Incidence and risk factor for short term postoperative cough after thyroidectomy

Junfu Wu
Zhengzhou University First Affiliated Hospital
Liyuan Dai
Henan Cancer Hospital
Weihua Lou (weihual2015@163.com)
Zhengzhou University First Affiliated Hospital

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Abstract

Background

The prevalence of and potential risk factors for postoperative cough after thyroidectomy remain unknown. The current study aimed to analyze postoperative cough in patients undergoing thyroidectomy using a prospective analysis.

Methods

Adult patients undergoing primary thyroidectomy were prospectively enrolled. Data regarding age, sex, BMI, pathology and surgical procedure were collected and analyzed. All patients were asked to complete the Leicester Cough Questionnaire (LCQ) preoperatively and at 2 weeks and 4 weeks postoperatively.

Results

There were 1264 patients enrolled in total. In patients with benign disease, postoperative cough occurred in 62 patients, with an prevalence rate of 17.2% compared to an prevalence rate of 32.9% in patients with malignant disease; the difference was significant. For benign patients, the factors of smoking and operation time were independently related to the occurrence of postoperative cough. For malignant patients, the factors of smoking, operation time, operation extent, and the number of positive nodes at level 6 were independently related to the occurrence of postoperative cough. There was no significant difference regarding the LCQ score in patients with benign or malignant disease at the preoperative and the postoperative 4-week time periods. Patients with malignant disease had a significantly lower LCQ score than patients with benign disease at the postoperative 2-week time point ($p = 0.001$).

Conclusions

Patients undergoing thyroid cancer surgery had a higher prevalence of postoperative cough and were also associated with a decreased cough-related quality of life. The factors of smoking and operation time were the most important predictors for postoperative cough after thyroidectomy.

Introduction

There has been a substantial increase in the proportion of thyroid cancer cases globally, mainly due to the actual increase in the prevalence of papillary thyroid cancer and/or the increased detection of the disease[1]. Clinical manifestations are usually asymptomatic, surgery is the primary treatment of choice, and thyroidectomy is regarded as an effective and safe surgical option for selected patients with a low risk of permanent vocal distortion, swallowing difficulties, and hypocalcemia when performed by experienced surgeons[2–4]; however, the symptoms of postoperative nausea and vomiting, transient

throat pain, local sensory disturbance, and prolonged swallowing time when taking medications are all common after thyroid surgery. In our cancer center, patients who have undergone thyroidectomy sometimes have severe cough; postoperative cough can even induce postoperative hematoma[2]. Patients complain that this phenomenon is quite worrisome, and doctor-patient conflicts may even occur[5], especially in patients without a previous history of cough. This suggests the importance of preoperative communication for postoperative cough. Factors including smoking history, surgical extent, and operation time might be associated with postoperative cough. However, there are few studies available in terms of its prevalence and potential predictors.

Since its first introduction by Birring et al.[6], the Leicester Cough Questionnaire (LCQ) has been regarded as a reliable tool for evaluating the cough in adults by a number of researchers[7–9]. Therefore, our goal was to prospectively analyze postoperative cough in patients undergoing thyroidectomy.

Materials And Methods

Ethical Considerations

Our study was approved by Henan Cancer Hospital institutional research committee, written informed consent for medical research was obtained from all patients at initial treatment. The study was conducted in accordance with the relevant guidelines and regulations.

From January 2018 to December 2018, adult (≥ 18 years) patients undergoing primary thyroidectomy were prospectively tracked. The exclusion criteria were as follows: the patient had chronic cough associated with smoking or gastroesophageal reflux or with other causes; resection of the trachea or larynx was performed; the recurrent laryngeal nerve was invaded by the tumor or metastatic nodes; and there was pulmonary infection. The symptom of cough had to begin on the first day after the operation, and was defined and assessed by our research group based on previous studies[10]. Smokers/drinkers were defined as patients who smoked/drank at diagnosis or who had stopped for less than 1 year[11]. The operation time was defined as the time from the beginning of endotracheal intubation to the point of extubation. Data regarding age, sex, BMI, operation time, postoperative pathology, operation type, and drinking and smoking status were collected and analyzed. Based on the Chinese Nutrition Society, overweight refers to a BMI from 24 to 28, and obesity refers to a BMI above 28.

