

## Assessment of the Early and Late Complication after Thyroidectomy

### Abstract

**Background:** The complications in thyroid surgery have been reported variable in literature. The aim of this study was to evaluate the early and late (3 months after surgery) complication rates of thyroidectomy in a cohort of patients undergoing thyroid surgery at two hospitals of Isfahan University of Medical Science, Iran. **Materials and Methods:** This study included 204 patients who candidates for thyroidectomy presenting at Medical Educational Centers of Al-Zahra and Kashani hospitals in Isfahan between March 2016 and March 2017. Clinical data are collected for all patients by continuous enrollment. The patients examined before and after thyroid surgery and the findings were recorded. **Results:** The highest prevalence of thyroidectomy was in women (81.9%). The most frequent thyroid surgery was total thyroidectomy and the most common indication for thyroid surgery was suspicious fine-needle aspiration for thyroid malignancy. Hypocalcemia was the most common complication with a frequency of 54.4%. The odds ratios for early complications were 2.375 and 2.542 for intermediate- and low-volume surgeons, respectively, compared to high-volume surgeons. **Conclusions:** According to the results of this study, the high level of surgeon's skill is effective to reduce the likelihood of late and early complications; furthermore, the chance of late complications increases with age.

**Keywords:** Complications, hypocalcemia, morbidity, surgery, thyroidectomy

### Introduction

Thyroid disorders are one of the most common endocrine diseases.<sup>[1]</sup> Surgical resection of the thyroid gland maybe necessary for the treatment of these disorders.<sup>[1]</sup> Thyroidectomy is recommended for benign condition such as symptomatic large goiters and for the treatment of malignant disease of the thyroid gland.<sup>[2]</sup>

Thyroidectomy has potential complications. The major postoperative complications are hypocalcemia, wound infection, hematoma, recurrent laryngeal nerve (RLN) injury, and Horner's syndrome.<sup>[3-5]</sup> Hypocalcemia is the important postoperative complication of thyroid surgery causing potentially severe symptoms and increasing hospitalization time.<sup>[6,7]</sup> Hypoparathyroidism is the usual cause of hypocalcemia, it results from accidental gland injury, removal, or devascularization.<sup>[6,7]</sup> Hoarseness is mostly caused by RLN injury, which often results in vocal and laryngeal dysfunction.<sup>[8]</sup> The patient's quality of life can be negatively influenced by the incidence of potential complications leading to increase in

individual's health-care costs and requiring a lifelong alternative therapy.<sup>[9]</sup> Complications associated with thyroidectomy are related to the type of disease, extent of disease, removal approaches, surgeon's training, and experience.<sup>[10-13]</sup> Several studies have shown that increased surgeon experience is significantly associated with decreases in complications after thyroid surgery.<sup>[10,14]</sup>

To the best of our knowledge, no published data have been found about the early and late complications of thyroid surgery in Isfahan. The aim of this study was to evaluate the early and late complication rates of thyroidectomy in a cohort of patients undergoing thyroid surgery at two hospitals of Isfahan University of Medical Science, Iran.

### Materials and Methods

This cross-sectional, descriptive analytic study was conducted in Isfahan, a large urban area located in the center of Iran. This study included 204 candidates for thyroidectomy presenting at Medical Educational Centers of Al-Zahra and Kashani hospitals in Isfahan between

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March 2016 and March 2017. Clinical data are collected for all patients by continuous enrollment. The study was approved by the Isfahan University of Medical Sciences, Medical Ethics Committee, and all patients gave informed consent for participation in the examination and registration.

The patients with hypocalcemia, vocal cord paralysis, Horner's syndrome, tracheal injury, and esophagus injury were excluded from the study. The patients were examined initially and the demographic characteristics, past medical history, and the indication of thyroid surgery were recorded. The height, weight, and blood pressure were measured, and a general examination was done.

Following thyroid surgery, the patients were examined for early and late (3 months after thyroid surgery) complications of thyroid surgery, including hypocalcemia, hoarseness, dysphagia, hematoma, infection, and Horner's syndrome. The findings were recorded.

Concentrations of total calcium in normal serum generally range between 8.5 mg/dl and 10.5 mg/dl. The corrected levels of total calcium for albumin concentration below 8.5 mg/dl were considered as hypocalcemia. Dysphagia was defined as a subjective sensation of difficulty or abnormality of swallowing. The term hoarseness was used to describe any change in voice quality. Surgeon volume was classified on the basis of the number of thyroid surgery performed per year as low volume (lesser than 10 thyroid surgery/year), intermediate volume (10–99 thyroid surgery/year), and high volume (>99 thyroid surgery/year).

