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Laryngeal nerve morbidity in 1.273 central node dissections for thyroid cancer

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ABSTRACT

Aim

We assess the prevalence and mechanism of recurrent laryngeal nerve (RLN) injury in central neck dissection (CND) for thyroid cancer.

Methods

CND with intraoperative neural monitoring was outlined in 1.273 nerves at risk (NAR). RLN lesions were stratified according to: timing (during thyroidectomy versus CND), segmental vs. diffuse injury, mechanism, severity, location, number of lymph nodes dissected and metastastatic. EMG parameters were recorded.

Results

49/1.273NAR (3,8%) documented RLN palsy. 25 nerves were injured during thyroidectomy, 8 while CND. In 16 no precise moment or mechanism of injury was identified. A disrupted point could be identified in 19/25 (76%) and 7/8 (87%) respectively for thyroidectomy and CND steps. Diffuse injury, occurred in 24% and 12,5% respectively for thyroidectomy and CND. Nerves were injured in the all cervical nerve course without any major location for incidence for CND; for thyroidectomy most nerves were injured in the last 1 cm course. Traction (36%) was the leading cause of RLN injury for thyroidectomy. For solely CND, traction, entrapment and thermal injuries were equally frequent. Permanent vs. transient injuries were respectively 8% (4/49) and 92% (n.45/49), overall. Permanent lesions were equally distributed.

Conclusions

During CND, RLN palsy still occurs with routine exposure of the nerve even combined with IONM. The incidence of nerve lesions during thyroidectomy is higher than that of CND.

1. Introduction

Therapeutic central neck dissection (CND) for patients with clinically involved lymph nodes accompanies thyroidectomy to provide disease clearance [1].

Prophylactic CND (ipsilateral or bilateral) is considered in papillary thyroid carcinoma (PTC) with clinically uninvolved nodes (cN0) who have advanced tumors (T3 or T4), involved lateral nodes (cN1b), rather to plan further therapy [1].

Recurrent laryngeal nerve (RLN) injury is increased in cancer surgery [1,2]. Lesion occurs at rates of up to 8% temporary and 1–2% permanent palsy [2]. Metastatic lymph nodes make RLN dissection more difficult [3–8].

Intraoperative neuromonitoring (IONM) has been advocated to elucidate the causes of RLN injury during thyroidectomy and result from transection, clamping, stretching, thermal and ligature entrapment [9–12].

This study prospectively delineates the prevalence, location and mechanism of RLN injury exclusively during CND.

2. Materials and methods

2.1. Patients

Protocol was approved by the Institutional Review Board of China-Japan Union Hospital, Jilin University, Division of Thyroid Surgery, Changchun (China). Written informed consent was obtained from each patient. Thyroidectomy without CND, "berry picking" dissection, pre-operatively paralyzed RLN, re-do procedure, lateral dissection exposing only the vagus nerve were excluded.

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2.2. Technique of CND

Guideline regarding the terminology of CND defines all perithyroidal, paratracheal soft tissue and lymph nodes with borders extending superiorly to hyoid bone, inferiorly to innominate artery, laterally to common carotid arteries [1,13]. The technique applied is identical and the procedure adopted provides as first step isolated thyroidectomy, subsequently, as a second step, the CND is accomplished. That is, CND dissection specimen is not excised en bloc during thyroidectomy. CND is accomplished caudal to cranial. The surgical technique for prophylactic nodal dissection includes ipsilateral CND. Depending on the surgical strategy, surgeon might go back and forth between the thyroidectomy and CND components of the operation. Efforts were given to precisely describe when IONM signal loss occurred during a specific portion of operation.

2.3. Technique of IONM

Procedures were offered with intermitted IONM. IONM (NIM-Response 2.0 and lately 3.0 Systems, Medtronic, Jacksonville, Florida, USA) was performed according to standards of equipment, set-up, induction and maintenance anesthesia, EMG tube positioning verification, EMG definitions [3,14]. Surface electrodes integrated with endotracheal tube were used. Nerves were stimulated using a monopolar electrode at 1 mA, 100 ms impulse duration and 4 Hz frequency [3]. Supplementary Table S1 summarizes the standardized IONM protocol technique. Vagal nerve and RLN were checked repeatedly at each step of CND according to the needs of the surgeon and to elucidate where and how the RLN was injured (Table S1). An unchanged signal is defined when V2.0, R2.0 signals, R2.1 signals, and V2.1 signals were obtained successfully with the same stimulation level during the CND, and no apparent change existed between the comparisons [3,14] (Table S1).