All patients received an open surgery under general anesthesia using both intravenous anesthesia and inhalation anesthesia, the frequently used narcotic drugs included cisatracurium, propoxate and fentanyl. Patients were extubated at the end of the operation and transferred to the ward after a brief stay in the recovery room. The extent of operation of the primary tumor consisted of two types: unilateral thyroid operation referred to surgery involving only one thyroid lobe, and bilateral thyroid operation referred to surgery involving both thyroid lobes. In our cancer center, central neck dissection was routinely performed for thyroid papillary and medullary carcinoma. Lateral neck dissection was performed if there were

positive nodes at level 3 or 4 according to frozen sections. All patients had atomised inhalation after surgical treatment.

All enrolled patients were required to complete the Mandarin Chinese Version of LCQ preoperatively in the ward, and patients with postoperative cough were required to complete the LCQ at 2 weeks and 4 weeks postoperatively via the out-patient department, email, or WeChat. The LCQ was usually used for measuring chronic cough, but recent evidence showed there was also high validity and responsiveness in assessing acute cough or postoperative cough[7, 12, 13]. The LCQ is easy to complete taking less than 5 minutes by themselves. There are 19 items, and each item represents an adverse event caused by cough. The responses were scored by a 7-point Likert scale. These 19 items were divided into three domains that considered the psychological impacts (such as the effect of cough on embarrassment/anxiety), physical impacts (such as the effect of cough on sputum production and stomach and chest pain), and social impacts (such as the inference of cough with job/daily life and enjoyment of life). A total score and three domain scores were calculated, with domain scores ranging from 1 to 7 and total scores from 3 to 21; a higher score reflects a better health status[14].

A univariate analysis (the Chi-square test) was used to evaluate the possible risk factors for postoperative cough, and then a multivariate analysis (logistic regression test) was used to determine the independent risk factors. The Wilcoxon rank sum test was used to compare the LCQ scores among different time periods. All statistical analyses were performed by using SPSS 20.0, and $p < 0.05$ was considered significant.

Results

A total of 1264 patients (922 females and 342 males) were enrolled in the analysis, and the mean age was 49.4 (range: 18–78) years. There were 39 smokers and 35 drinkers. A total of 577 patients were classified as overweight, and 171 patients were classified as obese. The postoperative pathology was benign in 361 patients and malignant in 903 patients. The mean operation time was 1.6 (range: 0.7–4.8) hours. Postoperative bleeding occurred in 19 patients, transient hypocalcemia occurred in 186 patients, and vocal cord palsy occurred in 11 patients.

A total of 359 patients had postoperative cough, and the overall prevalence was 28.4%. In patients with cough, 6 developed postoperative bleeding, and in patients without cough, 13 developed postoperative bleeding; the difference was not significant ($p = 0.747$). In patients with benign disease, postoperative cough occurred in 62 patients with an prevalence rate of 17.2%, in these 62 patients, 2 (3.2%) patients had postoperative bleeding, 4 (6.5%) patients had transient hypocalcemia, and 1 (1.6%) patients had vocal cord palsy, in 299 patients without cough, 2 (0.7%) patients had postoperative bleeding, 20 (6.7%) patients had transient hypocalcemia, and 1 (0.3%) patients had vocal cord palsy, the mean operation time was 1.3 (range: 0.7–2.4) hours.

In patients with malignant disease, postoperative cough occurred in 297 patients with an prevalence rate of 32.9%, in these 297 patients, 4 (1.3%) patients had postoperative bleeding, 42 (14.1%) patients had

transient hypocalcemia, and 1 (0.3%) patients had vocal cord palsy, in 606 patients without cough, 11 (1.8%) patients had postoperative bleeding, 120 (19.8%) patients had transient hypocalcemia, and 8 (1.3%) patients had vocal cord palsy, and the mean operation time was 1.7 (range: 0.8–4.8) hours.

The differences regarding cough occurrence and operation time between patients with benign disease and patients with malignant disease were both significant (both $p < 0.001$). There were no differences in age, sex, or BMI between the two groups (all $p > 0.05$).

To identify the risk factors for postoperative cough in patients with benign disease, as described in Table 1, in the univariate analysis, the factors of smoking, operation time, and operation extent were associated with the occurrence of postoperative cough (all $p < 0.05$). In further multivariate logistic regression analysis (Table 2), the factors of smoking and operation time were related to the occurrence of postoperative cough (all $p < 0.05$).

Table 1
Univariate analysis of risk factors for postoperative cough in patients with benign thyroid disease.

