Predictors of post-thyroidectomy complications, a tertiary centre experience: A retrospective cohort study

Original Article

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ABSTRACT

Purpose: Thyroidectomy is currently a common elective surgical procedure associated with a wide range of complications, from unnoticed events to lifelong problems and even life-threatening complications. The most troublesome events are bleeding, nerve injuries, and hypocalcaemia. The present study was conducted to report the incidence and predictive factors for perioperative complications, aiming to identify preventive measures.

Patients and Methods: A retrospective study of 241 patients who underwent elective thyroidectomy between 2013 and 2023. The incidence and types of complications were the primary outcomes, and the predictive factors for complications were the secondary outcomes. Patient demographic and perioperative data were collected, tabulated, and analyzed by SPSS version 26. Univariate analysis was performed with the chi-square test for factors predicting perioperative complications, and statistically significant factors were further analyzed by multivariate logistic regression analysis to determine the most significant factor.

Results: This study included 241 patients; 183 (75.8%) were females, 170 (71.5%) patients had thyroid cancer, and 71 (29.5%) patients had benign thyroid lesions. The mean hospital stay after surgery was 2 days, and one case of hospital death was reported (0.4%).

The overall postoperative complication rate was 34.4%. The most frequent complications were hypocalcaemia (19.9%), recurrent laryngeal nerve injury (2.45%), and bleeding (4.1%). The other complications reported were pneumothorax, surgical site infection (SSI), seroma, and chyle leakage.

The predictors of post-thyroidectomy complications were advanced age greater than or equal to 60 years ($P=0.003^*$), prior thyroid surgery ($P<0.001^*$), and lymph node dissection with total thyroidectomy ($P= 0.01^*$) according to univariate analysis. Multivariate analysis revealed that advanced age ($P=0.02^*$) and prior thyroid surgery ($P<0.001^*$) were the main significant predictors of complications.

Conclusion: Thyroid surgery is generally a safe procedure with acceptable surgical outcomes. Transient hypocalcaemia is the most frequent post thyroidectomy complication. Advanced age and prior thyroid surgery were the main significant predictors of overall post-thyroidectomy complications. Neck dissection with total thyroidectomy is safe but has a higher incidence of hypocalcaemia than thyroidectomy alone. Consequently, every effort should be made to avoid reoperation by performing a wise definitive initial treatment.

Key Words: Hypocalcaemia, recurrent laryngeal nerve, thyroidectomy, total thyroidectomy.

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INTRODUCTION

The first total thyroidectomy was reported by Abu-Al-Qasim in 925 AD[1]. In the Middle Ages, it was invariably associated with death, so the French Academy of Medical Sciences banned it in 1850. In the 19th century, Emil Theodore Kocher used precise surgical techniques and meticulous hemostasis to reduce the mortality rate to less than 1% in more than 5,000 thyroidectomies[1]. He received a Nobel Prize in 1909 for this great shift[2].

The main goals during thyroidectomy are always good hemostasis and avoidance of injury to the recurrent laryngeal nerve (RLN), the external laryngeal nerve (ELN), and the parathyroid glands[3].

A wide range of complications are associated with thyroidectomies, such as hypoparathyroidism (HP), RLN injury, injury to the external branch of the superior laryngeal nerve, postoperative bleeding (PB), thoracic duct injury, laryngeal edema, laryngospasm, tracheal injury, esophageal injury, stridor, and thyroid crisis[4,5]. The incidence of complications is associated with patient factors, the type of thyroid disease, the type of thyroid surgery, and surgeon experience[6].

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Thyroidectomy complications increase hospital stays and overall costs. Permeant nerve injury and hypocalcaemia have negative impacts on the quality of life of patients[7].

Clinical studies to define risk factors for perioperative complications might aid in reducing the incidence of perioperative complications by applying preventive measures. This study aimed to report the incidence and predictive factors for perioperative complications, aiming to identify preventive measures.

PATIENTS AND METHODS:

This retrospective study was carried out on patients with different thyroid pathologies admitted to Surgical Oncology Department, South Egypt Cancer Institute, Assiut University, who were treated with thyroidectomy. After obtaining ethical approval for this study from the local institutional ethics committee, we started collecting the data from completed hospital files of patients who underwent thyroid surgeries between January 2012 and December 2022. A total of 241 patients were found to have undergone thyroid surgeries; 170 (71.5%) patients had thyroid cancer, and 71 (29.5%) patients had benign thyroid lesions.

