ORATION*

Early prediction and prevention of thyroidectomy associated complications: A paradigm shift towards safer thyroid surgery

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Introduction

History of thyroidectomy

Thyroxine (T4) and Triiodothyronine (T3) hormones are produced by the thyroid gland, which are important in regulating the body's metabolic function. It is documented that 5% of the world population is affected by thyroid-related diseases such as goiter, hypothyroidism, or hyperthyroidism.[1] Leonardo da Vinci in 1500, Andreas Vesalius in 1543 described the anatomical definition of the thyroid gland. The term 'thyroid' is attributed to Bartholemeus Eustacius of Rome, while in London, Thomas Wharton named it glandular thyroidoeis.[4]

Figure 1. Drawing of Leonardo da Vinci.

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Figure 2. Thomas Wharton.

Goiter is the commonest problem encountered in surgical endocrinology. Enlarged thyroid glands were recognized by the Chinese as early as 2700 BC, while in the Indian Ayurvedic system, goiters were referred to as "Gala Ganda" as early as 1400 BC. Hippocratic writings from the 4th century BC mention the term *choiron* to identify a goiter.

The first recorded thyroid operation under anesthesia was performed in 1847.[3] In the year 1850, the French Academy of Medicine banned thyroid surgery due to unacceptable rates of complications.[4]

Thyroid surgery was re-established through the efforts of Theodore Kocher, who is also known as the father of thyroid surgery, along with the "Magnificent Seven" which included William Halsted, Charles Mayo, George Crile, Frank Lahey, and Thomas Dunhill.[3]

Anatomy of the thyroid gland

The thyroid gland is considered the largest endocrine gland of the human body and is situated at the level of C5 to T1 of the anterolateral surface of the trachea. The gland has a central isthmus and two lateral lobes. The pyramidal lobe is a variation that is present in 50% of the population.[1] The thyroid gland has two capsules, the true capsule formed by connective tissue condensation and the false capsule formed by the pretracheal fascia. Zuckerkandl's tubercle is an extension of the posterolateral lobes of the thyroid gland, which has a close relation to the recurrent laryngeal nerves.

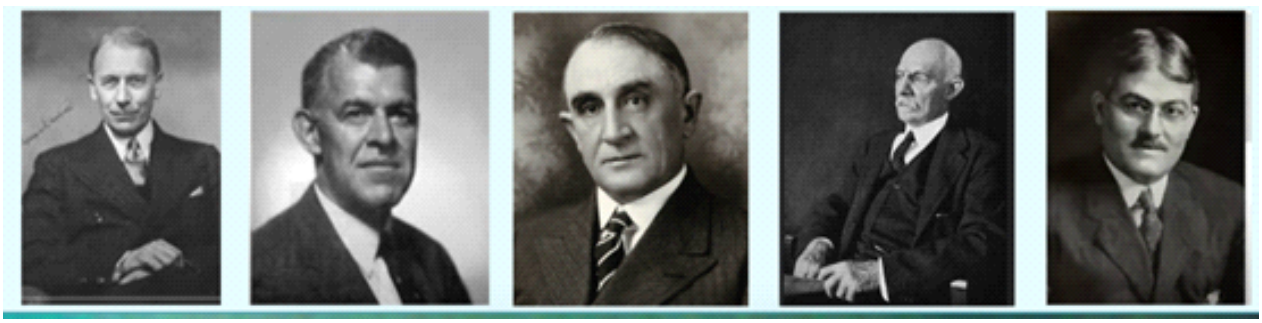

Figure 3. Magnificent Seven Surgeons.

The thyroid gland is supplied by the external carotid artery via the superior thyroid artery and the inferior thyroid artery, a branch from the thyrocervical trunk. The superior thyroid artery has a very close relation to the external branch of the superior laryngeal nerve. The recurrent laryngeal nerve has a close relation to the inferior thyroid artery, and it can be placed anterior, posterior, or between the branches of the artery. The thyroideaima artery arises from the aortic arch or innominate artery, and it is a third source of arterial supply to the gland. It courses to the inferior portion of the isthmus or inferior thyroid poles.[1]

The parathyroid glands are endocrine glands that produce Parathyroid Hormone (PTH), regulating the calcium metabolism of the body. The superior parathyroid glands are located at the posterolateral part of the upper pole, and the inferior parathyroid glands are located related to the inferior pole of the thyroid gland.

