Eur Arch Otorhinolaryngol (2014) 271:2267–2276
DOI 10.1007/s00405-013-2767-7

HEAD AND NECK

Risk factors for recurrent nerve palsy after thyroid surgery: a national study of patients treated at Danish departments of ENT Head and Neck Surgery

Christian Godballe · Anders Rørbæk Madsen · Christian Hjort Sørensen · Sten Schytte · Waldemar Trolle · Jens Helweg-Larsen · Lisa Barfoed · Larry Kristiansen · Vibeke Zederkof Sørensen · Grethe Samuelsen · Henrik Baymler Pedersen

Received: 12 July 2013 / Accepted: 7 October 2013 / Published online: 17 October 2013

Abstract Recurrent laryngeal nerve (RLN) injury is a well-known and serious complication to thyroid surgery. The objective was to estimate the frequency of post-thyroidectomy RLN palsy and to identify possible risk factors. Based on the Danish national thyroid surgery database, 6,859 patients treated with thyroid surgery from 1 January 2001 to the 31 December 2008 at the Danish departments of ENT-HNS were analyzed. Unilateral RLN palsy was found in 2.1 % and bilateral in 0.1 %. In benign histology, RLN palsies were registered in 1.3 %. Malignant histology and accordingly neck dissection were the most predominant risk factors with a relative risk (RR) of 5.4 and 5.8, respectively. In benign cases previous performed thyroid surgery had a RR of 10.4. High volume departments with more than 150 thyroid procedures per year seem to perform significantly better. Malignant histology, neck dissection and previous performed thyroid surgery are the strongest predictors for RLN palsy and patient information should be given accordingly. Incomplete resections should be reserved for isthmectomy only. Centralization of thyroid surgery in larger units might improve quality.

Keywords Thyroid surgery · Recurrent nerve palsy · Risk factors · National study

C. Godballe (✉) · A. R. Madsen
Department of ENT Head and Neck Surgery,
Odense University Hospital, 5000 Odense C, Denmark
e-mail: christian.godballe@rsyd.dk

A. R. Madsen
e-mail: arm@dadlnet.dk

C. H. Sørensen
Department of ENT Head and Neck Surgery,
Gentofte Hospital, Hellerup, Denmark
e-mail: chsor@geh.regionh.dk

S. Schytte
Department of ENT Head and Neck Surgery,
Aarhus University Hospital, Aarhus, Denmark
e-mail: sten.schytte@aarhus.rm.dk

W. Trolle
Department of ENT Head and Neck Surgery, Rigshospitalet,
Copenhagen University Hospital, Copenhagen, Denmark
e-mail: w.trolle@gmail.com

J. Helweg-Larsen
Department of ENT Head and Neck Surgery,
Vejle Hospital, Vejle, Denmark
e-mail: jens.peter.helweg-larsen@slb.regionsyddanmark.dk

L. Barfoed
Department of ENT Head and Neck Surgery,
Slagelse Hospital, Slagelse, Denmark
e-mail: lira@regionsjaelland.dk

L. Kristiansen
Department of ENT Head and Neck Surgery,
Viborg Hospital, Viborg, Denmark
e-mail: larry.kristiansen@viborg.rm.dk

V. Z. Sørensen
Department of ENT Head and Neck Surgery,
Køge Hospital, Køge, Denmark
e-mail: vzs@regionsjaelland.dk

G. Samuelsen
Department of ENT Head and Neck Surgery,
Hillerød Hospital, Hillerød, Denmark
e-mail: grethe.badsberg.samuelsen@regionh.dk

H. B. Pedersen
Department of ENT Head and Neck Surgery,
Aalborg University Hospital, Aalborg, Denmark
e-mail: hebp@rn.dk

Introduction

Recurrent laryngeal nerve (RLN) injury is a well-known and serious complication to thyroid surgery. It is related to significant morbidity and reduction in quality of life due to dysphonia, dysphagia and impaired control of breathing [1]. In bilateral cases, tracheotomy or other surgical intervention on the airway is in most cases necessary. Damage to the RLN may be caused by different mechanisms such as cutting, stretching, close dissection to the epineurium or heating by electro coagulation. The affection might be transient, often 4–6 weeks or permanent. When no function is detected 12 months postoperatively, permanent damage has to be assumed.

Before thyroid surgery, the patient must be precisely informed about the rationale for the procedure, the extent of surgery, the consequences and the risk of complications. Information about the risk of RLN injury is crucial and must not be omitted. Knowledge about risk factors and occurrence rate is, therefore, essential for the surgeon. The frequencies of permanent RLN injury vary a great deal in the literature and rates from 0 to 14 % have been reported [2]. Malignant diagnosis, intra-thoracic extension and re-operative procedure are factors which are known to influence the risk. But also the use of routine postoperative laryngeal examination seems to have a significant impact on reported RLN palsy frequencies. Results from Bergenfelz et al. [3] show a higher frequency of RLN injuries in patients who had routine postoperative laryngoscopy as compared to those without, indicating that the omitting of routine postoperative laryngoscopy may result in underestimation of the true rate. Most studies concerning postoperative RLN injury are retrospective and only a few prospective multicenter series have been published [3, 4].