The inclusion criterion was adult patients who underwent thyroid surgery for euthyroid goiter. Patients with incomplete hospital records, lack of operative notes, perioperative follow-up notes or histopathology, and confounding factors such as preoperative hypocalcaemia, preoperative ELN or RLN, involvement, preoperative vocal cord paralysis, tracheomalacia, or bleeding tendency were excluded.

The preoperative workup included patient history and examination, thyroid profile, radiological examination (thyroid and neck ultrasound and CT whenever indicated), and tissue biopsy. All patients underwent preoperative indirect or fiberoptic laryngoscopy for evaluation of vocal cord mobility.

Patients were operated on under general anesthesia in supine position. A transverse cervical skin incision 2 cm above the sternal notch was used (Fig. 1). The surgeries included lobectomy and total thyroidectomy (Fig. 2). Central neck dissection was performed for all patients with differentiated thyroid cancer, and lateral neck dissection was selectively added in patients proven to have lateral neck lymph nodes involvement (Fig. 3).

Vocal cord examination was performed routinely whenever possible by the anesthetist during extubation at the end of the procedure as the first step for assessment of vocal cord mobility. Postoperative clinical evaluation for nerve injuries was performed for all patients. Indirect or fiberoptic laryngoscopy was performed for suspected cases.

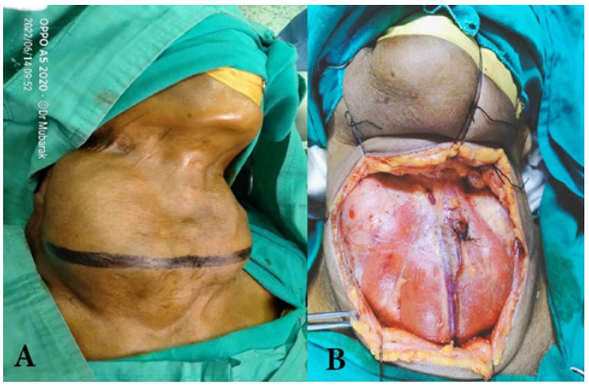

Fig. 1: Cervical collar incision for thyroidectomy: (a). Surgical marker demarcation. (b). Skin flaps elevated.

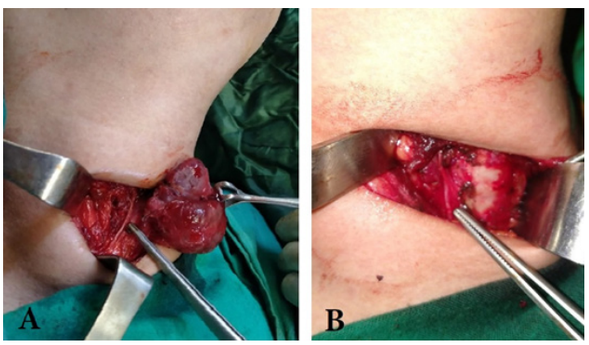

Fig. 2: Intraoperative photo taken during total thyroidectomy showing the following: (a). Identification and preservation of the recurrent laryngeal nerve. (b). The operative field after total thyroidectomy.

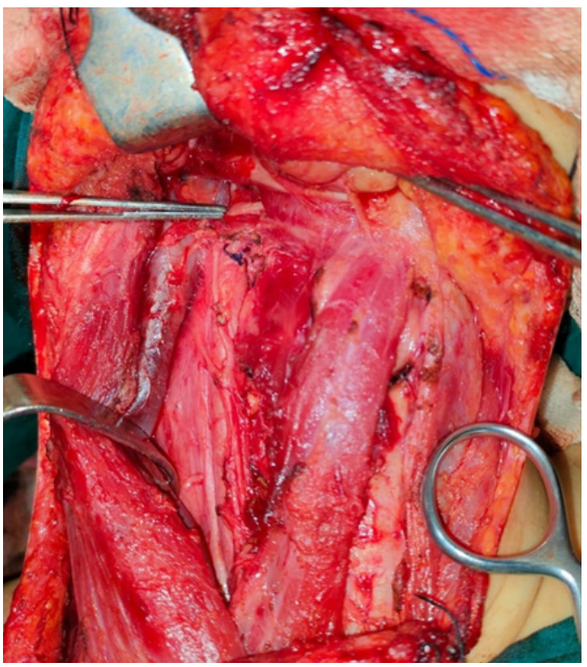

Fig. 3: Intraoperative photo showing operative field after modified radical neck dissection.

