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Thyroidectomy, especially total thyroidectomy, adversely affects erectile function in men

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Abstract

Objectives To evaluate the frequency of erectile dysfunction in male patients who undergo thyroidectomy using the International Index of Erectile Function (IIEF-5), and explore possible risk factors.

Methods 163 male patients who undergo partial, unilateral or bilateral thyroidectomy between December 2021 and September 2022 were retrospectively studied. The IIEF-5 questionnaires were completed 6 and 12 months after surgery, and patients who reported erectile dysfunction (ED) before surgery were not included. Sociodemographic factors (age, education status, and employment status) and health behavior (smoking and alcohol consumption) were also recorded. The above factors and clinical data were included for statistical analysis.

Results Fifty-five patients underwent total thyroidectomy (TT), 67 underwent hemithyroidectomy (HT), and 41 underwent partial thyroidectomy (PT). Six months after surgery, 33 patients (60%) in the TT group, 38 (56.7%) patients in the HT group, and 11(26.8%) patients in the PT group reported ED. The lowest scores were observed in the TT group (TT: 19.22 ± 3.895, HT: 20.67 ± 2.836, PT: 21.98 ± 1.651, $P < 0.05$). At the 12-month postoperative visit, the mean IIEF-5 scores were better in the HT and PT groups and worse in the TT group (TT: 18.36 ± 4.335, HT: 21.40 ± 2.692, PT: 22.54 ± 1.206, $P < 0.05$). Binary logistic regression analysis revealed that age and extent of resection significantly affected the onset of postoperative ED.

Conclusions Thyroidectomy, especially the total thyroidectomy, adversely affects erectile function. In addition to the operative procedure, age was also found to be significantly associated with postoperative ED.

Keywords Erectile dysfunction, Total thyroidectomy, Hemithyroidectomy

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Background

The incidence of thyroid cancer has increased in recent years [1], with a higher rate in women than in men [2]; however, the tumor grade of male patients is worse than that of female patients [3, 4], and a considerable number of male patients require total thyroidectomy (TT). Many studies have investigated physical changes after thyroidectomy, such as weight gain [5–7], chronic weakness [8–11], and an overall decrease in quality of life [12–14]. Some researchers reported that patients who underwent thyroidectomy frequently reported 'chronic asthenia', which worsened 1 year after surgery [9]. Patients are treated with L- thyroxine after removal of the thyroid since there is no intrinsic secretion or compensation.

Thyroid disease is considered a common factor affecting sexual function, which may be due to changes in thyroid hormones, autoantibodies, the patient's psychological state, or reproductive organs [15]. Some studies highlighted the intimate connection between thyroid hormones and sexual dysfunction [16–20] and revealed that hyperthyroidism and hypothyroidism can lead to male impotence, ejaculation dysfunction or low libido, all which improve after the restoration of thyroid hormones. ED is related to several risk factors, such as aging, thyroid disease, hypertension, diabetes, obesity and an unhealthy lifestyle [21].

Moreover, some patients often report impaired erectile function after thyroid resection even after adequate hormone replacement, and few studies have investigated the relationship between thyroid surgery and erectile dysfunction (ED). Therefore, we hypothesized that although the self-reported rate of ED may increase after thyroid surgery, patients who underwent partial thyroidectomy would still produce all kinds of thyroid hormones. It is reasonable to believe that postoperative ED is more common in patients who undergo TT and that some patients who undergo hemithyroidectomy (HT) and who suffer from postoperative ED will experience improvement in sexual function because of compensatory functions.

The purpose of this study was to investigate the frequency of post-thyroidectomy ED in male patients with adequate hormone replacement and explore the possible risk factors for post-thyroidectomy ED. We also evaluated the trends after a 12-month postoperative follow-up period.

Materials and methods

Participants

A total of 163 male patients who underwent partial, unilateral or bilateral thyroidectomy at the Second Affiliated Hospital of Chongqing Medical University between December 2021 and September 2022 and were followed up for 12 months were included in this retrospective study. After signing consent forms, they were asked to complete the IIEF-5 questionnaires online at 6 and 12 months after surgery. Sociodemographic factors (age, education status, and employment status), chronic diseases (hypertension, diabetes mellitus), and health behavior (smoking and alcohol consumption) were also collected. We assessed whether the IIEF-5 scores improved or worsened in the presence of these factors. The IIEF-5 is an efficient questionnaire for evaluating erectile function. It consists of 5 items. Each item has five response options ranging from 1 to 5, with a higher score indicating better sexual function, and its Chinese version has been proven effective and reliable in patients and the general population [22]. Scores ranging from 22 to 25 indicate normal sexual function, whereas scores 21 or less indicate sexual dysfunction, or ED. Serum calcium (s Ca) and parathyroid hormone (PTH) levels were measured prospectively on the first morning after surgery. Data from 3 periods (preoperative, 6 months after surgery, and 12 months after surgery) of hormone replacement with thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxin (FT4) were also collected.

