

Complications after Thyroidectomy-a Comparison Among Seven Different Surgical Procedures and the Impact of Central Compartment Lymph Nodes Sampling: a Cohort Study

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Abstract

Introduction: Thyroid nodules are commonly encountered in medical practice. The relation between the magnitude of thyroid surgery and its complications is not settled.

Objectives: We aim to examine the incidence of recurrent laryngeal nerve injury and hypoparathyroidism after thyroid surgery in different thyroid procedures, including local lymph nodes control.

Methods: The records of 345 patients who underwent thyroidectomy at the Jordan University Hospital from January 2010 to December 2016 were reviewed. They were divided into seven groups (total thyroidectomy, near-total thyroidectomy, hemithyroidectomy, completion thyroidectomy, redo surgery, hemithyroidectomy with completion, and near-total thyroidectomy with completion). A comparison among the groups was done. Ninety-one patients who underwent central lymph node biopsy were identified. They were divided into three groups (pre-tracheal lymph nodes excision, central neck dissection, and central neck sampling) and then compared.

Results: Transient hypocalcemia was significantly higher with total thyroidectomy in comparison to near-total thyroidectomy and hemithyroidectomy with or without completion. All groups were comparable regarding permanent hypocalcemia and recurrent laryngeal nerve palsy. No significant relationship between the type of dissection and complication rate was found.

Conclusion: Near-total thyroidectomy is a safe alternative to total thyroidectomy with a lower early complication rate. Redo surgery and central dissection are not associated with higher morbidity.

Keywords: Thyroid, Goiter, Papillary, Complications.

(J Med J 2024; Vol. 58 (1): 29–36)

Received

Accepted

May 18, 2019

June 7, 2023

INTRODUCTION:

Thyroid nodules are a medical condition observed all over the world. Its clinical presentation ranges from a small solitary nodule to a huge multinodular goiter, sometimes extending to the chest. The pathological processes responsible for these changes vary from a degenerative disease that does not affect life expectancy to anaplastic carcinoma, which is an aggressive cancer that kills in a few months (1). Due to this variability, many surgical techniques have been adopted in treating thyroid diseases; these techniques

include lobectomy, isthmectomy, subtotal thyroidectomy, near-total thyroidectomy, and total thyroidectomy. Sometimes, the excision of adjacent lymph nodes either in the central or the lateral compartment is done to secure loco-regional control (2). The surgical option is tailored for each case depending on the clinical-pathological presentation. A significant factor to be considered when designing the management is patient tolerance for possible complications; thus, understanding the complications of each procedure is fundamental for both the patient and the surgical team.

In the literature, many reports have described voice changes and hypoparathyroidism as specific complications after thyroid surgery. However, only a few of these studies have examined the magnitude of surgery in relation to complications, especially when considering near-total thyroidectomy and pre-tracheal

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lymph node dissection as specific entities (3). In this study, we set out to examine the incidence of recurrent laryngeal nerve (RLN) injury and hypoparathyroidism after thyroid surgery in relation to different thyroid procedures, including local lymph nodes control.

MATERIALS & METHODS:

Ethical approval was obtained from the ethical authority of the University of Jordan (IRB: 2015/2-290). The medical records of all patients who underwent thyroid surgery at The University of Jordan Hospital from January 2010 to December 2016 were reviewed. A total of 407 records were identified; of them, 62 records were excluded due to inadequate data or loss to follow-up. Thus, 345 patients were included in the study and analyzed. Data collected included age, gender, pre-operative diagnosis, final histopathological diagnosis, the magnitude of surgery, and complications. The patients were divided into seven groups according to the type of surgery; these include total thyroidectomy, near-total thyroidectomy, hemithyroidectomy, completion thyroidectomy, redo surgery, hemithyroidectomy with completion, and near-total thyroidectomy with completion. The last two groups represent those patients who had two surgeries at our institute: a primary thyroid operation and then a completion. Hypocalcemia was defined as serum calcium less than 8 mg/dl with or without manifestations. Vocal cord injury was defined as either immobility seen upon laryngoscopy or hoarseness documented in the file more than 48 hours after

