Thyroid Surgery

Contact endoscopy for identifying the parathyroid glands during thyroidectomy

Endoscopia da contatto per l'identificazione delle paratiroidi nel corso di tiroidectomia

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SUMMARY

Aim of this study was to analyse contact endoscopy as an auxiliary method for identifying parathyroid glands during thyroid surgery and to identify other variables that may interfere with this correlation. Overall, 125 patients underwent thyroid surgery between January 2004 and February 2006. The variables analysed were: the total duration of surgery; time taken to locate and identify parathyroid glands; improvement in identifying these; numbers of parathyroid glands located by the surgeon and confirmed by contact endoscopy; histopathological diagnosis; presence of thyroiditis; thyroid weight; number of parathyroid glands left in thyroid specimens; and number of parathyroid gland autotransplantations. A total of 331 parathyroid glands were observed by the surgeon. However, 282 glands were identified by contact endoscopy. Nine parathyroid glands (7.2%) were observed together with thyroid specimens (*Kappa* = 0.534). The longer the total duration of surgery ($p = 0.03$) and time taken to locate and identify ($p = 0.00$) the parathyroid glands by contact endoscopy, the lower the observed agreement. The second year of performing contact endoscopy led to better agreement between the results ($p = 0.02$). In conclusion, contact endoscopy is an efficient auxiliary method for identifying parathyroid glands during thyroid surgery. During the period studied, association between total duration of surgery and time taken to locate and identify parathyroid glands was statistically significant**.**

KEY WORDS: Parathyroid glands • Thyroid gland • Thyroidectomy • Contact Endoscopy

RIASSUNTO

Scopo di questo studio è stata la valutazione dell'endoscopia da contatto come tecnica ausiliaria nell'identificazione delle paratiroidi nel corso di interventi di tiroidectomia e la ricerca di altre variabili che possano interferire con questa correlazione. Un totale di 125 pazienti sono stati sottoposti a chirurgia tiroidea tra gennaio 2004 e febbraio 2006. Le variabili prese in considerazione sono state: la durata totale dell'intervento; il tempo necessario per l'identificazione delle paratiroidi; il miglioramento nella loro identificazione; il numero di paratiroidi localizzate dal chirurgo e confermate dall'endoscopia da contatto; la diagnosi istopatologica; la presenza di tiroidite; il peso della tiroide; il numero di paratiroidi identificate nel pezzo operatorio e il numero di paratiroidi auto-trapiantate. Un totale di 331 paratiroidi sono state identificate dal chirurgo, di cui 282 identificate mediante endoscopia da contatto. Sono state riscontrate 9 paratiroidi (7,2%) nel pezzo operatorio (Kappa = 0,534). Più lunga è stata la durata della chirurgia ($p = 0,03$) e il tempo necessario per la localizzazione delle paratiroidi mediante endoscopia da contatto ($p = 0,00$), più bassa è stata la concordanza osservata tra i due dati. Nel secondo anno di utilizzazione dell'endoscopia da contatto si è osservata una migliore concordanza tra i risultati. In conclusione, l'endoscopia da contatto risulta essere una metodica valida per l'identificazione delle paratiroidi durante la chirurgia della tiroide. Nel periodo studiato, è risultata statisticamente significativa l'associazione tra la durata totale della chirurgia e il tempo necessario per l'identificazione delle paratiroidi.

PAROLE CHIAVE: *Paratiroidi • Tiroide • Tiroidectomia • Endoscopia da contatto*

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Introduction

It is frequently observed that, during thyroidectomy, it is difficult to differentiate the parathyroid glands (PGs) from other tissues adjacent to the thyroid gland [1], thus leading to accidental removal of PGs or interruption of their vascularization [2-4]. Correct routine identification of PGs, by means of careful dissection, minimizes the risk of trauma in these glands, and may lead to reduced risk of hypoparathyroidism [5-9]. Any tissue suspected to be PG that is found in the capsular region of the thyroid, without a clear vascular pedicle, must be promptly removed by dissection and, if it is confirmed to be PG, in the frozen section biopsy, then this tissue must immediately be autotransplanted [10].

The incidence of hypocalcaemia following thyroidectomy is extremely variable in the literature and depends on several factors, such as the extent and type of disease in the thyroid gland, type of thyroidectomy, technique, concomitant cervical dissection, re-operation, asymptomatic or symptomatic hypocalcaemia, temporary or permanent hypocalcaemia, investigation of hypocalcaemia during the post-operative period, interval between the surgical procedure and laboratory investigation of calcaemia, and variations in the proportions of subjects in the initial cohort study [11-13]. Correct identification of PGs is essential for their preservation.

