

Peer Review File

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Reviewer A

A very interesting and well written article on an interesting topic. The sample is large. Please specify better what to do when a global LOS occurred. Do you control the tube positioning? How much time do you wait for an intraoperative recovery? Did you evaluate the patients at 6 or a 12 months? Did you stop your surgical procedure when there is a LOS?

>> Thank you for your advice. When a global LOS occurred, we followed the standard procedure according to the INMSG group guideline. We also check the tube positioning and machine error. The final decision was made 20 minutes after LOS occurred. We evaluate the vocal cord function every 2-3 months until the vocal cord movement recover.

When LOS occurs, we stop our surgical procedure and we pay attention the nerve stretch or traction.

We add the above to the text. (page 9 line 21-)

I think references can be improved and updated (see for example Calò PG et al. Interpretation of intraoperative recurrent laryngeal nerve monitoring signals: The importance of a correct standardization. Int J Surg. 2016 Apr;28 Suppl 1:S54-8.) {Calò, 2016 #236}

>> Thank you for your advice. We add this paper to the reference. And also, { International neural monitoring study group guideline 2018 part I: Staging bilateral thyroid surgery with monitoring loss of signal Schneider, 2018, Laryngoscope } { International neuromonitoring study group guidelines 2018: Part II: Optimal recurrent laryngeal nerve management for invasive thyroid cancer-incorporation of surgical, laryngeal, and neural electrophysiologic data Wu, 2018, Laryngoscope} were added.

Reviewer B

There are a few points I would like to address. There is a large number of cases and the data represented seems fine, and overall seems to be reasonably well written. But I'm not sure about the conclusions and clinical applications. It basically supports Schneider et al (and many other paper) results that a segmental injury is more like to result in vocal fold palsy and represent a more severe injury, whereas global is likely to have a higher rate of recovery. But that paper was also looking at identifying risk factors which makes it more clinically relevant. So first of all, I noticed overwhelmingly far more total thyroidectomies in the study than hemithyroidectomy. So I would like a comment about whether an intraoperative LOS changed the surgical approach. I.e. when the planned surgery was a total thyroidectomy, if a LOS occurred on the first side, would that mean that the second side wasn't completed? And why or why not. As usually this would be done in order to prevent the small but disastrous risk of bilateral cord palsy (unless there are particular case circumstances where it's necessary to complete the total thyroidectomy at that index operation).

>> Thank you for your advice. In our hospital, when hemithyroidectomy is planned, IONM was not routinely done, but total thyroidectomies were performed routinely IONM. So in this study, the number of hemithyroidectomy was small. When the imaging test (CT scan or ultrasonography) suggested the tumor has invasion to the recurrent laryngeal nerve palsy, but laryngeal fiber scope test showed normal vocal function, we performed IONM.

In Japan, surgeons prefer hemithyroidectomy rather than total thyroidectomy. In Japanese guideline for thyroid cancer, total thyroidectomy would be performed only for patients with preoperative recurrent laryngeal nerve palsy, tracheal invasion and/or lymph node metastasis > 3cm, and/or distant metastasis, etc. For benign tumor or Graves disease, the median of thyroid volume is more than 100g. For our cases with diffuse goiter, we feel that hemithyroidectomy is difficult because isthmus is very thick,

We add the above to the text.(page 10 line 17-)

This leads into a comment about your conclusion. You say that “we could change the management of the LOS nerves according to the clinical nerve LOS type and the histological type”. You basically only mention one line at the end of your discussion that you could refer the cancer and segmental LOS patients for additional therapy.

Whereas benign could wait at see. Is that the only difference it would make to your management?

I should imagine there are many more factors (voice assessment, laryngoscopy appearance, patient factors etc) that would impact your decision to refer for speech therapy anyway rather than just the type of LOS.

So it doesn't seem like that much of a benefit. Or that it would really change your management much at all.

>> We delete the sentences (we could change the management of the LOS nerves according to the clinical nerve LOS type and the histological type)

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And I think it would be worth commenting whether it could change your intraoperative management. For example, if in fact you wouldn't normally complete the contralateral side due to LOS on the first side... but with these results perhaps you would be happy completing the contralateral side if the LOS was global and benign rather than segmental and malignant, for example.

>> Thank you for your advice. We modified our text as advised (see page 14, line 5).

When the planned surgery was a total thyroidectomy, if the true LOS occurred on the first side, we have to decide whether to continue the surgery or stop it. The INMSG recommends that neural monitoring information should be used in planned bilateral procedures by staging the surgery in the case of ipsilateral LOS (10, 11). With our results, we would complete the contralateral side if the LOS was global and benign rather than segmental and malignant.

And in the case of global LOS especially, I think you need to address the possibility of false LOS. Such as monitor dysfunction, loss of the circuit, change in ETT position, neuromuscular agents from the anaesthetist etc. As this can be fairly common and present a dilemma for surgeons.

And whether this was considered and whether you had any strategies for assessing this intraoperatively. So I think the results support prognostic information about segmental vs global LOS, but this has already been presented many times before. I think that overall the discussion section in this paper could benefit from more expansion about the clinical application of this information, especially if your conclusion is that it would change your management.

>> Thank you for your advice. We modified our text as advised (see page 13, line 9).

When the LOS occurred, we have to exclude the possibility of false LOS. In the case of global LOS especially, we check the monitor dysfunction, change in electromyography (EMG) endotracheal tube position, neuromuscular agents from the anaesthetist, etc. At first, we check the result of neuromuscular monitoring. The train-of-four (TOF) monitoring is available for every patients who undergoes neuromuscular blockade during surgery in our hospital. The TOF ratio > 0.7 signifies a satisfactory recovery of the neuromuscular function and when the TOF ratio is low, some waiting time may be needed to wear off the effect, or selective reversal binding agents (sugammadex) should be given.

Next, we perform the contralateral vagus nerve stimulation. Negative contralateral vagus nerve stimulation means the possibility of the monitor equipment dysfunction. The recording electrodes, grounding electrode and associated connections at the interface-connector box and monitor might be dislodged or displaced and should be recheck. We also confirm the accurate surface electrode positions of an EMG tube by fiber-optic laryngoscope.