The inclusion criteria were as follows: male, aged 18 to 60 years, normal sexual function before surgery, underwent thyroid resection on the basis of a diagnosis of malignant cytology, diagnosed with unilateral malignancy, underwent HT plus isthmus, bilateral malignancies suitable for TT. Patients who underwent partial thyroidectomy (PT) to avoid compression were also included. Partial thyroidectomy is defined as the removal of less than 50% of the tissue of one gland, and considered suitable for the removal of benign thyroid tumors with lesions, as it can effectively preserve thyroid function. It is useful for patients with benign tumors with a diameter more than 3 to 4 cm, symptoms of compression, or a strong desire for surgery because the large volume of the nodule makes it more apparent, affecting normal life and work. The final operation aligned with the patients' wishes. The recurrent laryngeal nerve and parathyroid glands were protected well during the surgery. Postoperative pathology revealed thyroid papillary carcinoma in patients who underwent HT, bilateral thyroid papillary carcinoma in patients who underwent TT, and follicular adenoma in patients who underwent PT. After surgery, thyroid cancer patients who underwent TT or HT received supplementary or substitutive therapy with L-thyroxine. Thyroid hormone levels were measured 4 weeks after surgery, and the dose of L- thyroxine was adjusted according to the levels of TSH and FT4. Thyroid hormone levels returned to normal within 2 months (Table 1), and patients did not receive any other supplementary treatment, such as radiotherapy or chemotherapy after surgery. Then, they completed the IIEF-5 questionnaire by themselves or with the help of a relative at 6 and 12 months after surgery.

Table 1 The laboratory variables at different time intervals postoperatively

		Non-ED	ED	*P* value
Patients	163	108	55	
TSH(mIU/L)	Pre-operative	1.512 ± 0.479	1.501 ± 0.496	0.887
	6 months after surgery	1.411 ± 0.866	1.162 ± 0.423	0.015
	12 months after surgery	1.308 ± 0.566	1.215 ± 0.681	0.360
FT3(pmol/L)	Pre-operative	5.063 ± 0.609	5.518 ± 0.610	0.347
	6 months after surgery	4.957 ± 0.689	4.956 ± 0.627	0.995
	12 months after surgery	4.873 ± 0.616	4.700 ± 0.658	0.100
FT4(pmol/L)	Pre-operative	17.233 ± 2.413	17.277 ± 2.153	0.910
	6 months after surgery	17.702 ± 2.488	18.247 ± 2.109	0.166
	12 months after surgery	18.357 ± 2.446	18.262 ± 2.038	0.804
PTH(pg/ml)		15.367 ± 4.356	15.525 ± 4.687	0.831
sCa(mmol/L)		2.207 ± 0.099	2.223 ± 0.114	0.370

ED: Erectile dysfunction, TSH: Thyroid-stimulating hormone, FT3: Free triiodothyronine, FT4: Free thyroxin, PTH: Parathyroid hormone, s Ca: Serum calcium

Table 2 The rate of ED at different time intervals, postoperatively

	PT	HT	TT	*P* value
6 months after surgery	11/41 (26.8%)	38 /67(56.7%)	33/55 (60%)	0.854[a], 0.003[b], 0.002[c].
12 months after surgery	3/41 (7.3%)	21/67 (31.3%)	31/55 (56.4%)	0.006[a], 0.004[b], < 0.001[c].

a: PT vs. TT, b: PT vs. HT, c:HT vs. TT

ED: Erectile dysfunction, PT: Partial thyroidectomy, HT: Hemithyroidectomy, TT: Total thyroidectomy

