Unexpected mapping of recurrent laryngeal nerve by fluorescence-guided surgery using near-infrared indocyanine green angiography

Abstract. Background. The recurrent laryngeal nerve (RLN) damage and parathyroid gland injury are the most severe complications of thyroid surgery. The possibility of RLN confirmation in the near-infrared spectrum after the injection of indocyanine green (ICG) was not yet been studied. Aim: to evaluate the ICG angiography for the identification of RLN during thyroid and parathyroid surgery. Materials and methods. ICG angiography of RLN was performed in 7 patients. An intraoperative neuromonitoring was applied as a method of controlling RLN. During the operation, parathyroid glands and RLN were identified by visual inspection (naked eye). To further confirm the location of the parathyroid glands by autofluorescence, an intravenous injection of ICG was performed with a concentration of 0.25 mg/kg followed by the application of the image-based system. Results. A good signal was achieved in the near-infrared spectrum from the RLN in all cases after the ICG injection. Sufficient blood perfusion of the RLN could be considered as a reasonable explanation for the exhibition of a good ICG near-infrared signal. Conclusions. ICG use might be a helpful approach for the confirmation of the RLN in addition to routine visual identification. Such function could be applied during fluorescence-guided surgery to evaluate the parathyroid gland autofluorescence. Visualization of RLN by ICG angiography is considered as an additional useful feature to prevent RLN injury.

Keywords: recurrent laryngeal nerve; autofluorescence of parathyroid glands; fluorescence-guided surgery; indocyanine green; thyroid surgery; parathyroid surgery; prevention of postoperative complications

Introduction

The recurrent laryngeal nerve (RLN) damage and parathyroid gland injury are the most severe complications of thyroid surgery, accounting from 0.3 to over 38 % [1–4]. The risk for such complications is higher in the case of neck dissection or reoperations, in the central neck compartment, as well as in case of large goiters due to changes in anatomic landmarks [5–8]. The parathyroid glands might be evaluated by using fluorescence-guided surgery (FGS), judging their near-infrared autofluorescence (NIRAF), which could be enhanced by the application of contrast dye indocyanine green (ICG) [9–12].

To prevent RLN damage, intraoperative neuromonitoring (IONM) is widely used in after visual confirmation by the naked eye [4, 13]. Intraoperative localization of parathyroid glands is also mainly under visual identification, which could be a difficult task in case of reoperations or retrosternal localization [14–17]. Also, RLN detection is important to discriminate upper from lower parathyroid glands by evaluating their relation to the RLN in a patient with parathyroid adenomas [18]. The scientific discovery of the parathyroid autofluorescence in the NIRAF was given a new possibility for intraoperative parathyroid identification. A FGS is a useful approach to detecting parathyroid NIRAF by image-based or probe-based systems with or without a fluorophore. The commonly applied contrast fluorophore is ICG, which is a neurovascular dye [19]. The ICG is frequently used in FGS also to contrast various peripheral nerves [20, 21]. However, little is known about the role of the ICG to contrast the RLN.

The aim of this study was to evaluate the possibility of ICG angiography for the identification of the RLN during thyroid and parathyroid surgery.

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Materials and methods

This prospective study cohort comprised 7 patients, who were surgically treated for thyroid and parathyroid neoplasms at the Department of Surgery, Taras Shevchenko National University of Kyiv, Verum Expert Clinic (Kyiv, Ukraine). Preoperatively all patients underwent routine clinical investigations as demonstrated in our previous reports [14, 22]. Neck ultrasonography and fine needle aspiration biopsy were performed for all patients. Measurement of serum Ca²⁺ was performed before and on the next day after the operation, whereas parathormone was assessed on the 2nd day postoperatively. A capsular dissection technique was applied in all operations.

