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original article

IONM and minimally invasive videoassisted thyroidectomy

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SUMMARY: **IONM and minimally invasive videoassisted thyroidectomy.**

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Background. *We know that benefits of MIVAT are related to a better cosmetic result and lower post-operative pain in comparison to CT. The incidence of nerve cold palsy is related to a correct identification of the recurrent laringeal nerve (RLN) as standard procedure in thyroid surgery. From September 2014 we have introduced the use of intraoperative neural monitoring(I-IONM) in all thyroidectomies in the Unit of General Surgery of University Hospital of Parma, including in MIVAT.*

Patients and methods. *We have considered all patients treated from September 2014 to September 2017 for thyroid diseases using MIVAT and IONM. Intermittent neuromonitoring with NIM-3.0 equipment (Medtronic, Jacksonville, FL, USA) was used during all operations. We have recorded all data about age, sex, diagnosis, surgical time, i-IONM signal, postoperative pain, postoperative hypocalcemia after 24 hours, haematoma and vocal cord palsy. The mean hospital stay was collected from surgical procedure to hospital discharge. We have considered vocal dysfunctions that persist six months after surgery as permanent.*

Results. *From September 2014 to September 2017 we treated consecutively with both MIVAT and i-IONM 100 patients.*

Considering the extent of surgery, 26 pts underwent to hemithyroidectomy and 74 pts to total thyroidectomy. The mean surgical time was 61.8 minutes.

In 7 cases the patients were affected by preoperative clinical dysphonia. Using I-IONM during thyroidectomy, we recorded in 5 cases (5%) a loss of signal; in two cases (2%) we experienced a temporary postoperative vocal cord palsy.

Discussion. *In our experience the use of IONM has improved the safety during thyroidectomy because precision that can be achieved by endoscopic procedures is further improved by complementary use of IONM. The costs associated to a potential reduction of medical litigation have not been investigated.*

KEY WORDS: Minimmaly invasive thyroidectomy - IONM - Vocal cord palsy - Hypocalcemia - Thyroid surgery.

Background

The miniinvasive videoassisted thyroidectomy (MIVAT) was introduced in Italy from 2000. This procedure, as others endoscopic Endocrine surgical procedures, is used in only 15-20% of cases compared to conventional thyroidectomy (CT), (1-4) as in our experience.

We know that benefits of MIVAT are related to a better cosmetic result and lower post-operative pain in comparison to CT. In young age groups, the prevalence of thyroid disease is significantly higher in women than in men. Because of the emphasis on physical attractiveness in the media and modern society, cosmetic outcomes of thyroid surgery are particularly important to women (5).

The minimally invasive nature of the technique has not compromised its ability to accomplish its purpose both safely and effectively (6).

Furthermore, miniinvasive procedure has the same rate of adverse events and no statistical difference in postoperative hematoma, vocal cord palsy and persistent hypocalcemia bet.

In our experience the transitory hypocalcemia is lower in MIVAT than CT (7).

The incidence of nerve cold palsy is related to a correct identification of the recurrent laringeal nerve (RLN) as standard procedure in thyroid surgery. The causes of iatrogenic lesions are stretching, cutting, squeezing, pressure, ligature, heat spread. Anatomical variations are a risk factor for RLN injury as well as reoperation and extent of surgery (8). The rate of incidence of RLN palsy is

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related to surgical experience and to the volume rate of thyroidectomy/year and the range reported in literature is approaching 10% for temporary postoperative vocal cord palsy and 2.3% for permanent RLN injury (9). This rate increase to 12.5% for transient palsy and 3.8% for permanent injury in case of reoperation, where even skilled and experienced surgeons can have difficulty mapping the RLN and preventing inadvertent RLN injuries, particularly in non-anatomical fields with many scars from the first operation (10).

From September 2014 we have introduced the use of intermittent neural monitoring(I-IONM) in all thyroidectomies in the Unit of General Surgery of University Hospital of Parma, including in MIVAT.

In this article we present our results about use of I-IONM in MIVAT.

