What is the learning curve for intraoperative neuromonitoring in thyroid surgery?

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ABSTRACT

Background: The study describes the initial experience and learning curve of intraoperative neuro-monitoring (IONM) during thyroidectomy. We describe the prevalence and patterns of IONM technical problems.

Methods: Prospective series of 152 consecutive thyroid operations (304 nerves at risk) were analyzed. Standard technique consists of monitoring vagal and RLNs before, during and after resection. Personal gain of experience was defined by the preceding number of thyroid operations. To establish the number of thyroidectomies required before achieving an effective and safe IONM technique, all of the procedures were divided into three chronological groups of about 50 cases (groups 1, 2, and 3).

Results: Patients (90%) had successful IONM with initial endotracheal tube position. Fifteen patients (10%) needed further tube adjustment. Out of 15 patients 14 (93%) were due to non-optimal contact of endotracheal surface electrodes to vocal cords. Tube malrotation was the main reason for initial failure (53%). The success rates of prompt IONM technique were 80% in group 1, 92% in group 2, and 98% in group 3 ($p < 0.05$). Mean operating time was low in group 3 ($p < 0.03$). Vagus and RLNs were localized and monitored in all the cases (100%). The incidence of temporary RLN injury was 2.6%. No permanent complications occurred. Negative EMG response indicated an altered function of RLN and stage thyroidectomies were scheduled. Transient RLN palsies were seen without changes during the entire study period.

Conclusions: This is the first series of thyroidectomies with standardized IONM technique performed in Italy. Neuromonitoring was effective in providing identification and function of laryngeal nerves. IONM successful rates were affected considerably by the extent of surgical and anaesthesiological experiences, starting with relatively low rates in the beginner group and then increasing. We assessed the learning curve: improved operative variables and safe technique were seen in about 50 patients.

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1. Introduction

Intraoperative neuromonitoring (IONM) has been first proposed as an adjunct to standard visual identification of the recurrent laryngeal nerve (RLN) during thyroid surgery in 1966 by Shedd.[1]

Experience has shown that IONM allows the laryngeal nerves, both inferior and superior, to be reliably identified during neck surgery.[2] Authors stated that IONM is an important adjunct in dissection and functional neural prognosis.[3]

Recent technical advances currently allow accurate, non-invasive nerve monitoring.[4]

With numerous institutions beginning to perform thyroidectomy with IONM,[5] there is an increased interest in this new device that may facilitate the surgical procedure itself and reduce morbidity. The prevalence of monitoring is relatively high in the United States, United Kingdom,[5] Germany,[6] Asia and Oceania,[7,8] as opposed to Italy where no previous experience has been reported.

The objective of this study is to assess the role of IONM as a means of identifying, monitoring and assessing the function of the RLN on the performance of thyroidectomy. We describe in this study our learning curve and the prevalence and patterns of IONM technical problems. This would help to detect and resolve possible equipment failure.

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2. Methods

2.1. Patients

Starting in 2007, we modified our thyroidectomy procedure, introducing the neuromonitoring for localization of RLN in all elective bilateral thyroid operations. Between August 2007 and May 2008, 152 consecutive patients underwent IONM thyroid surgery, providing 304 nerves at risk for examination.

Exclusion criteria for IONM were thyroidectomies performed with local anesthesia and missing informed consent. Moreover, 2 RLNs were excluded from this study as it featured preoperatively cord palsy. Based on the exclusion criteria, 4 patients were withdrawn from the present study.

Main surgical outcome measures were mean operative and hospitalization times, intra- and postoperative complications, technical IONM setup problems or equipment malfunction and patient follow up.

The following complications were analyzed: intra- and postoperative bleeding, seromas, wound infections, transient or definitive laryngeal nerve lesions, uni- or bilateral, permanent or transient hypocalcemia and parathyroid gland autotransplantation.

Hypocalcemia was checked by preoperative and daily serum calcemia, starting from the first postoperative day and on the 7, 14 days postoperative, then 1, 3, 6 months after surgery. Intact parathyroid hormone (iPTH) levels were also determined postoperatively. Significant hypocalcemia was defined as experiencing signs or symptoms of hypocalcemia and/or having a serum calcium level that was $\leq$7.5 mg/dL (low end of normal for assay used = 8.5 mg/dL). Patients with postoperative hypocalcemia were discharged on a therapeutic regimen of oral calcium and cholecalciferol, which was continued until normalization of the calcium level.