During the operation, parathyroid glands and RLN were identified by visual inspection (naked eye). To further confirm the location of the parathyroid glands by their NIRAF signal, an intravenous injection of ICG was performed with a concentration of 0.25 mg/kg (Diagnostic Green, Germany) followed by application of the image-based system Fluobeam-800 or Fluobeam LX (Fluoptics, France). Both image-based systems were equipped with a near-infrared laser camera, a console to adjust near-infrared signal, and a monitor with a touchscreen. Assessment of ICG near-infrared signal was performed in a dark room with operation lights off. NIRAF of the parathyroid glands and near-infrared signals from the adjacent tissues were evaluated 1–2 minutes after the intravenous injection of ICG by the manual holding of a near-infrared camera at a distance of 20 cm over the operation field [10, 23]. RLN was also confirmed by IONM by using C2 NerveMonitor, equipped with a straight bipolar fork-shaped stimulation probe and adhesive electrodes for the laryngeal tube (Inomed, Germany). IONM was applied after the visual identification of RLN, before and after ICG injection. The ICG signal was assessed within the area of the RLN location with simultaneous confirmation by IONM while evaluating the parathyroid glands. Quantitative measurements were not performed. Indirect laryngoscopy was performed before surgery and on the 2nd postoperative day for evaluation of possible vocal cord disorders.

Results

The RLNs were identified with confidence in 6 cases by visual inspection, whereas in one case we had some doubts about its location. In view of our goal, we performed careful dissection of the RLN at a distance of 3–5 cm from the point of entering the larynx in the first 5 patients (Fig. 1). Then, in the next two patients (cases 6–7) we performed regular steps without careful dissection of the RLN in order to check the ICG angiography of the RLN in the routine surgical settings (Fig. 2). In all cases, the RLN was confirmed by IONM after the dissection, then an injection of ICG was performed resulting in a distinct NIR signal from the RLN (Fig. 3, 4). In cases 6 and 7 (without careful dissection of the RLN) a good intensity NIR signal was also detected through the undissected tissues covering the RLN (Fig. 4). After several applications of the IONM probe, good signals were obtained from the RLN, containing ICG in the blood vessels supplying the nerve (Fig. 1, 2). The parathyroid glands were identified at visual inspec-
tion followed by confirmation of their NIRAF using the image-based system in all patients. Pathologic changes in vocal cords were not identified by indirect laryngoscopy pre- or postoperatively in all patients.

Discussion

Our study underlined the importance of intraoperative confirmation of the RLN by an alternative approach in addition to routine visual identification and IONM validation. To the best of our knowledge, this is the first study, evaluating the RLN by using ICG fluorophore.

Sufficient blood perfusion of the RLN could be considered as a reasonable explanation for the exhibition of a good ICG near-infrared signal. Our findings are in line with Tanaka et al., who showed a strong signal for ICG fluorescent angiography in the vastus lateralis motor nerve and suggested presentation of the axial blood perfusion in the nervous tissue [21]. Also, a review article by Wu et al. summarized the utility of FGS to highlight such peripheral nerves as thoracic sympathetic nerves and phrenic nerve by using ICG in addition to electromyography [19].

ICG application might be considered as a helpful approach for the confirmation of the RLN in addition to routine visual identification. Such a feature could be applied during FGS for NIRAF evaluation of the parathyroid glands. Although confirmation of the parathyroid glands could be performed by FGS without ICG angiography [23], the injection of the latter could significantly improve discrimination of the tissues, which is important for the dissection of the central neck compartment or in case of neck reoperations. Also, ICG is a neurovascular dye, so it is appropriate also for RLN visualization [19]. Our study has also revealed that ICG angiography did not interfere with the electromyographic properties of the RLN as judged by the good IONM signal. However, one should take into consideration the small study group, indicating that different findings of the relations between ICG angiography and IONM signal from RLN might be seen in larger cohorts.

The evidence from this study suggests points towards the idea for the RLN confirmation during the visualization of parathyroid glands by NIRAF since FGS is more frequently applied in routine surgical settings. This present finding might help to detect RLN in case of unavailable IONM. In our opinion, application of NIRAF could be used as an initial step before the revision of the zone of RLN location, aiming to reduce the risk of RLN damage or its tiny branches while dissecting tissue. However, the cost of the procedure should be considered as a possible obstacle for the routine application of NIRAF for the RLN confirmation, including in Ukraine [10, 23, 24]. Although it is more common for endocrine surgery centers to get machines for the FGS, it is not always covered by the insurance and additional cost for the regular expenses for the operation might be too high for the patients in case of ordinary thyroid or parathyroid surgery. However, the benefit of FGS is high in case of reoperations on a zone of the thyroid gland to decrease the risk of RLN palsy.