Serum calcium was tested on the second postoperative day. Close observation of the patient was performed, and any complications were promptly diagnosed and properly managed.

Postoperative vocal cord palsy or paresis was defined as the presence of immobility or decreased movement of the vocal cords. Persisting vocal cord dysfunction after 6 months was considered permanent.

Hypocalcaemia was considered present whenever there was a need for exogenous calcium replacement to maintain normal serum levels (8–10.4 mg/dl) or to eliminate the clinical signs and/or symptoms of hypocalcaemia. Hypocalcaemia was considered permanent when calcium replacement was necessary for more than 6 months.

Outpatients followed-up at 1 week and at 1, 3, 6, and 12 months. Levothyroxine replacement therapy, radioactive iodine, or referral to medical oncology was started as appropriate according to the patient's condition. Nerve complications and tracheostomy were followed up and managed by Otorhinolaryngology, Head and Neck surgery department.

Statistics

Patient demographic and perioperative data (age, sex, comorbidity, tumor pathology, prior thyroid surgery, type of surgery, postoperative complications, and hospital death) were collected, tabulated, and analyzed by SPSS version 26 (Statistical Package for Social Sciences, PSS, Inc., Chicago, Illinois, USA). Qualitative data are presented as frequencies and percentages. Numerical data are expressed as the arithmetic mean ± standard deviation (M±SD). The chi-square test was used in univariate analysis for factors predicting postoperative complications. Binary logistic regression was used in multivariate analysis to determine the main significant factors predicting postoperative complications. A *P value* less than.05 was considered to indicate statistical significance.

RESULTS:

Patient demographics, histopathology and complications are presented in (Table 1). The mean age ranged from 20-78 (M±SD:50±16.62) years, 132 (54.8%) patients were greater than 60 years old, 183 (75.8%) were females, and 110 (45.6%) had prior thyroid surgery. Papillary thyroid cancer was the most common histopathology in 108 (44.8%) patients, followed by benign pathology in 71 (29.5%) patients. Total thyroidectomy was the most commonly performed procedure in 52.7% of patients. The duration of hospital stay was 2 (1–18) days.

Only one (0.4%) case of hospital death was reported. A total of 83 (34.4%) patients had postoperative complications, with transient hypocalcaemia being the most frequent complication in 44 (18.25%) patients. Other frequent complications with lower incidences were RLN, ELN palsy, seroma, hematoma, and SSI.

The overall rate of RLN palsy was 2.45% (six patients). Transient palsy occurred in 4 patients; full recovery occurred within 6 months. Permanent vocal cord palsy occurred in two patients. Tracheostomy was performed in 8 patients.

Postoperative hypocalcaemia occurred in 48 (19.9%) patients. Transient hypocalcaemia was found in 44 (18.25%) patients, full recovery occurred within 6 months. Four (1.6%) patients had permanent hypocalcaemia. The incidence of hypocalcaemia was significantly greater in patients who underwent thyroidectomy with neck dissection than in patients who underwent thyroidectomy alone (35.8% vs. 18.9%, *P value <.001*). (Table 2).

Seroma was a postoperative complication found in 10 (5%) out of the 200 patients with drain. None of the 41 patients in whom no drain was placed presented with this type of complication. Five (2.01%) patients developed postoperative SSI, 10 patients had postoperative bleeding, and four (1.65%) of them underwent reoperation. Chyle leaks occurred in two (0.82%) patients who underwent neck dissection.

The predictors of overall post-thyroidectomy complications were advanced age ≥ 60 years (*P=0.003*), prior thyroid surgery (*P<0.001*), and neck dissection with total thyroidectomy (*P=0.01*) according to univariate analysis (Table 3). Multivariate analysis revealed that advanced age (*P=0.02*) and prior surgery (*P<0.001*) were the main significant predictors of complications (Table 4).

