A comparative study of preoperative and intraoperative carbon nanoparticles injection in patients undergoing thyroid cancer surgery

Research program

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I.Background of the study

1. Thyroid Cancer and Thyroid Surgery

Thyroid cancer is a common malignant tumor in the neck, and its incidence accounts for about 1% of the total incidence of malignant tumors, and its incidence rate ranks fifth in the incidence of tumors. In recent years, with the improvement of residents' health awareness and the wide implementation of neck examination, the detection rate of thyroid cancer has been increasing rapidly, and the patient group is found to have a tendency to be younger, while female patients are predominant and significantly higher than male patients.

Except for undifferentiated cancer, surgery is still one of the most important treatments for all types of thyroid cancer, which is supplemented by radionuclide, TSH inhibition, and external radiation, etc. Surgery can effectively improve the prognosis of the disease by completely removing the lesions. Surgical treatment of the thyroid gland is mainly divided into two parts: thyroidectomy and cervical lymph node dissection. The extent of thyroidectomy is still divided, but there is a consensus that the lobes should be the minimum extent of resection. In recent years, total resection and subtotal resection have also been gradually accepted.

There is a basic consensus that the minimum scope of lymph node dissection is central lymph node (VI) dissection, because the main metastatic route of thyroid cancer is lymphatic metastasis, and it may appear earlier, for example, the lymphatic metastasis rate of initially treated patients with papillary thyroid cancer can be as high as 20% to 90%. For patients with positive lymph nodes or highly suspected in auxiliary examination, modified radical translymph node dissection is needed, i.e., on the basis of thyroidectomy, translymph node dissection in zone II-VI is performed while preserving sternocleidomastoid muscle, internal jugular vein and parasympathetic nerves. It is currently believed that under the premise of surgical safety, the number of central lymph node dissection can effectively reduce the risk of postoperative recurrence, and at the same time can be combined with the pathology to provide patients with precise treatment and clarify the stage of cancer.

In the past, open neck surgery was used in clinical practice, which would leave scarring on the neck and affect the appearance, and at the same time, patients could lose part of the function of the anterior cervical skin, and a few patients had a foreign body sensation and skin linkage during swallowing activities, which had an impact on the patients' satisfaction with the surgery. Thus, in recent years, with the development of minimally invasive medical technology, the luminal thyroid surgery has come into people's view. Currently, the more commonly performed laparoscopic surgeries can be categorized into axillary approach, oral vestibular approach, thoracic breast approach, etc., and there are also case reports of multi-approach combined surgeries. These new laparoscopic surgical treatments have been widely used in the clinic. While meeting the requirements of tumor resection as much as possible, laparoscopic surgery is gradually accepted by patients because of its smaller incision and stronger protection of the function and integrity of the neck skin.

2. Postoperative complications of thyroid cancer

Hypoparathyroidism and laryngeal recurrent nerve injury are the most common complications of radical thyroid cancer surgery, whether it is open surgery or luminal approach, and once these complications occur, they will have a serious impact on the patient's quality of life in the postoperative period.

(1). Hypoparathyroidism

A domestic study on the occurrence of hypoparathyroidism after radical thyroid cancer surgery in patients with differentiated thyroid cancer showed that the incidence of hypoparathyroidism after radical thyroid cancer surgery ranged from 0.5% to 65.0%. In clinical practice, hypoparathyroidism is usually categorized as temporary and permanent. Temporary hypoparathyroidism is mainly characterized by transient hypocalcemic symptoms such as numbness of hands and feet; permanent hypoparathyroidism is characterized by long-term hypocalcemic symptoms such as numbness of hands and feet and twitching of limbs, and in severe cases, it may also lead to convulsions and laryngeal spasms, which can seriously affect the patient's health and even cause death. Transient hypoparathyroidism with transient hypocalcemia is usually considered to be caused by destruction of the parathyroid blood supply (the blood supply of parathyroid glands mainly comes from the thyroid

artery, and ligation of the thyroid blood supply artery during bilateral thyroidectomy during surgery can have an effect on the blood supply to the parathyroid glands, which can become dysfunctional due to obstruction of venous return and stagnation of the parathyroid glands); whereas, permanent hypoparathyroidism is mostly related to the destruction of the blood supply to the parathyroid glands. Permanent hypoparathyroidism is mostly associated with disruption of the parathyroid blood supply leading to ischemic necrosis or misdirected parathyroidectomy.