It is also worth mentioning, that RLN visualization and confirmation by the naked eye and IONM are not always associated with normal functioning of RLN as one may judge by the minor voice changes in early post-operative period. The possible problem of RLN functionality in these cases could be associated with edema of adjacent to nerve tissues or edema of RLN itself, microtrauma due to tissue dissection as well as electric trauma in case of repeated application of IONM probe. Still, in case of confirmed RLN integrity, the impaired functionality of the RLN is temporary event.

We admit that this study has some limitations. For example, our results were obtained from the small sample size. It is also worth to mention, that only two devices for FGS were available, whereas different results could be obtained from other image-based systems. On the other hand, analyses of published data to show that almost all FGS image-based systems have approximate technical specifications, except the PTeye fiber probe-based system.

Still, we believe that the overall clinical utility of ICG angiography for RLN detection is relatively low because the near-infrared signal is presented during a short period, and reinjection of the ICG is limited by its toxic effect. However, the possible uses of ICG angiography for RLN detection might be in the case of the need to differentiate upper parathyroid from lower glands by judging their relation to the RLN, which is a difficult task in case of the retrosternal parathyroid adenomas.

Conclusions

To sum up, our study has fully supported the importance of the employment of the apparatus tools, such as IONM for the verification of the RLN, as well ICG angiography and NIRAF for the parathyroid gland confirmation.

Visualization of the RLN by the ICG angiography might be considered during fluorescence-guided surgery for thyroid and parathyroid lesions. Although this RLN identification by the ICG angiography could not be suggested for application in routine clinical settings, this observation might be considered as an additional useful tool for the prevention of RLN injury. Further studies, which take the RLN evaluation by ICG angiography into account will need to be undertaken.

Figure 4. Photograph of the RLN (patient ID 6) in the near-infrared spectrum showing strong signal after the ICG injection through the undissected tissues (indicated by the dotted ellipse)
References


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Неочікуване визначення зворотного гортанного нерва за допомогою флуоресцентно-керованої хірургії з використанням індоціаніну зеленого для ангіографії в ближній інфрачервоній ділянці

Резюме. Актуальність. Пошкодження зворотного гортанного нерва (ЗГН) і прищитоподібної залози є тяжким ускладненням операцій на щитоподібній залозі. Можливість підтвердження ЗГН у ближньому інфрачервоному спектрі після введення індоціаніну зеленого (ІЦЗ) не вивчалась. Мета: оцінити ангіографію з ІЦЗ для ідентифікації ЗГН під час хірургічного втручання на щитоподібні та прищитоподібні залози. Матеріали та методи. Ангіографія із застосуванням ІЦЗ виконана 7 хворим. Як метод контролю ЗГН застосовували інтраопераційний нейромоніторинг. Під час операції при візуальному огляді (неозброєним оком) виявлено прищитоподібні залози та ЗГН. Для подальшого підтвердження розташування прищитоподібних залоз шляхом їх автофлуоресценції було проведено внутрішньовенну ін'єкцію ІЦЗ у концентрації 0,25 мг/кг із подальшим застосуванням апаратної системи флуоресцентно-керованої хірургії. Результати. Сильний сигнал від ЗГН був ідентифікований в усіх випадках після ін'єкції ІЦЗ. Достатнє кровопостачання ЗГН можна розглядати як причину добого сигналу в ближній інфрачервоній ділянці. Висновки. ІЦЗ є додатковим інструментом підтвердження ЗГН на додаток до звичайної візуальної ідентифікації. Такий підхід може бути застосований під час флуоресцентно-керованої хірургії для оцінки автофлуоресценції прищитоподібних залоз. Візуалізація ЗГН за допомогою ангіографії з ІЦЗ розглядається як додатковий корисний інструмент для запобігання такому інтраопераційному ускладненню, як пошкодження ЗГН. Ключові слова: зворотний гортанний нерв; автофлуоресценція прищитоподібних залоз; флуоресцентно-керована хірургія; індоціанін зелений; хірургія щитоподібної залози; хірургія прищитоподібних залоз; профілактика післяопераційних ускладнень