The vagus nerve supplies the motor and sensory innervation to the larynx through the superior laryngeal nerve via its external and internal branches and the recurrent laryngeal nerves. Superiorly, sensory and motor innervation is divided between the internal and external branches of the superior laryngeal nerve. Inferiorly, the recurrent laryngeal nerves supply both sensory and motor innervation to the larynx.[11] The superior thyroid artery is related to the external branch of the superior laryngeal nerve, posing a potential risk of damage during ligation of the artery.[15]

The recurrent laryngeal nerves have a close relation to the inferior thyroid arteries and carry the risk of damage during inferior thyroid artery ligation. Both these nerves play an important role in laryngeal innervation and voice production.

Complications related to thyroidectomy

Before 1850, thyroid surgery carried a mortality rate of 40% and the mortality was attributed to hemorrhage, asphyxia, gangrene, and air embolism.[2] Due to the development of sterile surgical arenas, improvement in surgical techniques, and advances in general anesthesia, deaths related to thyroid surgery are extremely rare today. Even though the death rates are rare, the potential for the occurrence of major complications such as injury to the recurrent laryngeal nerve, superior laryngeal nerve, bleeding, hypoparathyroidism, hypothyroidism, thyrotoxic storm, and infection is still common.[5] The rate of injury to the recurrent laryngeal nerve is documented as approximately 1-2% of thyroid-related surgeries. The incidence of hypoparathyroidism can be as high as 20%, and the prevalence of haematoma is about 0.3-1.0%, which is potentially life-threatening.[6]

Voice change

Changes in phonation after thyroidectomy have been reported in many investigations.[7] The incidence of injury to the recurrent laryngeal nerve following thyroidectomy is reported as 2.3%. Voice change can occur in 14.6 -18.4% of thyroidectomy patients without nerve palsy related to the surgical procedures. The likely reasons for voice change include cricothyroid dysfunction, strap muscle traction, perithyroidal neural plexus abnormalities, laryngotracheal fixation with impaired vertical movement, and psychological stress reactions to the operation.[7] Injury to the external branch of the superior laryngeal nerve (EBSLN) is a possibility during the surgical dissection of the superior thyroid vessels, with reported prevalence of injury ranging from 0.5 to 58%. The damage to this nerve results in complete paralysis of the cricothyroid muscle, lowering fundamental voice frequency, and impaired performance in producing high-frequency sounds.[8] Pitch lowering has been one of the common symptoms related to voice-related complications. This type of voice change is not related to injury of the recurrent laryngeal nerves, and several factors may contribute to this complication following thyroidectomy. Preoperative and postoperative evaluation of the larynx to assess mobility of cords using fiberoptic laryngoscopy alone is a poor surrogate for assessment of voice, especially the quality of the voice.[9] A study done in Sri Lanka to evaluate the difference between preoperative and postoperative voice changes following thyroidectomy showed that 14.8% of patients failed to achieve preoperative pitch at two weeks, and 62.9% of patients had low voice intensity at two weeks.[5]

Hypocalcaemia

Post-operative hypocalcaemia results from devascularization or accidental removal of the parathyroid glands during thyroidectomy. Hypocalcaemia can be of two forms defined by the time of onset of symptoms and duration of symptoms, and their presentation. Early post-operative hypocalcemia occurs within a few days after thyroidectomy and is often a transient situation. Permanent hypoparathyroidism is a rare condition, manifesting when parathyroid function remains impaired for more than six months after surgery.[10] Considering the severity of these complications, one should be aware of these conditions and ideally prevent them during total thyroidectomy. According to the available Sri Lankan literature, Fernando et al have reported that the transient hypocalcemia rate is 11.7% and the permanent hypocalcemia rate is 1.96% following thyroidectomy.

