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Original Article

Prophylaxis of Postoperative Hypoparathyroidism in Thyroid Surgery

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Abstract

Introduction: There are a number of thyroid gland diseases that require surgical treatment. Therefore, it is important to improve the surgical approaches and treatment tactics in patients that need such surgery.

Aim: To provide an algorithm to prevent parathyroid gland damage during surgery.

Materials and methods: This work was based on treatment results of 226 patients with different thyroid diseases. All patients received extrafascial surgical interventions using modern methodological approaches. For prevention of postoperative hypoparathyroidism, we used the "stress-test", 5-aminolevulenic acid, and a method of double visual-instrumental registration of photosensitizer-induced fluorescence of parathyroid glands.

Results: Transient hypoparathyroidism was registered in four (1.8%) cases after surgery. Permanent hypocalcemia in patients was not recorded. Autotransplantation of parathyroid gland was required only in one case (0.44%). A deficiency or low level of vitamin D was detected in 35% of the cases, and in the majority of those cases, it was due to secondary hyperparathyroidism. The deficiency was corrected with the administration of vitamin D in all cases. In 10.17% (23 patients) of cases, there was no proper visual glow effect after administration of 5-aminolevulinic acid (5-ALA), which required proceeding to the second part of the proposed method (a helium-neon laser and registration of fluorescence using a laser spectrum analyzer).

Conclusions: The proposed methodological approach allows prevention of persistent hypoparathyroidism and reduces the frequency of transient hypoparathyroidism and other complications in surgical treatment of patients with various thyroid gland diseases.

Keywords

central neck dissection, hypoparathyroidism, hemithyroidectomy, lymph node dissection, thyroidectomy

INTRODUCTION

A number of thyroid gland diseases require surgical intervention. In such cases, it is important to use improved surgical approaches and treatment strategies for those patients who require such surgery.[1,2] The health-related quality of life directly depends on the method and technique of the surgical procedures.[3,4] The latter, unfortunately, are still accompanied by the development of various complications. Consequently, the parathyroid glands can be damaged, removed, or devascularized during endocrine surgeries, leading to postoperative complications.[5] Postoperative hypoparathyroidism is the most frequent complication in thyroid surgery that can be prevented.[6,7] Despite the apparent progress in thyroid surgery and the emergence of a number of modern methods, the frequency of postoperative hypoparathyroidism can reach up to 60% and leads to decreased quality of patient's life.[8-10]

AIM

Therefore, we present a study that analyzes the possibilities to reduce the overall risk for parathyroid gland damage during surgery.

MATERIALS AND METHODS

This study is a prospective cohort analysis of data obtained from the Department of Endocrine Surgery in Botkin State Clinical Hospital (Moscow, Russia). Two hundred twenty-six patients were operated due to thyroid diseases between 2017 and 2021. The patients underwent a comprehensive examination of the thyroid and parathyroid glands before operation. Laboratory analyses included serum ionized calcium, parathyroid hormone, and vitamin D.

Postoperative hypoparathyroidism was prevented with the use of a 'stress-test' and double visual-instrumental registration of photosensitizer-induced fluorescence of parathyroid glands according to an algorithm **(Fig. 1)**.

We performed migratory (translocatable) 3 to 10 cm surgical incision without crossing the neck muscles **(Fig. 2A)**. At the beginning of the operation, a special protective sterile latex-gauze casing (Epic, Austria) was used to protect the skin **(Fig. 2B)**.

In order to provide the surgeon with sufficient working space and allow migratory access with the correct position, we used a special retractor system developed in our clinic **(Fig. 3)**.

