

Intraoperative Ultrasonographic Assessment of Vocal Cord motion following pediatric thyroidectomy in the Era of COVID-19, a double-blind study

ABSTRACT

Unilateral vocal cord paralysis (UVCP) is a known complication of thyroid surgery, due to iatrogenic recurrent laryngeal nerve injury, with reported rates of 2-5% in children. The gold standard for assessing vocal cord function in flexible nasendoscopy (FNE) examination, which is considered high-risk for contraction of the COVID-19 virus. Intraoperative ultrasonographic assessment (IUA) of vocal cord function is a non-invasive and relatively simple procedure, performed in a supine position under general anesthesia.

Objectives: To evaluate the validity of IUA modality in children undergoing thyroidectomy, and to compare it to the standard FNE.

Design: A prospective double-blind study covering 24 months (March 2019-March 2021). Twenty thyroid lobectomies were performed, during 15 surgeries. Vocal cord function was assessed three times: Preoperatively by FNE, intraoperative (IUA) following extubation, and a second FNE on the first post-operative day.

Settings: A tertiary pediatric hospital.

Results: The overall accuracy of IUA results in our study was 92%. IUA sensitivity, specificity, positive and negative predictive values were 100%, 89%, 33%, and 100% respectively. Patient's age demonstrated borderline significance ($p=0.08$). The resident's experience was associated with a better correlation between IUA and FNE results ($p<0.05$).

Conclusions: IUA of vocal cord motion has a high accuracy rate for detection of iatrogenic vocal cord paralysis, similar to FNE. It is easily learned by residents, well tolerated by children, and it provides a safe and valid alternative modality while ensuring the safety of the medical staff in treating patients, especially in times of COVID-19 pandemic.

KEYWORDS

Ultrasound assessment, Friedman criteria, COVID-19, Paralysis, recurrent laryngeal nerve (RLN) injury, Nerve monitoring, IONM, pediatric.

Key points:

- Unilateral vocal cord palsy occurs in 5% of pediatric thyroid surgery.
- Intraoperative assessment of vocal cord function, according to the Friedman criteria is easy to learn and master by residents, with no additional costs, and without discomfort to the child.
- Level of agreement between IUA and FNE are 92%
- Recording and storage of examinations is beneficial for resident training and teaching by the attending physicians.
- IUA is safer than FNE in preventing exposure of medical staff to COVID-19 virus in the nasopharyngeal mucosa of the patients and can potentially lower infection rates.

Level of evidence: 4

Data availability statements:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest and financial disclosure:

The authors have no funding, financial relationships, or conflicts of interest to disclose.

INTRODUCTION

Complications of thyroid surgery, both in adults and children, include among others, transient and permanent unilateral vocal cord paralysis (UVCP) due to iatrogenic recurrent laryngeal nerve (RLN) injury¹. Clinical manifestations of such neurological damage vary from mild hoarseness to aspirations and respiratory distress, depending on the severity of injury and the extent of compensation from the contralateral vocal cord (VC)². When bilateral VC injury occurs, the patient often requires emergent tracheotomy. Reported rates of VC palsy among pediatric patients undergoing thyroidectomies range from 2-5%³.

The gold standard for the assessment of vocal cord mobility is flexible naso-endoscopy (FNE) examination, which enables a direct vision of the larynx⁴. Although it is relatively safe for the patient, this examination might generate aerosols. It is considered high-risk for contraction of the COVID-19 virus, detected in the mucosa of the upper airways⁵. Furthermore, FNE is an invasive procedure, which often in children is more complicated and time-consuming due to lack of cooperation from the child⁶.

Intraoperative ultrasonographic assessment (IUA) of VC function is a non-invasive and relatively simple procedure, performed in supine position under general anesthesia, similar to awake transcutaneous cervical ultrasonography^{7,8}. It is painless and non-traumatic and does not require patient cooperation. Since it is transcutaneous, it does not expose the examiner to aerosols and droplets contrary to FNE.

OBJECTIVES

We sought to evaluate the validity of intraoperative ultrasonographic assessment of VC motion in children undergoing thyroidectomy, and to compare this modality to the standard FNE.

METHODS

Study design

After receiving the institution review board (IRB) approval, and a written informed consent from the parents, we conducted a prospective study of pediatric patients undergoing thyroidectomies for various reasons, in the largest tertiary pediatric medical center in the country. The study period was 24 months (March 2019- March 2021). Half of the study period occurred during the COVID-19 pandemic.

Study protocol

All patients underwent preoperative neck ultrasonography (US) and fine-needle aspiration (FNA), as well as blood work for thyroid function (TSH, FT3, FT4). FNE was performed in all patients during preoperative evaluation, as well as COVID-19 nasopharyngeal swab test following the outburst of the epidemic. Following extubation, with the patient still sedated and in the supine position, an IUA of the VC was performed by a designated resident. On the first postoperative day (POD-1), a second double-blind FNE was done in our clinic, by a different resident, who did not participate in the surgery.