Table 1: Patient demographics, histopathology, and complications

Variables	Category	Number (Percentage (%))
Age years	≥60	109 (45.2)
	< 60	132 (54.8)
Gender	Female	183 (75.9)
	Male	58 (24.1)
Smoking	Smoker	41 (17)

	Nonsmoker		200 (83)
COPD	Yes		24 (10)
	No		217 (90)
Prior thyroid surgery	Yes		110 (45.6)
	No		131 (54.4)
Histopathology	Benign		71 (29.5)
	Pap thyroid cancer		108 (44.8)
	Follicular thyroid cancer		49 (20.3)
	Medullary thyroid cancer		10 (4.1)
	Anaplastic thyroid cancer		3 (1.2)
Type of Surgery	Thyroid lobectomy		47 (19.5)
	Total thyroidectomy(TTH)		127 (52.7)
	TTH with neck dissection		67 (27.8)
Indication	Benign		71 (29.5)
	Malignant		170 (71.5)
Complications	Number of patients with complications		83 (34.4)
	Hospital death		1 (0.4)
	Hypocalcaemia 48 (19.9%)	Transient	44 (18.25
		Permanent	4 (1.6)
	RLN palsy		6 (2.45)
	ELN palsy		10 (4.1)
	Bleeding		10 (4.1)
	Seroma		10 (4.1)
	Tracheostomy		8 (3.3)
	Pneumothorax		2 (0.8)
	Chyle leak		2 (0.8)
	SSI		5 (2)

Table 2: Postoperative hypocalcaemia and type of surgery

Type of Surgery	Number of surgeries (Total =241)	Number of cases of Hypocalcaemia (Total =48 (19.9%))	*P* value
Thyroid Lobectomy	47 (19.5%)	zero	
Total Thyroidectomy(TTH)	127 (52.7%)	24 (18.9%)	<0.001*
TTH with Neck Dissection	67 (27.8%)	24 (35.8%)	

Table 3: Univariate analysis of factors predicting postoperative complications

Variable	95% CI	*P* value
Age (≥60/<60)	0.01–0.12	0.003*
Gender (Female/Male)	0.84–0.93	0.12
Smoking (+/-)	0.8–0.92	0.135
COPD (+/-)	0.6–0.73	0.16
Pathology (Benign/Malignant)	0.9–1.00	0.117
Prior thyroid surgery	0.00–0.012	<0.001*
Type of Surgery (Lobectomy/TTH/TTH+ND)	0.00–0.026	0.01*

Table 4: Multivariate analysis of factors predicting postoperative complications

Variable	HR	95% CI	*P* value
Age (≥60/<60)	0. 64	0.40–0.65	0.02*
Prior thyroid surgery	1.27	0.62–0.94	<0.001*
Type of Surgery (Lobectomy/TTH/TTH+ND)	1.02	0.43–1.07	0.13

DISCUSSION

Thyroidectomy is the most frequently performed surgical procedure in endocrine surgery for treating a range of thyroid conditions, including thyroid nodules, goiters, and thyroid cancer. Although thyroid surgery is generally safe and most patients recover fully without any adverse events, there are potential complications associated with this procedure, especially in older patients who have had prior thyroid surgery or who have undergone thyroidectomy with neck dissection. Some complications, such as postoperative bleeding with airway compression and bilateral palsy of the RLN, can be life-threatening.

In this study, 241 patients who had undergone thyroidectomy for different thyroid pathologies were enrolled. Of these, 170 (71.5%) patients had thyroid cancer, and 71 (29.5%) patients had benign thyroid lesions.

The incidence of postoperative complications varies significantly in the literature, ranging from 7.4 to 53%. The overall postoperative complication rate in this study was 34.4%. Hypocalcaemia was identified as the most common complication in this study. The literature reports the incidence rates of temporary hypocalcaemia, ranging from 1.6 to 71%, while permanent hypocalcaemia incidence rates range from 0.4 to 13.8%[8–11].

In this study, postoperative hypocalcaemia occurred in 48 (19.9%) patients, transient hypocalcaemia in 44 (18.25%) patients and permanent hypocalcaemia in four (1.6%) patients.

Transient hypoparathyroidism and hypocalcaemia are the most common complications of thyroid surgery, and they occur in up to 50% of patients who undergo total thyroidectomy[12]. Hypoparathyroidism occurs due to damage or removal of the parathyroid glands during surgery, which leads to a decrease in parathyroid hormone secretion and a subsequent decrease in serum calcium levels. Transient hypoparathyroidism usually resolves within a few days to weeks, and patients may require calcium and vitamin D supplementation during this time. However, in some cases, permanent hypoparathyroidism may occur, which requires long-term calcium and vitamin D supplementation[12].