## Statistical analysis

The collected data were analyzed with SPSS software (version 20; SPSS Inc., Chicago, Ill., USA) Quantitative data were expressed as mean  $\pm$  standard deviation (SD) and qualitative data were reported by frequency (%). For interfered analysis, we used Fisher's exact test and Chi-square to compare qualitative data in frequency distribution. Based on the result of Kolmogorov–Smirnov test indicating the normality of data distribution, we used independent samples *t*-test to compare quantitative data in each gender. The logistic regression was applied to evaluate the association of factors such as sex, age, body mass index (BMI), past medical history, type of surgery, indication of surgery, and experience of surgeon, with the incidence of postoperative early and late complications. Thus, values for 95% confidence interval and odd ratio were reported. For all analyses, the significance level was considered <0.05.

## Results

This study included 204 patients undergoing thyroidectomy (37 [18.9%] men and 167 [81.9%] women). The mean (SD) of age, BMI, systolic blood pressure, diastolic blood pressure, and pulse rate at baseline were 41.2 (13.4) (years), 25.30 (3.6) (kg/m<sup>2</sup>), 119.7 (10.9) (mmHg), 73.7 (7.4) (mmHg), and 74.0 (6.1) (bpm), respectively. Table 1 presents baseline characteristics by gender. Hypertension was significantly more common among women than men and smoking was significantly more frequent among men than

**Table 1: Baseline characteristics of patients undergoing thyroidectomy**

Characteristics	Male (n=37)	Female (n=167)	Total (n=204)	P
Age (year)	42.7 $\pm$ 14.9	40.8 $\pm$ 13.1	41.2 $\pm$ 13.4	0.447
BMI (kg/m <sup>2</sup> )	25.0 $\pm$ 2.9	25.4 $\pm$ 3.7	25.3 $\pm$ 3.6	0.573
SBP (mmHg)	117.6 $\pm$ 10.6	120.1 $\pm$ 11.0	119.7 $\pm$ 10.9	0.226
DBP (mmHg)	73.7 $\pm$ 7.7	73.7 $\pm$ 7.4	73.7 $\pm$ 7.4	0.985
PR (bpm)	73.7 $\pm$ 4.8	74.0 $\pm$ 6.4	74.0 $\pm$ 6.1	0.814
Past Medical history* (%)				
Diabetes	1/37 (2.7)	13/167 (7.8)	14/204 (6.9)	0.276
Hypertension	2/37 (5.4)	32/167 (19.2)	34/204 (16.7)	0.007
Hyperlipidemia	6/37 (16.2)	23/167 (13.8)	29/204 (14.2)	0.826
IHD	0/37 (0)	6/167 (3.6)	6/204 (2.9)	0.589
COPD	2/37 (5.4)	3/167 (1.8)	5/204 (2.4)	0.248
Cancer	0/37 (0)	1/167 (0.6)	1/204 (0.5)	0.621
Smoking	6/37 (16.2)	4/167 (2.4)	10/204 (4.9)	0.003
None	23/37 (62.2)	109/167 (65.3)	132/204 (64.7)	0.708
Educational status (%)				
Illiterate	9/37 (24.3)	24/167 (14.4)	33/204 (16.2)	0.008
Elementary	10/37 (27.0)	57/167 (34.1)	67/204 (32.8)	
Diploma	6/37 (16.2)	62/167 (37.1)	68/204 (33.3)	
Bachelor	12/37 (32.4)	24/167 (14.4)	36/204 (17.6)	

Data shown mean $\pm$ SD or n/N (%). \*Some patients have more than one disease in past medical history. BMI: Body mass index, DBP: Diastolic blood pressure, SBP: Systolic blood pressure, PR: Pulse rate, IHD: Ischemic heart disease, COPD: Chronic obstructive pulmonary disease, SD: Standard deviation

women ( $P < 0.05$ ) [Table 1]. Other variables were not different between men and women ( $P > 0.05$ ).

Type of surgery and indication for thyroid surgery in patients undergoing thyroidectomy were shown in Table 2. Total thyroidectomy and suspicious fine-needle aspiration (FNA) for malignancy were the most frequent type of surgery and indication for thyroid surgery, respectively. Subtotal thyroidectomy and Graves' disease were the least frequent types of surgery and indication for thyroid surgery, respectively. There was no significant difference in frequency distributions of the type of surgery and indication for surgery by genders ( $P > 0.05$ ).

