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Original Article/ Оригинални рад

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Complications after total thyroidectomy in correlation with histopathological and hormonal findings

Компликације послије тоталне тиреоидектомије у корелацији са хистопатолошким и хормоналним налазима

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SUMMARY

IntroductionObjective Total thyroidectomy (TT) is frequently performed in head and neck surgery and is regarded as a relatively straightforward procedure, but is still accompanied by a number of complications. The study aimed to examine the role and significance of TT for the occurrence of postoperative complications in correlation with histopathological (HP) and endocrinological findings.

Methods A cross-sectional study was conducted involving 90 patients in the University Clinical Center of Republic of Srpska, Banja Luka, Bosnia and Herzegovina that in the period between 2022 and 2024 underwent the thyroid gland surgery. Preoperatively, hormonal analyses and thyroid ultrasound examination as well as endovideolaryngoscopy (EVLS) examination were performed. TT was performed in all patients. Postoperatively, HP diagnostics, control hormonal analyses, and EVLS examination were performed.

Results Vocal fold paralysis (VFP) was reported by 11 (12.2%) patients. HP analysis showed that in the majority of cases the cause was goiter with 37 (41.1%) patients, followed by follicular adenoma with 25 (27.8%), and papillary carcinoma with 18 (20%); other causes where with the remaining 10 (11%). According to endocrinological complications, hypocalcemia was present in 67 (74.4%) patients, and elevated parathyroid hormone levels in 4 (4.4%).

Conclusion Patients with VFP and hypocalcemia show the highest incidence of postoperative complications after TT due to HP diagnosed goiter, follicular adenoma, and papillary thyroid carcinoma. These findings may be potentially useful in identifying elderly patients that are at increased risk of complications after TT that may significantly affect their quality of life.

KEYWORDS: hypocalcemia; thyroid gland diseases; vocal fold paralysis

САЖЕТАК

Увод/Циљ Тотална тиреоидектомија (ТТ) се често изводи у хирургији главе и врата и сматра се релативно једноставном процедуром, али је још увек праћена бројним компликацијама. Студија је имала за циљ да испита улогу и значај ТТ за настанак постоперативних компликација у корелацији са хистопатолошким (ХП) и ендокринолошким налазима.

Методе Студија пресека је обухватила 90 болесника у Универзитетском клиничком центру Републике Српске, Бања Лука, Босна и Херцеговина у периоду од 2022. до 2024. године који су подвргнути операцији штитасте жлезде. Преоперативно су урађене хормонске анализе и ултразвучни преглед штитасте жлезде, као и ендовидеоларингоскопија (ЕВЛС). ТТ је урађена код свих болесника. Постоперативно је урађена ХП дијагностика, контролне хормонске анализе и преглед ЕВЛС.

Резултати Парализу гласница (ПГ) је имало 11 (12,2%) болесника. ХП анализа је показала да је у већини случајева узрок струма код 37 (41,1%) болесника, затим фоликуларни аденом код 25 (27,8%), папиларни карцином код 18 (20%) и остали узроци код 10 (11%). Према ендокринолошким компликацијама, хипокалцемија је била присутна код 67 (74,4%) болесника, а повишен ниво паратироидног хормона код четири (4,4%).

Закључак Болесници са ПГ и хипокалцемијом показују највећу учесталост постоперативних компликација након ТТ због ХП дијагностиковане струме, фоликуларног аденома и папиларног карцинома штитасте жлезде. Ови налази могу бити потенцијално корисни у идентификацији болесника старије животне доби с повећаним ризиком од компликација након тоталне тиреоидектомије, што може у значајној мери утицати на квалитет њиховог живота.

Кључне речи: хипокалцемија; болести штитасте жлезде; парализа гласница

INTRODUCTION

Thyroid disorders are among the most common endocrine system diseases, and thyroidectomy is a therapy of choice for benign changes, and is a surgical intervention normally used in cases of suspected malignancy after ultrasound examination and fine-needle aspiration (FNA) [1]. Other reasons for thyroid surgery also include enlargement of the thyroid gland in the form of

nodular or colloidal goiter that interferes with breathing or swallowing [2]. Even with recent adjustments to TT meant to reduce the financial strain on hospitals, expenses are still growing by 4.3% annually [3]. Currently, this surgical intervention is very common and is among the safest surgical procedures [4]. Ultrasound is a mandatory diagnostic procedure for thyroid disease, due to its reliability and non-invasiveness among diagnostic procedures, unlike computed tomography and nuclear magnetic resonance, both of which are reserved only for complex cases [5].