Contact Endoscopy (CE) is a relatively recent technique in Laryngology [14 15]. It enables very precise cytological and histological characterisation of the covering mucosa of the larynx, and particularly for the vocal folds and their blood vessels. It also allows observation of several pathological conditions, such as squamous cell carcinoma, and lesion mapping with more precise assessment of their margins [14]. CE has the advantage of enabling an *in vivo* histological study to be made, without the need for tissue removal.

The aim of this study was to analyse CE as an auxiliary method for identifying PGs during thyroid surgery and to identify other variables that may interfere with this correlation.

Methods

The study was started following approval from the Research Ethics Committee of the Medical School of Universidade Metropolitana de Santos, with a favourable report from the Ethics Committee for Research Projects of Hospital das Clínicas, University of São Paulo Medical School. The inclusion criterion was that the patients needed to have an indication for thyroidectomy. The exclusion criteria were: previous radiotherapy in the cervical region; patients under the age of 18 years; and haematoma or bleeding during surgery.

Overall, 125 patients underwent thyroid surgery, between January 2004 and February 2006, at the Head and Neck Services of Hospital Ana Costa de Santos and Santa Casa da Misericórdia de Santos. The age range of patients was 19-81 years (median: 45) and 13/125 (10.4%) were male. There were 67 lobectomies with isthmusectomies (53.6%), 51 total thyroidectomies (40.8%) and 7 total thyroidectomy with neck dissection (5.6%). Of these patients, 67 underwent lobectomy with isthmusectomy (53.6%), 51 total thyroidectomy (40.8%) and 7 total thyroidectomy with neck dissection (5.6%).

The histo-pathological diagnoses from the surgical specimens showed: goitre in 58 patients (46.4%), adenoma in 31 (24.8%), papillary cancer in 28 (22.4%) and other disorders in 8 (6.4%). The routine histo-pathological examinations diagnosed the presence of concomitant thyroiditis in 40 specimens (32%).

The routine histo-pathological examination showed PGs in 9 surgical specimens (7.2%), being extra-thyroidal in 5 cases (4%), sub-capsular in 3 (2.4%) and intra-thyroidal in 1 (0.8). Of these 9 cases, 7 had undergone total thyroidectomy and 2 had undergone lobectomy.

The weight of the specimens from surgical hemithyroidectomy procedures ranged from 6 g to 120 g (mean, 29.5 g). In cases of total thyroidectomy, the weight ranged from 8 to 290 g (mean, 57 g).

The total duration of surgery ranged from 50 to 160 minutes (mean, 75 min) for all the procedures assessed together. The duration of lobectomy varied between 50 and 85 minutes (mean, 72 min), for total thyroidectomy, it varied between 60 and 110 minutes (mean, 81 min) and for total thyroidectomy, associated with cervical dissection, it varied between 100 and 160 minutes (mean, 128 min).

The variables analysed were: the total duration of surgery, time taken to locate and identify PGs; improvement in identifying these; number of PGs located by the surgeon and confirmed by CE; histopathological diagnosis; presence of thyroid inflammation; thyroid gland weight; number of PGs left in thyroid specimens; and number of PG auto-transplantations.

CE was performed using a rigid straight endoscope model 8715A (Karl Storz®, Tuttlingen, Germany), 23 cm in length, with an angle of 0°, diameter of 5 mm, manual focus adjustment and image magnification of 60x or 150x. The magnification of 60x was used in the present study. The additional equipment included a 250 watt halogen light source (Ferrari® model HA, São Paulo, Brazil) and a colour microcamera (Toshiba® model IK M141-A, Tokyo, Japan) connected using a USB cable and operated using the Pinnacle® LINX digital software (Mountain View, USA), which allowed the images to be recorded on a laptop computer.

In all cases, it was initially attempted to macroscopically identify two PGs in each thyroid lobe. CE was performed on all tissue samples with suspected PGs. CE was performed in all cases in which the suspected PG presented signs of ischaemia or even in cases of inadvertent avulsion or removal because of the needs of cervical dissection. Next, a fragment of the supposed gland was subjected to frozen section histological examination. Auto-transplantation was performed after fragmentation to sizes of 1 mm^3, in individual spaces opened up by blunt dissection between the fibres of the ipsilateral sternocleidomastoid muscle.

After exposing the thyroid region, identifying the recurrent laryngeal nerve(s) and macroscopically recognizing the supposed PGs, a solution of methylene blue 1% was applied to each of them using a cotton swab. The excess staining medium was removed using gauze soaked in physiological serum (Fig. 1).