Table 3 Analyses of the IIEF-5 scores in the two periods of observation

	6 months after surgery	1 year after surgery	*P* value
TT	19.22 ± 3.895	18.36 ± 4.335	< 0.001
HT	20.67 ± 2.836	21.40 ± 2.692	< 0.001
PT	21.98 ± 1.651	22.54 ± 1.206	0.001
P value	< 0.001[a]	< 0.001[a]	
	0.008[b]	0.004[b]	
	0.023[c]	< 0.001[c]	

a: PT vs. TT

b: PT vs. HT

c: HT vs. TT

IIEF: International Index of Erectile Function questionnaire, PT: Partial thyroidectomy, HT: Hemithyroidectomy, TT: Total thyroidectomy

The exclusion criteria were as follows: a history of thyroid surgery or other malignancies, previous or current overt hypothyroidism or hyperthyroidism, current treatment for sexual dysfunction, no sex life, and refusal to participate. We excluded patients who complained of preoperative ED and patients who were treated with radioactive iodine. To reduce distractions, we excluded patients with postoperative hypocalcemia or hypoparathyroidism.

Statistical analyses

All the data were analyzed using SPSS (version 26). Continuous data are presented as means ± standard deviations (SDs), and categorical variables are presented as frequencies and percentages. For univariate analysis, Fisher's exact test was used to analyze categorical data (surgical type, tumor diameter > 1 cm, smoking status, alcohol consumption status, hypertension status, diabetes status, occupation and education), and an independent sample t test was used for continuous data (age, BMI). Variables that were significantly related to ED ($P < 0.05$) in the univariate analysis were assessed in the binary logistic regression analysis (age, surgical type and smoking status). A 2-tailed p value < 0.05 indicated statistical significance.

Results

A total of 163 patients were included in this study, including 55 in the total thyroidectomy (TT) group, 67 in the hemithyroidectomy (HT) group, and 41 in the partial thyroidectomy (PT) group. Six months after surgery, 33 patients (60.0%) in the TT group, 38 (56.7%) in the HT group, and 11(26.8%) in the PT group reported ED. The differences in the rates of postoperative ED at 6 months after surgery between the PT and HT groups and between the HT and TT groups were statistically significant (PT vs. HT: $P = 0.003$; HT vs. TT: $P = 0.002$). A total of 56.4% of patients in the TT group still had ED at the 12-month follow-up visit (31.3% in the HT group and 7.3% in the PT group), and there was an obvious difference in the incidence of ED at the 12-month follow-up visit (PT vs. TT: $P = 0.006$; PT vs. HT: $P = 0.004$; HT vs. TT: $P < 0.001$) (Table 2). Table 3 shows the mean IIEF-5 scores of the three groups. The lowest scores were observed in the TT group at 6 months after surgery (TT: 19.22 ± 3.895, HT: 20.67 ± 2.836, PT: 21.98 ± 1.651, $P < 0.05$). The IIEF-5 scores improved in the HT and PT groups during the follow-up, worsening in the TT group (HT: 21.40 ± 2.692, PT: 22.54 ± 1.206, TT: 18.36 ± 4.335, $P < 0.05$). The differences in the mean IIEF-5 scores between the three groups at 6 and 12 months after surgery were statistically significant (6 months after surgery, PT vs. TT: $P < 0.001$; PT vs. HT: $P = 0.008$; HT vs. TT: $P = 0.023$). Twelve months after surgery, PT vs. TT: $P < 0.001$; PT vs. HT: $P = 0.004$; HT vs. TT: $P < 0.001$). In addition, patients treated with TT had significantly lower scores than patients in the HT group did at 6 and 12 months after surgery ($P = 0.023$, < 0.001).

Patients were divided into two groups according to whether they had ED 12 months after thyroid surgery, and the sociodemographic and clinical characteristics of the patients in the two groups are summarized in Table 4. Overall, 55 of the 163 patients still reported ED 12 months after surgery. The mean ± SD age of the patients with ED was 43.47 ± 8.342 years, which was greater than that of the patients without ED ($P = 0.026$). In the ED group, 56.4% of the patients (31/55) had total TT, and 38.2% had HT (21/55). A total of 21.8% of the patients in the ED group had a smoking habit, which was lower in the non-ED group; the reason for this difference is not clear. Six months after surgery, the mean TSH level of the patients in the ED group was slightly lower than that of the patients in the non-ED group ($P = 0.015$). However, the difference in the mean TSH level between the two groups was not obvious 12 months after surgery. There was no significant difference in postoperative parathyroid hormone and serum calcium levels between the two groups (Table 1). Our univariate analysis indicated that the groups were balanced with respect to tumor size, BMI, alcohol consumption status, hypertension status, diabetes mellitus status, occupation and education (Table 4), and three variables namely, age, surgery type and smoking status were significantly different between the two groups ($P = 0.026$, < 0.001, 0.024). The binary logistic analysis indicated that there were two variables determining significant changes in the worsening of erectile function, and the significant associations were as follows: age ($P = 0.001$), HT ($P = 0.001$), and TT ($P < 0.001$) (Table 5).