Postoperative bleeding

Post-thyroidectomy haematoma formation is a rare but significant complication due to its life-threatening nature. Increasing age, male gender, presence of Graves' disease, pre-existing hypertension, usage of anti-thrombotic agents, low-volume centers, redo thyroidectomy, and association of neck dissection are considered significant risk factors for the development of postoperative haematomas in the neck.[6]

Difficulty in swallowing

Dysphagia following thyroidectomy is a common postoperative complication in the short or long term, leading to significant changes in the quality of life of those who have undergone thyroidectomy. Dysphagia related to thyroidectomy can be related to nerve damage or appear after an uncomplicated thyroidectomy.[11]

Both the superior laryngeal nerve (SLN) and the recurrent laryngeal nerve (RLN) are involved in the swallowing mechanism. The supraglottic space and vocal folds are supplied by the internal branch of the SLN. Lesions over the internal branch of the SLN can lead to dysphagia and aspiration.[12] The external branch (EBSLN) provides nerve supply to the cricothyroid muscle, which is responsible for tension of the vocal folds. However, damage to this nerve is followed by different rates of swallowing symptoms.[13]

Posterior branches of the recurrent laryngeal nerve are responsible for the innervation of the cricopharyngeal muscle. Due to this innervation, the patients with unilateral RLN paralysis show swallowing impairment in about 30% of cases.[14]

Results of the studies

The study included 128 patients who underwent total thyroidectomy at the University Hospital KDU from 01/01/2023 to 31/12/24.

Demographic data

Age distribution

The median age of the study group was 49 years (16 to 77 years).

Sex distribution

The majority of the patients who underwent thyroidectomy were female patients, accounting for 79.7%.

Table 1. Sex distribution

	Sex distribution
Female	102 (79.7%)
Male	26 (20.3%)

Table 2. Patterns of ultrasound scan reports of goiters

Type of goiter	*Number (%)*
Nodular goiter	95 (74.21%)
Thyroid carcinoma	15 (11.72%)
Other suspicious thyroid nodules	18 (14.06%)

Table 3. TIRADS Classification of goiters

	Number of patients
TIRADS 1	06
TIRADS 2	59
TIRADS 3	30
TIRADS 4	18
TIRADs 5	15

Table 4. Pre-operative fine needle cytology results of goiters

	Number of patients
Bethesda 1	06
Bethesda 2	72
Bethesda 3	08
Bethesda 4	09
Bethesda 5	18
Bethesda 6	15

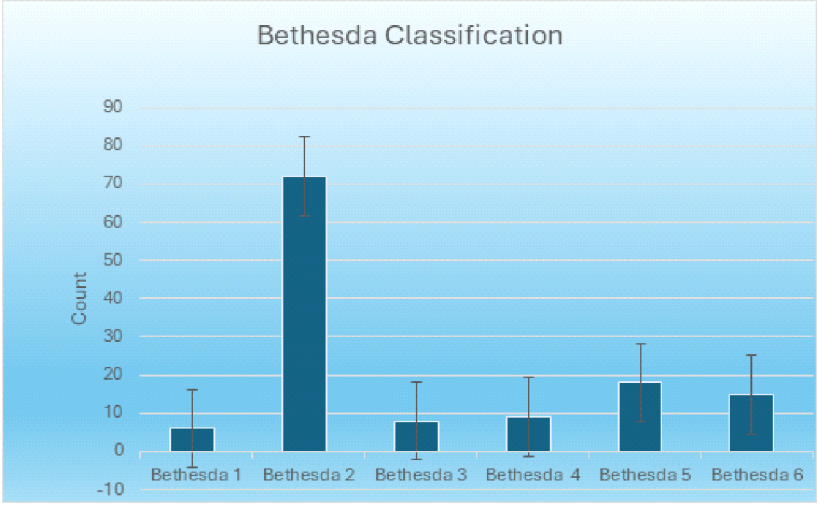

Figure 4. Distribution of the Bethesda categories.

Hypocalcaemia

Table 5. Pre-operative serum calcium levels

	Number of patients
Low pre-operative calcium level *(ionized calcium level less than 4.5 mg/dl)*	15
Normal preoperative calcium level *(ionized calcium levels between 4.5- 5.6 mg/dl)*	213

Table 6. Patients with post-operative hypocalcemia

	Number of patients
Patients with postoperative biochemical hypocalcemia *(ionized calcium level less than 4.5 mg/dl)*	59
Patients with postoperative normal calcium levels *(ionized calcium level between 4.5 - 5.6 mg/dl)*	59

Symptomatic hypocalcemia among patients with biochemical hypocalcemia

Symptomatic hypocalcemia was observed in 18 (30.5%) biochemically hypocalcemic patients, and 41 patients (69.5%) were asymptomatic.