However, thyroid surgery still carries a number of complications, regardless of whether it is performed using the classic open technique or micro-invasive surgery, and even includes a certain degree of mortality [6]. The most common complications include hypoparathyroidism (HPT), damage to the external branch of the superior laryngeal nerve, the recurrent laryngeal nerve, postoperative hemorrhage, laryngeal edema, and tracheospasm with dyspnea [6]. Post-thyroidectomy hypocalcemia occurs due to HPT, which can result from the devascularization or unintentional removal of the parathyroid glands [7]. A frequent and dangerous complication after TT is hypocalcemia [8]. Its incidence is about 1.2% and it most often, 40% of cases, occurs as a transient symptom, and permanent in only 3% of cases [7,8]. One common complication is damage to the recurrent laryngeal nerve.

The incidence of transient recurrent vocal-fold paralysis (VFP) ranges from 5% to 8%, while the rate of permanent recurrent VFP is between 0.3% and 3% [9]. The increase in the number of TT is associated with more postoperative complications. Surgeon experience, or lack of it, accounts for 46% to 56% of cases of unilateral and bilateral VFP, which can ultimately lead to dysphonia, dysphagia, and dyspnea [10]. Post-operative dysphonia can have significant implications and consequences for patients, so it is crucial to take all necessary measures to minimize this complication [11]. Postoperative hypocalcemia has a variety of causes. Since many of these characteristics may be changed, it is critical to identify them after surgery so that high-risk populations can be identified and early preventive measures can be put in place [12].

For patients who are experiencing changes in their voice, a multidimensional voice assessment and a postoperative laryngeal examination are advised [13]. After thyroid surgery, 80% of patients have voice disorders, meaning that roughly 10% of patients have recurrent laryngeal nerve damage [10]. Dysphonia after TT can significantly affect a patient's quality of life and interfere with their ability to effectively perform work and daily activities [11]. Preoperative voice education, handling anticipated voice changes during surgery, and thorough voice care after TT are all recommended by the guidelines [13].

This study aimed to examine the role and significance of TT for the occurrence of postoperative complications in correlation with HP and endocrinological findings.

METHODS

A cross-sectional study was conducted involving 90 patients with thyroid diseases who underwent TT at the University Clinical Center of Republic of Srpska (UCC RS) in Banja Luka between 2022 and 2024. Inclusion criteria were that the patients had thyroid diseases which were not surgically treated until arrival at the center. Patients under 18 years of age and those without a history of fine-needle aspiration were excluded. The research was approved by the Ethics Committee of UCC RS (approval no. 01-19-439-2/24) and complied with the revised ethical guidelines of the Declaration of Helsinki.

The patients underwent initial examination. Demographic characteristics and medical history were taken at the Clinic for Endocrine Diseases. Indications for surgery were set by endocrinologists who, based on anamnestic data, clinical examination, ultrasound examination of the thyroid gland, laboratory findings in the form of hormonal status and basic laboratory tests, diagnosed one of the thyroid diseases. Following TT, which involved removing all thyroid tissue, calcium, parathyroid hormone (PTH) and FT4 levels were measured at the Clinic for Endocrinology. After 48 h the patients were examined in the phoniatrics office to detect the condition of the vocal folds, when endovideolaryngoscopy (EVLS) was performed to diagnose whether there is proper mobility of both vocal folds, or whether there is unilateral or bilateral damage to the n. laryngeus recurrens.

Data analysis was conducted using SPSS v22.0 (IBM, USA). Descriptive statistics are presented as the mean, median and standard deviation. Quantitative values are expressed as absolute numbers (n) and percentages (%). For analysis of categorical variables, we used the χ^2-test and Fisher's exact test. Depending on the normality of the data distribution, we used the Student's t-test for independent samples or the Mann–Whitney test. For dependent variables, we used the t-test for dependent samples or the Wilcoxon test. For numerical variables, either Spearman's or Pearson's correlation was used. Results were considered significant if $p < 0.05$.