It is important to note that we began every manipulation of the thyroid gland after ligation and intersection of the thyroid vessels. We started with mobilization of the upper pole of the gland typically after clarifying the anatomical landmarks. In special cases, we displaced the infrahyoid muscles in the medial direction, but not in the lateral one. After the mobilization of the upper thyroid pole, we moved to the lower thyroid pole separately ligating the main trunks and the smaller thyroid branches in the thyroid capsule. To prevent postoperative hypoparathyroidism, we identified the parathyroid glands along with the feeding arterial branches. The integrity of the parathyroid glands was preserved under visual control. The parathyroid glands have their own capsule, feeding arteries (unlike the adipose tissue), and soft, almost imperceptible consistency (unlike the lymph nodes of the neck).

We used several additional methods to identify the parathyroid glands in addition to careful consideration of their anatomical features. One of the tests was the 'stress-test'. It is based on the sensitivity of epithelial cells to hypoxia and traumatization. The tissue that is presumed to be the parathyroid glands is gently tapped (or 'stroked') by the tip of a blunt tool. The color of the gland changes to darker one

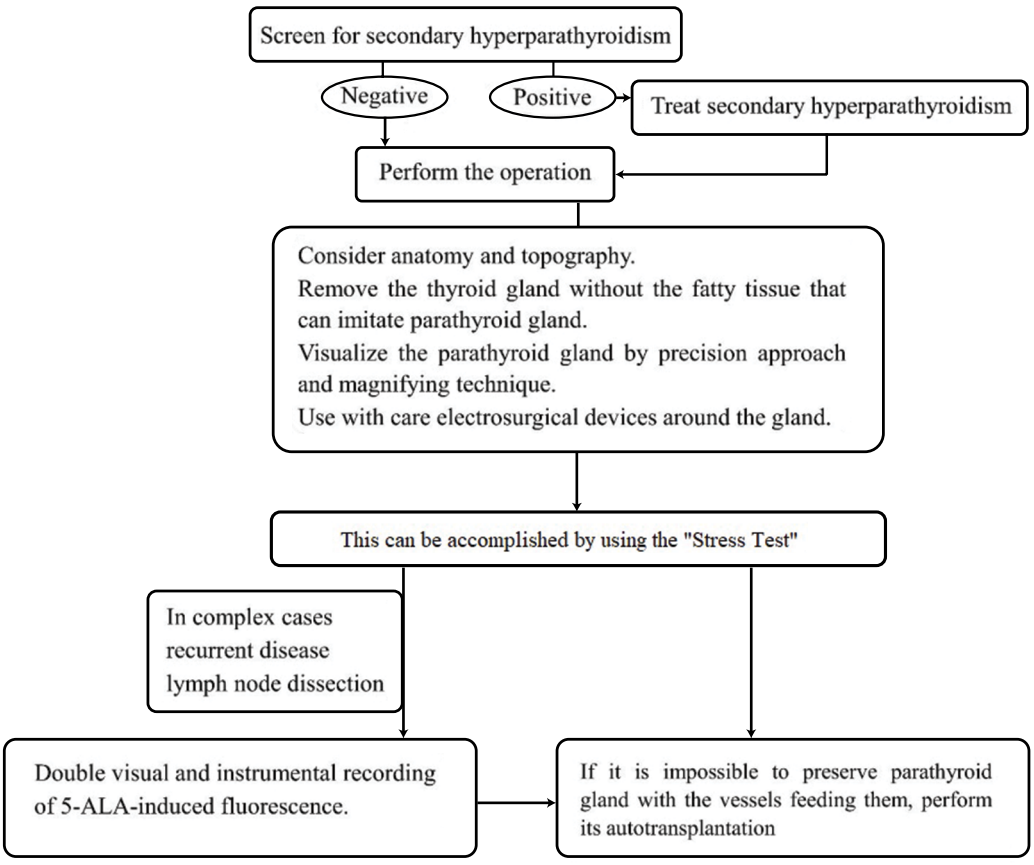

Figure 1. Algorithm for parathyroid gland preservation during operation. 5-ALA: 5-aminolevulinic acid.