In Denmark, more and more thyroid surgery is performed inside the specialty of ENT Head and Neck surgery (ENT-HNS). From 2001 to 2008, the percentage performed by ENT-HNS has increased from 41 to 72 %, and today almost all thyroid surgery in Denmark is performed by head and neck surgeons or by teams including such. To monitor surgical quality, a national database (THYKIR) was established in January 2001. The hope was to register all thyroid surgeries performed at the Danish departments of ENT-HNS. The database was started on initiative of The Danish Society for Head and Neck Surgery and is internet-based. Programming and maintenance are performed inside the organization of the Danish Head and Neck Cancer Group (DAHANCA). The database has been used for an earlier publication in 2009 in which we presented data regarding post-thyroidectomy hemorrhage showing a 4.2 % overall hemorrhage frequency with a wide variation among departments [5]. We have since improved data by contacting all departments concerning missing patients and follow-up resulting in a near-complete data set. The THYKIR database is unique in offering an unselected, consecutive and almost complete nationwide dataset from a whole specialty.

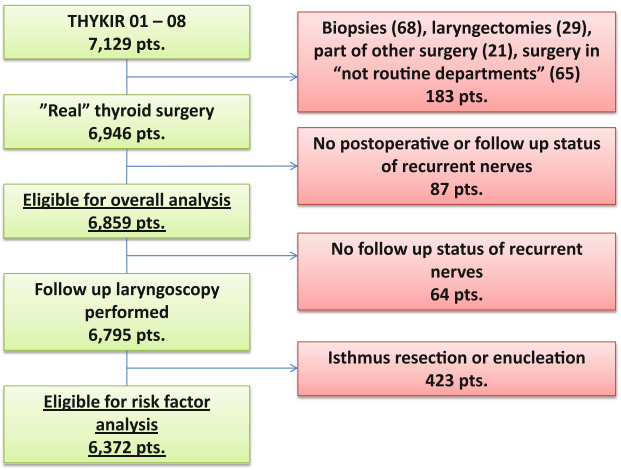

Fig. 1 Flow diagram showing in- and exclusion of patients for the analysis of recurrent nerve palsy after thyroid surgery in patients treated at the Danish departments of ENT-HNS from 2001 to 2008

The objective of the present study was to estimate the frequency of post-thyroidectomy RLN injury in an unselected national series of patients treated at departments of ENT-HNS and to identify possible risk factors which might improve patient information and treatment planning.

Materials and methods

This cohort study of patients treated with thyroid surgery is nationwide and represents all the twelve Danish departments of ENT-HNS doing thyroid surgery on a regular basis in the analyzed time interval. The registration is based on an online internet form enabling surgeons to report prospectively to the THYKIR database. Due to the daily work load, some departments have reported part of their data retrospectively. Patients treated from 1 January 2001 to the 31 December 2008 were included for analysis. To secure maximal completeness of patient material, a cross check with the National Patient Register (NPR) was performed. Thirty-eight patients from NPR were not registered in the THYKIR database resulting in a completeness of more than 99.5 %.

All data were analyzed as reported to the database except the variable for sub sternal/intra-thoracic involvement and the use of drainage, which has been adjusted because of changes in database structure during the registration period. Due to the nature of the database only one thyroid procedure per patient was registered. Figure 1 shows the inclusion and exclusion of patients for the study.

Patients were excluded if only biopsied or if the procedure was part of surgery not related to the thyroid or parathyroid gland (e.g., tracheotomy or laryngectomy).

This resulted in 6,946 patients of whom 87 (1.3 %) did not have a postoperative or follow-up laryngoscopy. Patient-, surgery- and tumor characteristics from these patients are shown in Table 1. Excluding these patients, the final group eligible for recurrent nerve palsy analysis consisted of 6,859 patients. The median age was 50 years (range 6–100 years) and the sex distribution was 5,428 women (79 %) and 1,431 men (21 %). All patients were hospitalized. Previous thyroid surgery (defined as all types of thyroid surgery, since no specification of the previous procedures was registered) had been performed in 553 patients (8 % of 6,826 registered cases). Patients were referred from departments of medical endocrinology (48 %), general practitioners (18 %), ENT-specialists in private sector (17 %), departments of internal medicine (8 %), departments of general surgery (5 %) and from other sources (5 %). Preoperative standard ENT examination (100 %) was performed including visualization of vocal cord motility (99 %). Also fine needle aspiration (75 %), ultrasound (85 %), scintigraphy (87 %), chest X-ray (27 %) and MR/CT-scan (9 %) were part of the preoperative evaluation. Blood sampling showed that 6,223 (92 %) were euthyroid, while 355 (5 %) had hyperthyroidism, and 158 (2 %) hypothyroidism. In 48 patients (1 %), the thyroid status was not examined and in 75 patients, no data were registered. Tables 2 and 3 show the indications for and the extent of performed thyroid surgery. In 444 patients (7 %), a neck dissection was performed. Use of the harmonic scalpel (Ultracision®) has been registered in the THYKIR database since 2005 and has been used in 638 of 3,115 registered cases (20 %). Magnifying spectacles were used in 17 % of procedures and surgical microscope in 19 %. Nerve monitoring and/or stimulator were used in 80 %. Intra-thoracic involvement was registered in 768 patients (12 %) based on imagining techniques and overall clinical evaluation, the rest of the patients were considered to have no intra-thoracic involvement. Visualization of the LRN(s) was considered a standard method in all surgical thyroid procedures when total lobectomy was part of the surgical strategy. Among 6.272 patients with data registered on the aspect visualization of the RLN (uni- or bilaterally) was done in 97.6 % of procedures. The histological distribution is shown in Table 4.