Pre- and postoperative follow ups included for all patients direct laryngoscopy to check vocal cord mobility performed at 24–48 h before and within 2 weeks after the surgical procedure by an independent laryngologist (ear, nose and throat department), because patients may have vocal cord paralysis without changes in their voice. Any reduction in the movement of the cord was recorded as postoperative cord paralysis. For those patients with documented postoperative cord palsy, repeated examinations were performed periodically at 1, 2, 6, and 12 months after the operation until full recovery of the vocal cord function had been confirmed.

Hypoparathyroidism and RLN palsy were defined as permanent when there was no evidence of recovery within 6 months of surgery.

Hospital discharge was at 48–72 h after the operation if no signs of complications were present.

All procedures were performed by the same surgeon (GD) with 6 years of experience in endocrine surgery and having performed more than 150 procedures per year in an academic setting. All patients were intubated for general anesthesia by the same anesthesiologist (AB).

The attending surgeon and anesthesiologist completed a perioperative data sheet that included the number of applications of IONM per case, intraoperative complications or equipment malfunction. Moreover, we tested the hypothesis that the use of IONM could prolong overall operative time thus intubation. We routinely measured all the surgical procedure; in particular we classified and calculated the anaesthetist operative time (AOT) from patient entering the operating room to the correct endotracheal tube placement (i.e. confirmed by the correlation of EMG with respiratory activity). Care was taken in positioning the electrode accurately, since the adjustment of the head and neck after intubations can change the relative position of the tube and hence the electrode. Furthermore, the surgical operative time (SOT) was recorded by the circulating nurse as the time from skin incision to the application of the wound dressing.

Patients were followed pre- and postoperatively in collaboration with the Division of Endocrinology of the University of Insubria, Varese, Italy. For cancer patients, after surgery, patients were submitted to thyroid remnant ablation by radioactive iodine (^{131}I) and placed under TSH-suppressive L-thyroxine therapy.[9] Preoperative diagnosis was based on ultrasound-guided fine needle aspiration cytology and serum calcitonin measurement.[9]

2.2. Operative technique

The technique of IONM was standardized and has been described.[4,6] Succinylcholine (1 mg/kg) was used in the initial phase of the general endotracheal anesthesia. No additional neuromuscular blocking agents were used following intubation. The Nerve Integrity Monitor (NIM-Response 2.0 System, Medtronic Xomed, Jacksonville, Florida) was used for laryngeal nerves monitoring. A dedicated tube (NIM Contact EMG Tube) is used and functions as a normal endotracheal tube, except that it contains bipolar, stainless steel contact electrodes for monitoring both vocal cords. The tube is placed with the exposed electrodes well in contact with the true vocal cords under direct laryngoscopy.

RLN is located, mapped and stimulated in the surgical field by the application of a sterile single-use pulse-generated monopolar stimulator probe (no. 8225101, Medtronic Xomed). This stimulator measured 10 cm in handle, 9 cm long in probe with a flexible and adaptable tip of 0.5 mm. The probe delivers an electric current that ranged from 0.5 to 2 mA. The probe is insulated at the tip to prevent current shunting. The identity of an intact nerve is confirmed through a series of audible acoustic signals generated by the machine. The probe is applied directly, perfectly and minutely to the nerve for approximately 1 s to elicit a response. The stimulation level was set at 0.5 mA as a starting point; if no signal was elicited, the stimulation was increased. Equipment failure was considered if pre-resection vagal stimulation signal could not be received at a level of 2.0 mA.

Our standard IONM technique is to stimulate both the vagus nerve and the RLN before, during and after thyroid resection.[4,6,10] The ispilateral vagus nerve is stimulated directly by a 1–3 cm dissection of the carotid sheath or in some cases only by simply applying the stimulator on the carotid shift without dissection (usually in patients with low fat in the neck). The absence of a signal that was generated by the stimulator at any precise point along the nerve would be regarded as a positive test. Nonpathologic and pathologic EMG responses were recorded. The identification of the disrupted point was located by stimulating the distal point of the RLN at the entry to the larynx and the proximal portion of the exposed RLN to the upper portion until a signal was elicited. Thus, the disrupted point could be located and potentially pinpointed.