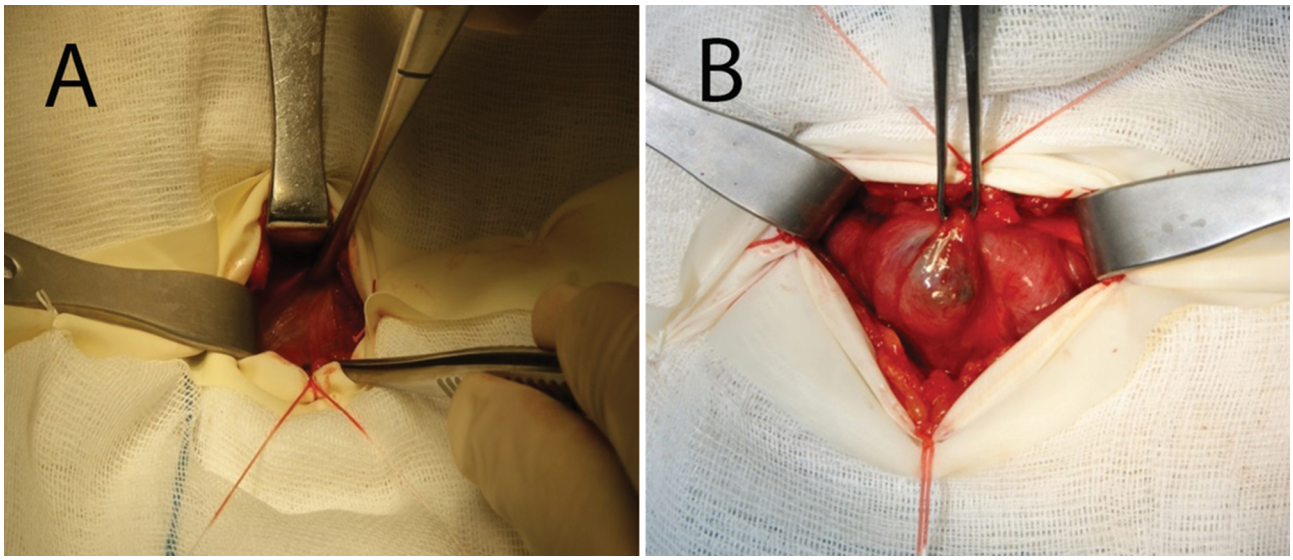

Figure 2. A. An intraoperative view of a minimal surgical incision; **B.** A view of a fixed protective casing.

with prominent vessels after 2-4 minutes. Furthermore, this allowed to identify and preserve the vascular supply **(Fig. 4)**.

In complicated cases, the parathyroid gland was identified by registration of photosensitizer-induced fluorescence. This was achieved with the use of 5-aminolevulinic acid (protoporphyrin precursor IX) which is a source of polarizing blue light. The patients were given 5-aminolevulinic acid (30 mg/kg of body mass diluted in 50-100 ml of isotonic solution) two hours before operation. The operated area of the parathyroid gland was irradiated with blue light with a wavelength of 435-440 nm from a portable source at the appropriate stages of intervention. The parathyroid gland would have pink fluorescence **(Fig. 5A)**. In the absence of a proper visual glow effect, a helium-neon laser with a wavelength of 630-640 nm would light the surgical area. The registration of fluorescence was performed by graphical and digital methods using a laser spectrum analyzer LESA-01-BioSpec **(Figs 5B, 6)**.

In the final stage, the thyroid lobe was mobilized and dissected in the area of Berry ligament with separation and ligation of all vascular collaterals. After visualization and preservation of recurrent laryngeal nerve and upper parathyroid gland, the thyroid lobe was carefully removed. For the purpose of a precision approach, a magnifying technique was used with microsurgical instruments **(Figs 7A, 7B)**.

The functional state of parathyroid gland was examined after surgery by determining the level of calcium and phosphorus in the blood. To examine the motility of the vocal cords, all patients underwent laryngoscopy check-up pre- and postoperatively. The cosmetic effect was evaluated according to the patient and observer scar assessment scale (POSAS v. 2.0).[11] The volume of surgery performed on patients with thyroid carcinoma was monitored by radioactive iodine scintigraphy **(Fig. 8)**.

