

Review

A Comparison Between Complications Following Total Versus Subtotal Thyroidectomy: A Literature Review

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Abstract

Thyroidectomy is a common procedure performed for various medical conditions such as hyperthyroidism, thyroid nodules, and thyroid cancer. As with any other procedure, thyroidectomy has several complications such as Recurrent Laryngeal Nerve (RLN) injury, hypocalcemia, and hematoma. Total thyroidectomy and subtotal thyroidectomy are two main types of procedures performed with each having their own common complications. This literature review aims to compare common complications that occur in total thyroidectomy and subtotal thyroidectomy. Three main complications, RLN injury, hypocalcemia, and hematoma formation, are reviewed using PubMed/MEDLINE and Google Scholar with a Synthesis Without Meta-analysis (SWiM) approach to ensure a clear and reliable reporting of findings. Complications post thyroidectomy may be life threatening where prompt attention and follow up is needed to insure effective management. Risk factors for hematoma formation include age >45, gender (male sex), Graves' disease, systolic blood pressure >150, and the use of Ketorolac or Aspirin. Identification of the RLN intra-operatively is an important step in order to decrease the risk of occurrence. While hypocalcemia is the most common post-operative complication, an increased risk of developing both hypocalcemia and hypoparathyroidism occurs in total thyroidectomy in comparison to subtotal thyroidectomy. In conclusion, complications from thyroidectomy may be life threatening indicating the necessity of post-operative care. The incidence and measures for decreasing the risk of post-operative complications may vary with the type of thyroidectomy performed.

Keywords: Total Thyroidectomy, Subtotal Thyroidectomy, Recurrent Laryngeal Nerve Injuries, Hypocalcemia,

Introduction

Thyroidectomy has become the treatment choice for many malignant and benign lesions (tumors) of the thyroid gland (1). It is an important topic in the surgical field as it shifts attention to the preceptive of inductions, complications and recent developed techniques. In the past decades, a major development of thyroid surgery techniques took place. This made thyroidectomy a safe procedure with a well-established safety profile that considered the dangerous areas and vital structures involved in it (2, 3). Although the surgery helps to treat various benign and malignant conditions, it has some serious complications that occur when the surgery is not performed by an experienced surgeon (4).

As the incidence of thyroid disease, including thyroid cancer, is increasing worldwide, thyroid surgery became a common procedure in clinical practice (5, 6). In the United States, the number of thyroidectomies performed for inpatients and outpatients increased by 39% from 66,864 to 92,931 between 1996 and 2006 (7). This number is expected to rise in the future. On the other hand, there are several indications that signal the need for performing thyroidectomy such as thyroid nodules (8), hyperthyroidism (9), substernal or obstructive goiter (10) and thyroid cancer (1). The main two types of thyroidectomies are often performed in the common practice namely are Total Thyroidectomy (TT) and Subtotal Thyroidectomy (ST) (11, 12).

Total thyroidectomy aims to remove both thyroid lobes and preserve the parathyroid gland. However, subtotal thyroidectomy removes the gland but preserves small bilateral or unilateral remnant of the thyroid tissue. The latter type helps to maintain the thyroid function with much less post operation complications. Although the incidence of death following the thyroid surgery is rare, several serious complications occur (13). This is due to the delicate anatomy of the thyroid after the procedure that varies in the percentage of incidence depending on the surgery techniques. Examples of common complications include neck hematoma, transient or permanent hypocalcemia, and transient or permanent Recurrent Laryngeal Nerve (RLN) injury (11, 14-19). To provide further insights into the topic, this literature review presents an updated comparative analysis of total thyroidectomy (TT) and subtotal thyroidectomy (ST) and the common complications that occur in each type.

Methodology

This review draws on relevant literatures to examine the complications of total and subtotal thyroidectomy micronutrients. It attempts to cover the three main complications which are RLN injury, hypocalcemia and Hematoma. Two authors used PubMed/MEDLINE and Google Scholar to apply the following search terms to titles and abstracts: “total thyroidectomy” OR “subtotal thyroidectomy” AND “complications” OR “RLN injury” OR “hypocalcemia” OR “Hematoma”. Also, the authors separately sifted through the vast literature on these topics and, by consensus, selected the ones that best answered the research questions. The review used the Synthesis Without Meta-analysis (SWiM) approach to ensure a clear and reliable reporting of findings.

