

Paratracheal lymph node dissection does not negatively affect thyroid dysfunction in patients undergoing laryngectomy

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Received: 10 September 2009 / Accepted: 26 October 2009 / Published online: 14 November 2009
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Abstract The aim of this retrospective study was to evaluate the prognostic significance of paratracheal lymph node dissection including hemithyroidectomy for the development of hypo(para)thyroidism. From 1990 to 2004, 169 patients with a carcinoma of the larynx or hypopharynx who underwent paratracheal lymph node dissection were selected. Data of 137 patients (23 women, 114 men) were analyzed. Hundred patients were tested on thyroid function. Patient, tumor and treatment characteristics were noted including age, gender, site, TNM stage and details of surgery, radiotherapy and chemotherapy. Seventy percent of the tested patients had hypothyroidism (36% clinical, 34% subclinical); 33% had hypoparathyroidism. All patients with hypo(para)thyroidism underwent various lymph node treatment modalities. For the various treatment combinations, no increase of hypo(para)thyroidism was found if a bilateral paratracheal lymph node dissection was performed. The incidence of hypo(para)thyroidism after laryngectomy in combination with hemithyroidectomy, neck dissection and paratracheal lymph node dissection is high. An additional risk of paratracheal dissection for the development of hypo(para)thyroidism could not be shown.

Keywords Carcinoma · Larynx · Hypopharynx · Paratracheal lymph node dissection · Hypothyroidism · Hypoparathyroidism

Introduction

The incidence of endocrine dysfunction after treatment for laryngeal and hypopharyngeal carcinoma is high, especially after combination treatment of radiotherapy and surgery. The incidence of hypothyroidism is between 10 and 78%, depending on treatment modalities [1–3]. In our previous cross-sectional study we found an incidence of hypothyroidism of 77% in patients after total laryngectomy, hemithyroidectomy and radiotherapy. Risk factors for the development of hypothyroidism were laryngectomy, hemithyroidectomy and ipsilateral neck dissection [4].

Hypothyroidism causes symptoms such as weight gain, cold intolerance, dry skin, constipation, depression, cognitive impairment and a decrease in gastrointestinal tract motility. These symptoms may have significant impact on the quality of life [5, 6].

Hypoparathyroidism is a rare condition and most commonly occurs because of damage or removal of (para)thyroid glands at the time of thyroid surgery [7, 8]. Hypoparathyroidism is estimated to occur in between 12 and 31% of cases with regard to laryngectomy combined with hemithyroidectomy [7].

In advanced laryngeal and hypopharyngeal carcinoma paratracheal lymph node (PTLN) dissection is frequently performed [9]. The reported incidence of PTLN metastases varies between 9 and 36% depending on the site and stage of the primary tumor [10–13].

The vascular supply of the (remaining part of the) thyroid gland may be injured during PTLN dissection, which

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may contribute to the development of hypo(para)thyroidism [14].

To our knowledge no studies reported the relationship between PTLN dissection and development of hypothyroidism. The purpose of this study is to examine if PTLN dissection is an additional risk factor for the development of (para)thyroid function [4].

Patients and methods

A retrospective analysis was performed on 169 patients who underwent laryngectomy and paratracheal lymph node dissection because of primary or recurrent laryngeal or hypopharyngeal carcinoma between 1990 and 2004. Thirty-two patients who underwent total thyroidectomy were excluded. In the remaining group of 137 patients thyroid function was tested on indication only. Results were obtained from 100 patients.

Patient, tumor and treatment parameters were collected including age, gender, site, TNM stage and details of surgery, radiotherapy and chemotherapy. Thyroid function was classified as euthyroidism (normal TSH, 0.3–4.5 mU/L) and normal free T4 (11.0–24.0 pmol/L), clinical hypothyroidism (high TSH and low free T4) and subclinical hypothyroidism (high TSH and normal free T4). Parathyroid function was classified as normal if calcium serum levels were between 2.20 and 2.60 mmol/L with a serum albumin of 35–52 G/L. Corrected calcium levels were used.

Comparison contingency tables were made with Pearsons χ^2 for nominal data.

Results

Data of 23 females and 114 males were analyzed (shown in Table 1). The mean age was 61.9 years. Fifty-five patients died during follow-up. The primary tumors were located in the supraglottis ($n = 45$), glottis ($n = 64$), subglottis ($n = 1$), piriform sinus ($n = 19$) and posterior pharyngeal wall or post-cricoid area ($n = 8$). One-hundred and seventeen tumors were located unilaterally and 20 had a midline location.