Methylene blue enables staining of the nuclei of cells from the first layers [14]. Thus, the superficial layers of these organs were stained dark blue, which, in particu-

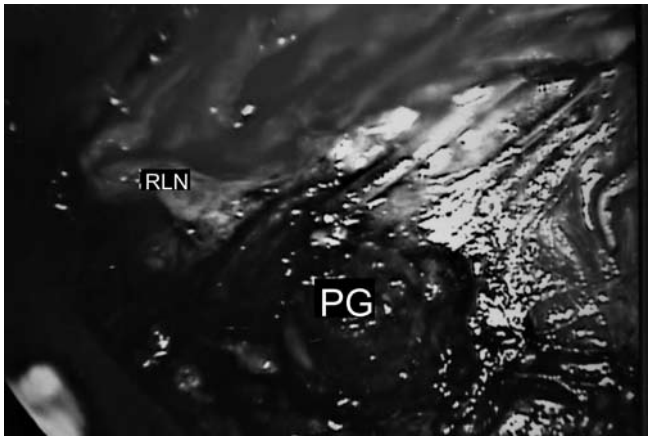

Fig. 1. Surgical field showing parathyroid gland stained with methylene blue 1%, and its relationship with the recurrent laryngeal nerve (PG: parathyroid gland, RLN: recurrent laryngeal nerve).

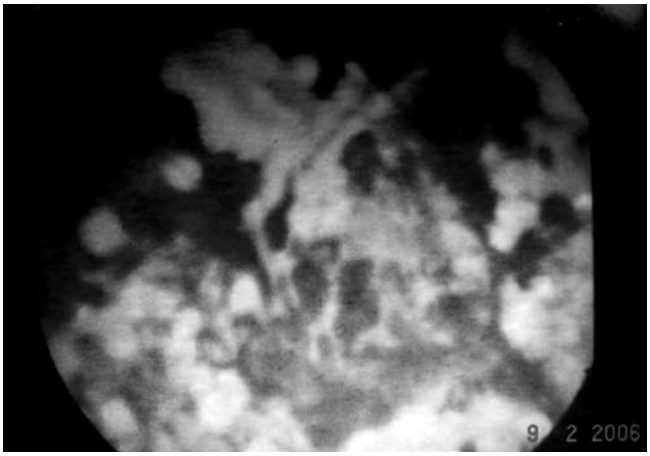

Fig. 2. View of parathyroid gland observed using CE. HE, 60x.

lar, revealed the nuclei. The end of the optic endoscope was brought to lightly touch the stained surface and thus the image could be observed on the computer screen. The focus, at 60x magnification, was adjusted manually, and the end of the endoscope was smoothly slid along the tissue under analysis. When the characteristic images of the parathyroid gland were found to be similar to those on a histological section, the identification was confirmed and concluded (Fig. 2). In cases of tissues that were compatible with adipose tissue or thyroid gland, a new dissection was performed to search for the PG.

The total duration of surgery was counted from the skin incision until skin closure. The time taken to locate and identify the PGs was counted from immediately after identifying and dissecting the recurrent laryngeal nerve(s) until obtaining the corresponding image of each PG by means of CE.

Statistical analysis was performed by means of Student's t test for paired samples from the same patient, and the significance level was taken to be 5%. The Kappa correlation index was used to compare the identification of the supposed PG by the surgeon (macroscopic examination) and identification using CE (microscopic examination). The influence of the following variables was investigated: total duration of surgery, time taken to locate and identify the PGs, weight of the thyroid gland, presence of thyroiditis, histo-pathological diagnosis and the period during which the surgery was carried out.

Results

A total of 331 PGs were observed by the surgeon. On the other hand, 282 glands were identified by CE. Nine PGs (7.2%) were observed together with the thyroid specimens, and the Kappa index was 0.534. The longer the total duration of surgery ($p = 0.03$) and the time taken to locate and identify ($p = 0.00$) the PG by means of CE, the lower the observed agreement was. The results from the second year of routine use of CE showed better agreement ($p = 0.02$). All the 17 auto-transplanted PGs were identified by CE and confirmed by the frozen section method.

For 16 patients, it was necessary to re-implant 17 PGs. In this group of 16 patients, 6 had undergone cervical dissection, 8 had undergone total thyroidectomy and 2 had undergone lobectomy. In all cases, the re-implanted PGs were identified by CE and the histological diagnosis was confirmed by frozen sections.

The anatomical distribution of each PG, in relation to its macroscopic identification by the surgeon and by means of CE, is outlined in Table I. The results of comparisons between PGs, identified by the surgeon and by CE, taking into consideration the total number of PGs observed with the two methods, are given in Table II.