To gain experience in this field, scientific background of the first author included two University internships at the Thyroid and Parathyroid Surgical Division, Harvard Medical School, Boston (USA) and the Department of General Surgery, Martin Luther University, Halle (Germany).

Personal gain of experience was defined by the preceding number of thyroid operations. All operations were indexed consecutively with a running number.

Option for controlling haemostasis during thyroidectomy included the vessel sealing system (LigaSure™, Precise, Valley Lab).

If a parathyroid gland appeared to be damaged or hypovascularized, we reimplanted it in the sternocleidomastoid muscle. No patients received antibiotics prophylaxis.[11]

2.3. Statistical analysis

According to Chiang and Dralle,[6,10] loss of IONM signal was defined as true positive (TP) if RLN palsy was confirmed on postoperative laryngoscopy; false positive (FP) with a no verifiable RLN palsy. Intact IONM signal was defined as false negative (FN) in case of RLN palsy diagnosed on postoperative laryngoscopy and true negative (TN) with normal postoperative laryngoscopic finding. Sensitivity was calculated as $TP/(TP + FN)$; specificity as $TN/(FP + TN)$. Positive predictive value (PPV): $TP/(TP + FP)$; negative predictive value (NPV): $TN/(FN + TN)$ and accuracy: $TP + TN/$total number.

Unless otherwise stated, all data for continuous variables were expressed as median and range. All patients' data were collected in a prospective manner with a dedicated electronic Microsoft Office Access Database (Microsoft Corp, Redmond, Washington). Data are collected daily until the day of discharge, then there was a regular contact between the study coordinator and the participating specialist (endocrinologist, laryngologist, etc.). The database is part of our department's quality-improvement program. The use of this database for clinical research has been approved by our institutional review board. Primary outcome measure was the morbidity and mortality. In case of dichotomous variables, group differences were examined by χ^2 or Fisher exact tests as appropriate. Statistical analysis was computed with SPSS, release 15.0 for Windows (SPSS Inc, Chicago–Ill, USA) in cooperation with the Institution of Biomedical Statistics of the University of Insubria. The level of significance was set at p less than 0.05. All efforts were made to avoid sources of bias such as the loss of individuals to follow up during the study.

3. Results

The study group included 97 women and 55 men with a mean age of 39.8 (age range 19–77 years). The mean thyroid volume estimated by preoperative ultrasonography was 41 (range 11–149) mL. Mean size of dominant nodules was 3.5 cm (range 1.2–7.9 cm). The treated pathologies were mainly nodular goiter and tumors (Table 1). Complete follow up was available for all patients.

3.1. IONM setup

About 137 (90%) patients had successful IONM with the initial endotracheal tube position. Fifteen (10%) patients needed further tube adjustment under fiberoptic bronchoscopy (initial unsuccessful monitoring). All these patients (15/15 patients, 100%) had no EMG signal on the first pre-resection vagal nerve stimulation. Specific reasons for initial unsuccessful IONM were tube malrotation in 8 patients (53%); in 5 patients (33%) the endotracheal surface electrodes were inserted too deep ($n = 4$) (mean 23.25 cm, range 22–24 cm from oral) or too high ($n = 1$); improper tube size in 1 patient (7%); and displacement of the external sternal wires in 1 case (7%).

As for tube malrotation, 6 of the 8 patients (75%) were towards the right side (clockwise tube turn following intubation).

In the only case of improper tube size, the tube tends to rotate clockwise; in this case, the anesthesiologist needs to change the dedicated tube with a bigger one of one size, from 7 mm to 8 mm internal diameter (ID).

Thus, in 93% of cases (14/15), causes of unsuccessful IONM were due to a non-optimal contact of the endotracheal surface electrodes to the vocal cords (Table 2).

After adjustment of tube position and electrodes, all patients had final successful IONM prior thyroid resection with optimal vagal EMG signal.

To establish the number of thyroidectomies required before achieving an effective and safe IONM technique, all of the procedures were divided into three chronological groups of about 50 cases (groups 1, 2, and 3). There were no statistical difference between the three groups for distribution of epidemiological characteristics, thyroid pathology, and mean weight of the thyroid ($p > 0.05$) (data not shown). There were 10 unsuccessful cases in group 1, 4 cases in group 2, and 1 in group 3. Thus, the success rates of prompt IONM technique were 80% (40/50 patients) in group 1, 92% (46/50 patients) in group 2, and 98% (49/50) in group 3, respectively ($p < 0.05$). Details of each group are shown in Table 3.