Discussion

Hematoma

Hematoma in Total Thyroidectomy

Rare but life-threatening complications may develop in the highly-vascularized thyroid gland. As such, an uncontrolled collection of post-operative bleeding rapidly progresses and compression/obstruction ensues, thereby leading to airway compromise. This prompts urgent management to relieve airway obstruction and ensure effective intra-operative hemostasis. It is also important to know the common sources of bleeding (20). Therefore, it is essential to establish a profile of patients who are at a high risk of developing hematoma and identify those who are at a lower risk on an outpatient basis.

A precise percentage on the incidence of this complication may vary; however, some studies identify it as somewhere between 0.5% to 4% while others state it is around 1-2% (21). Moreover, the timing of developing hematomas is also essential as it helps to determine the appropriate time to discharge the patient. As Burkey et al. reported, 43% of hematoma occur within 6 hours post thyroidectomy while 81% of cases occur within 24 hours (22). As a result, a vigilant monitoring of patients is important in the early post-operative period (23, 24). This signals the presence of various factors that affect the overall risk of developing a hematoma post-thyroidectomy.

Studies have shown that age and male gender are independent risk factors for developing hematoma (25, 26). After performing a systematic review with meta-

analysis, Fan et al. (2019) states that the occurrence of post-operative hematoma is greater in males with a percentage of 2.10% compared to that in females with only 1.27% (26). Likewise, age is another factor that increases the risk of developing hematoma. In a study by de Carvalho et al. they argued that 0.7% of patients who are less than 45 years old develop hematoma compared to 1.4% of patients who are 45 years old or more with an odds ratio of 2.03 (27). Graves' disease is another well-established risk factor in existing literature. It is an autoimmune thyroid condition in which the thyroid gland's vascularity increases. This makes thyroidectomy more challenging as the increased intra-operative bleeding may hinder the visual field and exposure, thereby leading to increased morbidity (28). According to a systematic with meta-analysis conducted by Quimby et al. (29), the overall rate of post-operative hematoma formation is 1.66% in the Graves' disease group and is higher than the "other" group at 1.44% with an odds ratio of 1.58 and a p-value of 0.02.

Besides, a retrospective case-control study shows that a 22-fold increase in the risk of developing hematoma occurs after taking two or more doses of ketorolac, another 55-fold increase occurs due to antithrombotic agents' usage, and a 10-fold increase post-operative hematoma accompanied with significant post-operative pain (23). On another note, a study by Morton et al. reports an increased risk of bleeding with hypertension defined as a systolic blood pressure that is greater than 150 mmHg in the pre- or post-operative period. Other factors include excessive coughing, vomiting, and pain, all of which increase blood pressure and the risk for hematoma (30).

A controversial practice commonly used by surgeons is the placement of a surgical drain. Many authors do not support the placement of a drain because it is not evidence-based (31). They argue that it is a traumatic practice that dislodges the already ligated vessels. They also claim that negative pressure causes bleeding from vessels with affected integrity in the operative bed (32). This suggests that drains lead to more post-operative pain which feeds into the cycle of pain, thereby leading to hypertension and indirectly increasing the risk of hematoma (5). From another perspective, some studies fail to show the link between the histology of thyroid cancer and the fact that it does not affect the rate of post-operative hematoma. Similar findings report the relationship between the use of conventional ligation and coagulation methods or alternative energy-based vessel

sealing devices, such as Ligasure and Harmonic scalpel (33).

When it comes to comparing total thyroidectomy and subtotal thyroidectomy in terms of developing hematoma, the scientific community reports conflicting findings. A large number of studies has not found a significant statistical difference (34). However, some members of the scientific community argue otherwise and claim that total thyroidectomy results in a higher risk of developing post-operative hematoma because it leaves a larger dead space. This view aligns with a study in Austria which states that subtotal thyroidectomy lowers the risk of hematoma at a 1.6%, compared to its total counterpart at a 2% of patients. These conflicting views show that sufficient evidence to support both theories is still unavailable (35).

In terms of total thyroidectomy combined with central neck dissection, no significant association is identified between it and the risk for developing a post-operative hematoma (36). The last factor that contributes to hematoma is hospital volume. Studies show that thyroidectomies performed in low volume hospitals (< 75 per year) have a higher propensity that results in post-operative hematoma compared to higher volume hospitals that have an odds ratio of 1.32 (26, 37).

Hematoma in Subtotal Thyroidectomy

Studies on neck hematomas post-thyroidectomy report mixed findings on the matter of occurrence in subtotal vs. total thyroidectomies. They conclude that more extensive neck resections in thyroidectomy lead to a greater risk of developing post-operative bleeding. This conclusion is made despite the discrepancies in the occurrence rates between the two groups. To elaborate more, six studies will be analysed as follows.