Tumor stage was T2, T3 and T4 in 3, 28 and 40 cases, respectively, whereas 66 patients had a recurrence after radiotherapy. Thirty-six patients were staged as a N0 neck. Fifteen patients were classified with a N1 neck, 16 with N2, 4 with N3 and all 66 patients with a local recurrence with a N0 neck.

All, but one patient underwent total laryngectomy. Hundred and thirty-two patients underwent hemithyroidectomy.

Table 1 Patient, tumor and treatment characteristics associated with hypothyroidism

	TSH < 4.5	%	TSH > 4.5	%	Not tested	<i>P</i>
Sex						
Male	28	33	56	67	30	0.096
Female	2	12	14	88	7	
Age (years)						
<60	8	20	32	80	10	0.032
61–70	13	33	28	67	20	
>70	9	47	10	53	7	
Site						
Supraglottis	7	21	26	79	12	0.429
Glottis	19	37	32	63	13	
Subglottis	0		0		1	
Piriform sinus	3	27	8	73	8	
Hypopharynx	1	20	4	80	3	
Side						
Left	12	32	26	68	17	0.409
Median	0		4	100	16	
Right	18	31	40	69	4	
Stage						
T1	0		0		0	0.495
T2	0		0		3	
T3	4	20	16	80	8	
T4	11	35	20	65	9	
Recurrence						
N0	9	32	19	68	8	0.768
N1	4	36	7	64	4	
N2	2	22	7	78	7	
N3	0		3	100	1	
N4	0		0		0	
Recurrence	15	31	34	69	17	
Laryngectomy						
Total	30	30	70	70	36	1.00
Partial	0		0		1	
Hemithyroidectomy						
Yes	29	29	70	70	33	0.125
No	1	100	0		4	
Neck dissection						
Ipsilateral						
Yes	18	27	49	73	23	0.330
No	12	36	21	64	14	
Contralateral						
Yes	10	26	28	74	11	0.529
No	20	32	42	68	26	
Paratracheal dissection						
Ipsilateral						
Yes	30	30	70	70	37	

Table 1 continued

	TSH < 4.5	%	TSH > 4.5	%	Not tested	<i>P</i>
Contralateral						
Yes	17	35	32	65	21	0.315
No	13	26	38	74	16	
Radiotherapy						
Yes	28	29	68	71	32	0.373
No	2	50	2	50	5	
Chemotherapy						
Yes	0		2	100	1	0.350
No	30	31	68	69	36	

137 patients were included in our study of which 100 patients were tested

Ninety patients underwent a modified radical or selective neck dissection on the ipsilateral side and 49 patients a bilateral neck dissection. All 137 patients underwent a paratracheal lymph node dissection of the ipsilateral side and 70 (51%) bilaterally. All patients except 9 received radiotherapy; 67 patients received radiotherapy as primary treatment (3 patients combined with chemotherapy) and 61 patients received radiotherapy postoperatively.

Thirty-seven patients were not tested for hypothyroidism (30 men, 7 women) during follow-up. The prevalence of thyroid dysfunction was 70%. Thirty-six patients (36%) had clinical hypothyroidism and 34 patients (34%) had subclinical hypothyroidism. Thirty patients had normal laboratory results. Fourteen women (87.5%) and 56 men (66.7%) had hypothyroidism.

Table 2 shows the incidence of hypothyroidism after several combinations of paratracheal lymph node dissection (ipsilateral or bilateral) and neck dissection (ipsilateral or bilateral). In the PTLN dissection only group, consisting of 33 patients, 67% of the patients with unilateral PTLN dissection developed hypothyroidism versus 60% of the patients with a bilateral PTLN dissection. In the ipsilateral

Table 2 The incidence of hypothyroidism after several lymph node treatment modalities [paratracheal lymph node dissection (PTLN) and/or neck dissection (ND)]

ND		PTLN		TSH < 4.5	TSH > 4.5	HT (%)
Ipsi	Contra	Ipsi	Contra			
		X		6	12	67
		X	X	6	9	60
X		X		4	19	83
X		X	X	4	2	33
X	X	X		3	7	70
X	X	X	X	7	21	75

PTLN paratracheal lymph node dissection, ND modified radical neck dissection or selective neck dissection, HT hypothyroidism

neck dissection group, consisting of 29 patients, these figures were 83 and 33% and in the bilateral neck dissection group, consisting of 38 patients, 70 and 75%, respectively.