Surgeries

All thyroidectomies were performed by the same two highly trained pediatric head and neck surgeons. Some of the surgeries were primaries, and some were revisions, either hemi-thyroidectomy or total thyroidectomy. Some of the patients underwent central compartment and/or lateral neck dissections, according to clinical indications, which were benign and malignant lesions. Intraoperative nerve monitoring (IONM) system was applied in all surgeries, using intermittent RLN stimulation with a monopolar probe, and a specialized pediatric oro-tracheal tube.

Assessment of VC function

Assessment of VC function using ultrasound required autodidactic training of 2 hours following basic instructions from a pediatric anesthesiologist and online videos. A flexible pediatric endoscope (Karl Storz©) was used in all FNE examinations. IUA were performed by Zonare Pro Ultrasound system© available in our operating rooms. Ultrasonographic assessment was performed using a midline approach. The transducer was placed transversely over the thyroid cartilage in the frontal midline plane. During spontaneous respiration, VC motion, according to Friedman criteria⁹, was assessed for asymmetry between right and left VC (adduction and abduction), abnormal arytenoid movements, lengths and alignment of both VC and anterior bowing.

Statistical Analysis

Descriptive statistics was used to quantify different patient demographics and information related to the surgeries, including complications. Receiver operating characteristic (ROC) analysis assessed accuracy of IUA against the gold standard; i.e.

FNE. Diagnostic tests for test validity included sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Multivariate logistic regression analysis assessed different prognostic factors with the level of agreement between IUA and FNE results on POD1 (either normal function or paralysis).

Reporting guidelines:

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RESULTS

Thirteen children (8 girls, 5 boys) underwent 20 thyroid lobectomies (15 surgeries in total) during the study period. The average age was 11.8 years (6.1-16.5 years). Two children had a history of bone marrow transplantation in early childhood. The indications for surgery were mostly oncologic (primary or completion surgery). Preoperative cytology for 15 lobes according to Bethesda classification was B1 (13%), B2 (13%), B3 (35%), B4 (27%), B6 (13%). VC function assessed on preoperative FNE was normal for all children (100%). During COVID-19 era, all patients underwent nasopharyngeal swab test. All patients were COVID-19 negative. Twenty thyroid lobes were resected. Surgeries included 8 hemithyroidectomies (53%), 5 total thyroidectomies (33%) and 2 completion hemithyroidectomies (13%). Four children (31%) underwent bilateral level 6 neck dissection, and one patient (7.7%) underwent lateral neck dissection. The final pathology was papillary thyroid

carcinoma (PTC) in 8 lobes (40%), Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) in 2 lobes (10%), Hashimoto or lymphocytic thyroiditis in 3 (15%), one multi-nodular goiter (5%) and the rest were benign cysts (30%). Two cases of PTC had extrathyroid extension (ETE) and one had nodal extracapsular extension (ECE). All 5 children with malignant pathology received post-operative radioiodine therapy (RAI). Post-operative hypocalcemia was not seen in any of the patients. Results are depicted in table 1. Malignancy rates according to preoperative Bethesda classification and final pathology results for B1, B2, B3, B4, B6 were- 100%, 50%, 0%, 25% and 100%, respectively (table 2).

VC assessments post operatively were performed on all patients with IUA and FNE on POD1. In three children IUA was inconclusive, in whom FNE was normal in two and paralysis was noted in one (patient H). Level of agreement between IUA and FNE was 92%. Area under the curve (AUC) was 96%, and the overall model quality was 0.87, although not meeting statistical significance criteria ($p=0.1$). Results were not associated with gender, prior history, VC side, indication for surgery or nodule size. Patient's age demonstrated borderline significance ($p=0.08$), as patients older than 10 years had higher levels of agreement. Level of experience was associated with better IUA accuracy, demonstrated by higher levels of agreement between the two modalities in the second half of the study period compared to the first period ($p<0.05$). Diagnostic studies for IUA demonstrated sensitivity, specificity, PPV and NPV of 100%, 89%, 33% and 100% respectively (table 3).

During the surgery of patient H, a large benign cyst compressed and dislodged the left VC, causing loss of signal on IONM. The IUA of the left VC showed no movement, which was consistent with the Friedman criteria¹⁰ (figure 1). FNE results on POD1 were consistent with the diagnosis of UVCP. On first follow up visit, six weeks after

surgery, a second IUA and FNE assessments in the clinic revealed no change in outcome (VC paralysis), shown in picture 1. The patient exhibited mild hoarseness, with no respiratory distress and no signs or complaints of aspiration.