There was no correlation between epidemiological characteristics, thyroid volume, thyroid pathology and the equipment malfunctions (data not shown).

The overall mean operative time was 91.6 (range 59–130) min. In group 1, the overall mean operative time was 111.0 (78–139) min, while operative time in group 2 was 93 (66–134) min and group 3 86 (59–130) min ($p < 0.03$). Both AOT and SOT of group 1 were significantly higher than groups 2 and 3.

The mean supramaximal current was 1 mA. The maximal current used for supramaximal stimulation was 1.5 mA, and the minimal current was 0.5 mA.

The nerve stimulator/probe was applied a mean of 13 times (range 8–19 times) per case, for a total of 1798 applications. There were no significant differences in the number of probe applications per period study, thyroid volume or treated pathologies (data not shown).

Table 1
Preoperative characteristics and operative parameters in 152 patients undergoing elective bilateral thyroidectomy with IONM.

	N
Age (years)	39.8 (19–77)
Women	97
Men	55
Thyroid volume (mL)[a]	41 (11–149)
Dominant nodule diameter (cm)	3.5 (1.2–7.9)
Nerves at risk	304
Thyroid pathology	
-Non toxic nodular goiter	88 (58)
-Hyperthyroidism[b]	39 (26)
-Thyroid cancer[c]	25 (16)

Data are numbers or mean with percentages or ranges in parentheses.
[a] Estimated by preoperative ultrasonography (US).
[b] Toxic nodular goiter ($n = 23$), Graves's disease ($n = 16$).
[c] Papillary carcinoma ($n = 19$), follicular carcinoma ($n = 5$), and medullary carcinoma ($n = 1$).

Table 2
Details of IONM setup problems.

|	N	%
Endotracheal surface electrodes		
●Malrotation[a]	8	53
●Insertion to deep[b]	4	26
●High insertion	1	7
●Improper tube size[c]	1	7
External wires		
●Displacement of sternal wires	1	7
Total	15	10 (15/152)

About 93% (14/15) non-optimal contact of endotracheal surface electrodes to the vocal cords.
[a] About 6/8, 75% clockwise rotation to right.
[b] Mean 23.25 cm, range 22–24 cm from oral.
[c] Tube small and rotated: anesthesiologist changed tube from 7 mm to 8 mm ID.

Table 3
Learning curve.
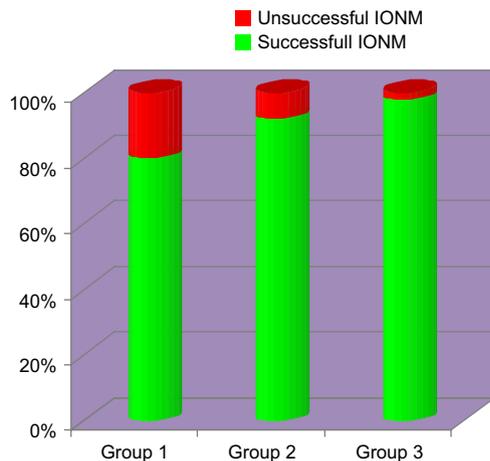
Group 1(from first IONM thyroidectomy to 50th) :
  IONM successful rate 80% (40/50 patients)
Group 2(from 51st to100) :
  IONM successful rate 92% (46/50) $p < 0.05$}
Group 3 (from 101 to 152): IONM successful rate 98% (49/50)

3.2. Morbidity

As for systemic interaction, we found no cardiac interaction (arrhythmia), no pulmonary (bronchospasm) interaction intra- and postoperatively due to vagal nerve stimulation. No patient had any motility disorders of the gastrointestinal tract postoperatively.

About 76% of patients experienced a 48 h hospital stay, 24% of patients a 72 h stay.

No mortality was observed. Overall morbidity was as high as 16.4% ($N = 25$) and in most cases included transient complications (Table 4).

No patient required reoperation. There were no other peri-operative incidents: in particular no hemorrhagic complications or cervical hematoma was observed. One patient experienced a wound seroma. One patient reported wound infection.

No bilateral vocal cord paresis or paralysis occurred in the study period. There was 1 case of permanent hypocalcemia. No case of permanent RLN paralysis was reported in the study group.