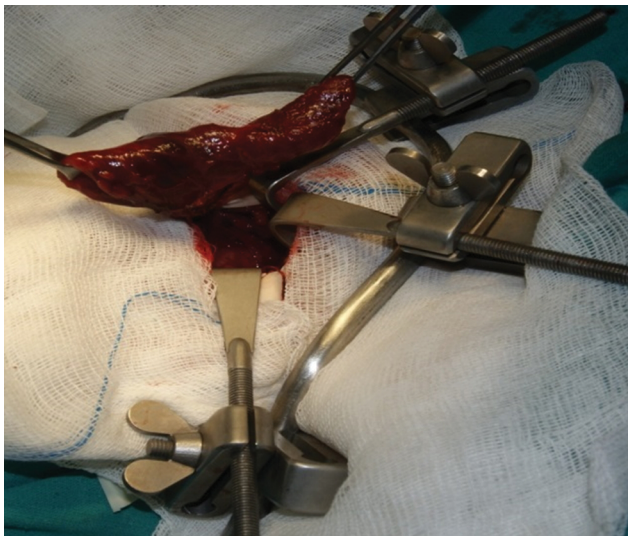

Figure 3. Stages of thyroidectomy from migratory access using the proposed retractor system.

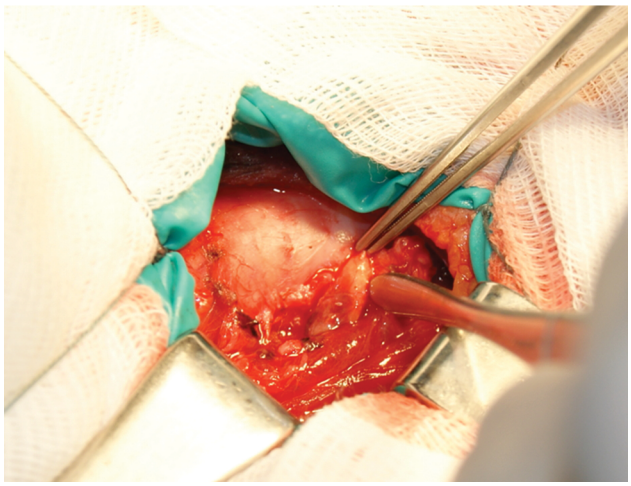

Figure 4. Darkened upper parathyroid gland after the 'stress-test'.

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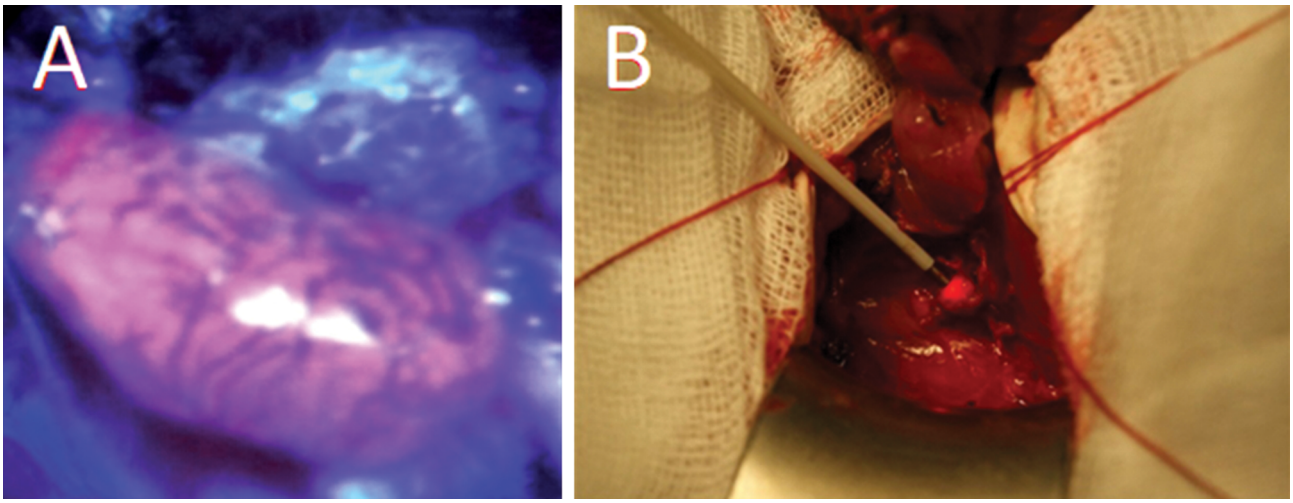