Previous studies have suggested that the incidence of postoperative temporary hypoparathyroidism ranges from 7% to 38%, with most patients returning to normal within 6 months as serum parathyroid hormone levels rise. In contrast, the incidence of permanent hypoparathyroidism ranges from 1% to 7% of patients who do not have complete resolution of symptoms at 6 months after surgery and who also require oral calcium to maintain normal calcium levels. There is no doubt that hypothyroidism can have a serious impact on the quality of life and health of patients and greatly reduces their satisfaction with surgery.

(2). Injury to the recurrent laryngeal nerve

Injury to the recurrent laryngeal nerve usually occurs during dissection of the thyroid artery, ligation, or freeing of the trachea after severing the thyroid isthmus. Patients with unilateral recurrent laryngeal nerve injury will suffer from hoarseness, mild respiratory and swallowing difficulties, and choking on drinking water; patients with bilateral recurrent laryngeal nerve injury will suffer from respiratory difficulties, respiratory failure, and even asphyxia in severe cases. At this stage, it is usually advocated to expose the laryngeal recurrent nerve in the process of freeing the trachea, which can reduce the incidence of laryngeal recurrent nerve injury to a certain extent.

3. carbon nanoparticles and carbon nanoparticles negative contrast technology

Carbon nanoparticles is an effective and harmless negative developer, and there have been many studies confirming that carbon nanoparticles can be used to identify parathyroid glands in thyroid surgery. Nanocarbon suspensions consist of nanocarbon particles with an average diameter of 150 nm. The cellular gap between capillary

endothelial cells ranges from 20 to 50 nm, and the gap between capillary lymphatic endothelial cells ranges from 120 to 500 nm, with an underdeveloped basement membrane. Therefore, carbon nanoparticles cannot enter the blood vessels when injected into the thyroid tissue; it rapidly enters the lymphatic vessels or lymphatic capillaries through phagocytosis by macrophages and is retained in the lymph nodes. In thyroid surgery, by injecting nano-charcoal into the thyroid gland, the nano-charcoal can diffuse through the gland and the lymphatic system, thus staining the thyroid tissue and lymph nodes black, while the tissues not subject to the lymphatic return of the thyroid gland will not be stained, such as parathyroid glands, the trachea and the supraglottic laryngeal reentrant nerve, which can keep their original color, different from the thyroid tissue and lymph nodes, thus playing an effective role in the protection. Protecting effect.

As a third-generation tracer, carbon nanoparticles suspension is highly conductive to the lymphatic system, especially in the display of small lymph nodes (<2mm), and the staining is fast-acting, long-lasting, effective in identifying parathyroid glands, and mildly toxic. The importance of charcoal carbon nanoparticles in parathyroid protection has been noted by many thyroid surgeons and many clinical trials have been conducted. It has been demonstrated that intraoperative injection of carbon nanoparticles can effectively increase the quality of intraoperative parathyroid gland detection and lymph node dissection, and reduce postoperative hypocalcemia and other adverse reactions, and at the same time, the carbon nanoparticles suspension injections in this trial have a high degree of safety, and no patients had allergic reactions to the injections.

However, there is no complete clinical guideline for preoperative intraglandular injection of carbon nanoparticles, and there is no standardized dosage for the appropriate injection time, injection dose, and injection method. Meanwhile, there is still the problem of carbon nanoparticles leakage during the procedure, which may affect the recognition and protection of the parathyroid glands by accidentally coloring the thyroid region black.