Three departments averaged more than 150 thyroid operations per year (high volume departments) and accounted for 61 % of the thyroid surgery performed, four departments performed more than 50 but not more than 150

Table 1 Comparison of selected patient-, treatment- and tumor-related characteristics for patients with and without laryngoscopy after thyroid surgery performed at Danish departments of ENT-HNS from 2001 to 2008

	Laryngoscopy performed ($N = 6.859$)[a]	Laryngoscopy not performed ($N = 87$)[a]	Significance
Median age	50 years	54 years	NS
Male sex	21 %	30 %	NS
Previous thyroid surgery	8 %	18 %	$P < 0.05$
Bilateral surgery	29 %	34 %	NS
Median weight of specimen	35 g	44 g	NS
Malignant histology	14 %	40 %	$P < 0.05$
Treated at high volume department (>150/year)	62 %	22 %	$P < 0.05$

NS not significant

[a] Postoperative or follow-up laryngoscopy

Table 2 Indications for thyroid surgery in 6,843 patients treated at Danish departments of ENT-HNS from 2001 to 2008

Indication	Number	Percentage
Risk of malignancy	2,244	33
Pressure symptoms	2,163	32
Neck tumor	1,365	20
Thyrotoxicosis	394	6
Thyroid cancer	355	5
Respiratory distress	160	2
Cosmetic	63	1
Parathyroid disease	49	1
Other	50	1

In 16 patients no information was available

Table 3 Extent of surgical procedure in 6,859 patients treated at Danish departments of ENT-HNS from 2001 to 2008

Surgical procedure	Number	Percentage
Lobectomy	4,365	63
Total thyroidectomy	1,501	22
Resection of isthmus	338	5
Lobectomy + resection	209	3
Subtotal thyroidectomy	164	2
Unilateral resection	97	2
Enucleation	91	1
Lobectomy + enucleation	55	1
Bilateral resection	39	1

Table 4 Histological distribution in 6,859 patients treated with thyroid surgery at Danish departments of ENT-HNS from 2001 to 2008

Histology	Number	Percentage
Multinodular colloid goiter	3,597	52
Adenoma	1,412	21
Benign cyst	336	5
Other benign histology	327	5
Hashimotos thyroiditis	151	2
Normal thyroid tissue	108	2
Papillary carcinoma	617	9
Follicular carcinoma	174	3
Medullary carcinoma	50	1
Undifferentiated carcinoma	44	1
Metastasis	13	0
Lymphoma	14	0
Other malignant histology	16	0

(intermediate volume departments) and accounted for 31 % and finally five departments did 50 procedures or less per year (low volume departments) and accounted for 8 %. Because of uncertainty about inclusion of neck dissection specimen in the reported weight this variable has only been used in analysis of procedures with benign histology.

Vocal cord mobility was evaluated by indirect laryngoscopy or fiber optic visualization. Any vocal cord impairment caused by the surgical procedure was registered in predefined forms. The answer possibilities were: "no impairment", "unilateral partial palsy", "unilateral complete palsy", "bilateral partial palsy", "partial palsy + complete palsy", "bilateral complete palsy", "not evaluated". Postoperative examination was typically performed the day after surgery and latest before discharge from department. Follow-up examination was defined as laryngoscopy performed after discharge from department and no fixed time intervals were used. The end point—"permanent RLN palsy" was defined as vocal cord palsy (partial, complete, unilateral or bilateral) caused by surgery and present at the last performed laryngoscopy. If no follow-up laryngoscopy was performed, the result of the postoperative laryngoscopy was used for the overall analysis. In the risk factor analyses, only patients with a follow-up laryngoscopy and a surgical procedure more extensive than enucleation and resection of the isthmus were included. The group eligible for this part of the study consisted of 6.372 patients (see also Fig. 1).

Data were statistically analyzed in the medical database and analysis program Medlog 2008-2. χ^2 statistics, Wilcoxon rank sum test, *t* test and multiple logistic regression analyses were used. Odds ratio (OR) was interpreted as the relative risk (RR).

Table 5 Results of postoperative and follow-up laryngoscopies in 6,859 patients treated with thyroid surgery at Danish departments of ENT-HNS from 2001 to 2008

Laryngeal evaluation	Number	Unilateral palsy (%)	Bilateral palsy (%)
Only postoperative laryngoscopy—no follow-up evaluation registered	64	9 (14.0)	0 (0.0)
Both postoperative laryngoscopy- and follow-up laryngeal evaluation registered	6,565	133 (2.0)	4 (0.1)
Only follow-up laryngoscopy registered	230	0 (0.0)	1 (0.4)
Total	6,859	142 (2.1)	5 (0.1)

Results

A total of 6,859 patients fulfilled the inclusion criteria. Follow-up vocal cord palsy specified according to laryngeal evaluation is presented in Table 5. According to our definition of permanent RLN palsy—also patients with no follow-up laryngoscopy and a RLN palsy detected at the postoperative laryngoscopy were considered events. Based on this we found permanent unilateral RLN palsy in 142 of 6,859 patients (2.1 %) and bilateral in 5 (0.1 %) resulting in 147 patients (2.1 %) with RLN palsy. Using nerves at risk (NAR) for calculation, the frequency of vocal cord palsy at last laryngeal examination was 1.7 % (8,827 NAR/152 RLN palsies).

The median follow-up time for the 142 patients with RLN palsy was 7 months (range 6–9 years). Fifty percent had a follow-up time below 6 months, 15 % between 7–12 months and 35 % more than 12 months.