surgery. The cut-off point between transient and permanent complications was 6 months. Other complications considered in this study are bleeding, hematoma, and wound infection. The seven groups were compared based on the complications of the surgery. The whole group was also divided into four groups according to the type of lymph nodes dissection performed: central, pre-tracheal (lymph nodes around pyramidal lobe), and no dissection; a particular fourth group was considered when one or more lymph nodes in the central compartment were picked and sent for frozen section or permanent pathology. A comparison between the four groups was made regarding complications. Statistical analysis was performed using the Statistical Package for the Social Sciences version 16.0 (SPSS Inc., Chicago, IL, USA). Comparisons among the groups were performed using chi-square tests, and statistical significance was set at $p < 0.05$.

RESULTS:

The most common preoperative diagnosis was multinodular goiter, followed by a solitary nodule, as shown in Table 1. A total of 235 patients had a benign disease, representing 68.1% of the whole group; the remaining 110 patients had malignant tumors. The most common benign disease was degenerative goiter alone or with other pathologies, while papillary thyroid cancer was the most malignant disease seen in our group. Surprisingly, follicular thyroid cancer was seen only in 3% of malignant patients. A full description of pathological distribution is demonstrated in Table 2.

Table 1: Preoperative clinical diagnosis.

Preoperative diagnosis	Frequency	Percent	Cumulative Percent
Multi-nodular goiter	124	35.9	35.9
Toxic multi-nodular goiter	7	2.0	38.0
Solitary nodule	114	33.0	71.0
Grave's	35	10.1	81.2
Recurrence	3	0.9	82.0
Cancer	62	18.0	100.0
Total	345	100.0	

Table 2 Postoperative pathological diagnosis.

Pathological type	Frequency	Percent	Cumulative Percent
Benign Follicular nodule	105	30.4	30.4
Chronic lymphocytic	39	11.3	41.7
Other benign diseases	108	31.3	73.0
Papillary carcinoma	78	22.6	95.7
Follicular carcinoma	3	0.9	96.5
Medullary carcinoma	3	0.9	97.4
Malignant; others	9	2.6	100.0
Total	345	100.0	

The overall rate of complications was 34.5%, and the vast majority of which was transient hypocalcemia. Around 90% of the patients with transient hypocalcemia recovered within two weeks, but this was significantly higher in those patients with total thyroidectomy in comparison to near-total

thyroidectomy and hemithyroidectomy cases. Only one patient developed a local hematoma that required surgical evacuation, and no cases of wound infection were documented. All groups were comparable regarding permanent hypocalcemia and RLN palsy, as seen in Tables 3 and 4.

Table 3. Complications in relation to the type of surgery

		Type of Surgery							Total
		Total thyroidectomy	Near-total thyroidectomy	Hemi-thyroidectomy	Completion thyroidectomy	Redo surgery	Hemi-thyroidectomy and completion	Near total and completion	
No Complications	Count	131 _a	39 _{b, c}	36 _c	9 _{a, b}	2 _{a, b, c}	4 _{a, b, c}	3 _{a, b, c}	224
	% *	57.2%	78.0%	92.3%	69.2%	100.0%	66.7%	100.0%	65.5%
Transient vocal cord paralysis	Count	2 _a	1 _a	0 _a	0 _a	0 _a	0 _a	0 _a	3
	%	0.9%	2.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.9%
Transient Hypocalcemia	Count	89 _a	10 _b	3 _b	3 _{a, b}	0 _{a, b}	2 _{a, b}	0 _{a, b}	107
	%	38.9%	20.0%	7.7%	23.1%	0.0%	33.3%	0.0%	31.3%
Permanent Hypocalcemia	Count	5 _a	0 _a	0 _a	0 _a	0 _a	0 _a	0 _a	5
	%	2.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	1.5%
Transient Hypocalcemia and others	Count	1 _a	0 _a	0 _a	0 _a	0 _a	0 _a	0 _a	1
	%	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%
Transient vocal cord paralysis and transient hypocalcemia	Count	1 _a	0 _a	0 _a	0 _a	0 _a	0 _a	0 _a	1
	%	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%
Permanent vocal cord paralysis	Count	0 _a	0 _a	0 _{a, b}	1 _b	0 _{a, b}	0 _{a, b}	0 _{a, b}	1
	%	0.0%	0.0%	0.0%	7.7%	0.0%	0.0%	0.0%	0.3%
Total	Count	229	50	39	13	2	6	3	342
	%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Each subscript letter denotes a subset of Type of Surgery categories whose column proportions do not differ significantly from each other at the .05 level.