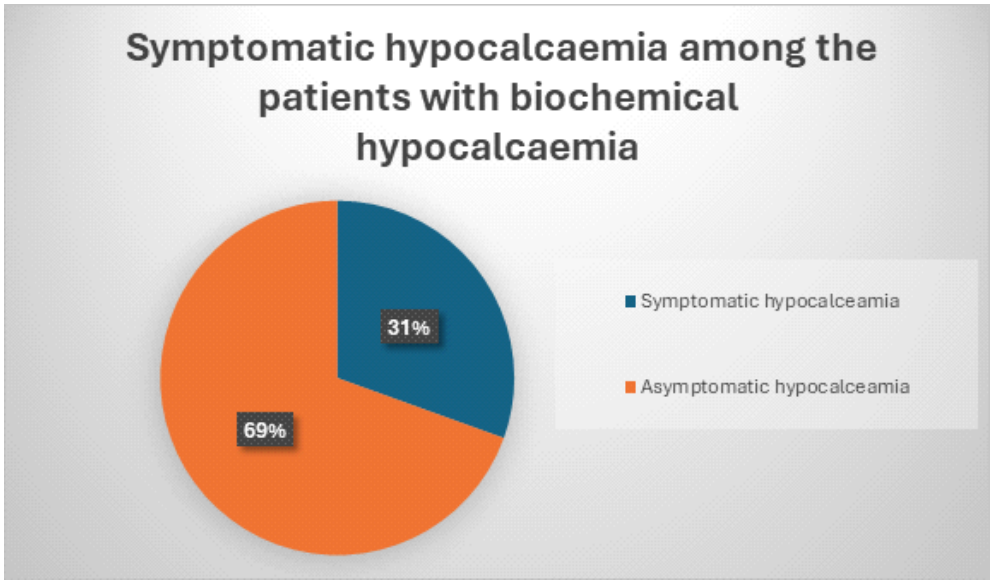

Figure 5. Incidence of symptomatic hypocalcaemia among patients with biochemical hypocalcaemia.

Relationship between preoperative and postoperative hypocalcaemia

There is no statistically significant relationship between preoperative and postoperative hypocalcaemia (p= 0.3).

Table 7. Preoperative Vitamin D level

	Number of patients
Sufficient level (30 - 60 ng/ml)	08
Insufficient level (12 - 30 ng/ml)	86
Deficient level (less than 12 ng/ml)	34

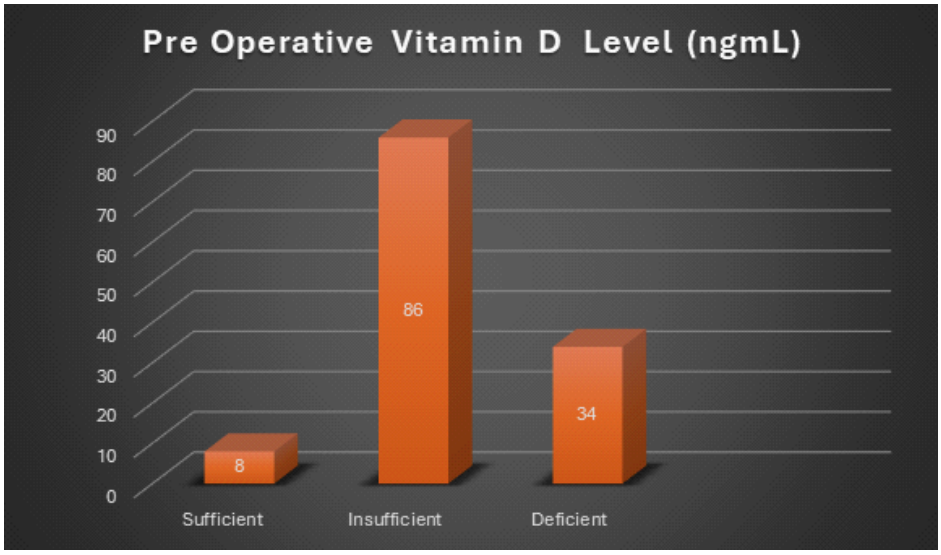

Figure 6. Pre-operative Vitamin D level.