The differences within these three groups consisted thus in the bilateral paratracheal lymph node dissection. However, no statistical relevance in univariate and multivariate studies was found.

Comparison contingency tables were made with Pearsons χ^2 for nominal data which showed no statistical significance for paratracheal lymph node dissection or any other variable except for age ($P = 0.003$). Therefore, stepwise logistic regression analysis was not done.

We found 43 patients (33%) with hypoparathyroidism. Six of the patients tested for thyroid dysfunction were not tested for hypoparathyroidism (Table 3). Thirty-six patients developed hypoparathyroidism within 6 months after surgery, mostly within 7 days postoperatively, 1 patient more than 6 months after surgery and 6 patients more than 1 year after surgery. Of the patients with hypoparathyroidism, 35 patients were tested for thyroid function as well. Seventy-one percent had thyroid dysfunction (37% clinical hypothyroidism and 34% subclinical hypothyroidism). Patients with bilateral PTLN dissection did not develop more often hypoparathyroidism than patients with ipsilateral.

Discussion

In the present study the incidence of hypothyroidism after laryngectomy with PTLN dissection was 70%. The incidence of hypoparathyroidism was 33%. If it is considered that patients who are not tested on indication did not have hypo(para)thyroidism, the incidence of hypothyroidism and hypoparathyroidism would be 51% (70 out of 137) and 31% (43 out of 137), respectively. However, our cross-sectional study showed a high incidence of occult hypothyroidism [4]. On the other hand, if all patients who are not tested would have had hypothyroidism and hypoparathyroidism, these figures would be 78% (107 out of 137) and 58% (80 out of 137). Therefore, it can be anticipated that if all patients, who undergo total laryngectomy, hemithyroidectomy, paratracheal lymph node dissection and radiotherapy, were tested the incidences of hypothyroidism would be somewhere between 51 and 78%. Only in a prospective study in which all patients are routinely screened on hypo(para)thyroidism will provide more precise figures. In our previous cross-sectional study we found an incidence of hypothyroidism of 77% in patients after total laryngectomy, hemithyroidectomy and radiotherapy [4].

In our previous study no parathyroid dysfunction was found [4]. Geminiani et al. [7] found no parathyroid dysfunction following laryngeal surgery while Thorp et al. [15] found after surgery with or without radiotherapy an incidence

Table 3 The number of patients with hypoparathyroidism in relation with hypothyroidism and paratracheal neck dissection in months after surgery

Months	Hypoparathyroidism	PTLN dissection		Thyroid function			
		Ipsi (%)	Bilateral (%)	Normal	Clinical HT (%)	Subclinical HT (%)	Not tested
<6	36	18 (50)	18 (50)	7	12 (40)	12 (40)	5
>6	1		1	1			
>12	6	2 (30)	4 (70)	2	1 (20)		3

HT hypothyroidism, *normal* normal thyroid function

of 63–89%. Most patients in our present study developed hypoparathyroidism immediately postoperative. This could suggest vascular injury after hemithyroidectomy [14] or after PTLN dissection. Therefore, it is advised to determine serum calcium directly postoperatively frequently. Most patients with hypoparathyroidism suffer also from hypothyroidism. Therefore, all patients with hypothyroidism should be tested for hypothyroidism and the reverse.

In the present study almost all patients underwent at least laryngectomy, hemithyroidectomy, radiotherapy together with PTLN dissection. Therefore, it could be anticipated that there is no clear additional risk of PTLN dissection for the development of hypothyroidism. Moreover, we did not find an additional effect of a bilateral PTLN dissection on the development of hypothyroidism in the various treatment groups.

In the present study age was the only significant prognostic factor for the development of hypothyroidism. It is known that with aging more persons generally develop hypothyroidism. In a previous study hemithyroidectomy was one of the most important prognostic factors [4]. In the present study all patients underwent hemithyroidectomy.

There are no general guidelines in performing a PTLN dissection. Usually a PTLN dissection is performed in advanced laryngeal and hypopharyngeal carcinomas with subglottic involvement [8, 12]. It still remains to be identified in which patients PTLN dissection is really indicated [9]. Therefore, for clinical decision making and counseling it is important to know that even bilateral PTLN dissection does not contribute to the risk of development of hypothyroidism after treatment of laryngeal or hypopharyngeal cancer.

In conclusion, the incidence of (para)hypothyroidism after laryngectomy combined with hemithyroidectomy and PTLN dissection is high. PTLN dissection can be performed without additional risk of hypo(para)thyroidism.

Conflict of interest The authors declare that they have no conflict of interest.

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