RESULTS

This cross-sectional study included 90 patients of both genders. Demographic data, indications for surgery, symptoms before and after surgery, TSH (thyroid-stimulating hormone) before and after surgery, postoperative serum calcium level, PTH and occurrence of paralysis of one or both vocal folds were collected. Of the total number of patients, 81 (90%) were female, average age 54.18 ± 11.8 years. The most common indication for TT was the isolated presence of goiter in 51 (56.7%), followed by Hashimoto's thyroiditis in 11 (12.2%) (Figure 1).

Five (5.6%) patients had preoperative symptoms, all of whom were women, while 85 (94.4%) patients had no preoperative symptoms. The most common postoperative symptoms were dyspnea on exertion, dizziness, neck pain, dysphagia, and cough. Laryngeal symptoms after TT were present in 13 (14.4%) patients and were reported as: hoarseness; hoarseness and difficulty swallowing; difficulty swallowing and cough (Figure 2). HP findings showed the highest presence of goiter in 37 (41.1%) patients, followed by follicular adenoma in 25 (27.8%) and papillary carcinoma in 18 (20%). VFP occurred in 11 patients (12.2%). The highest incidence of VFP occurred in patients with an HP diagnosis of goiter in 4 (4.4%) patients and papillary carcinoma in 4 (4.4%) patients, but it was not statistically significant ($\chi^2 = 3.88$, df = 3, p = 0.27) (Table 1). In the total sample, 11 (12.2%) had unilateral VFP, while bilateral VFP was not detected.

In the total sample, 12 (13.3%) patients had clinical endocrinological symptoms postoperatively. Among the symptoms they mentioned calf pain, leg cramps, tingling sensation and a general feeling of weakness. Sixty-seven (74.4%) patients had hypocalcemia, of which 51 (56.7%) had mild (1.9–2.2 mmol l^{-1}) and 16 (17.8%) severe hypocalcemia (< 1.9 mmol l^{-1}). Four (4.4%) patients had elevated PTH levels. A statistically significant correlation was found between age and postoperative Ca levels ($r_s = 0.2$, p = 0.05). However, no statistically significant associations were observed between age and postoperative TSH ($r_s = -0.09$, p = 0.37), age and preoperative TSH ($r_s = 0.004$, p = 0.97) or postoperative PTH ($r_s = 0.02$, p = 0.84) (Table 2).

There is a statistically significant correlation between postoperative PTH levels and the onset of postoperative symptoms overall (U = 470.0, p = 0.005). Age does not show a statistically significant correlation with postoperative symptoms (U = 671.5, p = 0.35), nor do preoperative TSH (U = 670.0, p = 0.35), postoperative TSH (U = 662.0, p = 0.31) or postoperative pH (Table 3).

Logistic-regression analysis was conducted to evaluate the influence of age, HPT presence, preoperative TSH levels, pH and gender on the total incidence of postoperative symptoms. The overall model did not show a statistically significant difference when compared with the null model ($\chi^2 = 5.013$, $p = 0.658$), accounting for 8% of the variation in postoperative symptoms (Nagelkerke R^2). There was no statistically significant effect of individual factors on the occurrence of postoperative symptoms: age ($p = 0.45$), hyperthyroidism ($p = 0.68$), preoperative TSH ($p = 0.88$), pH ($p = 0.57$), and gender ($p = 0.20$) (Table 4).

DISCUSSION

The analysis of post-thyroidectomy complications reveals that, while these procedures are typically routine and relatively safe, they do carry some risks. The most common complications, including VFP and HPT, can significantly affect patients' quality of life [14].

TT still has an overall complication rate of up to 54.4% [1]. Our study reveals several key findings regarding laryngeal complications after TT, highlighting their association with HP findings and the patient's hormonal status [9]. The findings also align with earlier research on complications following thyroid surgery, particularly highlighting hypocalcemia and recurrent laryngeal-nerve dysfunction as the most frequently encountered negative outcomes. We demonstrated that the rate of recurrent laryngeal-nerve dysfunction is 12.2%, with symptoms observed in 14.4% of individuals. Our results align with previous studies that have reported comparable complications [15].