The incidence of postoperative hypocalcaemia did not significantly correlate with patient sex, age, or pathology. However, extension of thyroidectomy and neck dissection were significantly associated with the risk of transient and permanent hypocalcaemia than was thyroidectomy alone (35.8% vs. 18.9%, *P value <.001*).

The British Association of Endocrine and Thyroid Surgeons (BAETS) Six National Audit Report in 2021 revealed that the incidence of hypocalcaemia was 7.3–8.5%. Malignancy and redo-thyroidectomy were identified as significant risk factors for hypocalcaemia.

Other less frequent complications observed in the study included RLN and ELN palsy, hematoma, seroma, SSI, postoperative bleeding, and chyle leakage. The incidence of RLN injury after thyroidectomy varies widely in the literature, with reports ranging from 0.4 to 13% for temporary paresis and from 0 to 5.2% for permanent paralysis[13–16]. Injury to the RLN can result in vocal cord palsy, which can cause hoarseness, difficulty speaking, and breathing difficulties. Most cases of RLN injury are transient and resolve within a few months. However, in some cases, permanent vocal cord palsy may occur[17].

The risk of RLN injury is greater in patients who have undergone extensive thyroid surgery or who have a history of previous neck surgery. Malignancy was not reported to be statistically significant in overall nerve palsy[18]. Recurrent goiter surgery, nonidentification of the RLN, and total thyroidectomy were shown to be associated with a significantly increased risk of postoperative RLN palsy in other studies[19].

In this study, RLN palsy was observed in six (2.49%) patients, temporary palsy in four (1.66%) patients, and permanent palsy in two (0.83%) patients. The type of thyroidectomy, patient sex, and the association with neck dissection did not significantly correlate with the incidence of vocal cord palsy.

ELN injury is less common than RLN injury, with reported incidence rates ranging from 0 to 3%[17]. Injury to the ELN can result in dysphonia, which can cause difficulty speaking and singing. Most cases of ELN injury are transient and resolve within a few weeks to months[20].

One potential complication of thyroid surgery is bleeding, which can occur during or after surgery. Bleeding can be caused by injury to blood vessels during the surgical procedure or can occur later due to SSI, inflammation, or other factors. The incidence of postoperative bleeding after thyroid surgery ranges from 0.5 to 4%[21–23]. In severe cases, bleeding can lead to airway obstruction, which requires urgent intervention. In the current study, 10 patients had postoperative bleeding. Five patients managed conservatively by close follow-up, among them, blood transfusion was needed in one patient. Four patients required reoperation to secure hemostasis, slipped superior thyroid artery ligature was found in one patient, no bleeding points was found in the other three patients at the time of wound exploration. One (0.4%) patient died from airway compression secondary to bleeding, in spite of presence of drain, bedside wound opening and evacuation of the huge compressing hematoma once a family member alarm the medical staff for patient difficult respiration. The event happened 4 h after uneventful total thyroidectomy for recurrent goiter in 68 years old woman. That event might give us insight about how postoperative life-threatening hematoma could be encountered even after straightforward thyroidectomy procedure especially in recurrent goiter. Early postoperative close follow-up and readiness for bedside opening of the wound to release hematoma followed by hemostasis in operative theatre is a must in all patients.

In the current study, pneumothorax was encountered intraoperatively in two (0.8%) patients, and was managed by intercostal tube under water seal, it was removed within 48 h after full lung expansion in daily follow-up chest radiography, and maintenance of normal oxygen saturation in room air.

Regarding tracheostomy, it was needed in eight patients. Four patients, due to laryngeal edema, which diagnosed by laryngoscopy during extubation, that revealed oedematous swollen larynx associated with airway obstruction. Hydrocortisone was given and the condition was resolved within 3–7 days. Worthy to mention is that the authors realized, anecdotally, that, laryngeal edema mostly happened in prolonged surgery and excessive electrocautery around trachea.

Tracheostomy was also needed in other three patients, due to tracheomalacia. The eighth patient was acromegalic and suffered from a redundant pharyngeal wall after surgery, which resulted in respiratory obstruction. This patient improved after 2 months of follow-up at the Otorhinolaryngology, Head and Neck Surgery Department.