Among 5,931 patients with benign histology, a total of 80 permanent RLN palsies were registered (1.3 %). In 76 patients (1.3 %), the affection was unilateral and in 4 patients (0.1 %), it was bilateral. In 6,565 patients with both postoperative- and follow-up laryngoscopy, a total of 172 transient RLN palsies were diagnosed (2.6 %).

To identify patient-, tumor- or treatment-related risk factors, univariate analysis of selected variables was performed. Only patients with a follow-up laryngoscopy and a surgical procedure more extensive than enucleation and resection of the isthmus were included for this part of the study. The results are presented in Table 6. In continuous variables (patient age at the time of surgery, bleeding during surgery and weight of surgical specimens), the median value was used as cut point in a dichotomizing process.

In univariate analysis of all patients eligible for risk factor analysis ($N = 6,372$), age, previous performed thyroid surgery, sub sternal involvement, charge of surgeon

Table 6 Univariate analyses of selected variables concerning risk of recurrent laryngeal nerve (RLN) palsy in 6,372 patients treated with thyroid surgery at Danish departments of ENT-HNS from 2001 to 2008

Variable	Dichotomization	Observations	Events	Percentage	*P* value	Odds ratio
Age	≥50 years	3,169	93	2.9	<0.05	2.1
	<50 years	3,203	44	1.4		
Gender	Male	1,323	34	2.6	NS	1.3
	Female	5,049	103	2.0		
Previous thyroid surgery	Yes	516	19	3.7	<0.05	1.9
	No	5,825	116	2.0		
Previous radioiodine treatment	Yes	280	7	2.5	NS	1.2
	No	5,991	122	2.0		
Hyperthyroidism before surgery	Yes	346	3	0.9	NS	0.4
	No	5,921	129	2.2		
Sub sternal involvement[a]	Yes	748	28	3.7	<0.05	1.9
	No	5,624	109	1.9		
Charge of surgeon	Consultant	4,947	117	2.4	<0.05	1.8
	Other charges	1,414	19	1.3		
Extent of surgery	Bilateral	1,905	80	4.2	<0.05	3.3
	Unilateral	4,467	57	1.3		
Bleeding during surgery	≥50 ml	3,748	102	2.7	<0.05	3.0
	<50 ml	2,163	20	0.9		
Intraoperative nerve-monitoring/stimulation	Used	5,254	116	2.2	NS	1.3
	Not used	1,038	17	1.6		
Neck dissection performed	Yes	431	37	8.6	<0.05	5.2
	No	5,907	98	1.7		
Magnifying spectacles or microscope used	Used	2,333	48	2.1	NS	0.8
	Not used	3,886	85	2.2		
Histology	Malignant	892	62	7.0	<0.05	5.1
	Benign	5,480	75	1.4		
Volume in department	≤150/year	2,678	77	2.9	<0.05	1.7
	>150/year	3,935	67	1.7		
Time interval for surgery	2001–2004	2,680	48	1.8	NS	1.3
	2005–2008	3,692	89	2.4		

Only patients with a follow-up laryngoscopy and a surgical procedure more extensive than enucleation and resection of the isthmus were included for risk factor analysis

[a] Because of the structure of this variable "no" includes also patients with no registered information

(consultant versus other charges), extent of surgery (unilateral versus bilateral procedure), amount of bleeding during surgery, performed neck dissection, histology (benign versus malignant) and departmental volume of thyroid procedures were found to have significant influence on the frequency of RLN palsy. These variables were analyzed in a logistic regression model using a step-down procedure. The result is shown in Table 7.

Malignant histology and accordingly neck dissection were the most predominant risk factors with a relative risk of RLN palsy of 5.4 and 5.8, respectively. But also sub sternal involvement, extent of surgery, patient age, previous thyroid surgery and departmental volume of thyroid surgery procedures showed significant influence on the risk of surgically-induced RLN palsy.

To eliminate the very high influence from malignant histology, similar analyses were performed for patients with benign histology ($N = 5{,}480$). The results of univariate analysis are shown in Table 8 and the final multivariate model in Table 9. In this set-up, previous performed thyroid surgery turned out to be a very strong risk factor with a RR of 10.4. Large specimen weight, more extensive surgery and treatment in a low volume department significantly increased the risk of RLN palsy.

The influence of intraoperative nerve monitoring (IONM) on the frequency of RLN paralysis was tested in

Table 7 Resulting model from logistic regression analysis of 5,859 patients treated with thyroid surgery at Danish departments of ENT-HNS from 2001 to 2008 with all information available

Variable	Relative risk (RR)	Confidence interval RR	*P* value
Neck dissection performed	5.8	[4.0; 8.3]	<0.0001
Malignant histology	5.4	[3.8; 7.6]	<0.0001
Bilateral thyroid surgery performed	2.4	[1.3; 2.7]	<0.0001
Sub sternal involvement	1.8	[1.5; 3.2]	0.0016
Patient age ≥50 years	1.7	[1.3; 2.3]	0.0003
Low volume department (≤150/year)	1.6	[1.2; 2.1]	0.0020
Previous thyroid surgery performed	1.6	[1.1; 2.3]	0.0228

a unilateral set-up of +/−IONM in surgery of patients with malignant histology, weight of specimen above the median of 35 g, bilateral surgery, and in patients with previous thyroid surgery. In none of the analysis, the use of IONM reduced the frequency of RLN palsies significantly.

To see if the use of IONM influenced the operation time (from incision to the last suture), comparable groups were established (Tables 10, 11). A significant longer operation time for both lobectomy and total thyroidectomy was found when IONM was used.