2.4. Definition of loss of signal and identification of injured nerve

The following prerequisite issues are constitutive to loss of V2.1 and R2.1 signals (LOS): (a) normal VC movement at preoperative laryngeal examination; (b) initial EMG satisfactory (V1.0 and V2.0 > 500mcV); (c) no EMG response with stimulation at 1–2 mA or (d) low response <100mcV with stimulation at 1–2 mA; (e) no laryngeal twitch; (f) loss of the primary normal biphasic waveform; (g) the troubleshooting algorithm applied systematically [3,15,16]. If R2.1 and V2.1 signals were lost after complete dissection of the RLN, the disrupted point of conduction was located by the procedures that follow: the RLN was tested from the distal portion of RLN at the entry to the larynx with stimulation between 0.5 and 1 mA [3,14–16]. If a signal was obtained, then the lower portion of the nerve was tested until a response could not be elicited. Conversely, the RLN was tested from the proximal portion of the exposed nerve to the upper portion until a response was elicited. Thus, the disrupted point was located [3,14–16].

2.5. Outcomes measured

Parameters recorded on each NAR were: transient or permanent lesions, either uni- or bilateral; amplitude and latency in a standardized fashion (Table S1), the success in identifying the injured RLN, the manner in injury was identified (visual vs. IONM), circumstances that determined nerve injury [13]; location of injury; relationship between EMG parameters and number of lymph nodes resected, EMG parameters and number of positive/metastatic lymph nodes, therapeutic dissection vs. prophylactic dissection, TNM staging. RLN injuries were stratified in accordance with Chiang's classification [13].

2.6. Follow-up

Pre- and postoperative follow-up included direct laryngoscopy performed at 24 h before surgery and on the first postoperative day [17]. Dysfunction was considered permanent if persisted for >12 months [17].

2.7. Statistical analysis

Patients' data were collected in a prospective manner with a dedicated electronic Microsoft Office Access Data Base. Measurement of RLN palsy rate was based on the number of NAR. Statistical analysis was computed with SPSS, release 15.0 for Windows (SPSS Inc, Chicago-Ill, USA). The level of significance was set at P less than R.05.

3. Results

3.1. Patients

From July 2016–December 2016, 1.119 patients with PTC underwent CND. There were 237 men, 882 women; mean age 45.2 (18–82) years. 1.007 therapeutic and 112 prophylactic CNDs constituted this investigation. 154 bilateral CND and 965 ipsilateral CND were performed, covering 1.273NAR. 1.112 (99%) were PTC, 3 (0,25%) follicular, 2 (0,17%) medullary, 2 (0.17%) coexisting PTC and medullary. Mean tumor size was 22 ± 5 (4–72) mm (Table S2).

3.2. Lymph node histology

6.636 lymph nodes were extracted. 5,9 mean lymph nodes were dissected per procedure (range 0–45) (Table S2). In 58 (5,1%) CNDs, no nodes were detected. In 593 (52%) > 5 nodes were detached. 489 (43%) were pN1. There was a positive correlation between the total number of excised lymph nodes and metastases ($r = 0.183$, $P < .01$). There was a negative correlation test between the lymph nodes excised and T1a tumors ($r = -0.242$, $P < .01$), while a positive difference with T1b, T3a, T4a ($r = 0.068$, $P < .05$, $r = 0.091/0.086$, $P < .01$ respectively) (Table S2).

3.3. Normative EMG data

Complete follow-up was available for all NAR. Vagus nerve and the RLNs were correctly localized and monitored in all procedures. 1.221 (95,9%) NAR showed unchanged EMG signals after complete CND; all had normal vocal fold movement after operation. The mean ± standard deviation response amplitudes were 1.250 ± 879 µV for *V1,* 1.436 ± 749 µV for *R1*. Mean response amplitudes of *R2.1* and *V2.1* were 1.466 ± 721 µV and 1.592 ± 616 µV respectively. No false negative cases were noticed.

3.4. RLN injury

49/1.273 NAR (3,8%) documented LOS with RLN palsy at postoperative laryngoscopy.