Excessive use of alcohol, due to its toxic effect, can be one of the risk factors for thyroid cancer [16]. We found that VFP occurred in 11 (12.2%) patients after TT, with no statistically significant association with gender, age, presence of goiter, or hyperthyroidism. However, goiter and papillary carcinoma were present in the majority of patients with VFP [17]. EVLS offers insights into the anatomical structures and functional changes of the vocal folds, including their appearance and vibratory patterns, without any complications [18]. These results align with research conducted by other authors, which found that a notable proportion of patients experienced VFP, with its occurrence being influenced by the surgeon's level of expertise and the scope of the operation [19]. In this regard, the importance of standardizing recurrent laryngeal-nerve identification activities was emphasized to prevent nerve damage during surgery [20].

Regardless of changes in laryngeal mobility, individuals may experience swallowing issues following thyroidectomy. Although they are more frequently noticed in the late postoperative

phase, these problems, characterized by delayed triggering and stasis of food, may be seen in the early postoperative period [21]. A study assessing a tool designed to calculate the likelihood of hypocalcemia following TT discovered that the decline in PTH levels 1 h and 8 h after surgery, in addition to magnesium levels on the second postoperative day, were reliable indicators of more severe hypocalcemia [22].

These results are in line with research showing that hypocalcemia is the most frequent side effect following thyroidectomy, with a frequency as high as 54.4%. Postoperative endocrinological symptoms, such as tingling, muscle cramps and fatigue, were reported in 12 (13.3%) patients. The most important factor influencing the occurrence of these symptoms was the degree of hypocalcemia ($p = 0.001$), while other factors such as the presence of goiter, hyperthyroidism and histopathological findings did not show a significant association. This confirms previous findings linking hypoparathyroidism with postoperative hypocalcemia [23]. Increased surgeon operative volume has been linked to better outcomes across various procedures, including thyroidectomy. A study showed that thyroidectomies on elderly persons were less common among high-volume thyroid surgeons, who had fewer difficulties [24]. Risk-factor analysis showed that the presence of goiter alone significantly influences the occurrence of postoperative symptoms, which is consistent with the results of our study [25].

The decision regarding which surgical approach to take should be guided by the patient's risk factors, tumour characteristics and overall clinical context [26]. Thoracoscopy is considered the technique of choice for large retrosternal goiters descending into the mediastinum [27]. The treatment of autoimmune diseases of the thyroid gland such as Hashimoto's thyroiditis also requires surgical therapy. The solution would be improvement of diagnostics, good preoperative preparation, adequate intraoperative monitoring of the *n. laryngeus recurrens* and preoperative use of corticosteroids. Adequate and good results are directly related to precise surgical techniques, good operator experience and early voice rehabilitation [28].

CONCLUSION

Patients with VFP and hypocalcemia show the highest incidence of postoperative complications after TT due to HP-diagnosed goiter, follicular adenoma and papillary thyroid carcinoma. These findings may be useful in identifying elderly patients at increased risk of complications after TT that can significantly affect their quality of life.

Conflict of interest: None declared.

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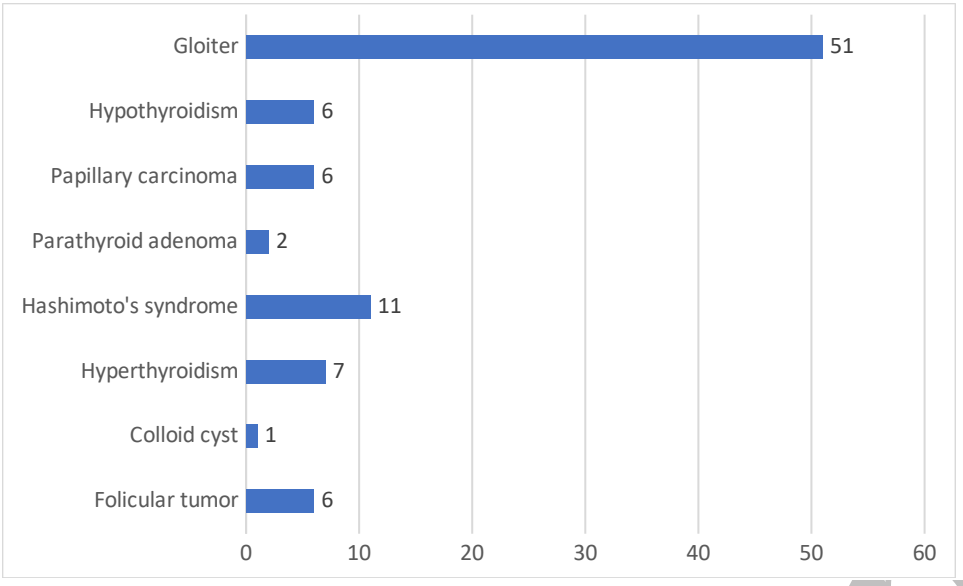