Use of harmonic scalpel was only registered in a minor part of the study period (2005–2008) and was, therefore, not included in the overall analyses. However, a separate analysis did not show any significant influence on the frequency of RLN palsy.

Table 8 Univariate analyses of selected variables concerning risk of recurrent laryngeal nerve palsy in 5,480 patients with benign histology having thyroid surgery at Danish departments of ENT-HNS from 2001 to 2008

Variable	Dichotomization	Observations	Events	Percentage	*P* value	Odds ratio
Age	≥50 years	2,703	47	1.7	<0.05	1.7
	<50 years	2,777	28	1.0		
Gender	Male	1,059	8	0.8	NS	0.5
	Female	4,421	67	1.5		
Previous thyroid surgery	Yes	410	15	3.7	<0.05	3.1
	No	5,044	59	1.2		
Previous radioiodine treatment	Yes	257	5	2.0	NS	1.5
	No	5,149	66	1.3		
Hyperthyroidism before surgery	Yes	318	1	0.3	NS	0.2
	No	5,084	72	1.4		
Sub sternal involvement[a]	Yes	652	13	2.0	NS	1.5
	No	4,396	59	1.3		
Charge of surgeon	Consultant	4,166	62	1.5	NS	1.5
	Other charges	1,304	13	1.0		
Extent of surgery	Bilateral	1,423	30	2.1	<0.05	1.9
	Unilateral	4,057	45	1.1		
Bleeding during surgery	≥50 ml	3,143	51	1.6	<0.05	1.9
	<50 ml	1,985	17	0.9		
Intraoperative nerve-monitoring/stimulation	Used	4,527	59	1.3	NS	0.9
	Not used	893	13	1.5		
Magnifying spectacles or microscope used	Used	1,934	30	1.6	NS	1.3
	Not used	3,421	41	1.2		
High weight of surgical thyroid specimen	≥35 g	2,562	43	1.7	<0.05	1.9
	<35 g	2,497	22	0.9		
Volume department	≤150/year	2,038	39	1.9	<0.05	1.8
	>150/year	3,442	36	1.1		
Time interval for surgery	2001–2004	2,294	23	1.0	NS	0.6
	2005–2008	3,186	52	1.6		

Only patients with a follow-up laryngoscopy and a surgical procedure more extensive than enucleation and resection of the isthmus were included for risk factor analysis

[a] Because of the structure of this variable "no" includes also patients with no registered information

Table 9 Resulting model from logistic regression analysis of 4,921 patients treated with thyroid surgery for benign lesions at Danish departments of ENT-HNS from 2001 to 2008 with all information available

Variable	Relative risk (RR)	Confidence interval RR	*P* value
Previous thyroid surgery performed	10.4	[6.8; 15.9]	<0.0001
Weight of specimen ≥35 g	1.7	[1.1; 2.5]	0.0257
Bilateral thyroid surgery performed	1.6	[1.0; 2.5]	0.0294
Low volume department (≤150/year)	1.6	[1.0; 2.3]	0.0358

Table 10 Operation time (from incision to last suture) in lobectomies with benign histology from patients treated at Danish departments of ENT-HNS from 2001 to 2008

	Mean	SE	Significance
Operation time IONM not used ($N = 686$)	82 min	1.0	$P < 0.05$
Operation time IONM used ($N = 3{,}058$)	86 min	0.7	
Bleeding during surgery IONM not used ($N = 624$)	77 ml	5.2	NS
Bleeding during surgery IONM used ($N = 3{,}009$)	69 ml	2.4	
Specimen weight IONM not used ($N = 624$)	44 g	2.2	NS
Specimen weight IONM used ($N = 2{,}977$)	48 g	1.0	

Table 11 Operation time (from incision to last suture) in total thyroidectomies with benign histology from patients treated at Danish departments of ENT-HNS from 2001 to 2008

	Mean	SE	Significance
Operation time IONM not used ($N = 108$)	111 min	3.6	$P < 0.05$
Operation time IONM used ($N = 886$)	123 min	1.5	
Bleeding during surgery IONM not used ($N = 104$)	172 ml	21.5	NS
Bleeding during surgery IONM used ($N = 882$)	205 ml	9.9	
Specimen weight IONM not used ($N = 105$)	106 g	10.3	NS
Specimen weight IONM used ($N = 860$)	126 g	4.0	

Discussion

Several studies have addressed RLN palsy after thyroid surgery. However, most of these are retrospective single center series and only two prospective multicenter studies dealing with risk factors for RLN palsy after thyroidectomy have been identified in the literature [3, 4]. Thomusch et al. [4] published a series of 7,266 surgically-treated patients with benign goiter from 45 German hospitals, and Bergenfelz et al. [3] reported 3,660 patients from The Scandinavian Register for Thyroid and Parathyroid Surgery. The presumably most comprehensive study is a retrospective observational analysis performed by Rosato et al. [6] including 14,934 patients. In this study, a number of Italian departments provided data from 50 unselected thyroid surgery patients each year in a 5-year period for centralized analysis and follow-up. Comparable larger studies are presented in Table 12. In Denmark, more and more thyroid surgery is performed by ENT-HNS and in 2010 the Danish National Board of Health declared that: "To secure future education and competency it must be considered to concentrate the function (thyroid surgery) in one specialty—together with other benign and malignant neck surgery". Since then almost all thyroid surgeries has been performed by ENT-HNS or in constructive collaborations between departments of general surgery and ENT-HNS. The present study is based on a prospectively registered and unselected cohort of patients having thyroid surgery at the Danish departments of ENT-HNS from 2001 to 2008. A very high completeness of the series on the patient level (close to 100 %) has been confirmed by cross checking with The Danish National Patient Registry as described in a previous publication [5]. This study represents, to our knowledge, the first nationwide evaluation of risk factors for RLN palsy after thyroidectomy performed inside the specialty of ENT-HNS.