Early and late postoperative complications in patients undergoing thyroidectomy were shown in Table 3. 152 patients (74.5%) experienced early complications. 111 patients (54.4%) were with hypocalcaemia (41.4% [ $n = 46$ ] on the first day, 54.9% [ $n = 61$ ] on the second day, and 3.6% [ $n = 4$ ] on the third day), 68 patients (33.3%) with hoarseness, 7 patients (3.4%) with wound infection, 9 patients (5.9%) with hematoma, 67 patients (32.8%) with dysphagia to solids, and 1 patient with other complications.

Furthermore, in 3-month follow-up after surgery from 194 evaluated patients (10 patients were not responding), 164 (84.5%) had no complication and 30 (15.5%) were associated with late complications; as 12 patients (6.2%) had hypocalcemia, 16 (8.2%) had hoarseness, and 7 (3.6%) had dysphagia. Furthermore, 6 (3.1%) patients died after 3 months [Table 3].

Of the 6 patients died after 3-month follow-up, 4 were female and 2 were male, with the mean age of  $66 \pm 14.45$  years. Early complications of hypocalcemia, hoarseness, and dysphagia were seen in 4, 4, and 3 cases,

respectively. The cause of surgery in the majority of them (4 cases) was FNA, and the type of surgery in 5 cases was total thyroidectomy and in one case was near-total thyroidectomy. The volume surgeon was also low in 1 case, intermediate in 3 cases, and high in 2 cases [Table 4].

Ultimately, evaluation of the effect of factors including sex, age, BMI, past medical history, type of surgery, indications for surgery, and experience of surgeon, on the surgical complications using logistic regression showed that surgeon's skill is associated with the incidence of complication; the likelihoods of the incidence of complication for low-volume surgeon and intermediate-volume surgeon were, respectively, 2.54 and 2.375 times more than that for high-volume surgeon ( $P < 0.05$ ). Increasing age was also associated with an increased risk of late complications so that the incidence of late complications in patients with the age range of greater than 60 years was 4.80 times higher than the patients under the age of 40 years [Table 5].

## Discussion

In our study, the highest prevalence of thyroidectomy was in women (81.9%). The most frequent thyroid surgery was total thyroidectomy and the most common indication for thyroid surgery was suspicious FNA for thyroid malignancy. Hypocalcemia was the most common complication with a frequency of 54.4% and surgeon experience is associated with the incidence of complication.

In line with this study, Yan *et al.* showed that of 7385 patients undergoing thyroidectomy, 71% were female<sup>[15]</sup> and Huang *et al.* reported that among 3428 patients undergoing thyroidectomy, the ratio of female to male was 5.24:1, while the mean age of patients was more than 40 years.<sup>[16]</sup> In fact, overall,

**Table 2: Surgical variables in patients undergoing thyroidectomy**

Variables	Male (n=37)	Female (n=167)	Total (n=204)	P
Type of surgery (%)				
Lobectomy	2 (5.4)	17 (10.2)	19 (9.3)	0.666
Total thyroidectomy	21 (56.8)	95 (56.9)	116 (56.9)	
Subtotal thyroidectomy	1 (2.7)	5 (3)	6 (2.9)	
Near-total thyroidectomy	4 (10.8)	24 (14.4)	28 (13.7)	
Other*	9 (24.3)	26 (15.6)	35 (17.2)	
Indication for surgery (%)				
Grave's disease	1 (2.7)	0 (0)	1 (0.5)	0.319
Multinodular goiter	10 (27)	50 (29.9)	60 (29.4)	
Suspicious FNA for malignancy	22 (59.5)	96 (57.5)	118 (57.8)	
MTC	2 (5.4)	11 (6.6)	13 (6.4)	
Other†	2 (5.4)	10 (6)	12 (5.9)	
Clinical factors				
Albumin (g/dl)	3.8±0.4	3.85±0.2	3.8±0.2	0.063
Phosphorus (mg/dl)	3.2±0.6	3.34±0.7	3.3±0.7	0.373
Calcium (mg/dl)	8.4±0.8	8.37±0.7	8.4±0.7	0.909

Data shown n (%). \*Other type of surgery: Lymph node dissection (central or lateral) + thyroidectomy, †Other indications for surgery: Included physician recommended or reason undocumented. Suspicious FNA: Suspicious fine-needle aspiration, MTC: Medullary thyroid carcinoma

the findings of many epidemiologic studies indicated a higher prevalence of thyroid disorders among women than men.<sup>[16,17]</sup>