Variables	**Univariate**		
	Cough (n = 62)	No cough (n = 299)	
Age ≥45	42	184	
45	20	115	0.358
Sex Female	48	200	
Male	14	99	0.104
Smoker No	54	289	
Yes	8	10	0.002
Drinker No	57	289	
Yes	5	10	0.090
Operation time 1.3 h	40	234	
≥1.3 h	22	65	0.021
BMI Normal	27	103	
24 ~ 28	24	129	
>28	11	67	0.380
Operation extent Unilateral	24	167	
Bilateral	38	132	0.014

Table 2
Multivariate analysis of risk factors for postoperative cough in patients with benign thyroid disease.

Variables	Multivariate analysis	
	p	HR [95% CI]
Smoker	0.001	3.336 [1.542–7.886]
Operation time	0.008	1.896 [1.278–4.481]
Operation extent	0.475	2.772 [0.664–5.112]

Table 3
Univariate analysis of risk factors for postoperative cough in patients with malignant thyroid disease.

Variables	Univariate		
	Cough (n = 297)	No cough (n = 606)	
Age ≥45	190	367	
45	107	239	0.322
Sex Female	214	460	
Male	83	146	0.211
Smoker Yes	12	9	
No	285	597	0.017
Drinker Yes	10	10	
No	287	596	0.100
Operation time ≥1.3 h	203	300	
1.3 h	94	306	< 0.001
BMI Normal	116	270	
24 ~ 28	141	283	
>28	40	53	0.056
Operation extent Unilateral	83	308	
Bilateral	214	298	< 0.001
Number of positive nodes in level 6			
≥3	118	195	
<3	179	511	< 0.001
Lateral neck dissection			
Yes	99	256	
No	198	350	0.010
Cancer type			
PTC	287	577	
others	10	29	0.325
PTC: papillary carcinoma			

To identify the risk factors for postoperative cough in patients with malignant disease, as described in Table 2, in the univariate analysis, the factors of smoking, operation time, operation extent, the number of positive nodes at level 6, and lateral neck dissection were associated with the occurrence of postoperative cough (all $p < 0.05$). In further multivariate logistic regression analysis (Table 4), the factors of smoking, operation time, operation extent, and the number of positive nodes at level 6 were related to the occurrence of postoperative cough (all $p < 0.05$).

Table 4
Multivariate analysis of risk factors for postoperative cough in patients with malignant thyroid disease.

Variables	Multivariate analysis	
	p	HR [95% CI]
Smoker	0.003	4.004 [1.672–8.462]
Operation time	0.005	2.556 [1.448–5.132]
Operation extent	0.014	2.988 [1.264–4.874]
Number of positive nodes in level 6	< 0.001	5.654 [2.003–9.439]
Lateral neck dissection	0.087	2.432 [0.922–7.583]

In coughing patients with benign disease, the mean preoperative LCQ score was 21, and the mean LCQ score was 18.8 (SD: 3.7) at the second week after the operation; the difference was significant ($p < 0.001$). The mean LCQ score was 20.9 (SD: 0.2) at the fourth week after the operation, and when compared to the preoperative level, the difference was not significant ($p = 0.961$).

In coughing patients with malignant disease, the mean preoperative LCQ score was 21, and the mean LCQ score was 16.8 (SD: 5.7) the second week after the operation; the difference was significant ($p < 0.001$). The mean LCQ score was 20.8 (SD: 0.3) the fourth week after the operation, and when compared to the preoperative level, the difference was not significant ($p = 0.903$).

When comparing the scores among different time periods in patients with benign or malignant disease, there was no significant difference between the two groups at the preoperative and postoperative 4-week time periods (both $p > 0.05$), but patients with malignant disease had significantly lower LCQ scores than patients with benign disease at the postoperative 2-week time period ($p = 0.001$).

Discussion

One of the main findings in the current study was that postoperative cough was relatively common after thyroid surgery, with an overall prevalence rate of 28.4%, and it was more common in patients with malignant disease than in patients with benign disease. In a study by Jung et al.[15], the authors aimed to determine the effects of a humidifier with heated wire circuits on the prevalence and severity of cough

after thyroidectomy, and they reported that in patients undergoing active humidification of inspired gases, the prevalence of postoperative cough was significantly decreased compared to patients without a heated humidifier. In the current study, all patients had routine postoperative atomization inhalation, and the overall prevalence of postoperative cough was consistent with the results of the above study.

The finding of a higher rate of postoperative cough in patients with malignant disease than in patients with benign disease was interesting. Most previous authors have analyzed cough in patients with a flexible reinforced laryngeal mask airway or a plain endotracheal tube[16–18]; although they described that a flexible reinforced laryngeal mask airway placed during surgery decreased the prevalence and severity of laryngo-pharyngeal symptoms and was a feasible anesthetic tool compared with the use of a conventional endotracheal tube for thyroidectomy, no authors have evaluated whether the type of pathology affects postoperative cough. The variation between the two groups might be explained by the following: surgical trauma, anesthesia, tracheal intubation, and recurrent laryngeal nerve dissection are all potential causes for cough following surgical procedures[19], and patients with malignant disease had longer operation times and more instances of routine central neck dissection in the current study.