Preoperative Vitamin D level and post-operative hypocalcemia

There is a statistically significant relation between preoperative Vitamin D deficiency and postoperative hypocalcemia (p=0.0075). Pearson correlation coefficient of 0.816 indicates a strong positive correlation between preoperative Vitamin D deficiency and postoperative hypocalcemia.

Recurrent laryngeal nerve palsy

Table 8. Incidence of vocal cord palsy among the study group

	Number of patients
Preoperative vocal cord palsy	08
Normal vocal cord function	120

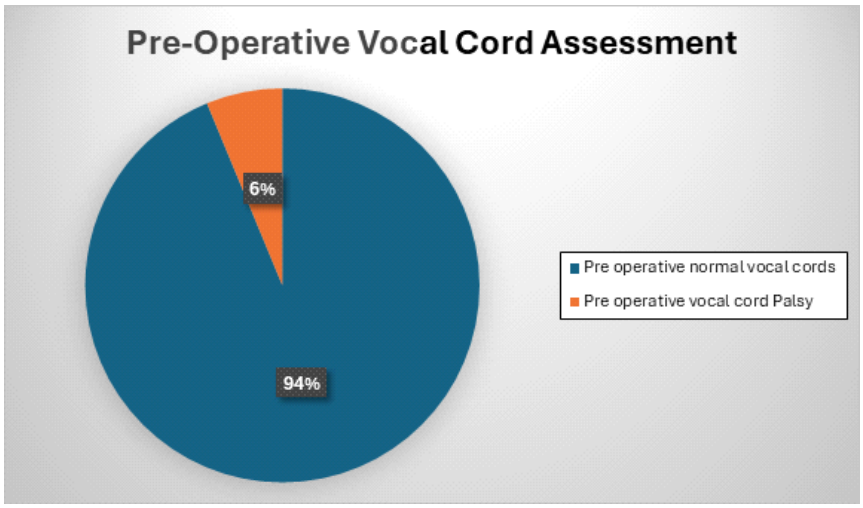

Figure 7. Pre-operative vocal cord assessment.

No incidence of post-operative recurrent laryngeal nerve palsy in this study group.

Continuous intraoperative nerve monitoring

Recurrent laryngeal nerve palsy has been documented as a commonly occurring complication following thyroidectomy. The reported incidence of temporary vocal cord palsy is 2 - 26%, whereas that of permanent palsy is in the range of 0.3 - 6%. During revision surgery, the rate of vocal cord palsy is as high as 14%. Visualization and preservation of the recurrent laryngeal nerve during thyroidectomy is the GOLD standard to prevent vocal cord palsy.

Intraoperative identification of nerves during thyroidectomy has shown significant improvement along with the development of laryngeal nerve monitoring techniques. The recurrent laryngeal nerve can be monitored intraoperatively as continuous or intermittent nerve monitoring. During the surgical procedure, intraoperative monitoring of the nerve using the nerve monitor prevents thermal and traction injuries. This type of monitoring plays an important role in revision thyroidectomies, thyroidectomies done for malignancies, and patients with preoperative vocal cord palsy.

During the surgical procedure, intermittent and continuous monitoring of the recurrent laryngeal nerve is performed to detect signal loss. In contrast, continuous nerve monitoring intraoperatively helps to minimize traction and thermal injury by detecting them. Further, continuous intraoperative monitoring facilitates the functional real-time monitoring of the entire nerve with detailed EMG documentation for reference. Intraoperative nerve monitoring (Figure 2) can be used as a supporting method of identifying the nerve, which is compatible with the gold standard method, minimizing the risk of damaging the recurrent laryngeal nerve, especially where the nerve is at high risk.