Overall, 152 cases (74.5%) were with postoperative complications of thyroidectomy, in which the most common complication was hypocalcemia with a frequency of 54.4%. In many previous studies, hypocalcemia is identified as the most common postoperative complication. In a previous study, the incidences of temporary hypocalcemia and permanent hypocalcemia were reported about 2%–53% and 0.4%–13.8%, respectively.<sup>[6,18–20]</sup> Suwannasarn *et al.* reported immediate hypocalcemia was observed in 38.5% patients.<sup>[20]</sup> Early postoperative hypocalcemia was 42% in Seo *et al.* study.<sup>[19]</sup> The higher rate in our study maybe due to higher percentage of total thyroidectomy. Hypoparathyroidism is the usual cause of hypocalcemia; it results from accidental gland injury, removal, or devascularization.<sup>[6,7]</sup> Signs and symptoms of hypocalcemia are paresthesia, numbness around the mouth and fingertips, tetany, carpopedal spasm, positive Chvostek’s sign, positive Trousseau’s sign, convulsion, laryngospasm, prolonged QT interval on the electrocardiogram, coma, and death.<sup>[3]</sup> Hypocalcemia was mostly occurred on first and second days after surgery and most physicians obtain serial serum calcium measurements after surgery to recognize and manage appropriately the low levels of calcium. Transient hypocalcemia, generally,

responds well to calcium replacement therapy within a few days or weeks. Hypocalcemia is considered permanent when it does not return to normal within 6 months.<sup>[6,7]</sup>

In our study, this complication was reported as 6.2% in 3 months’ follow-up after surgery. In fact, the timely diagnosis of this complication (in the first 24 h after surgery) and early onset of complementary therapies prevented the symptom and long-term complications. According to some studies, the delayed hypocalcemia can occur in the first postoperative week and has been reported to occur months and even years following thyroidectomy.<sup>[6,21]</sup> Of significant concern and consequence is the development of hypocalcemia after thyroidectomy for Graves’ disease.<sup>[22]</sup> Despite excellent surgical technique and anatomical preservation of the parathyroid glands and their blood supply, these patients can demonstrate a delayed and rapid drop in serum calcium 2–3 days after total thyroidectomy.

Other complications in our study were hoarseness, dysphagia to solids, hematoma, and wound infection. Hypocalcemia, hoarseness, and dysphagia were more common in our study. Hematoma and wound infection were less common. Furthermore, previous studies have reported RLN injury, transient hypocalcemia, and hypoparathyroidism as the common complications of thyroidectomy, while other complications such as cellulitis, infection, and damages to the carotid artery, jugular vein, and esophagus are uncommon.<sup>[23,24]</sup> It is considered that the incidence of postoperative complications can be influenced by the extent of surgery and the experience of the surgeon.<sup>[10,25,26]</sup>

In the current study, the experience of the surgeon was influenced significantly in the incidence of early and late complications. The higher volume surgeons had lower complication rates. The relationship between surgeon volume and patient outcomes has been studied extensively over the last 20 years. Other studies have made similar results.<sup>[10,25,26]</sup> Sosa *et al.* found a strong association between higher surgeon volume and favorable patient outcomes.<sup>[10]</sup> In a recent study of patients undergoing thyroidectomy in the Health Care Utilization Project Nationwide Inpatient Sample, high-volume surgeons had the lowest complication rates.<sup>[26]</sup> It can be concluded that referral of patients to high-volume thyroid surgeons is associated with better outcomes.

**Table 3: Early and late postoperative complications in patients undergoing thyroidectomy**

Complication*	Early complication (n=204)	Late complication (n=194)**
Uncomplicated	52/204 (25.5)	164/194 (84.5)
Hypocalcemia	111/204 (54.4)	12/194 (6.2)
8-8.5 (mg/dl)	68/111 (61.3)	7/12 (58.3)
7.5-8 (mg/dl)	24/111 (21.6)	3/12 (25)
<7.5 (mg/dl)	19/111 (17.1)	2/12 (16.7)
Hoarseness	68/204 (33.3)	16/194 (8.2)
Dysphagia	67/204 (32.8)	7/194 (3.6)
Wound infection	7/204 (3.4)	0/194 (0)
Death	0/204 (0)	6/194 (3.1)
Other†	1/204 (0.4)	0/194 (0)

Data shown mean±SD or n/N (%). \*Some patients have more than one complication, \*\*Late complications assessed within 3 months, †Other complications: Cervical numbness. SD: Standard deviation