SSI is also a potential complication of thyroid surgery. The incidence of SSI after thyroid surgery ranges from 0.5 to 5%[24]. Risk factors for SSI include obesity, diabetes, immunosuppression, and the presence of preexisting infection. In our study, postoperative SSI occurred in five (2.01%) patients.

Additionally, other complications of thyroid surgery include seroma and chyle leakage.

Regarding Chyle leak in our study, two (0.82%) patients, from those who had lateral neck dissection, was diagnosed by having milky drain output. The triglyceride level greater than 100 mg/dl and presence of chylomicrons in the drain output confirmed the diagnosis. The two patients had low output chyle fistula, and successfully closed by conservative management, one patient in the 10th day, and the second patient in the 14th day.

Patients were restricted to bed, and took intravenous fluids, low fat and medium-chain fatty acid diet. Octreotide 100 micrograms was given subcutaneously three times a day continues for 48 h after complete cessation of chyle leak.

Seroma was encountered in 10 (4.1%) patients and managed by aspiration only whenever necessary.

Another potential complication is damage to the trachea or oesophagus, which can occur due to injury during surgery or due to the development of a fistula after surgery[25]. In our study, no cases of tracheal and oesophageal injury encountered.

Unsuccessful removal of all the thyroid tissue is another problem that may lead to the need for additional surgery or radioactive iodine treatment. The risk of recurrence depends on several factors, including the extent of the initial surgery, the presence of cancer, and the patient's age and overall health[26].

Finally, thyroid surgeries might result in psychological side effects such as anxiety, depression, and issues with body image. Changes in a patient's self-image, voice, or level of energy following thyroid surgery might be detrimental to their quality of life[27,28].

Age older than 60 years and a history of thyroid surgery were found in our study to be important predictors of overall post-thyroidectomy complications. According to multivariate analyses, advanced age and prior surgery were the most important significant predictors of perioperative complications. These findings are consistent with those of a study by Atiq and colleagues which revealed that hypocalcaemia was significantly predicted by the extent of thyroidectomy and the association with neck dissection, while overall post-thyroidectomy complications and prior thyroid surgery were significantly predicted by age (older than 60 years) and prior thyroid surgery[29].

The spectrum and incidence of complications in the current study learned us many lessons. Preoperative serum calcium should be done before surgery. Patients with low or borderline serum calcium level are at higher risk for developing postoperative symptomatic hypocalcaemia. Preoperative laryngoscopy to evaluate vocal cords mobility should be done, the presence of non-mobile vocal cord in one side will alert surgeon to give extreme caution to other RLN during dissection, any bleeders in Berry's ligament or in proximity to RLN are better be controlled with non-absorbable suture not by energy source.

Intraoperatively, every effort should be done to avoid inadvertent surgical trauma to the parathyroid glands or its blood supply or inadvertent removal of parathyroid gland, every parathyroid gland should be treated as if it is the only one the patient have. Vasculature-preserving technique in the form of ligation of the tertiary branches not the inferior thyroid artery main trunk, might reduce the risk of postoperative hypocalcaemia. Intracapsular dissection of thyroid gland reduces the risk of inadvertent removal of parathyroid glands. Avoiding use of energy sources in proximity of the parathyroid glands and the anticipated location RLN, nerve monitoring, magnification with surgical loupes might reduce the risk of harm. In case of accidental removal of parathyroid gland, autotransplantion is recommended. These precautions should be applied even during hemithyroidectomy procedures, as hypocalcaemia after hemithyroidectomy has not been well investigated till now. Recently Jae *et al*. published interesting study which revealed that manipulation of even one thyroid lobe can result in a transient hypocalcaemia and hypoparathyroidism in 5% of patients and be symptomatic in 2.5%[30].

CONCLUSION

Thyroid surgery is a generally safe procedure, with acceptable surgical outcomes. Transient hypocalcaemia is the most frequent post-thyroidectomy complication. Advanced age and prior thyroid surgery were the main significant predictors of overall post-thyroidectomy complications. Neck dissection with total thyroidectomy is safe but has a higher incidence of hypocalcaemia than thyroidectomy alone. Consequently, every effort should be made to avoid reoperation by performing a wise definitive initial treatment.

CONFLICT OF INTEREST

There are no conflicts of interest.

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