Discussion

ED is defined as the inability to achieve or sustain a satisfactory erection to engage in sexual intercourse [23] and is associated with advanced age, obesity, smoking, alcohol consumption, and thyroid disorders; however, the mechanism is not fully understood [24]. The effects of changes in thyroid hormone levels on erectile function have been previously studied [17, 19, 25, 26]. Keller et al. [25] reported that patients with ED were 1.64 times more likely to have hyperthyroidism than controls were. Corona et al. [19] reported that the inhibition of TSH caused by overt hyperthyroidism was associated with increased rates of severe ED, and the treatment of hyperthyroidism significantly reduced rates of severe ED. These reports suggest an association between impotence and hyper and hypothyroidism, and the mechanism by which thyroid hormone disorders affect sexual function may involve pathways including endocrine, sympathetic, and psychiatric pathway [16, 17, 27–31]. Most published studies to date have addressed the effects of thyroid hormone alterations on sexual function, but few studies have addressed the impact of thyroidectomy on sexual

Table 4 Patients with ED vs. non-ED 12 months after surgery

		Non-ED	ED	*P* Value
Patients		108	55	/
Age(years)		40.09 ± 9.467	43.47 ± 8.342	0.026
BMI(kg/m^2)		25.90 ± 3.170	25.77 ± 4.205	0.819
Surgical type				< 0.001
	Partial thyroidectomy	38	3	
	Hemithyroidectomy	46	21	
	Total thyroidectomy	24	31	
Tumor>1 cm				0.069
	No	52	35	
	Yes	56	20	
Smoke				0.024
	No	65	43	
	Yes	43	12	
Drink				1
	No	92	47	
	Yes	16	8	
Hypertension				0.804
	No	94	49	
	Yes	14	6	
Diabetes mellitus				0.878
	No	102	53	
	Yes	6	2	
Occupation				0.434
	Civil service	16	7	
	Technicians	7	4	
	Clerk	53	21	
	Business or service	32	23	
Education				0.069
	Primary school or below	3	1	
	Junior high school	25	22	
	College or higher	80	32	

ED: Erectile dysfunction

Table 5 The binary logistic regression between the group Non-ED and ED

		OR (95% CI)	*P*
Age		1.076 (1.030–1.125)	0.001
Surgical type			
	Partial thyroidectomy	Reference	
	Hemithyroidectomy	9.189(2.356–35.843)	0.001
	Total thyroidectomy	26.478(6.537-107.248)	< 0.001
Smoke			
	No	Reference	
	Yes	0.575(0.250–1.319)	0.191

function. In this study we evaluated the prevalence of post-thyroidectomy ED. As a consequence of thyroidectomy in patients adequately treated with L-thyroxine, the postoperative incidence of ED was 56.4% in the TT group and 31.3% in the HT group, both of which were higher than the incidence of ED in the PT group.