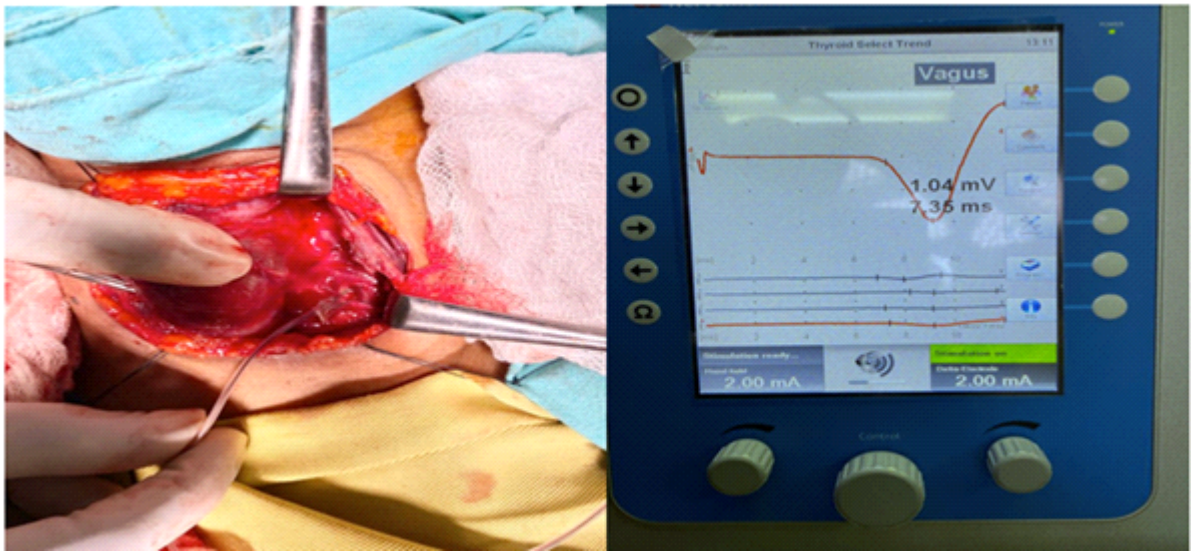

Figure 8. Intra-operative monitoring of the vagus nerve.

Table 9. Surgical operations in which nerve monitoring was used

	Number of patients
Pre-operative unilateral vocal cord palsy	08
Multinodular goiter	07

Identification of External Branch of Superior Laryngeal Nerve (EBSLN)

The superior laryngeal nerve is a branch of the vagus nerve that gives an internal branch and an external branch. The external branch innervates the cricothyroid muscle to promote lengthening and thinning of the vocal fold, thus increasing voice pitch. The external branch of the superior laryngeal nerve also supplies the pharyngeal plexus and inferior constrictor muscle, playing a significant role in the swallowing mechanism. The nerve has a close relation to the superior thyroid artery and the upper pole of the gland. Identification of the nerve is crucial in preventing damage during the thyroidectomy.

Kierner categorized the EBSLN into four types based on its relationship to the superior thyroid artery (STA) and surrounding structures:

- **Type 1** – The EBSLN crosses the STA more than 1cm above the superior pole of the thyroid gland
- **Type 2** – The nerve crosses less than 1 cm above the superior pole
- **Type 3** – The nerve crosses below the superior pole of the thyroid gland, often under the cover of the thyroid tissue or the inferior constrictor muscle
- **Type 4** – The nerve runs dorsally to the STA, passing through or behind its branches near the superior thyroid pedicle

Identification of the external branch of the superior laryngeal nerve

A total of 78 nerves were identified during thyroidectomy surgeries.

Table 10. Types of external branches of the superior laryngeal nerve

	Number of patients
Type 01	69
Type 02	06
Type 03	02
Type 04	01

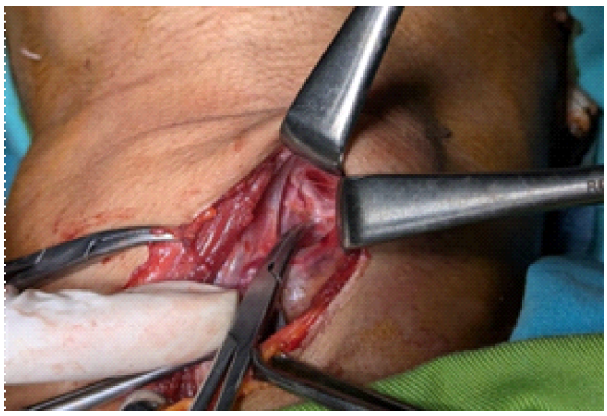

Figure 9. External branch of superior laryngeal nerve.

Post-operative haematoma formation

There was one (1) case with major bleeding leading to reopening, and another five (5) cases with mild haematoma formation.

Case 1

A 48-year-old patient diagnosed with hyperthyroidism, on carbimazole, underwent a total thyroidectomy. He was euthyroid preoperatively. The patient was managed in the ICU post-operatively and developed voice change and neck swelling two hours after surgery. Immediate reopening of the surgical site was done in the operating theater, and found to have bleeding from a branch of the inferior thyroid artery. Artery ligation was done, and the postoperative period was uneventful.