*% within type of surgery

Table 4. Chi-Square tests for complications in relation to the type of surgery

Chi-Square Tests	Value	df	Asymptotic Significance (2-sided)	Monte Carlo Sig. (2-sided)			Monte Carlo Sig. (1-sided)		
				Significance	99% Confidence Interval		Significance	99% Confidence Interval	
					Lower Bound	Upper Bound		Lower Bound	Upper Bound
Pearson Chi-Square	53.879 ^a	36	.028	.160 ^b	.151	.170			
Likelihood Ratio	41.692	36	.237	.002 ^b	.001	.003			
Fisher's Exact Test	76.874			.008 ^b	.006	.010			
Linear-by-Linear Association	9.884 ^c	1	.002	.003 ^b	.001	.004	.000 ^b	.000	.001
N of Valid Cases	342								

a. 42 cells (85.7%) have expected count less than 5. The minimum expected count is .01.

b. Based on 10000 sampled tables with starting seed 726961337.

c. The standardized statistic is -3.144.

In the whole group, 91 patients received a lymph node pathological examination, including central neck dissection, pre-tracheal lymph node excision, and lymph node sampling. Twenty-six patients had intraoperative frozen section examination, and the

rest were sent for definitive pathology. No significant relationship between the type of dissection and complications was identified, as seen in Tables 5 and 6.

Table 5. Complications in relation to the type of neck dissection

										Total	
		No neck dissection		Pretracheal LN (Delphian L.N)		Central Neck dissection		Lymph node sampling			
		Count	% within new group	Count	% within new group	Count	% within new group	Count	% within new group	Count	% within new group
Complications	None	166	65.4%	25	83.3%	23	53.5%	13	72.2%	227	65.8%
	Transient v cord paralysis	3	1.2%	0	0.0%	0	0.0%	0	0.0%	3	0.9%
	transient hypocalcemia	78	30.7%	4	13.3%	20	46.5%	5	27.8%	107	31.0%
	Permanent hypocalcemia	5	2.0%	0	0.0%	0	0.0%	0	0.0%	5	1.4%
	Transient hypocalcemia and others	0	0.0%	1	3.3%	0	0.0%	0	0.0%	1	0.3%
	Transient vocal cord paralysis and transient hypocalcemia	1	0.4%	0	0.0%	0	0.0%	0	0.0%	1	0.3%
	Permanent vocal cord paralysis	1	0.4%	0	0.0%	0	0.0%	0	0.0%	1	0.3%
Total		254	100.0%	30	100.0%	43	100.0%	18	100.0%	345	100.0%

Table 6. Chi-Square tests for complications in relation to the type of neck dissection

Chi-Square Tests	Value	df	Asymptotic Significance (2-sided)	Monte Carlo Sig. (2-sided)			Monte Carlo Sig. (1-sided)		
				Significance	99% Confidence Interval		Significance ^e	99% Confidence Interval	
					Lower Bound	Upper Bound		Lower Bound	Upper Bound
Pearson Chi-Square	23.018 ^a	18	.190	.283 ^b	.271	.294			
Likelihood Ratio	20.284	18	.317	.091 ^b	.084	.099			
Fisher's Exact Test	23.161			.243 ^b	.232	.254			
Linear-by-Linear Association	.002 ^c	1	.960	.960 ^b	.955	.965	.501 ^b	.488	.514
N of Valid Cases	345								

a. 20 cells (71.4%) have expected count less than 5. The minimum expected count is .05.

b. Based on 10000 sampled tables with starting seed 20000000.

c. The standardized statistic is -.050.