The incidence of temporary hypoparathyroidism was 11.8% (18/152). One patient was readmitted with a diagnosis of symptomatic hypocalcemia 2 days after discharge.

The vagus nerve and the RLN were intraoperatively correctly localized and monitored bilaterally in all cases (100%, 304 nerves at risk). The overall incidence of temporary RLN injury was 2.6% (4 patients). Transient recurrent nerve palsies were seen without changes during the entire study period. Loss or decrease in amplitude of EMG signals was seen in all these patients with RLN injury (true positive IONM signal, 100%).

Table 4
Morbidity.

	N (%)
Wound complication	2 (1.3)
Permanent hypoparathyroidism	1 (0.65)
Permanent RLN injury	0
Temporary hypocalcemia	18 (11.8)
Temporary RLN injury	4 (2.6)
Total	25 (16.4%)

In detail, a modified EMG amplitude signal was seen in 2 patients during the *first* lobectomy (two left lobectomies); in 2 patients during the *second* lobectomy (one right, one left RLNs).

The first 2 patients were scheduled for a total thyroidectomy for a bilateral diffuse multinodular goiter (one video-assisted thyroidectomy). The procedures were stopped after the first lobectomy to avoid the potential for bilateral vocal cord paralysis (one-stage thyroidectomy).[4,6,10] Early intraoperative and post-operative steroid administration was given. Both patients were dysphonic and laryngoscopy performed at 48 h postoperatively confirmed a reduction in the movement of the left vocal cord. A repeated examination was performed at 1, 2, and 3 months after the operation until full recovery of vocal cord function was confirmed after speech therapy. The patients underwent complete thyroid-ectomy after 3 and 4 months, respectively, from first operation without complications.

Patients 3 and 4 had a minimal vocal cord dysfunction which was diagnosed laryngoscopically. Full recovery of vocal cord function was confirmed after logopedy at 2 and 6 months postoperatively.

By mapping with IONM the cervical course of the RLN, proximally and distally, we found in all cases the disrupted point of conduction. In detail, in 3/4 cases the RLN was injured in last 2 cm of its course, in 1 case more proximally. In all these cases an external RLN branching was present. Visually it was hard to judge the nerve injury in 3/4 cases (probably was a stretch or blunt injuries).

Postoperative laryngoscopy confirms no case of false negative IONM signal.

We were not involved in any lawsuit as a result of these RLN injuries.

4. Discussion

The availability of a non-invasive monitoring device for RLN led us to introduce this tool for all elective bilateral thyroid procedures. To our knowledge, this is the first series of patients undergoing thyroidectomy with the use of IONM in Italy.

Standardization of IONM technique, surgical training, specific experience and a interdisciplinary collaboration are essential for optimal use of this new device.

A standardized technique includes both vagal and RLNs stimulation before, during and after thyroid resection. This is in concordance with Timmermann, Dralle and Chiang remarks.[4,6,10] Based on the same principle, Ulmer developed a real-time RLN monitoring by continuous stimulation of the vagal nerve with an implanted tripolar cuff electrode.[12] Pre-resection vagal nerve stimulation has the advantage to detect equipment failures early before thyroid-ectomy.[4,6,10] Vagus and RLNs stimulation during and after resection prove RLN anatomy and function.[4,6,10]

Using the neuromonitoring procedure we were able to exclude the presence of RLN in each step of dissection and ligation. A negative EMG response indicates a non-nerve structure or altered function of the RLN. IONM allowed us to stage contralateral surgery if RLN damage is diagnosed at *first* lobectomy, thereby avoiding the potential for bilateral vocal cord paralysis. No bilateral paralysis was diagnosed in the study period. In the case of patients with pre-existing RLN morbidity, intraoperative assessment of RLN function with IONM may facilitate reoperations.[6] Moreover, all patient with intraoperative diagnose of RLN injury were given early intra-operative and postopearive steroid administration.[13]

With IONM we were able to locate routinely the disrupted point of conduction of RLN (immediately and intraoperatively) in all cases with lost or decrease EMG signal. Several studies have shown how poor the surgeon is at judging RLN injury intraoperatively.[14–16] RLN

injury during thyroidectomy may be caused by traction, pressure, crush, electrical injury, ligature, ischemia, or suction injury without transaction.[10,17] In this study, in 3/4 cases (75%) the injured RLN appears intact to the surgeon's eye. Other authors found that in only 1 of 10 cases of RLN injury were surgeons aware of the injury.[14–16]