The protocol followed to prevent post-operative haematoma formation

Edafe has proposed an intraoperative protocol (ITSRED Fred) to practice during surgery to minimize the risk of postoperative bleeding (Table 11).

Table 11. ITSRED fred protocol

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Table 4 ITSRED Fred Protocol for preventing post-surgical neck haematoma after thyroid and/or parathyroid surgery

	Parameters
I	Irrigation of wound with water – to clear field and look for minor points [11,25]
T	Time – wait a few miniutes
S	Systolic blood pressure to be > 100 mmHg at time of closure
R	Relieve neck extension – either by deflating bag under shoulders, removing sand bag, or flexing the neck
E	Elevate venous pressure – either by Valsalva manoeuvre [25,26], head-down position, or both [27]
D	Do not drain it, deal with it and consider sealants such as fibrillar [25,26]
Fred	Flaps – evaluation of bleeding under subplatysmal flaps prior to closure

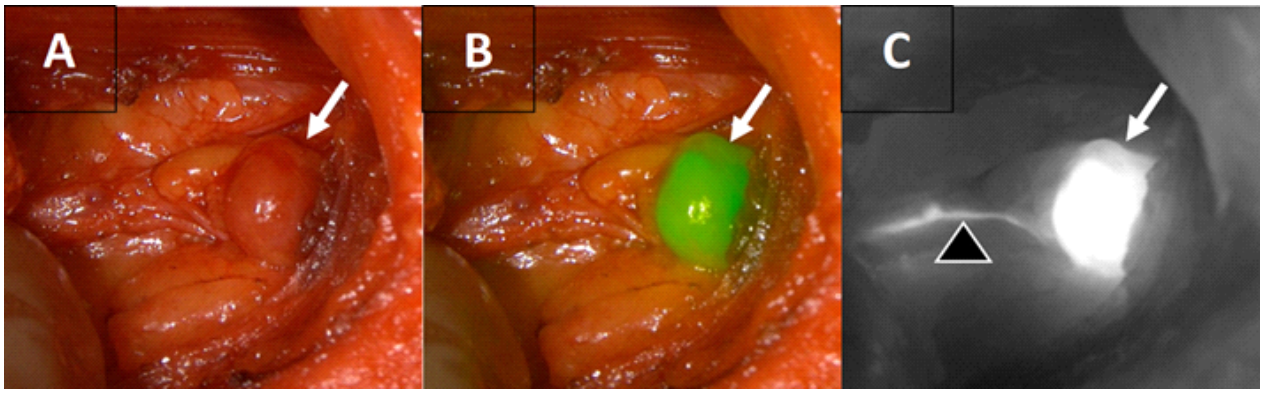

Figure 10. Parathyroid gland fluorescence following injection of ICG and excitation with NIR light.

Hypoparathyroidism

Literature describes different methods for identifying the parathyroid glands during the surgical procedure.

1. Identification of the glands using anatomical landmarks.
2. Intraoperative Indocyanine Green (ICG) angiography.
3. Near Infrared (NIR) autofluorescence imaging during thyroidectomy.

Table 12. Identification of parathyroid glands

	Number of patients
All four glands identified	20
At least two glands identified	108

Conclusion

Even though mortality related to thyroidectomy is rare in the modern surgical era, complications related to thyroidectomy are associated with significant morbidity and reduction of the quality of life of patients. Adherence to the available preventive strategies is the responsibility of the surgical team to give the most favorable outcome to the patient. Vitamin D insufficiency and deficiency were highly prevalent among patients who underwent total thyroidectomy, and a statistically significant association was observed with post-operative hypocalcemia and Vitamin D deficiency. Pre-operative hypocalcemia does not show a statistically significant association with the occurrence of postoperative hypocalcemia. Further, proper identification of the parathyroid gland is crucial in preventing hypocalcemia following thyroidectomy. Intraoperative nerve monitoring is beneficial in patients with a high risk of vocal cord palsy. Adherence to a protocol before the closure of the surgical procedure has an impact on the prevention of postoperative bleeding following total thyroidectomy. Swallowing problems following thyroidectomy need to be evaluated further in future research.

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