The International Journal for Clinical and Experimental Medicine aims to assess post-operative early complications of total and Bilateral Subtotal Thyroidectomy (BST) for benign multi-nodular goiter (38). They examined 409 patients, out of them, 258 underwent total thyroidectomy and 151 underwent bilateral subtotal thyroidectomy. In both groups, only 3 patients developed hematoma accounting for 1.9% of the BST group and 1.1% of the TT group. Given the study findings, the researchers concluded that while the rate is in fact higher in the BST group, there are no statistically significant differences between the two groups with a P value of >0.05. By contrast, a study by Rifaat et al. examined the formation of hematoma in 244 patients who represent both subtotal and total thyroidectomies

(39). Three cases are reported in the ST group (2.5%) compared to four ones in the TT group (3.3%) which results in a statistically insignificant differences between the two groups.

To analyse the extent of resection as a risk factor, Dixon et al. investigated the rates following bilateral and unilateral procedures (40). They examined a total of 4,140 cases of thyroid and parathyroid operations and analysed the outcomes. The latter show the occurrence of hematoma as 0.66 % (n = 11) for bilateral thyroid procedures and 0.21 % (n = 3) for unilateral thyroid procedures, thereby displaying a more concrete difference than the previous study. Another study examines the same factor in 30,142 participants (35). The authors argue that more extensive resections contribute to a greater risk of post-operative bleeding. They demonstrated that bilateral near-total resection results in 75 cases of hematomas out of 3,403 patients (2.2 %) and 60 cases out of 2,975 (2.0 %) for total thyroidectomy. These rates can be compared with the bilateral subtotal group, where 144 cases out of 9,124 patients are reported (1.6 %). Comparing the risks of bilateral and unilateral shows that a twofold increased risk of postoperative bleeding is associated with bilateral procedures, with 427 of 21359 (2.0 %) operations compared with 92 of 8783 (1.0 %) unilateral operations. Thus, the authors concluded that bilateral thyroid surgery doubled the risk compared with a unilateral procedure. The extent of thyroid resection was also a risk factor". In terms of total and Bilateral Near-Total (BNT) vs. bilateral subtotal, the TT and BNT groups show a total of 135 cases of 6,378 (2.1%) compared with the 1.6% occurrence in the SBT group.

Another finding is presented by Morton et al. where they examined 355 thyroid operations and report 7 cases of hematoma in the TT group (1.97% of total cases) despite being a normotensive pre-operative occurrence (30). That is, none of the patients in the subtotal group has developed post-operative bleeding. The study also underlines other factors that contribute to this outcome, such as gender, ethnicity, neck dissection, and thyroid etiology. Although it concludes that the institution where the surgery is performed is the most significant risk factor in that subgroup, the occurrence is greater in the TT group.

Post thyroidectomy hematoma is a life-threatening complication that risks the compromising of airway patency. With a 2% risk of occurrence, proper profiling of higher risk patients is essential in decreasing the rates of post-op morbidity and mortality. Common risk factors

that develop hematoma include age >45, gender (male sex), Graves' disease, systolic blood pressure >150 (pre and post operatively), and the use of Ketorolac or Aspirin. The risk of developing a hematoma associated with a total or subtotal thyroidectomy is currently unknown due to conflicted findings from different studies. Consequently, there is no evidence to support the presence of thyroid cancer on histopathology as a risk factor that develops post thyroidectomy hematomas.

Recurrent Laryngeal Nerve Injury

Recurrent Laryngeal Nerve Injury in Total Thyroidectomy

Many causes of RLN injury have been reported including malignancy, endotracheal intubations, viral illnesses, and diabetic neuropathy. However, one of the most common causes of RLN injuries is the surgical intervention of the chest, neck and skull base (41). Jiang et al. examined the prevention and treatment of RLN injury in thyroid surgery in 623 patients with different thyroid pathologies (42). They state that thyroid surgeries are a significant cause of RLN injury whether it is unilateral or bilateral. Besides, the injury can lead to hoarseness of the voice, coughing, micro-aspiration, aphonia, dyspnea, and asphyxia. In the surgery, about 528 patients have been exposed to RLN compared to 95 ones with no exposure. Among those patients, only 189 patients underwent unilateral resection of the total thyroid. The incidence of RLN injury is 4.61% during the first surgery and 10.81% in the second or multiple surgeries. As for the exposed and unexposed RLN, the incidence of injury is 3.79% and 11.58%, respectively.