Figure 5. A. Parathyroid gland fluorescence under magnification; **B**. Local spectrometry of the parathyroid gland.

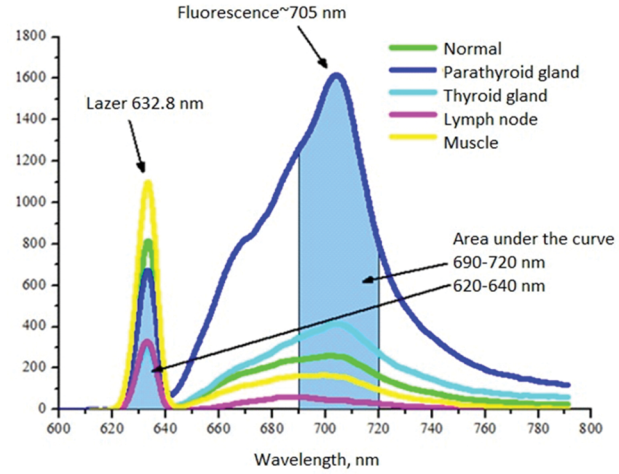

Figure 6. Registration of fluorescence by graphical and digital method.

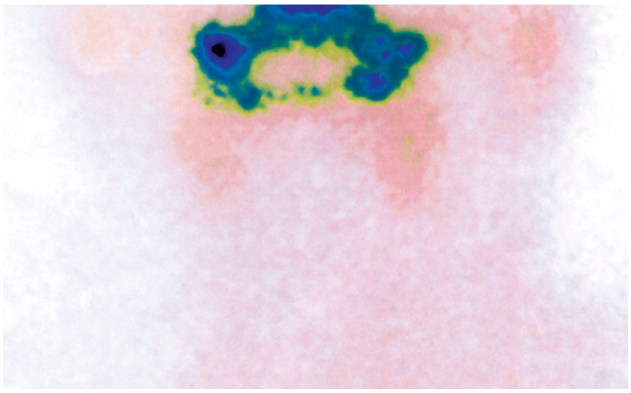

Figure 8. Thyroid scintigraphy after thyroidectomy for papillary cancer.

