [18].

The unilateral recurrent laryngeal nerve injury usually causes hoarseness of voice or dysphonia because of laryngeal paralysis with unilateral vocal cord immobility. It is usually linked to upper airway dyspnea and swallowing deficits, specifically for liquids. Bilateral recurrent laryngeal nerve palsy causes significant clinical manifestations of acute life-threatening dyspnea. This is considered to be a rare complication; its occurrence is challenging to assess from the literature but is estimated to be about 0.4 percent by Rosato. There is an important risk of recurrent nerve injury following any thyroid surgical operation. The risk increases according to the type of the surgery (re-operation vs. initial surgery), the underlying thyroid etiology, the size of resection, and the volume of the surgeon's experience. Risk is also elevated by the presence of cancer needing a central nodal dissection or invading near structures (3.6% vs. 2.3%) [19]. A previous meta-analysis included about 14,934 patients and concluded a 3.4 percent incidence of recurrent laryngeal nerve paralysis for all thyroid conditions. The incidence rate was more in patients with malignant tumor (5.7 percent) and varied based on the type of thyroid cancer from 1.4 percent for low-grade cancers to 16.5 percent for high-grade cancers where the recurrent laryngeal nerve might be directly invaded. The presence of chronic thyroiditis or Grave's disease emphasizes the risk of recurrent nerve injury. The size of the goiter or the operated thyroid lobe could also elevate the risk of recurrent laryngeal nerve injury, specifically with substernal goiter where the nerve is stretched and highly exposed to trauma during surgical operation.

The extent of surgical activity and surgeon' experience have also been found to influence the risk of recurrent nerve injury. Other predisposing factors that have been studied include neck hyperextension with resultant nerve traction, the degree of recurrent laryngeal nerve branching the anterior branches always being motor nerves) and the extent of the recurrent nerve, since small nerves seem to be more fragile. In addition, spontaneous recovery of nerve function and axonal regrowth are less good in old patients, smokers, patients with diabetes mellitus and patients who have relatively severe comorbidities.

Neural monitoring (NM) has been used in thyroid surgical operations for the last decade by several centers; it was initially introduced to aid in the intra-operative detection of the nerve and to elucidate the implied mechanisms of post-operative nerve trauma [20]. In a prospective study of more than 440 patients, Neural monitoring had a forty percent positive predictive value and a one hundred percent negative predictive value for nerve injury with a sensitivity of sixty three percent and a specificity of ninety seven percent. In a comparison of recurrent laryngeal nerve identification by standard dissection versus Neural monitoring in a series of one thousand patients undergoing total thyroidectomy, Barczynski demonstrated that Neural monitoring decreased the occurrence of transient recurrent laryngeal nerve paresis (about three percent for high-risk patients and bout one percent for low-risk patients). A meta-analysis by Higgins, comprising a randomized trial and seven cohort studies, demonstrated that systematic visualization of the recurrent laryngeal nerve was considered the best approach to prevent nerve injury, with a recurrent laryngeal nerve injury rate of 3.25 percent using the nerve stimulator versus 3.12 percent for visualization of the nerve. The use of neural monitoring in preoperative cases was not found to decrease the risk of recurrent laryngeal nerve injuries. All the same, despite that Neural monitoring needs a long learning curve, its use changes the dissection technique, and helps in detection of the recurrent nerve, even when the nerve does not follow the classical recurrent trajectory (occurrence of a non-recurrent laryngeal nerve may be as high as six percent).

Unilateral recurrent laryngeal nerve trauma might cause minor clinical manifestations, so visualization of vocal cord function must be systematically performed post-operatively, even in cases where there is no dysphonia. Management must be symptomatic and, once the diagnosis of recurrent laryngeal nerve injury is made, it falls into the domain of an ENT specialist. On the other hand, Bilateral vocal cord paralysis in adduction manifests as the development of acute dyspnea and is evident at the time of extubation, needing urgent airway re-intubation. The essential first gesture is to maintain/restore ventilation. High-dose corticosteroid therapy is administered for forty-eight hours to reduce laryngeal edema (intravenous solumedrol twenty to sixty mg by slow intravenous infusion over thirty minutes every eight to twelve hours, or dexamethasone four to ten mg/day). Cortico-therapy is usually accompanied by broad-spectrum antibiotic coverage and the use of PPI agents, which seems to decrease the risk of laryngeal granuloma formation [21].

Postoperative hemorrhage

The occurrence of post-operative bleeding can vary from zero to six percent. Bleeding adverse events are frequently due to slippage of a ligature on one of the bif arterial pedicles, to bleeding from the transected parenchymal surface, or to a jugular vein injury. Compressive hematoma developing in the neck compartment might be fatal and needs immediate surgical decompression. This might develop beyond the first 6 post-operative hours. In a series of more than 6,700 patients, Leyre., *et al.* reported seventy compressive hematomas, ten percent of which developed later than twenty-four hours following surgery. Factors that might lead to an increased risk of bleeding include male gender, the presence of a thyroid malignancy, the size of the surgery and surgeon's experience. Anti-coagulant or anti-platelet use or coagulopathy do not seem to be predisposing factors as long as intra-operative hemostasis is meticulous. The first warning sign is usually blood in the drains or respiratory difficulty. It is important that the source of bleeding is identified only in about seventy-three percent of patients who undergo neck re-exploration. Prevention must start pre-operatively with control of hyperthyroidism, intra-operatively by rigorous and meticulous hemostasis and by performance of Valsalva maneuver in coordination with the anesthesiologist following completion of the dissection to identify the presence of bleeding, and post-operatively by the prompt resumption of anti-hypertensive pharmacological agents.

Drainage of the cervical space following thyroidectomy has been found by a Cochrane meta-analysis to be of no benefits. Management usually consists of immediate evacuation of the hematoma from the cervical space, at the patient's bedside when necessary, followed by careful re-exploration of the operative site with copious lavage of blood clots to detect the source of hemorrhage. Either passive or suction drains are put based on the circumstances. If a non-compressive hematoma is found, it could be decompressed by simple needle aspiration, but careful surveillance for recurrent collections is crucial in all cases. Other complications like Dysphagia or other minor swallowing problems are usually reported following thyroidectomy. They are often due to post-operative inflammation of the periesophageal musculature. Daily massage of the cervical region positively improves these clinical manifestations, which often disappear after the next few months. Lymphorrhea or seroma are more likely to develop following the surgical excision of relatively large goiters, extensive nodal dissection, and due to lymphatic injury (thoracic duct or right cervical-brachial trunk). Simple needle aspiration is usually enough to repair such problem. If lymph drainage persists, re-intervention with ligation of the thoracic duct may be used.

Conclusions

The surgical techniques of thyroidectomy, as well as surgical technologies, remained to improve. Recently, several new instruments (for example, the introduction of harmonic technology) and advanced approaches like video-assisted thyroidectomy and robot-assisted thyroidectomy have improved. This review discusses the preoperative evaluation, intraoperative considerations, surgical technique(s), and postoperative concerns for patients undergoing thyroidectomy.

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