Table I. Anatomical location of the supposed PGs, as identified by the surgeon, in relation to their identification by CE.

	Position				
	Right		Left		
	Superior	Inferior	Superior	Inferior	N.
Identified by surgeon	90	76	79	74	319
Identified by CE	88	59	75	60	282
Not identified by surgeon	6	20	8	13	47
Not identified by CE	8	37	12	27	84

Table II. Comparison between PGs identified by macroscopic examination and by endoscopy, in relation to central trend measurements.

	N.	Mean	Median	SD	Minimum	Maximum
Parathyroid glands identified by macroscopic examination	125	2.7	2.0	1.1	0.0	4.0
Parathyroid glands identified by endoscopy	125	2.3	2.0	0.95	0.0	4.0

p value: 0.000; SD: Standard deviation.

Table III. Distribution of PGs identified by the surgeon and by CE, to obtain the Kappa correlation index.

			Parathyroid glands identified by CE (> 0)				
			1	2	3	4	Total
Parathyroid glands identified by the surgeon	1	N	12				12
		%	9.8				9.8
	2	N	12	44			56
		%	9.8	35.8			45.5
	3	N		3	12		15
		%		2.4	9.8		12.2
	4	N		6	20	14	40
		%		4.9	16.3	11.4	32.5
Total		N	24	53	32	14	123
		%	19.5	43.1	26.0	11.4	100.0

p: 0.000; Kappa: 0.534

The Kappa test was used to analyse these comparisons, and the results were considered to be statistically significant ($p < 0.05$), thus indicating the existence of concordance (Table III).

After excluding 2 cases that did not have at least one parathyroid gland identified by CE, the results were concordant in 82 cases (66.7%).

The results of a comparison between the concordant and non-concordant groups, with qualitative variables analysed by means of the chi-square test, taking 5% as the significance level, are presented in Table IV.

A statistically significant difference was found only between the concordant and non-concordant groups, in relation to total duration of surgery and the time taken for macroscopic identification of parathyroid glands (Table V).

When the descriptive values are observed, it can be seen that the total surgical time was longer for patients with non-concordant results. The same can be seen concerning the time taken for location and identification, which was also longer for the group of patients with non-concordant results. As there were some aberrant weight values, the standard deviation value was large for this variable.

After exclusion of two patients with aberrant values, Student's t test was carried out. There was no difference in the mean weight for these two groups.

Discussion

PGs play a vital role in human homeostasis and hypoparathyroidism is almost synonymous with complications

Table IV. Analysis of qualitative variables, comparing patient groups with concordant and non-concordant results from identification of PGs by the surgeon and by CE.

		Identification by surgeon and by CE				
		Non-concordant results		Concordant results		
		N	%	N	%	P
Thyroiditis	Absent	30	69.8	55	67.1	0.759
	Present	13	30.2	27	32.9	
Histopathological diagnosis	Papilliferous carcinoma	14	32.6	14	17.1	0.135
	Goitre	17	39.5	41	50.0	
	Adenoma	8	18.6	23	28.0	
	Miscellaneous	4	9.3	4	4.9	
Year	2004	24	55.8	28	34.1	0.020
	2005/06	19	44.2	54	65.9	

Table V. Analyses of quantitative variables comparing patient groups with concordant and non-concordant results from identification of PGs by the surgeon and by CE.

		Concordance between surgeon's evaluation and CE		
		Non-concordant results	Concordant results	p
Total duration of surgery (min)	N	43	82	0.003
	Mean	86.4	74.8	
	Median	80.0	75.0	
	SD	23.5	10.0	
	Minimum	60.0	50.0	
	Maximum	160.0	100.0	
Time taken to identify parathyroid glands	N	43	82	< 0.000
	Mean	7.7	6.3	
	Median	8.0	6.0	
	SD	1.8	2.2	
	Minimum	3.0	3.0	
	Maximum	11.0	12.0	
Weight of thyroid gland (grams)	N	43	82	0.506
	Mean	45.8	40.4	
	Median	26.0	30.0	
	SD	49.4	40.0	
	Minimum	6.0	4.0	
	Maximum	276.0	290.0	

SD: Standard deviation.

during total thyroidectomy. This complication is less frequent when the surgeon is more experienced [12]. Knowledge of how to preserve viable PGs, either by maintaining them *in situ* with intact vascularization or by means of auto-transplantation, is an essential technical element in thyroid gland surgery [1 2].

Despite the clear description of the anatomical criteria for identifying PGs, such as the chestnut-brown colour, vascularization in the shape of leaf nervures and elliptical shape, there is still some doubt regarding their identification. The main difficulty seems to be in relation to adjacent structures, like adipose tissue, the thymus, the thyroid or even lymph nodes[1]. It is not always easy to locate these, especially because they can be in a sub-capsular position, or even in an intra-thyroid [16 17] or ectopic [18] location.