It is well known that the use of charcoal CNS is usually performed during surgery, but in our medical center, we found that preoperative injection of carbon nanoparticles by fine needle aspiration under ultrasound guidance can have better results by reducing CNS leakage in the surgical area. Possible reasons for this include: (i) preoperative ultrasound-guided intra-glandular lobe injection of carbon

nanoparticles does not have to open the surgical peritoneum of the thyroid gland, which reduces possible lymphatic vessel damage and makes lymphatic drainage more consistent with normal physiology; (ii) preoperative injection allows for a more adequate time for lymphatic dispersion of the carbon nanoparticles; and (iii) preoperative labeling of suspected metastatic lymph nodes by carbon nanoparticles injection further improves the tracing effect of the lymph nodes.

II.Purpose of the study

The purpose of this study was to investigate the effect of carbon nanoparticles injections at different preoperative and intraoperative times on surgical procedures and postoperative complications in patients with unilateral and bilateral papillary thyroid cancer or lymph node metastases.

III.Study population

One hundred and fifty patients who came to our hospital from January 2025 to June 2025, who were diagnosed with unilateral bilateral PTC or lateral LN metastasis by preoperative FNA (fine needle aspiration) or preoperative ultrasonography suggestive of TRAIDs grading 4a and above, and who were proposed to undergo laparoscopic thyroid surgery, were selected. Based on the objective conditions and subjective requirements of the patients, these patients were first divided into a partial thyroidectomy group (i.e., a unilateral lobectomy or partial thyroidectomy was performed) and a total thyroidectomy group (a total thyroidectomy was performed), and under the two groups, according to the timing of carbon nanoparticles injections, they were divided into two subgroups: a preoperative subgroup and a suboperative subgroup. In the preoperative subgroup, carbon nanoparticles was injected into the thyroid gland 2-6 hours prior to surgery, whereas in the suboperative subgroup, carbon nanoparticles was injected intraoperatively.

Inclusion Criteria:

(1).Preoperative pathological assessment indicated the presence of thyroid cancer

with a maximum diameter of less than 4 cm.

(2).Postoperative pathological evaluation confirmed bilateral thyroid cancer or lateral lymph node metastasis.

(3). Vocal cord examination conducted one week prior to surgery revealed no abnormalities.

(4). The patient had no history of prior thyroid surgery and required a total thyroidectomy.

(5). Blood pressure was stably controlled.

(6). The patient regained consciousness and was able to communicate normally.

Exclusion criteria

(1) Prior to enrollment, the patient had received radiotherapy, chemotherapy, or isotope therapy;

(2) A documented history of thyroid surgery;

(3) Age under 16 years;

(4) Known allergies to the medications under investigation or an inability to tolerate surgical intervention;

(5) Presence of a retrosternal thyroid tumor;

(6) Tumor invasion of the parathyroid glands and/or the recurrent laryngeal nerve during surgical procedures;

(7) Postoperative pathology suggestive of medullary carcinoma or undifferentiated carcinoma;

(8) Development of a postoperative tracheal fistula.

IV.Observation indicators

(1). General information: age; gender; height; weight; BMI; tumor size; tumor location; pathology results; preoperative serum calcium; preoperative thyroid hormone;

(2). Preoperative parathyroid hormone levels; preoperative TSH; preoperative vocal cord movement problems.

(3). Carbon nanoparticles injections: carbon nanoparticles injection site; number of carbon nanoparticles injection needles; carbon nanoparticles injection dose.

(4). Carbon nanoparticles staining: thyroid staining; lymph node staining; parathyroid staining; nanocarbon leakage.

(5). Intraoperative data: length of surgery, number of lymph nodes cleared, amount of intraoperative bleeding.

(6). Postoperative data: postoperative pain duration; postoperative drainage; postoperative hospitalization; postoperative serum parathyroid hormone; postoperative laryngeal recurrent nerve stimulation and injury; postoperative hematoma; postoperative tracheal fistula.