DISCUSSION

Thyroid surgery is a risk factor for UVCP. The most common clinical presentation of UVCP is stridor in 70% of cases, followed by dysphonia (50%) and aspiration of food (25%)¹⁰. Although rare, in cases of bilateral VC palsy, respiratory distress can develop which may require re-intubation or tracheotomy¹¹. The indications for pediatric thyroidectomies vary from benign to malignant pathologies¹². The incidence of Grave's disease in children 1:10,000 children¹³, with 70% failure rate under medical treatment, that ultimately require surgical intervention or RAI. Papillary thyroid carcinoma (PTC) is the most common malignant tumor of the thyroid gland, both in adults and in children, and it has a 3% yearly-increase in incidence in children¹⁴. In a study that assessed UVCP in children undergoing thyroid surgery, Baumgarten et al. found a 2% risk for temporary neuropraxia among 464 participants¹⁵. In another study, Bussi res et al. reported 4.2% risk for RLN injury in 118 pediatric thyroidectomies¹⁶. The use of IONM assists the surgeon in avoiding intraoperative nerve injuries. In the last two decades it has become the standard of care¹⁷. In our medical center, all thyroidectomies are performed using this system.

Assessment of VC function following thyroidectomies is therefore of clinical value. FNE in children can be challenging due to the discomfort nature of the examination⁶. Still, in our medical center FNE on POD1 following thyroid surgery is the standard of care. Otolaryngologists, are at increased risk for contracting the COVID-19 virus

when treating patients, especially when performing FNE among other procedures¹⁸. A need for differentiating between elective and urgent procedures exists, to minimize unnecessary exposure to nasopharyngeal mucosa, and when possible, telemedicine is preferred¹⁹. If endoscopy is required, remote fiberoptic endoscopy, with the use of personal protective equipment (PPE), either N95 masks or sometimes powered air purifying respirators (PAPR) is required to avoid contamination, and to maintain safety of medical teams²⁰.

Awake transcutaneous ultrasonographic VC examination in the clinic is a safe and non-invasive alternative for FNE, as reported in the literature. Wang et al. compared the maximal glottis angle (MGA) and vocal fold arytenoid angle (VAA) in 45 normal-functioning VC and known UVCP children²¹. He reported 96% agreement between FNE and awake sonographic findings. Vats et al.⁷ compared FNE results with IUA of VC in 55 children and reported 82% agreement in children over 1 year of age. Shaath et al.²² published results on iatrogenic UVCP following heart surgery diagnosed with IUA, in ten children who developed respiratory distress after extubation. The reported sensitivity and specificity were 100% and 80%, respectively. Similar results were published by Jadcherla et al.²³ In our study of 20 thyroid lobectomies, transient UVCP occurred in 5% of cases, which is consistent with previous reports, mentioned above. Diagnostic tests for IUA in our study demonstrated sensitivity, specificity, PPV and NPV of 100%, 89%, 33% and 100% respectively. These results are similar to Jadcherla et al.²³ The overall agreement between IUA and FNE results in our study was 92%, which represents a remarkably high accuracy rate of IUA modality. Results were not associated with gender, prior history, VC side, indication for surgery or nodule size with IUA success rates. IUA was more accurate in older patients (more than 10 years), although only borderline significance was seen ($p=0.08$). Higher

accuracy levels were seen later in the study period highlighting the importance of personal experience of the device operator ($p<0.05$).

Neck ultrasound (US) is an important imaging modality for an otolaryngologist in all areas of cervical assessments. By mastering this skill intraoperatively, post-operative FNE can potentially be avoided. Apart from diagnosis, the US is an excellent teaching modality for residents. By recording examinations, residents can later consult with attending physicians and get a second opinion. In the era of COVID-19 there is a need for adjustment in the clinical training of otolaryngology residents worldwide^{24,25}. The use of US, and specifically IUA, is an excellent opportunity to do so. In terms of costs, although US machines are not common in an outpatient clinic, they are commonly used by anesthesiologists around the world in operating rooms. Therefore, IUA assessments does not require any additional costs or expenses. Furthermore, in clinics where US device is available, the recorded examinations can also be used to monitor UVCP during follow-up visits by comparing images from previous examinations.

Limitations

The relatively small sample and the low UVCP rate is an important limitation. We believe that future studies with a large number of participants are required.

Conclusions

To the best of our knowledge, our clinical study is the first to report the use of IUA of VC function following pediatric thyroidectomies by residents. In this era of COVID-

19, IUA provides additional benefit compared to the standard FNE, as a valid non-invasive modality with high detection rates of UVCP, without exposing the otolaryngologist to the patient's nasopharynx and without causing inconveniences to the child.

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