Stratifying by the timing-step of operation most lesions occurred while performing thyroidectomy: 25 nerves (1,9%) were injured during thyroidectomy, 8 (0,62%) nerves while CND (Tables S3 and S4).

In 16 (1,2%) we couldn't locate the precise moment and mechanism of injury (Fig. 1). Mean number of lymph nodes dissected was 9 (range 2–17). Positive nodes were 2,5 (0–11). 50% of CNDs injured nerves were negative for metastases. No bilateral vocal fold paralysis occurred. By mapping the cervical integrity of the RLN using stimulation, a disrupted point (type 1 injury) could be identified in 19/25 (76%) and 7/8 (87%) respectively for thyroidectomy and CND (Table S5). We found that the nerve was injured in the all cervical nerve course without any major location for incidence for CND. For thyroidectomy, most nerves were injured in the distal 1 cm (Fig. 2). Type 2 global injury, occurred in 24% and 12,5% respectively for thyroidectomy and CND (Table S5).

Traction (36%) was the leading cause of RLN injury, entrapment (24%), nerve invasion (12%) during thyroidectomy. For solely CND, there was different distribution of causes: traction, entrapment and thermal (25%), ligation (12,5%) (Table S6). We hypothesized a combination of injury mechanism in 2 RLN (traction plus entrapment) in CND procedure, and 3 RLNs lesions in the thyroidectomy step (2 traction plus entrapment, 1 thermal and traction).

Macroscopic change of the nerves could be identified in only 1 case (ligation).

Over the 154 bilateral CNDs, 4 (2.5%) procedures were staged due to transient LOS of the first dominant side. Completion thyroidectomy and CND was performed within 4 months form initial surgery.

The long term results in terms of permanent vs transient were respectively 8% (4/49) and 92% (45/49), overall. Permanent lesions were equally distributed (2 per CND and thyroidectomy steps).

3.5. EMG data during CND

Compared with the amplitude of the RLN just after thyroidectomy alone (R2.0), the RLN amplitude (R2.1) subsequently to CND is significantly lower (p<.0001) (Tables S7a and b). With the increase of the total number of node dissected, RLN amplitude gradually decreased (r=−0.066, P<0,5) (Tables S7a and b). With the increase of the number of node dissected, the RLN latency increased gradually (r=0.058, P<0,5). These results were consistent with the EMG data obtained by monitoring the VN (V2.0 vs. V2.1, P=.008). Furthermore, there was a significant difference in RLN and VN latency (increase) and amplitude (decrease) with increased number of metastases excised (p=.002) (Tables S7a and b).

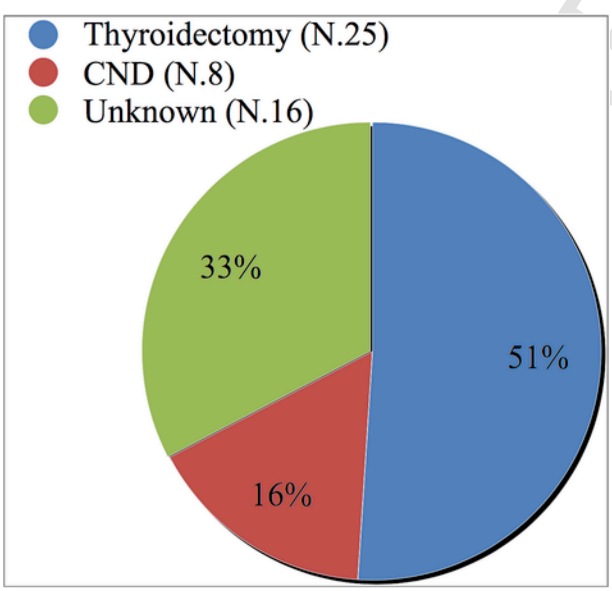

Fig. 1. Procedural distribution of RLN injuries (N.49).