The root cause of postoperative ED is unknown, and the hypothalamus–pituitary–thyroid axis may be the main cause of postoperative ED. The production of thyroid hormone is regulated by the hypothalamus–pituitary–thyroid axis, which is closely related to the hypothalamic–pituitary–gonadal axis. Thyroid hormone is associated with thyroid-releasing hormone (TRH) secondary to thyroid-stimulating hormone (TSH), which stimulates the release of prolactin (PRL) by the anterior pituitary. The presence of PRL links thyroid hormones and gonadal dysfunction by regulating the release of gonadotropin-releasing hormone (GnRH) [32], causing disturbances in testosterone, dehydroepiandrosterone (DHEA), and metabolites of DHEA, sex hormone-binding globulin (SHBG) [17], which bind androgens with higher affinity than estrogens do, leading to a relatively hyperestrogenism state and a reduction in bioavailable testosterone, ultimately leading to sexual dysfunction including ED and reduced libido [27, 28]. Some studies have revealed a link between thyroid disorders and the impairment of nitric oxide synthase (NOS) in corpora cavernosa tissue [30], which plays a role in dilating blood vessels through cyclic guanosine monophosphate (cGMP) signaling. Reduced NOS leads to the weakening of penile blood vessels, causing ED. In addition, some thyroid hormones are produced by deiodination and other biochemical pathways in the thyroid gland [33], and the neurotransmitters produced by parafollicular cells such as calcitonin-related peptides, may play a role in erection [34]. In 1991, researchers reported that an intracavernous injection of 500 mg or more of calcitoningene-related peptides induced a dose-dependent erectile response. At all doses, a long-lasting increase in arterial inflow at all doses and a significant increase in the arterial flow were observed. An injection of 5 μg of calcitoningene-related peptides resulted in electrical silencing (and subsequent cavernous smooth muscle relaxation) for a mean of 92 s. In 3 of 4 patients, a significant decrease in maintenance flow was observed after an intracavernous injection of 5 μg of calcitonin-gene-related peptides. A functional study revealed that an intracavernous injection of calcitonin-gene-related peptides induces a dose-dependent erectile response by increasing arterial flow, relaxing cavernous smooth muscles and activating the cavernous occlusive mechanisms. The effect of calcitoningene-related peptides on the cavernous artery is much longer than that on the cavernous smooth muscles [34]. Resection of the thyroid results in the loss of a stable thyroid hormone system that is critical to the hypothalamic–pituitary–gonadal axis. Even if patients are treated with L-thyroxine, those atypical hormones are insufficient after thyroid resection. Additional studies are necessary to elucidate the mechanisms by which thyroidectomy leads to ED. In this study we also compared their mean IIEF-5 scores. Our results revealed that patients treated with total thyroid resection had significantly lower IIEF-5 scores, which were worse at the 12-month follow-up. The trend of toward worsening erectile function in patientswho underwent TT in our study is consistent with the onset of chronic asthenia reported by patients who underwent TT [9]. The extent of resection and age were identified as independent risk factors via multivariate analysis, and variables such as obesity, diabetes, and hypertension were not associated with the incidence of postoperative ED, probably because of the small number of patients with diabetes or hypertension in our study, not to mention the small sample size as a whole. Interestingly, the ED group had a mild TSH inhibition compared with the non-ED group, but the TSH, FT3 and FT4 levels in both groups were within the normal range. If the difference in erectile function between the two groups is related to the difference in TSH levels, there would still be a significant difference in TSH levels between the two groups at the 12-month follow-up, and more studies are needed on this issue. The incidence of postoperative hypocalcemia is 1.2–40%[35]. To reduce distractions, we excluded patients with postoperative hypocalcemia or hypoparathyroidism.

Postoperative sexual dysfunction has received little attention. Although this was a small-sample, single-center study, our data revealed that patients with thyroid cancer who underwent TT are more likely to have ED, and more large-sample studies are needed to confirm our results and explore other changes in the endocrine system in male patients after thyroidectomy, which may affect clinical decisions regarding the extent of thyroid resection in male patients with thyroid cancer.

Conclusion

This study is the first to demonstrate that thyroidectomy, especially total thyroidectomy, adversely affects erectile function in men. Moreover, a significant positive correlation was found between erectile dysfunction and age. Further studies involving more patients are needed to confirm our results.

Abbreviations

IIEF-5	International Index of Erectile Function
ED	Erectile dysfunction
TT	Total thyroidectomy
HT	Hemithyroidectomy
PT	Partial thyroidectomy
sCa	Serum calcium
PTH	Parathyroid hormone
TSH	Thyroid-stimulating hormone

FT3	Free triiodothyronine
FT4	Free thyroxin
TRH	Thyroid-releasing hormone
PRL	Prolactin
GnRH	Gonadotropin-releasing hormone
DHEA	Dehydroepiandrosterone
SHBG	Sex hormone-binding globulin
NOS	Nitric oxide synthase
cGMP	Cyclic guanosine monophosphate

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Author contributions
Study design: DG and YH. Questionnaires collection: QD. Clinical data collection: YH and YY. Statistics analysis: YH. Manuscript writing: YH. Manuscript critical revision: YH and DH. All authors read and approved the final version of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The studies involving human participants were reviewed and approved by the local Ethics Committee of the Chongqing Medical University. Informed consent to participant was obtained from all of the participants in the study.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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