Patients and methods

We have considered all patients treated from September 2014 to September 2017 for thyroid diseases using MIVAT and IONM. Surgery was performed with standardized technique using an Energy Device, camera of 5 mm 30° and dedicated Stortz Kit for MIVAT. All cases were treated by a single endocrine-surgeon, with experience in both miniinvasive and traditional thyroidectomy.

Intermittent neuromonitoring with NIM-3.0 equipment (Medtronic, Jacksonville, FL, USA) was used during all operations. A monopolar stimulating probe with a handle was used for nerve stimulation with a current amplitude of 1 mA to 2 mA. The electromyographic (EMG) signal was obtained using surface electrodes integrated in the endotracheal tube (NIM Flex EMG tube, Medtronic); in female patients 7 mm tubes were used and in males 7.5-8 mm tubes were used.

The technique of IONM performed was intermittent (I-IONM) with standardized analysis as proposed by the International Neural Monitoring Study Group (L1 preoperative laryngoscopy, V1 Vagus test before lobectomy; R1 RLN test before lobectomy; R2 RLN test post lobectomy; V2 Vagus test post lobectomy) (11).

Only in patient affected by loss of signal Type 1 or 2, L2 (postoperative laryngoscopy) was performed.

We have recorded all data about age, sex, diagnosis, surgical time, I-IONM signal, postoperative pain, postoperative hypocalcemia after 24 hours, haematoma and vocal cord palsy. The mean hospital stay was collected from surgical procedure to hospital discharge. We have considered vocal dysfunctions that persist six months after surgery as permanent.

All patients signed an informed consent to a possible two-stage thyroidectomy, performed in case of loss of signal during or after the first lobectomy. In this case the patient should wait until full nerve recovery and undergoes to a new laryngoscopy before the second surgical procedure to evaluate the vocal cord performance.

This work is approved by Institutional Ethics Committee to collect the data about IONM.

The data were analyzed with t test, chi square test, Positive predictive value (PPV) and Negative Predictive Value (NPV).

$P<0.05$ was considered statistical significant.

Results

From September 2014 to September 2017 we treated consecutively with both MIVAT and i-IONM 100 patients.

The patients (pts) were 87 females and 13 males, with a mean age at time of surgery of 45.9 years old in the female group and 57.4 years old in the male group.

The preoperative diagnosis was in 13 pts goiter, 6 pts toxic goiter, 6 pts THYR3, 30 pts THYR 4, 3 pts THYR 5, 39 pts THYR 6 and 3 pts positive RET (Table 1).

Considering the extent of surgery, 26 pts underwent to hemithyroidectomy and 74 pts to total thyroidectomy. The mean surgical time was 61.8 minutes.

The preoperative mean PTH level (pg/ml) was 53.2 (range 23-132).

The mean preoperative calcemia was 9.28+/-0.31 mg/dL (range 8.8-10) versus mean postoperative calcemia of 7.95+/-0.69 mg/dl (range 5.8-9.1) ($p<0.0001$).

We detected a clinical postoperative transitory hypocalcemia in 6 pts (6%); no postoperative hematoma was recorded.

In 7 cases the patients were affected by preoperative clinical dysphonia. Using I-IONM during thyroidectomy, we recorded in 5 cases (5%) a loss of

Table 1 - PATIENTS' CHARACTERISTICS.

		N°
SEX	**Male**	13
	Female	87
MEAN AGE	**Male**	45.9 years
	Female	57.4 years
PREOPERATIVE DIAGNOSIS	**Goiter**	13
	Toxic goiter	6
	Thyr 3	6
	Thyr 4	30
	Thyr 5	3
	Thyr 6	39
	RET pos	3
EXTENT OF SURGERY	**Total thyroidectomy**	74
	Hemithyroidectomy	26
MEAN SURGICAL TIME		61.8 min

signal; in two cases (2%) we experienced a temporary postoperative vocal cord palsy in 1 pts (1%) (Table 2).

In cases treated the correct results of standardized IONM was associated to a NPV of 100% and a PPV of 40%.