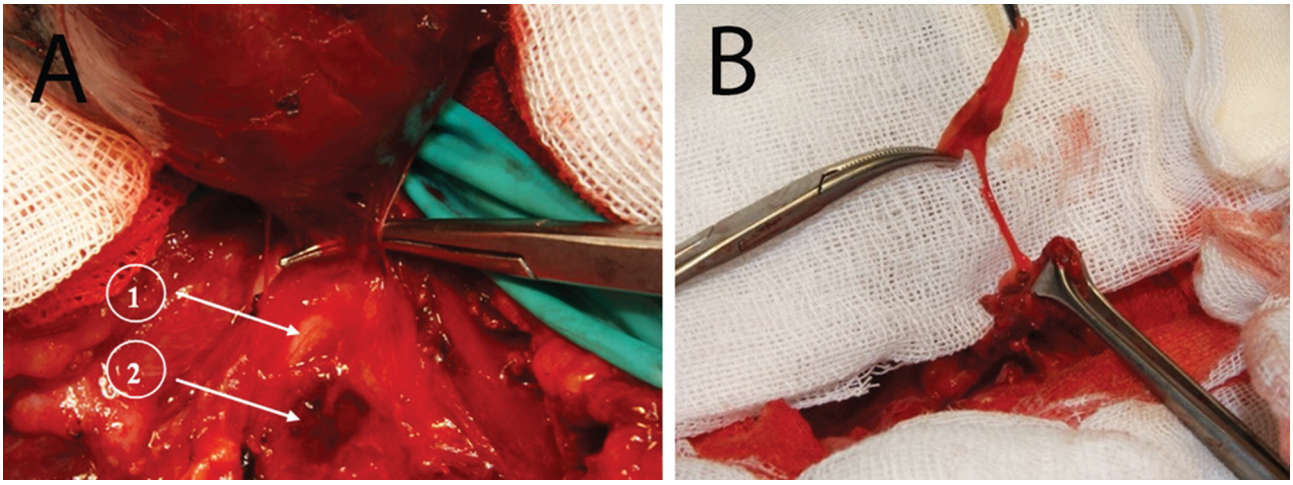

Figure 7. A. Dissection of Berry ligament with preservation of recurrent laryngeal nerve (1) and parathyroid gland (2); **B**. Preservation of the lower parathyroid gland with a feeding vascular branch during central lymph node dissection.

The study was approved by the ethical commission of Russian Medical Academy of Continuous Professional Education (No. 67/12.06.2016).

RESULTS

Hemithyroidectomy was performed in 76 (33.6%) patients, and thyroidectomy in 103 (45.6%), while 28 (12.4%) cases of thyroidectomy were followed by central lymph node dissection, and 19 (8.4%) – with neck dissection. The age of the patients ranged from 18 to 78 years. The men/women ratio was 1:8 (25/201).

Deficiency or low level of vitamin D was detected in 35% of the cases and in the majority of cases, this was due to secondary hyperparathyroidism. It was corrected with the administration of vitamin D in all cases.

In 10.17% (23 patients) of cases, there was no proper visual glow effect after administration of 5-aminolevulinic acid, which required proceeding to the second part of the proposed method (helium-neon laser with registration of fluorescence using a laser spectrum analyzer).

There were 68 (30.1%) cases of nontoxic multinodular goiter, 37 (16.4%) cases of diffuse toxic goiter, 64 (28.3%) cases of thyroid adenoma, and 57 (25.2%) cases of thyroid cancer. Twenty-six patients (10.2 %) had retrosternal location of a part of the thyroid gland, and 19 (6.3%) were previously operated. The patients with thyroid cancer were found to have papillary thyroid carcinoma in 32 (14.2%) cases, follicular carcinoma in 21 (9.3%) cases, and medullary thyroid cancer in 4 (1.8%) cases. Where it was necessary, preoperative correction of thyrotoxicosis was carried out. Extrafascial interventions were performed after a comprehensive examination.

There were no cases of bleeding, laryngeal paralysis, wound suppuration, and no recurrence of the disease. Several patients had serum calcium deviations. On the first day, 61 (27%) patients showed a decrease in the level of ionized calcium within the reference values (level of ionized calcium 1.12–1.32 mmol/l, total calcium 2.2–2.56 mmol/l) without clinical manifestations. They did not require medical correction. Twenty-three (10.17%) patients had asymptomatic transient hypocalcemia (ionized calcium level 1.0–1.12 mmol/l, total calcium 1.9–2.1 mmol/l). These patients were prescribed calcium carbonate (1–2 g/day) and 1-hydroxycholecalciferol (0.5–1 μg/day). The treatment was stopped after normalization of the calcium level (within 3 to 10 days).