DISCUSSION:

Total thyroidectomy is indicated for all patients with a pre-operative diagnosis of differentiated thyroid carcinoma (4). It is also beneficial in the treatment of benign diseases with the benefit of lower recurrence and elimination of the risk of malignancy in the rest of the thyroid gland (5). Hemi-thyroidectomy and subtotal thyroidectomy are suggested to have lesser morbidity since theoretically, one RLN and two parathyroid glands are not exposed to trauma. However, those patients with cancer after surgery are usually scheduled for a completion thyroidectomy with a higher overall complication rate (6). This is the reason some surgeons suggest total thyroidectomy for benign diseases (7-9). The concept of near-total thyroidectomy was introduced by some surgeons as a midway solution between total thyroidectomy and subtotal thyroidectomy, where a small remnant of the thyroid is left around the RLN and parathyroid glands. If a malignant disease is identified in the final pathology, the remnant part is dealt with by radioactive iodine ablation.

The relationship between the magnitude of thyroid surgery and complications is not settled in the literature. For example, Pelei et al. performed a meta-analysis on different surgical methods for

multi-nodular goiter and concluded that there was no significant difference in postoperative complications among them (10). Barczynski et al. compared the results of Dunhill thyroidectomy, total thyroidectomy, and bilateral subtotal thyroidectomy methods and showed that the lower incidence of postoperative transient hypocalcemia and transient RLN palsy belonged to the total thyroidectomy group (11). On the contrary, Li et al. concluded that total thyroidectomy involves a significantly higher risk of postoperative transient hypoparathyroidism (12).

Thyroiditis and redo surgery are two categories that make thyroidectomy more difficult. Chen et al. reported a higher rate of complications after thyroidectomy for patients known to have Hashimoto's thyroiditis (13). Müller et al. showed that the risk of permanent RLN palsy is five times greater after repeat surgery for recurrent goiter than after the primary surgery, even when the operation is performed by an experienced endocrine surgeon (14). Regarding transient hypoparathyroidism after re-operative thyroid surgery, one study reported an unusually high rate of 38.7% (15). Other studies reported rates that ranged from 3% to 20.7% (2). Rudolph et al. observed that as compared to patients who underwent unilateral lobectomy for

multinodular goiter, those who had previously undergone subtotal thyroidectomy had a significantly higher permanent RLN injury rate (3.44% vs. 0.77%) and higher permanent hypoparathyroidism (5.1% vs. 1.5%) (16). Our results are consistent with those of Kurmann et al., whose retrospective study showed no statistical difference in permanent RLN nerve injury between patients undergoing ipsilateral and those undergoing contralateral redo surgery (17).

Para-tracheal lymph node metastases are common; grossly positive nodal disease is seen in 10 to 30% of patients with papillary thyroid tumor while the microscopic disease is reported to be prevalent in 40 to 70% of patients (18, 19). However, the impact of central neck dissection on the prognosis of grossly negative patients is still unclear. A few studies suggest that microscopically positive lymph nodes do not appear to progress to recurrence whether operated on or not (20, 21). Other reports indicate that central neck dissection in microscopic disease decreases locoregional recurrence and improves survival (22, 23).

Many reports suggest that central lymph nodal dissection is associated with higher morbidity, especially injury to the parathyroid glands with rates of transient hypoparathyroidism ranging from 14 to 60%, permanent hypoparathyroidism from 3 to 11%, transient vocal cord paralysis from 3 to 7%, and permanent RLN injury from 0 to 4% (24-26).

In this study, transient hypocalcemia was the only complication that was significantly higher with total thyroidectomy in comparison to near-total thyroidectomy and hemithyroidectomy. Transient hypocalcemia carries significant morbidity that includes numbness, pain, and occasionally, muscle spasms. The treatment of hypocalcemia also has an added burden on the patients; it may require

hospitalization for parenteral calcium, and its oral treatment has some annoying side effects, especially heartburn and constipation. Therefore, although transient hypocalcemia is reversible, it is considered a significant complication after thyroid surgery. Leaving a rim of thyroid tissue around parathyroid glands will decrease the incidence of this complication. Our study showed no significant relationship between the type of dissection and complications, including hypoparathyroidism. This finding can be explained by the surgical approach adopted by our team, which focuses on the identification of the inferior thyroid artery and preservation of small branches that supply both parathyroids before proceeding to central neck dissection. Local recurrence could not be assessed due to short follow-up.