Figure 1. Frequency of preoperative thyroid disease diagnosis

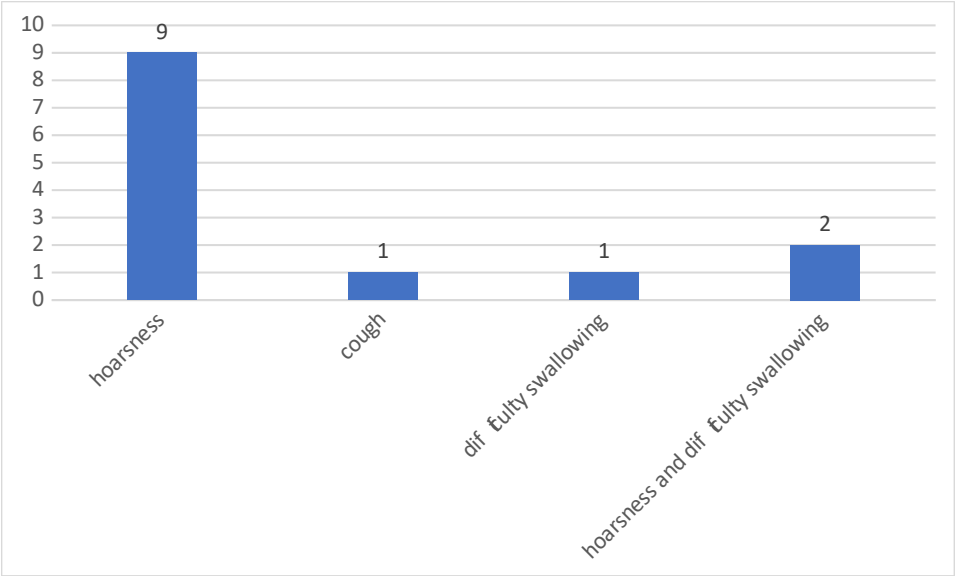

Figure 2. Presentation of laryngeal symptoms after surgery

Table 1. Correlation of pathohistological findings and paralysis

Paresis	HP				p
	Goiter	Papillary carcinoma	Follicular adenoma	Other	
Yes	4 (4.4)	4 (4.4)	1 (1.1)	2 (2.2)	> 0.05
No	33 (36.7)	14 (15.6)	24 (26.7)	8 (8.9)	

$\chi^2 = 3.88$, df = 3, p = 0.27**;** HP – histopathological

Table 2. Correlation of endocrinological complications with laboratory parameters

Laboratory parameters	N	Min.	Max.	Mean	SD
TSH preoperatively	90	0	4.33	1.55	1.14
TSH postoperatively	90	0.01	45	13.84	10.56
PTH postoperatively	90	1	75	32.7	16.28
Hypocalcemia postoperatively	90	1.06	2.56	2.02	0.32

* SD – standard deviation, TSH – thyroid-stimulating hormone; PTH – parathyroid hormone

Table 3. Correlation of the occurrence of postoperative symptomatology overall with age and laboratory parameters

	Age	**PTH postoperatively**	**TSH preoperatively**	**TSH postoperatively**
p	0.35	0.005	0.35	0.31

U = 470, p=0.005; PTH – parathyroid hormone; TSH – thyroid-stimulating hormone

Table 4. Correlation of demographic laboratory and endocrinological and PH factors with postoperative complications

Variable		Coef. (B)	SE	Odds ratio (Exp B)	95% confidence interval		p
					Lower	Upper	
Age		0.016	0.022	0.984	0.943	1.026	0.45
Hyperthyroidism	No			1			
	Yes	0.476	1.159	1.610	0.166	15.592	0.68
TSH before		0.033	0.222	1.034	0.669	1.598	0.88
HP							0.57
1		-0.952	0.794	0.389	0.081	1.828	0.23
2		-0.210	0.846	0.476	0.154	4.257	0.80

χ^2-test=5.013, p=0.658, TSH - thyroid-stimulating hormone; HP – histopathological