Knowledge about the risk of RLN palsy is important for the preoperative information of patients. As earlier mentioned, frequencies between 0 and 14 % have been reported in the literature [2]. However, prospective multicenter studies including a large number of patients have shown that the risk seems to be in the lower part of the cited interval. Thomusch et al. [4] analyzed patients with benign histology and found transient and permanent RLN palsy rates of 2.1 and 1.1 %, respectively. In an analysis of both benign and malignant cases The Scandinavian Register for Thyroid and Parathyroid Surgery estimated the frequency of permanent LRN palsy to be between 0.9 and 1.7 % [3]. Rosato et al. [6] reported transient RLN lesions in 3.4 % of all patients and a frequency of unilateral definitive lesions of 1.0 % and a bilateral of 0.4 %. Our results seem comparable. We found an overall frequency of 2.6 % transient cases and 2.1 % unilateral and 0.1 % bilateral permanent lesions. Considering only patients with a benign histology, we found 1.3 % unilateral and 0.1 % bilateral permanent RLN lesions. So, it might seem fair to inform the patients

Table 12 Comparable larger studies of thyroid surgery complications listed by size

Author, publication, data collection.	Patients	Design	Recurrent laryngeal nerve palsy (RLN) palsy frequency	Significant risk factors for RLNP by multiple logistic regression (odds ratio)	Remarks, laryngoscopy practice
Rosato et al. [6] World J Surg 2004 Data: 1995–2000	14,934	Retrospective cohort, multicenter, Italy	Transient 2.0 % Permanent 1.0 % Bilateral 0.4 %	–	42 Italian endocrine surgery units Postoperative optical fiber laryngoscopy Assessment in "all" patients
Thomusch et al. [4] World J Surg 2000 Data: 1998	7,617	Prospective cohort, multicenter, 45 German hospitals	Transient 2.1 % NAR Permanent 1.1 % NAR	Extent of resection (2.1) Recurrent goiter (3.4) Patient gender (1.4) Hospital volume (1.3)	Benign goiter only Pre- and post-operative laryngoscopy in "all" patients
Godballe et al. Present study Data: 2001–2008	6,859	Prospective cohort, nationwide, Denmark	Transient 2.6 % (2.0 % NAR) Permanent 2.1 % (1.7 % NAR). Bilateral 0.1 %.	Neck dissection (5.8) Malignancy (5.4) Bilateral surgery (2.4) Sub sternal involvement (1.8) Patient age (1.7) Low volume department (1.6) Previous thyroid surgery (1.6)	Postoperative laryngoscopy in 99 % Median follow-up 7 months Data completeness 99.5 % compared to National Patient Registry
Bergenfelz et al. [3] Langenbecks Arch Surg, 2008 Data: 2004–2006	3,660	Prospective cohort, multicenter, Scandinavia	Transient 3.9 % (3.0 % NAR) After 6 Months 0.97 %. Bilateral 0.2 %	Older age (1.02) Sub sternal goiter (1.8) Thyrotoxicosis (1.9) Postop. laryngoscopy (1.9)	26 Scandinavian departments Postoperative laryngoscopy was not performed in 2,054 patients (56.1 %)
Hayward et al. [14] ANZ J Surg 2012 Data: 2007–2011	2,422	Retrospective cohort, single institution, Australia	Transient 1.25 % Permanent 0.16 %	–	Fiber optic evaluation in "the majority of cases"

NAR nerves at risk

that the overall risk for a permanent RLN lesion after thyroid surgery is somewhere between 1 and 3 %.

However, the risk might differ among patients. Our study shows that malignant histology and performed neck dissection are two very strong risk factors for RLN lesions with RR of 5.4 and 5.8, respectively. And in fact patients with malignant histology had RLN palsies in 7 % and if a neck dissection was performed the frequency was as high as 9 %. Therefore the cancer patients naturally have to be advised in another way than patients with small benign lesions.

Considering patients with benign histology, our results seem in accordance with other prospective multicenter studies which found recurrent goiter, extension of resection and patient age as risk factor for RLN lesions [3, 4]. In our multivariate regression analysis, the factor "previous thyroid surgery performed" was the absolutely strongest with a RR of 10.4. The frequency of RLN lesions in this group was 3.7 %. This result emphasizes the importance of sufficient surgery already at the first procedure. In our opinion, the number of partial resections must be reduced to an absolute minimum and perhaps it should be reserved for isthmectomy alone.

Since the amount of thyroid surgery has increased at the Danish departments of ENT-HNS during the study period, the possibility for a learning curve has to be considered. Therefore, an analysis of RLN palsies according to time interval was performed. However, no difference between the two time intervals was found indicating that no larger change had occurred.

In this study, we have only focused on damage to the RLN. However, voice impairment after thyroid surgery

may also come from other sources such as damage to the external branch of the superior laryngeal nerve, injury to laryngeal external muscles and prelaryngeal strap muscles or adhesions to these muscles [7–9]. The vocal cord mobility will in such cases be normal, but the patients might have dysphonia which will be a catastrophe for the professional singer. Therefore, introduction of objective voice analysis should be considered as a standard examination before and after thyroid and parathyroid surgery at least for professional voice users.