Discussion

The use of miniinvasive thyroidectomy is increased in the last years and today we recognize the benefits of these procedures related to equal adverse events, reduced postoperative pain and better cosmetic results in comparison to traditional surgery. The smaller surgical trauma allowed by MIVAT accounts for this more positive outcome (6). Even considering the more recent robotic-assisted transaxillary thyroidectomy (RATT), experienced authors assessed that RATT seems not to supersede MIVAT in patient satisfaction when two groups of patients are compared (12).

Table 2 - RATE OF ADVERSE EVENTS.

		N°
Clinical transitory hypocalcemia		6
Postoperative vocal cord palsy	**transitory**	2
	permanent	0
Postoperative hematoma		0

The reports on the use of IONM in miniinvasive thyroidectomy are few; furthermore, in a recent literature review, considering studies published during 2000-2015, Dionigi G. et al. outlined the delayed acceptance of IONM in endoscopic procedures in comparison with conventional open thyroidectomy. They deduced that only 5% studies used monitoring in endoscopic thyroidectomies; of them, in 75% IONM was used in all procedures and in 25% only in selected cases. In 92% they used i-IONM and in 8% c-IONM. Only 31% of studies reported a standardized use of IONM, with V1, R1, R2 and V2 stimulation, according to INMSG guidelines, while 69% reported RLS stimulation only (5).

The first report of IONM in endoscopic surgery was published in 2007 (13).

We report our experience in MIVAT using IONM. Even in mininvasive procedures, the use of IONM is feasible and is an additional help to surgeon to value the correct functional ability of nerve.

During endoscopic procedures we use Harmonic Scalpel and we perform a thyroid gland retraction and elevation in medial direction in order to extract the lobe from the mini-incision and gain space laterally. This is the most dangerous surgical step of the miniinvasive procedure because the use of excessive tension on the lobe, that remains attached with the latest fibers of Berry ligament to the neural branch, increases the risk of distraction of NLR compared to CT, especially in cases of thyroiditis (4, 14). Indeed the event that can be related to dysphonia are stretching and squeezing, in addiction to aspiration, ligature, edema, inflammation, electric shock, thermal injury and section (8). Endoscopic procedures should be performed without excessive traction on the thyroid to avoid injury over the nerve by Berry's ligament (13, 15, 16).

We know that the gold standard during thyroidectomy is still visual identification of inferior laryngeal nerve but many authors demonstrated that a rate of patients should be affected by postoperative dysphonia even with a visually intact nerve identified intraoperatively (17-20). Bergenfelz et al., in a multicenter study, highlighted that only a few injured nerves can be visually identified intraoperatively, 11.3% for unilateral and 16.7% for bilateral cases (18). Dralle et al. and Goretzki et al., in two German publications, recommended the use of IONM as the most reliable method to identify nerve injury in an anatomically intact nerve (17, 20).

The bilateral vocal cord palsy is the worse adverse event. The use of IONM and the implementation of strategy of two-stage thyroidectomy in case of loss of signal during or after the first lobectomy can minimize the risk of bilateral RLN to nearly 0% (21).

We adopt in all cases a protocol with two-stage thyroidectomy when after the first lobectomy we highlight a loss of signal to avoid a bilateral risk of injury.

The clinical utility of IONM can be expressed in terms of its negative (NPV) and positive predictive values (PPV). Owing the rarity of RLN palsy, NPV and specificity for intermittent IONM are high, whereas PPV and sensitivity are lower (22). In our experience, the PPV of IONM is 40% of patients affected by loss of intraoperative signal but patients have accepted the risk after a correct and informed indication. The most frequent causes of false positive are as follows: endotracheal tube displacement, equipment problems both on the stimulation side and on the recording side, blood covering the stimulated nerve segment, neuromuscular blockage and early neural recovery. Strict adherence to IONM standards, avoiding technical pitfalls, can improve NPV and PPV.

The use of I-IONM is rising, especially in Europe. More than 90% of German surgical departments use IONM in thyroids procedures (19). In the United States 53% of general surgeons use IONM for some or all thyroids operation (23).