Our study has some limitations. First, it is a retrospective study, and the number of cases is relatively limited, especially in the redo and neck dissection categories. This is probably due to the relative rarity of this surgical procedure. Postoperative vocal cord assessments were not routinely performed. Thus, the real rate of vocal cord paralysis cannot be reported since voice changes may not be recorded in patients with unilateral vocal cord paralysis. Furthermore, the lack of facilities such as intraoperative laryngeal nerve monitoring may also have affected the RLN outcomes. Since intraoperative laryngeal nerve monitoring may reduce the morbidity of redo thyroid surgery, further studies assessing its ability to minimize RLN injury rates after thyroid reoperation are warranted.

In conclusion, near-total thyroidectomy is a safe alternative to total thyroidectomy with a lower early complication rate. Central neck dissection and redo surgery were not associated with higher morbidity in our group.

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المضاعفات بعد استئصال الغدة الدرقية. مقارنة بين سبع عمليات جراحية مختلفة وتأثير استئصال العقد الليمفاوية المركزية عليها

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الملخص

الخلفية والأهداف : تحدث عقيدات الغدة الدرقية بشكل شائع في الممارسة الطبية. لم يتم تسوية العلاقة بين حجم جراحة الغدة الدرقية ومضاعفاتها. وهدفنا هو فحص حدوث إصابة العصب الحنجري المتكرر ونقص جارات الدرقية بعد جراحة الغدة الدرقية في عمليات الغدة الدرقية المختلفة بما في ذلك استئصال في الغدد الليمفاوية المحلية.

منهجية الدراسة : تمت مراجعة سجلات 345 مريضاً خضعوا لعملية استئصال الغدة الدرقية في مستشفى الجامعة الأردنية من كانون الثاني 2010 إلى كانون الأول 2016. تم تقسيمهم إلى سبع مجموعات (استئصال الغدة الدرقية الكلي، استئصال الغدة الدرقية شبه الكلي، استئصال نصف الغدة الدرقية، استئصال الغدة الدرقية الاستكمالي، إعادة الجراحة، استئصال نصف الغدة الدرقية و من ثم الاستكمال، واستئصال الغدة الدرقية شبه الكامل و من ثم الاستكمال). تم إجراء مقارنة بين المجموعات. تم تحديد 91 مريضاً خضعوا لاستئصال الغدد الليمفاوية المركزية. تم تقسيمهم إلى ثلاث مجموعات (استئصال العقد الليمفاوية حول القصبة الهوائية، ونشر العنق المركز، وأخذ عينات من الرقبة المركزية) ثم تمت مقارنتها.

النتائج: كان نقص الكالسيوم الدم العابر أعلى بشكل ملحوظ مع استئصال الغدة الدرقية الكلي مقارنة باستئصال الغدة الدرقية شبه الكلي واستئصال الغدة الدرقية مع أو بدون استكمال. كانت جميع المجموعات قابلة للمقارنة فيما يتعلق بنقص الكالسيوم الدائم وشلل العصب الحنجري المتكرر. لم يتم العثور على علاقة ذات دلالة إحصائية بين طريقة التعامل مع العقد الليمفاوية المركزية ومعدل المضاعفات.

الاستنتاجات : يعتبر استئصال الغدة الدرقية شبه الكامل بديلاً آمناً لاستئصال الغدة الدرقية الكلي مع معدل مضاعفات مبكرة أقل. حسب الدراسة لا ترتبط جراحة الإعادة واستئصال العقد الليمفاوية المركزية بارتفاع معدلات المضاعفات.

الكلمات الدالة: الغدة الدرقية، تضخم الغدة الدرقية، الحليمي، المضاعفات.