No fixed time limits have been used in the follow-up of patients in the THYKIR database. Therefore, we have not been able to give an exact six-month or one-year follow-up status, which might be considered a weakness of the study. From the very start of the database, we accepted the differences in follow-up strategy among participating departments and instead of fixed dates we have used the actual/precise date at which the patients met for control. The consequence has been that we have some very short follow-up intervals for some of the patients with RLN palsies. In some cases we only have the postoperative laryngoscopy and in other cases the follow-up time is significantly below 6 months. Therefore, it is possible that a proportion of the patients who have been characterized as permanent RLN palsies, in fact, might be transient. So, the presented complication frequencies might very well be overestimated. However, we assume that the distribution in length of follow-up time is without bias and, therefore, we consider the statistical calculations reliable.

The issue regarding frequency of complications and the surgeons experience has been addressed by several authors. Our results are in agreement with other studies [2, 4, 10, 11] showing that the charge of the surgeon is without influence on the frequency of permanent RLN lesions, indicating that trainees very well can do thyroid surgery if just the supervision is sufficient. However, Sosa et al. showed in their study from Baltimore, Maryland that the experience of the surgeon is important and that complication rates to a higher degree were determined by surgeon experience than hospital volume. This is presumably correct. But there might be some correlation between experience of the surgeons and the hospital volume. Evaluating benign cases, our multivariate regression analysis showed an increased rate of RLN lesions (RR 1.6), if surgery was performed in a low volume department. Another aspect is that thyroid surgeons do not start as high volume experts—they have to start somewhere. In our opinion, it is, therefore, very important, that surgery—and especially surgery of delicate structures as the RLN—is performed by teams including experienced surgeons as well as trainees, and if departmental volume is sparse it is important that the surgeons find the time to do the surgery together for sharing of experience. Identification of the individual surgeon has not been possible in the THYKIR database until now. Therefore, we have not been able to add information concerning experience on the surgeon level. Recently an identification variable has been added and such analysis will be possible in the future.

Iodine fortification of salt was made mandatory in Denmark in 2000 because of mild-to-moderate iodine deficiency. In a nationwide Danish study of 26,456 operations and 39,149 iodine treatments of benign thyroid disorders made from 1990 to 2007, Cerqueira et al. [12] found a slight fall in radioiodine treatments after iodization was fully introduced, while surgery rates remained almost constant. We, therefore, find that our study can be compared to countries with iodine deficiency, as well as countries without.

In our multivariate regression analyses, we find low departmental volume to be a significant risk factor and the results are in favor of continuing the already started centralization process which for the time being is going on in Denmark. Also continued surveillance of the surgical quality seems important.

IONM was used in 79 % of all surgical procedures. Overall univariate analyses did not show any significant reduction in RLN palsies by the use of IONM. Neither did subgroup analyses of patients with malignant histology, high weight of specimen, bilateral surgery nor previous thyroid surgery. The results are in line with other studies [13]. Dralle et al. [14] have done a systematic literature review and point out that IONM has a nonsignificant effect on RLN palsy rate when compared with the very low rate observed when visual identification is used alone. In the Danish departments of ENT-HNS, IONM has developed to be part of the standard equipment for thyroid surgery. Our study does not support this routine use of IONM and the value and cost-effectiveness of routine use have been discussed by other authors [15, 16]. Further, we cannot demonstrate any decrease in operation time using IONM. In fact it was found that both benign lobectomy and total thyroidectomy were performed faster when IONM was not used. We have no obvious explanation for this—except the possibility that the procedures without IONM were performed by the more experienced surgeons. However, it is still our opinion that IONM is a good tool for identifying the RLN and we find it a valuable instrument in the teaching situation. Also IONM adds a functional aspect enabling the thyroid surgeon to choose only lobectomy in case of loss of signal on one side to avoid the risk of bilateral palsy and subsequent postoperative respiratory distress [17]. Also, preservation of the external branch the superior laryngeal nerve is important and is facilitated by the use of IONM [18]. Furthermore surgeons are increasingly forced to consider medicolegal reasons for using IONM routinely [19]. Therefore, we find it justified to use IONM in routine as well as complicated thyroid surgery.

Conclusion

Malignant histology, neck dissection and previous performed thyroid surgery are the strongest predictors for RLN palsy and patient information should be given accordingly. Incomplete resections should be reserved for isthmectomy only. Centralization of thyroid surgery in larger units might improve quality.

Acknowledgments We thank all colleagues who have participated in the establishment of the actual dataset.

According to Danish law permission to collect patient data has been approved by the Danish Data Protection Agency (journal number 2000-41-0010). The local ethical committee has been informed about the project.

Conflict of interest The authors have no conflicts of interest.