Four (1.8%) patients developed hypocalcemia with clinical manifestations in the form of paresthesia of the fingers of the hands (the level of ionized calcium 0.8–1.05 mmol/l, total calcium 1.8–2.1 mmol/l). These patients underwent thyroidectomy with central lymph node dissection and had atypical location of the parathyroid gland, which required their complex microsurgical isolation or relocation while preserving the feeding vascular structures. The parathyroid glands in these patients were located in the thickness of the removed tissue, far from the usual areas of localization and under the thyroid capsule. This group required a combination therapy (10% calcium gluconate 20–40 ml/day, calcium carbonate 1.5–3 g/day) and 1-hydroxycholecalciferol 0.5–1.5 μg/day. Drug therapy was discontinued after confirmation of persistent normocalcemia at 3 and 5 weeks.

Therefore, four (1.8%) patients developed transient hypocalcemia in the postoperative period, and no persistent hypocalcemia was detected. At the same time, the cosmetic result assessed by POSAS was excellent in 212 (93.8%) patients.

DISCUSSION

The above-mentioned algorithm was especially important for thyroid cancer (15.2% of patients) and in cases when patients were previously operated (6.3% of patients). Performance of lymph node dissection and surgery in the presence of scars poses special risks for damage of parathyroid glands. In such cases, parathyroid gland should be differentiated from other tissues, primarily from the fatty tissue and neck lymph nodes, due to its visual similarity It should be noted also that in 3 (1.3%) patients such an arrangement of parathyroid glands was noted, when it was possible to separate them from the removed tissues with some traumatization, but preserving part of their feeding vessels. It should be noted that hypoparathyroidism in these patients was in all cases transient.

The methods we used during surgery have their advantages and disadvantages. Their comparison is presented in **Table 1**.

Surgery with the use of magnifying glasses is an accessible and useful method during thyroid surgery. Magnification glasses can be used to assist parathyroid dissection. Although, this is a logical conclusion to use magnification during dissection of small anatomical structures, there is no clear data that there is decreased hypoparathyroidism or reduced incidence of postoperative transient hypocalcemia. The use of magnification techniques to identify recurrent laryngeal nerves and parathyroid glands appears to be as safe as direct vision.[12] Overall active search of the parathyroid gland is not recommended due to the increased risk of gland lesion, mainly by devascularization.[13]

A promising technique is to use 5-aminolevulinic acid to localize the normal parathyroid glands during thyroid surgery in humans.[14] The diagnostic accuracy depended on the thickness of the tumor capsule, timing of 5-aminolevulinic acid administration, the appropriate timing of illumination, differences in vascularity, and inflammation of the surrounding tissue.[15]

In future clinical application, intraoperative fluorescence diagnosis is expected to increase the ease of identification of atypically located or multiple parathyroid glands and help to avoid persistent hypercalcemia.[16]

There are several classical methods that are used to identify the parathyroid gland such as intraoperative parathy-

Table 1. Comparison of the advantages and disadvantages of the proposed tests

	Advantages	Disadvantages
'Stress-test'	Fast results Easy to use Doesn't require preparation Identifies arterial supply Low cost Doesn't require equipment	Isn't accurate Subjective
5-aminolevulinic acid	Accurate (effective in up to 89.93% of cases)	Requires preparation Requires equipment Requires contrast agent Subjective
5-aminolevulinic acid Helium-neon laser	Accurate Reproducible Objective	Requires equipment Requires contrast agent

roid hormone measurement, intraoperative gamma probe application, intraoperative ultrasonography, parathyroid imaging with methylene blue, and frozen section examination. Recently, several new techniques were described such as indocyanine green imaging with autofluorescence, autofluorescence imaging with methylene blue, autofluorescence imaging with 5-aminolevulinic acid, optical coherence tomography, laser speckle contrast imaging, dynamic optical contrast imaging, and Raman spectroscopy.[17]

Intraoperative methylene blue spray helps to identify the parathyroid glands in 82% to 92.31% of cases.[18,19] Fluorescence imaging techniques is an actively developing filed based on the interaction between serum proteins and fluorescent dyes. However, recent advances demonstrated that tissues can possess the capability of autofluorescence.[20] The accuracy of near-infrared/indocyanine green imaging method is 82%-87.3% for identifying parathyroid glands based on their autofluorescence.[21,22]