**Table 4: Died patients during the follow-up after surgery (3-month follow-up)**

Sex	Age	BMI	Hypocalcemia	Hoarseness	Dysphagia	Indication for surgery	Type of surgery	Volume surgeon
Female	69	24.22	Yes	Yes	No	FNA	Total thyroidectomy	Low
Female	73	28.65	No	Yes	Yes	FNA	Near-total thyroidectomy	High
Male	69	29.63	No	Yes	Yes	Unknown	Total thyroidectomy	High
Female	72	24.22	Yes	No	No	Multinodular goiter	Near-total thyroidectomy	Intermediate
Male	37	23.78	Yes	No	No	FNA	Total thyroidectomy	Intermediate
Female	76	26.30	Yes	Yes	Yes	FNA	Total thyroidectomy	Intermediate

FNA: Fine-needle aspiration, BMI: Body mass index

**Table 5: Association of factors with the incidence of early and late complications of thyroidectomy**

Covariates	Early complications		Late complications	
	OR (95% CI)	P	OR (95% CI)	P
Sex				
Male	Reference		Reference	
Female	1.090 (0.45-2.65)	0.850	1.011 (0.353-2.897)	0.984
BMI categories				
Normal	Reference		Reference	
Low weight	3.591 (0.42-10.50)	0.242	4.679 (0.963-16.746)	0.065
Over weight	0.655 (0.30-1.42)	0.282	0.890 (0.318-2.489)	0.824
Obesity	1.206 (0.29-4.94)	0.794	0.009 (0.000-0.021)	0.999
Age categories (year)				
<40	Reference		Reference	
40-60	0.616 (0.28-1.37)	0.235	1.260 (0.495-3.205)	0.627
>60	1.166 (0.31-4.39)	0.820	4.800 (1.586-14.530)	0.006
Past Medical history	1.625 (0.78-3.36)	0.191	1.860 (0.730-4.744)	0.194
Surgical indications				
Multinodular goiter	Reference		Reference	
Grave's disease	-	-	-	-
FNA	0.716 (0.31-1.64)	0.429	1.649 (0.578-4.700)	0.349
MTG	1.106 (0.25-4.90)	0.894	1.585 (0.249-10.093)	0.626
Surgical type				
Lobectomy	Reference		Reference	
Total thyroidectomy	1.222 (0.32-4.65)	0.769	1.890 (0.395-9.051)	0.426
Subtotal thyroidectomy	0.244 (0.02-2.61)	0.244	0.003 (0.000-0.009)	0.999
Near-total thyroidectomy	0.939 (0.20-4.39)	0.936	3.442 (0.406-29.157)	0.257
Other*	1.675 (0.34-8.32)	0.529	3.462 (0.556-23.871)	0.178
Volume surgeon				
High-volume surgeon	Reference		Reference	
Intermediate-volume surgeon	2.375 (1.75-7.50)	0.040	2.723 (1.099-6.742)	0.030
Low-volume surgeon	2.542 (1.216-5.31)	0.013	2.931 (0.887-9.684)	0.038

\*Other surgical type: Lymph node dissection (central or lateral) + thyroidectomy. Suspicious FNA: Suspicious fine-needle aspiration, MTG: Medullary thyroid carcinoma, BMI: Body mass index, CI: Confidence interval, OR: Odd ratio

Some studies reported that the incidences of RLN injuries, hypocalcemia, and other postoperative complications in patients undergoing total thyroidectomy were significantly higher than patients undergoing unilateral thyroidectomy.<sup>[16,27]</sup> In our study, the complication rates did not influence by the extent of surgery.

The likelihood of late complications also increases in older patients (over 60 years of age). It has been also confirmed in previous studies as reported that the patients over 65 years of age, and especially those over 80, have significantly more complications and a longer hospital stay than younger patients.<sup>[28]</sup> Older patients have a greater risk for transient vocal fold paralysis and hematoma than other adult patients, with odds ratios of 1.04 and 1.92, respectively, in the study by Bergenfelz *et al.*<sup>[29]</sup> Vitamin D deficiency is also more prevalent in elderly patients and has been shown to be a risk factor for transient postoperative hypoparathyroidism.<sup>[30,31]</sup> This issue should be addressed preoperatively when treating elderly patients.

Our study was prospective study to evaluate the patients who candidate for thyroid surgery before and after

operation. The prospective design of the study can show more accurate data about the early postoperative complication rate. It is known that retrospective studies often fail to detect all cases and some complications are missed using the database.

## Conclusions

This study showed that higher surgeon volume is associated with improved patient outcomes after thyroid surgery. Furthermore, it has been revealed that the chance of complications increases with the patient's age during the 3-month postoperative follow-up.

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## Conflicts of interest

There are no conflicts of interest.

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