References

1. Zumtobel M, End A, Bigenzahn W, Klepetko W, Schneider B (2006) Reduced quality of life in patients with unilateral vocal cord paralysis after thoracic surgery. Chirurg 77(6):518–522. doi:10.1007/s00104-006-1156-9
2. Sosa JA, Bowman HM, Tielsch JM, Powe NR, Gordon TA, Udelsman R (1998) The importance of surgeon experience for clinical and economic outcomes from thyroidectomy. Ann Surg 228(3):320–330
3. Bergenfelz A, Jansson S, Kristoffersson A, Martensson H, Reihner E, Wallin G, Lausen I (2008) Complications to thyroid surgery: results as reported in a database from a multicenter audit comprising 3,660 patients. Langenbecks Arch Surg 393(5):667–673
4. Thomusch O, Machens A, Sekulla C, Ukkat J, Lippert H, Gastinger I, Dralle H (2000) Multivariate analysis of risk factors for postoperative complications in benign goiter surgery: prospective multicenter study in Germany. World J Surg 24(11):1335–1341
5. Godballe C, Madsen AR, Pedersen HB, Sorensen CH, Pedersen U, Frisch T, Helweg-Larsen J, Barfoed L, Illum P, Monsted JE, Becker B, Nielsen T (2009) Post-thyroidectomy hemorrhage: a national study of patients treated at the Danish departments of ENT Head and Neck Surgery. Eur Arch Otorhinolaryngol: Off J Eur Fed Otorhinolaryngol Soc 266(12):1945–1952. doi:10.1007/s00405-009-0949-0
6. Rosato L, Avenia N, Bernante P, De PM, Gulino G, Nasi PG, Pelizzo MR, Pezzullo L (2004) Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years. World J Surg 28(3):271–276
7. Aluffi P, Policarpo M, Cherovac C, Olina M, Dosdegani R, Pia F (2001) Post-thyroidectomy superior laryngeal nerve injury. Eur Arch Otorhinolaryngol: Off J Eur Fed Otorhinolaryngol Soc 258(9):451–454
8. Bellantone R, Boscherini M, Lombardi CP, Bossola M, Rubino F, De Crea C, Alesina P, Traini E, Cozza T, D'Alatri L (2001) Is the identification of the external branch of the superior laryngeal nerve mandatory in thyroid operation? Results of a prospective randomized study. Surgery 130(6):1055–1059. doi:10.1067/msy.2001.118375
9. Musholt TJ, Musholt PB, Garm J, Napiontek U, Keilmann A (2006) Changes of the speaking and singing voice after thyroid or parathyroid surgery. Surgery 140(6):978–988. doi:10.1016/j.surg.2006.07.041 (discussion 988–979)
10. Reeve TS, Curtin A, Fingleton L, Kennedy P, Mackie W, Porter T, Simons D, Townend D, Delbridge L (1994) Can total thyroidectomy be performed as safely by general surgeons in provincial centers as by surgeons in specialized endocrine surgical units? Making the case for surgical training. Arch Surg 129(8):834–836
11. Shindo ML, Sinha UK, Rice DH (1995) Safety of thyroidectomy in residency: a review of 186 consecutive cases. Laryngoscope 105(11):1173–1175. doi:10.1288/00005537-199511000-00006
12. Cerqueira C, Knudsen N, Ovesen L, Laurberg P, Perrild H, Rasmussen LB, Jorgensen T (2010) Nationwide trends in surgery and radioiodine treatment for benign thyroid disease during iodization of salt. Eur J Endocrinol/Eur Fed Endocr Soc 162(4):755–762. doi:10.1530/EJE-09-0965
13. Lee C, Stack BC Jr (2011) Intraoperative neuromonitoring during thyroidectomy. Expert Rev Anticancer Ther 11(9):1417–1427. doi:10.1586/era.11.97
14. Dralle H, Sekulla C, Lorenz K, Brauckhoff M, Machens A (2008) Intraoperative monitoring of the recurrent laryngeal nerve in thyroid surgery. World J Surg 32(7):1358–1366
15. Sanabria A, Silver CE, Suarez C, Shaha A, Khafif A, Owen RP, Rinaldo A, Ferlito A (2013) Neuromonitoring of the laryngeal nerves in thyroid surgery: a critical appraisal of the literature. Eur Arch Otorhinolaryngol: Off J Eur Fed Otorhinolaryngol Soc 270(9):2383–2395. doi:10.1007/s00405-013-2558-1
16. Randolph GW, Dralle H, Abdullah H, Barczynski M, Bellantone R, Brauckhoff M, Carnaille B, Cherenko S, Chiang FY, Dionigi G, Finck C, Hartl D, Kamani D, Lorenz K, Miccolli P, Mihai R, Miyauchi A, Orloff L, Perrier N, Poveda MD, Romanchishen A, Serpell J, Sitges-Serra A, Sloan T, Van Slycke S, Snyder S, Takami H, Volpi E, Woodson G, International Intraoperative Monitoring Study G (2011) Electrophysiologic recurrent laryngeal nerve monitoring during thyroid and parathyroid surgery: international standards guideline statement. Laryngoscope 121(Suppl 1):S1–S16. doi:10.1002/lary.21119
17. Sadowski SM, Soardo P, Leuchter I, Robert JH, Triponez F (2013) Systematic use of recurrent laryngeal nerve neuromonitoring changes the operative strategy in planned bilateral thyroidectomy. Thyroid 23(3):329–333. doi:10.1089/thy.2012.0368
18. Barczynski M, Randolph GW, Cernea CR, Dralle H, Dionigi G, Alesina PF, Mihai R, Finck C, Lombardi D, Hartl DM, Miyauchi A, Serpell J, Snyder S, Volpi E, Woodson G, Kraimps JL, Hisham AN, International Neural Monitoring Study G (2013) External branch of the superior laryngeal nerve monitoring during thyroid and parathyroid surgery: international neural monitoring study group standards guideline statement. Laryngoscope 123 Suppl 4:S1–S14. doi:10.1002/lary.24301
19. Dralle H, Lorenz K, Machens A (2012) Verdicts on malpractice claims after thyroid surgery: emerging trends and future directions. Head Neck 34(11):1591–1596. doi:10.1002/hed.21970