In cases with extensive surgical procedures, there is an increased incidence of both transient and persistent hypoparathyroidism [19]. PGs present terminal vascularisation, although it has been observed that the ligature of the inferior thyroid arteries does not simultaneously contribute towards a higher incidence of hypoparathyroidism. Thus, other variables are probably also involved [20].

With the aim of identifying PGs with low morbidity, some Authors started using different methods, such as studying imprints in surgical specimens for the differential diagnosis between the thyroid, parathyroid and fat, in cases of hyperparathyroidism, and achieved 100% accuracy [21]. Histological studies by means of imprints, with preservation of PGs *in situ*, showed low sensitivity and allowed correct identification in only 66% of the cases [22]. When this value is compared with the results from CE in our data, CE identified all the cases of re-implanted PGs and these cases were confirmed by frozen section biopsy. A prospective cytological study on tissue scraped during a surgical procedure showed that 29 PGs were identified, with accuracy of 88.2%, sensitivity of 86% and specificity of 100% [23].

The excessive use of biopsies for identifying PGs, even in cases of hyperparathyroidism, increases the risk of hypoparathyroidism [24]. Therefore, sampling of part of one or more PGs, together with the association of cervical dissection, may increase the incidence of this complication.

A study on locating normal PGs was made using intravenous injections of sestamibi (a selective radio-labelled drug also used for parathyroid adenomas) [25]. The PGs were marked for subsequent location by means of a portable gamma camera during the surgical procedure. The most interesting finding, in that study, was that 50% of the cases occurred during re-operation, indicating that these cases had the potential for higher levels of hypoparathyroidism. This is the only method that simultaneously brings together PG location and identification data. Although the removal of PGs could not be avoided, the glands could be recovered and auto-transplanted. There were no cases of permanent hypoparathyroidism.

Contact laryngoscopy is a method performed during suspension laryngoscopy that is still at the experimental stage, and it enables assessment both of healthy mucosa and a variety of lesions, such as tumours, to establish the pat-

tern for the covering mucosa and vascularization [14 15 26-28]. Mapping of diseases, such as malignant tumours, to establish the transitional limit between the normal and pathological mucosa, is one of the aims of this technique. With the accumulated knowledge from future experiences, this technique will be safe to use.

An experimental study was conducted in which PG and adipose tissue images, during surgical procedures for thyroidectomy were reproduced using the same CE method [29]. In 2006, the same Authors compared the findings from CE with the histological examinations from four fresh corpses and concluded that CE was precise in identifying PGs, without false positive results, thereby validating the method [30].

Histo-pathological examinations performed on tissue biopsies are still the gold standard diagnostic method. On the one hand, it is easy, and part of the routine, to perform histo-pathological examinations on frozen sections during surgery, in order to assess the presence or absence of disease in given tissue samples. On the other hand, this diagnostic method may lead to an increased risk of lesions in small tissues that are prone to avulsion and loss of vascularisation.

There was a statistically significant difference between the variables of total duration of surgery and identification of PGs, such that the shorter the total duration of surgery and the time taken to identify the PGs, the greater the concordance observed. The explanation for these facts lies in the initial difficulty in identifying PGs using endoscopy because of their lack of exposure. If there was any tissue between the surface of the PG and the optical extremity of the endoscope, identification was more difficult. An additional technical problem related to situations in which there was initial difficulty in locating the PG, i.e., when it took longer to identify it. The increased number of attempts gave a bluish appearance to the surgical field. Never the less, previous dissection of the recurrent laryngeal nerve allowed the procedure to continue.

There was no statistically significant difference between the concordant and non-concordant groups regarding the weight. This may have been because the median values were very close to each other (between 26 and 30 grams).

All 16 cases in which auto-transplantation of PGs was necessary because of suspected loss of vascularization had been previously identified by CE and confirmed by frozen section biopsy. In the present investigation, the incidence of resection of PGs was nine cases (7.2%), but in three cases, the PGs were subcapsular and in one case showed an intra-thyroid location. It is unlikely that CE would have avoided such occurrences.

It is likely that correct identification of PGs is also the way to reduce hypoparathyroidism. Although the initial cost of the endoscope is considerable, its long life and low maintenance cost should allow it to be used routinely as a tool for identifying various tissues.

Conclusions

CE is an efficient auxiliary method for identifying PGs during thyroid surgery. The period studied, total duration of surgery and time taken to locate and identify PGs were statistically significant.

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