Recent systematic reviews pointed towards a benefit of IONM in decreasing RLN palsy rates, but failed to reach statistical significance for persistent RLN palsy (24, 25). A recent reanalysis of the Scandinavian Quality Register for Thyroid, Parathyroid and Adrenal Surgery found that the use of IONM was not independently associated with a lower risk of early cord palsy but independently decreased the risk of permanent vocal cord palsy (26).

Whether neuromonitoring reduces the RLN paralysis rate during endoscopic procedures remains unclear because of the low numbers of endoscopic procedures performed with IONM and because the number of complications is too small to draw firm conclusions (5).

The literature agrees that IONM performed complementary to endoscopic thyroidectomy enhances the quality and safety of the procedures (5, 27). In at least two prospective studies, the efficacy of IONM in endoscopic procedures was demonstrated by more rapid recovery of voice function (28).

Effectiveness of IONM is related to a correct use of standardized technique, as previously reported. In our experience, in MIVAT as in CT, the use of IONM help the surgeon to reduce the risk of bilateral cord palsy, facilitating RNL identification and allowing testing of RLN function, and to recognize anatomical laryngeal nerve variants. These include the variable course of RLN at the level of inferior thyroid artery, the relationship between the RLN and posterior tubercle (Zuckerkandl's tubercle), nonrecurrent laryngeal nerves and extralaryngeal bifurcation (29). In add to this, use of IONM helps younger surgeon in thyroidectomy and increase their confidence in endoscopic procedures. Furthermore, IONM enables corrective actions at three stage of surgery: during blunt dissection, during use of energy-based devices and during gland retraction (5).

The standardization of IONM, the surgical training and the multidisciplinary collaboration are essential for a correct use of IONM. The intraoperative report of functional state in all stages of thyroidectomy is important to prevent nerve injuries caused by a lack of recognition of the nerve.

Nevertheless, surgeons need to be cognizant of the methodological limitations of intermittent IONM in both time and space: limited in time because the period between the stimulation cycles goes unsupervised, limited in space because RLN function is monitored only between the levels of the stimulation and recording electrodes, missing proximal RLN lesions (22).

Techniques and technologies applied for thyroid surgery such as laryngeal examination (30, 31), intraoperative pathological examination (32), energy-based devices (33) and robotics (34) are important drivers for increased operating and hospitalization costs.

In endoscopic procedures the use of energy devices is higher than CT, increasing the overall cost of the operation; equipment and consumables for IONM are expansive and consequently the costs associated to IONM should be an obstacle to routinary use.

Hospitalization and operating room costs for a thyroidectomy with IONM were between 5-7% and 10-12%, respectively, higher than those for traditional thyroidectomy; these costs were sensitive to the number of procedure performed (35).

In a recent study, Wang et al. used simulation economic modelling to asses clinical and cost-effectiveness utility of IONM implementation. The analysis demonstrated that the importance of IONM is variable depending on the duration, the severity and the prevalence of RLN damage, in addition to the clinical setting in which IONM is applied. The results suggest that IONM is cost-effective when the prevalence of transient nerve injury encountered is higher than 38%. This scenario is rare in a clinical setting. Considering permanent injuries, the cost-effectiveness is determined when these are estimated at about 3% of cohort population simulated. Moreover, the study confirms that the volume utilization of IONM is an important, modifiable factor for cost-effectiveness. The above described cost-effective scenario is cost-effective only in high volume setting with more than 5 IONM procedures/week (36).

The IONM tecnique can hardly be cost-effective when only direct costs of RLN injuries are considered. RLN morbidity has its economic weight on patients and on society (37, 38). To be cost-effective, all indirect costs of RLN injuries, including speech therapy, repeat laryngeal examinations, VF surgery and legal claims must be factored into the cost-effectiveness equation (22).

Future trials should also seek to clarify the aspects related to the quality of life of patients with vocal cord paralysis, that matter the most to the patients, and to characterize the changes in the quality of life that occur during the follow up. The assessment of modified clinical strategies as the opportunity given by IONM for an intraoperative corrective action is not measurable either (36). In our experience the use of IONM has improved the feel safety during thyroidectomy because precision that can be achieved by endoscopic procedures is further improved by complementary use of IONM. The costs associated to a potential reduction of medical litigation have not been investigated.

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