Wound protector with silicone can significantly prevent the drying of the surgical wound and reduces the incidence of infection. There is a significant improvement in POSAS scale, especially in patient younger than 35 years.[23,24]

The current study was based on an algorithm that is useful for parathyroid gland protection **(Fig. 1)**. The algorithm has several principles from basic to more advanced. Prior to the operation, the patients should be screened for vitamin D deficiency with the elimination of the consequences of secondary hyperparathyroidism. In order to detect parathyroid gland, first of all, carefully consider their anatomical and topographic-anatomical features. While performing operations for benign thyroid pathology, try to remove the thyroid gland without the fatty tissue segments that can imitate parathyroid gland. In the visualization and detaching of parathyroid gland use a precision approach and magnifying technique. When visualizing and detaching parathyroid gland, use electrosurgical devices with care. To identify the parathyroid gland, use the 'stress-test'. In complex cases, especially in the case of a recurrent process and lymph node dissection, apply the technique of double visual and instrumental recording of 5-aminolevulenic-induced fluorescence. If it is impossible to preserve the parathyroid gland with the feeding vessels, perform its autotransplantation into the neck muscles. In our experience, an autotransplantation was required only in one case (0.44%).

There are several limitations of our study. One limitation is the relatively low number of cases included in the study. Another limitation is that we analyzed a heterogeneous group of patients who had different thyroid diseases and volume of surgery. These limitations are balanced to some degree by the fact that the main aim of the study was to introduce a method to decrease parathyroid gland damage during surgery.

CONCLUSIONS

The proposed methodological approach allows prevention of persistent hypoparathyroidism and reduces the frequency of transient hypoparathyroidism, with controlling other complications in the surgical treatment of patients with various thyroid gland diseases. Only four patients developed transient hypocalcemia, only one required parathyroid gland autotransplant, and none had permanent hypocalcemia.

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Профилактика послеоперационного гипопаратиреоза в хирургии щитовидной железы

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Резюме

Введение: Существует ряд заболеваний щитовидной железы, требующих хирургического лечения. Поэтому важно совершенствовать хирургические доступы и тактику лечения больных, нуждающихся в таком оперативном вмешательстве.

Цель: Предложить алгоритм предотвращения повреждения паращитовидной железы во время операции.

Материалы и методы: В основу работы положены результаты лечения 226 больных с различными заболеваниями щитовидной железы. Всем пациентам выполнены экстрафасциальные оперативные вмешательства с применением современных методических подходов. Для профилактики послеоперационного гипопаратиреоза использовали «стресс-тест», 5-аминолевуленовую кислоту, метод двукратной визуально-инструментальной регистрации фотосенсибилизатор-индуцированной флуоресценции паращитовидных желез.

Результаты: Транзиторный гипопаратиреоз зарегистрирован в 4 (1.8%) случаях после операции. Стойкой гипокальциемии у больных не зарегистрировано. Только в одном случае (0.44%) потребовалась аутотрансплантация паращитовидной железы. Дефицит или низкий уровень витамина D выявлен в 35% случаев, и в большинстве случаев он был обусловлен вторичным гиперпаратиреозом. Дефицит был устранён введением витамина D во всех случаях. В 10.17% (23 пациента) случаев после введения 5-аминолевулиновой кислоты (5 – ALA) не было должного эффекта визуального свечения, что потребовало перехода ко второй части предлагаемого метода (гелий-неоновый лазер и регистрация флуоресценции с помощью лазерного анализатора спектра).

Заключение: Предложенный методический подход позволяет предотвратить персистирующий гипопаратиреоз и снизить частоту транзиторного гипопаратиреоза и других осложнений при хирургическом лечении больных с различными заболеваниями щитовидной железы.

Ключевые слова

центральная диссекция шеи, гипопаратиреоз, гемитиреоидэктомия, лимфодиссекция, тиреоидэктомия