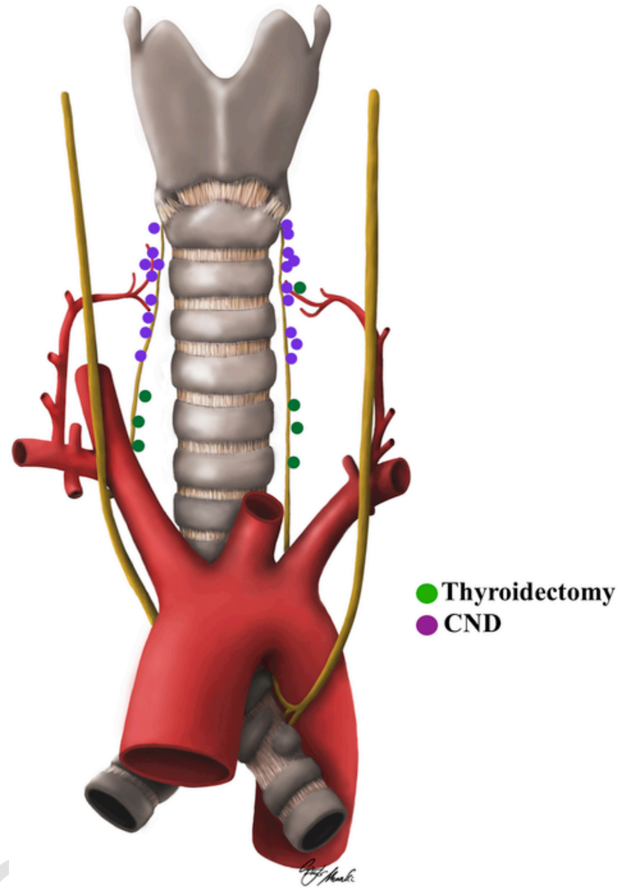

Fig. 2. Location of type 1 segmental nerve injuries in thyroidectomy (n.19) vs. CND (n.7).

4. Discussion

Figures are lacking regarding details of the RLN status and mechanism of injury during CND: 51% of RLN injuries were at the time of thyroidectomy, followed by CND (16%) step (Fig. 1). In 33% of lesions a precise moment and mechanism was not possible to clarify. The reader should carefully interpret the results of the study: if the EMG signal is lost early on during the thyroidectomy, then function cannot be lost while CND, since injury has already happened. This is essentially bias toward a mechanism of injury that happens during an earlier portion of the cancer case.

CND may determine RLN injury with different mechanism of injuries than thyroidectomy. Traction (36%) was the leading cause, entrapment (24%), nerve invasion (12%) for thyroidectomy procedure. The causes of injury during exclusively CND are equally: traction (25%), entrapment (25%), thermal injury (25%) and ligation (12,5%) (Table S6). Chiang described 15 RLN injuries during thyroidectomy: 80% were thought to be stretch injuries, 13% from clamping, 7% due to constriction [11]. Snyder analyzed 25 nerve injuries: 56% traction, 12% related to transection or ligatures, 8% compression insults [10]. Fourteen injured nerves in endoscopic thyroidectomy were analyzed: the mechanisms of injury were traction (70%), thermal (30%) [12].

The incidence and distribution of type 1 and 2 injuries during CND was similar to that described for thyroidectomy with slight prevalence of segmental ones [10–12].

Nerve injuries occurred also in N0 level 6 dissections (50%) (Table S3).

During the thyroidectomy procedure, the last 1 cm of RLN course, appears to be the most critical site for traction injury. Studies have indicated that the region of Berry's ligament is the area of greatest risk for RLN injury during thyroidectomy [10–12]. In the present study, differently, RLN was injured in all its course in the level VI (Fig. 3) and most injures were not visible. For this reason, standardized VN stimulation to assure the full integrity of RLN is mandatory [9,14].

Any modifications to the established CND operative technique should result in improved patient outcomes with lower rates of complications. The advice to take particular care to free the lymph node from the nerve before applying traction is sound and obvious. Clearly to make further impact on RLN injury incidence following CND there must be more cautious of lymph node entrapment and use of traction control on nerve while dissecting (Fig. 3a,b,c). Injuries were created during the extraction of the lymph nodes from the cervical incision and subsequent retraction and elevation of the RLN in an upward direction. The RLN may be insufficiently dissected both anteriorly, posteriorly and laterally and medially away from the lymph node capsule and beyond and fixed to bands of connective tissue (Fig. 3a,b,c). More thorough dissection of the RLN away from all the lymph nodes capsule prior to node extraction is essential in order to minimize the likelihood of traction. Surgeon must free the inferior laryngeal nerve meticulously and completely, at 360°, for both the lymph nodes located posterior to it than the front ones. Surgeon may also pay attention during dissection to other near lymph nodes that may be the cause of entrapment and traction (Fig. 3a,b,c). We suggest meticulous dissection of the RLN away from the lymph node capsule before extraction of the node in CND.