IONM in thyroid surgery is appealing. However, the adoption of this technique is hampered by the steep learning curve and the fear of exposing patients to excessive prolongation of operative time and morbidity. Equipment malfunction or improper endotracheal tube position can result in unsuccessful monitoring which could potentially give rise to misleading information that might increase the risk of RLN injury.[18] We assessed how many patients should be monitored to overcome this learning curve. In this study, the success rates of IONM technique were considerably associated with experience. A clear turning point, with improved operative variables and safe IONM technique, was seen in about 50 patients. In fact, patients were not exposed to excessive morbidity during this learning curve. Vagal nerve stimulation did not cause any cardiac, pulmonary, or gastrointestinal interaction. The procedural malfunctions significantly decreased after the first 50 procedures. The length of operation decreased after the first 50 cases. Other authors stated that the intraoperative neuromonitoring in thyroid surgery is associated with a longer learning curve lasting several years.[19] A minimum of 100 operations using IONM are required according to Dralle.[20]

In this study, 93% of unsuccessful IONM cases were due to a non-optimal contact of the endotracheal surface electrodes to the vocal cords for displacement. The position of the electrodes can be displaced and not be detected when the patient's head and neck position is changed from the initial for tracheal intubation to full extension for thyroid surgery.[18] Displacement must be detected easily by checking the impedance imbalance of the NIM EMG monitor.

The study represents the result of the collaboration at the University Hospital of Varese between the Department of Surgical Sciences, the Division of Endocrinology, Anesthesiology and Neurology. Our good results of IONM can be explained by a combination of conscientious preparation of the equipment and the routine and experience of the multidisciplinary team. In fact, each IONM thyroidectomy was performed cooperatively with different specialties. This is in concordance with the interdisciplinary neuromonitoring study groups recently proposed in literature.[4,6] Moreover, surgeons need to implement all their knowledge with this new technology and be experienced in neurophysiology to make optimal surgical decision for their patients: in fact, IONM provides original data on RLN and vagal neurophysiology and pathology.[6]

IONM in thyroid surgery has, more than any other new technology, created extreme controversy and debate, particularly within the establishment.[8,21,22] On reflection this is not surprising given that few specialist surgeons are trained to do it. With continuous technical refinements, learning curve and experience, more patients could become candidates for IONM.[5] Currently, in our academic setting, residents use the RLN monitoring during their training in endocrine surgery. The use of neuromonitoring provides new instructive information for operation by ascertaining where and how the RLN has been injured.

IONM during thyroidectomy may be easily organized in centers of endocrine surgery. However, most patients with thyroid problems are still treated in smaller surgical units in Italy. Therefore, IONM may be a logistical problem.

IONM has been claimed in some studies to reduce rates of nerve injury, whereas other studies have found no benefit.[8,23] Hermann concluded in a prospective study that neuromonitoring is useful for identifying the recurrent laryngeal nerve, in particular if the anatomic situation is complicated by prior surgery, large tissue masses.[24] In this study, RLN palsy still occurred with routine identification of RLN combined with IONM, although all cases were temporary. No permanent palsies were diagnosed in the study period. Studies have shown that only routine exposure of the RLN is associated with very low rates of injury in high volume centers.[25,26]

A significant reduction in the rates of postoperative complications was not possible to be demonstrated in the present study. In order to compare the use of IONM, a multi-center trial with large numbers and well-defined groups is needed. Eisele noted that to show a reduction in RLN paralysis rates from 2% to 1% per nerve at risk, a study group of approximately 1000 patients would be necessary.[27]

The gold standard is still thyroidectomy with routine visualization of the RLN: this approach is essential in case of malfunction of this novel technology.

There are other criticisms on the use of IONM, focused mainly on the cost: the device is expensive. In consideration of its cost, we did not perform any statistical study in this study. Recently, authors stated that the implementation of the clinical pathway for thyroid operations had successfully reduced clinically variability, hospital stay and mean cost.[28]

Perhaps, the monitoring of nerves during surgical procedures potentially reduces the medico-legal liability for surgeons.[29]

Acknowledgements

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