In addition, a retrospective review was conducted by Zakariya et al. in the surgical department at King Fahad Hospital in Saudi Arabia to examine 340 patients of thyroid surgery between 1990-2005 (43). The study assessed the risk factors of RLN during thyroid surgery and emphasized that the type of procedure, whether total or subtotal thyroidectomy, significantly influences the rate of RLN injury. According to the authors, the incidence of RLN injury is higher in total thyroidectomy compared to subtotal which is 7.2% and 1.9%, respectively. However, a non-randomized controlled trial study Sajid et al. was done in 2016 on 177 patients in Rawalpindi to compare between total and subtotal thyroidectomy in terms of RLN injury (44). The incidence of RLN injury in total thyroidectomy is 2.3% compared to 3.3% in subtotal one. The study thus concludes that the difference between total and subtotal thyroidectomy is not considerable. Even though RLN is

commonly injured during surgery, there are various methods that can preserve it if applied. The six practical methods to prevent the injury are a) enhancing preoperative examination, b) identifying the RLN and dissecting it safely during the operation, c) utilizing good basic surgeon skills, d) avoiding a forcible traction of thyroid tissues, e) intraoperative neuromonitoring, and f) avoiding unessential dissection of RLN in patients with large substernal goitres because the thyroid membrane retention in the back can decrease the injury (42).

Recurrent Laryngeal Nerve Injury in Subtotal Thyroidectomy

Vocal cord paresis or paralysis occurs due to the iatrogenic injury of the RLN. The injury is one of the main problems in thyroid surgery. Although many procedures have been introduced to prevent the nerve injury, the incidence of recurrent laryngeal nerve palsy varies between 1.5-14% (43). A randomized controlled trial was conducted on 90 patients of subtotal thyroidectomy at the surgery and Ear Nose and Throat department of Ayub Teaching Hospital Abbottabad and Combined Military Hospital Rawalpindi between 2013 and 2014 (44). The patients had preoperative indirect laryngoscopy examination repeated postoperatively to check for injury to the recurrent laryngeal nerve and showed that only three patients have developed recurrent laryngeal nerve injury (3.3%). Another study and a retrospective review examined patients who had thyroid surgery between 1990 and 2005 in the surgical department at King Fahd Hospital in Al-Khobar, Saudi Arabia (43). Only 202 patients had subtotal thyroidectomy during this period contributing of 132 patients who underwent bilateral ST compared with 70 ones of unilateral ST. The results demonstrated the presence of transient unilateral RLN paralysis in 3 patients (2.2%) of bilateral ST compared with only 1 (1.4%) patient of unilateral subtotal thyroidectomy who has developed transient unilateral RLN paralysis (43).

Another study published in 1984 by Kark et al. assessed the voice function in 325 patients after thyroidectomy (45). Permanent changes have occurred in 35 patients (25%) after subtotal thyroidectomy and in 19 ones (11%) after lobectomy. The common cause of voice change here is injury to the external laryngeal nerves on one or both sides. Damage to the recurrent laryngeal nerve, which is routinely identified and protected, is rarely a cause. A

An observational study on 310 patients of thyroidectomy was carried out in the department of surgery at Fauji

Foundation Hospital, Rawalpindi. The study examines patients who have had subtotal thyroidectomy between January 2000 to December 2005 (46). They reported only 3 patients (1.53 %) out of 196 (63.23%) that developed transient recurrent laryngeal nerve (RLN) palsy, 1 patient of lobectomy (2.63%) out of 38 (12.26%) has developed transient RLN palsy, and 2 patients of lobectomy and ST (6.25%) out of 16 (5.16 %) have developed transient RLN palsy and permanent RLN palsy, respectively. In brief, the findings of the above studies show that recurrent laryngeal nerve Injury is low in subtotal thyroidectomies (nearly 1.9 %) compared to total/near total ones (7.2 %). Thus, there is no significant difference in the incidence of RLN injury between unilateral and bilateral subtotal thyroidectomy.