Thermal injuries represented 25% of nerve lesions in CND. Energy-based devices have the potential for unapparent and undesirable heat-related collateral/proximity iatrogenic injury to adjacent structures such as the laryngeal nerves [18,19]. The tip of the device must be carefully assessed while used as a dissecting tool for CND. Cooling time and a safer distance >3 mm are suggested.

The long term results in terms of permanent vs transient were respectively 8% and 92%. Permanent lesions were equally distributed per CND and thyroidectomy step. This is a critical issue since the permanent injuries are the ones of most concern.

When evaluating EMG parameters from thyroidectomy to CND (Tables S7a and b), interestingly a significant decrease of amplitude combined with increased latency was noticed, possible predictors of RLN stress [20,21].

Future studies with continuous monitoring of the RLN by vagal nerve stimulation may provide even more information regarding changes in the RLN EMG signal in CND to enhance safety and optimize the surgical procedure and understanding those injures with unknown cause [20,21].

Author contributions

(I) Conception and design: Liu Xiaoli, Fu Yantao, Li Shijie, Zhao Yishen, Li Changlin, Che-Wei Wu, Feng-Yu Chiang, Gianlorenzo Dionigi, Sun Hui;
(II) Administrative support: Liu Xiaoli, Zhang Daqi, Zhang Guang, Zhao Lina, Zhou Le, Fu Yantao, Li Shijie, Zhao Yishen, Li Changlin,
(III) Collection and assembly of data: Gianlorenzo Dionigi, Hui Sun
(IV) Data analysis and interpretation: Gianlorenzo Dionigi, Hui Sun
(V) Manuscript writing: Liu Xiaoli;
(VI) Final approval of manuscript: All authors

Compliance with ethical standards

Ethical approval

The Institution's Ethical Board Committee approved the review.

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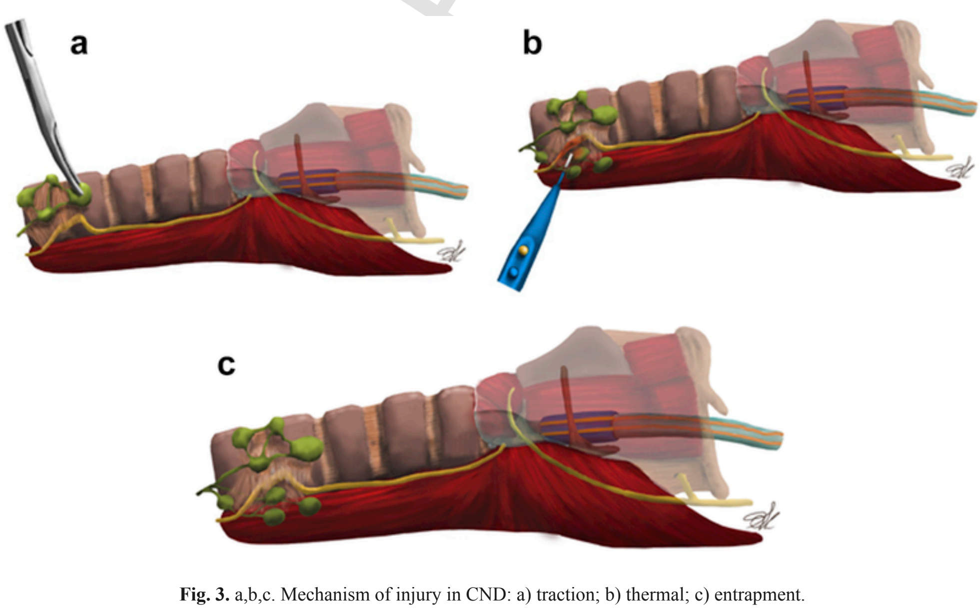

Fig. 3. a,b,c. Mechanism of injury in CND: a) traction; b) thermal; c) entrapment.

Conflict of interest

The authors Liu Xiaoli, Zhang Daqi, Zhang Guang, Zhao Lina, Zhou Le, Fu Yantao, Li Shijie, Zhao Yishen, Li Changlin, Che-Wei Wu, Feng-Yu Chiang, Gianlorenzo Dionigi, Sun Hui have no conflict of interest to disclose, and no other funding or financial relationship with the surgical industry.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.suronc.2018.01.003.

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