Risk factors for postoperative cough following surgical procedures have been occasionally analyzed. Lin et al.[20] demonstrated that a long duration of anesthesia time, female sex, subcarinal node resection and lower paratracheal node resection were independent risk factors related to cough in non-small-cell lung cancer patients after surgery. Chen et al.[21] reported a correlation between pulmonary surgery and postoperative cough, and the probability of postoperative cough was higher in more invasive patients. The current study was the first to analyze the predictors of postoperative cough after thyroidectomy. Similar to previous reports, we also noted that operation time was an independent predictor for postoperative cough. Moreover, smoking has been proven to be associated with chronic cough by Colak et al.[22], and there was also a positive linkage with acute cough based on our outcome.

Another interesting finding was that postoperative cough was more common in patients with more than 3 positive central nodes. In our view, the most likely cause of this finding is associated with the branches of the recurrent laryngeal nerve. Small branches of the nerve, such as the tracheal branch, are often encountered during thyroidectomy, and they may inadvertently be resected during central neck lymph node dissection. However, the actual frequency of branch excision has not been clearly documented. More studies are needed to clarify this question. Another potential explanation is the tracheal thermal damage associated with the usage of high-frequency electric surgical knives and ultrasonic scalpels during operation.

It is important to evaluate the impact of postoperative cough on quality of life. The LCQ is a reliable method and has been used in many clinical trials as an outcome measure[13, 19, 23]. Lin et al.[20] described that in patients receiving video-assisted thoracoscopic surgery for lung cancer, the mean postoperative total score was 16.35, which was significantly lower than the mean follow-up score after 1 month, but the authors did not provide the data of preoperative levels. In our previous study, we found that thyroidectomy was significantly associated with a decreased LCQ score compared to baseline

scores, but the study did not report when the LCQ scores returned to preoperative levels. In the current study, we were the first to note that for patients undergoing thyroidectomy regardless of the presence of benign or malignant disease, the mean postoperative LCQ score returns to baseline level in 4 weeks. The time interval found in this study was significantly shorter than in patients undergoing lung surgery, which can be attributed to the different types of operation.

Moreover, we found that the 2-week mean LCQ score was significantly lower in patients with malignant disease than in patients with benign disease. One possible reason for this difference is that patients with malignant disease were associated with a longer operation time and more surgical trauma, including routine dissection of the main trunk and branches of the recurrent laryngeal nerve.

The limitations of this study must be acknowledged. First, cough assessment usually consists of objective and subjective measures. Although the LCQ is a reliable method for subjective assessment, more objective analyses are needed to clarify postoperative cough after thyroidectomy. Second, postoperative cough can be caused by laryngitis or laryngeal trauma related to orotracheal intubation, but we did not routinely examine the larynx using flexible laryngoscopy for patients with cough, and any misclassification would bias our analysis. Third, the BMI and lifestyle characteristics were significantly different in this group to a western group, it remained unclear whether this finding could be confirmed in western studies.

In summary, compared to patients with benign disease, patients undergoing thyroid cancer surgery had a higher prevalence of postoperative cough and a lower 2-week postoperative LCQ score. However, the 4-week postoperative LCQ score returned to the preoperative level in patients undergoing thyroidectomy regardless of the presence of benign or malignant disease. The factors of smoking and operation time were the most important predictors for postoperative cough after thyroidectomy.

Abbreviations

Leicester Cough Questionnaire
LCQ

Declarations

Statement of Ethics

Henan Cancer Hospital institutional research committee approved our study and all participants signed an informed consent agreement for medical research before initial treatment. And all the related procedures were consistent with Ethics Committee regulations.

Consent to publish

All the material came from our cancer center, and the publish consent have been obtained from all the patients.

Availability of data and materials

All data generated or analyzed during this study are included in this published article. And the primary data could be achieved from the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

JW and WL contributed to the study design, supported statistical analysis, recruited patients, provided inputs for data interpretation and contributed to the writing and review of the content of the manuscript. JW and LD recruited patients and critically reviewed the content of the manuscript. JW and LD supported statistical analysis and was involved in writing and critical review of the content of the manuscript. All authors read and approved the final draft of the manuscript for publication.

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