A key factor that affects the outcomes of RLN injury is the identification of the nerve intraoperatively. Here, recurrent laryngeal nerve monitoring (RLNM) is believed to reduce postoperative RLN paralysis (RLNP). According to a 2004 study conducted in Germany (1), the analysis of 16,448 consecutive multi-institutional operations has resulted in 29,998 nerves at risk. Three groups of different RLN treatment were compared: Group 1: no RLN identification, Group 2: visual RLN identification, and Group 3: visual RLN identification and electromyographic monitoring (47). RLNM has been performed with a bipolar needle electrode placed through the cricothyroid ligament into the vocal muscle. The study results identified the risk factors for permanent RLNP as recurrent benign and malignant goiter, primary surgery in thyroid malignancy, lobectomy , no nerve identification, low or medium volume hospital, and low volume surgeons (47). The conclusion based on these data shows that the visual nerve identification is the standard of RLN treatment in thyroid surgery. RLNM thus becomes a promising tool for nerve identification and protection in extended procedures of thyroid resection.

RLN injuries can cause disability, morbidity and mortality. They also increase prevalence in total thyroidectomies compared to subtotal thyroidectomy. As for lobectomies, they carry the least risk of occurrence. However, the most important risk factor for occurrence is the identification of the RLN intra-operatively. There have been higher rates of occurrences in thyroidectomies without RLN identification or monitoring. This makes the latter an important intervention in reducing the rate of RLN injury occurrences. The majority of occurring RLN injuries are transient while permanent ones are less common.

Hypocalcemia

Hypocalcemia in Total Thyroidectomy

Post-thyroidectomy hypocalcemia is one of the prevalent complications of thyroidectomy. The mechanisms of hypocalcemia following thyroidectomy include parathyroid removal and damage or devascularization which leads to transient or permanent hypoparathyroidism. Other possible mechanisms are vitamin D deficiency and acute increase in calcitonin levels during surgery (48). As for transient initial post-operative hypocalcemia, it is defined as a serum calcium below 2.0 mmol/l during the first 48h following thyroidectomy, whereas persistent hypocalcemia is serum calcium below 2.0 mmol/l am following the six months of surgery where vitamin D supplementation is needed (48).

Hypocalcemia in Subtotal Thyroidectomy

A retrospective study was conducted at Theni Medical College to evaluate thyroidectomy causes and post-operative complications (49). The patients were from different age groups, had different thyroid problems (with female predominance), and all of them underwent similar evaluation measurements and follow-up plan as a management of their results. Only 12 out of 73 patients underwent subtotal thyroidectomy. This suggests that hypoparathyroidism rate is lower in subtotal thyroidectomy despite the superiority of total thyroidectomy in terms of recurrence (49).

Another meta-analysis study compared total thyroidectomy with bilateral subtotal thyroidectomy in patients with multi-nodular non-toxic goiter between 1990-2004 (50). The study examined 528 patients who underwent total thyroidectomy and 550 ones who had a bilateral subtotal thyroidectomy. Data analysis showed that transient hypoparathyroidism was 11% in total thyroidectomy and 4.9% in bilateral subtotal thyroidectomy. As for permanent hypoparathyroidism, it was 0.6% in total thyroidectomy and 0.2% in bilateral subtotal. This was marked as an insignificant difference that did not overweigh the risk of recurrence that was higher in bilateral subtotal thyroidectomy. This implies that the latter carries a higher risk of re-operation with its higher complication rate (50).

Another retrospectives study by Karamanakos et al. was conducted in Greece to examine the complications and risk factors related to different types of thyroidectomies. The study data were collected from 2,043 patients (with female predominance) who had a thyroidectomy for

different thyroid problems. According to the data, even though subtotal thyroidectomy was associated with a significantly lower incidence of permanent and transient hypoparathyroidism, it was not the best surgical option due to the high risk of re-operation that in turn had a higher risk of complications (51).

Hypocalcemia is the most common post-operative complication, where transient hypocalcaemic occurs in one fifth of patients. The selected studies show an increased risk of developing both hypocalcaemic and hypoparathyroidism in total thyroidectomies in comparison to subtotal thyroidectomies.

Conclusion

Although thyroidectomy is a common procedure performed, life threatening complications may occur in both total and subtotal thyroidectomy. An increased risk of hematoma formation is not associated with either approach. On the other hand, recurrent laryngeal nerve injury and hypocalcemia have an increased risk with total thyroidectomy in comparison to subtotal thyroidectomy.

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Data availability

Data that support the findings of this study are embedded within the manuscript.

Authors' contribution:

NA, SA and BM contributed to conception and design of the study, writing – original draft, drafting the article, revising it critically for important intellectual content, final approval of the version to be submitted. LA, RA, KM and AA contributed to Conception and design of the study, revising it critically for important intellectual content, final approval of the version to be submitted.

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